

rifampin-soaked prosthetic grafts.¹⁴² The graft excision and replacement may be done concurrently or in a staged manner, depending on the patient's clinical status.

If patients are known to be MRSA-positive, a decolonization strategy should be pursued prior to the surgery whenever possible. Moreover, given the devastating complications associated with prosthetic graft infections, some have advocated for regular preoperative screening and, when detected, decolonization of MRSA. Lee and colleagues analyzed the economic impact of screening all vascular surgery patients prior to a vascular surgical procedure, and demonstrated that testing and decolonizing patients for MRSA may be cost-effective.¹⁴³

FUTURE ADVANCES

Despite substantial advancements in prosthetic graft technologies and their associated clinical outcomes, current grafts are still inferior to autogenous vein grafts. As such, the quest continues for a durable prosthetic conduit that is resistant to intimal hyperplasia and infection while providing patients with long-term patency. Bioengineered human acellular vessels have emerged as a promising technology. These conduits are constructed from banked human vascular smooth muscle cells cultured on a biodegradable polymer. A process of de-cellularization then removes viable tissue elements leaving an intact conduit with preservation of mechanical properties. A recently published trial utilized this conduit for dialysis access at six centers in the United States and Poland.¹⁴⁴ Trial endpoints were freedom from adverse events (immune reaction, pseudoaneurysm, infection) and patency rates. The acellular vessel was implanted into sixty patients with mean follow-up of 16 months. These bioengineered conduits demonstrated no dilation and minimal postcannulation bleeding with 6-month primary patency of 63% (primary assisted patency 73%, secondary patency 97%). Thrombosis at 12 months resulted in a 28% primary patency (primary assisted patency, secondary patency 89%). The rate of reintervention was similar to reported rates with ePTFE including 16 venous anastomotic revisions showing no demonstrable reduction in anastomotic hyperplasia. There were, however, no reports of systemic immune reaction or excessive inflammatory response. Although cannulation-related pseudoaneurysms were noted in some patients, no true aneurysmal degeneration of the vessels occurred. Although patency rates were acceptable, there was not an obvious improvement over prosthetic graft results and patency was not as good as that with arteriovenous fistula construction. However, the potential benefits and significant scientific efforts surrounding this conduit support further testing and a larger controlled clinical study.

Another future avenue for improving prosthetic conduit outcomes includes the use of remote monitoring of graft function to detect early hemodynamic changes prior to graft failure. As noted above, prosthetic grafts fail due to myointimal

hyperplastic stenosis and thrombosis. Graft surveillance is used to monitor function; however, graft failure can occur between these episodic examinations. An innovative microsensor with wireless, microchip technology may allow automated surveillance with assessment of graft function using a cloud-based algorithm. *In vitro* flow data has demonstrated the ability of the device to determine factors related to prosthetic graft function under varied hemodynamic flow conditions. Wireless signal acquisition using Bluetooth technology allows remote data analysis reflecting graft flow parameters through changes in microsensor voltage and frequency. Waveform analysis was applied to construct an algorithm using proprietary software thereby determining parameters for graft flow characteristics as well as determination of degree of stenosis and location of stenosis. Subsequent *in vivo* experiments have confirmed the ability of the system to generate signal acquisition through skin and soft tissue under biologic conditions.¹⁴⁵ This automated system shows promise to deliver real-time data that can be analyzed by cloud-based algorithms alerting the clinician of a change in graft function or development of stenosis for further diagnostic study or intervention prior to graft failure.

SELECTED KEY REFERENCES

- Anand SS. Efficacy of oral anticoagulants compared with aspirin after infrapopliteal bypass surgery (The Dutch Bypass Oral Anticoagulants or Aspirin Study): a randomised trial. *Lancet*. 2000;355:346–351.
- Dorigo W, Pulli R, Piffaretti G, et al. Results from an Italian multicentric registry comparing heparin-bonded ePTFE graft and autologous saphenous vein in below-knee femoro-popliteal bypasses. *J Cardiovasc Surg.* 2012;53:187–194.
- Greenberg RK, Ouriel K. A multi-modal approach to the management of bypass graft failure. *Vasc Med.* 1998;3:215–220.
- Heyligers JM, Lisman T, Verhagen HJ, et al. A heparin-bonded vascular graft generates no systemic effect on markers of hemostasis activation or detectable heparin-induced thrombocytopenia-associated antibodies in humans. *J Vasc Surg.* 2008;47:324–329.
- Kreienberg PB, Darling 3rd RC, Chang BB, et al. Early results of a prospective randomized trial of spliced vein versus polytetrafluoroethylene graft with a distal vein cuff for limb-threatening ischemia. *J Vasc Surg.* 2002;35:299–306.
- Neville RF, Tempesta B, Sidway AN. Tibial bypass for limb salvage using polytetrafluoroethylene and a distal vein patch. *J Vasc Surg.* 2001;33:266–271; discussion 71–72.
- Singh N, Sidawy AN, DeZee KJ, et al. Factors associated with early failure of infrapopliteal lower extremity arterial bypass. *J Vasc Surg.* 2008;47:556–561.
- Twine CP, McLain AD. Graft type for femoro-popliteal bypass surgery. *Cochrane Database Syst Rev.* 2010;(5):CD001487.
- Visser K, Idu MM, Buth J, et al. Duplex scan surveillance during the first year after infrapopliteal autologous vein bypass grafting surgery: costs and clinical outcomes compared with other surveillance programs. *J Vasc Surg.* 2001;33:123–130.
- Voorhees Jr AB, Jaretzki 3rd A, Blakemore AH. The use of tubes constructed from vinyon "N" cloth in bridging arterial defects. *Ann Surg.* 1952;135:332–336.

A complete reference list can be found online at www.expertconsult.com.

REFERENCES

1. Voorhees AB Jr, Jaretzki A. 3rd, Blakemore AH. The use of tubes constructed from vinyon "N" cloth in bridging arterial defects. *Ann Surg.* 1952;135:332–336.
2. Hobson 2nd RW, Lynch TG, Jamil Z, et al. Results of revascularization and amputation in severe lower extremity ischemia: a five-year clinical experience. *J Vasc Surg.* 1985;2:174–185.
3. Bandyk DF, Kaebnick HW, Stewart GW, et al. Durability of the in situ saphenous vein arterial bypass: a comparison of primary and secondary patency. *J Vasc Surg.* 1987;5:256–268.
4. Goodney PP, Beck AW, Nagle J, et al. National trends in lower extremity bypass surgery, endovascular interventions, and major amputations. *J Vasc Surg.* 2009;50:54–60.
5. Kannan RY, Salacinski HJ, Butler PE, et al. Current status of prosthetic bypass grafts: a review. *J Biomed Mater Res B Appl Biomater.* 2005;74:570–581.
6. Kapadia MR, Popowich DA, Kibbe MR. Modified prosthetic vascular conduits. *Circulation.* 2008;117:1873–1882.
7. Branchereau A, Rudondy P, Gournier JP, et al. The albumin-coated knitted Dacron aortic prosthesis: a clinical study. *Ann Vasc Surg.* 1990;4:138–142.
8. den Hoed PT, Veen HF. The late complications of aorto-ilio-femoral Dacron prostheses: dilatation and anastomotic aneurysm formation. *Eur J Vasc Surg.* 1992;6:282–287.
9. Matsumoto H, Hasegawa T, Fuse K, et al. A new vascular prosthesis for a small caliber artery. *Surgery.* 1973;74:519–523.
10. Neville RF, Elkins CJ, Alley MT, et al. Hemodynamic comparison of differing anastomotic geometries using magnetic resonance velocimetry. *J Surg Res.* 2011;169:311–318.
11. Edwards WS. Arterial grafts: past, present, and future. *Arch Surg.* 1978;113:1225–1233.
12. Greisler HP, Tattersall CW, Henderson SC, et al. Polypropylene small-diameter vascular grafts. *J Biomed Mater Res.* 1992;26:1383–1394.
13. Lumsden AB, Morrissey NJ. Randomized controlled trial comparing the safety and efficacy between the FUSION BIOLINE heparin-coated vascular graft and the standard expanded polytetrafluoroethylene graft for femoropopliteal bypass. *J Vasc Surg.* 2015;61:703–712.e1.
14. McAllister TN, Maruszewski M, Garrido SA, et al. Effectiveness of haemodialysis access with an autologous tissue-engineered vascular graft: a multicentre cohort study. *Lancet.* 2009;373:1440–1446.
15. Wystrychowski W, McAllister TN, Zagalski K, et al. First human use of an allogeneic tissue-engineered vascular graft for hemodialysis access. *J Vasc Surg.* 2014;60:1353–1357.
16. Farber A, Major K, Wagner WH, et al. Cryopreserved saphenous vein allografts in infrainguinal revascularization: analysis of 240 grafts. *J Vasc Surg.* 2003;38:15–21.
17. Ziza V, Canaud L, Gander T, et al. Outcomes of cold-stored venous allograft for below-knee bypasses in patients with critical limb ischemia. *J Vasc Surg.* 2015;62:974–983.
18. Hartranft CA, Noland S, Kulwicki A, et al. Cryopreserved saphenous vein graft in infrainguinal bypass. *J Vasc Surg.* 2014;60:1291–1296.
19. Guevara-Noriega AK, Lucar-Lopez GA, Pomar JL. Cryopreserved allografts for treatment of chronic limb-threatening ischemia in patients without autologous saphenous veins. *Ann Vasc Surg.* 2019;60:379–387.
20. Hirth-Voury A, Massiot N, Giauffret E. Comparison of cryopreserved arterial allografts versus heparin-bonded vascular grafts in infragenicular bypass for chronic limb threatening ischemia. *Ann Vasc Surg.* 2020;64:33–42.
21. Rychlik IJ, Davey P, Murphy J, et al. A meta-analysis to compare Dacron versus polytetrafluoroethylene grafts for above-knee femoropopliteal artery bypass. *J Vasc Surg.* 2014;60:506–515.
22. Twine CP, McLain AD. Graft type for femoro-popliteal bypass surgery. *Cochrane Database Syst Rev.* 2010;(5):CD001487.
23. Dardik H, Silvestri F, Alasio T, et al. Improved method to create the common ostium variant of the distal arteriovenous fistula for enhancing crural prosthetic graft patency. *J Vasc Surg.* 1996;24:240–248.
24. Nguyen BN, Neville RF, Abugideiri M, et al. The effect of graft configuration on 30-day failure of infrapopliteal bypasses. *J Vasc Surg.* 2014;59:1003–1008.
25. Andersen LI, Nielsen OM, Buchardt Hansen HJ. Umbilical vein bypass in patients with severe lower limb ischemia: a report of 121 consecutive cases. *Surgery.* 1985;97:294–299.
26. Allon M, Lok CE. Dialysis fistula or graft: the role for randomized clinical trials. *Clin J Am Soc Nephrol.* 2010;5:2348–2354.
27. Lok CE, Huber TS, Lee T, et al. KDOQI Vascular Access Guideline Work Group. KDOQI clinical practice guideline for vascular access: 2019 update. *Am J Kidney Dis.* 2020;75(4 Suppl 2):S1–S164.
28. Kakkos SK, Haddad R, Haddad GK, et al. Results of aggressive graft surveillance and endovascular treatment on secondary patency rates of Vectra Vascular Access Grafts. *J Vasc Surg.* 2007;45:974–980.
29. Al Shakarchi J, Houston G, Inston N. Early cannulation grafts for haemodialysis: a systematic review. *J Vasc Access.* 2015;16:493–497.
30. Akoh JA. Prosthetic arteriovenous grafts for hemodialysis. *J Vasc Access.* 2009;10:137–147.
31. Schild AF, Perez E, Gillaspie E, et al. Arteriovenous fistulae vs. arteriovenous grafts: a retrospective review of 1,700 consecutive vascular access cases. *J Vasc Access.* 2008;9:231–235.
32. Pineda DM, Dougherty M, Wismer MC, et al. Bovine carotid artery xenografts for hemodialysis access. *J Vasc Surg.* 2017;65:1729–1734.
33. Marcus P, Echeverria A, Cheung M, et al. Early cannulation of bovine carotid artery graft reduces tunneled dialysis catheter-related complications: a comparison of bovine carotid artery graft versus expanded polytetrafluoroethylene grafts in hemodialysis access. *Vasc Endovasc Surg.* 2019;53(2):104–111.
34. Abdoli S, Mahajan A, Han SM, et al. Early cannulation of bovine carotid artery grafts (Artegraft) after primary vascular access and fistula revision procedures. *J Vasc Surg.* 2018;68:1865–1871.
35. Caldarelli G, Minervini A, Guerra M, et al. Prosthetic replacement of the inferior vena cava and the iliofemoral vein for urologically related malignancies. *BJU Int.* 2002;90:368–374.
36. Huguet C, Ferri M, Gavelli A. Resection of the suprarenal inferior vena cava. The role of prosthetic replacement. *Arch Surg.* 1995;130:793–797.
37. Bower TC, Nagorney DM, Cherry Jr KJ, et al. Replacement of the inferior vena cava for malignancy: an update. *J Vasc Surg.* 2000;31:270–281.
38. Sarkar R, Eilber FR, Gelabert HA, et al. Prosthetic replacement of the inferior vena cava for malignancy. *J Vasc Surg.* 1998;28:75–81; discussion 82–83.
39. Comerota AJ, Harwick RD, White JV. Jugular venous reconstruction: a technique to minimize morbidity of bilateral radical neck dissection. *J Vasc Surg.* 1986;3:322–329.
40. Norton L, Eiseman B. Replacement of portal vein during pancreatectomy for carcinoma. *Surgery.* 1975;77:280–284.
41. Sarfeh IJ, Rypins EB, Mason GR. A systematic appraisal of portacaval H-graft diameters. Clinical and hemodynamic perspectives. *Ann Surg.* 1986;204:356–363.
42. Collins JC, Ong MJ, Rypins EB, et al. Partial portacaval shunt for variceal hemorrhage: longitudinal analysis of effectiveness. *Arch Surg.* 1998;133:590–592; discussion 592–594.
43. Dalsing MC, White JV, Yao JS, et al. Infrapopliteal bypass for established gangrene of the forefoot or toes. *J Vasc Surg.* 1985;2:669–677.
44. Bergan JJ, Veith FJ, Bernhard VM, et al. Randomization of autogenous vein and polytetrafluoroethylene grafts in femoral-distal reconstruction. *Surgery.* 1982;92:921–930.
45. Whittemore AD, Kent KC, Donaldson MC, et al. What is the proper role of polytetrafluoroethylene grafts in infrainguinal reconstruction? *J Vasc Surg.* 1989;10:299–305.
46. Londrey GL, Ramsey DE, Hodgson KJ, et al. Infrapopliteal bypass for severe ischemia: comparison of autogenous vein, composite, and prosthetic grafts. *J Vasc Surg.* 1991;13:631–636.
47. Neville RF, Sidawy AN. Myointimal hyperplasia: basic science and clinical considerations. *Semin Vasc Surg.* 1998;11:142–148.

48. Miller JH, Foreman RK, Ferguson L, et al. Interposition vein cuff for anastomosis of prosthesis to small artery. *Aust N Z J Surg.* 1984;54:283–285.
49. Taylor RS, Loh A, McFarland RJ, et al. Improved technique for polytetrafluoroethylene bypass grafting: long-term results using anastomotic vein patches. *Br J Surg.* 1992;79:348–354.
50. Kansal N, Pappas PJ, Gwertzman GA, et al. Patency and limb salvage for polytetrafluoroethylene bypasses with vein interposition cuffs. *Ann Vasc Surg.* 1999;13:386–392.
51. Stonebridge PA, Prescott RJ, Ruckley CV. Randomized trial comparing infrainguinal polytetrafluoroethylene bypass grafting with and without vein interposition cuff at the distal anastomosis. The Joint Vascular Research Group. *J Vasc Surg.* 1997;26:543–550.
52. Kreienberg PB, Darling 3rd RC, Chang BB, et al. Adjunctive techniques to improve patency of distal prosthetic bypass grafts: polytetrafluoroethylene with remote arteriovenous fistulae versus vein cuffs. *J Vasc Surg.* 2000;31:696–701.
53. Kreienberg PB, Darling 3rd RC, Chang BB, et al. Early results of a prospective randomized trial of spliced vein versus polytetrafluoroethylene graft with a distal vein cuff for limb-threatening ischemia. *J Vasc Surg.* 2002;35:299–306.
54. Neville RF, Attinger C, Sidawy AN. Prosthetic bypass with a distal vein patch for limb salvage. *Am J Surg.* 1997;174:173–176.
55. Neville RF, Tempesta B, Sidwy AN. Tibial bypass for limb salvage using polytetrafluoroethylene and a distal vein patch. *J Vasc Surg.* 2001;33:266–271; discussion 271–272.
56. Neville RF, Capone A, Amdur R, et al. A comparison of tibial artery bypass performed with heparin-bonded expanded polytetrafluoroethylene and great saphenous vein to treat critical limb ischemia. *J Vasc Surg.* 2012;56:1008–1014.
57. Heyligers JM, Verhagen HJ, Rotmans JI, et al. Heparin immobilization reduces thrombogenicity of small-caliber expanded polytetrafluoroethylene grafts. *J Vasc Surg.* 2006;43:587–591.
58. Lin PH, Chen C, Bush RL, et al. Small-caliber heparin-coated ePTFE grafts reduce platelet deposition and neointimal hyperplasia in a baboon model. *J Vasc Surg.* 2004;39:1322–1328.
59. Walluscheck KP. Heparin-bonded expanded polytetrafluoroethylene vascular graft for occlusive vascular disease of the lower extremity. *Ital J Vasc Endovasc Surg.* 2006;13:137–147.
60. Peeters P, Verbist J, Deloose K, et al. Will heparin-bonded PTFE replace autologous venous conduits in infrapopliteal bypass? *Ital J Vasc Endovasc Surg.* 2008;15:143–148.
61. Devine C, McCollum C. Heparin-bonded Dacron or polytetrafluoroethylene for femoropopliteal bypass: five-year results of a prospective randomized multicenter clinical trial. *J Vasc Surg.* 2004;40:924–931.
62. Daenens K, Schepers S, Fournier I, et al. Heparin-bonded ePTFE grafts compared with vein grafts in femoropopliteal and femorocrural bypasses: 1- and 2-year results. *J Vasc Surg.* 2009;49:1210–1216.
63. Gessaroli M, Tarantini S, Leone M, et al. A comparison of femorocrural bypasses performed with modified heparin-bonded expanded polytetrafluoroethylene grafts and those with great saphenous vein grafts to treat critical limb ischemia. *Ann Vasc Surg.* 2015;29:1255–1264.
64. McPhee JT, Barsnes NR, Ozaki CK, et al. Optimal conduit choice in the absence of single-segment great saphenous vein for below-knee popliteal bypass. *J Vasc Surg.* 2012;55:1008–1014.
65. Dorigo W, Pulli R, Piffaretti G, et al. Results from an Italian multicentric registry comparing heparin-bonded ePTFE graft and autologous saphenous vein in below-knee femoro-popliteal bypasses. *J Cardiovasc Surg.* 2012;53:187–194.
66. Wheatcroft MD, Greco E, Tse L, et al. Heparin-induced thrombocytopenia in the presence of a heparin-bonded bypass graft. *Vascular.* 2011;19:338–341.
67. Thakur S, Pigott JP, Comerota AJ. Heparin-induced thrombocytopenia after implantation of a heparin-bonded polytetrafluoroethylene lower extremity bypass graft: A case report and plan for management. *J Vasc Surg.* 2009;49:1037–1040.
68. Lester J, Silver D. Heparin-coated catheters and heparin-induced thrombocytopenia. *J Vasc Surg.* 1988;7:667–672.
69. Whiffen JD, Beeckler DC. The fate of the surface heparin of GBH-coated plastics after exposure to the blood stream. *J Thorac Cardiovasc Surg.* 1966;52:121–125.
70. Kasirajan K. PROPATEN graft: an unlikely heparin-induced thrombocytopenia culprit. *Vascular.* 2012;20:299.
71. Heyligers JM, Lisman T, Verhagen HJ, et al. A heparin-bonded vascular graft generates no systemic effect on markers of hemostasis activation or detectable heparin-induced thrombocytopenia-associated antibodies in humans. *J Vasc Surg.* 2008;47:324–329; discussion 329.
72. Stonebridge PA, Brophy CM. Spiral laminar flow in arteries? *Lancet.* 1991;338:1360–1361.
73. Stonebridge PA, Buckley C, Thompson A, et al. Non spiral and spiral (helical) flow patterns in stenoses. In vitro observations using spin and gradient echo magnetic resonance imaging (MRI) and computational fluid dynamic modeling. *Int Angiol.* 2004;23:276–283.
74. Stonebridge PA. Three-dimensional blood flow dynamics: spiral/helical laminar flow. *Methodist DeBakey Cardiovasc J.* 2011;7:21–26.
75. Stonebridge PA, Vermassen F, Dick J, et al. Spiral laminar flow prosthetic bypass graft: medium-term results from first-in-man structured registry study. *Ann Vasc Surg.* 2012;26:1093–1099.
76. Ascer E, Gennaro M, Pollina RM, et al. Complementary distal arteriovenous fistula and deep vein interposition: a five-year experience with a new technique to improve infrapopliteal prosthetic bypass patency. *J Vasc Surg.* 1996;24:134–143.
77. Hamsho A, Nott D, Harris PL. Prospective randomised trial of distal arteriovenous fistula as an adjunct to femoro-infrapopliteal PTFE bypass. *Eur J Vasc Endovasc Surg.* 1999;17:197–201.
78. Neville RF, Dy B, Singh N, et al. Distal vein patch with an arteriovenous fistula: a viable option for the patient without autogenous conduit and severe distal occlusive disease. *J Vasc Surg.* 2009;50:83–88.
79. Neville RF, Babrowicz J, Spinoza D, Comerota A. Deep venous arterialization in conjunction with prosthetic distal bypass for limb preservation. *Southern Assoc Vasc Surg.* 2020;20-A:156.
80. Neville R, Parker M, Babrowicz J, Comerota A. Deep venous arterialization in conjunction with prosthetic distal bypass for limb preservation. *Society for Clinical Vascular Surgery.* 2019;20-A:147.
81. Mutirangura P, Ruangestakit C, Wongwanit C, et al. Pedal bypass with deep venous arterialization: the therapeutic option in critical limb ischemia and unreconstructable distal arteries. *Vascular.* 2011;19(6):313–319.
82. Ho VT, Gologorski R, Kibrik P, et al. Open, percutaneous, and hybrid deep venous arterialization technique for no-option foot salvage. *J Vasc Surg.* 2020;71:2152–2160.
83. Giudice CD, Jeuvel D, Willie J, et al. Percutaneous deep venous arterialization for severe critical limb ischemia in patients with no option of revascularization: early experience from two European centers. *Cardiovasc Interv Radiol.* 2018;41:1474–1480.
84. Efficacy of oral anticoagulants compared with aspirin after infrainguinal bypass surgery (The Dutch Bypass Oral Anticoagulants or Aspirin Study): a randomised trial. *Lancet.* 2000;355:346–351.
85. Johnson WC, Williford WO. Benefits, morbidity, and mortality associated with long-term administration of oral anticoagulant therapy to patients with peripheral arterial bypass procedures: a prospective randomized study. *J Vasc Surg.* 2002;35:413–421.
86. Belch JJ, Dormandy J, Biasi GM, et al. Results of the randomized, placebo-controlled clopidogrel and acetylsalicylic acid in bypass surgery for peripheral arterial disease (CASPAR) trial. *J Vasc Surg.* 2010;52:825–833, 833.e1–2.
87. Bedenis R, Lethaby A, Maxwell H, et al. Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery. *Cochrane Database Syst Rev.* 2015;(2):CD000535.
88. Conte MS, Bandyk DF, Clowes AW, et al. Results of PREVENT III: a multicenter, randomized trial of edifoligide for the prevention of vein graft failure in lower extremity bypass surgery. *J Vasc Surg.* 2006;43:742–751; discussion 751.
89. Singh N, Sidawy AN, DeZee KJ, et al. Factors associated with early failure of infrainguinal lower extremity arterial bypass. *J Vasc Surg.* 2008;47:556–561.

90. Maufus M, Pernod G. Antithrombotic therapy after infrainguinal bypass. *J Vasc Surg.* 2014;60:1367–1375.
91. van Oostenbrugge TJ, de Vries JP, Berger P, et al. Outcome of endovascular reintervention for significant stenosis at infrainguinal bypass anastomoses. *J Vasc Surg.* 2014;60:696–701.
92. Norgren L, Hiatt WR, Dormandy JA, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg.* 2007;45(Suppl S):S5–67.
93. Bandyk DF. Surveillance after lower extremity arterial bypass. *Perspectives Vasc Surg Endovasc Ther.* 2007;19:376–383; discussion 384–385.
94. Brumberg RS, Back MR, Armstrong PA, et al. The relative importance of graft surveillance and warfarin therapy in infrainguinal prosthetic bypass failure. *J Vasc Surg.* 2007;46:1160–1166.
95. Sanchez LA, Suggs WD, Veith FJ, et al. Is surveillance to detect failing polytetrafluoroethylene bypasses worthwhile?: Twelve-year experience with ninety-one grafts. *J Vasc Surg.* 1993;18:981–989; discussion 989–990.
96. Lundell A, Lindblad B, Bergqvist D, et al. Femoropopliteal-crural graft patency is improved by an intensive surveillance program: a prospective randomized study. *J Vasc Surg.* 1995;21:26–33; discussion 34.
97. Visser K, Idu MM, Buth J, et al. Duplex scan surveillance during the first year after infrainguinal autologous vein bypass grafting surgery: costs and clinical outcomes compared with other surveillance programs. *J Vasc Surg.* 2001;33:123–130.
98. Gorbet MB, Sefton MV. Biomaterial-associated thrombosis: roles of coagulation factors, complement, platelets and leukocytes. *Biomaterials.* 2004;25:5681–5703.
99. Davie EW, Fujikawa K, Kisiel W. The coagulation cascade: initiation, maintenance, and regulation. *Biochemistry.* 1991;30:10363–10370.
100. Coughlin SR. Thrombin signalling and protease-activated receptors. *Nature.* 2000;407:258–264.
101. Morrell CN, Sun H, Swaim AM, et al. Platelets an inflammatory force in transplantation. *Am J Transplant.* 2007;7:2447–2454.
102. Ito RK, Rosenblatt MS, Contreras MA, et al. Monitoring platelet interactions with prosthetic graft implants in a canine model. *ASAIO Trans.* 1990;36:M175–178.
103. McCollum CN, Kester RC, Rajah SM, et al. Arterial graft maturation: the duration of thrombotic activity in Dacron aortobifemoral grafts measured by platelet and fibrinogen kinetics. *Br J Surg.* 1981;68:61–64.
104. Stratton JR, Thiele BL, Ritchie JL. Platelet deposition on Dacron aortic bifurcation grafts in man: quantitation with indium-111 platelet imaging. *Circulation.* 1982;66:1287–1293.
105. Stratton JR, Thiele BL, Ritchie JL. Natural history of platelet deposition on Dacron aortic bifurcation grafts in the first year after implantation. *Am J Cardiol.* 1983;52:371–374.
106. Stratton JR, Ritchie JL. Reduction of indium-111 platelet deposition on Dacron vascular grafts in humans by aspirin plus dipyridamole. *Circulation.* 1986;73:325–330.
107. Mazur C, Tschopp JF, Faliakou EC, et al. Selective alpha IIb beta 3 receptor blockage with peptide TP9201 prevents platelet uptake on Dacron vascular grafts without significant effect on bleeding time. *J Lab Clin Med.* 1994;124:589–599.
108. De La Cruz C, Haimovich B, Greco RS. Immobilized IgG and fibrinogen differentially affect the cytoskeletal organization and bactericidal function of adherent neutrophils. *J Surg Res.* 1998;80:28–34.
109. Greisler HP, Petsikas D, Cziperle DJ, et al. Dacron stimulation of macrophage transforming growth factor-beta release. *Cardiovasc Surg.* 1996;4:169–173.
110. Mattana J, Effiong C, Kapasi A, et al. Leukocyte-polytetrafluoroethylene interaction enhances proliferation of vascular smooth muscle cells via tumor necrosis factor-alpha secretion. *Kidney Int.* 1997;52:1478–1485.
111. Clowes AW, Kirkman TR, Reidy MA. Mechanisms of arterial graft healing. Rapid transmural capillary ingrowth provides a source of intimal endothelium and smooth muscle in porous PTFE prostheses. *Am J Pathol.* 1986;123:220–230.
112. Greisler HP, Dennis JW, Endean ED, et al. Derivation of neointima in vascular grafts. *Circulation.* 1988;78:I6–12.
113. Golden MA, Hanson SR, Kirkman TR, et al. Healing of polytetrafluoroethylene arterial grafts is influenced by graft porosity. *J Vasc Surg.* 1990;11:838–844; discussion 845.
114. Hazama K, Miura H, Shimada T, et al. Relationship between fibril length and tissue ingrowth in the healing of expanded polytetrafluoroethylene grafts. *Surg Today.* 2004;34:685–689.
115. Takahashi T, Kalka C, Masuda H, et al. Ischemia- and cytokine-induced mobilization of bone marrow-derived endothelial progenitor cells for neovascularization. *Nat Med.* 1999;5:434–438.
116. Hattori K, Dias S, Heissig B, et al. Vascular endothelial growth factor and angiopoietin-1 stimulate postnatal hematopoiesis by recruitment of vasculogenic and hematopoietic stem cells. *J Exp Med.* 2001;193:1005–1014.
117. Chavakis E, Carmona G, Urbich C, et al. Phosphatidylinositol-3-kinase-gamma is integral to homing functions of progenitor cells. *Circulation Res.* 2008;102:942–949.
118. Veith FJ, Weiser RK, Gupta SK, et al. Diagnosis and management of failing lower extremity arterial reconstructions prior to graft occlusion. *J Cardiovasc Surg.* 1984;25:381–384.
119. Oresanya L, Makam AN, Belkin M, et al. Factors associated with primary vein graft occlusion in a multicenter trial with mandated ultrasound surveillance. *J Vasc Surg.* 2014;59:996–1002.
120. Hincliffe RJ, Braithwaite BD, Hopkinson BR. The thrombo-lytic management of bypass graft occlusion. *Acta Chirurgica Belgica.* 2003;103:541–547.
121. Funaki B. Lower extremity arterial thrombolysis. *Semin Intervent Radiol.* 2010;27:431–437.
122. Sicard GA, Schier JJ, Totty WG, et al. Thrombolytic therapy for acute arterial occlusion. *J Vasc Surg.* 1985;2:65–78.
123. Gardiner Jr GA, Koltun W, Kandarpa K, et al. Thrombolysis of occluded femoropopliteal grafts. *AJR.* 1986;147:621–626.
124. McNamara TO, Bomberger RA. Factors affecting initial and 6 month patency rates after intraarterial thrombolysis with high dose urokinase. *Am J Surg.* 1986;152:709–712.
125. Koltun WA, Gardiner Jr GA, Harrington DP, et al. Thrombolysis in the treatment of peripheral arterial vascular occlusions. *Arch Surg.* 1987;122:901–905.
126. Durham JD, Geller SC, Abbott WM, et al. Regional infusion of urokinase into occluded lower-extremity bypass grafts: long-term clinical results. *Radiology.* 1989;172:83–87.
127. Nackman GB, Walsh DB, Fillinger MF, et al. Thrombolysis of occluded infrainguinal vein grafts: predictors of outcome. *J Vasc Surg.* 1997;25:1023–1031; discussion 1031–1032.
128. Spence LD, Hartnell GG, Reinking G, et al. Thrombolysis of infrapopliteal bypass grafts: efficacy and underlying angiographic pathology. *Am J Roentgenol.* 1997;169:717–721.
129. Weaver FA, Comerota AJ, Youngblood M, et al. Surgical revascularization versus thrombolysis for nonembolic lower extremity native artery occlusions: results of a prospective randomized trial. The STILE Investigators. Surgery versus Thrombolysis for Ischemia of the Lower Extremity. *J Vasc Surg.* 1996;24:513–521; discussion 521–523.
130. Ouriel K, Veith FJ, Sasahara AA. Thrombolysis or peripheral arterial surgery: phase I results. TOPAS Investigators. *J Vasc Surg.* 1996;23:64–73; discussion 74–75.
131. Greenberg RK, Ouriel K. A multi-modal approach to the management of bypass graft failure. *Vasc Med.* 1998;3:215–220.
132. Zetrenne E, McIntosh BC, McRae MH, et al. Prosthetic vascular graft infection: a multi-center review of surgical management. *Yale J Biol Med.* 2007;80:113–121.
133. FitzGerald SF, Kelly C, Humphreys H. Diagnosis and treatment of prosthetic aortic graft infections: confusion and inconsistency in the absence of evidence or consensus. *J Antimicrob Chemother.* 2005;56:996–999.
134. Edwards Jr WH, Martin RS 3rd, Jenkins JM, et al. Primary graft infections. *J Vasc Surg.* 1987;6:235–239.
135. Liekweg Jr WG, Greenfield LJ. Vascular prosthetic infections: collected experience and results of treatment. *Surgery.* 1977;81:335–342.

136. Kaebnick HW, Bandyk DF, Bergamini TW, et al. The microbiology of explanted vascular prostheses. *Surgery*. 1987;102:756–762.
137. Siracuse JJ, Nandivada P, Giles KA, et al. Prosthetic graft infections involving the femoral artery. *J Vasc Surg*. 2013;57:700–705.
138. Roll S, Muller-Nordhorn J, Keil T, et al. Dacron vs. PTFE as bypass materials in peripheral vascular surgery--systematic review and meta-analysis. *BMC Surgery*. 2008;8:22.
139. Orton DF, LeVeen RF, Saigh JA, et al. Aortic prosthetic graft infections: radiologic manifestations and implications for management. *Radiographics*. 2000;20:977–993.
140. Dosluoglu HH, Schimpf DK, Schultz R, et al. Preservation of infected and exposed vascular grafts using vacuum assisted closure without muscle flap coverage. *J Vasc Surg*. 2005;42:989–992.
141. Cowie SE, Ma I, Lee SK, et al. Nosocomial MRSA infection in vascular surgery patients: impact on patient outcome. *Vascular Endovasc Surg*. 2005;39:327–334.
142. Furlough CL, Jain AK, Ho KJ, et al. Peripheral artery reconstructions using cryopreserved arterial allografts in infected fields. *J Vasc Surg*. 2019;70(2):562–568.
143. Lee BY, Tsui BY, Bailey RR, et al. Should vascular surgery patients be screened preoperatively for methicillin-resistant *Staphylococcus aureus*? *Infect Control Hosp Epidemiol*. 2009;30:1158–1165.
144. Lawson JH, Glickman MH, Ilzecki M, et al. Bioengineered human acellular vessels for dialysis access in patients with end-stage renal disease: two phase 2 single-arm trials. *Lancet*. 2016;387:2026–2034.
145. Neville RF, Gupta SK, Kuraguntla DJ. Initial in vitro and in vivo evaluation of a self-monitoring prosthetic bypass graft. *J Vasc Surg*. 2017;65:1793–1801.

Biologic Grafts

JEFFREY KALISH and ALIK FARBER

GRAFT PROPERTIES 864

- Fresh Vascular Allografts 864
- Cryopreserved Allografts 864
 - Methods of Preparation 864
 - Histology and Physiology 865
 - Immunology 865
- Structurally Modified Biologic Grafts 866
- Other Grafts 866

CLINICAL USE IN VASCULAR SURGERY 866

- Indication 866
 - Extremity Bypass 866
 - Arteriovenous Access 867
 - Replacement of Infected Prosthetic Grafts 867
- Biologic Graft Preparation 867
- Cryopreserved Allografts 867

Structurally Modified Allografts 868

- CLINICAL OUTCOMES 868
 - Cryopreserved Saphenous Vein Allografts 868
 - Graft Patency 868
 - Role of Anticoagulation and Immunosuppression 869
 - Limb Salvage 869
 - Aneurysmal Degeneration 869
 - Summary and Indications for Use 870
 - Cryopreserved Femoral Vein Allografts 870
 - Cryopreserved Arterial Allografts 870
 - Human Umbilical Vein Grafts 872
 - Bovine Carotid Artery Xenografts 872
 - Bovine Mesenteric Vein Xenografts 873
 - Tissue-Engineered Vascular Grafts 873
- FUTURE DIRECTIONS 873

In the field of vascular surgery, the use of surgical bypass is fundamental to the treatment of a wide variety of arterial and venous disorders. In turn, the technical conduct and success of surgical bypass are directly dependent on the conduit used. The ideal conduit should be readily available, easy to handle, resistant to thrombosis and infection, durable, inexpensive, and should have characteristics similar to the vessel that it is replacing.

Although the perfect conduit does not exist, autogenous blood vessels are closest to the ideal. Autogenous arterial conduits, such as the internal mammary, radial, and gastroepiploic arteries, have been used with great success in the coronary circulation.^{1–3} The internal iliac and radial arteries have been used in the visceral vascular bed,^{4,5} and the superficial temporal artery has been used for extracranial–intracranial bypass.⁶ Unfortunately, short conduit length and invasive harvest have limited the use of autogenous arterial grafts to a relatively small number of clinical scenarios.

Autogenous vein has been the preferred conduit for infringuinal bypass because long lengths of vein can be harvested, removal is inconsequential, and harvest complexity is minimal.⁷ Autogenous veins have been used for the bypass of upper extremity,⁸ carotid,⁹ coronary,¹ and visceral¹⁰ arterial beds.

They have also been preferentially used in the construction of arteriovenous fistulae (AVFs) for hemodialysis.¹¹

Although autogenous vascular grafts perform well, there are multiple clinical situations in which these conduits are inadequate, unavailable, or improperly matched to the recipient vascular bed. These unmet demands led to the development of artificial grafts. Although multiple materials have been tried, polyethylene terephthalate (Dacron, DuPont, Wilmington, DE) and polytetrafluoroethylene (PTFE) have emerged as the standard materials for prosthetic vascular grafts. These grafts have been used with excellent success for the bypass of large vessels, such as the aorta and iliac arteries,¹² and medium-sized vessels, such as the subclavian artery.⁹ Prosthetic grafts have also been used extensively for dialysis access¹¹ and with mixed results for infrainguinal revascularization.¹³ Dacron and PTFE grafts offer “off-the-shelf” availability and a variety of sizes to permit replacement of even the largest vessels. In general, however, they cannot be used in infected fields and, compared with autogenous conduits, are at increased risk for infection, structural deterioration, and occlusion. Although patency rates are acceptable for aortoiliac reconstruction because of high flow rates and low outflow resistance, bypass to smaller targets, such as the tibial arteries, is associated with low graft patency.

Limitations of autogenous and prosthetic grafts have fueled exploration for other potential conduits, and this investigative effort has led to the evaluation of biologic grafts for bypass. Biologic grafts, or biografts, are bypass conduits made of non-autogenous biologic vessels modified for use in clinical practice. Allografts or homografts refer to arteries or veins that are transplanted from one individual to another within the same species. Xenografts or heterografts are vessels transplanted from an individual of one species to an individual of another species.

Carrel¹⁴ was first to experiment with fresh allografts and xenografts in dogs during the first decade of the 20th century. The first recorded human use of allografts, obtained from casualties, occurred during World War I.¹⁵ In 1948, Gross et al.¹⁶ described the first clinical series of fresh arterial allografts, and less than a decade later, Linton¹⁷ published his series of fresh venous allografts. Various methods of allograft cryopreservation were developed in the 1950s,¹⁷ refined in the 1970s,^{18,19} and standardized and commercialized in the late 1980s.²⁰ In parallel, enzymatically treated and tanned bovine carotid artery (BCA) xenografts were evaluated and first described in a clinical setting in 1966.²¹ Application of similar techniques to human vessels led to development of the human umbilical vein (HUV) graft by Dardik and Dardik in 1976.²²

Theoretically, biografts promise to be the optimal vascular conduit. They can potentially offer “off-the-shelf” availability, a wide variety of sizes, excellent handling characteristics, and patency rates similar to those of autogenous vessels. These attractive features prompted scientific investigation and clinical use of these conduits that has spanned the course of almost a century. Although this collective experience with an assortment of biografts in a variety of clinical settings led to specific clinical indications for their use, biologic grafts have failed to become the “Holy Grail” of vascular surgery.

GRAFT PROPERTIES

Fresh Vascular Allografts

Fresh arterial and venous allografts have been studied in animal experiments.^{14,23,24} In one canine model, fresh venous allografts had a patency rate of 69% at 20 months. Pathologic analysis of explanted veins revealed intimal proliferation, medial inflammation, medial degeneration, and periadventitial fibrosis.²³ In another canine venous allograft experiment, dogs that were immunosuppressed with azathioprine demonstrated slightly better graft patency than did those that were not.²⁴ Conversely, in a murine model, fresh venous allografts implanted in rats had excellent patency rates and minimal intimal thickening on histologic analysis.²⁴

In humans, fresh venous allografts used for infrainguinal bypass had a failure rate of 55% in one series; failed grafts either occluded or became aneurysmal. Patency rates of allografts appeared to be higher in patients whose grafts were harvested from blood types ABO compatible donors.²⁵ In another study, fresh arterial allografts placed in the aortic position were noted to be highly immunogenic, with evidence of both a humoral and cellular immune response.²⁶ These animal and human

data suggest that fresh vessel allografts initiate a host immune response. Furthermore, the patency of these grafts appears to vary among species.

Aside from their immunogenicity, the use of fresh vascular allografts in the clinical setting has been hampered by logistic factors. Scarce availability of fresh arteries and veins and a need to successfully store such vessels for future use have led to the development of a number of preservation and modification techniques. These techniques can be divided into those that involve preservation without a planned significant change in graft integrity and those in which the graft is intentionally chemically altered. Cryopreservation is the most common example of the preservation technique, whereas proteolytic enzymatic digestion and dialdehyde starch tanning are examples of the modification technique. In addition to creating a conduit that would be more readily available, it is hoped that these techniques will inhibit the host immune response and thereby increase graft patency.²⁷

Over the past century, multiple vessel preservation techniques have been tested. Grafts were stored in a number of solutions, including nutrient broths,¹⁶ glycerol,²⁸ and plasminate.²⁹ A variety of storage temperatures ranging from room temperature to -70°C were tried.^{17,28} Finally, a number of adjunctive sterilization techniques, including ethyl dioxide and irradiation, were attempted.¹⁷ Early techniques focused on preservation without much regard to viability of the vascular tissue. Initial results with preserved vascular grafts were inconsistent, probably because significant cellular and structural damage occurred in many of these vessels and made them nonviable.^{25,30}

Cryopreserved Allografts

Methods of Preparation

There is evidence that cryopreservation can result in significant cellular damage unless appropriate precautions are taken.³¹ During the cryopreservation process, the extracellular matrix freezes at a higher temperature than cellular cytoplasm. This leads to a vapor pressure gradient between the intracellular and extracellular components. When cooling occurs slowly, this gradient can result in cellular dehydration, whereas rapid cooling can lead to plasma membrane rupture. Work with cell suspensions, such as blood and semen, has revealed that certain substances, when added during the freezing process, can significantly improve cell viability.³² These substances, called cryoprotectants, include dimethylsulfoxide and glycerol. Their mechanism of action is to enter cellular cytoplasm and decrease the vapor pressure gradient that exists between the intracellular and extracellular components.²⁰

Over the last 20 years, cryopreservation techniques have been optimized and commercialized. Important variables inherent in modern cryopreservation processes include the type and amount of cryoprotectant used, freezing rate, storage temperature, duration of storage, and additives used.²⁰ The most common cryoprotectant in use today is dimethylsulfoxide at 10% to 20% dilution. The freezing rate varies among protocols, and there is some evidence that rapid freezing at 5°C/s

may work best. Storage temperature may vary from -102°C to -196°C . The duration of cryopreservation may be important, and longer duration has been shown to have an adverse influence on vessel wall morphology but not on graft patency in one animal model.³³ Finally, there is evidence that the addition of certain additives such as chondroitin sulfate to the storage solution enhances vein viability and function.³⁴

Histology and Physiology

Cryopreserved arteries and veins are affected by both cryopreservation and immune rejection; a large body of research has been performed to define and dissect these processes from one another. Cryopreservation has effects on the mechanical properties, histology, and physiology of the treated vessel. Elasticity and compliance of a vessel are important mechanical characteristics that affect its performance as a conduit. Changes in these properties lead to an increased difference in compliance between the conduit and host vessel, which can adversely affect graft patency. *In vitro* models comparing the mechanical properties of cryopreserved and freshly harvested arteries and veins reveal that cryopreservation does not significantly affect elasticity, contractility, compliance, and the mechanical buffering function of the treated vessel.^{19,35,36}

Cryopreservation of blood vessels leads to changes in the intima, media, and adventitia. Although appropriate cryopreservation does not affect the gross morphology of the endothelial layer, histologic changes such as focal microvillous projection, cytoplasmic vacuolization, nuclear prominence, and interruption of tight junctions have been visualized.^{33,37} These changes increase with the duration of cryopreservation^{33,37} and lead to partial endothelial cell loss.³⁷⁻³⁹ Endothelial loss is significant when the cryopreserved graft is exposed to arterial flow. Although autogenous grafts re-establish an endothelial layer, only minimal re-endothelialization is observed in allografts.^{20,29} Because of a compromise in intimal integrity, cryopreserved grafts accumulate low-density lipoprotein cholesterol at an accelerated rate as measured in an *ex vivo* organ perfusion system.⁴⁰

Endothelial vasodilatory function, as measured by response to acetylcholine, thrombin, and calcium ionophore, appears to be retained, but is somewhat diminished, with cryopreservation.⁴¹ With regard to coagulation homeostasis, although cryopreservation of vein grafts is not associated with increased platelet deposition,⁴¹ it does cause decreased thrombomodulin activity.³⁸ Fibrinolytic activity appears to be similar in both fresh and cryopreserved canine jugular veins, but this activity may be adversely affected by the duration of cryopreservation.³⁷

The medial layer of cryopreserved vascular grafts appears to have grossly normal smooth muscle cells, although slight lysis and minimal mitochondrial edema were observed in a rabbit model. In that model, implantation of autologous veins into an arterial circuit led to the preservation of both smooth muscle cells and the elastic lamina. The smooth muscle cells displayed a synthetic, rather than a contractile, phenotype characterized by dilatation of the endoplasmic reticulum.³³ Despite these findings, collagen synthesis in cryopreserved veins was diminished in a canine model.³⁹ Smooth muscle cells in cryopreserved

canine saphenous autografts were noted to have a diminished relaxation response to nitric oxide,⁴¹ although contraction induced by norepinephrine, potassium chloride, and serotonin was unaltered.²⁰

Immunology

Allogeneic implantation of cryopreserved vessels leads to a different histologic and physiologic picture than that seen with cryopreserved autologous grafts. These observed changes are caused by immune mechanisms. Endothelial loss, encountered when an allograft is exposed to arterial flow, is not appreciably reversed, and exposed subendothelial elements are noted on electron microscopy.^{20,29} Smooth muscle cell viability is lost,^{23,42} severe medial fibrosis and disruption of elastic fibers occur,^{23,29,42} and medial necrosis has been described.⁴³ Significant lymphocytic infiltration of the media and adventitia has been observed.²⁹ These alterations in vessel wall biology are not routinely observed with autologous conduits.⁴³

Although it is well known that transplanted allograft and xenograft organs elicit an immune response, it was initially believed that the host-mediated immune response of transplanted vessel allografts was minor^{44,45} and could be successfully blunted by the cryopreservation process.²⁷ Recent literature, however, suggests that vascular allografts do trigger a significant immune response.^{20,26} Endothelial cells present surface antigens that stimulate a cell-mediated immune response⁴⁶ against the donor graft. An immunoglobulin-G-mediated humoral immune response to donor-specific antigens has been described.^{26,47} Transplanted canine venous allografts, but not autografts, demonstrated extensive medial fibrosis and lymphocytic infiltration consistent with immunologic rejection.⁴⁸ In a human model, analysis of 22 explanted cryopreserved saphenous vein (CSV) allografts revealed moderate to severe intimal, medial, and adventitial inflammatory infiltrates. Immunohistochemical analysis demonstrated an abundance of activated T lymphocytes containing cytotoxic granules.⁴⁹ In another experiment, cryopreservation did not alter antigenic expression and the immunologic response of a murine host to allograft transplantation in a number of studies.^{50,51} Chronic immunologic rejection clearly plays a role in allograft biology and appears to be responsible for both diminished patency of cryopreserved vascular grafts and the predilection of these grafts to aneurysmal degeneration.⁴³ A number of investigators hypothesized that manipulating the host immune response to vascular allografts may attenuate immune rejection and improve graft patency. Matching of ABO blood groups was suggested by Ochsner et al.,²⁵ who noted improved patency of allografts transplanted to ABO-matched patients. However, a recent study of seventy-two implanted allografts revealed that ABO-mismatch had no effect on death, thrombosis, rupture, stenosis, or aneurysmal degeneration.⁵² In animal models, immunosuppression with cyclosporine has been demonstrated to diminish immunologic rejection of aortic⁴³ and venous allografts.⁵³ Azathioprine has likewise been shown to decrease the effects of rejection in venous allografts.²⁴

Based on these findings, attempts were made to improve the results of allograft use in humans by modulating the host

immune response. Carpenter and Tomaszewski,⁵⁴ in a prospective, randomized trial of 40 CSV allografts implanted in patients treated with low-dose azathioprine, failed to show a significant improvement in graft patency at 1 year. Azathioprine immunosuppression, however, was associated with a decreased presence of T-lymphocyte cytotoxic granules in that study.⁴⁹ In another small human trial, a combination of low-dose cyclosporine, azathioprine, prednisone, warfarin, aspirin, and vasodilators was used in patients who underwent CSV bypass. Grafts treated with this immunosuppressive regimen demonstrated increased patency rates. This regimen, however, was associated with an increased incidence of complications and graft aneurysmal degeneration.⁵⁵ In one series of patients with prosthetic aortic infection, 10 of 30 patients who underwent aortic allograft replacement were concomitantly treated with cyclosporine. Although the measured humoral immune response was blunted in patients who received cyclosporine, no differences in graft patency or graft complication rates were appreciated.²⁶ In contrast, Randon et al.⁵⁶ contended that a low-dose cyclosporine immunosuppressive regimen for lower extremity bypass using CSV was effective at reducing the risk of rejection while facilitating host cell repopulation of biograft endothelium.

Furthermore, an immunologic response evoked by a cryopreserved allograft can induce allosensitization, which may interfere with future organ transplantation. This mostly affects the use of cryopreserved femoral vein (CFV) allografts in hemodialysis access. A case-matched series of 20 patients who underwent creation of hemodialysis access with this graft demonstrated host allosensitization in all patients as measured by the panel-reactive antibody assay.⁵⁷ Allosensitization, however, did not occur when the CFV graft was processed to remove cellular elements.⁵⁸ Diminution of the immune response by removal of antigenic epitopes has led to multiple attempts to structurally modify biologic grafts.

Structurally Modified Biologic Grafts

In parallel with the development of cryopreservation techniques, further research was conducted to modify blood vessels so that an acceptable vascular substitute could be developed. The goal was to transform a harvested blood vessel into a durable nonimmunogenic graft that could be easily produced and stored. During early experiments in the 1950s, animal arteries were modified by enzymatic digestion of the musculoelastic portion of the vessel wall with ficin, a proteolytic enzyme isolated from figs, to remove immunologically reactive proteins. The resultant collagenous vascular skeleton was strengthened by collagen cross-linking through subsequent tanning with dialdehyde starch.^{21,59} This modified graft was then sterilized and stored in a 1% propylene oxide-50% ethanol solution.²¹

In the earliest experiments, modified BCA grafts were implanted as xenografts first in dogs and then in patients with symptomatic lower extremity occlusive disease. Although no graft ruptures had occurred at 3 years of follow-up, early neointimal hyperplasia and diminished patency were observed.²¹ An unacceptable late rate of graft infection and aneurysmal

degeneration led to a change to glutaraldehyde-based tanning protocols.^{59,60}

Bovine mesenteric veins (BMVs) have also been modified by a patented process of glutaraldehyde cross-linking and sterilized by γ radiation.⁶¹ Both BCAs and BMVs have been used as xenografts in a number of clinical applications.

HUV is a modified biologic conduit that was first evaluated in baboons²² in the early 1970s and subsequently used in humans^{22,62} in 1975. Umbilical vessels are uniform in caliber, valveless, and branchless. The umbilical vein was removed from the umbilical cord by a variety of techniques, including enzymatic digestion and mechanical stripping. Polyester fiber mesh was then sutured in place about the length and outside circumference of the graft for added support.²² The reduced immunogenicity of this graft was hypothesized to be secondary to pretreatment with glutaraldehyde, which was thought to bind to graft histocompatibility antigen sites and thereby shielded them from the host immune response.⁶³

Other Grafts

The search for an ideal blood vessel substitute led to the investigation of a number of nonconventional biologic grafts in animal models. Vascular prostheses fashioned from pericardium⁶⁴ and small intestinal mucosa⁶⁵ have been evaluated. Chemically modified human⁶⁶ and bovine⁶⁷ ureters have been used as vascular conduits with some success. Modified bovine ureters have been used clinically with acceptable patency rates in femoral to popliteal bypass in one small Australian series.⁶⁸ In addition, a small randomized trial claimed clinical equivalence between bovine ureters and PTFE used for hemodialysis access in patients with no vein options.⁶⁹

CLINICAL USE IN VASCULAR SURGERY

Indication

Biologic grafts have been used in modern vascular surgery mostly in three distinct clinical settings: extremity bypass in the absence of suitable autogenous conduit, arteriovenous (AV) access for hemodialysis, and replacement of infected prosthetic grafts.

Extremity Bypass

Acute or chronic ischemia of an extremity is caused by a number of conditions, including atherosclerosis, trauma, embolization, and *in situ* thrombosis. Treatment of extremity ischemia involves revascularization by endovascular or surgical techniques. During infrainguinal surgical bypass, autogenous great saphenous vein has proven to be the preferred conduit for infrainguinal revascularization.^{70,71} When the autogenous great saphenous vein is not available, alternative autogenous conduits, such as an arm vein,⁷² the small saphenous vein,⁷³ and the composite autogenous vein,⁷⁴ have been used with good results. The ever-increasing age and complexity of patients with infrainguinal arterial occlusive disease has brought about increasingly frequent clinical scenarios in which the autogenous

vein is not available and an alternative conduit must be found. Although prosthetic grafts have been used with moderate success above the knee, they have been disappointing when used for infrageniculate bypass.^{75,76} Distal modification of prosthetic grafts with a vein cuff or distal AVF may improve patency rates,⁷⁷⁻⁷⁹ but is more cumbersome.

Given the absence of reliable conduit options for infrageniculate bypass when a suitable autogenous vein is lacking, the feasibility of biologic grafts has been evaluated. In this setting, CSV allografts,⁸⁰ cryopreserved femoro-popliteal artery (CFA) allografts,⁴² HUV grafts,⁸¹ BCA xenografts,⁵⁹ and BMV xenografts⁸² have been used with varying degrees of success.

Arteriovenous Access

End-stage renal disease is a significant public health problem in the United States; its prevalence is increasing steadily, and it is forecast that by the year 2030, more than 2 million patients will be undergoing hemodialysis.^{83,84} Long-term hemodialysis is best performed through a surgically created AVF that connects the arterial and venous circulations via a conduit. The ideal AV conduit carries high flow for efficient dialysis, is superficial enough for easy access, is sufficiently durable to withstand multiple cannulations, allows rapid sealing of cannulation sites, and is resistant to infection, stenosis, and thrombosis. A mature, native vein AVF comes closest to the ideal, and its use is strongly encouraged.¹¹ Unfortunately, many individuals lack suitable veins for native AVF construction because of small vein size, previous access procedures, or vein harvest for extremity or coronary bypass. Furthermore, up to 60% of native AVFs fail to mature, and therefore, cannot be used successfully.^{85,86} Although prosthetic AV grafts are widely used, they have lower patency rates, require more frequent revision, and are at higher risk than vein AVFs for infection.⁸⁷ The search for optimal hemodialysis access in patients who are not candidates for a native vein AVF has led to the use of biologic grafts. CFV allografts,⁸⁸ BCA xenografts,⁸⁹ bovine ureter xenografts,⁶⁹ and BMV xenografts⁶¹ have been used in a variety of settings with variable results.

Replacement of Infected Prosthetic Grafts

Prosthetic graft infection, particularly when the aorta is involved, is one of the most dreaded complications in vascular surgery and is associated with high morbidity and mortality.⁹⁰ Treatment of an infected aortic prosthesis includes excision of the infected segment and extra-anatomic prosthetic bypass⁹⁰ or reconstruction with an antibiotic-soaked or antibiotic-bonded prosthetic graft,⁹¹ femoral vein,⁹² or aortic allograft.⁹³ Extra-anatomic bypass and aortic ligation are associated with long operative times, risk of remote infection, bypass thrombosis, and aortic stump rupture.^{90,94} Antibiotic-soaked prosthetic grafts may work well for infections caused by relatively indolent *Staphylococcus epidermidis*, but are much less effective against more virulent organisms.⁹¹ Finally, use of the femoral vein for aortic reconstruction is tedious and associated with harvest-related complications.⁹²

Cryopreserved aortic allografts offer “off-the-shelf” availability, good handling properties, and the potential for expeditious *in situ* repair. Cryopreserved aortic allografts were more

resistant than prosthetic grafts to *S. epidermidis* infection in a canine model.⁹⁵ Resistance of vascular allografts to infection has led to the wide use of arterial allografts to treat aortoiliac infection,⁹⁶ CFV allografts to treat infection involving prosthetic AV grafts,⁹⁷ and CSV allografts to replace infected infrainguinal prosthetic bypass grafts.⁹⁸

Biologic Graft Preparation

Cryopreserved Allografts

A number of tissue banks and commercial companies prepare, store, and supply cryopreserved blood vessels. Despite similarities in conduit preparation, many have proprietary cryopreservation protocols.⁹⁹ The great saphenous vein, femoral vein, and arterial segments are harvested from multiorgan donors who are screened for an array of viral, bacterial, and fungal infections. Branches are suture ligated, and the allografts are sized with calibrated dilators. They are tested for presence of pathogens, rinsed in an antibiotic solution, placed in a proprietary cryoprotectant solution, and stored in the vapor phase of liquid nitrogen at -110°C to -196°C. Allografts are shipped and stored in a solution of dimethylsulfoxide at -96°C until needed. At the start of the procedure, the allograft is rapidly thawed by submersion in a warm water bath at 37°C to 42°C for 20 minutes. After rinsing in a series of solutions provided by the manufacturer, it is ready for use.

CSV allografts are available in a number of lengths and diameters. Most commonly, the vein measures 3 to 5 mm in diameter. These grafts look, feel, and handle like the autogenous saphenous vein. During an infrainguinal bypass, the allograft is usually reversed and placed in a superficial tunnel for easy access.⁸⁰ Postoperative surveillance was not considered useful in one large series.⁸⁰

CFV allografts are usually less than 25 cm in length and have a diameter between 5 and 7 mm. They have most commonly been used in hemodialysis in the setting of prosthetic AV graft infection. When used for dialysis access, this allograft is appropriately reversed and tapered to a 5-mm diameter at the arterial anastomosis to decrease the incidence of ischemic steal syndrome.⁸⁸ It is allowed to mature for 3 to 4 weeks before it is accessed for hemodialysis. Revision of these grafts is very difficult because of their thin wall and surrounding fibrosis.⁹⁷

Arterial allografts have most frequently been used for aortic replacement in the setting of primary or prosthetic aortic infection. Given this clinical setting and the need to replace a large artery such as the aorta, these allografts have to withstand particularly hostile conditions. Technical modifications for the use of these allografts have been developed, including vigilance in following thawing instructions, use of appropriately long grafts, and construction of tension-free anastomoses, taking great care that suture ligation of branches is performed with polypropylene sutures that include the graft wall along with the branches. Aggressive excision of infected tissue and wound drainage is required, and other adjuncts include circumferential anastomotic reinforcement with allograft strips, use of gentamicin-impregnated fibrin glue, and coverage of the graft with viable tissue, such as a pedicled omental or muscle flap.^{93,100}

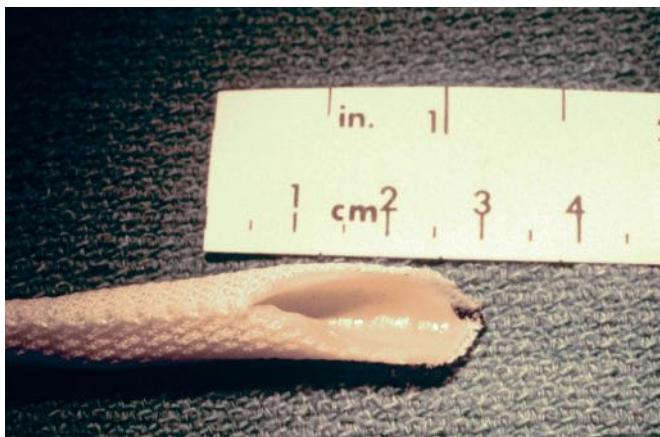


Figure 67.1 Human Umbilical Vein Graft. (Courtesy Herbert Dardik.)

Structurally Modified Allografts

The HUV graft (Fig. 67.1) was stored in 50% ethanol and provided on a glass mandril. This graft did not tolerate traction or the application of standard vascular clamps. To avoid injury, it needed to be passed through a metal or plastic conduit during tunneling and preferably controlled with a tourniquet. To decrease the risk of pseudoaneurysm formation during suturing, both the vein and the Dacron mesh needed to be incorporated into the suture line. Manufacturing of the umbilical vein graft by Synovis Life Technologies, Inc. (St. Paul, MN) stopped in May 2005 in compliance with new US Food and Drug Administration (FDA) guidelines governing combination tissue medical devices.¹⁰¹ A next-generation HUV graft that fulfilled FDA regulations never became commercially available.

The BCA graft (Fig. 67.2) is supplied in a specially designed tube containing a proprietary solution of 1% propylene oxide in 40% aqueous ethyl alcohol. It is naturally compliant, soft, and relatively easy to use. It is presently available in 6-, 7-, and 8-mm diameters and 15- to 50-cm lengths (Artegraft; Artegraft, Inc., New Brunswick, NJ). The BMV graft (Fig. 67.3) is shipped in a sterile saline solution and is available in 6-mm diameters and 10- to 40-cm lengths (ProCol Vascular Bioprostheses, Hancock Jaffe Laboratories, Irvine, CA). This graft is compliant and handles much like a saphenous vein.⁶¹ Both xenografts require a series of rinsing steps in the operating room before use.

CLINICAL OUTCOMES

Cryopreserved Saphenous Vein Allografts

Numerous reports on the utility of CSV allografts for infrainguinal revascularization have been published (Table 67.1).^{54–56,80,102–112} However, this literature has confounding factors that may affect the interpretation of outcomes. CSV has been distributed by a number of vendors who use similar, but not identical, cryopreservation techniques. There is significant variability pertaining to patients, location of the proximal and distal anastomoses, use of anticoagulation, and use of immunosuppressive agents. The majority of these reports



Figure 67.2 Bovine Carotid Artery Graft. (Courtesy Artegraft, Inc., North Brunswick, New Jersey.)



Figure 67.3 Bovine Mesenteric Vein Graft. (Courtesy ProCol Vascular Bioprostheses, Hancock Jaffe Laboratories, Irvine, California.)

are retrospective, and the two largest studies contain 115¹⁰⁷ and 240⁸⁰ grafts. One of the more recently published reports spanned a 15-year period of implantation.⁵⁶ Four prospective studies have been published, but they include small numbers of patients.^{54,55,80,106}

Graft Patency

Although use of CSV allografts has been reported in a number of settings, these grafts are generally used for the treatment of limb-threatening ischemia.^{80,107} The primary patency rate of CSV grafts has been noted to be relatively low in most retrospective series (see Table 67.1).^{80,104–110,112} The largest case series reported a 30% primary patency rate at 1 year,⁸⁰ similar to the 37% primary patency rate noted in the second largest series.¹⁰⁷ Although Buckley et al.¹¹⁰ published an impressive 87% primary patency rate in their prospective study of 26 patients, Carpenter and Tomaszewski⁵⁴ found a dismal 13% primary patency rate in their prospectively monitored patient cohort. Randon et al.⁵⁶ showed slightly better than average

TABLE 67.1

Summary of Published Cryopreserved Saphenous Vein Allograft Series Containing More than 25 Grafts

Series	No. of Grafts	Primary Patency at 1 Year (%)	Secondary Patency at 1 Year (%)	2-Year Limb Salvage (%)
Farber et al. ⁸⁰	240	30	NR	71
Martin et al. ¹⁰⁷	115	37	40	66*
Randon et al. ⁵⁶	108	56	73	70†
Chang et al. ¹⁰³	81	27	NR	43‡
Harris et al. ¹⁰⁴	80	36.8	NR	62‡
O'Banion et al. ¹¹²	73	35	NR	73‡
Bannazadeh et al. ¹¹¹	66	19	42	73‡
Hartranft et al. ¹⁰²	60	53	NR	70‡
Shah et al. ¹⁰⁸	43	66	NR	NR
Carpenter and Tomaszewski ⁵⁴	40	13	NR	42‡
Walker et al. ¹⁰⁹	39	28	46	67*
Buckley et al. ¹¹⁰	26	87	NR	80
Harris et al. ¹⁰⁵	25	NR	36	74‡
Leseche et al. ¹⁰⁶	25	NR	52	78

NR, not reported.

*At last follow-up.

†At 3 years.

‡At 12 months.

patency and limb salvage rates in CSV recipients treated with low-dose cyclosporine. Chang et al.¹⁰³ reported that CSV performed better in patients with rest pain compared to tissue loss when evaluating amputation-free survival, particularly in those who could be anticoagulated with warfarin.

Secondary procedures on failing or failed grafts generally seem to yield little gain. Primary-assisted and secondary patency of CSV grafts were not significantly higher than primary patency in the two largest allograft series.^{80,107} Once the graft failed, it was abandoned, and secondary grafting was performed when indicated.⁸⁰ Other authors, however, almost doubled their secondary patency rates by adopting an aggressive posture toward allograft thrombectomy and revision.^{109,111}

Multiple patient and procedural variables were evaluated for their influence on allograft patency. In the largest published series, multivariate analysis identified that diabetes negatively affected graft patency. Age, gender, hypertension, smoking, renal dysfunction, indication for surgery, history of bypass grafting, and site of distal anastomosis did not have an effect.⁸⁰ A recent series likewise noted a negative effect of diabetes on graft patency,⁵⁶ although others found no significant effect.^{107,109} Two separate investigations found that secondary and composite allograft reconstructions adversely affected graft patency.^{108,111} Lastly, in a recent study, statin use was noted to improve graft patency.⁵⁶

Role of Anticoagulation and Immunosuppression

A number of studies have evaluated the effect of anticoagulation on allograft patency. Aspirin and warfarin, alone or in combination, did not improve graft patency in most series.^{54,80,105,107,108} Although Chang et al.¹⁰³ identified a benefit to anticoagulation with warfarin in terms of limb salvage, this benefit was most pronounced in patients with rest pain and not tissue loss. Buckley et al.,¹¹⁰ however, reported an impressive 87% primary patency rate in their prospective cohort of 26 patients who were treated with an intensive anticoagulation protocol consisting of preoperative aspirin, perioperative low-dose heparin and dextran, and postoperative warfarin, aspirin, and dipyridamole. Of note, 42% of grafts in that series underwent distal anastomotic modification with either vein cuffs or AVFs. A limitation of most retrospective studies is that the precise level of therapeutic anticoagulation was not rigorously followed for each individual patient. The true effect of an anticoagulation protocol on allograft patency awaits a prospective randomized study that will closely monitor the adequacy of postoperative oral warfarin therapy.

Immunosuppressive regimens have been evaluated clinically. In a prospective randomized trial of 40 grafts in patients treated with low-dose azathioprine, Carpenter and Tomaszewski⁵⁴ failed to show a significant improvement in graft patency at 1 year. In contrast, Randon et al.⁵⁶ declared their low-dose cyclosporine immunosuppressive regimen to be effective at reducing the risk of graft rejection and thrombosis, and reported minimal side effects. Although immunosuppressive protocols may be effective, potentially serious side effects of therapy may not justify routine use in this patient population.⁵⁵

Limb Salvage

Despite discouraging graft patency, use of CSV allografts has been associated with acceptable limb salvage rates (see Table 67.1). In the largest published series, a 71% 2-year limb salvage rate was achieved,⁸⁰ whereas Randon et al.⁵⁶ reported a 5-year limb salvage rate of 64%. The discrepancy between graft patency and limb salvage can be explained, in part, by secondary bypass procedures performed after primary graft failure. Others have reported that repetitive bypass grafting significantly extends limb salvage.¹¹³ Another possibility is that the saphenous allografts remained patent long enough to enable healing of lower extremity ulceration in a large proportion of patients. The ulcers may not have recurred despite graft failure.^{80,106,107} Unfortunately, this hypothesis can only be proven in a trial in which ulcer healing is prospectively monitored, along with limb salvage.

Of the various clinical factors that could potentially influence limb salvage, multivariate analysis found the site of distal anastomosis to be significant.^{80,112} Patients who underwent allograft bypass to the popliteal artery had better limb salvage than did those who underwent tibial bypass. Martin et al.¹⁰⁷ found patient age to be inversely related to limb salvage.

Aneurysmal Degeneration

CSV allografts that remain open for a prolonged period are prone to aneurysmal degeneration,^{55,80,107} which is probably

related to the immune response by the recipient against the graft. The true incidence of allograft aneurysm formation cannot be accurately determined because the majority of these grafts occlude long before a clinically detectable aneurysm can develop. In one series, aneurysmal degeneration developed in nine grafts, for a 2-year aneurysm incidence of 44%.⁸⁰ Martin et al.¹⁰⁷ reported a 25% aneurysm formation rate at 2.5 years. The development of aneurysms in allografts necessitates close surveillance of those few patients whose graft remains open for a prolonged period. Because allograft aneurysm rupture has been reported,^{55,80} preemptive graft revision is recommended.

Summary and Indications for Use

Although CSV allografts look, feel, and handle like an autogenous vein, they are far from being the “Holy Grail” of conduits for infrainguinal reconstruction. Their poor patency rates are worsened by several risk factors, including diabetes, previous bypass, and composite reconstruction. Postoperative anticoagulation has not significantly improved graft patency,⁸⁰ although some authors believe that an intensive peri- and postoperative anticoagulation regimen has merit.¹¹⁰ Given the immunologic mechanism of graft failure, it is unlikely that anticoagulation alone is sufficient to prevent graft occlusion. Grafts that stay open for extended periods, perhaps as a result of chance matching of important immunologic loci, are prone to aneurysmal degeneration. Finally, CSV allografts are expensive, costing approximately \$12,000 (in 2020 US dollars), depending on the length of the graft.

Given published clinical data, many authors conclude that the use of CSV allografts should be limited.^{55,80,104,106,107} Nevertheless, these grafts clearly have a place in the armamentarium of the modern vascular surgeon. Because they have been reported to be relatively resistant to graft infection,⁹⁸ they have an advantage when revascularization needs to be performed in an infected field. They also have an advantage when distal bypass needs to be extended onto the foot because closure of the wound is considerably easier than if a prosthetic graft is used. Finally, CSV allografts typically remain patent long enough to allow healing of an ischemic ulcer or minor amputation. The final piece of evidence supporting the continued role of this graft is persistent demand for the product by the vascular surgery community as evidenced by the number of grafts that continue to be sold.

Cryopreserved Femoral Vein Allografts

Femoral vein allografts have been used for hemodialysis access in the setting of prosthetic AV graft infection, multiple graft failures, or compromised venous outflow sites. In one series of 48 allografts, 1-year primary and secondary patency rates of 49% and 75%, respectively, were achieved. No allograft infection or aneurysmal degeneration was noted.⁸⁸ In another series of 337 allografts, primary patency rates of 58%, 35%, and 17% were reported after 1, 3, and 5 years, with secondary patency of 90%, 78%, and 58%. Although no infection was noted during follow-up, two pseudoaneurysms required repair.¹¹⁴ Madden et al.¹¹⁵ compared the outcomes of 90 femoral allografts with

100 concurrent PTFE AV grafts and noted similar patency rates. No infections were seen in the allograft group, whereas 10% of the PTFE AV grafts became infected. In 18% of the allografts, however, aneurysmal degeneration developed.¹¹⁵ In a prospective, randomized trial between CFV and PTFE grafts (suspended by the FDA after enrollment of 27 patients into each group), need for fistulography and aneurysmal degeneration was higher in the CFV cohort.¹¹⁶ Others found that the use of CFV for AV access was associated with a 55% rate of infection, which was particularly common in thigh grafts. Allograft rupture occurred in 46% of infected grafts.¹¹⁷

CFV allografts do not have a primary role in hemodialysis access. They may have a secondary role in the setting of infected prosthetic access in a patient with limited reconstructive options. Because of alloimmunization, they should not be used in patients who are candidates for future kidney transplantation,⁵⁷ although de-cellularized femoral vein allografts appear to be safer in that regard.⁵⁸ Symptomatic pseudoaneurysms may develop in these allografts and should elicit a low threshold for repair. Finally, CFV placement in the thigh should be avoided.

More recently, the use of CFV allografts has been described in cases of venous reconstruction during pancreaticoduodenectomy¹¹⁸ and liver transplantation.¹¹⁹ In a study of 36 patients requiring portal vein–superior mesenteric vein resection during 144 Whipple procedures for pancreatic adenocarcinoma, 18 of the 36 underwent reconstruction with cryopreserved homologous veins; there was no significant difference in postoperative morbidity/mortality or patency based on type of venous reconstruction.¹²⁰ In living donor liver transplants, cryopreserved homologous veins can be used for the hepatic vein reconstructions to secure the large outflow of the graft, with excellent patency rates and graft survival rates.¹¹⁹

Cryopreserved Arterial Allografts

Although most experience with arterial allografts has been gained with aortic replacement in the setting of prosthetic graft infection, CFAs have been used for infrainguinal revascularization. Cryopreserved femoropopliteal arterial allografts used for infrageniculate revascularization had primary patency rates of 60%, 56%, and 26% at 1, 2, and 5 years in a 10-year series following 42 bypasses.¹²¹ Because of short conduit length, a composite bypass was necessary in 53% of cases. Another series of 35 allografts reported a 39% primary patency and 59% secondary patency rate at 18 months of follow-up. Two grafts required replacement as a result of aneurysmal degeneration.¹²² A 5-year primary patency rate of 16% was achieved in a retrospective multicenter trial of 165 fresh and cryopreserved arterial allografts.¹²³ A more recent study compared 39 peripheral reconstructions using CFAs with 35 non-CFA bypasses, including extra-anatomically tunneled prosthetic grafts, autogenous veins, and endarterectomized superficial femoral artery grafts performed in the setting of infection. Total graft-related morbidity was 18% in the CFA group and 57% in the non-CFA group.¹²⁴ In this study, mortality at 18 months of follow-up was high in both groups: 31% in the CFA group and 43% in the non-CFA group.¹²⁴ These results suggest that in lower

extremity bypass, cryopreserved arterial allografts have low patency rates, are predisposed to aneurysmal degeneration, do not offer any significant advantage over the use of saphenous vein allografts, and have the additional potential drawback of the need to connect two or more arterial segments together to create a conduit of sufficient length.

Arterial allografts have been used extensively for the management of primary and prosthetic aortic infection. To this end, fresh aortic allografts stored for less than 1 month at 4°C have been used with some success.^{93,125,126} An Italian study of 44 patients treated with 13 fresh and 31 cryopreserved aortic allografts did not find a difference in patient outcomes.¹²⁵ A French study of 179 patients treated with 111 fresh and 68 cryopreserved grafts, however, did note long-term differences in graft behavior: fresh allografts were associated with allograft rupture and an increased incidence of late graft-related complications.⁹³

There are nine published studies using more than 40 grafts that provide information about the outcomes of cryopreserved aortic allografts for the treatment of aortic infection (Table 67.2). Most of these represent multi-institutional registries with relatively short follow-up periods.^{96,127–129} Although many patients had polymicrobial aortic infections, staphylococcal species were the most common organisms cultured.^{96,100,125,129–132} As expected, perioperative mortality rates were high and ranged between 5% and 36%. Factors associated with increased mortality included emergent or urgent surgery and the presence of an aortoenteric fistula.^{100,129} Aortic allograft repair in patients with aortoenteric fistulae was associated with prohibitive long-term mortality rates of 80% in one recent series¹³³ and 83% in an older series.¹²⁹

As expected, these patients had very high perioperative complication rates, ranging between 18% and 55%. Allograft rupture was seen in the immediate postoperative period and up to 4 years of follow-up.¹⁰⁰ This devastating complication occurred in 2% to 14% of cases and was associated with high mortality. Allograft aneurysmal dilatation was noted to occur in as many as 8% of patients in one series.¹²⁹ Graft stenosis and thrombosis were more often associated with grafts extending to the iliac or femoral arteries.⁹³ Amputation rates ranged between 1% and 14%. Despite these sobering statistics, 87% and 60% of patients were free of aortic and iliofemoral complications or interventions, respectively, at 7 years in one large single-institution series.⁹³ Furthermore, the largest study of cryopreserved aortoiliac allografts indicates that this modality allows aortic reconstruction in the setting of infection or those at high risk of infection, with lower early and long-term morbidity and mortality than previously reported.¹²⁷ A recent systematic review and meta-analysis of 31 studies, including 1377 patients, also concluded that the use of cryopreserved allograft appears to be a safe and durable option with acceptable outcomes for the treatment of aortoiliac infections.¹³⁴

Aortic infection is one of the gravest conditions in vascular surgery. Therefore, allograft performance needs to be viewed against the results of other treatment options for the management of infected aortic grafts. Graft excision with extra-anatomic bypass was associated with a 30-day mortality of 13% and an amputation rate of 10%.⁹⁰ Likewise, *in situ* aortic graft replacement with a rifampicin-bonded prosthetic graft had a perioperative mortality rate of 18%.⁹¹ Although cryopreserved aortic allografts clearly have a place in the management of prosthetic aortic graft infection, their precise role has yet to

TABLE 67.2 Summary of Published Cryopreserved Aortic Allograft Series Containing More than 40 Grafts

Series	Total No. of Grafts	No. of Aortic Grafts	Follow-up (months)	30-Day Mortality (%)	No. with Perioperative Major Complications (%)	No. of Allograft Ruptures (%)	Amputation Rate (%)	No. of Graft Thromboses (%)	Graft Dilatation (%)
Harlander-Locke et al. ¹²⁷	220	220	30 ^t	20 (9)	53 (24)	8 (4)	NR	9 (4)	6 (3)
Bisdas et al. ¹³²	110	57	36*	5 (9)	10 (18)	0	NR	1 (2)	1 (2)
Verhelst et al. ¹²⁹	90	66	36 ^t	16 (17)	40 (44)	12 (13)	1 (1)	8 (9)	7 (8)
Ben Ahmed et al. ¹³⁰	71	71	45 ^t	11 (17)	15 (21)	5 (7)	NR	5 (7)	0 (0)
Kieffer et al. ⁹³	68	68	34 ^t	9 (13) ^t	31 (45)	1 (2)	0	2 (3)	NR
Noel et al. ¹²⁸	56	56	5.3 ^t	7 (13)	28 (55)	8 (14)	3 (5)	5 (9)	1 (2)
McCready et al. ¹³³	51	43	46 ^t	11 (26)	11 (26)	0	NR	NR	NR
Vogt et al. ¹⁰⁰	49	49	27 ^t	3 (6)	10 (20)	5 (10)	NR	NR	NR
Zhou et al. ⁹⁶	42	42	12.5 ^t	7 (17)	21 (50)	0	6 (14)	1 (6)	0

NR, not reported.

*Median follow-up.

^tMean follow-up.

^tIn-hospital mortality.

be clearly defined. They are associated with allograft dilatation and rupture, probably because of the previously discussed immunologic mechanisms.^{20,23,29,44,45} Graft surveillance protocols have yet to be standardized and validated. Although the use of current immunosuppressive regimens in these very ill patients is not practical, the development of more focused immunosuppressive therapy in the future may better define the role of aortic allografts in the armamentarium of vascular surgeons.

Human Umbilical Vein Grafts

The first large clinical experience with the use of HUV grafts was reported in 1988 by Dardik et al.⁸¹ A total of 907 lower limb bypass procedures were performed in 799 limbs of 715 patients. The 5-year primary-assisted patency rates were 57% and 32% for femoropopliteal and femorotibial bypasses, respectively. The 5-year limb salvage rate ranged between 70% and 80%. Fifty-seven percent of the grafts exhibited aneurysmal dilatation at a mean follow-up of 5 years. In 1989, ownership and manufacture of the HUV graft changed hands. In an attempt to address the issue of time-dependent graft degradation, a second-generation graft was developed to resist aneurysmal degeneration.¹⁰¹ In parallel, Dardik et al.⁷⁹ attempted to improve the patency of femorotibial HUV grafts by using adjunctive distal AVFs. These investigators published an updated experience with 283 second-generation HUV grafts in 2002. Five-year primary patency rates for this graft were 60% and 50% for below-knee popliteal and tibial bypass, respectively. Five-year limb salvage rates were 80% and 65% for below-knee popliteal and tibial bypass, respectively. No graft aneurysmal degeneration was noted on duplex surveillance of these grafts.¹³⁵

The largest randomized trial of HUV grafts was a Veterans Administration-sponsored trial in the United States in which the outcomes of HUV, saphenous vein, and PTFE grafts were evaluated in 752 patients who underwent above-knee femoropopliteal bypass. At 5 years, primary-assisted patency rates were 73%, 53%, and 39% for saphenous, umbilical vein, and PTFE grafts, respectively. Although HUV grafts outperformed PTFE grafts, they were associated with a higher incidence of early graft thrombosis and amputation.¹³⁶

Although HUV grafts demonstrated adequate outcomes and improved patency rates compared with PTFE grafts, they never became part of mainstream vascular practice. Nevertheless, vascular surgeons must be aware of the HUV graft and its unique complexities and complications given the possibility of encountering a patient with this type of bypass in clinical practice. Currently, the HUV graft is not commercially available.

Bovine Carotid Artery Xenografts

The BCA xenograft was first used for dialysis access by Chinitz et al.,¹³⁷ who found that the graft tolerated frequent cannulation and maintained flow sufficient for successful hemodialysis. Patency rates of this graft range from 21% to 86% at 1 year and 45% to 76% at 2 years.^{138–143} With the advent of PTFE and its

TABLE 67.3

Published Reports Comparing the Cumulative Patency of Bovine Carotid Artery and Expanded Polytetrafluoroethylene Grafts

Series	Year	Grafts (n)	CUMULATIVE PATENCY (%)		
			6 months	12 months	24 months
Kaplan et al. ¹⁴⁴	1976	BCA (16)	NR	NR	NR
		ePTFE (15)	NR	NR	NR
Butler et al. ¹⁴³	1977	BCA (103)	94	83	76
		ePTFE (184)	85	75	74
Telli et al. ¹⁴⁵	1979	BCA (71)	NR	33*	NR
		ePTFE (66)	NR	62*	NR
Lilly et al. ¹⁴⁶	1980	BCA (113)	NR	73	NR
		ePTFE (83)	NR	84	NR
Anderson et al. ¹⁴²	1980	BCA (76)	NR	70*	45*
		ePTFE (100)	NR	87*	73*
Sabanayagam et al. ¹⁴⁰	1980	BCA (402)	57*	21*	NR
		ePTFE (225)	94*	91*	NR
Hurt et al. ¹⁴⁷	1983	BCA (62)	NR	84	72
		ePTFE (78)	NR	65	63
Anderson et al. ¹⁴¹	2005	BCA (245)	NR	86	NR
		ePTFE (446)	NR	82	NR
Arhuidese et al. ¹⁴⁹	2017	BCA (52)	NR	30	16
		ePTFE (68)	NR	43	29

BCA, bovine carotid artery; ePTFE, expanded polytetrafluoroethylene; NR, not reported.

*Significant difference between conduits.

Adapted from Scott EC, Glickman MH: Conduits for hemodialysis access. *Semin Vasc Surg* 20:158, 2007.

use in hemodialysis access in the mid-1970s, multiple studies comparing BCA xenografts with PTFE grafts have been published (Table 67.3).^{140–149} A prospective, controlled, randomized trial of 140 BCA and PTFE AV grafts found no significant differences in patency and complication rates.¹⁴⁷ Other studies, however, revealed PTFE grafts to have superior patency rates.^{140,142,145} BCA xenografts are associated with higher infection^{140,142} and aneurysmal degeneration^{140,145} rates than PTFE AV grafts. A 9% to 20% infection rate^{140,142,150} and a 1% to 8% aneurysmal degeneration rate^{140,143,145,150} have been observed. Although BCA xenografts elicit a dense desmoplastic reaction, they are predisposed to aneurysmal degeneration, which is exacerbated by repeated cannulation during hemodialysis. They are prone to infection, and when it occurs, they are very difficult to excise because of intense inflammation and the fragile nature of the graft.¹⁴⁵ Finally, they are more expensive than PTFE grafts. These issues have limited widespread use of this graft for hemodialysis access.¹⁴⁸

There have been a few published series on the use of different BCA xenografts for infrainguinal revascularization. In one series, 30% of the grafts underwent degeneration within 4 months of insertion.¹⁵¹ A study of 124 grafts used for

femoropopliteal and femorotibial bypass yielded primary patency rates of 86.5% at 1 year and 67.5% at 5 years.¹⁵² Another study of 58 grafts used for above-knee femoropopliteal bypass yielded a 56% 5-year primary-assisted patency rate. No graft infections or aneurysmal degeneration was noted.⁵⁹ Short available lengths, wide availability of PTFE, and concern about graft degeneration have damped enthusiasm for the use of BCA xenografts in lower extremity bypass.

Bovine Mesenteric Vein Xenografts

BMV xenografts have been successfully used for hemodialysis access. In one series of 50 grafts placed in 49 patients who had an average of 3.6 previous AVFs, a primary patency rate of 62% was noted at 30 months. Four infections but no aneurysmal degeneration developed.¹⁵³ In one prospective, multicenter registry, 183 patients with previously failed synthetic grafts were treated with a BMV hemodialysis access. Outcomes were compared with a concomitant nonrandomized group of patients who received PTFE grafts. One-year primary and secondary BMV patency rates were 36% and 66%, respectively. Although primary rates were similar to those of PTFE AV grafts, secondary rates were significantly higher for bovine xenografts. Graft infection was less common in the BMV xenograft group, and the pseudoaneurysm formation rate was similar to that seen with PTFE grafts. However, significant dilatation occurred in six grafts.⁶¹ In another recent series of 62 BMV grafts used for hemodialysis access, 30% primary and 58% secondary patency rates were reported. Thirteen infections occurred, and six (10%) grafts required surgical excision. Significant graft dilatation was noted in two patients.¹⁵⁴

BMV xenografts appear to have acceptable patency rates that are similar to those seen with PTFE grafts. Although data are limited, these grafts do not appear to be any more predisposed than PTFE grafts to infection or pseudoaneurysm formation. The significance of the dilatation that occurs in some of these grafts is not yet clear. More research will be required before the role of this graft for hemodialysis access is more precisely defined.

BMV xenografts have been used for infrainguinal revascularization. In one small trial involving six patients, all grafts failed within 4 months.⁸² In another trial of 32 patients with critical limb ischemia, a 16% primary patency rate was noted at 1 month. Most of the occlusions occurred within 1 day of the operation.¹⁵⁵ Given these results, this conduit cannot be recommended for infrainguinal bypass.

Tissue-Engineered Vascular Grafts

Spurred by repeated failures of commercially available xenografts and allografts, numerous researchers started to focus on tissue engineering as a tool to improve functionality of current biologic grafts. These new graft concepts aim to utilize the patient's own cells grown on a variety of supportive scaffolds.

Such grafts hold promise to eliminate immunogenicity and propensity for infection that have plagued many biologic grafts. A number of researchers have experimented with different scaffold systems and have created both *in vitro* and animal models for such grafts; tissue-engineered vascular grafts for humans have started to be evaluated in clinical trials conducted by multiple companies (see Ch. 68, Bioengineered Vascular Grafts).

FUTURE DIRECTIONS

Biologic grafts differ from one another in composition and method of preparation. They are useful in a number of clinical scenarios and have earned a place in the armamentarium of modern vascular surgeons. They have not, however, delivered on the expectations that many early vascular surgeons had for these conduits. Despite an enormous amount of basic and clinical investigation they have failed to become the ideal conduit. The search for such a conduit is still progressing.

Significant research is currently being conducted in an attempt to create a biologic nonimmunogenic graft, mainly through improvements using vascular tissue engineering. It is still conceivable that in the future a biologic graft with little or no immunogenicity and characteristics similar to that of a normal artery or vein can be developed, in an acceptable period of time and without prohibitive cost.

SELECTED KEY REFERENCES

- Farber A, Major K, Wagner WH, et al. Cryopreserved saphenous vein allografts in infrainguinal revascularization: analysis of 240 grafts. *J Vasc Surg*. 2003;38:15–21.
- Largest single-center series of CSV allografts for infrainguinal revascularization.*
- Harlander-Locke MP, Harmon LK, et al. Vascular Low-Frequency Disease Consortium. The use of cryopreserved aortoiliac allograft for aortic reconstruction in the United States. *J Vasc Surg*. 2014;59:669–674.
- Largest multicenter study of aortic allografts for the treatment of aortic infection.*
- Katzman HE, Glickman MH, Schild AF, et al. Multicenter evaluation of the bovine mesenteric vein bioprosthesis for hemodialysis access in patients with an earlier failed prosthetic graft. *J Am Coll Surg*. 2005;201:223–230.
- Largest multicenter registry of the use of BMV grafts for dialysis access.*
- Madden RL, Lipkowitz GS, Browne BJ, Kurbanov A. Experience with cryopreserved cadaveric femoral vein allografts used for hemodialysis access. *Ann Vasc Surg*. 2004;18:453–458.
- One of the largest single-center series of CFV allografts for hemodialysis access.*
- McAllister TN, Maruszewski M, Garrido SA, et al. Effectiveness of haemodialysis access with an autologous tissue-engineered vascular graft: a multicentre cohort study. *Lancet*. 2009;373:1440–1446.
- First series of patients implanted with tissue-engineered biologic graft for hemodialysis access.*

A complete reference list can be found online at www.expertconsult.com.

REFERENCES

1. Loop FD, et al. Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. *N Engl J Med.* 1986;314:1–6.
2. Hayward PA, et al. Which arterial conduit? Radial artery versus free right internal thoracic artery: six-year clinical results of a randomized controlled trial. *Ann Thorac Surg.* 2007;84:493–497.
3. Hirose H, et al. Coronary artery bypass grafting using the gastroepiploic artery in 1,000 patients. *Ann Thorac Surg.* 2002;73:1371–1379.
4. Piercy KT, et al. Renovascular disease in children and adolescents. *J Vasc Surg.* 2005;41:973–982.
5. Patterson R, Smail D. Radial artery as conduit for distal renal artery reconstruction. *J Vasc Surg.* 2003;38:609–612.
6. Amin-Hanjani S, et al. Extracranial-intracranial bypass in the treatment of occlusive cerebrovascular disease and intracranial aneurysms in the United States between 1992 and 2001: a population-based study. *J Neurosurg.* 2005;103:794–804.
7. Pomposelli FB, et al. A decade of experience with dorsalis pedis artery bypass: analysis of outcome in more than 1000 cases. *J Vasc Surg.* 2003;37:307–315.
8. Hughes K, et al. Bypass for chronic ischemia of the upper extremity: results in 20 patients. *J Vasc Surg.* 2007;46:303–307.
9. Synn AY, et al. Is there a conduit of preference for a bypass between the carotid and subclavian arteries? *Am J Surg.* 1993;166:157–162.
10. Modrall JG, et al. Comparison of superficial femoral vein and saphenous vein as conduits for mesenteric arterial bypass. *J Vasc Surg.* 2003;37:362–366.
11. NKF-K/DOQI clinical practice guidelines for vascular access: update 2006. *Am J Kidney Dis.* 2006;48(Suppl 1):S176.
12. Prager M, et al. Collagen versus gelatin coated Dacron versus stretch polytetrafluoroethylene in abdominal aortic bifurcation graft surgery: results of a seven year prospective randomized multicenter trial. *Surgery.* 2001;130:408–414.
13. Faries PL, et al. A comparative study of alternative conduits for lower extremity revascularization: all autogenous conduit versus prosthetic grafts. *J Vasc Surg.* 2000;32:1080–1090.
14. Carrel A. Ultimate results of aortic transplants. *J Exp Med.* 1912;15:389–392.
15. Jeger E. Zur Technik der Blutgefäßnaht. *Beitr Klin Chir.* 1915;97:553.
16. Gross RE, et al. Preliminary observations of the use of human arterial grafts in the treatment of certain cardiovascular defects. *N Engl J Med.* 1948;239:578.
17. Linton RB. Some practical considerations in the surgery of blood vessel grafts. *Surgery.* 1955;38:817.
18. Boren CH, Roon AJ, Moore WS. Maintenance of viable arterial allografts by cryopreservation. *Surgery.* 1978;83:382–391.
19. L'Italien GJ, Maloney RD, Abbott WM. The preservation of the mechanical properties of venous allografts by freezing. *J Surg Res.* 1979;27:239–243.
20. Fagioli GL, Ricotta JJ. The role of cryopreserved vein allografts in infringuinal reconstructions. *Adv Vasc Surg.* 1995;3:173.
21. Rosenberg N, et al. Tanned collagen arterial prosthesis of bovine carotid origin in man. *Ann Surg.* 1966;164:247–256.
22. Dardik H, Dardik I. Successful arterial substitution with modified human umbilical vein. *Ann Surg.* 1976;183:252–258.
23. Barner HB, DeWeese JA, Schenk EA. Fresh and frozen homologous venous grafts for arterial repair. *Angiology.* 1966;17:389–401.
24. Perloff LJ, et al. The venous homograft: an immunological question. *Surgery.* 1972;72:961–970.
25. Ochsner JL, DeCamp PT, Leonard GL. Experience with fresh venous allografts as arterial substitute. *Ann Surg.* 1971;173:933–939.
26. Mirelli M, et al. Fresh and cryopreserved arterial homografts: immunological and clinical results. *Transplant Proc.* 2005;37:2688–2691.
27. Weber TR, et al. Cryopreservation of venous homografts. *Surg Forum.* 1975;26:291–293.
28. Bortolotti U, et al. Coronary artery bypass with glycerol-preserved saphenous vein allografts. *Bull Tex Heart Inst.* 1981;8:250–258.
29. Balderman SC, et al. Preparation of venous allografts: a comparison of techniques. *Ann Surg.* 1984;200:117–130.
30. Stephen M, Sheil AGR, Wong J. Allograft vein arterial bypass. *Arch Surg.* 1978;113:591–593.
31. Livan GG. Mechanism of cryoinjury in biological systems. *Cryobiology.* 1972;9:182–191.
32. Mazur P. Cryobiology: the freezing of biological systems. *Science.* 1970;168:939–949.
33. Fagioli GL, Gargiulo M, Pasquinelli G. Long-term cryopreservation of autologous veins in rabbits. *Cardiovasc Surg.* 1994;2:259–265.
34. Brockbank KGM. Effects of cryopreservation upon vein function in vivo. *Cryobiology.* 1994;31:71–81.
35. Pukacki F, et al. The mechanical properties of fresh and cryopreserved arterial homografts. *Eur J Vasc Endovasc Surg.* 2000;20:21–24.
36. Muller-Schweinitzer E, et al. Impact of freezing/thawing procedures on the post-thaw viability of cryopreserved human saphenous vein conduits. *Cryobiology.* 2007;54:99–105.
37. Malone JM, et al. Venous cryopreservation: endothelial fibrinolytic activity and histology. *J Surg Res.* 1980;29:209–222.
38. Bambang LS, et al. Effects of cryopreservation on the proliferation and anticoagulant activity of human saphenous vein endothelial cells. *J Thorac Cardiovasc Surg.* 1995;110:998–1004.
39. Brockbank KGM, et al. Functional analysis of cryopreserved veins: preliminary report. *J Vasc Surg.* 1990;11:94–100.
40. Ligush J, et al. First results on the functional characteristics of cryopreserved human saphenous vein. *Cell Mat.* 1991;1:359.
41. Elmore JR, et al. Cryopreservation affects endothelial and smooth muscle function of canine saphenous vein grafts. *J Vasc Surg.* 1991;13:584–592.
42. Alonso M, et al. Cryopreserved arterial homografts: preliminary results in infrainguinal arterial reconstructions. *Ann Vasc Surg.* 1999;13:261–267.
43. Schmitz-Rixen T, et al. Immunosuppressive treatment of aortic allografts. *J Vasc Surg.* 1988;7:82–92.
44. Schwartz SI, et al. Antigenicity of homografted veins. *Surgery.* 1967;61:471–477.
45. Tice DA, Zerbino V. Clinical experience with preserved human allografts for vascular reconstruction. *Surgery.* 1972;72:260–267.
46. Pober JS, et al. Interactions of T lymphocytes with human vascular endothelial cells: role of endothelial cell surface antigens. *Immunobiology.* 1984;168:483–494.
47. Balzer KM, et al. Donor-specific sensitization by cadaveric venous allografts used for arterial occlusive vascular disease. *Tissue Antigens.* 2004;64:13–17.
48. Bank HL, et al. Transplantation of cryopreserved canine venous allografts. *J Surg Res.* 1991;50:57–64.
49. Carpenter JP, Tomaszewski JE. Human saphenous vein allograft bypass grafts: immune response. *J Vasc Surg.* 1998;27:492–499.
50. Axthelm SC, et al. Antigenicity of venous allografts. *Ann Surg.* 1979;189:290–293.
51. Cochran RP, Kunzelman KS. Cryopreservation does not alter antigenic expression of aortic allografts. *J Surg Res.* 1989;46:597–599.
52. Della Schiava N, et al. Cryopreserved arterial allografts and ABO and Rhesus compatibility. *Ann Vasc Surg.* 2016;33:173–180.
53. Miller VM, et al. Cryopreserved venous allografts: effects of immunosuppression and antiplatelet therapy on patency and function. *J Vasc Surg.* 1993;18:216–226.
54. Carpenter JP, Tomaszewski JE. Immunosuppression for human saphenous allograft bypass surgery: a prospective randomized trial. *J Vasc Surg.* 1997;26:32–42.
55. Posner MP, et al. Early results of infrageniculate arterial reconstruction using cryopreserved homograft saphenous conduit (CADVEIN) and combination low-dose systemic immunosuppression. *J Am Coll Surg.* 1996;183:208–216.
56. Randon C, et al. Fifteen years of infrapopliteal arterial reconstruction with cryopreserved venous allografts for limb salvage. *J Vasc Surg.* 2010;51:869–877.

57. Benedetto B, et al. Use of cryopreserved cadaveric vein allograft for hemodialysis access precludes kidney transplantation because of allo-sensitization. *J Vasc Surg.* 2001;34:139–142.
58. Madden R, et al. Decellularized cadaver vein allografts used for hemodialysis access do not cause allo-sensitization or preclude kidney transplantation. *Am J Kidney Dis.* 2002;10:1240–1243.
59. Holdsworth RJ, et al. Glutaraldehyde-tanned bovine carotid artery graft for infrainguinal vascular reconstruction: 5 year follow-up. *Eur J Vasc Endovasc Surg.* 1997;14:208–211.
60. Rosenberg N. The modified bovine arterial graft. *Arch Surg.* 1972;105:547–548.
61. Katzman HE, et al. Multicenter evaluation of the bovine mesenteric vein bioprosthesis for hemodialysis access in patients with an earlier failed prosthetic graft. *J Am Coll Surg.* 2005;201:223–230.
62. Dardik H, et al. Clinical experience with modified human umbilical cord vein for arterial bypass. *Surgery.* 1976;79:618–624.
63. Schechter I. Prolonged survival of glutaraldehyde treated skin homografts. *Proc Natl Acad Sci USA.* 1971;68:1590–1593.
64. Love C, et al. Rapid intraoperative construction of autologous small caliber blood vessels. *ASAIO J.* 1998;44:M648–652.
65. Lantz GC, et al. Small intestinal submucosa as a small-diameter arterial graft in a dog. *J Invest Surg.* 1990;3:217–227.
66. Uematsu M, Okada M. A modified human ureter graft tanned by a new crosslinking agent polyepoxy compound for small diameter arterial substitutions: an experimental preliminary study. *Artif Organs.* 1998;22:909–913.
67. Ketharanathan V, Christie BA. Bovine ureter as a vascular prosthesis: a preliminary report of an experimental study in dogs. *Aust N Z J Surg.* 1982;52:590–593.
68. Field PL. The chemically treated bovine ureter—clinical performance of a novel biological vascular prosthesis. *Cardiovasc Surg.* 2003;11:30–34.
69. Chemla ES, Morsy M. Randomized clinical trial comparing decellularized bovine ureter with expanded polytetrafluoroethylene for vascular access. *Br J Surg.* 2009;96:34–39.
70. Taylor LM, Edwards JM, Porter JM. Present status of reversed vein bypass grafting: five-year results of a modern series. *J Vasc Surg.* 1990;11:193–206.
71. Shah DM, et al. Long term results of in situ saphenous vein bypass. Analysis of 2058 cases. *Ann Surg.* 1995;222:438–448.
72. Faries PL, et al. The use of arm vein in lower-extremity revascularization: result of 520 procedures performed in eight years. *J Vasc Surg.* 2000;31:50–59.
73. Chang BB, et al. The lesser saphenous vein: an underappreciated source of autogenous vein. *J Vasc Surg.* 1992;15:152–157.
74. Londrey GL, et al. Infrainguinal reconstruction with arm vein, lesser saphenous vein and remnants of greater saphenous vein: a report of 257 cases. *J Vasc Surg.* 1994;20:451–457.
75. Veith FJ, et al. Six-year prospective multicenter randomized comparison of autologous saphenous vein and expanded polytetrafluoroethylene grafts in infrainguinal arterial reconstruction. *J Vasc Surg.* 1986;3:104–114.
76. Hobson RW, et al. Results of revascularization and amputation in severe lower extremity ischemia: a five year clinical experience. *J Vasc Surg.* 1985;2:174–185.
77. Pappas PJ, et al. Patency of infrainguinal polytetrafluoroethylene grafts with distal interposition vein cuffs. *Cardiovasc Surg.* 1998;6:19–26.
78. Neville RF, Tempesta B, Sidway AN. Tibial bypass for limb salvage using polytetrafluoroethylene and a distal vein patch. *J Vasc Surg.* 2001;33:266–272.
79. Dardik H, et al. Improved method to create the common ostium variant of the distal arteriovenous fistula for enhancing crural prosthetic graft patency. *J Vasc Surg.* 1996;24:240–248.
80. Farber A, et al. Cryopreserved saphenous vein allografts in infrainguinal revascularization: analysis of 240 grafts. *J Vasc Surg.* 2003;38:15–21.
81. Dardik H, et al. A decade of experience with the glutaraldehyde-tanned human umbilical cord vein graft for revascularization of the lower limb. *J Vasc Surg.* 1988;7:336–346.
82. Kovalic AJ, Beattie DK, Davies AH. Outcome of ProCol, a bovine mesenteric vein graft, in infrainguinal reconstruction. *Eur J Vasc Endovasc Surg.* 2002;24:533–544.
83. Szczech LA, Lazar IL. Projecting the United States ESRD population: issues regarding treatment of patients with ESRD. *Kidney Int Suppl.* 2004;90. S3–7.
84. Xue JL, et al. Forecast of the number of patients with end-stage renal disease in the United States to the year 2010. *J Am Soc Nephrol.* 2001;12:2753–2758.
85. Patel ST, Hughes J, Mills JL. Failure of arteriovenous fistula maturation: an unintended consequence of exceeding Dialysis Outcome Quality Initiative guidelines for hemodialysis access. *J Vasc Surg.* 2003;38:439–445.
86. Dember LM, et al. Effect of clopidogrel on early failure of arteriovenous fistulas for hemodialysis: a randomized controlled trial. *JAMA.* 2008;299:2164–2171.
87. Woo K, et al. Evaluation of the efficacy of the transposed upper arm arteriovenous fistula: a single institutional review of 190 basilic and cephalic vein transposition procedures. *J Vasc Surg.* 2007;46:94–99.
88. Matsuura JH, et al. Cryopreserved femoral vein grafts for difficult hemodialysis access. *Ann Vasc Surg.* 2000;14:50–55.
89. Hutchin P, et al. Bovine graft arteriovenous fistulas for maintenance hemodialysis. *Surg Gynecol Obstet.* 1975;141:255–258.
90. O'Hara PJ, et al. Surgical management of abdominal aortic grafts: review of 25 year experience. *J Vasc Surg.* 1986;3:725–731.
91. Hayes PD, et al. In situ replacement of infected aortic grafts with rifampicin-bonded prostheses: the Leicester experience (1992–98). *J Vasc Surg.* 1999;30:92–98.
92. Clagett GP, Valentine RJ, Hagino RT. Autogenous aortoiliac/femoral reconstruction from superficial femoral-popliteal veins: feasibility and durability. *J Vasc Surg.* 1997;25:255–270.
93. Kieffer E, et al. Allograft replacement for infrarenal aortic graft infection: early and late results in 179 patients. *J Vasc Surg.* 2004;39:1009–1017.
94. Quinones-Baldrich WJ, Hernandez JJ, Moore WS. Long-term results following surgical management of aortic graft infection. *Arch Surg.* 1991;126:507–511.
95. Knosalla C, et al. Treatment of vascular infection by in situ replacement with cryopreserved aortic allografts: an experimental study. *J Vasc Surg.* 1998;27:689–698.
96. Zhou W, et al. In situ reconstruction with cryopreserved arterial allografts for management of mycotic aneurysms or aortic prosthetic graft infections: a multi-institutional experience. *Tex Heart Inst J.* 2006;33:14–18.
97. Matsuura JH, et al. Hemodialysis graft infections treated with cryopreserved femoral vein. *Cardiovasc Surg.* 2002;10:561–565.
98. Fujitani RM, et al. Cryopreserved saphenous vein allogeneic homografts: an alternative conduit in lower extremity arterial reconstruction in infected fields. *J Vasc Surg.* 1992;15:519–526.
99. Buzzi M, et al. Vascular tissue banking: state of the art. *Transplant Proc.* 2005;37:2428–2429.
100. Vogt PR, et al. Technical details with the use of cryopreserved arterial allografts for aortic infection: influence on early and midterm mortality. *J Vasc Surg.* 2002;35:80–86.
101. Dardik H. A 30-year odyssey with the umbilical vein graft. *J Am Coll Surg.* 2006;203:582–583.
102. Hartranft CA, et al. Cryopreserved saphenous vein graft in infrainguinal bypass. *J Vasc Surg.* 2014;60:1291–1296.
103. Chang CK, et al. Defining utility and predicting outcome of cadaveric lower extremity bypass grafts in patients with critical limb ischemia. *J Vasc Surg.* 2014;60:1554–1564.
104. Harris L, O'Brien-Irr M, Ricotta JJ. Long term assessment of cryopreserved bypass grafting success. *J Vasc Surg.* 2001;33:528–532.
105. Harris RW, et al. Allograft vein bypass: is it an acceptable alternative for infrapopliteal revascularization? *J Vasc Surg.* 1993;18:553–560.
106. Leseche G, et al. Femorodistal bypass using cryopreserved venous allografts for limb salvage. *Ann Vasc Surg.* 1997;11:230–236.
107. Martin RS, et al. Cryopreserved saphenous vein allografts for below-knee lower extremity revascularization. *Ann Surg.* 1994;219:664–672.
108. Shah RM, et al. Early results with cryopreserved saphenous vein allografts for infrainguinal bypass. *J Vasc Surg.* 1993;18:965–971.

109. Walker PJ, et al. Early experience with cryopreserved saphenous vein allografts as a conduit for complex limb-salvage procedures. *J Vasc Surg.* 1993;18:561–569.
110. Buckley CJ, et al. Suggested treatment protocol for improving patency of femoral-infrapopliteal cryopreserved saphenous vein allografts. *J Vasc Surg.* 2000;32:731–738.
111. Bannazadeh M, et al. Reoperative lower extremity revascularization with cadaver vein for limb salvage. *Ann Vasc Surg.* 2009;23:24–31.
112. O'Banion LA, et al. Cryopreserved saphenous vein as a last-ditch conduit for limb salvage. *J Vasc Surg.* 2017;66:844–849.
113. Dalsing MC, et al. Infrapopliteal bypass for established gangrene of the forefoot or toes. *J Vasc Surg.* 1985;2:669–677.
114. Harlander-Locke MP, et al. Cryopreserved venous allograft is an acceptable conduit in patients with current or prior angioaccess graft infection. *J Vasc Surg.* 2017;66:1157–1162.
115. Madden RL, et al. Experience with cryopreserved cadaveric femoral vein allografts used for hemodialysis access. *Ann Vasc Surg.* 2004;18:453–458.
116. Madden RL, et al. A comparison of cryopreserved vein allografts and prosthetic grafts for hemodialysis access. *Ann Vasc Surg.* 2005;19:686–691.
117. Bolton WD, et al. The use of cryopreserved femoral vein grafts for hemodialysis in patients at high risk for infection: a word of caution. *J Vasc Surg.* 2002;36:464–468.
118. Sgroi M, et al. Vascular reconstruction plays an important role in the treatment of pancreatic adenocarcinoma. *J Vasc Surg.* 2015;61:475–480.
119. Ito K, et al. Outflow reconstruction using cryopreserved homologous venous grafts in living donor liver transplantation. *Transplant Proc.* 2017;49:109–114.
120. Yamamoto M, et al. Safety and efficacy of cryopreserved homologous veins for venous reconstruction in pancreateoduodenectomy. *Surgery.* 2017;161:385–393.
121. Masmejan S, et al. Ten year experience using cryopreserved arterial allografts for distal bypass in critical limb ischemia. *Eur J Vasc Endovasc Surg.* 2019;57:823–831.
122. Castier Y, et al. Early experience with cryopreserved arterial allografts in below-knee revascularization for limb salvage. *Am J Surg.* 1999;177:197–202.
123. Albertini JN, et al. Long-term results of arterial allograft below-knee bypass for limb salvage: a retrospective multicenter study. *J Vasc Surg.* 2000;31:426–435.
124. Brown KE, et al. Arterial reconstruction with cryopreserved human allografts in the setting of infection: a single-center experience with midterm follow-up. *J Vasc Surg.* 2009;49:660–666.
125. Chiesa R, et al. Fresh and cryopreserved arterial homografts in the treatment of prosthetic graft infections: experience of the Italian Collaborative Vascular Homograft Group. *Ann Vasc Surg.* 1998;12:457–462.
126. Locati P, et al. The use of arterial allografts in aortic graft infection: a three year experience on eighteen patients. *J Cardiovasc Surg.* 1998;39:735–741.
127. Harlander-Locke MP, et al. The use of cryopreserved aortoiliac allograft for aortic reconstruction in the United States. *J Vasc Surg.* 2014;59:669–674.
128. Noel AA, et al. Abdominal aortic reconstruction in infected fields: early results in the United States Cryopreserved Aortic Allograft Registry. *J Vasc Surg.* 2002;35:847–852.
129. Verhelst R, et al. Use of cryopreserved arterial homografts for management of infected prosthetic grafts: a multicenter study. *Ann Vasc Surg.* 2000;14:602–607.
130. Ben Ahmed S, et al. Cryopreserved arterial allografts for in situ reconstruction of abdominal aortic native or secondary graft infection. *J Vasc Surg.* 2018;67:468–477.
131. Nevelsteen A, et al. Experience with cryopreserved arterial allografts in the treatment of prosthetic graft infections. *Cardiovasc Surg.* 1998;6:378–383.
132. Bisdas T, et al. Eight-year experience with cryopreserved arterial homografts for the in situ reconstruction of abdominal aortic infections. *J Vasc Surg.* 2010;52:323–330.
133. McCready RA, et al. Long-term results with cryopreserved arterial allografts (CPAs) in the treatment of graft or primary arterial infections. *J Surg Res.* 2011;168:149–153.
134. Antonopoulos CN, et al. Cryopreserved allografts for arterial reconstruction after aorto-iliac infection: A systematic review and meta-analysis. *Eur J Vasc Endovasc Surg.* 2019;58:120–128.
135. Dardik H, et al. Comparative decades of experience with glutaraldehyde-tanned human umbilical cord vein graft for lower limb revascularization: an analysis of 1275 cases. *J Vasc Surg.* 2002;35:64–71.
136. Johnson WC, Lee KK. A comparative evaluation of polytetrafluoroethylene, umbilical vein, and saphenous vein bypass for femoral-popliteal above-knee revascularization: a prospective randomized Department of Veterans Affairs cooperative study. *J Vasc Surg.* 2000;32:268–277.
137. Chinitz JL, et al. Self-sealing prosthesis for arteriovenous fistula in man. *Trans Am Soc Artif Intern Organs.* 1972;18:452–457.
138. Harlander-Locke, et al. Bovine carotid artery (Artegraft) as a hemodialysis access conduit in patients who are poor candidates for native arteriovenous fistulae. *Vasc Endovascular Surg.* 2014;48:497–502.
139. Pineda DM, et al. Bovine carotid artery xenografts for hemodialysis access. *J Vasc Surg.* 2017;65:1729–1734.
140. Sabanayagam P, et al. A comparative study of 402 bovine heterografts and 225 reinforced expanded PTFE grafts as AVF in the ESRD patient. *Trans Am Soc Artif Intern Organs.* 1980;26:88–92.
141. Anderson C, et al. Renewed interest in bovine heterograft for vascular access: a comparison between polytetrafluoroethylene and bovine. In: Henry ML, ed. *Vascular Access for Hemodialysis IX.* Los Angeles, CA: Bonus Books; 2005:185–193.
142. Anderson CB, Sicard GA, Etheredge EE. Bovine carotid artery and expanded polytetrafluoroethylene grafts for hemodialysis vascular access. *J Surg Res.* 1980;29:184–188.
143. Butler HG, Baker LD, Johnson JM. Vascular access for chronic hemodialysis: polytetrafluoroethylene versus bovine heterograft. *Am J Surg.* 1977;134:791–793.
144. Kaplan MS, et al. Comparison of PTFE and bovine grafts for blood access in dialysis patients. *Trans Am Soc Artif Intern Organs.* 1976;22:388–393.
145. Tellis VA, et al. Expanded polytetrafluoroethylene graft fistula for chronic hemodialysis. *Ann Surg.* 1979;189:101–105.
146. Lilly L, et al. Comparison between bovine heterograft and expanded PTFE grafts for dialysis access. *Am Surg.* 1980;46:694–696.
147. Hurst AV, Batello-Cruz M, Skipper BJ. Bovine carotid artery heterografts versus polytetrafluoroethylene grafts: a prospective, randomized study. *Am J Surg.* 1983;146:844–847.
148. Scott EC, Glickman MH. Conduits for hemodialysis access. *Semin Vasc Surg.* 2007;20:158–163.
149. Arhuidese I, et al. Bovine carotid artery biologic graft outperforms expanded polytetrafluoroethylene for hemodialysis access. *J Vasc Surg.* 2017;65:775–782.
150. Hertzler NR, Beven EG. Venous access using the bovine heterograft: techniques, results, and complications in 75 patients. *Arch Surg.* 1978;113:696–700.
151. Broyn T, et al. Early complications with a new bovine arterial graft (Solcograft P). *Acta Chir Scand.* 1986;152:263–266.
152. Lindsey P, et al. Lower extremity bypass using bovine carotid artery graft (Artegraft): An analysis of 124 cases with long-term results. *World J Surg.* 2018;42:295–301.
153. Bourquelot P. ProCol bioprosthetic vascular grafts for dialysis access. In: Henry ML, ed. *Vascular Access for Hemodialysis VI.* Chicago, IL: Precept Press; 1999:223–229.
154. Widmer MK, et al. Intermediate outcome and risk factor assessment of bovine vascular heterografts used as AV-fistulas for hemodialysis access. *Eur J Vasc Endovasc Surg.* 2004;27:660–665.
155. Schmidli J, et al. Bovine mesenteric graft (ProCol) in critical limb ischaemia with tissue loss and infection. *Eur J Vasc Endovasc Surg.* 2004;27:251–253.

Bioengineered Vascular Grafts

LAURA E. NIKLASON and JEFFREY H. LAWSON

BASIC PRINCIPLES 874

- Initial History 875
- Intact Isolated Blood Vessels 875
 - Artegraft 875
 - Procol 875
 - Cryovein 875
- Luminal Modification (Biohybrids) 876
- Tissue-Engineered Vascular Grafts 876
 - Grafts Created In Vivo ("Bioreactors") 876
 - Scaffold-Based 877
 - BIODEGRADABLE SCAFFOLDS 877
 - XENOGENEIC TISSUE SCAFFOLDS 878
 - HUMAN TISSUE SCAFFOLDS 878
 - Tissue Engineered Sheets 879

CLINICAL EXPERIENCE 881

- Intact Isolated Blood Vessels 881
- Biohybrids 881
- Tissue-Engineered Vascular Grafts 881
 - CytoGraft – Tissue-Engineered Vascular Grafts for Hemodialysis Vascular Access – 2004* 881
 - Olausson – Decellularized Human Donor Vessel Scaffold – 2012* 881
 - Humacyte, Inc. – Tissue-Engineered Vascular Grafts for Hemodialysis Vascular Access and Peripheral Arterial Bypass – 2013* 882
- LIMITATIONS AND RISKS 883
- FUTURE ADVANCES 883
- CONCLUSION 884
- DISCLOSURE 885

BASIC PRINCIPLES

Surgical repair or replacement of diseased blood vessels, including aortic reconstruction for aneurysmal disease, bypass of occlusive atherosclerotic lesions, vascular trauma, oncologic vascular reconstruction, and creation of durable arteriovenous access for hemodialysis, remains a mainstay of modern vascular surgery. All of these procedures require implantation of a vascular conduit to replace diseased vessels or to augment normal anatomy. When available, autogenous blood vessels are generally the conduit of choice.¹ This is limited as individuals have a finite number of available vessels that can be utilized for reconstruction, and options may be further limited due to concomitant disease of the desired vessels. Wound complications and infection from vessel harvest sites remain a vexing problem. Devitalization of the vessel during surgical excision prematurely injures the conduit and may contribute to poor performance or failure. Even in the best of conditions, autogenous venous tissue eventually remodels in high resistance arterial or high flow arteriovenous circuits in a manner that more closely resembles a hyperplastic injury response than the more desirable development of a vessel-like structure with functional adventitial, medial, and intimal layers. Synthetic alternatives provide additional options when autologous conduit is not

available, but these grafts pose a clear disadvantage to host tissue in terms of patency, compliance, infection, and durability.

The development of an ideal arterial substitute has been referred to as the "Holy Grail" of vascular surgery.² Since the initial concept of tissue engineering in the 1980s, the field of regenerative medicine has been steadily growing in search of novel, engineered tissue replacements to create these substitute vessels. Such research has focused on creating conduits with exquisitely exact design criteria, including adequate tensile and recoil strength to withstand long-term cardiac cycles, as well as an antithrombotic and anti-inflammatory blood-contacting surface to prevent conduit failure. Conduits would require low risk for immunogenicity, foreign body response, and development of infection that could impact the long-term patency. The vessel would need to be immediately functional and combine durability, both for maintaining suture strength and resistance to subsequent mechanical stresses, with a capacity to remodel into a functional tissue and to respond to physiologic stimuli. Lastly, it would need to be cost-effective and ready to use "off the shelf".^{3,4}

Although the search remains ongoing for an ideal conduit that encompasses all of these design elements, dramatic advancements have been made in the past several decades, due to developments in the field of tissue engineering. Indeed, in

2020 alone, there were over 600 cell-based or engineered tissue-based clinical trials currently registered as “ongoing” on [ClinicalTrials.gov](#). In this chapter, we review a brief history on the field of bioengineered grafts, highlight important advances in the field, provide an update on current clinical activity, and look to the future of bioengineered vascular conduit.

Initial History

The origin of vascular surgery is frequently traced back to the development of the triangulated vascular anastomosis in the early 20th century by Alexis Carrel,⁵ a French surgeon who received the Nobel Prize in Physiology or Medicine in 1912 for this advancement. Carrel would later partner with aviator and engineer, Charles Lindberg, to develop perfusion pumps and incubators that would allow maintaining of organs for prolonged periods of time, paving the way for organ culture that would anticipate many modern approaches in tissue engineering.⁶ Although venous interposition grafts had been used for trauma and aneurysmal disease, it was not until 1948 that saphenous vein was used successfully as a bypass graft for atherosclerotic vascular disease.⁷ In the 1950s Michael DeBakey, Denton Cooley, and colleagues reported the use of Dacron grafts for aortic reconstruction.⁸ Shortly thereafter, in the 1960s, the field of nephrology was revolutionized when Michael Brescia and James Cimino developed the radiocephalic arteriovenous fistula as an alternative to the Scribner shunt.^{9,10} By the 1970s, the earlier pioneering investigations into the use of synthetic vascular conduits progressed to using polytetrafluoroethylene (PTFE) and expanded PTFE (ePTFE) as replacements for small arteries and as hemodialysis access.^{11,12}

Somewhat surprisingly, the first investigations into the use of bioengineered blood vessels were conducted in the 1940s when Robert Gross and colleagues experimented with aortic transplantation in dogs.¹³ This work demonstrated that, although preservation of graft vessels by freezing alone carried unacceptable rates of thrombosis and hemorrhage, biological modification of donor aortas by storage in a nutrient solution at temperatures slightly above freezing resulted in long-term patency even after several weeks of extracorporeal storage. Those experiments led to the successful translation of these techniques to human tissue. Cadaveric human arteries were successfully treated and used both for aortic reconstruction in pediatric patients with aortic coarctation and as shunt material in patients with tetralogy of Fallot. This type of tissue preservation strategy, although successful, was quite volatile and required significant improvement in order to produce a therapy that was reliable and readily available.

Intact Isolated Blood Vessels

Gross’ work spurred the earliest examples of bioengineered blood vessels: intact blood vessels isolated from either animals (xenogeneic grafts) or later from humans (allogeneic grafts).¹⁴ While intact isolated blood vessels come from donor cells, they can be considered bioengineered grafts because they undergo an extensive process to biologically modify the tissue so that it

can be implanted without producing an immune-mediated response. A common way to prepare xenogeneic grafts for use is by treating the tissue with a chemical decellularization process and then fixation of the remaining collagen, connective tissue proteins, and cells with glutaraldehyde to reduce antigenicity. This technique fixes or “tans” the tissue, cross-linking proteins to prevent an immunogenic reaction. Unfortunately, variations in xenogeneic graft fixation¹⁵ and inability of the chemically cross-linked vascular matrix to become repopulated with host cells^{16,17} introduce the potential for aneurismal degradation over time.

The use of isolated intact blood vessels, first reported in the 1960s, persists in several grafts commercially available today.

Artegraft

Rosenberg and colleagues successfully translated enzyme treatment of bovine arteries follow by chemically fixing the vessels to pre-clinical and clinical models. In this early work, bovine arteries were stripped of most of their parenchymal proteins and subjected to “decellularization” by controlled enzyme action, leaving a tubular prosthesis composed mostly of collagen.¹⁸ The first clinical application of this technology was reported in 1966, when a conduit made from collagen matrix of a bovine carotid artery treated with enzymatic removal of the musculoelastic portion of the vessel was used for lower extremity bypass.¹⁴ These processes were refined and the Bovine Carotid Artery Graft technology was ultimately developed by Artegraft (North Brunswick, NJ). In 1970, these xenogeneic grafts were FDA approved for use as conduit for dialysis access, and the graft is also currently approved for peripheral arterial bypass and as an arterial patch.

Procol

Decades after the introduction of bovine carotid artery xeno-grafts, Hancock Jaffe Laboratories Inc (Irvine, CA) developed a method to treat bovine mesenteric veins with a decellularization process, followed by fixation with glutaraldehyde cross-linking and gamma radiation.¹⁶ The muscle content of the bovine mesenteric vein, as well as its relatively high content of elastin, provided a theoretical advantage of improved vessel compliance and thus decreased rate of venous stenosis. This xenograft technology, Procol (now LeMaitre Vascular, Inc., Burlington, MA) was FDA approved in 2003 for vascular access in patients who have failed at least one prosthetic access graft.

Cryovein

In the 1970s, Ochsner and colleagues built on efforts to develop vascular homografts from cadavers or living donors and demonstrated the superiority of venous homografts to arterial homografts; however, due to the dependence of arteries on the vasa vasorum, the techniques used for fixation and decellularization of xenogeneic grafts did not translate to allogeneic grafts.¹⁹ Ultimately a combination of cryopreservation and fixation with either glutaraldehyde or dialdehyde improved upon early results in terms of vein integrity and tissue handling, although long-term patency remained a significant concern with allogeneic grafts through the remainder of the 20th century.^{20,21}

Subsequent improvements in cryopreservation and tissue fixation led to the development of the CryoVein graft by CryoLife (Kennesaw, GA), which is currently approved for both hemodialysis access and as a peripheral bypass conduit.

Luminal Modification (Biohybrids)

The endothelium is a dynamic environment, not simply an inert blood-contacting surface. The endothelium, and particularly vascular endothelial cells (ECs), play a central role in regulating cardiovascular physiology. ECs regulate vascular tone and thus modulate hemodynamics. In addition to providing an antithrombotic surface for blood flow under normal conditions, ECs control platelet activation and adhesion as well as the adhesion and migration of both leukocytes and vascular smooth muscle cells in response to pathological stimuli.²² The benefits of an intact and functional endothelium are clear, leading several investigators to develop “biohybrid” grafts by modifying the luminal surfaces of conduits in order to recreate the physiologic function of the native endothelium.

The concept of transplanting autogenous ECs into grafts emerged in the late 1970s. This can be done as either a single stage or two stage method. In one stage methods, ECs are both harvested and seeded at the time of surgery. Two stage methods require seeding of the recipient graft with ECs via serial passaging in a bioreactor and incubation for several weeks prior to implant.²³ In the 1990s, Zilla, Deutsch and colleagues in Europe and South Africa developed means of seeding autologous endothelium into the lumen of ePTFE conduits,^{24–26} where ECs derived from small vein biopsies were expanded and cultured on ePTFE grafts over approximately 4 weeks. These endothelialized grafts were then implanted as infrainguinal femoropopliteal grafts in more than 300 patients with severe peripheral arterial disease. Primary and secondary patency rates were successfully comparable to those of native saphenous vein.²⁶ However, the need for harvesting suitable numbers of autologous ECs from vein segments, and challenges with long-term EC adherence to artificial surfaces, has prevented widespread adoption of this technology.

Later investigators were able to improve cell retention as well as cell growth structure and adaption, by exposing the EC-treated conduit *in vitro* to hydrostatic pressure, laminar shear stresses, and circumferential and longitudinal stretching.^{27,28} Indeed, some suggest that shear stresses from prolonged laminar flow (as opposed to turbulent flow) play a crucial role in the signal transduction, gene expression, cell proliferation, and cell survival of both ECs and vascular smooth muscle cells (VSMC). This is hypothesized to reduce the incidence of both thrombotic complications and the development of atherosclerotic lesions *in vivo*.^{29–31}

Tissue-Engineered Vascular Grafts

Tissue-engineered vascular grafts (TEVGs) are cellular or tissue-based vascular conduits designed to have any synthetic components degrade over time with progressive replacement by autogenous tissues resulting in a functional blood vessel

with an intact endothelium and a capacity to respond appropriately to physiologic stimuli. This technology has been made possible only recently by groundbreaking advances in the field of tissue engineering, although it truly represents the extension of half a century of continuous exploration and improvement.

TEVGs may be classified by the method used to construct the conduit. At present there are three main categories of TEVGs: grafts created *in vivo* by “bioreactors,” scaffold-based TEVGs, and sheet-based TEVGs.

Grafts Created In Vivo (“Bioreactors”)

One of the earliest methods utilized to generate TEVGs leverages the ability of a host to generate a foreign body reaction when a cylindrical mandril or inert tubing is inserted into the body, forming connective tissue around the foreign body which can be isolated and used as vascular conduit. This process is usually described as using the host’s body as a “bioreactor.” The first descriptions of the bioreactor technique come from the late 1960s, when Charles Sparks and colleagues implanted a tubular silicone rubber mandril, comprised of an inner cylindrical steel and outer Dacron graft, into the leg of intended patients. After 5 to 12 weeks the tube was explanted, and both the mandril and Dacron layers were removed and the tube of fibrocollagenous materials that formed in the interval was implanted for use as a vascular conduit.^{32,33} Clinical trials with these “Sparks mandril” grafts continued into the 1970s; however, it was not widely adopted due to poor patency, tendency of the scar tissue-based tissue to thrombose, aneurysmal degeneration, and the prolonged incubation period.^{33–35} Use of these mandril grafts was abandoned in the 1980s.

Several decades later, a modification of Sparks’ techniques was reported by Julie Campbell and colleagues^{36,37}; placing silastic tubing into the peritoneal cavities of rats, rabbits, and dogs. The resulting host response produced a structure with an inner layer of collagen, a middle layer of myofibroblasts, and an outer layer of mesothelium. After removal of the synthetic material the tube could be turned inside out thus producing a conduit lined entirely with mesothelium. Histologic examination demonstrated that the myofibroblasts in the graft were derived of a bone marrow origin.³⁸ While the conduits were relatively successful in animal models, this technique was not successfully translated to humans largely owing to the need for a prolonged incubation period of several weeks and the requirement for an additional surgical procedure.

To eliminate the need for an incubation period within the intended recipient, Ketharanathan and colleagues experimented with the use of sheep as a bioreactor for grafts to be inserted in humans. Silicone tubes were implanted beneath the subcutaneous layer of adult sheep. Upon explantation 12 weeks later, the tubes were covered with ovine collagen.^{39,40} The collagen tubes were then fixed in a glutaraldehyde solution, rinsed in a buffered saline, and then stored in 50% alcohol at room temperature. Early results in dogs were extremely positive with the ability to comply with arterial pressures and resist degradation for up to 3 years.⁴¹ This initial design was later augmented by the incorporation of a polyester mesh over the tube to improve burst strength and reduce the risk of aneurysmal degeneration.

Eventually Bio Nova (North Melbourne, Australia) used this technology to produce Omniflow, a glutaraldehyde-tanned ovine collagen tube grown around a Dacron mesh template in a sheep bioreactor.⁴² These grafts were first approved for use as a hemodialysis access in Australia, Germany, and Canada. An improved version of the original Omniflow device, the Omniflow II (now LeMaitre Vascular, Inc., Burlington, MA), was released in 1990.⁴³ Subsequent studies have demonstrated primary and secondary patency rates approaching that of an arteriovenous fistula, with reported secondary patency at two years of 75% as well as a lower infection rate than ePTFE.⁴⁴

More recently, work has been rekindled on creating TEVGs by foreign body response. Rothuizen and colleagues has successfully modulated the histological composition and architecture of the fibrocellular capsule produced by the foreign body reaction by utilizing templates with different physiochemical properties.^{45,46} Following early work using polymer rods in rats the investigators have more recently used a large animal porcine carotid interposition model. Their early results demonstrate acceptable patency, acceptable mechanical and physiologic characteristics, as well as positive vascular remodeling of the graft post implant.⁴⁷ Geelhoed and colleagues in the Netherlands are using revised approaches wherein mandrels are pre-treated with TGF β , collagen, or plasma etching, in efforts to improve the foreign body response to the implants and one day grow conduits for patients needing vascular access for hemodialysis.⁴⁸

Scaffold-Based

Concerted efforts at *in vitro* arterial engineering arguably began in the 1980s at MIT, where Eugene Bell and colleagues reported the first culture of an engineered vessel made from vascular cells.⁴⁹ Weinberg and Bell, credited with the first TEVG prototype, developed a process using bovine aortic tissue to create the TEVGs that took approximately 4–6 weeks. First a rigid scaffold was created *in vitro* by casting a culture medium of collagen and smooth muscle cells and molding around an annular mold. This mixture was dehydrated over the course of a few days to form a rigid lattice before a Dacron mesh sleeve was slipped over the lattice to improve the TEVG integrity. Adventitial fibroblasts were then cast around the collagen/Dacron structure and allowed to cure for 2 weeks. The tube was then slipped off the mandrel and seeded with ECs over the course of 1 week.⁴⁹ The result was a TEVG with 3 distinct layers of vascular cells with physical and biosynthetic function. Rupture strengths of these conduits were only 90 mm Hg at maximum, and the conduits required support by external Dacron sleeves to enable handling and to increase burst strength. In addition, the surrounding synthetic conduit was still subject to many familiar problems including infection and stenosis. Others attempted to improve upon this initial design by surrounding the inner cell lining with stronger biologic materials; however, none of these solutions were able to combine adequate strength to resist high pressure and degradation with sufficient compliance comparable to native vessels.^{50,51} Nonetheless, this team gets credit for being the first to show the feasibility of culturing a macroscopic vascular analogue *in vitro*. This work in vascular engineering, along with Bell's work on engineered skin, served

as the basis for the creation of the biotechnology company Organogenesis, based in Massachusetts, which currently markets a number of regenerative medicine products, although none are blood vessel replacements.⁵²

Biodegradable scaffolds

In the wake of Bell's pioneering work proving the principle of arterial tissue regeneration *in vitro*, numerous investigators took up the problem using a variety of approaches. Early work on the development and utilization of bioabsorbable polymers as a scaffold for cell transplantation and tissue engineering can be attributed to Joseph Vacanti and Robert Langer. Their investigation into cell transplantation and experimentation with various polymers as tissue scaffolds had far-reaching effects on hepatic, cartilage, and bone tissue bioengineering.^{53–58} By the mid-1990s, considerable progress had been made towards the development of tubular structures composed of biodegradable polymer scaffolds.^{59,60} The initial foray into the cardiovascular system came when Christopher Breur and Toshiharu Shinoka developed autologous lamb heart leaflets on a polyglycolic acid (PGA) scaffold.^{61,62} PGA is the same polymer that has been used commercially for biodegradable surgical sutures for decades (i.e., Vicryl, Ethicon, Somerville, NJ).

As techniques to develop tubular structures improved, this technology was translated to clinical applications. In 2001, Shinoka and colleagues reported the first successful application of a TEVG produced *in vitro* with autologous bone marrow-derived mononuclear cells on a biodegradable scaffold composed of L-lactide and E-caprolactone reinforced with a PGA-woven fabric.⁶³ A pediatric patient with a single ventricle and pulmonary atresia underwent a pulmonary artery reconstruction after the patient's ECs were used to seed the conduit prior to surgical implant. After this initial success, this method was applied to two other successful cases, followed by clinical success in 22 more patients.⁶⁴ This approach provides the potential benefit of producing a tissue graft that may continue to grow with a young child thereby minimizing the need for reinterventions. Ultimately, this TEVG was acceptable for the low-pressure system; however, it was not structurally robust enough to be used under systemic arterial pressure. One point of concern was that PGA, a foreign material, may generate an inflammatory reaction that could weaken the integrity of the graft.⁶⁵

Niklason and Langer implemented further improvements focused on the integrity of the bioengineered vessels in order to withstand systemic arterial pressures.⁶⁶ A comparison of autologous bovine vessels grown under pulsatile conditions mimicking systemic pressure demonstrated improved vessel integrity and strength relative to vessels grown without exposure to pulsatile flow.^{67,68} When examined histologically, vessels exposed to radial strain and pulsatility demonstrated improved SMC matrix deposition, alignment, and orientation, as well as increased extracellular byproducts. VSMCs in these vessels also exhibited contractile reactivity to chemical stimuli. Burst strengths greater than 2000 mm Hg and suture retention strengths as high as 90 g were recorded, representing the strongest bioengineered vessels produced up to that point.

Following the validation of the structural integrity and mechanical durability of this conduit came the challenge of developing an appropriate decellularization process to eliminate antigenic materials.⁶⁹ Although several decellularization processes have previously been outlined for decellularizing native connective tissues, none had been successfully applied to bioengineered tissues. Ultimately, a protocol described in 1995 was found to adequately treat the conduit without unacceptably compromising the compliance and mechanical properties of the graft.⁷⁰ Importantly, these experiments led these investigators to hypothesize that bioengineered vessels may not require re-seeding of the vessels with host cells prior to implant, owing to the migration of host cells, such as VSMCs, into the conduit extracellular matrix.

These findings were successfully translated into several large animal models including canine, porcine, and Old-World primates. In 2011, Dahl et al. (now as Humacyte, Inc., Durham, NC) reported success in a translational model of TEVGs created from allogeneic dog cells to be used in the canine models and from allogeneic human aortic cells in the Old World primate baboon models, combining decellularized technology and biodegradable scaffolds.⁷¹ This species of primate was chosen to provide a genetic phylum that was the most similar to humans, which could allow non-cross-linked human matrix-containing bioengineered vessels to be implanted without immunosuppression. Canine vessels were re-endothelialized with autologous cells prior to implant, but the human vessels were not.

For primate experiments, allogeneic smooth muscle cells from human donors were grown on biodegradable PGA mesh scaffolds, positioned over a silastic mandril. The PGA mesh degraded slowly as the vessels grew *in vitro* over the course of 8–12 weeks. A final decellularization process using a series of detergents and hypertonic solution rinses rendered the vessels acellular and free from antigenic material, subsequently termed the human acellular vessel (HAV).⁷¹ As Table 68.1 shows, this model is robust enough for arterial pressure, with burst strength *in vitro* of between 2651 and 3337 mm Hg while retaining compliance between saphenous vein and internal mammary artery. The Humacyte HAV has been implanted in primates in a model for dialysis access with 88% patency when measured at various time points between 1 month and 6 months. Figure 68.1 shows the graft *in situ* in a non-human primate with angiography demonstrating graft patency. Figure 68.2 shows histology of the graft, with the decellularized allogeneic tube composed of collagen, fibronectin, and vitronectin and containing only minimal residual PGA.

Similar decellularization approaches have been taken to producing engineered, acellular heart valves.⁷² Baaijens, Hoerstrup and colleagues cultured human fibroblasts on a PGA scaffold fashioned as a tri-leaflet valve within a tubular conduit for 4 weeks, then decellularized the human valve using Triton and sodium deoxycholate detergents, combined with Benzonase nuclease and buffer washes. Valves implanted as pulmonary heart valves into chacma baboons and harvested after up to 8 weeks did demonstrate evidence of retraction at time of explant; however, overall valves demonstrated good function

TABLE 68.1

Suture Strength, Burst Pressure and Compliance for Tissue Engineered Vascular Grafts

	Suture strength (g)	Burst pressure (mm Hg)	% compliance per 100 mm Hg
Human Saphenous Vein ¹⁰⁰	196 ± 29	1599	0.7–1.5
Human Internal Mammary Artery ¹⁰⁰	138 ± 50	3196	11.5 ± 3.9
ePTFE ¹¹¹		28,391	1.6 ± 0.2
Omniflow II ⁴²	>400	*1688	3.1 ± 1.3
Humacyte HAV ⁷¹	178 ± 11	3337	3.3 ± 0.8
Lifeline ¹⁰⁰	152 ± 50	3523	3.4–8.8 (at 6 months)

*Omniflow II withstood 1688 mm Hg, which is equivalent of human saphenous vein, but additional pressures were not reported.

Human internal mammary artery and saphenous vein parameters provided for comparison. Values when available are mean (M) ± standard deviation (SD).

with minimal or modest valvular regurgitation. Notably, the cellular repopulation of the engineered valves was more rapid and complete than decellularized native human heart valves, which may imply that cellular migration and remodeling of engineered matrix is easier than for decellularized native adult tissues.

Xenogeneic tissue scaffolds

An alternative approach to biodegradable scaffolds is the use of xenogeneic tissue as the scaffold for a bioengineered vessel. The benefits of this method are that animal tissue is readily available and their vessels have a supportive extracellular matrix pre-manufactured and, with adequate decellularizing, their connective tissue matrix could be used as a scaffold for human EC seeding. In 2000, Augustinus Bader and colleagues reported the first such “humanization” of a xenogenic vessel. Porcine aortas were enzymatically decellularized before being seeded sequentially with human ECs and myofibroblasts were isolated from human great saphenous vein. The result was a porcine extracellular matrix fully endothelialized with human ECs and a myofibroblast media.⁷³ This work was expanded upon by Jörg Heine and colleagues, ultimately demonstrating that these “humanized” xenogeneic vessels regained vasomotor contractility and function.⁷⁴

Human tissue scaffolds

Analogous to the method generating “humanized” xenogeneic grafts are the work done by Michael Olausson and his group in Sweden. This group performed the first and only procedure in using a bioengineered vessel that they created from a decellularized human donor iliac vein.⁷⁵ This was done for a pediatric patient with thrombocytopenic purpura with extrahepatic portal vein thrombosis. With no autogenous options for conduit available and with a family extremely resistant to

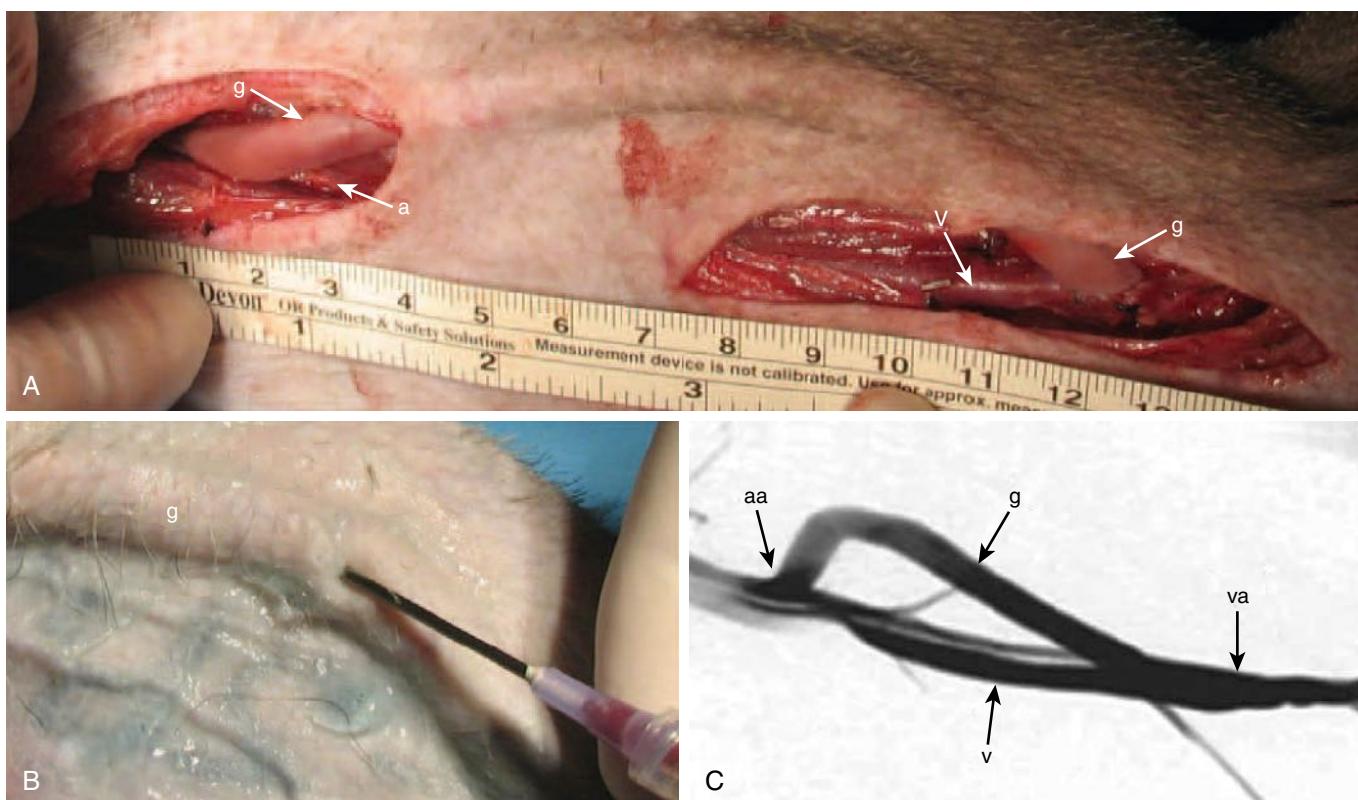


Figure 68.1 Images of decellularized allogeneic graft in pre-clinical trial (Humacyte, Durham, NC). (A) Human cell-derived 6-mm grafts (*g*) were implanted between the axillary artery (*a*) and the brachial vein (*V*) in a baboon model. (B) Arteriovenous grafts (*g*) were first accessed with 16-gauge needles at 4 weeks after implant. (C) A representative angiogram of the graft demonstrates that the graft was patent (*g*). The arterial anastomosis (*aa*), venous anastomosis (*va*), and brachial vein (*v*) are shown. (Reproduced with permission from Dahl et al.⁷¹)

the immunosuppressive medications required for transplantation, it was decided that a bioengineered vessel would be most suitable. The donor vessel decellularization process was similar to that described and ECs and VSMCs differentiated and isolated from the recipient BMCs were seeded to the luminal surface of the decellularized human vessel scaffold over the course of 1 week.

Tissue Engineered Sheets

The last sub-category of TEVGs is sheet-based grafts which are cells grown in culture to create a sheet of cells which can then be formed into a tubular structure by wrapping the sheet repeatedly around a mandril. Initial work with this methodology by Nicholas L'Heureux and colleagues was limited by the same difficulties with structural integrity that had previously limited Weinberg and Bell.⁷⁶ However, by 1998 this group had created a completely biological tissue-engineered human blood vessel with sufficient burst strength and suture retention to be used in humans.⁷⁷ This relied upon a novel sheet-based manufacturing process. In brief, human umbilical vein ECs and VSMCs were isolated. VSMCs and fibroblasts were cultured in flasks to form sheets of cells and corresponding extracellular matrix. A fibroblast sheet was wrapped around a mandril and dehydrated. A subsequent sheet-layer of SMCs, followed by fibroblasts, were wrapped around the initial dehydrated scaffold, and finally, the luminal surface of the conduit was seeded with ECs. The total

duration of this manufacturing process is approximately 4 to 6 months. Overall, if cell expansion time is factored in, this process requires approximately 4–6 months to complete.

In pre-clinical studies, L'Heureux and colleagues were able to demonstrate positive results with placement of human-derived xenografts in rodent, canine, and non-human primate models.⁷⁸ The group (Cytograft, Novato, CA) demonstrated that these bioengineered vessels had structural integrity for human use and entered clinical trials and developed the Lifeline.^{79,80} Indeed, the tubular structure was capable of burst pressures greater than 3500 mm Hg, greater than that needed to support arterial pressure, with vessel compliance between that of saphenous vein and internal mammary artery (Table 68.1).

Cytograft has subsequently experimented with use of frozen, devitalized autologous vessels which allow autologous tissue biopsies to be taken far in advance of when the need for a vessel is anticipated. The vessel can then be manufactured, a process that takes 6 to 7 months, and stored safely at -80°C until it is needed. The vessel requires just 2 weeks of lead-time to thaw and seed the lumen with ECs prior to implant. In the first case report of this device, the vessel maintained patency and high flow rates up to the time of publication (8 weeks).⁸¹ An alternative attempt to improve production efficiency has been the utilization of decellularized allogeneic tissue from healthy donors. Production of these vessels occurs as described previously up to the point of EC seeding, which is deferred. The vessel is

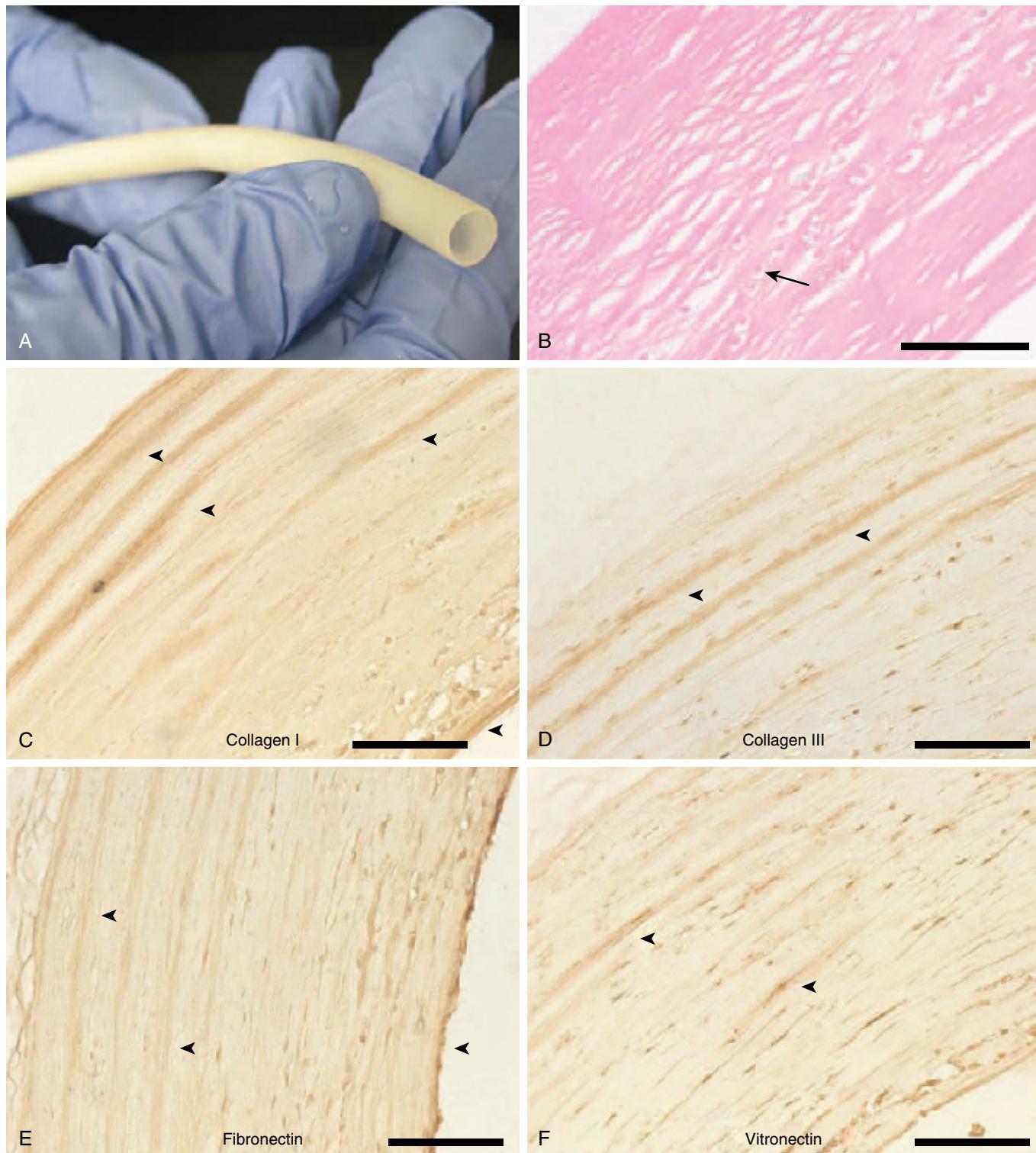


Figure 68.2 Histologic analysis of decellularized allogeneic graft before implant (Humacyte, Durham, NC). (A) A 6-mm-diameter graft before implant. (B) Representative histology with no cells in H&E-stained sections (arrow points to residual PGA), and the porous structure typical of decellularized TEVGs. (C–F) Decellularized TEVGs stain strongly and diffusely for collagen type I (C), and also stain for organized (D) collagen type III, (E) fibronectin, and (F) vitronectin. Areas staining positive for extracellular matrix proteins are noted with arrowheads. Note that DAB staining masks the porous structure in C–F. Scale bars, 100 μ m. (Reproduced with permission from Dahl et al.⁷¹)

dehydrated and frozen to -80°C until needed. Results from a case series of three patients demonstrated acceptable results without any rise in either immunologic or inflammatory blood markers following implantation.⁷⁹

CLINICAL EXPERIENCE

Intact Isolated Blood Vessels

The first significant clinical experience with intact isolated blood vessels came in 1970 after FDA approval of Artegraft. As a hemodialysis vascular access, patency rates have been similar to ePTFE.^{82,83} However there have been reports of the medial layer of the bovine artery developing calcifications which have in some cases resulted in structural degradation and aneurysmal degeneration.⁸⁴ Although early experience with the bovine mesenteric vein xenograft Procol reported improved patency over ePTFE for dialysis access, with primary patency at 2 years of 70%, these findings did not translate to improved outcomes in infrainguinal reconstruction.⁸⁵⁻⁸⁷ Indeed, despite the positive performance of this product in terms of patency and decreased infection, Procol has not gained widespread clinical adoption.

CryoVein is currently approved for use as a conduit for both hemodialysis access and for peripheral bypass. Primary and secondary patency for CryoVein when used as primary conduit for dialysis access was reported to have been comparable when compared to ePTFE.⁸⁸ Due to the presumed resistance of CryoVein to infection relative to synthetic materials, some report using this as a salvage option for localized prosthetic graft infection.^{89,90} Importantly other investigators report no decrease in infectious complications, at least not when these are used as thigh grafts.⁹¹ Additionally, despite treatment to remove blood type proteins and reduce immunogenicity, these grafts carry concerns about blood type compatibility and elevating panel reactive antibodies (PRA), which may be of concern in patients on the kidney transplant waiting list. Indeed, the survival of cardiac and kidney allografts is often limited not by rejection of the organ parenchyma, but by adaptive immunity directed against the donor blood vessels.⁹²

Biohybrids

The first clinical application of the luminal modification process was reported in 1978. Malcolm Herring and colleagues utilized ECs harvested from superficial veins to seed the luminal surface of a Dacron graft at the time of a peripheral bypass.⁹³ Unfortunately, subsequent trials using this technique failed to reproduce the promising outcomes seen in early reports.^{94,95} In later decades, investigators were able to improve upon this early methodology by extracting ECs from fat, omentum, and other tissues rich in ECs in order to improve cell density and performance in pre-clinical models.^{22,23,96}

An alternative to seeding vascular grafts with differentiated ECs is to use endothelial progenitor cells (EPCs).²² In the 1990s, Noishiki and colleagues seeded bone marrow cells (BMCs) harvested from dogs onto ePTFE grafts which

resulted in fully endothelialized grafts with superior patency to non-seeded ePTFE grafts at 6 months.⁹⁷ Ultimately despite these and other advances, investigation into biohybrid grafts has declined in favor of fully tissue-engineered vascular grafts.

Tissue-Engineered Vascular Grafts

The earliest clinical experiences with totally autologous grafts on biodegradable scaffold were reported in 2001 after Shinoka performed a reconstruction of the pulmonary artery of a pediatric patient using autologous bone marrow cells seeded onto a PGA-reinforced L-lactide and E-caprolactone.⁶³ In 25 pediatric patients in Japan undergoing extracardiac total cavo-pulmonary connection using engineered vessels, all grafts were patent at 30 days,⁹⁸ and after 10 years, roughly 30% of patients displayed some degree of graft stenosis, which was successfully treated with balloon angioplasty.⁹⁹ No patients suffered aneurysm formation or graft rupture of the engineered vessels in this low-pressure implantation site. These Japanese results formed the basis for an ongoing US phase 1 trial of similar conduits in patients with single-ventricle physiology, which was completed in 2018 ([ClinicalTrials.gov](#) identifier: NCT01034007). Although this technique was subsequently replicated, the limited mechanical strength of this material prevented use in the adult systemic circulation.⁶⁴

Cytograft – Tissue-Engineered Vascular Grafts for Hemodialysis Vascular Access – 2004

In the mid-2000s, L'Heureux and McAllister formed the company Cytograft. Between 2004 and 2007, the company conducted their first phase 1/2 clinical trial utilizing the Lifeline sheet-based TEVG as hemodialysis access conduit in patients with end-stage renal disease.^{78,80} This was the first clinical trial using autologous cells to create a patient-specific bioengineered vessel and the first human use of TEVG in the arteriovenous access circulation. [Figure 68.3](#) shows a Lifeline TEVG implanted in human subject.

Even though the Lifeline is composed of human cells, which should have minimal immune reaction, investigators noted an early failure rate of approximately 30% within 90 days. This was ultimately attributed to the use of bovine proteins during early vessel production, which generated an immune reaction that was not seen in subsequent productions. In addition, the layered fibroblast-based tissues suffered some early failures and dilatation over time.^{80,81} Further, the Lifeline is not available as a truly “off the shelf” conduit as the manufacturing process requires autologous cell culture over 24 weeks. Decellularized allogeneic grafts and devitalized, frozen grafts may expand the use of this vessel¹⁰⁰; however, clinical development has not progressed with this product.

Olausson – Decellularized Human Donor Vessel Scaffold – 2012

The 2012 use of a decellularized human iliac vein for bypass of an extrahepatic portal vein thrombosis in a pediatric patient remains the only reported use of a TEVG derived from a fully decellularized intact human blood vessel.⁷⁵ The direct application

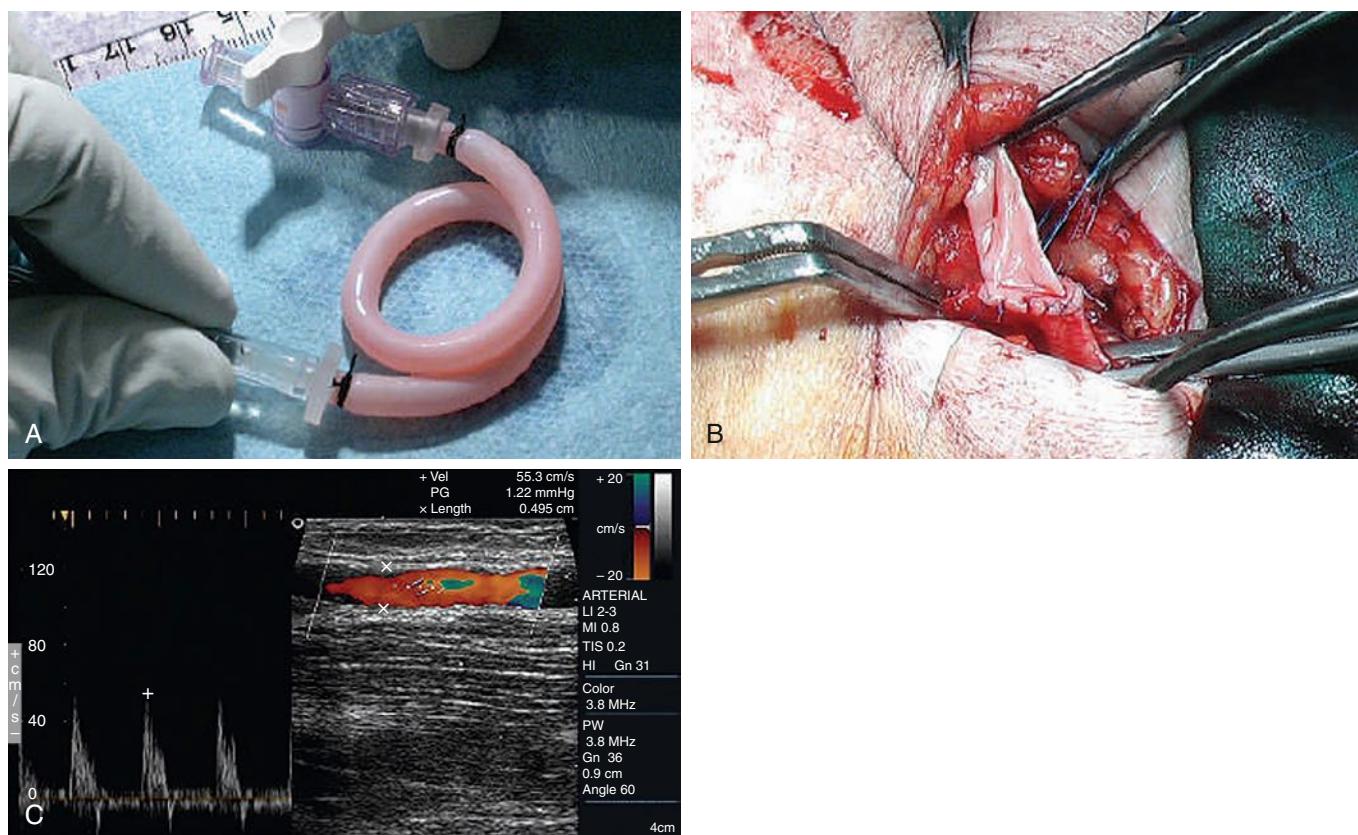


Figure 68.3 Images of a sheet-based graft (Lifeline, Cytovine, Novato, CA). (A) An autologous graft was implanted in a human recipient as an arteriovenous shunt between the humeral artery and the axillary vein. (B) The tissue-engineered blood vessel during implantation. (C) On duplex at 6 months the graft maintains high flow without signs of stenosis or aneurysm. (Reproduced with permission from Konig et al.¹⁰⁰)

of this technique to further clinical practice is limited both by the availability of suitable donor tissue and the need for prolonged seeding of the conduit with recipient cells.

Humacyte, Inc. – Tissue-Engineered Vascular Grafts for Hemodialysis Vascular Access and Peripheral Arterial Bypass – 2013

Following successful pre-clinical work with decellularized, allogeneic human bioengineered vessels, Humacyte initiated its first phase 1/2 clinical trial in December 2012 using the human acellular vessel (HAV) as a conduit for hemodialysis access. This study was conducted as two single-arm trials in the United States and Poland, where 60 patients with ESRD who were not candidates for AVF creation received the HAV and were followed for a period of 24 months. Overall, the acellular vessel was well tolerated by all subjects without evidence for immune response to the HAV as illustrated by no significant change in a panel of reactive antibodies. The incidence of HAV infection in the phase 2 AV access studies was extremely low with only one reported vessel infection during more than 82 patient-years of follow-up. There were no reports of spontaneous aneurysmal dilation or post-cannulation bleeding. At 6 months, primary, primary assisted, and secondary patency was 63%, 73%, and 97%, respectively. At 12 months, primary, primary assisted, and secondary patency was 12%, 38%, and 89%, respectively. Histology from isolated HAV explants

(Fig. 68.4) during surgical interventions revealed evidence of host VSMC and EC infiltration into the walls of the vessel; essentially rendering the bioengineered vessel a new living tissue in the recipient host.¹⁰¹ Some patients from these studies are beginning to approach 5 to 6 years post-implantation, with no evidence of dilation over long-term dialysis use (Fig. 68.5), supporting durability of the HAV.

In May of 2016, the first phase 3 clinical trial using a bioengineered implantable tissue was initiated in a multinational, double-arm, randomized clinical trial to compare the HAV to the current standard of ePTFE for patients unsuitable for creation of an AVF. The primary endpoint is secondary patency at 2 years and the goal for total enrollment is 350 patients. In June 2017, a second phase 3 clinical trial was initiated to compare the HAV to AV fistulas in ESRD patients. The primary endpoints are functional patency at 6 months and secondary patency at 12 months.

Detailed histological analysis of vessels that have been explanted from these ESRD patients has been reported¹⁰² and is summarized in Figure 68.4. Results were supportive of repopulation of host cells into the vessel to create multilayered living tissues that maintain blood transport and exhibit self-healing after cannulation injury. In vessels explanted 16 to 200 weeks after implantation, histological analysis indicated spatial pattern of the host cell response to the HAV after implantation, indicating substantial influx of alpha smooth muscle

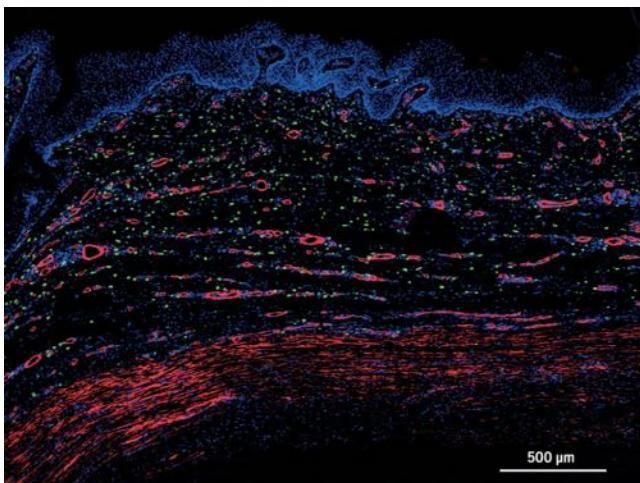


Figure 68.4 Cellular repopulation and remodeling of an implanted HAV. The figure demonstrates the infiltration of the vessel wall with host-derived vascular smooth muscle cells (stained in red) and the development of a neo-adventitia with the in-growth of host capillaries into the vessel wall.

actin-expressing cells that progressively matured and circumferentially aligned in the HAV wall. These cells were supported by microvasculature initially formed by CD34⁺/CD31⁺ cells in the neoadventitia and later maintained by CD34⁻/CD31⁺ endothelial cells in the media and lumen of the HAV.

Humacyte has also completed a phase 2 study in Poland using the HAV as a bypass conduit for superficial femoral artery occlusion, and the company is conducting a similar trial in the US. Both are single arm, safety-focused studies with a collective target enrollment of 40 patients (20 in the US, 20 in Poland). The study in the US is ongoing; however, results from the 20 patients from Poland are available.¹⁰³ They indicate HAVs were well tolerated, with no evidence of structural failure or rejection. No patients required amputations over a 2-year period. Primary, primary assisted, and secondary patency was 79%, 79%, and 90%, respectively, at 6 months and 63%, 63%, and 84% at 12 months. At 24 months, secondary patency was 74%. There was only one report of a pseudoaneurysm, which occurred after a suspected iatrogenic injury. Rates of infection were also low; there were three surgical site infections and no HAV infections in 34 patient-years of follow-up. There was no evidence for an immunogenic response.

To date, clinical experience indicates that the HAV remains mechanically strong over implantation periods of more than 45 months with no evidence of dilatation. During more than 150 patient-years of follow-up across the three phase 2 studies (ESRD and PAD), only one case of infection of the HAV material itself has been reported. The serious adverse event profile has been typical of that expected in the dialysis and PAD populations. Secondary patency of the HAVs is substantially higher than the historical data for both ePTFE and AVF (accounting for non-maturation). No evidence of immunogenicity of the HAV has been found and the HAV remains mechanically robust even after repeated puncture for hemodialysis. The HAV in the decellularized form has a shelf life of at least 12 months

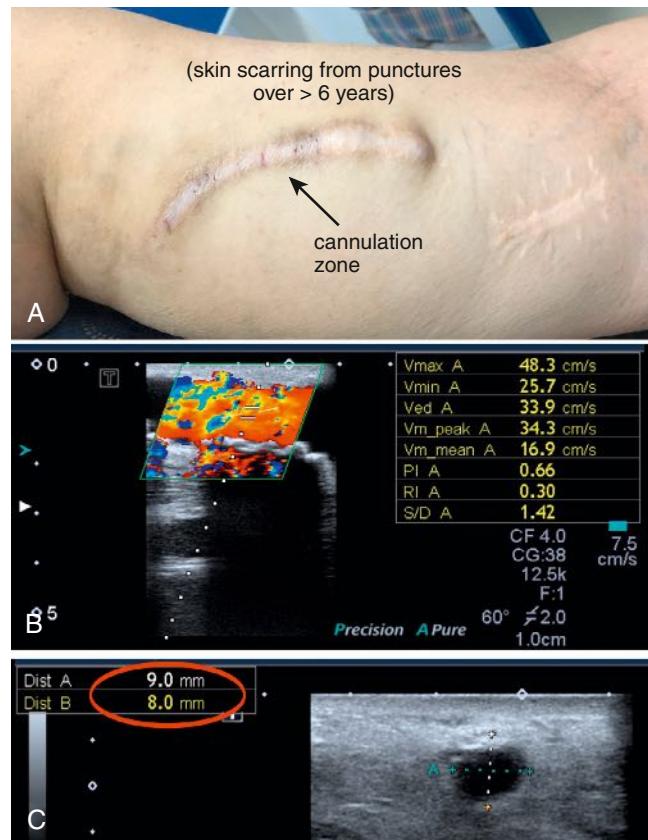


Figure 68.5 Ultrasound and computed tomography (CT) angiogram of human acellular vessel (HAV) from a patient from Poland (phase 2 study) who has been using the HAV for dialysis for 6 years. (A) Image of arm with HAV implant. The cannulation zone is indicated with a black arrow. Skin scarring occurred from approximately 6 years of dialysis. (B) CT angiogram of the HAV indicates patency. (C) Some degree of small dilation is noted, as the conduit diameter is 8 to 9 mm, slightly increased from the original 6-mm diameter.

according to tests, but there is ongoing work to extend that window to 18 months.

LIMITATIONS AND RISKS

Despite rapid progress in the development of durable bioengineered vascular grafts, each of the products and technologies presented in this chapter have limitations. Use of intact isolated blood vessels continues to raise concern for decreased patency and durability (Table 68.2). Biohybrids have fallen out of favor due to the difficulty of harvesting and seeding ECs, as well as the potential need for a two-stage surgery. Although early clinical experience with fully tissue-engineered vascular grafts has shown promising results, large-scale clinical trials remain ongoing. Thus, both cost-effectiveness and long-term outcomes remain incompletely understood.

FUTURE ADVANCES

Though acellular engineered conduits seem to hold great promise for the future, alternative technologies continue to develop. Three-dimensional (3D) printing is a rapidly evolving technology that holds significant promise for the future of engineered

TABLE 68.2

A Comparison of the Preparation, Patency Rates, Complications and Availability Between Isolated Vessels and Tissue-Engineered Vascular Tubes

	Preparation	Patency (Primary)	Patency (Secondary)	Complication Rate	Availability
Isolated Vessels					
Artegraft 1976 ¹¹² 2011 ¹¹³	Bovine carotid artery treated with glutaraldehyde	87% (87/100) at 18 months 60.5% – 12 months (16/26)	n/a 60.1% – 12 months (16/26)	3% (1/26) thrombosis	Off the shelf
Procol 2004 ⁸⁶ 2005 ¹⁶	Bovine mesenteric vein treated with glutaraldehyde	80% – 12 months 70% – 24 months (N = 25) 35.6% at 12 months (N = 183)	65.6% at 12 months 60.3% at 24 months (N = 183)	0.77 thromboses/year	Off the shelf
CryoVein (Cryolife) 2004 ⁸⁸	Cryopreserved human saphenous vein	60% – 6 months 30% – 12 months (N = 93)	82% – 12 months 63% – 24 months	18% aneurysmal 12% thromboses	Off the shelf
Tissue-Engineered Vascular Tubes					
Omniflow II 1992 ⁴² 1994 ¹¹⁴ 1996 ¹¹⁵	Ovine collagen + polyester mesh grown in sheep, treated with glutaraldehyde	68% (N = 110) at 4 yrs ⁴² 77% at 1 year, 58% at 2 years, 48% at 3 years, 34% at 4 years (N = 47) ¹¹⁵	78% (N = 110) at 4 years ¹¹⁴	Aneurysm 0.96%, infection 1.92% ¹¹⁵	Off the shelf
Humacyte 2011 ⁷¹	Decellularized allogeneic cells grown on PGA scaffold (dissolved prior to implantation in sub-human primates)	88% (7/8) at 3–6 months	n/a	(1/8)-thrombosis at 3 months	Off the shelf
Lifeline (Cytograft) 2009 ⁸⁰	Autologous fibroblasts in sheets, seeded with ECs	78% at 1 month (7/9)	60% at 6 months (5/8)	22% (2/9) dilated 11% (1/9) aneurysm	24 weeks
Allogeneic sheet-based (Cytograft) 2014 ⁷⁹	Decellularized allogeneic cells in sheets	100% at 1–7 months (N = 3)	n/a	None reported	Off the shelf

Current technologies available on the market are listed by name; others by best descriptor available based on preparation.
ECs, endothelial cells; PGA, polyglycolic acid.

tissues. This process, in which the repetitive deposition of materials layer-by-layer is used to generate complex 3-dimensional structures, has been adapted to produce biological and biocompatible materials in a process known as “bioprinting.”¹⁰⁴ Using a combination of cells and biological polymers as “bio-ink” this has already been used to produce *in vitro* models of blood vessels lined with endothelial cells and this may ultimately overcome some of the limits of existing methods for bioengineered vessel production.^{105–107}

Another technology that is being investigated for its potential applications for bioengineered blood vessels is electrospinning. This is an established technology in which an electrical field is used to guide the deposition of polymers onto a grounded platform. A source material, which can be chemicals, biopolymers, nanoparticles, or cells, is “sprayed” onto this platform with an electrical charge guiding the orientation of the resulting structure.¹⁰⁸ This can be used to produce either tubular structures or flat sheets and provides the potential benefit of producing improved scaffolds that more accurately reproduce the

triple-layered structure of human blood vessels. Additionally, co-spinning of multiple substrates may result in improved strength and compliance of conduits relative to existing methods.^{109,110}

CONCLUSION

The field of bioengineered vascular tissues spans a period of more than 50 years. In this time, we have benefited from the brilliant and diligent work of several teams from around the world. The processes of developing conduit for use as blood vessel replacements has progressed at an astonishing rate. Early work aimed at utilizing autologous conduit gave way to later processes attempting to decellularize these vessels and ultimately to the creation of entirely tissue-engineered vascular grafts.

Tissue engineering technologies have advanced to the degree that the manufacturing of an allogeneic, readily available, bio-mimicking vascular tube is now feasible. There exists convincing evidence to support that strong, non-immunogenic, human-derived vessels are well received by the recipient host

and may even become a living tissue within the patient who requires blood vessel replacement. Cost, scale, manufacturing, biocompatibility, thrombogenicity, and durability remain important focuses on the horizon for this innovative technology. Continued careful, safety- and efficacy-focused clinical trials with progression to long-term, randomized clinical studies will be necessary to eventually validate this promising technology in hopes that it may one day provide a benefit to the millions of patients in need.

DISCLOSURE

Dr. Niklason: Humacyte, Inc., Employee, BOD
Dr. Lawson: Humacyte, Inc., Employee, BOD

SELECTED KEY REFERENCES

- Benrashid E, et al. Tissue engineered vascular grafts: Origins, development, and current strategies for clinical application. *Methods*. 2016;99:13–19.
Overview of the history, current status, and future directions of BEVG development.
- Boland ED, et al. Electrospinning collagen and elastin: preliminary vascular tissue engineering. *Front Biosci*. 2004;9:1422–1432.
Description of biospinning used to produce a scaffold for use as a vascular conduit.
- Dahl SL, et al. Readily available tissue-engineered vascular grafts. *Sci Transl Med*. 2011;3(68):68ra9.
Description of preclinical animal model studies of the Humacyte human acellular vessel (HAV).
- Heine J, et al. Tissue engineering human small-caliber autologous vessels using a xenogenous decellularized connective tissue matrix approach: preclinical comparative biomechanical studies. *Artif Organs*. 2011;35(10):930–940.
Description of the histological and mechanical properties of decellularized xenogenous vascular scaffolds seeded with human cells.
- Lawson JH, et al. Bioengineered human acellular vessels for dialysis access in patients with end-stage renal disease: two phase 2 single-arm trials. *Lancet*. 2016;387(10032):2026–2034.
Reports of two clinical trials with Humacyte HAV used as a hemodialysis graft.
- Livesey SA, et al. Transplanted acellular allograft dermal matrix. Potential as a template for the reconstruction of viable dermis. *Transplantation*. 1995;60(1):1–9.
Description of methodology for the decellularization of tissue.
- McAllister TN, et al. Effectiveness of haemodialysis access with an autologous tissue engineered vascular graft: a multicentre cohort study. *Lancet*. 2009;373(9673):1440–1446.
Case series of patients receiving sheet-based BEVG derived from autologous tissues and seeded with autologous endothelium for hemodialysis access.
- Palumbo R, et al. Long-term favorable results by arteriovenous graft with Omniflow II prosthesis for hemodialysis. *Nephron Clin Pract*. 2009;113(2):c76–80.
Long-term results of the Omniflow II BEVG as a hemodialysis access graft.
- Weinberg CB, Bell E. A blood vessel model constructed from collagen and cultured vascular cells. *Science*. 1986;231(4736):397–400.
Description of the development of an early BEVG prototype.
- Wystrychowski W, et al. First human use of an allogeneic tissue-engineered vascular graft for hemodialysis access. *J Vasc Surg*. 2014;60(5):1353–1357.
Case series of patients receiving decellularized allogeneic sheet-based BEVG for hemodialysis access.

A complete reference list can be found online at www.expertconsult.com.

REFERENCES

1. Veith FJ, Gupta SK, Ascer E, et al. Six-year prospective multicenter randomized comparison of autologous saphenous vein and expanded polytetrafluoroethylene grafts in infrainguinal arterial reconstructions. *J Vasc Surg.* 1986;3(1):104–114.
2. Conte MS. The ideal small arterial substitute: a search for the Holy Grail? *FASEB J.* 1998;12(1):43–45.
3. Benrashid E, McCoy CC, Youngwirth LM, et al. Tissue engineered vascular grafts: Origins, development, and current strategies for clinical application. *Methods.* 2016;99:13–19.
4. Manson RJ, Unger JM, Ali A, et al. Tissue-engineered vascular grafts: autologous off-the-shelf vascular access? *Semin Nephrol.* 2012;32(6):582–591.
5. Menzoian JO, Koshar AL, Rodrigues N, Alexis Carrel, Rene Leriche, Jean Kunlin, and the history of bypass surgery. *J Vasc Surg.* 2011;54(2):571–574.
6. Carrel A, Lindbergh C. *The Culture of Organs.* New York: Hoeber, Paul B; 1938.
7. Kunlin J. [Long vein transplantation in treatment of ischemia caused by arteritis]. *Rev Chir.* 1951;70(7–8):206–235.
8. DeBakey ME, Cooley DA, Crawford ES, Morris GCJ. Clinical application of a new flexible knitted Dacron arterial substitute. 1958. *Am Surg.* 2008;74(5):381–386.
9. Brescia MJ, Cimino JE, Appel K, Hurwicz BJ. Chronic hemodialysis using venipuncture and a surgically created arteriovenous fistula. *N Engl J Med.* 1966;275(20):1089–1092.
10. Scribner BH, Caner JE, Buri R, Quinton W. The technique of continuous hemodialysis. *Trans Am Soc Artif Intern Organs.* 1960;6:88–103.
11. Johnson JM, Goldfarb D, Baker LDJ. Expanded polytetrafluoroethylene as a small artery replacement. A preliminary report. *Am J Surg.* 1976;132(6):723–727.
12. Baker LDJ, Johnson JM, Goldfarb D. Expanded polytetrafluoroethylene (PTFE) subcutaneous arteriovenous conduit: an improved vascular access for chronic hemodialysis. *Trans Am Soc Artif Intern Organs.* 1976;22:382–387.
13. Gross RE, Hurwitt ES. Preliminary observations on the use of human arterial grafts in the treatment of certain cardiovascular defects. *N Engl J Med.* 1948;239(16):578.
14. Rosenberg N, Martinez A, Sawyer PN, et al. Tanned collagen arterial prosthesis of bovine carotid origin in man. Preliminary studies of enzyme-treated heterografts. *Ann Surg.* 1966;164(2):247–256.
15. Schmitz-Rixen T, Megerman J, Anderson JM, et al. Longterm study of a compliant biological vascular graft. *Eur J Vasc Surg.* 1991;5(2):149–158.
16. Katzman HE, Glickman MH, Schild AF, et al. Multicenter evaluation of the bovine mesenteric vein bioprostheses for hemodialysis access in patients with an earlier failed prosthetic graft. *J Am Coll Surg.* 2005;201(2):223–230.
17. Manduz S, Katrancioglu N, Ozker E, Dogan K. Early thrombosis in bovine mesenteric vein grafts after infrainguinal reconstruction. *Int J Angiol.* 2008;17(1):37–39.
18. Douglas JF, Gaughran ER, Henderson J, et al. The use of segmental arterial implants prepared by enzymatic modification of heterologous blood vessels. *Surg Forum.* 1956;6:242–246.
19. Ochsner JL, DeCamp PT, Leonard GL. Experience with fresh venous allografts as an arterial substitute. *Ann Surg.* 1971;173(6):933–939.
20. Ochsner JL, Lawson JD, Eskin SJ, et al. Homologous veins as an arterial substitute: long-term results. *J Vasc Surg.* 1984;1(2):306–313.
21. Martin 3rd RS, Edwards WH, Mulherin JLJ, et al. Cryopreserved saphenous vein allografts for below-knee lower extremity revascularization. *Ann Surg.* 1994;219(6):662–664.
22. Allobaid N, Alnaeb ME, Sales KM, et al. Endothelial progenitor cells and their potential clinical applications in peripheral arterial disease. *Endothelium.* 2005;12(5–6):243–250.
23. Allobaid N, Salacinski HJ, Sales KM, et al. Single stage cell seeding of small diameter prosthetic cardiovascular grafts. *Clin Hemorheol Microcirc.* 2005;33(3):209–226.
24. Zilla P, Deutsch M, Meinhart J, et al. Clinical in vitro endothelialization of femoropopliteal bypass grafts: an actuarial follow-up over three years. *J Vasc Surg.* 1994;19(3):540–548.
25. Deutsch M, Meinhart J, Fischlein T, et al. Clinical autologous in vitro endothelialization of infrainguinal ePTFE grafts in 100 patients: a 9-year experience. *Surgery.* 1999;126(5):847–855.
26. Deutsch M, Meinhart J, Zilla P, et al. Long-term experience in autologous in vitro endothelialization of infrainguinal ePTFE grafts. *J Vasc Surg.* 2009;49(2):352–362.
27. Rademacher A, Paulitschke M, Meyer R, Hetzer R. Endothelialization of PTFE vascular grafts under flow induces significant cell changes. *Int J Artif Organs.* 2001;24(4):235–242.
28. Lehoux S, Castier Y, Tedgui A. Molecular mechanisms of the vascular responses to haemodynamic forces. *J Intern Med.* 2006;259(4):381–392.
29. Yoshizumi M, Abe J-I, Tsuchiya K, Berk BC, Tamaki T. Stress and vascular responses: atheroprotective effect of laminar fluid shear stress in endothelial cells: possible role of mitogen-activated protein kinases. *J Pharmacol Sci.* 2003;91(3):172–176.
30. Chien S. Mechanotransduction and endothelial cell homeostasis: the wisdom of the cell. *Am J Physiol Heart Circ Physiol.* 2007;292(3):H1209–1224.
31. Daculsi R, Rémy-Zolghadri M, Grellier M, et al. Signal transduction and procoagulant state of human cord blood–progenitor-derived endothelial cells after interleukin-1alpha stimulation. *Endothelium.* 2007;14(3):163–171.
32. Sparks CH. Autogenous grafts made to order. *Ann Thorac Surg.* 1969;8(2):104–113.
33. Sparks CH. Silicone mandril method for growing reinforced autogenous femoro-popliteal artery grafts in situ. *Ann Surg.* 1973;177(3):293–300.
34. Hallin RW. Complications with the mandril-grown (Sparks) dacron arterial graft. *Am Surg.* 1975;41(9):550–554.
35. Hallin RW, Sweetman WR. The Sparks' mandril graft. A seven year follow-up of mandril grafts placed by Charles H. Sparks and his associates. *Am J Surg.* 1976;132(2):221–223.
36. Campbell JH, Efendi JL, Campbell GR. Novel vascular graft grown within recipient's own peritoneal cavity. *Circ Res.* 1999;85(12):1173–1178.
37. Chue W-L, Campbell GR, Caplice N, et al. Dog peritoneal and pleural cavities as bioreactors to grow autologous vascular grafts. *J Vasc Surg.* 2004;39(4):859–867.
38. Campbell JH, Efendi JL, Han C, et al. Haemopoietic origin of myofibroblasts formed in the peritoneal cavity in response to a foreign body. *J Vasc Res.* 2000;37(5):364–371.
39. Christie B, Ketharanathan V, Perloff LJ. Patency rates of minute vascular replacements: the glutaraldehyde modified mandril-grown conduit. *J Surg Res.* 1980;28(6):519–532.
40. Perloff LJ, Christie BA, Ketharanathan V, et al. A new replacement for small vessels. *Surgery.* 1981;89(1):31–41.
41. Ketharanathan V, Christie BA. Glutaraldehyde tanned ovine collagen compared with polytetrafluoroethylene (Gore-Tex) as a conduit for small calibre artery substitution; an experimental study in dogs. *Aust N Z J Surg.* 1981;51(6):556–561.
42. Edwards GA, Roberts G. Development of an ovine collagen-based composite biosynthetic vascular prosthesis. *Clin Mater.* 1992;9(3–4):211–223.
43. Koch G, Gutschi S, Pascher O, et al. Analysis of 274 Omniflow Vascular Prostheses implanted over an eight-year period. *Aust N Z J Surg.* 1997;67(9):637–639.
44. Palumbo R, Niscola P, Calabria S, et al. Long-term favorable results by arteriovenous graft with Omniflow II prosthesis for hemodialysis. *Nephron Clin Pract.* 2009;113(2):c76–80.

45. Rothuizen TC, Damanik FFR, Anderson JM, et al. Tailoring the foreign body response for in situ vascular tissue engineering. *Tissue Eng Part C Methods*. 2015;21(5):436–446.
46. Damanik FFR, Rothuizen TC, van Blitterswijk C, et al. Towards an in vitro model mimicking the foreign body response: tailoring the surface properties of biomaterials to modulate extracellular matrix. *Sci Rep*. 2014;4:6325.
47. Rothuizen TC, Damanik FFR, Lavrijsen T, et al. Development and evaluation of in vivo tissue engineered blood vessels in a porcine model. *Biomaterials*. 2016;75:82–90.
48. Geelhoed WJ, Moroni L, Rotmans JI. Utilizing the foreign body response to grow tissue engineered blood vessels in vivo. *J Cardiovasc Transl Res*. 2017;10(2):167–179.
49. Weinberg CB, Bell E. A blood vessel model constructed from collagen and cultured vascular cells. *Science*. 1986;231(4736):397–400.
50. Girton TS, Oegema TR, Grassl ED, et al. Mechanisms of stiffening and strengthening in media-equivalents fabricated using glycation. *J Biomech Eng*. 2000;122(3):216–223.
51. Cummings CL, Gawlitza D, Nerem RM, Stegemann JP. Properties of engineered vascular constructs made from collagen, fibrin, and collagen-fibrin mixtures. *Biomaterials*. 2004;25(17):3699–3706.
52. MIT. Remembering Eugene Bell. MIT Technology Review. Available at: <https://www.technologyreview.com/2007/10/15/223430/remembering-eugene-bell/>; 2007.
53. Vacanti CA, Kim W, Upton J, et al. Tissue-engineered growth of bone and cartilage. *Transplant Proc*. 1993;25(1 Pt 2):1019–1021.
54. Vacanti JP, Morse MA, Saltzman WM, et al. Selective cell transplantation using bioabsorbable artificial polymers as matrices. *J Pediatr Surg*. 1988;23(1 Pt 2):3–9.
55. Mikos AG, Bao Y, Cima LG, et al. Preparation of poly(glycolic acid) bonded fiber structures for cell attachment and transplantation. *J Biomed Mater Res*. 1993;27(2):183–189.
56. Mikos AG, Sarakinos G, Leite SM, et al. Laminated three-dimensional biodegradable foams for use in tissue engineering. *Biomaterials*. 1993;14(5):323–330.
57. Fontaine M, Hansen LK, Thompson S, et al. Transplantation of genetically altered hepatocytes using cell-polymer constructs. *Transplant Proc*. 1993;25(1 Pt 2):1002–1004.
58. Cohen S, Baño MC, Cima LG, et al. Design of synthetic polymeric structures for cell transplantation and tissue engineering. *Clin Mater*. 1993;13(1–4):3–10.
59. Mooney DJ, Breuer C, McNamara K, et al. Fabricating tubular devices from polymers of lactic and glycolic Acid for tissue engineering. *Tissue Eng*. 1995;1(2):107–118.
60. Mooney DJ, Organ G, Vacanti JP, Langer R. Design and fabrication of biodegradable polymer devices to engineer tubular tissues. *Cell Transplant*. 1994;3(2):203–210.
61. Shinoka T, Ma PX, Shum-Tim D, et al. Tissue-engineered heart valves. Autologous valve leaflet replacement study in a lamb model. *Circulation*. 1996;94(9 Suppl):II164–168.
62. Breuer CK, Shin'oka T, Tanel RE, et al. Tissue engineering lamb heart valve leaflets. *Biotechnol Bioeng*. 1996;50(5):562–567.
63. Shin'oka T, Imai Y, Ikada Y. Transplantation of a tissue-engineered pulmonary artery. *N Engl J Med*. 2001;344(7):532–533.
64. Matsumura G, Hibino N, Ikada Y, et al. Successful application of tissue engineered vascular autografts: clinical experience. *Biomaterials*. 2003;24(13):2303–2308.
65. Weiler A, Helling HJ, Kirch U, et al. Foreign-body reaction and the course of osteolysis after polyglycolide implants for fracture fixation: experimental study in sheep. *J Bone Joint Surg Br*. 1996;78(3):369–376.
66. Niklason LE, Langer RS. Advances in tissue engineering of blood vessels and other tissues. *Transpl Immunol*. 1997;5(4):303–306.
67. Niklason LE, Gao J, Abbott WM, et al. Functional arteries grown in vitro. *Science*. 1999;284(5413):489–493.
68. Niklason LE, Abbott W, Gao J, et al. Morphologic and mechanical characteristics of engineered bovine arteries. *J Vasc Surg*. 2001;33(3):628–638.
69. Dahl SLM, Koh J, Prabhakar V, Niklason LE. Decellularized native and engineered arterial scaffolds for transplantation. *Cell Transplant*. 2003;12(6):659–666.
70. Livesey SA, Herndon DN, Hollyoak MA, et al. Transplanted acellular allograft dermal matrix. Potential as a template for the reconstruction of viable dermis. *Transplantation*. 1995;60(1):1–9.
71. Dahl SLM, Kypson AP, Lawson JH, et al. Readily available tissue-engineered vascular grafts. *Sci Transl Med*. 2011;3(68):68ra9.
72. Weber B, Dijkman PE, Scherman J, et al. Off-the-shelf human decellularized tissue-engineered heart valves in a non-human primate model. *Biomaterials*. 2013;34(30):7269–7280.
73. Bader A, Steinhoff G, Strobl K, et al. Engineering of human vascular aortic tissue based on a xenogeneic starter matrix. *Transplantation*. 2000;70(1):7–14.
74. Heine J, Schmiedl A, Cebotari S, et al. Tissue engineering human small-caliber autologous vessels using a xenogenous decellularized connective tissue matrix approach: preclinical comparative biomechanical studies. *Artif Organs*. 2011;35(10):930–940.
75. Olausson M, Patil PB, Kuna VK, et al. Transplantation of an allogeneic vein bioengineered with autologous stem cells: a proof-of-concept study. *Lancet*. 2012;380(9838):230–237.
76. L'Heureux N, Germain L, Labbé R, Auger FA. In vitro construction of a human blood vessel from cultured vascular cells: a morphologic study. *J Vasc Surg*. 1993;17(3):499–509.
77. L'Heureux N, Pâquet S, Labbé R, et al. A completely biological tissue-engineered human blood vessel. *FASEB J*. 1998;12(1):47–56.
78. L'Heureux N, Dusserre N, Konig G, et al. Human tissue-engineered blood vessels for adult arterial revascularization. *Nat Med*. 2006;12(3):361–365.
79. Wystrychowski W, McAllister TN, Zagalski K, et al. First human use of an allogeneic tissue-engineered vascular graft for hemodialysis access. *J Vasc Surg*. 2014;60(5):1353–1357.
80. McAllister TN, Maruszewski M, Garrido SA, et al. Effectiveness of haemodialysis access with an autologous tissue-engineered vascular graft: a multicentre cohort study. *Lancet*. 2009;373(9673):1440–1446.
81. Wystrychowski W, Cierpka L, Zagalski K, et al. Case study: first implantation of a frozen, devitalized tissue-engineered vascular graft for urgent hemodialysis access. *J Vasc Access*. 2011;12(1):67–70.
82. Kaplan MS, Mirahmadi KS, Winer RL, et al. Comparison of “PTFE” and bovine grafts for blood access in dialysis patients. *Trans Am Soc Artif Intern Organs*. 1976;22:388–393.
83. Hutchin P, Jacobs JR, Devin JB, et al. Bovine graft arteriovenous fistulas for maintenance hemodialysis. *Surg Gynecol Obstet*. 1975;141(2):255–258.
84. Dale WA, Lewis MR. Further experiences with bovine arterial grafts. *Surgery*. 1976;80(6):711–721.
85. Bacchini G, Del Vecchio L, Andrulli S, et al. Survival of prosthetic grafts of different materials after impairment of a native arteriovenous fistula in hemodialysis patients. *ASAIO J*. 2001;47(1):30–33.
86. Hatzibaloglu A, Velissaris I, Kaitzis D, et al. ProCol vascular bioprostheses for vascular access: midterm results. *J Vasc Access*. 2004;5(1):16–18.
87. Kovalic AJ, Beattie DK, Davies AH. Outcome of ProCol, a bovine mesenteric vein graft, in infringuinal reconstruction. *Eur J Vasc Endovasc Surg*. 2002;24(6):533–534.
88. Madden RL, Lipkowitz GS, Browne BJ, Kurbanov A. Experience with cryopreserved cadaveric femoral vein allografts used for hemodialysis access. *Ann Vasc Surg*. 2004;18(4):453–458.
89. Matsuura JH, Rosenthal D, Wellons ED, et al. Hemodialysis graft infections treated with cryopreserved femoral vein. *Cardiovasc Surg*. 2002;10(6):561–565.
90. Lin PH, Brinkman WT, Terramani TT, Lumsden AB. Management of infected hemodialysis access grafts using cryopreserved human vein allografts. *Am J Surg*. 2002;184(1):31–36.
91. Bolton WD, Cull DL, Taylor SM, et al. The use of cryopreserved femoral vein grafts for hemodialysis access in patients at high risk for infection: a word of caution. *J Vasc Surg*. 2002;36(3):464–468.
92. Merola J, Jane-Wit DD, Pober JS. Recent advances in allograft vasculopathy. *Curr Opin Organ Transplant*. 2017;22(1):1–7.

93. Herring M, Gardner A, Glover J. A single-staged technique for seeding vascular grafts with autogenous endothelium. *Surgery*. 1978;84(4):498–504.
94. Herring MB, Compton RS, LeGrand DR, et al. Endothelial seeding of polytetrafluoroethylene popliteal bypasses. A preliminary report. *J Vasc Surg*. 1987;6(2):114–118.
95. Bordenave L, Rémy-Zolghadri M, Fernandez P, et al. Clinical performance of vascular grafts lined with endothelial cells. *Endothelium*. 1999;6(4):267–275.
96. Tiwari A, Salacinski HJ, Hamilton G, Seifalian AM. Tissue engineering of vascular bypass grafts: role of endothelial cell extraction. *Eur J Vasc Endovasc Surg*. 2001;21(3):193–201.
97. Noishiki Y, Yamane Y, Tomizawa Y, Matsumoto A. Transplantation of autologous tissue fragments into an e-PTFE graft with long fibrils. *Artif Organs*. 1995;19(1):17–26.
98. Drews JD, Miyachi H, Shinoka T. Tissue-engineered vascular grafts for congenital cardiac disease: Clinical experience and current status. *Trends Cardiovasc Med*. 2017;27(8):521–531.
99. Shoji T, Shinoka T. Tissue engineered vascular grafts for pediatric cardiac surgery. *Transl Pediatr*. 2018;7(2):188–195.
100. Konig G, McAllister TN, Dusserre N, et al. Mechanical properties of completely autologous human tissue engineered blood vessels compared to human saphenous vein and mammary artery. *Biomaterials*. 2009;30(8):1542–1550.
101. Lawson JH, Glickman MH, Ilzecki M, et al. Bioengineered human acellular vessels for dialysis access in patients with end-stage renal disease: two phase 2 single-arm trials. *Lancet*. 2016;387(10032):2026–2034.
102. Kirkton RD, Santiago-Maysonet M, Lawson JH, et al. Bioengineered human acellular vessels recellularize and evolve into living blood vessels after human implantation. *Sci Transl Med*. 2019;11(485):eaau6934.
103. Gutowski P, Gage SM, Guziewicz M, et al. Arterial reconstruction with human bioengineered acellular blood vessels in patients with peripheral arterial disease. *J Vasc Surg*. 2020;72(4):1247–1258.
104. Murphy SV, Atala A. 3D bioprinting of tissues and organs. *Nat Biotechnol*. 2014;32(8):773–785.
105. Zhao L, Lee VK, Yoo S-S, et al. The integration of 3-D cell printing and mesoscopic fluorescence molecular tomography of vascular constructs within thick hydrogel scaffolds. *Biomaterials*. 2012;33(21):5325–5332.
106. Lee VK, Kim DY, Ngo H, et al. Creating perfused functional vascular channels using 3D bio-printing technology. *Biomaterials*. 2014;35(28):8092–8102.
107. Cui X, Boland T. Human microvasculature fabrication using thermal inkjet printing technology. *Biomaterials*. 2009;30(31):6221–6227.
108. Matthews JA, Wnek GE, Simpson DG, Bowlin GL. Electrospinning of collagen nanofibers. *Biomacromolecules*. 2002;3(2):232–238.
109. Stitzel JD, Pawlowski KJ, Wnek GE, et al. Arterial smooth muscle cell proliferation on a novel biomimicking, biodegradable vascular graft scaffold. *J Biomater Appl*. 2001;16(1):22–33.
110. Boland ED, Matthews JA, Pawlowski KJ, et al. Electrospinning collagen and elastin: preliminary vascular tissue engineering. *Front Biosci*. 2004;9:1422–1432.
111. Walden R, L'Italien GJ, Megerman J, Abbott WM. Matched elastic properties and successful arterial grafting. *Arch Surg*. 1980;115(10):1166–1169.
112. Katzman HE, Schild AF, Vanderwerf BA. Bovine arterigraft arteriovenous fistulas for hemodialysis in one-hundred patients after “conventional” arteriovenous fistulas failed. *Vasc Surg*. 1976;10(3):169–175.
113. Kennealey PT, Elias N, Hertl M, et al. A prospective, randomized comparison of bovine carotid artery and expanded polytetrafluoroethylene for permanent hemodialysis vascular access. *J Vasc Surg*. 2011;53(6):1640–1648.
114. Werkmeister JA, White JF, Ramshaw JA. Evaluation of the Omniproflow collagen-polymer vascular prosthesis. *Med Prog Technol*. 1994;20(3–4):231–242.
115. Wang SS, Chu SH. Clinical use of omniproflow vascular graft as arteriovenous bridging graft for hemodialysis. *Artif Organs*. 1996;20(12):1278–1281.

Nonaortic Stents and Stent Grafts

DANIELLE C. SUTZKO, WILLIAM D. JORDAN JR., and BENJAMIN J. PEARCE

HISTORICAL BACKGROUND	886
STENT–VESSEL INTERACTION	887
Vessel Injury	887
<i>Fluid Dynamics</i>	887
<i>Strut Characteristics</i>	887
<i>Stent Composition</i>	887
STENT TYPES AND CHARACTERISTICS	887
Important Characteristics	888
Cell Size: Open and Closed Cells	888
Balloon-Expandable Stents	889
Self-Expanding Stents	890
Stent Grafts (Covered Stents)	890
SELECTION OF STENT	891
Plaque Morphology	891
External Forces	892
Anatomic Location	892
Branch Location	893
FAILURE MODES	894
Drug-Eluting Technology for Neointimal Failure	894
Treatment of In-Stent Restenosis	895
NEW DEVELOPMENTS	895
Absorbable Stents	895
FUTURE DEVELOPMENTS	896

Endovascular therapy has changed the landscape of vascular surgical practice. A major thrust into catheter-based therapy was initiated in 1999 with the US Food and Drug Administration (FDA) approval of endografts for aneurysmorrhaphy. As this important technique became ubiquitous, surgeons began to utilize stents in other vascular beds both for initial therapy and as secondary treatment after failed surgical grafts. Endovascular therapy with stents is now utilized throughout the vascular system, including arteries and veins spanning from the intracranial circulation to the tibial vessels.

As the use of endovascular stents has undergone more critical investigation, it has become evident that various vascular beds react differently to stent placement.^{1–3} Furthermore, angioplasty and stenting alter the biology of the treated vessel, a finding that has implications for both short-term and long-term results. The nature of the lesion, as well as the vascular bed to be treated, dictate specific nuances that guide the surgeon in choosing an appropriate stent.

This chapter focuses on factors that relate to the choice of stents and stent grafts for endovascular intervention in the nonaortic vascular beds. The indications for stent use in

conjunction with balloon angioplasty as well as the interaction between vessel and stent are reviewed. The multiple factors that influence the optimal stent choice in a given circumstance are considered, including device characteristics such as cell design, deployment precision, treatment length, deliverability, and adjunctive stent designs that may affect therapy.

HISTORICAL BACKGROUND

Isolated dilation of vessels using dilation catheters was first introduced in 1964 by Dotter and Judkins.⁴ This technique was refined in the 1970s by Gruentzig et al.,⁵ who used smaller catheters with attached balloons that could be delivered through the vascular tree from a remote location. Balloon angioplasty became a popular technique in the 1980s but remained inferior to surgical reconstruction because of the high acute occlusion rate and intermediate restenosis rate. Acute technical failure occurred as a result of elastic recoil, vasospasm, plaque rupture, or dissection. Recurrent stenosis, caused by an intense hyperplastic response, was commonly seen within the first 2 years after intervention. In the initial series of coronary angioplasty, interval

restenosis occurred in 30% to 50% of treated lesions.^{6–8} Likewise, angiographic failure of isolated angioplasty in the renal, iliac, and femoropopliteal arteries occurred in up to 26%,^{9,10} 32%,¹ and 50%,^{11,12} of cases, respectively.

Stenting was introduced with the goal of improving results of angioplasty by ensuring an adequate vessel lumen, maintaining flow, and reducing embolic load. Achieving optimal luminal diameter lessens the impact of in-stent neointimal formation. However, paradoxically, the stent itself has inherent properties that alter the normal vascular intimal development and can lead to maladaptive remodeling through direct intimal damage related to the procedure and the interaction between the arterial wall and the stent itself.

STENT–VESSEL INTERACTION

Vessel Injury

The degree of intimal response to stent placement has been linked directly to the extent of vessel injury. Sullivan et al.¹³ used an experimental stent with beveled struts to demonstrate this negative remodeling effect *in vivo*, utilizing a swine model. This experimental stent was designed to violate the internal elastic lamina. In comparison with Palmaz stents deployed in control animals, the experimental stent was associated with significantly greater neointimal formation. Furthermore, the extent of vessel injury demonstrated a linear effect on the absolute neointimal formation.

In addition, an inflammatory response to stent placement has been demonstrated histologically. In an early autopsy series, Farb et al.¹⁴ demonstrated inflammatory cell infiltration in the area of the vessel directly adjacent to the stent struts. The absolute number of inflammatory cells present was significantly increased when stent struts violated the internal lamina and penetrated into the lipid core of the plaque. Subsequent analysis demonstrated that inflammatory mediators were present more than 6 months after implantation. Another study showed that, in addition to the effect of the stent itself, bacterial contaminants introduced to the vessel wall during stent delivery also play a role in neointimal formation.¹⁵

Fluid Dynamics

Endovascular stents have been demonstrated to alter the fluid dynamics of the stented vessel segment. The most widely studied impact of stent placement on flow and negative remodeling is the creation of areas of low (<5 dyne/cm²) wall shear stress (WSS). Alteration in WSS occurs as a result of both a change in luminal diameter of the treated vessel and the presence of the stent itself. In a computational flow model, LaDisa et al.^{16,17} demonstrated several characteristics of stent placement that create a low shear stress environment. The factor that led to the most significant increase in the proportion of vessel wall exposed to a low shear environment was overdistention of the stented segment. Although some degree of stent oversizing is necessary for appropriate apposition of the stent to the vessel wall, LaDisa's group demonstrated a 13-fold increase in the total native vessel exposed to low WSS with 20% stent oversizing

compared with that seen with 10% oversizing. The low WSS can subsequently lead to greater neointimal hyperplasia and recurrent stenosis. This finding is validated clinically, as other studies have shown that along with other factors such as burden of calcified plaque, oversizing is associated with a higher incidence of in-stent restenosis.¹⁸ Most surgeons aim for a 10% oversizing when stenting infrainguinal occlusive lesions because of this evidence.

Strut Characteristics

The tolerances for stent construction are very strict, and minimal alteration of the strut height can have a significant impact on shear stress and neointimal formation. Intuitively, the area of the vessel wall adjacent to the stent struts has the greatest potential for negative remodeling. Eddy currents created as blood flows over the stent struts lead to regions of low shear. This effect results in a proportional change in shear stress with alterations of strut thickness. The formation of neointima in such areas of low shear stress has been reproduced in several models, and the thickness of the resultant neointima correlates with strut coverage, configuration, and thickness.^{19–21} Sprague et al.²² demonstrated that positive remodeling, as measured by endothelial cell migration, is hampered in low WSS environments. In normal shear models, migration of endothelial cells increased 2.5-fold within 1 week after implantation of steel struts onto the endothelial surface. However, in stented models with low shear, this migration was delayed up to several months.²³ The clinical effect of these findings was demonstrated by the angiographic restenosis rates of two nearly identical coronary stents that differed only by stent heights of 50 µm and 140 µm. The stent with the lower-profile design had less restenosis.²⁴

Stent Composition

The material composition of the stent also plays a role in neointimal formation. The most common bare metal (BM) stent components are stainless steel, nitinol (nickel and titanium alloy), cobalt chromium alloy, and tantalum. Although the actual mechanism of vessel injury from stent components is unclear, corrosive products from alloys have been found within sections of vessel wall. In addition, hypersensitivity of some patients to certain metals has been observed.²⁵ Palmaz et al.²⁶ demonstrated that galvanic currents are created within stented arteries and lead to corrosion and subsequent vessel injury.

STENT TYPES AND CHARACTERISTICS

Each stent has intrinsic properties that determine whether or not it is suitable for any given lesion.^{26–32} On the basis of the biologic interaction between vessel and stent, an ideal stent would be easy to deliver through a small-caliber sheath, be readily visible on fluoroscopy, conform to the vessel upon deployment, prevent acute procedural failure, provide long-term resistance to negative remodeling, and be fracture-resistant.

Generally, stents are divided into two groups according to their construction and mode of deployment – self-expanding (SE) versus balloon-expandable (BE) (Table 69.1).

TABLE 69.1

Comparison of Balloon-Expandable and Self-Expanding Stents Based on Intrinsic Characteristics and Clinical Use

Characteristic	Balloon Expandable	Self-Expanding
Radial force	High	Low
Flexibility	Low	High
Requires delivery sheath	Yes	No
Radiopacity	High	Variable
Oversizing recommended	No	Yes
Treats lesions with variable diameter	No	Yes
Resistant to external compression/bending	No	Yes

Important Characteristics

In a comparison of SE and BE stents, the major characteristics that determine suitability are radial force, flexibility, and precision of deployment. Both SE and BE stents can be covered with polytetrafluoroethylene or polyester, and such stent grafts combine the advantages of a stent with those of a graft.

Radial force is defined as the force required to produce a 50% reduction in the luminal diameter of the stent. The radial force of the stent maintains its apposition to the vessel wall and tucks down intimal flaps that may obstruct flow. It also provides the support to resist immediate vessel recoil and acute occlusion. This outward force may lead to a better technical result than that of balloon angioplasty alone. As the stent becomes incorporated into the vessel, the radial force resists deformation and negative remodeling to maintain luminal diameter over time.

Ultimately, radial force is a product of both stent design and composition. The original Palmaz stent has a stainless steel slotted/diamond design. The slotted configuration allows the stent to maintain a low profile for loading on the balloon. Once expanded, the slots become diamonds, resisting further conformational change and providing a high radial force. The Wallstent (Boston Scientific, Natick, MA, USA) also has a diamond configuration, but is designed to change lengths with its diameter. Therefore, its radial force is related to both its design and the degree of endothelialization within the artery. As the stent becomes more securely anchored, it resists shortening and leads to increased radial force. Various BE and SE stents are shown in [Figure 69.1](#), demonstrating the variability in stent design.

Conversely, nitinol stents rely on the inherent nature of their metallic composition to provide resistance to deformation. The nitinol alloy assumes a predetermined configuration at a desired temperature. At low temperatures, the alloy exists in the martensite state (metallurgic property of shape-memory alloys in which the crystalline structure of the alloy is elongated or asymmetric at cooler temperatures), which is flexible and aids both mounting on the catheter shaft and deliverability.

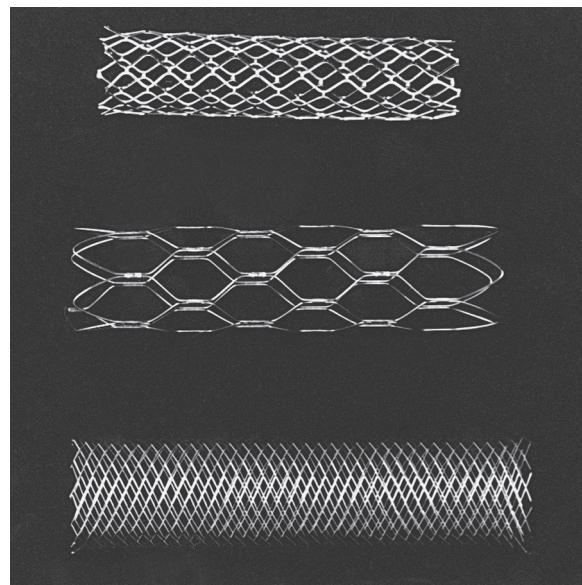


Figure 69.1 Comparison of Stents. From top to bottom are the balloon-expandable Palmaz stent, the self-expanding nitinol Symphony stent, and the self-expanding stainless steel Wallstent.

At higher temperatures, the alloy adopts a crystalline austenite state (metallurgic property of shape memory alloys in which the crystalline structure is symmetric) which makes the stent rigid, thereby providing more radial force.

Flexibility is determined by the same properties that govern radial force. BE stents require a force to change conformation. Thus, these stents are less able to maneuver through tortuous vessels. BE stents are susceptible to deformation in mobile arteries because the torque required to maneuver them may enact a conformational change in the stent. In contrast, the nitinol stent, while in the martensite state, can be easily deformed and, therefore, is more suitable for arterial anatomy, which requires significant maneuverability to reach the target lesion. Interestingly, nitinol may change states not only in the setting of temperature change, but also in response to external compression. These qualities afford nitinol stents improved flexibility in mobile arteries after implantation. Such is not the case for BE stents ([Fig. 69.2](#)).

Radiopacity is a consideration important in stent deployment. The material used in stent construction is a major determinant of radiopacity. Stainless steel is more visible than nitinol; thus BE stents are, generally, more visible on radiographic imaging than SE stents. Improved visibility leading to increased accuracy of deployment must be considered in the choice of the appropriate stent for a given indication ([Fig. 69.3](#)).

Cell Size: Open and Closed Cells

Stent cell size should be considered in the selection of the best stent for a given clinical situation. *Cell size* refers to the area outlined by connected metallic components within a stent. Stents with a large cell size are labeled “open cell” stents, and those with a small cell size are termed “closed cell” stents. The cell size of a stent and the connection of the metallic wires to each other may influence performance. A closed cell stent has consistent

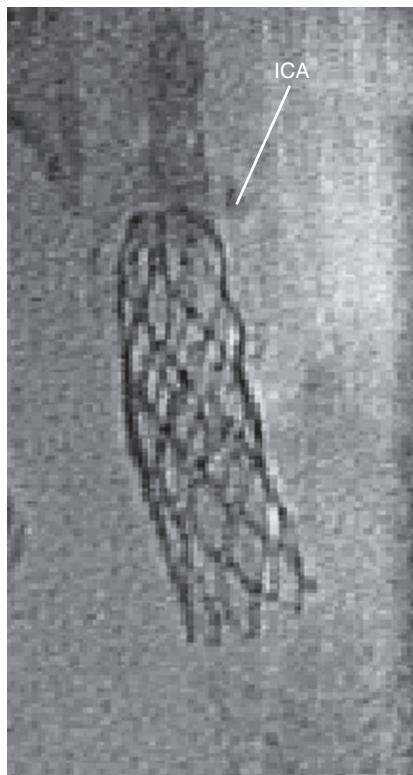


Figure 69.2 This balloon-expandable stent in the cervical portion of the internal carotid artery (ICA) is deformed at the distal endpoint where the carotid artery is mobile and susceptible to external compression.

interconnection of all stent wires throughout its length. This consistency provides a fixed area of interstices within the stent and uniform coverage of the vessel wall. Such construction decreases the free cell area, and may trap fractured plaque at the time of deployment, limiting distal embolization. However, this configuration makes a stent less flexible and conformable. Considering the previously mentioned advantage of the SE stent, the closed cell stent may have more difficulty matching the tortuosity and change in luminal diameter across a vessel length. Conversely, in open cell stents, the wires are not interconnected throughout the entire stent. This feature allows for a greater range of movement between the stent components and leads to added flexibility and conformability. It also results in significantly more vessel wall exposure between stent struts and greater potential for debris to embolize during deployment or balloon dilatation. Free cell area can vary from 1.08 mm^2 in the smallest closed cell stent to 11.48 mm^2 in the largest open cell stent.²⁷

The efficacy of cell design to decrease the risk of embolic phenomena during stenting has yet to be determined. Stent cell size has received the most attention in the treatment of carotid lesions but may also have implications at other sites. Hart et al.³³ demonstrated a significant reduction in rates of stroke, transient ischemic attack, and death when closed cell stents were compared with open cell stents in a series of 701 carotid stent implantations. The odds ratio was most significant in treatment of symptomatic lesions. A larger study combining patients from 10 European centers demonstrated no significant difference, even in symptomatic lesions, between the two stent designs.³⁴ Because closed cell stents are less flexible, a bias

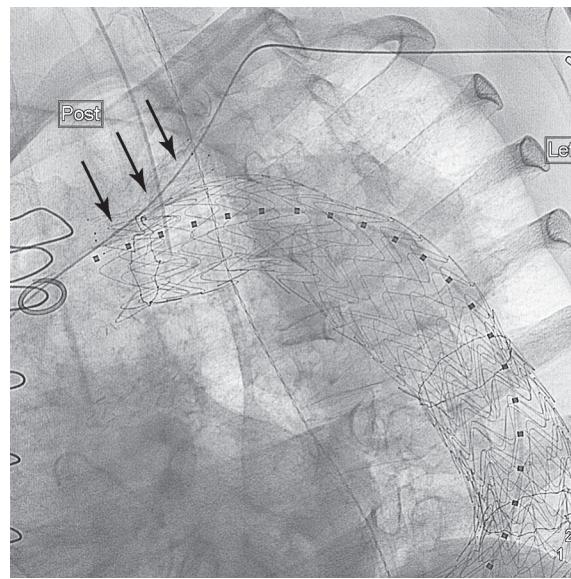


Figure 69.3 A flexible nitinol stent is placed across the subclavian artery origin (arrows) to maintain patency when a thoracic endograft has covered the ostium.

may exist to use them in straighter, less complicated lesions. Ultimately, the use of an open or closed cell stent remains the prerogative of the clinician because there is no convincing evidence of the superiority of one over the other. The operator should seek ideal stent characteristics based on both the nature of the lesion and its location.

Balloon-Expandable Stents

BE stents are optimal in clinical scenarios where high radial force and precise deployment are imperative. Unfortunately, the characteristics of BE stents may also limit deliverability to target lesions. Because they are mounted on balloons, BE stents are at risk for dislodgement both during transit to their target and while crossing the lesion. For this reason, it is recommended that a BE stent be delivered through a guiding catheter, or sheath, over a stiff guide wire. The guiding sheath should be advanced beyond the target lesion before the stent is delivered to the deployment site. Once the stent is positioned at the lesion, the sheath is retracted to allow for stent deployment. The BE stent is deployed as the balloon is inflated to nominal pressure. The balloon is designed to inflate at both ends simultaneously to prevent forward slippage (“watermelon seeding”) of the stent off the balloon before complete deployment.

The BE stent achieves a size corresponding to the degree to which the balloon is expanded. Because this stent is deployed by expansion, vigorous oversizing of the stent in relation to the vessel is not recommended. However, one advantage of the BE stent is that it can be distended to a larger diameter if optimal vessel apposition is not obtained. Of note, aggressive oversizing of the stent with a larger balloon will foreshorten the stent and weaken its struts, leading to increased risk of stent failure.

Innate characteristics of BE stents, including minimal displacement with deployment, make them ideal for treating difficult lesions in which precise placement is paramount. Thus, BE stents are widely used to treat ostial lesions of aortic branch

vessels, such as renal, common iliac, and subclavian arteries, where the lesions are anatomically fixed and thus have little potential for stent deformation with movement. In addition, plaque at bifurcations tend to be more calcific and prone to dissection.

The construction of the BE stent also accounts for its major limitations. When the segment being treated transitions across a branch point from a larger into a smaller artery, the high radial force across arteries that have different diameters make a BE stent inappropriate; examples of such branch points include the iliac and carotid bifurcations. In these settings, the rigid size constraints of the BE stent may not allow for adequate apposition to the entire treated segment. Furthermore, these transitions are frequently mobile and may lead to stent deformation. In certain situations, such as treatment of renal and carotid stenoses, the consequences of embolization are severe. Predilation should be considered with small balloons to improve subsequent stent deliverability and to prevent embolism or dissection. Finally, a BE stent may fracture or retain a new conformation when stressed by outside forces. This risk of deformation affects the decision to use a BE stent across the inguinal ligament or joints. In these positions, the risk of stent compression with fracture and subsequent vessel occlusion is increased. Care must also be taken when one is operating on an artery treated with a BE stent, as clamping may lead to permanent conformational change or stent fracture.

Self-Expanding Stents

SE stents are better suited for tortuous lesions or those traversing vessels of variable diameters. These stents are more flexible than BE stents (Fig. 69.4) and can be delivered through vessels that create more torque within the catheter. To maintain the stent in its constrained form during transit to the lesion, the stent is covered by an outer sheath on the mounting catheter. When this sheath is withdrawn, the stent is allowed to take its natural shape. As such, SE stents do not require that guiding catheters or sheaths be advanced beyond the target lesion first. Deployment of SE stents requires sequential pull-back of the constraining sheath from the distal to proximal end of the delivery catheter. During this maneuver, the stent can inadvertently advance forward or be retracted by the operator. This can lead to maldeployment and must be considered by the operator prior to final deployment maneuvers.

Another factor to consider in the use of an SE stent is the need for adequate oversizing. As mentioned previously, flow dynamic models demonstrate optimal shear environments at 10% oversizing. It is essential to choose a stent that apposes the vessel wall on deployment given it cannot be overdilated. In the instance in which a deployed SE stent is undersized for a given vessel, a second, larger-diameter stent can be deployed within it to aid with stent fixation. A BE stent is preferred in this circumstance since its increased radial force can overcome the nominal diameter of the SE stent.

Stent Grafts (Covered Stents)

Stent grafts, or covered stents, have expanded the use of endovascular technology beyond their contribution to the treatment

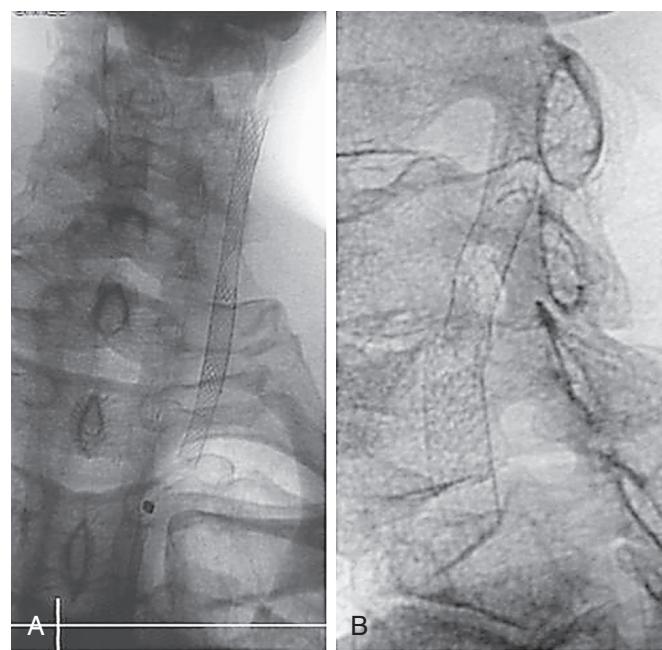


Figure 69.4 Plain radiographs of a stainless steel self-expanding stent (A) and a nitinol self-expanding stent (B) show the superior visibility of the stainless steel stent.

of aortic aneurysms. A covered stent may be considered the ultimate closed cell stent, with the inherent applications and limitations of complete coverage of the treatment area. Stent grafts can be categorized on the basis of graft material or deployment characteristics. Polyester (e.g., Wallgraft [Boston Scientific]) and polytetrafluoroethylene stent grafts (e.g., Viabahn and VBX [W.L. Gore, Flagstaff, AZ]; iCAST [Atrium USA, Hudson, NH]; Jostent [Abbott, Abbot Park, IL]; and Fluency [Bard Peripheral Vascular, Inc., Tempe, AZ]) are currently available. Some stent grafts are balloon-expandable (e.g., VBX and iCAST) whereas others are self-expanding (e.g., Viabahn, Jostent, Wallgraft). Amongst stent grafts, different deployment mechanisms and delivery characteristics can impact clinical utility. SE stent deployment can be distal to proximal (Jostent, Wallgraft, W.L. Gore Internal Iliac branch component) or proximal to distal (Viabahn). This variability allows stent grafts to be utilized in a wide variety of lesions.

Stent grafts provide the inherent advantage of continuous exclusion of the vessel wall from luminal flow. Historically, this feature allows for complete exclusion of vessel defects, such as aneurysm, arteriovenous fistula, pseudoaneurysm, embolic plaque, and perforation. Several case reports have demonstrated the utility of stent grafts in acute vascular trauma. True aneurysms of peripheral arteries, such as popliteal or visceral artery aneurysms, are also amenable to treatment with covered stents.³⁵ Stent grafts have been deployed into the subclavian artery to treat aneurysmal degeneration, although special care should be taken to rule out an associated thoracic outlet syndrome in those patients who may require further surgical cervical or first rib resection.³¹

Stent grafts can be utilized to trap debris within the treated lesion. This approach, in theory, lessens the risk of embolization during vessel dilation. Embolization has been shown to occur

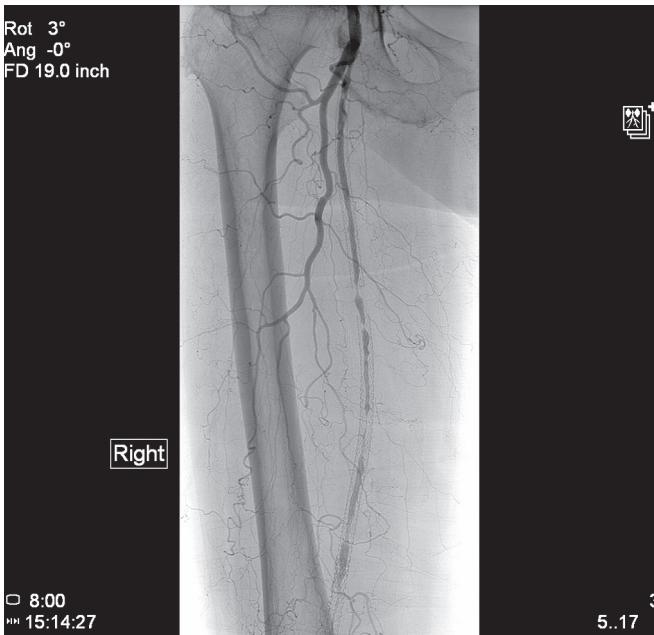


Figure 69.5 Angiographic image of dense neointimal reaction through the interstices of a stent that was placed in a superficial femoral artery 12 months earlier.

in both *ex vivo* and *in vivo* models of angioplasty in several arterial beds.^{32,36,37} Therefore, the use of stent grafts may prove to be an effective treatment of lesions in which embolization risks causing significant morbidity. However, stent graft use may be limited in certain locations where coverage of branch points or collateral vessels is not acceptable.

Another potential use for stent grafts is to treat long lesions of the superficial femoral artery (SFA). In this position, the covered stent provides protection from embolization during deployment and theoretically provides a barrier to smooth muscle cell migration and neointimal growth within the treated segment. The SFA often has a large plaque burden that can hasten failure of a BM stent due to an aggressive neointimal response and ingrowth by medial smooth muscle cells (Fig. 69.5). In a randomized comparison, Kedora et al.³⁸ demonstrated equivalent rates of patency and limb salvage in a stent graft and a prosthetic bypass for various lesions in the above-knee position, treating various lesions with comparable runoff. However, a rigorous, randomized trial has not compared stent graft placement with popliteal bypass from femoral to above the knee using a vein conduit. A drawback of stent graft use is the potential of exclusion of important branches or collaterals. When the stent graft is deployed, collaterals may be covered within the treated segment; therefore, subsequent stent thrombosis may lead to worse limb ischemia than was present before treatment.

SELECTION OF STENT

After consideration of the various stent characteristics, the selection of an appropriate stent depends on plaque morphology, external forces, anatomic location, and branch locations. First and foremost, the stent must treat the primary lesion.



Figure 69.6 (A, B) Photographs of an endarterectomized carotid plaque that had embolized and caused symptoms. This type of plaque is thought to be a greater risk for periprocedural embolization when an open-cell stent is used to cover the stenosis.

Plaque Morphology

If there is concern about microembolization of debris with stent deployment, a covered stent or closed-cell stent should be used. Procedural and early postprocedural embolization associated with carotid stenting can have significant clinical sequelae (Fig. 69.6). Additional data about plaque morphology may help predict which lesions are more likely to embolize through the interstices of the stent. Some researchers have used ultrasound technology to evaluate a gray-scale median to determine the embolization potential of a specific carotid plaque.³⁹ Magnetic resonance or computed tomographic imaging may also provide morphologic plaque information about lipid content that can help the clinician choose a stent type.⁴⁰

Additionally, if stenting is indicated in the setting of possible fresh thrombus, one should consider selecting a covered stent. Although it may be difficult to differentiate a stenotic plaque from an organized thrombus, clinical or angiographic evidence of distal embolization should raise concern about a proximal lesion that is unstable and prone to repeated embolization.

during manipulation. Jeyabalan et al. reported on 25 cases treated with endovascular strategies for treatment of embolizing thoracoabdominal lesions. They describe using a combination of preoperative CT, intraoperative transesophageal echocardiography (TEE) and intravascular ultrasound (IVUS) for device selection, treatment length and ensuring only mobile plaque was covered. In this study, no clinical signs of recurrent embolization were seen during the follow-up period.⁴¹ If a covered stent cannot be used, one should consider various embolic protection methods, such as filter wires or flow reversal devices. Alternatively, open arterial exposure may be used to flush debris away from the distal vascular bed.

External Forces

After assessment of the luminal surface of the artery and its lesion-specific pathology, the clinician must also consider the potential external forces that may affect the stent in its designated location. Extrinsic forces on the origins of supra-aortic trunks are often minimal, but the extrathoracic carotid or subclavian arteries can be subject to significant compressive forces from the surrounding musculoskeletal structures. Examples include compression of the subclavian artery by a cervical rib, or the axillary artery by a hypertrophic pectoralis muscle or axillary manipulation. A potentially catastrophic example includes compression or possible thrombosis of a carotid stent from aggressive rotation or external pressure on the neck, resulting in decreased cerebral perfusion or stroke. Because of these concerns, SE stents are often chosen for these more mobile areas given their greater resistance to external forces.

Anatomic Location

In atherosclerotic lesions involving the **celiac artery**, BE stents are commonly used and are associated with good patency. Although access can be gained by either the brachial or femoral approach, historically brachial approach is preferred because it allows for easier cannulation of the celiac artery, however the introduction of steerable sheaths (e.g. Destino [Oscor, Palm Harbor, FL], TourGuide [Medtronic, Minneapolis, MN]) have made successful cannulation of challenging target vessels from a femoral approach a feasible option.⁴² Careful angiographic evaluation in multiple planes is warranted to ensure exact deployment of the stent short of the main division of the celiac artery, extending into the aorta slightly. When stenosis of the celiac artery origin is related to compression by the median arcuate ligament, stenting is contraindicated and open surgical or laparoscopic division of the arcuate ligament followed by endovascular or open reconstruction of the celiac lesion is typically indicated.

Superior mesenteric artery and renal ostial stenoses are typically treated with BE stents because disease is typically associated with extensive atherosclerotic plaque extending from the aortic wall (Fig. 69.7). An adequate landing zone proximal to the middle colic and inferior pancreaticoduodenal arteries must exist to avoid occlusion of these important branches. A covered BE stent may provide better embolic protection than

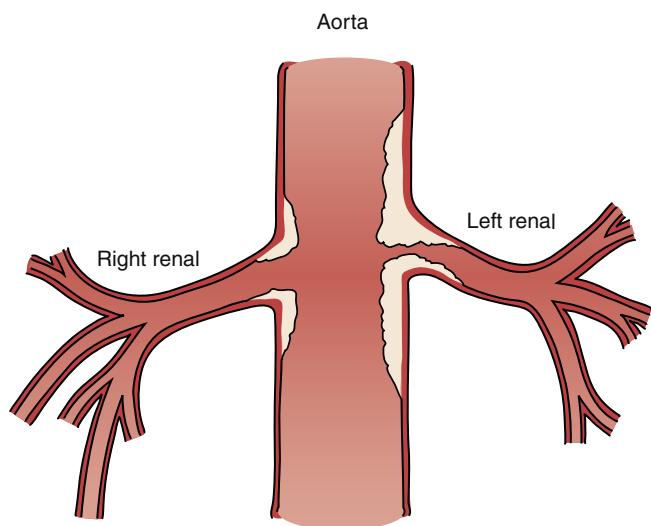


Figure 69.7 The atherosclerotic plaque of a renal artery stenosis originates in the aortic wall as the line drawing depicts. This type of plaque is susceptible to elastic recoil with angioplasty alone, and is best treated with a balloon-expandable stent that protrudes slightly into the aortic lumen to maintain improved luminal flow.

a BM stent. There are some preliminary reports that covered stents may have more resistance to restenosis than BM stents in the mesenteric circulation.⁴³ Covered stents are commonly used in mesenteric and renal arteries as adjuncts in complex endovascular thoracoabdominal aneurysm repair with good patency.^{44,45} Additionally, with increased complexity of endovascular approaches to thoracoabdominal aneurysms, Khouri et al. has recently described a combination of covered and bare devices, with the use of BM stents beyond covered stents to prevent kinks in complex anatomy.⁴⁶

SE stents may be superior for non-orificial lesions in the renal and mesenteric vasculature, particularly those associated with dissection. Covered SE stents can be ideal in nonatherosclerotic pathologies, such as pseudoaneurysms associated with pancreatitis. More distal occlusive lesions of the mesenteric and renal vessels often can be treated with balloon angioplasty alone because of the high flow and small caliber of these vascular beds.

The **left common iliac vein** is another location where stents are often used to treat compression, in this case, related to the overlying right common iliac artery (May–Thurner syndrome). Although most patients with anatomic left common iliac vein compression are asymptomatic, edema or deep venous thrombosis (DVT) may result. After lytic therapy for DVT, the underlying stenosis/compression may be exposed, revealing an indication for treatment. Most clinicians recommend utilizing an oversized BM SE stent in this anatomic location to provide the appropriate radial force and avoid stent migration. BE stents are more likely to cause perforation and are relatively contraindicated in venous disease.

The **distal abdominal aorta and the iliac arteries** are prone to extensive plaque formation that can cause ischemic symptoms in the lower extremities. Treating a proximal common iliac stenosis often requires a “kissing stent” technique,^{47,48} in which stents are placed concurrently in both common iliac

arteries to prevent the shift of the aortic bifurcation plaque into the contralateral lumen. The two stents are deployed simultaneously, matching their position in the distal aorta and proximal iliac arteries. Although both covered and BM stents can be used in this location, the Covered Versus Balloon Expandable Stent Trial (COBEST) found that covered stents had a significantly higher freedom from restenosis when compared with BM stents (hazard ratio [HR], 0.35; 95% confidence interval [CI], 0.15–0.82; $P = 0.02$), however freedom from occlusion was not statistically different in all TASC lesions.⁴⁹ The COBEST trial 5-year results found that covered stents had a significantly higher patency at long-term follow-up (18, 24, 48 and 60 months) with particular benefit for TASC C and D lesions. They did find, however, that the choice of stent was not associated with the rate of limb amputations.⁵⁰ The covered stent used in the trial was the Advanta V12 balloon-expandable covered stent (Atrium Medical Corp, Hudson, NH) compared to multiple BM balloon expandable stents including Palmaz Genesis (Cordis Corp, East Bridgewater, NJ); Express LD iliac stent (Boston Scientific, Natick, MA); Assurant Cobalt iliac stent (Medtronic, Minneapolis, MN); Peiron (Biotronik, Berlin, Germany); and AVE-Bridge (Medtronic, Minneapolis, MN). A small number of devices used (5.8%) were SE stents. Since the COBEST trial, other covered balloon-expandable stents are available including the Gore Viabahn balloon-expandable endoprosthesis (VXB Stent-Graft). Panneton et al. conducted a prospective, multicenter, nonrandomized clinical study which has demonstrated 94.5% 1-year primary patency and 99% assisted primary patency with most patients maintaining or improving in their baseline functional status.⁵¹ Although both BE and SE stent types are used in the proximal iliac arteries, the BE type are more often used for short lesions and the SE type for longer lesions that traverse the change in artery caliber past the iliac bifurcation. Lesions in the external iliac artery are usually treated with SE stents because of the typical tortuosity of the artery, however short BE stents can be used also.

Primary patency of endovascular repair has traditionally fallen short of open revascularization for complex aortoiliac pathology, but secondary patency rates have been favorable.⁵² A recent multicenter study demonstrated similar primary, primary-assisted and secondary patency rates between kissing stents and open surgery.⁵³ Published series show promise for the use of covered SE stents extending from the distal external iliac into the common femoral arteries.^{54,55} The covered construction theoretically makes stent fracture less relevant because the graft may prevent the stent from injuring the underlying vessel wall. Stent grafts in this position can be sewn directly, allowing for femoral patch angioplasty or interposition grafting, if needed, to obtain adequate outflow. Additionally, femoral endarterectomy can be completed first followed by deployment of SE stents in the external iliac artery with the distal end of the stent landing just distal to the proximal endarterectomy ledge as described by Nelson et al.⁵⁶

For the **infrainguinal arteries**, SE stents are utilized preferentially with a few exceptions. Stents in the common femoral arteries are generally contraindicated for two reasons. First,

the stent could cover the origin of the profunda femoris artery and compromise flow into this vital artery. Although arteries often remain patent after they have been “jailed” (e.g., hypogastric artery, external carotid artery), the extent of disease in the common femoral artery and the potential consequences of occluding the profunda femoris have a more serious effect on long-term limb salvage. Second, the common femoral artery is a major access point for vascular procedures throughout the body, and a stent in this position may adversely affect subsequent access. The common femoral artery is easily accessible surgically, and repair or endarterectomy can be performed with minimal risk. Stenting of the infrainguinal arteries for occlusive disease is indicated for the failure of primary angioplasty. Yajun et al.⁵⁷ demonstrated in a meta-analysis that short-term results are better with adjunctive stenting, but long-term patency is no different.

Dialysis outflow tracts are prone to treatment failure owing to the unique hemodynamic environment created by AV fistulas or grafts. Stent-supported revascularization of the axillo-subclavian veins and cephalic arch have been proven to improve access salvage over that with angioplasty alone.⁵⁸ Because central stenosis often occurs in areas of significant mobility, careful evaluation for thoracic outlet compression should be made before deployment of a stent. Given these considerations, a large SE stent is recommended. The failure mode in these situations relates to neointimal hyperplasia, so use of a stent graft is not unreasonable and is preferred in cases of venous disruption from high-pressure angioplasty. Quaretti et al. conducted a 10-year retrospective review in 70 dialysis patients comparing patency of covered vs. BM stents for the treatment of symptomatic central venous stenosis. They found stent grafts had higher primary patency (follow-up 3–24 months) and lower restenosis rates as well as fewer reinterventions when compared to BM stents.⁵⁹

The hemodynamics of the cephalic arch results in a common failure mode of cephalic vein-based access. Initial experience with BM stenting demonstrated a high incidence of recurrence. SE covered stents have been shown to be superior to BM stents in the treatment of these lesions.⁶⁰ Care must be taken to avoid encroachment of the stent into the axillary vein.

The venous anastomosis is the most common failure site of prosthetic AV grafts.⁶¹ The use of covered stents has been especially promising in treating these lesions. In a randomized trial, Haskal et al.⁶² demonstrated the superiority of stent grafts over angioplasty alone for the treatment of venous anastomotic stenosis. Covered stents change the hemodynamics of these anastomoses, converting them to a functional end-to-end anastomosis, reducing the neointimal hyperplastic response. Stent grafts in dialysis access commonly fail secondary to thrombosis. However, secondary patency of these grafts is promising, and they appear to be an appropriate first line of therapy in venous anastomotic complications of AV grafts.

Branch Location

Once the external forces that may affect stent choice have been reviewed, the clinician must also consider the extent of disease



Figure 69.8 This endarterectomy specimen shows the extent of the plaque that originates in the aortic wall but impedes flow through the branch vessel.

relative to vessel branch points. When plaque radiographically appears at the origin of a vessel, histologically it will extend into the “parent” artery (Fig. 69.8). For example, an ostial renal artery stenosis may appear isolated to the renal artery on angiography when, in fact, the majority of the plaque is within the wall of the aorta. This extensive plaque requires a high radial force stent with accurate deployment, therefore the BE stent works best in this scenario. The BE stent is typically deployed with a small portion extending into the aorta to fully address the aortic portion of the plaque.

FAILURE MODES

Although stents are designed to maintain patency of the treated vessel, the presence of a foreign material in the arterial bed may lead to failure through neointimal hyperplasia and vessel restenosis or thrombosis. Studies have demonstrated that acute inflammatory changes occur with the disruption of the endothelial surface. After the acute phase, the arterial wall continues to react through a remodeling process, which includes acute and chronic changes with a smooth muscle response that can be seen as neointimal hyperplasia.¹⁴ This chronic inflammatory change can lead to an obstructing lesion that creates a recurrent stenosis or *in situ* thrombosis.

Stents are designed using various metallic components that have long, but finite, lifespans under the mechanical stress of the cardiac cycle. Stent fracture or failure may be the result of metallic corrosion, which may, in turn, be related to the local vascular environment, external forces, and interaction with other intravascular materials^{63–67} (Fig. 69.9). In a common clinical scenario, when two overlapping stents are placed, the materials of the two stents can be additive in the corrosive process (Fig. 69.10). The use of an appropriate-length stent to avoid device overlap may lead to fewer fracture-induced occlusions and long SE stents are now available (>20 cm). Overlap within tortuous segments seems to be especially prone to failure.⁶⁸ Strategies to decrease occlusion within stented segments include the use of drug-eluting stents (DESs) in overlapped segments⁶⁹ and telescoping of a covered stent inside a bare stent, the graft material theoretically inhibiting the corrosive effect of metal-on-metal interaction. Stents can also release ions into the local vascular environment that can adversely affect

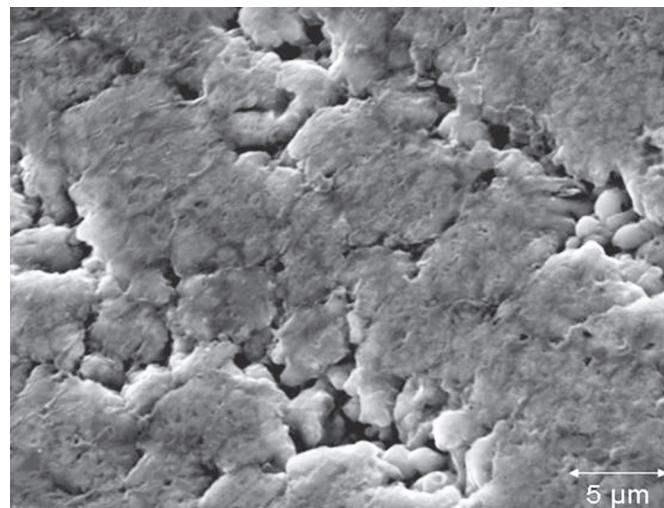


Figure 69.9 Scanning electron microscopy of a corroded nitinol stent that had been deployed in the iliac artery. The stent occluded and the patient ultimately required aortobifemoral bypass and stent explantation. (Photo courtesy Dr. Britta Brott.)

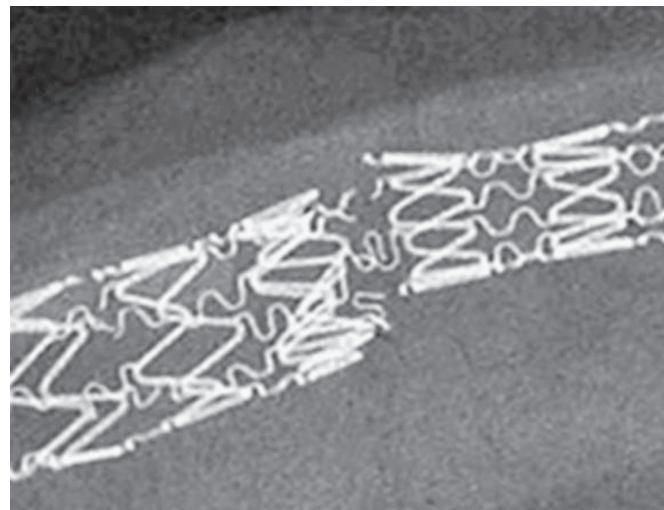


Figure 69.10 Two overlapping coronary stents placed at a tortuous portion in the coronary artery created a stress point that led to galvanic corrosion, stent fracture and recurrent stenosis. (Photo courtesy Dr. Britta Brott.)

the treated lesion. Both stainless steel and nitinol stents have been shown to release cytotoxic agents that may contribute to smooth muscle necrosis, affecting the response of the artery to such a stent.^{25,70}

Drug-Eluting Technology for Neointimal Failure

Many modalities to control the hyperplastic response to an arterial implant have been investigated. Specifically, stents have become a conduit to deliver medication to the local vascular environment in an effort to limit this response to injury. Three chemotherapeutic agents have been attached to BE stents for utilization in the coronary arteries: paclitaxel, sirolimus, and everolimus. These agents have been shown to aggressively inhibit the neointimal response and thereby improve patency

rates. Paradoxically, DESs have created a new late-failure mode of delayed stent thrombosis, due to the lack of endothelialization and minimal incorporation into the associated vessel wall. The exposed raw surface of the stent carries a risk of stent thrombosis as high as 4% after 1 year in the coronary arteries.⁷¹ When evaluating the use of DESs in the peripheral circulation, one must consider that late stent thrombosis of the femoral artery carries a significantly different risk from that of a coronary artery.

Initial clinical trials of DESs in the SFA did not demonstrate better patency than with BM stents. The Sirolimus-Coated Cordis Self-Expandable Stent (SIROCCO) trial compared the results of a SE DES and a SE BM stent, and found near-equivalent restenosis rates: 22.9% for the DES and 22.1% for the BM SE stent at 2 years.⁷² A prospective industry-sponsored trial of a nonpolymer, paclitaxel-coated SFA stent (Zilver PTX, Cook Medical, Bloomington, IN) has shown more promising results. The main arm of the study demonstrated noninferiority of the DES to primary angioplasty, although these data may be unreliable because of an overly high primary failure rate of percutaneous transluminal angioplasty. Interestingly, a separate arm compared BM stents to DESs in patients with failed percutaneous transluminal angioplasty and showed statistically significant better patency with DESs at 1 year.⁷³ Enthusiasm for DES use in the SFA on the basis of these results is hampered by the large number of short lesions and the high percentage of patients with claudication (90%) enrolled in the trial. Subsequent analysis from 12-month results for patients with *de novo* TASC II C & D lesions treated with Zilver PTX stents showed results similar to those of open surgical bypass (77% primary patency rate), fueling the interest in continued investigation into long-term efficacy.⁷⁴

The Preventing Amputations using Drug eluting StEnts (PaRADISE) trial attempted to quantify the impact of DES technology on patients at greatest risk of amputation.⁷⁵ In this noncontrolled prospective study of DESs in tibial intervention, the major amputation rate was 6% at 3 years in patients presenting with critical limb ischemia. Maintenance of limb salvage required a re-intervention rate of 36% at a mean of less than 1 year, but overall survival, renal failure, and limb salvage rates were better than those in historical controls. Although many of these RCTs have shown promise with paclitaxel-coated stents and balloons, Katsanos et al. called urgent attention to this treatment modality when they conducted a meta-analysis of these trials and found a significant increase in all cause death at 2 years in the paclitaxel group compared to controls (7.2% vs. 3.8%, risk ratio [RR] 1.68, 95% CI, 1.15–2.47), with an even increased risk seen at 5 years following intervention (14.7% vs. 8.1%, RR 1.93, 95% CI, 1.27–2.93). Additionally, the authors found a significant relationship between the dose of paclitaxel utilized with a 0.4±0.1% excess risk of death per paclitaxel mg/year ($P<0.001$).⁷⁶ Since this publication many vascular interventionalists have been hesitant to continue to use this technology despite subsequent studies suggesting no such mortality risk.^{77,78} It may be reasonable to use the technology but only in select cases where a discussion is had between the patient and provider regarding the previously published risks.

Treatment of In-Stent Restenosis

As endovascular interventions have become increasingly common in use for the management of *de novo* femoropopliteal stenoses, strategies for maintaining patency have also become of utmost importance. The long-term interaction between stent and vessel can lead to the development of late stenosis or occlusion via neointimal hyperplasia. Various mechanisms have been proposed for the management of in-stent stenosis, including repeat percutaneous transluminal angioplasty (PTA), stenting, atherectomy, or angioplasty or stenting with drug-coated technology. The EXCITE ISR Trial (EXCImer Laser Randomized Controlled Study for Treatment of Femoropopliteal In-Stent Restenosis) demonstrated superiority of laser atherectomy with PTA compared with PTA alone in patients with in-stent stenosis following the prior placement of bare nitinol stents, for both target lesion revascularizations and 30-day major adverse events.⁷⁹ The FAIR (Femoral Artery In-Stent Restenosis) Trial examined the effects of drug-coated balloon (DCB) angioplasty for SFA in-stent restenosis, in comparison with conventional PTA. Lower rates of recurrent restenosis at both 6- and 12-month intervals were seen with interventions using DCBs compared to conventional PTA.⁸⁰ Building off known data regarding utility of DESs for coronary in-stent stenosis, data from the Zilver PTX Global Registry showed favorable results for the treatment of femoropopliteal in-stent restenosis with implantation of the Zilver PTX stent, with 6- and 12-month primary patency rates of 96% and 79%, respectively.⁸¹ The Viabahn-covered stent also demonstrated superiority over PTA at 1- and 2-year primary patency in the RELINE trial.⁸² Interestingly, the lesion lengths treated were nearly double in the RELINE trial compared to trials of drug-coated technology, indicating that stent graft treatment is likely the modality of choice in complex restenotic lesions of the SFA.

NEW DEVELOPMENTS

Absorbable Stents

One approach to mitigate the effect of the long-term interaction between stent and vessel is to create stents composed of biodegradable material. Bioabsorbable stents theoretically provide scaffolding for healing of the vessel before they are eventually absorbed. Although lower extremity data are sparse, absorbable stents in the coronary arteries have shown a 30% mass reduction of neointimal hyperplasia at 12 months, and 60% reduction at 18 months.⁸³ Tamai et al.⁸⁴ reported the use of a poly-L-lactic acid (PLLA) bioabsorbable stent in the coronary arteries of 15 patients with a restenosis rate of 10.5% at 6 months. Even with imaging at 4 years, these investigators found some hyperplasia related to the local stent reaction, but no late stent thromboses were seen.⁸⁵ The effect of bioabsorbable stent degradation may lead to late events, such as embolization with resulting small vessel ischemia. However, this clinical phenomenon has not been well documented. After the initial reports of success with the PLLA stent, Ormiston et al.⁸³ reported the success of attaching everolimus to the PLLA stent to obtain the

benefit of a medicated stent that reduces the intimal response while potentially removing the nidus for late stent thrombosis. These investigators found a decreased neointimal response and reduced cardiac event rate (3.3%) in a series of 30 patients. Although these results seemed promising, the ABSORB II trial fell short with the bioresorbable vascular scaffold being associated with higher post-procedural asymmetry and eccentric morphology.⁸⁶ The Absorb stent was eventually removed from the market in 2017, as the technology had failed to compare to current coronary DES devices. More recently, long-term results of the BIOSOLV-II and -III trials, showed use of a second-generation magnesium based sirolimus-eluting absorbable scaffold in the coronary circulation to be safe, with target lesion failure seen in 6.3% at 3 years.⁸⁷

The bulk of the data regarding the use of bioabsorbable stents in the peripheral circulation examine their efficacy in the femoral segments, with only a small number evaluating their utility in the infrapopliteal circulation. Substantive conclusions regarding efficacy relative to standard therapies are limited, due to the small sample size and heterogeneity in the study designs. Initial 30-day results in the femoral segment appeared promising, however 6-month data demonstrated patency as low as 60%. The AMS INSIGHT trial compared infrapopliteal PTA versus PTA and stenting with bioabsorbable stents. These data showed no difference in 30-day outcomes of amputation or death, but the stenting group showed worse 6-month primary patency than PTA alone.⁸⁸ Ultimately, the currently studied bioabsorbable scaffolds demonstrate safety and technical success in implantation without long-term clinical success in the infrainguinal circulation. Future research may improve this by incorporating various drug technologies into the scaffolds.⁸⁹

FUTURE DEVELOPMENTS

The progressive refinement of revascularization technology remains a consistent goal for clinicians treating vascular disease. Considering that open surgery has been developed over the last 50 years, the endovascular era is still relatively young. Simple dilation of diseased vessels has had limited clinical success, thus leading to intensive efforts to improve those results with intravascular devices, such as stents, and with antiproliferative medications. As with any new technology, new problems have been created. The alteration of hemodynamic variables, such as vessel compliance and shear stress, continues to limit the patency of endovascular intervention. Fortunately, this alteration appears to come at the cost of repeat interventions rather than limb loss. Stents have improved some of these catheter-based treatments, but further modifications are necessary to provide more effective therapies for the patient with vascular disease.

Looking forward, the modification of existing technology, such as bioabsorbable scaffolds, DCBs, or novel treatments for occlusive disease will likely focus on the elimination of stents, and their inherent limitations, completely. The combined use of plaque debulking with drug technology is already being utilized in clinical practice but has not been studied in a systematic fashion. Similarly, the introduction of stem cell technology or genetically engineered constructs, such as viruses to modulate the neointimal response, may render stenting obsolete.⁹⁰

SELECTED KEY REFERENCES

Dyer JF, Watts WG, Ettles DF, Nicholson AA. Mechanical properties of metallic stents: how do these properties influence the choice of stent for specific lesions? *Cardiovasc Interv Radiol.* 2000;23(1):47–54.

The experiment design of this study is pertinent to all physicians who perform peripheral interventions. The key components of stent choice – flexibility, trackability, radiopacity, etc. – are evaluated for several stent types. The results and discussion serve as an excellent guide to optimal stent choice for various lesions.

LaDisa JF Jr, Olson LE, Guler I, et al. Stent design properties and deployment ratio influence indexes of wall shear stress: a three-dimensional computational fluid dynamics investigation within a normal artery. *J Appl Physiol.* 2004;97(1):424–430; discussion 416.

Provides a mathematical basis for stent selection in avoiding negative shear environments and defines a precise indication for proper stent sizing.

Mauri L, Hsieh W, Massaro JM, Ho KL, D'Agostino R, Cutlip DE. Stent thrombosis in randomized clinical trials of drug-eluting stents. *N Engl J Med.* 2007;356:1020–1029.

Late stent thrombosis continues to be a major limitation to the utilization of drug-eluting stents (DESs). The implications of the need for continued antiplatelet therapy affect both cardiovascular treatments, but can impact other patient outcomes such as need for abdominal procedures. This article summarizes the data on antiplatelet therapy for DESs and nuances for proper perioperative management.

Palmaz JC, Bailey S, Marton D, Sprague E. Influence of stent design and material composition on procedure outcome. *J Vasc Surg.* 2002;36(5):1031–1039.

Dr. Palmaz's contributions to stent technology are as great as that of any single individual. He provides a comprehensive review of several factors that lead to stent failure, including stent topography, metallic composition, corrosion, and contamination.

Sullivan TM, Ainsworth SD, Langan EM, et al. Effect of endovascular stent strut geometry on vascular injury, myointimal hyperplasia, and restenosis. *J Vasc Surg.* 2002;36(1):143–149.

Demonstrates the potential for vessel injury and negative remodeling that can be caused by the stent itself. Presents a pertinent review of the histologic findings associated with peri-stent inflammation.

A complete reference list can be found online at www.expertconsult.com.

REFERENCES

1. Lee ES, et al. Comparing patency rates between external iliac and common iliac artery stents. *J Vasc Surg.* 2000;31(5):889–894.
2. Ward MR, et al. Response to balloon injury is vascular bed specific: a consequence of de novo vessel structure? *Atherosclerosis.* 2000;151(2):407–414.
3. Schillinger M, et al. Inflammatory response to stent implantation: differences in femoropopliteal, iliac, and carotid arteries. *Radiology.* 2002;224(2):529–535.
4. Dotter CT, Judkins MP. Transluminal treatment of arteriosclerotic obstruction. Description of a new technic and a preliminary report of its application. *Circulation.* 1964;30:654–670.
5. Gruentzig AR. Percutaneous transluminal coronary angioplasty. *Semin Roentgenol.* 1981;16(2):152–153.
6. Gruentzig AR, et al. Long-term follow-up after percutaneous transluminal coronary angioplasty. The early Zurich experience. *N Engl J Med.* 1987;316(18):1127–1132.
7. Nobuyoshi M, et al. Restenosis after successful percutaneous transluminal coronary angioplasty: serial angiographic follow-up of 229 patients. *J Am Coll Cardiol.* 1988;12(3):616–623.
8. Nobuyoshi M, et al. Restenosis after percutaneous transluminal coronary angioplasty: pathologic observations in 20 patients. *J Am Coll Cardiol.* 1991;17(2):433–439.
9. Isles CG, Robertson S, Hill D. Management of renovascular disease: a review of renal artery stenting in ten studies. *QJM.* 1999;92(3):159–167.
10. Kandarpa K, et al. Transcatheter interventions for the treatment of peripheral atherosclerotic lesions: part II. *J Vasc Interv Radiol.* 2001;12(7):807–812.
11. Gray BH, et al. High incidence of restenosis/reocclusion of stents in the percutaneous treatment of long-segment superficial femoral artery disease after suboptimal angioplasty. *J Vasc Surg.* 1997;25(1):74–83.
12. Schillinger M, et al. Restenosis after percutaneous transluminal angioplasty in the femoropopliteal segment: the role of inflammation. *J Endovasc Ther.* 2001;8(5):477–483.
13. Sullivan TM, et al. Effect of endovascular stent strut geometry on vascular injury, myointimal hyperplasia, and restenosis. *J Vasc Surg.* 2002;36(1):143–149.
14. Farb A, et al. Pathology of acute and chronic coronary stenting in humans. *Circulation.* 1999;99(1):44–52.
15. Whelan DM, van Beusekom HM, van der Giessen WJ. Foreign body contamination during stent implantation. *Cathet Cardiovasc Diagn.* 1997;40(3):328–332.
16. LaDisa Jr JF, et al. Stent design properties and deployment ratio influence indexes of wall shear stress: a three-dimensional computational fluid dynamics investigation within a normal artery. *J Appl Physiol.* 2004;97(1):424–430; discussion 416.
17. LaDisa Jr JF, et al. Alterations in wall shear stress predict sites of neointimal hyperplasia after stent implantation in rabbit iliac arteries. *Am J Physiol Heart Circ Physiol.* 2005;288(5):H2465–H2475.
18. He HP, et al. Impact of plaque calcification and stent oversizing on clinical outcomes of atherosclerotic femoropopliteal arterial occlusive disease following stent angioplasty. *Eur J Vasc Endovasc Surg.* 2019;58(2):215–222.
19. Sommer CM, et al. Impact of stent design on in-stent stenosis in a rabbit iliac artery model. *Cardiovasc Interv Radiol.* 2010;33(3):565–575.
20. Garasic JM, et al. Stent and artery geometry determine intimal thickening independent of arterial injury. *Circulation.* 2000;101(7):812–818.
21. Rogers C, Edelman ER. Endovascular stent design dictates experimental restenosis and thrombosis. *Circulation.* 1995;91(12):2995–3001.
22. Sprague EA, Luo J, Palmaz JC. Human aortic endothelial cell migration onto stent surfaces under static and flow conditions. *J Vasc Interv Radiol.* 1997;8(1 Pt 1):83–92.
23. Palmaz JC, Benson A, Sprague EA. Influence of surface topography on endothelialization of intravascular metallic material. *J Vasc Interv Radiol.* 1999;10(4):439–444.
24. Kastrati A, et al. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STERO) trial. *Circulation.* 2001;103(23):2816–2821.
25. Shih CC, et al. The cytotoxicity of corrosion products of nitinol stent wire on cultured smooth muscle cells. *J Biomed Mater Res.* 2000;52(2):395–403.
26. Palmaz JC, et al. Influence of stent design and material composition on procedure outcome. *J Vasc Surg.* 2002;36(5):1031–1039.
27. Flueckiger F, et al. Strength, elasticity, and plasticity of expandable metal stents: in vitro studies with three types of stress. *J Vasc Interv Radiol.* 1994;5(5):745–750.
28. Dyet JF, et al. Mechanical properties of metallic stents: how do these properties influence the choice of stent for specific lesions? *Cardiovasc Interv Radiol.* 2000;23(1):47–54.
29. Grenacher L, et al. Resistance to hoop stress in balloon expandable stents: evaluation in an ex vivo model. *Invest Radiol.* 2003;38(2):65–72.
30. Grenacher L, et al. In vitro comparison of self-expanding versus balloon-expandable stents in a human ex vivo model. *Cardiovasc Interv Radiol.* 2006;29(2):249–254.
31. Schoder M, et al. Elective and emergent endovascular treatment of subclavian artery aneurysms and injuries. *J Endovasc Ther.* 2003;10(1):58–65.
32. Edwards MS, et al. Atheroembolism during percutaneous renal artery revascularization. *J Vasc Surg.* 2007;46(1):55–61.
33. Hart JP, et al. Do device characteristics impact outcome in carotid artery stenting?. *J Vasc Surg.* 2006;44(4):725–730; discussion 730–731.
34. Schillinger M, et al. Does carotid stent cell design matter? *Stroke.* 2008;39(3):905–909.
35. Sfyroeras GS, et al. Flow-diverting stents for the treatment of arterial aneurysms. *J Vasc Surg.* 2012;56(3):839–846.
36. Lam RC, et al. Incidence and clinical significance of distal embolization during percutaneous interventions involving the superficial femoral artery. *J Vasc Surg.* 2007;46(6):1155–1159.
37. Rapp JH, et al. Subclinical embolization after carotid artery stenting: new lesions on diffusion-weighted magnetic resonance imaging occur postprocedure. *J Vasc Surg.* 2007;45(5):867–872; discussion 872–874.
38. Kedora J, et al. Randomized comparison of percutaneous Viabahn stent grafts vs prosthetic femoral-popliteal bypass in the treatment of superficial femoral arterial occlusive disease. *J Vasc Surg.* 2007;45(1):10–16; discussion 16.
39. Biasi GM, et al. Carotid plaque echolucency increases the risk of stroke in carotid stenting: the Imaging in Carotid Angioplasty and Risk of Stroke (ICAROS) study. *Circulation.* 2004;110(6):756–762.
40. Altaf N, et al. Detection of intraplaque hemorrhage by magnetic resonance imaging in symptomatic patients with mild to moderate carotid stenosis predicts recurrent neurological events. *J Vasc Surg.* 2008;47(2):337–342.
41. Jeyabal G, et al. Endovascular strategies for treatment of embolizing thoracoabdominal aortic lesions. *J Vasc Surg.* 2014;59(5):1256–1264.
42. Gallitto E, et al. Steerable Sheath for Cannulation and Bridging Stenting of Challenging Target Visceral Vessels in Fenestrated and Branched Endografting. *Ann Vasc Surg.* 2020;67:26–34.
43. Oderich GS, et al. Comparison of covered stents versus bare metal stents for treatment of chronic atherosclerotic mesenteric arterial disease. *J Vasc Surg.* 2013;58(5):1316–1323.
44. Grimme FA, et al. Visceral stent patency in fenestrated stent grafting for abdominal aortic aneurysm repair. *J Vasc Surg.* 2014;59(2):298–306.
45. Spear R, et al. One Year Outcomes of 101 BeGraft Stent Grafts used as Bridging Stents in Fenestrated Endovascular Repairs. *Eur J Vasc Endovasc Surg.* 2018;55(4):504–510.
46. Khoury MK, et al. Visceral stent patency after fenestrated endovascular aneurysm repair using bare-metal stent extensions versus covered stents only. *J Vasc Surg.* 2020;71(1):23–29.
47. Mendelsohn FO, et al. Kissing stents in the aortic bifurcation. *Am Heart J.* 1998;136(4 Pt 1):600–605.
48. Scheinert D, et al. Stent-supported reconstruction of the aortoiliac bifurcation with the kissing balloon technique. *Circulation.* 1999;100(19 Suppl):II295–300.

49. Mwipatayi BP, et al. A comparison of covered vs bare expandable stents for the treatment of aortoiliac occlusive disease. *J Vasc Surg.* 2011;54(6):1561–1570.
50. Mwipatayi BP, et al. Durability of the balloon-expandable covered versus bare-metal stents in the Covered versus Balloon Expandable Stent Trial (COBEST) for the treatment of aortoiliac occlusive disease. *J Vasc Surg.* 2016;64(1):83–94.e1.
51. Panneton JM, et al. Three-year follow-up of patients with iliac occlusive disease treated with the Viabahn balloon-expandable endoprosthesis. *J Endovasc Ther.* 2020;27(5):728–736.
52. Jongkind V, et al. A systematic review of endovascular treatment of extensive aortoiliac occlusive disease. *J Vasc Surg.* 2010;52(5):1376–1383.
53. Dorigo W, et al. A comparison between aortobifemoral bypass and aortoiliac kissing stents in patients with complex aortoiliac obstructive disease. *J Vasc Surg.* 2017;65(1):99–107.
54. Calligaro KD, et al. Results of polytetrafluoroethylene-covered nitinol stents crossing the inguinal ligament. *J Vasc Surg.* 2013;57(2):421–426.
55. Chang RW, et al. Long-term results of combined common femoral endarterectomy and iliac stenting/stent grafting for occlusive disease. *J Vasc Surg.* 2008;48(2):362–367.
56. Nelson PR, et al. Early results of external iliac artery stenting combined with common femoral artery endarterectomy. *J Vasc Surg.* 2002;35(6):1107–1113.
57. Yajun E, et al. Percutaneous transluminal angioplasty (PTA) alone versus PTA with balloon-expandable stent placement for short-segment femoropopliteal artery disease: a metaanalysis of randomized trials. *J Vasc Interv Radiol.* 2008;19(4):499–503.
58. Kakisis JD, et al. Balloon angioplasty vs nitinol stent placement in the treatment of venous anastomotic stenoses of hemodialysis grafts after surgical thrombectomy. *J Vasc Surg.* 2012;55(2):472–478.
59. Quaretti P, et al. Stent grafts provided superior primary patency for central venous stenosis treatment in comparison with angioplasty and bare metal stent: a retrospective single center study on 70 hemodialysis patients. *Vasc Endovascular Surg.* 2016;50(4):221–230.
60. Shemesh D, et al. Angioplasty with stent graft versus bare stent for recurrent cephalic arch stenosis in autogenous arteriovenous access for hemodialysis: a prospective randomized clinical trial. *J Vasc Surg.* 2008;48(6):1524–1531, 1531.e1–2.
61. Naoum JJ, Irwin C, Hunter GC. The use of covered nitinol stents to salvage dialysis grafts after multiple failures. *Vasc Endovascular Surg.* 2006;40(4):275–279.
62. Haskal ZJ, et al. Stent graft versus balloon angioplasty for failing dialysis-access grafts. *N Engl J Med.* 2010;362(6):494–503.
63. Couris AJ. *Degradation of materials in the biological environment.* 2nd ed. Elsevier Academic Press; 2004.
64. Rondelli G, Vicentini B. Localized corrosion behaviour in simulated human body fluids of commercial Ni-Ti orthodontic wires. *Biomaterials.* 1999;20(8):785–792.
65. Shih CC. Electrochemical and SEM characterization of gold-coated stents in vitro. *J. Electrochem Soc.* 2007;154:C326–C330.
66. Thomas KA, et al. Tissue reaction to implant corrosion in 38 internal fixation devices. *Orthopedics.* 1988;11(3):441–451.
67. Cook SD, et al. The in vivo performance of 250 internal fixation devices: a follow-up study. *Biomaterials.* 1987;8(3):177–184.
68. Kapnisis KK, et al. Stent overlapping and geometric curvature influence the structural integrity and surface characteristics of coronary nitinol stents. *J Mech Behav Biomed Mater.* 2013;20:227–236.
69. Aoki J, et al. Chronic arterial responses to overlapping paclitaxel-eluting stents: insights from serial intravascular ultrasound analyses in the TAXUS-V and -VI trials. *JACC Cardiovasc Interv.* 2008;1(2):161–167.
70. Eliades T, et al. Characterization and cytotoxicity of ions released from stainless steel and nickel-titanium orthodontic alloys. *Am J Orthod Dentofacial Orthop.* 2004;125(1):24–29.
71. Mauri L, et al. Stent thrombosis in randomized clinical trials of drug-eluting stents. *N Engl J Med.* 2007;356(10):1020–1029.
72. Duda SH, et al. Drug-eluting and bare nitinol stents for the treatment of atherosclerotic lesions in the superficial femoral artery: long-term results from the SIROCCO trial. *J Endovasc Ther.* 2006;13(6):701–710.
73. Dake MD, et al. Paclitaxel-eluting stents show superiority to balloon angioplasty and bare metal stents in femoropopliteal disease: twelve-month Zilver PTX randomized study results. *Circ Cardiovasc Interv.* 2011;4(5):495–504.
74. Bosiers M, et al. The Zilver® PTX® Single Arm Study: 12-month results from the TASC C/D lesion subgroup. *J Cardiovasc Surg (Torino).* 2013;54(1):115–122.
75. Feiring AJ, et al. Preventing leg amputations in critical limb ischemia with below-the-knee drug-eluting stents: the PaRADISE (PReventing Amputations using Drug eluting StEnts) trial. *J Am Coll Cardiol.* 2010;55(15):1580–1589.
76. Katsanos K, et al. Risk of death following application of paclitaxel-coated balloons and stents in the femoropopliteal artery of the leg: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc.* 2018;7(24):e011245.
77. Katsuki T, et al. Mortality risk following application of a paclitaxel-coated stent in femoropopliteal lesions. *J Endovasc Ther.* 2019;26(5):593–599.
78. Dinh K, et al. Mortality after paclitaxel-coated device use in patients with chronic limb-threatening ischemia: a systematic review and meta-analysis of randomized controlled trials. *J Endovasc Ther.* 2020;27(2):175–185.
79. Dippel EJ, et al. Randomized controlled study of excimer laser atherectomy for treatment of femoropopliteal in-stent restenosis: initial results from the EXCITE ISR trial (EXCImer Laser Randomized Controlled Study for Treatment of Femoropopliteal In-Stent Restenosis). *JACC Cardiovasc Interv.* 2015;8(1 Pt A):92–101.
80. Krankenbergh H, et al. Drug-coated balloon versus standard balloon for superficial femoral artery in-stent restenosis: the randomized Femoral Artery In-Stent Restenosis (FAIR) trial. *Circulation.* 2015;132(23):2230–2236.
81. Zeller T, et al. Treatment of femoropopliteal in-stent restenosis with paclitaxel-eluting stents. *JACC Cardiovasc Interv.* 2013;6(3):274–281.
82. Bosiers M. RELINE study: Randomized comparison of endoluminal grafting with Viabahn vs. PTA for femoral artery in-stent restenosis – 6 month results. Paper presented at: Leipzig Interventional Course. Leipzig, Germany.
83. Ormiston JA, et al. A bioabsorbable everolimus-eluting coronary stent system for patients with single de-novo coronary artery lesions (ABSORB): a prospective open-label trial. *Lancet.* 2008;371(9616):899–907.
84. Tamai H, et al. Initial and 6-month results of biodegradable poly-L-lactic acid coronary stents in humans. *Circulation.* 2000;102(4):399–404.
85. Tsuji T. Four year follow up of biodegradable stent (IGAKI-TAMAI Stent). *Circ J.* 2004;68:135.
86. Suwannasom P, et al. The impact of post-procedural asymmetry, expansion, and eccentricity of bioresorbable everolimus-eluting scaffold and metallic everolimus-eluting stent on clinical outcomes in the ABSORB II trial. *JACC Cardiovasc Interv.* 2016;9(12):1231–1242.
87. Haude M, et al. Sustained safety and performance of the second-generation sirolimus-eluting absorbable metal scaffold: Pooled outcomes of the BIOSOLV-II and -III trials at 3 years. *Cardiovasc Revasc Med.* 2020;21(9):1150–1154.
88. Bosiers M, et al. AMS INSIGHT-absorbable metal stent implantation for treatment of below-the-knee critical limb ischemia: 6-month analysis. *Cardiovasc Interv Radiol.* 2009;32(3):424–435.
89. van Haelst ST, et al. Current status and future perspectives of bioresorbable stents in peripheral arterial disease. *J Vasc Surg.* 2016;64(4):1151–1159.e1.
90. McCormick S, et al. Evidence for the Use of multiple mechanisms by herpes simplex virus-1 R7020 to inhibit intimal hyperplasia. *PLoS One.* 2015;10(7):e0130264.

Novel and Evolving Aortic Endovascular Devices

JORDAN R. STERN and JASON T. LEE

INTRODUCTION	897
AORTIC ARCH AND THORACIC AORTA	897
Standard Thoracic Endografts	897
Arch Branch Devices	898
<i>Single-Branch Design</i>	898
<i>Multi-Branch Design</i>	898
THORACOABDOMINAL	899
Fenestrated and Branched Technology	900

Dissection Systems	901
ABDOMINAL	902
Devices Available in the United States	902
Devices Available Outside the United States	903
ILIAC	903
NONTRADITIONAL DEVICES	904
SUMMARY AND CONCLUSIONS	904

INTRODUCTION

Endovascular aortic surgery is nearly ubiquitous in modern vascular practice, and has largely supplanted open surgery for appropriate anatomy across virtually the entire length of the aorta.¹ With medical device companies vying for market share, device innovation has been rapid and there are now multiple commercially available options for both standard thoracic endovascular aortic repair (TEVAR) and endovascular abdominal aortic repair (EVAR). While some grafts have stood the test of time and only undergone minor updates, newer technology has also emerged to challenge the status quo with improvements in profile, materials, and deployment systems.

With the advent of fenestrated and branched technology as well as adjunctive techniques, aortic disease near the branch vessels has more recently moved towards endovascular treatment as well. This includes the aortic arch and supra-aortic branches, the thoracoabdominal aorta and visceral segment, and the iliac bifurcation. In this chapter, we review some of the standard and more advanced endovascular aortic devices currently on the market, as well as new and emerging technologies still in the pipeline, in order to highlight their relative advantages and clinical utility.

AORTIC ARCH AND THORACIC AORTA

Standard Thoracic Endografts

The Gore TAG device (W.L. Gore & Associates, Flagstaff, AZ) became the first commercially available thoracic endograft in the

United States in 2005. The device has since been redesigned into a conformable version (CTAG), and most recently to CTAG with Active Control (CTAG-AC). Consistent with other Gore endografts, CTAG-AC is comprised of an expandable polytetrafluoroethylene (ePTFE) fabric with a nitinol exoskeleton and requires an external sheath for delivery. This newest iteration includes a mechanism that allows controlled deflection of the proximal portion of the graft in order to better conform to angulated anatomy. The graft is first partially deployed to 50% diameter, and the angulation mechanism is then used to the extent of the operator's preference. A final deployment step then allows full expansion of the graft and release. Several single center experiences have been published, which have reported high accuracy and technical success in challenging anatomy.^{2,3}

Medtronic (Santa Rosa, CA) recently updated their Valiant thoracic graft to the Navion platform. This newer generation TEVAR device has a lower profile delivery system than its predecessor (18–22 F outer diameter [OD]), and is offered both with a proximal bare metal stent (FreeFlo) and without (CoveredSeal). Valiant Navion is made of a woven polyester fabric with external nitinol stents. In the pivotal trial leading to FDA approval, there were zero access or deployment failures in 87 patients with high tortuosity of both access vessels and aorta. One patient (1.2%) had a type 1a endoleak at 30 days.⁴ One unique feature of this graft is that there are several sizes which are available in very short lengths, as short as 52 mm, expanding its potential clinical uses particularly in locations requiring large diameter, short length devices. *Unfortunately, due to issues*

related to stent fractures leading to type III endoleak, this stent graft was recently subject to an FDA Class I recall and is no longer available. This unexpected problem reinforces the need for post-market surveillance of approved devices.

The current thoracic stent graft from Cook Medical (Bloomington, IN) is the Zenith Alpha device. This graft is very low profile (18 F OD for smaller sizes), and designed to be delivered without an external sheath. The Alpha device is also comprised of woven polyester material with self-expanding nitinol stents. One hundred and ten patients were treated with Zenith Alpha in their international, multicenter pivotal trial, with a technical success rate of 98.2%.⁵ At one-year follow-up, freedom from all-cause mortality was 95% and freedom from aortic-related mortality was 99%.

Terumo Aortic (Sunrise, FL) is currently in the process of updating the Relay Plus stent graft to a newer version as well (Relay Pro). While clinical results with the Relay Plus have been favorable, the current drawback has remained the relatively larger profile access required.⁶ Relay Pro maintains many of the positive aspects of the prior generation such as a flexible inner sheath for accurate deployment, while lowering the profile to better align with its competitors. Much like its predecessor, Relay Pro will also be available in both bare stent and non-bare stent configurations at the proximal edge. Relay Pro is currently in clinical trial for aneurysm, dissection, and traumatic aortic injury indications.

Finally, the E-Vita Thoracic 3G stent graft (Jotec GmbH, Hechingen, Germany) is an option currently available only outside the United States. This graft is available in both bare spring and covered spring stent options similar to several of the other grafts described here, and in a variety of lengths and tapered configurations as well. The E-Vita is deployed via a unique, stepwise release mechanism, which uncovers 4 mm of graft per click to enhance accuracy. Jotec was recently purchased by CryoLife (Kennesaw, GA), with plans to expand into the US market in the upcoming years.

Arch Branch Devices

Endovascular repair of the aortic arch remains a significant challenge in minimally invasive aortic surgery. The traditional approach to arch pathology has been open surgical arch replacement via either median sternotomy or thoracotomy, generally requiring cardiopulmonary bypass and deep hypothermic circulatory arrest.⁷ Hybrid techniques have become more common in recent years, in an attempt to mitigate some of the significant perioperative risk associated with open surgery.⁸ Hybrid options include open repair with placement of a thoracic endograft at the distal end of the surgical graft in a “frozen elephant trunk” configuration,^{8,9} and approaches involving extra-anatomic debranching of the supra-aortic branch vessels in combination with standard TEVAR.^{10–12}

Total endovascular solutions for the aortic arch have also become increasingly prevalent, mostly involving off-the-shelf solutions such as parallel grafting^{13,14} and *in situ* laser fenestration.¹⁵ These techniques have allowed for proximal extension of endovascular therapy into zones 0–2, but are limited by various issues related to the interfaces between components and are considered “off-label” uses of standard FDA-approved devices.

Dedicated branched devices for the aortic arch are still in the early stages of development but should allow for more durable repair in the proximal arch once the technology is more mature. At the time this chapter was written, these devices are all still in various stages of investigational use both in and outside the US, therefore not yet commercially available.

Single-Branch Design

There are several single-branch devices currently in active US clinical trials (Fig. 70.1). Because there is only one branch, these devices can be used either for zone 2 repair with branching into the left subclavian artery, or more proximally in combination with surgical supra-aortic debranching. The design of the Gore Thoracic Branch Endoprosthesis (TBE) is based on the CTAG platform, with an ePTFE graft material and nitinol stent frame. The side branch, located 20 to 40 mm from the proximal bare stent, is accessed through an internal portal that is oriented caudally to allow retrograde cannulation via femoral access. The dedicated branch component is tapered for a smooth transition from the portal to the target vessel.

Results from the TBE early feasibility trial were published in 2016, with 100% technical success in 22 patients treated into zone 2 for thoracic aortic aneurysms.¹⁶ Four type 1a endoleaks were seen (18.2%), all of which had resolved by 1-month follow-up without reintervention. Importantly, there were no cerebrovascular complications noted. Side branch patency was 100% at 1 month, and Kaplan–Meier overall survival was 94.7% at 6 months. Based on these encouraging results, TBE has now moved into the pivotal trial phase.

The Medtronic Valiant Navion LSA device (formerly Mona LSA) is based on its Valiant TEVAR counterpart, with a polyester fabric and a helical nitinol stent lattice. Rather than an internal portal, the opening for the side branch is a flexible, external, volcano-shaped cuff. This is cannulated via femoral access in order to deliver the bridging component.

Early feasibility results of the Mona LSA were favorable.¹⁷ Nine patients were treated for thoracic aortic aneurysm or penetrating ulcers, with main body placement into zone 2 and branch revascularization of the left subclavian artery. Technical success was 100%, with no perioperative or 30-day mortality. Four minor strokes were observed in three patients, but there were no major, disabling strokes. Four endoleaks were seen on initial postoperative imaging, two type II and two undefined; none required reintervention. There was also no loss of branch patency during the follow-up period. The Mona LSA recently underwent a redesign onto the newer Navion platform but was unfortunately shelved with the base Navion design following the FDA recall. Its future remains unclear at this time.

Multi-Branch Design

Devices with more than one side branch can be used in the more proximal zones of the aortic arch, potentially lessening, or even eliminating, the need for adjunct surgical debranching procedures for revascularization. The Terumo Relay dual-branch arch system contains two internal branches, positioned side-by-side and directed in an antegrade fashion (Fig. 70.2). Because of the direction of the branches, these are generally cannulated from either upper extremity or direct carotid

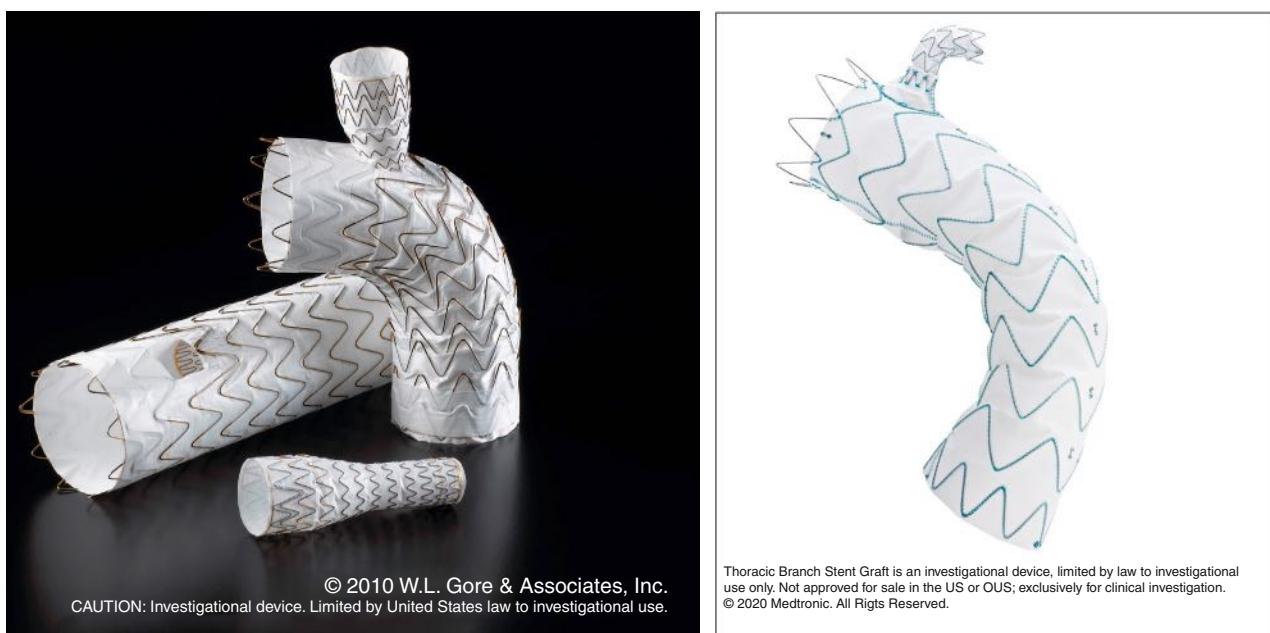


Figure 70.1 Thoracic Single Side Branch Aortic Devices. (A) Gore Thoracic Branch Endoprosthesis. (B) Medtronic Valiant Navion LSA device. (A, Image provided courtesy GORE® EXCLUDER® Iliac Branch Endoprostheses. ©2021. B, Reproduced with permission Medtronic, Inc.)



Figure 70.2 Terumo Relay Dual-Branch Arch System. Two antegrade-directed branches arise from the main body. (Image provided courtesy Bolton Medical, Inc. dba Terumo Aortic, Sunrise, FL.)

arterial access. This system is based on the Relay thoracic endograft platform, formerly of Bolton Medical (Sunrise, FL), with whom Terumo has merged. This device is offered either with or without a leading bare metal stent, and custom configurations are also available.

The largest experience with the Terumo Dual branch graft thus far comes from the Italian TRIUMPH registry, with 24 high-risk patients treated in nine centers.¹⁸ Technical success was achieved in 100%, and there were no type I or III endoleaks noted. However, the in-hospital mortality rate was 16.7% and cerebrovascular complications occurred in 25% (12.5% major strokes). There were two (8.3%) retrograde type A dissections seen as well. An additional, single center study from the Netherlands included another 11 patients considered unfit for open surgery, two of whom died from perioperative stroke (18.2%).¹⁹

The Cook Arch Branch device is a fully customizable option for aortic arch pathology, based on the Alpha thoracic platform. The graft is available in a variety of diameters with 1 to 3 side branches specifically oriented based on patient anatomy, the most common configuration being the two-branch design. The largest experience with multi-branch arch repair was published in 2019 from a single center in Europe, which reported on 54 patients treated with double-branched grafts and adjunctive left carotid–subclavian bypass.²⁰ Patients underwent treatment for aneurysms, dissections and penetrating ulcers, in both the elective and emergent settings. Technical success was 98%, and complication rates were reasonable, with 30-day mortality and major stroke rates of 5.5% each. Importantly, despite landing in the ascending aorta, there were no retrograde type A dissections or cardiac injuries.

THORACOABDOMINAL

Aortic pathology involving the visceral branches necessitates the use of more complex devices in order to maintain perfusion

to the vital organs of the abdomen. This includes both extensive thoracoabdominal aneurysms (TAAA) and Stanford type B aortic dissections (TBAD), with or without aneurysmal degeneration. For the purposes of this chapter, we review the current and upcoming technology specifically designed for these pathologies and forgo a detailed discussion of other techniques using off-the-shelf components, such as chimney/snorkel repair (ChEVAR).

Fenestrated and Branched Technology

The only commercially available fenestrated graft in the United States is the Cook Zenith Fenestrated device (ZFEN), which has been on the market since 2012. Although customized to patient anatomy, the ZFEN is somewhat limited in its configuration options, and mainly indicated for short-neck infrarenal aneurysms. The graft can be designed with a maximum of three fenestrations or scallops, somewhat limiting its applicability to the juxta- and pararenal aneurysms for which it was designed. Results from both the pivotal clinical trial and post-approval usage have proven the safety, utility and durability of ZFEN,^{21,22} and this continues to be an excellent option for short-neck and juxtarenal aneurysm repair. A four-vessel fenestrated option, the ZFEN-Plus device, indicated for pararenal and suprarenal aneurysms, is currently in development and about to begin its pivotal trial. This device design should expand the treatment zone across the entire visceral segment.

Another option for fenestrated aortic aneurysm repair (FEVAR) available in Europe is the Anaconda Fenestrated device, originally produced by Vascutek (Renfrewshire, Scotland) and now owned by Terumo Aortic. In contrast to the ZFEN device, the fenestrations in Anaconda are placed in an unsupported area of the graft, which allows for more

flexibility with design since there is no interference from crossing stent struts. The graft is also able to be repositioned even after full deployment, theoretically improving the success rate of target vessel cannulation.²³ Mid-term outcomes in 60 patients with 140 fenestrations (2.3 fenestrations/patient) showed primary and secondary target vessel patency of 95.0% and 98.6% at a mean follow-up of 16.4 months. Of some concern was a reported type 1a endoleak rate of 11.6%, but all of these resolved spontaneously without need for reintervention.²⁴

One of the major issues with custom fenestrated devices is the protracted wait time for manufacturing and delivery, limiting utilization in urgent or emergent treatment scenarios. In order to address this problem, Cook Medical introduced the Zenith Pivot Branch (P-branch) device. P-branch is an off-the-shelf option for treatment of juxta- and pararenal aortic aneurysms, and is designed with a scalloped fenestration for the celiac axis and a reinforced standard fenestration for the superior mesenteric artery (SMA) (Fig. 70.3). There are two configurations for the pivoting renal fenestrations, either at the same level or offset. The pivoting function allows the graft to adapt to a range of renal anatomic variations, and by some estimates can treat 55%–72% of patients.^{25–27} In pivotal trial, there were no technical failures after the first two cases, and no patients required dialysis or developed mesenteric ischemia.²⁸ Nine of 28 patients (32%) did require secondary interventions however, most commonly for branch stenosis, kinking or occlusions. The P-branch device has completed its enrollment in the pivotal trial and is awaiting the process for FDA submission at the time of this chapter writing.

Multi-branched grafts for treatment of thoracoabdominal aneurysms are also in development, as an alternative or adjunct to fenestrated repair. Cook Medical offers both custom

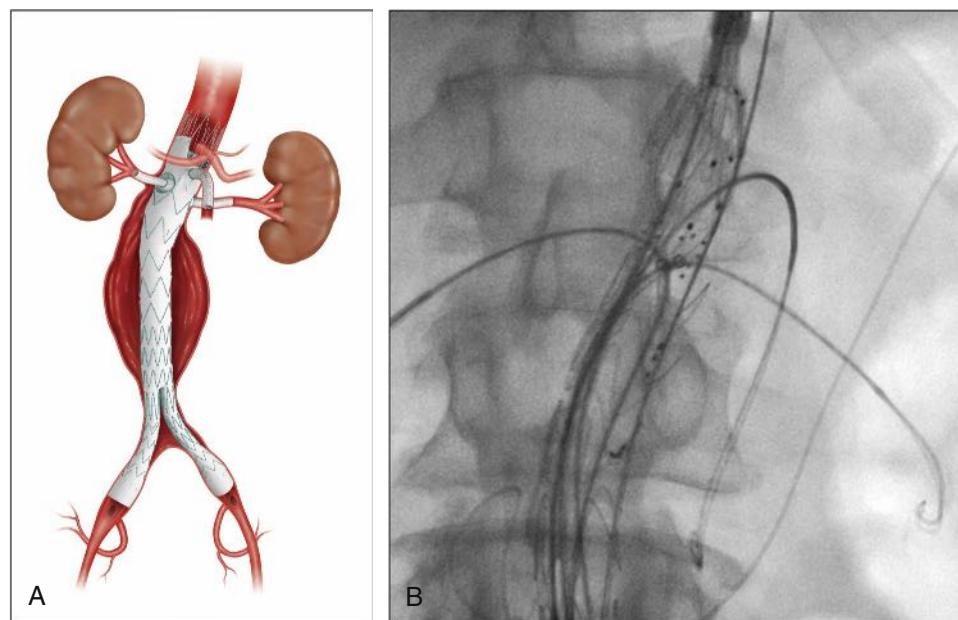


Figure 70.3 Cook Pivot-Branch (P-branch) Device. (A) Schematic drawing with branches to superior mesenteric artery (SMA) and bilateral renal arteries. (B) Deployment with guide wires positioned into target vessels. (Image provided courtesy, and permission for use granted by, Cook Medical, Bloomington, IN.)

branched and fenestrated grafts as well as T-branch, which is an off-the-shelf 4-branch design. These devices are currently available for use in Europe and Canada, but not yet in the United States, where they still require an Investigational Device Exemption (IDE) from the Food & Drug Administration (FDA). A recent publication from the US Fenestrated and Branched Aortic Research Consortium, comprised of those physicians with such IDEs, described outcomes using these devices in 240 patients for both degenerative and post-dissection TAAAs.²⁹ These patients had a mean of 3.7 renovisceral target vessels treated, indicating more extensive repairs. At 2 years, freedom from aortic-related mortality was 94%–98% and primary and secondary target vessel patency was >95%. While these are truly outstanding outcomes, all procedures were performed by a select cohort of high-volume experts and it remains to be seen how generalizable the results may be.

Outside the United States, Jotec/Cryolife offers both a custom thoracoabdominal branch graft program (E-xtra) and an off-the-shelf branched graft (E-nside), the latter of which was granted *Conformité Européenne* (CE) mark status in Europe in late 2019. The company estimates that 70% of TAAA patients can be treated with this standard configuration, eliminating the need for prolonged waiting times associated with patient-specific designs. The E-nside graft has 4 antegrade-directed inner branches that are pre-wired to aid in target vessel cannulation.

The most recent development in aortic branch grafts is the Thoracoabdominal Branched Excluder (TAMBE) device from W.L. Gore, which is an off-the-shelf, 4-branch design aimed at treating a wide range of patients with a single configuration. TAMBE is designed with two sets of parallel, antegrade-directed branches with the upper two intended for the celiac axis and SMA, and the lower two for the renal arteries (Fig. 70.4). Similar to other Gore devices, TAMBE is designed with nitinol stents over an ePTFE graft base, and branches are bridged to their respective target vessels using the Gore

Viabahn Balloon-Expandable Endoprosthesis (VBX) stent graft.

In the first 13 patients treated in a prospective early feasibility study there were zero deaths, aneurysm ruptures, need for dialysis, conversion to open surgery, or spinal cord injuries.³⁰ TAMBE is now actively accruing patients for its multicenter pivotal clinical trial at the time of this chapter writing.

Dissection Systems

The Petticoat technique (Provisional ExTension To Induce COnplete ATtachment) was first described in 2006 as a treatment option for extensive TBAD, including those involving the visceral segment.³¹ Here, a standard TEVAR device is deployed to cover the proximal entry tear, and an open-cell stent is then used to extend distally. This secondary stent serves to expand the true lumen and seal any distal re-entry tears, while maintaining flow to the visceral arteries through its interstices.

The FDA recently approved the Cook Zenith Dissection Endovascular System (Fig. 70.5), whose stent forms are based on the TX2 thoracic stent graft. The dissection stent is available in two diameters (36 and 46 mm), and lengths of 80–185 mm. The STABLE-1 trial was a single-arm study to evaluate outcomes using this system in patients with acute and subacute TBAD, and recently reported its 5-year data.³² Freedom from all-cause mortality was 79.9% and 70.1%, and freedom from dissection-related mortality was 83.9% and 90.1% for acute and subacute TBAD patients, respectively. Perhaps most notably, the system appeared to promote positive aortic remodeling in the majority of patients. This likely contributed to the very respectable freedom from reintervention rates of 65.5% and 71.2% in acute and subacute patients. With widespread adoption, this will likely translate to lower rates of late aneurysmal degeneration in these patients going forward.



Figure 70.4 Gore Thoracoabdominal Branched Excluder (TAMBE). (A) TAMBE device with four antegrade-directed branches. (B) 3-D reconstruction of type 4 thoracoabdominal aneurysm, pre-repair. (C) Completed 4-vessel TAMBE repair, coronal view. (D) Completed 4-vessel TAMBE repair, sagittal view. (A, Image provided courtesy W.L. Gore & Associates.)

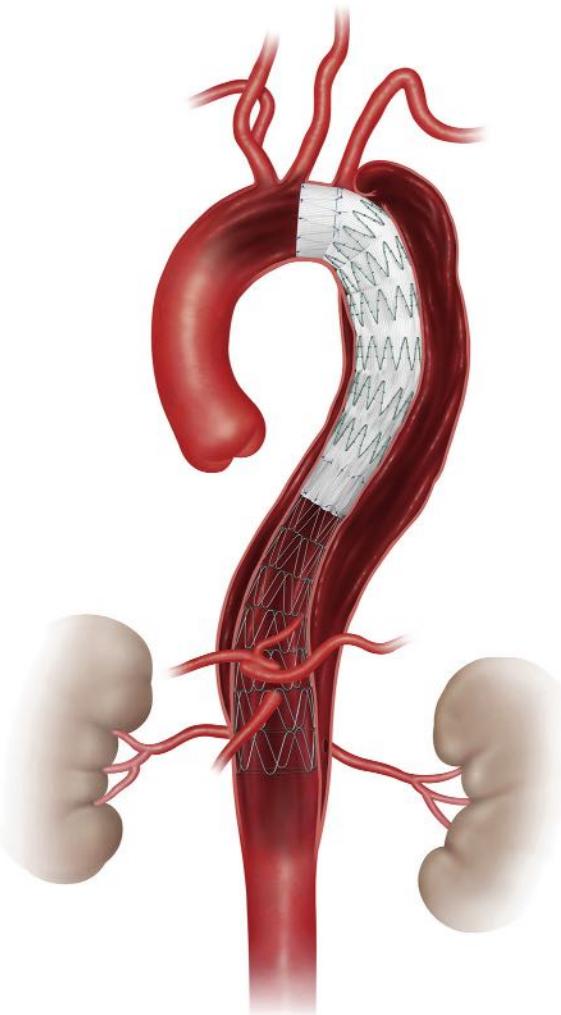


Figure 70.5 Cook Dissection Stent System. A standard, covered TEVAR is deployed proximally, and extended across the visceral segment with the open-cell dissection stent. (Image provided courtesy, and permission for use granted by, Cook Medical, Bloomington, IN.)

ABDOMINAL

Endovascular repair of infrarenal abdominal aortic aneurysms (EVAR) has seen many advances since the initial physician-made stent grafts were first used in the 1990s and the AneuRx device (Medtronic, Santa Rosa, CA) became the first commercially available device in 1999. Here, we review many of the currently available options for EVAR and their relative benefits and differences.

Devices Available in the United States

The Cook Zenith device was first introduced to market in 2003, and has since undergone few design changes or updates. The current version, Zenith Flex, is a modular system comprised of a bifurcated main body and iliac limb extensions, made of woven Dacron with stainless steel Z-stents. There is a suprarenal stent on the main body for active fixation. Unlike many other grafts, the main body is available in variable lengths, which may have implications for proximal reinterventions. Because

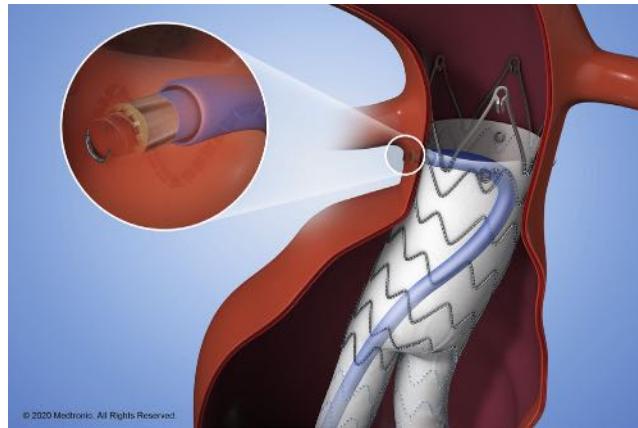


Figure 70.6 Medtronic Endurant Endograft with Heli-FX Endoanchors. Anchors are deployed at the proximal edge for additional fixation. (Reproduced with permission Medtronic, Inc.)

this device has been on the market for so long, there are now long-term data demonstrating its durability with very low rates of aneurysm-related mortality, endoleaks and reintervention.^{33,34} A lower-profile version, Zenith Alpha Abdominal, is currently available in Europe and set to begin study in the US in the near future.

Medtronic is now offering the second generation of their abdominal stent graft system, the Endurant II and IIs. This newer version of the well-established Endurant platform is one of the most widely used stent graft systems in the world. Endurant is also a modular, three-component system, comprised of a polyester graft with nitinol stents and a suprarenal stent. The ENGAGE registry, including over 1200 patients, recently published very positive 5-year results with 95.2% freedom from type Ia endoleak, and 97.8% freedom from aneurysm-related mortality.³⁵ Endurant has the shortest aortic neck length indication alone (≥ 10 mm), and recently acquired an additional approval for use in even shorter necks (≥ 4 mm) with adjunctive use of the Heli-FX Endoanchor system (Fig. 70.6) (Medtronic, Santa Rosa, CA). This indication was based on a study of 70 patients with a mean neck length³⁶ of 6.7 mm treated with Endurant and Endoanchors, which showed only a 2% type Ia endoleak rate and 1.4% proximal endoleak-related reintervention at 1 year.

The Gore Excluder is the only widely used device on the market to employ both seal and fixation in the infrarenal segment without crossing the renal arteries. It can be used as a two-component modular system in appropriately selected patients, or a more traditional three-component system when an ipsilateral limb extension is desired. Much like the rest of W.L. Gore's portfolio, the graft is comprised of nitinol stents and an ePTFE graft, which is delivered through a separate sheath and deployed via a ripcord mechanism. The most recent innovation in Excluder is the addition of an active control mechanism, similar to the technology used in the thoracic device, which allows for deflection of the proximal main body to accommodate severe angulation up to 90°. The Conformable Excluder with Active Control is currently under investigation in a pivotal clinical trial.



Figure 70.7 Terumo Aortic TREO Abdominal Stent Graft. TREO is a modular device for endovascular abdominal aortic aneurysm repair (EVAR), and employs both suprarenal and infrarenal fixation. (Image reproduced by permission Bolton Medical, Inc dba Terumo Aortic, Sunrise, FL.)

The newest addition to the US infrarenal market is the TREO graft from Terumo Aortic (Fig. 70.7). TREO (formerly Treovance), which has been available in Europe since 2015, received FDA approval in early 2020 following a successful IDE study. There are several unique features, including both infra- and suprarenal fixation barbs, fixation within the contralateral gate and iliac limbs to prevent component separation, and a leave-behind sheath for continued use following deployment. TREO is currently being utilized across the United States in limited markets.

Endologix (Irvine, CA) currently offers two infrarenal devices in the US, the Ovation iX and AFX grafts. Ovation iX is a modular, PTFE-based device. The graft seals at the proximal neck with use of two polymer-filled sealing rings and is anchored by a large suprarenal stent. Initial enthusiasm was based on the ultra-low profile, with the main body deliverable through a 14-F (OD) sheath. However, in June 2020 the FDA issued a Class I recall for Ovation, due to concerns about polymer leaking during implantation. The latest iteration, the Ovation Alto device, has completed its pivotal trial and awaits the FDA approval process.

AFX is a unique graft designed to sit on the native aortic bifurcation and has its stent support on the interior aspect of the graft material, a so-called “endoskeleton.” The contralateral gate is pre-cannulated and requires only an 8-F sheath to deliver the contralateral limb extension. AFX has also come under some scrutiny, primarily due to fabric tears in the crotch of the Strata fabric in the first-generation device

(AFX1) leading to type IIIb endoleaks.³⁷ Although the fabric was updated to Duraply for the second-generation device (AFX2), there have been reports of similar issues in this device as well.³⁸

Although not widely distributed, several other devices are FDA-approved for use in the United States. This includes the Incraft (Cordis, Hialeah, FL), as well as the Aorfix (Lombard Medical, Irvine, CA). Since these grafts are not commonly used, an in-depth discussion of their features is beyond the scope of this chapter.

Devices Available Outside the United States

The Nellix Endovascular Sealing (EVAS) system (Endologix, Irvine, CA) is a unique device, which uses a double-barrel technique rather than a traditional bifurcated main body, and aims to achieve total aneurysm exclusion by filling the residual sac with a polymer-filled bladder or “endobag.” Initial enthusiasm for EVAS stemmed from its pivotal clinical trial, which reported 30-day outcomes of only one type Ia endoleak (0.7%) and 6% overall endoleak rate in 150 patients.³⁹ However, longer-term data has since questioned its durability. One study from London, UK reported 4-year estimates of therapeutic failure to be 54.4%, sac rupture 8.8%, and aneurysm-specific mortality 6.3%.⁴⁰ Failures were mainly due to graft migration (29.1%), leading to type Ia endoleak (27.4%) and sac expansion (25.6%). Given these ongoing issues, the future of EVAS is unclear.

There are several more traditional-style grafts available for infrarenal EVAR outside the US, including Anaconda (Terumo Aortic), E-tegra and E-vita (Jotec GmbH), and Altura (Lombard Medical). Again, detailed discussion of these devices fall beyond the scope of this chapter.

ILIAC

Preservation of internal iliac artery patency during endovascular iliac aneurysm repair has several known benefits, including reducing rates of buttock claudication, sexual dysfunction and pelvic ischemia.⁴¹ While techniques such as parallel grafting via the sandwich technique have been used with good success, there are now dedicated iliac branch devices for this purpose.

At present, the Gore Iliac Branch Endoprosthesis (IBE) is the only available iliac branch device for use in the United States. The Gore IBE is intended for the treatment of common iliac artery aneurysms, with an ipsilateral external iliac component and an internal gate that is cannulated from the contralateral groin for bridging into the internal iliac artery. The device is 23 mm in diameter at the proximal graft, which is intended to fit with an Excluder main body and limb extension, and does not contain any fixation barbs. Results from the IBE multicenter pivotal trial demonstrated external iliac patency of 100%, internal iliac patency of 95.1%, and freedom from reintervention of 93.7% at 2-year follow-up.⁴² There were no adverse events of new-onset buttock claudication or sexual dysfunction, even in the few patients in whom the internal iliac branch occluded.



Figure 70.8 Cardiatis Multilayer Braided Stent. (Courtesy Cardiatis, Isnes, Belgium.)

Outside of the US, there are several other approved iliac branch devices. The Cook Zenith Branch Iliac Endovascular Graft is constructed similarly to the Gore IBE device, except for a much narrower proximal diameter of only 12 mm and variable iliac segment length. There is also no dedicated component for the internal iliac branch, and the majority of cases are performed using the Atrium iCast balloon-expandable covered stent graft (Getinge, Gothenburg, Sweden). This clinical trial has completed in the US and is awaiting the FDA approval process. The E-liac branched system from Jotec is also available in Europe and parts of South America, and has shown excellent results as well with 12-month primary patency of 98% for both internal and external iliac arteries.⁴³

NONTRADITIONAL DEVICES

Endovascular repair of the aorta is generally predicated on exclusion of the aneurysm sac or other pathology by way of a fabric-covered stent. When branch vessels are involved, this necessitates the use of fenestrations or other modifications in order to maintain their patency. An alternative approach has recently been proposed with the Multilayer Flow Modulator device (MFM, Cardiatis, Isnes, Belgium) (Fig. 70.8). This device is

comprised of multiple layers of braided, self-expanding stents and is used to preferentially direct flow through the stent and reduce pressure in the aneurysm sac while preserving branch vessel perfusion.⁴⁴ The stent can therefore, in theory, be placed across these vessels without the need for custom design. Studies have demonstrated a reduction in pressure in the aneurysm sac of over 90% while permitting a porosity of 65%.^{45,46}

Because flow to the sac is not completely eliminated, there are concerns about continued risk of rupture. Short-term results with MFM have been moderate, with one study of 67 patients showing a 25% reintervention rate and 10% aneurysm rupture at 12-months follow-up. At this point, these types of devices should still be considered experimental.

SUMMARY AND CONCLUSIONS

There have been incredible advancements in the endovascular repair of aortic disease, and vascular surgeons now have a significant minimally invasive armamentarium with which to treat complex aortic pathology. Given the rapidity with which innovation continues, it is important to keep in mind that the information contained in this chapter, while accurate and relevant at the time of writing, may soon be outdated. Physicians should always stay up to date by continually reviewing the published primary literature, conference proceedings and press releases.

SELECTED KEY REFERENCES

- Farber MA, Oderich GS, Timaran C, et al. Zenith p-Branch Feasibility Study Investigators. Results from a prospective multicenter feasibility study of Zenith p-Branch stent graft. *J Vasc Surg*. 2019;70(5):1409–1418.e3.
- Oderich GS, Farber MA, Silveira PG, et al. Technical aspects and 30-day outcomes of the prospective early feasibility study of the GORE EXCLUDER Thoracoabdominal Branched Endoprostheses (TAMBE) to treat pararenal and extent IV thoracoabdominal aortic aneurysms. *J Vasc Surg*. 2019;70(2):358–368.e6.
- Oderich GS, Greenberg RK, Farber M, et al. Results of the United States multicenter prospective study evaluating the Zenith fenestrated endovascular graft for treatment of juxtarenal abdominal aortic aneurysms. *J Vasc Surg*. 2014;60(6):1420–1428.e1-5.
- Lombardi JV, Cambria RP, Nienaber CA, et al. Five-year results from the Study of Thoracic Aortic Type B Dissection Using Endoluminal Repair (STABLE I) study of endovascular treatment of complicated type B aortic dissection using a composite device design. *J Vasc Surg*. 2019;70(4):1072–1081.e2.
- Schneider DB, Milner R, Heyligers JMM, et al. Outcomes of the GORE Iliac Branch Endoprostheses in clinical trial and real-world registry settings. *J Vasc Surg*. 2019;69(2):367–377.e1.
- Vemuri C, Oderich GS, Lee JT, et al. Postapproval outcomes of juxtarenal aortic aneurysms treated with the Zenith fenestrated endovascular graft. *J Vasc Surg*. 2014;60(2):295–300.

A complete reference list can be found online at www.expertconsult.com.

REFERENCES

1. Suckow BD, Goodney PP, Columbo JA, et al. National trends in open surgical, endovascular, and branched-fenestrated endovascular aortic aneurysm repair in Medicare patients. *J Vasc Surg.* 2018;67(6):1690–1697.e1.
2. Antonello M, Squizzato F, Dall'Antonia A, et al. GORE TAG thoracic endograft with active control system: landing accuracy and wall apposition in an initial clinical experience. *Ann Vasc Surg.* 2019;58: 261–269.
3. Mariani C, van der Weijde E, Smith T, et al. The GORE TAG conformable thoracic stent graft with the new ACTIVE CONTROL deployment system. *J Vasc Surg.* 2019;70(2):432–437.
4. Azizzadeh A, Desai N, Arko FR, et al. Pivotal results for the Valiant Navion stent graft system in the Valiant EVO global clinical trial. *J Vasc Surg.* 2019;70(5):1399–1408.e1.
5. Illig KA, Ohki T, Hughes GC, et al. One-year outcomes from the international multicenter study of the Zenith Alpha Thoracic Endovascular Graft for thoracic endovascular repair. *J Vasc Surg.* 2015;62(6):1485–1494.e2.
6. Farber MA, Lee WA, Szeto WY, et al. Initial and midterm results of the Bolton Relay Thoracic Aortic Endovascular Pivotal Trial. *J Vasc Surg.* 2017;65(6):1556–1566.e1.
7. Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with Thoracic Aortic Disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Circulation.* 2010;121(13):e266–369.
8. Bozso SJ, White A, Nagendran J, et al. Hybrid aortic arch and frozen elephant trunk reconstruction: bridging the gap between conventional and total endovascular arch repair. *Expert Rev Cardiovasc Ther.* 2018;16(3):209–217.
9. Ouzounian M, Hage A, Chung J, et al. Hybrid arch frozen elephant trunk repair: evidence from the Canadian Thoracic Aortic Collaborative. *Ann Cardiothorac Surg.* 2020;9(3):189–196.
10. Benrashid E, Wang H, Keenan JE, et al. Evolving practice pattern changes and outcomes in the era of hybrid aortic arch repair. *J Vasc Surg.* 2016;63(2):323–331.e1.
11. Iida Y, Kawaguchi S, Koizumi N, et al. Thoracic endovascular aortic repair with aortic arch vessel revascularization. *Ann Vasc Surg.* 2011;25(6):748–751.
12. Chiesa R, Melissano G, Tshomba Y, et al. Ten years of endovascular aortic arch repair. *J Endovasc Ther.* 2010;17(1):1–11.
13. Wang T, Shu C, Li M, et al. Thoracic endovascular aortic repair with single/double chimney technique for aortic arch pathologies. *J Endovasc Ther.* 2017;24(3):383–393.
14. Shu C, Fan B, Luo M, et al. Endovascular treatment for aortic arch pathologies: chimney, on-the-table fenestration, and in-situ fenestration techniques. *J Thorac Dis.* 2020;12(4):1437–1448.
15. Kopp R, Katada Y, Kondo S, et al. Multicenter analysis of endovascular aortic arch in situ stent-graft fenestrations for aortic arch pathologies. *Ann Vasc Surg.* 2019;59:36–47.
16. Patel HJ, Dake MD, Bavaria JE, et al. Branched endovascular therapy of the distal aortic arch: preliminary results of the feasibility multicenter trial of the gore thoracic branch endoprosthesis. *Ann Thorac Surg.* 2016;102(4):1190–1198.
17. Roselli EE, Arko FR, Thompson MM. Results of the Valiant Mona LSA early feasibility study for descending thoracic aneurysms. *J Vasc Surg.* 2015;62(6):1465–1471.e3.
18. Ferrer C, Cao P, Coscarella C, et al. iTalian RegIstry of doUble inner branch stent graft for arch PatHology (the TRIUmPH Registry). *J Vasc Surg.* 2019;70(3):672–682.e1.
19. van der Weijde E, Heijmen RH, van Schaik PM, et al. Total endovascular repair of the aortic arch: initial experience in the Netherlands. *Ann Thorac Surg.* 2020;109(6):1858–1863.
20. Tsilimparis N, Detter C, Law Y, et al. Single-center experience with an inner branched arch endograft. *J Vasc Surg.* 2019;69(4):977–985.e1.
21. Vemuri C, Oderich GS, Lee JT, et al. Postapproval outcomes of juxtarenal aortic aneurysms treated with the Zenith fenestrated endovascular graft. *J Vasc Surg.* 2014;60(2):295–300.
22. Oderich GS, Greenberg RK, Farber M, et al. Results of the United States multicenter prospective study evaluating the Zenith fenestrated endovascular graft for treatment of juxtarenal abdominal aortic aneurysms. *J Vasc Surg.* 2014;60(6):1420–1428.e1-5.
23. Bungay PM, Burfitt N, Sirtharan K, et al. Initial experience with a new fenestrated stent graft. *J Vasc Surg.* 2011;54(6):1832–1838.
24. Blankenstein LL, Dijkstra ML, Tielliu IFJ, et al. Midterm results of the fenestrated Anaconda endograft for short-neck infrarenal and juxtarenal abdominal aortic aneurysm repair. *J Vasc Surg.* 2017;65(2):303–310.
25. Schroeder M, Donas KP, Stavroulakis K, et al. Anatomical suitability of the Zenith Off-the-Shelf (p-Branch) Endograft in juxtarenal aortic aneurysms previously treated using the chimney technique. *J Endovasc Ther.* 2017;24(2):223–229.
26. Ou J, Cheng SWK, Chan YC. The compatibility of p-branch “off-the-shelf” fenestrated endovascular graft in Asian patients with juxtarenal aortic aneurysm. *J Vasc Surg.* 2015;61(6):1417–1423.
27. Farber MA, Vallabhaneni R, Marston WA. “Off-the-shelf” devices for complex aortic aneurysm repair. *J Vasc Surg.* 2014;60(3):579–584.
28. Farber MA, Oderich GS, Timaran C, et al. Zenith p-Branch Feasibility Study Investigators. Results from a prospective multicenter feasibility study of Zenith p-Branch stent graft. *J Vasc Surg.* 2019;70(5):1409–1418.e3.
29. Tenorio ER, Oderich GS, Farber MA, et al. Outcomes of endovascular repair of chronic postdissection compared with degenerative thoracoabdominal aortic aneurysms using fenestrated-branched stent grafts. *J Vasc Surg.* 2020;72(3):822–836.e9.
30. Oderich GS, Farber MA, Silveira PG, et al. Technical aspects and 30-day outcomes of the prospective early feasibility study of the GORE EXCLUDER Thoracoabdominal Branched Endoprostheses (TAMBE) to treat pararenal and extent IV thoracoabdominal aortic aneurysms. *J Vasc Surg.* 2019;70(2):358–368.e6.
31. Nienaber CA, Kische S, Zeller T, et al. Provisional extension to induce complete attachment after stent-graft placement in type B aortic dissection: the PETTICOAT concept. *J Endovasc Ther.* 2006;13(6): 738–746.
32. Lombardi JV, Cambria RP, Nienaber CA, et al. Five-year results from the Study of Thoracic Aortic Type B Dissection Using Endoluminal Repair (STABLE I) study of endovascular treatment of complicated type B aortic dissection using a composite device design. *J Vasc Surg.* 2019;70(4):1072–1081.e2.
33. Ramirez JL, Schaller MS, Wu B, et al. Late graft failure is rare after endovascular aneurysm repair using the Zenith stent graft in a cohort of high-risk patients. *J Vasc Surg.* 2019;70(5):1456–1462.
34. Hiramoto JS, Reilly LM, Schneider DB, et al. Long-term outcome and reintervention after endovascular abdominal aortic aneurysm repair using the Zenith stent graft. *J Vasc Surg.* 2007;45(3):461–466.
35. Teijink JAW, Power AH, Böckler D, et al. Editor's Choice - Five year outcomes of the endurant stent graft for endovascular abdominal aortic aneurysm repair in the ENGAGE Registry. *Eur J Vasc Endovasc Surg.* 2019;58(2):175–181.
36. Arko FR, Stanley GA, Pearce BJ, et al. Endosuture aneurysm repair in patients treated with Endurant II/IIs in conjunction with Heli-FX EndoAnchor implants for short-neck abdominal aortic aneurysm. *J Vasc Surg.* 2019;70(3):732–740.
37. Lemmon GW, Motaganahalli RL, Chang T, et al. Failure mode analysis of the Endologix endograft. *J Vasc Surg.* 2016;64(3):571–576.
38. Lemmon G, Barleben A, Nelson P, Garrett HE. Diagnosis and relining techniques for delayed type IIIIB endoleaks with the second-generation AFX endograft. *J Vasc Surg Cases Innov Tech.* 2019;5(1):51–53.

39. Carpenter JP, Cuff R, Buckley C, et al. Results of the Nellix system investigational device exemption pivotal trial for endovascular aneurysm sealing. *J Vasc Surg.* 2016;63(1):23–31.e1.
40. Stenson KM, de Bruin JL, Loftus IM, Holt PJE. Migration and sac expansion as modes of midterm therapeutic failure after endovascular aneurysm sealing. *J Vasc Surg.* 2020;71(2):457–469.e1.
41. Giosdekos A, Antonopoulos CN, Sfyroeras GS, et al. The use of iliac branch devices for preservation of flow in internal iliac artery during endovascular aortic aneurysm repair. *J Vasc Surg.* 2020;71(6):2133–2144.
42. Schneider DB, Milner R, Heyligers JMM, et al. Outcomes of the GORE Iliac Branch Endoprosthesis in clinical trial and real-world registry settings. *J Vasc Surg.* 2019;69(2):367–377.e1.
43. Brunkwall JS, Vaquero-Puerta C, Heckenkamp J, et al. Prospective study of the Iliac Branch Device E-liac in patients with common iliac artery aneurysms: 12 month results. *Eur J Vasc Endovasc Surg.* 2019;58(6):831–838.
44. Sultan S, Hynes N, Kavanagh EP, Diethrich EB. How does the Multi-layer Flow Modulator work? The science behind the technical innovation. *J Endovasc Ther.* 2014;21(6):814–821.
45. Tolva VS, Bianchi PG, Cireni LV, et al. Multiple multilayer stents for thoracoabdominal aortic aneurysm: a possible new tool for aortic endovascular surgery. *Int J Gen Med.* 2012;5:629–632. Available at: <http://www.dovepress.com/multiple-multilayer-stents-for-thoracoabdominal-aortic-aneurysm-a-poss-peer-reviewed-article-IJGM>.
46. Ibrahim W, Spanos K, Gussmann A, et al. Early and midterm outcome of Multilayer Flow Modulator stent for complex aortic aneurysm treatment in Germany. *J Vasc Surg.* 2018;68(4):956–964.

Arterial Aneurysms: Etiology, Epidemiology, and Natural History

PETER F. LAWRENCE and DAVID A. RIGBERG

INTRODUCTION	905
HISTORICAL PERSPECTIVE	906
ANEURYSM CLASSIFICATION	906
Size Definitions	906
Aortic	906
Peripheral	907
True vs. False Aneurysms	907
Location and Extent	907
Morphology	907
Etiology	909
Degenerative	909
Inflammatory	909
Aneurysms Associated with Arterial Dissection	909
Traumatic	910
Developmental and Congenital Anomalies	910
Infectious	910

SPECIFIC ARTERIES	910
Aortic	910
Iliac	911
Femoral	911
Popliteal	911
Visceral	911
Renal	911
Cerebrovascular	912
Upper Extremity	912
MULTIPLE ANEURYSMS	912
Aortic	912
Peripheral	912
Familial	912
Connective Tissue Disorders	912
Cystic Medial Degeneration	913
CURRENT ANEURYSM MANAGEMENT	913

INTRODUCTION

The term *aneurysm* describes dilatation of any blood vessel. Arterial aneurysms occur throughout the body but are most prevalent in the infrarenal aorta (AAA). These aneurysms represent the primary cause of the death and disability attributed to arterial aneurysms. In the United States, AAAs were directly responsible for 9928 deaths in 2017 and roughly 120,000 procedures are performed annually to prevent ruptured AAAs.^{1,2} The incidence of aneurysms increases with age, but aneurysmal disease can occur in any decade of life. These lesions may be the result of several processes, including degenerative, inflammatory, infectious, genetic, and traumatic conditions. Although aneurysms can cause a variety of clinical conditions

(embolism, compression on adjacent organs, and fistulas) the primary danger from intracavitory aneurysms, such as aortic, is rupture with uncontrolled hemorrhage, and death. Nonaortic aneurysms may also rupture, but they more often embolize, thrombose, or compress surrounding structures, and they rarely rupture into an open space where blood loss is catastrophic.

The risk of rupture of any aneurysm is related to both the absolute size of the aneurysm and its size relative to the normal diameter of the inflow and outflow artery from which it arises. The normal sizes for arteries in men and women have been reported, with normal ranges, based on location. A variety of other factors, including etiology, growth rate, and aneurysm morphology (i.e., fusiform vs. saccular) are also critical in assessing aneurysm risk.

HISTORICAL PERSPECTIVE

The presence of arterial calcification and atherosclerotic change has been documented in Egyptian mummies from 3500 years ago. The Ebers Papyrus (*c.* 2000 BCE) clearly identifies an arterial aneurysm, recommending, “Treat it with a knife and burn it with a fire so that it bleeds not too much.”³ Antyllus repaired aneurysms of the extremities with proximal and distal ligation, followed by packing of the aneurysm sac.⁴ Few advances occurred during the next 1000 years, until John Hunter ushered in the era of modern vascular surgery based on a scientific understanding of anatomy and physiology. He studied the collateral circulation resulting from the occlusion of arteries, and in 1785 successfully ligated the superficial femoral artery to treat a popliteal aneurysm. The patient did well and maintained function of his lower extremity.⁵

Rudolph Matas (1860–1957), in 1888, was the first to perform endo-aneurysmorrhaphy in the treatment of a brachial artery aneurysm. This procedure augmented the principle of proximal and distal ligation by Hunter, using evacuation of the aneurysm sac and ligation of tributaries from within, while preserving important collaterals, and remains an important principle in modern surgery.^{6,7} In 1923, Matas performed the first successful aortic ligation.⁸ Little progress was made during the next two decades. Bigger’s summary of therapy for aortic aneurysms at the 1940 American Surgical Association meeting probably represented the consensus of the era: “Judging from the literature, only a small number of surgeons have felt that direct surgical attack upon aneurysms of the abdominal aorta was justifiable, and it must be admitted that the results obtained by surgical intervention have been discouraging.”⁹

The modern era of aneurysm therapy was ushered in by Charles Dubost in 1951 with the first successful graft replacement of the aorta with an aortic homograft. The introduction of Vinyon N cloth aortic prostheses, by Voorhees, Jaretski, and Blakemore,⁹ addressed the poor availability of aortic homograft and initiated the era of prosthetic vascular reconstruction.* The eventual introduction of polyester, championed by DeBakey, and the introduction of new knitting machine technologies to make seamless grafts of multiple sizes and shapes led to wider availability of materials and ultimately diffusion of surgical techniques for repairing aneurysms.¹⁰ In the 1990s, many surgical series documented mortality for open aneurysm repair below 5%, with some at 1% or lower.

* Large samples of Vinyon N were made available for research following World War II. The material was manufactured to make parachutes for an invasion of Japan, which was cancelled following the atomic bombings of Hiroshima and Nagasaki and Japan’s subsequent surrender. Interestingly, polytetrafluoroethylene (PTFE) was used to help contain uranium hexafluoride, a toxic byproduct of atomic bomb production during the Manhattan Project. (Foundation CH, Plunkett RJ, 2013. Available from: <<http://www.chemheritage.org/discover/online-resources/chemistry-in-history/themes/petrochemistry-and-synthetic-polymers/synthetic-polymers/plunkett.aspx>>.)

The era of endovascular, or transcatheter, repair of aortic and other peripheral aneurysms was introduced in 1991 by Juan Parodi, who used available balloon-expandable stents in combination with standard polyester grafts to create a device that could be delivered from the femoral artery into the infrarenal aorta, where it effectively excluded the aneurysm. The first devices approved for use in the United States by the US Food and Drug Administration were in June 1999. Today there are numerous endografts available for use and current estimates are that more than 70% of all aortic aneurysm therapy is performed with endograft technology (see Ch. 75, Aortoiliac Aneurysms: Endovascular Treatment). Both approved devices and off-label combinations of various endovascular devices have been increasingly used where critical branches are present, leading to the technical ability to repair virtually any aneurysm, from the aortic valve to the popliteal and brachial artery. Formal clinical trials of protocol-driven endograft designs for treating the mesenteric and arch segments of the aorta are numerous and represent the most active area of current endograft innovation (see Ch. 81, Aortic Stent Graft and Endovascular Treatment of Thoracoabdominal and Aortic Arch Aneurysms: Strategies for Operative Repair).

Modern approaches to peripheral aneurysm and nonaortic cavitary aneurysmal (e.g., splenic, renal) repair typically use techniques to bypass the vessel, after proximal and distal ligation of the aneurysm; their development has paralleled techniques used for arterial bypass. As with aortic aneurysms, a variety of endografting techniques for peripheral aneurysms have been introduced during the last 20 years, with both self-expanding and balloon-expandable stent-grafts. Embolization techniques have also been selectively used for the treatment of saccular visceral artery aneurysms and aneurysm providing blood supply to noncritical organs, or where good collateral circulation exists (see Ch. 85, Lower Extremity Aneurysms and Ch. 87, Visceral Artery Aneurysms).

ANEURYSM CLASSIFICATION

Size Definitions

The size required to define an artery as aneurysmal, which is “a permanent localized (i.e., focal) dilatation of an artery having at least a 50% increase in diameter compared with the expected normal diameter of the artery in question” was determined by the Ad Hoc Committee on Reporting Standards of the Society for Vascular Surgery in 1991.¹¹

Aortic

Magnetic resonance imaging of 70-year-old men and women in Sweden determined aneurysmal size and ratio to normal on the basis of a 2 SD difference from normal in the ascending and descending thoracic aorta, supraceliac aorta, and infrarenal aorta (Tables 71.1 and 71.2). Other definitions for infrarenal aortic aneurysms have used a 3.0-cm threshold for definition across all adults or a 50% increase relative to an adjacent normal-appearing segment.

TABLE 71.1 Normal Mean Aortic Diameter in 70-Year-Old Men and Women

Aortic Segment	MEN			WOMEN			<i>P</i> *
	N	Mean Diameter (cm)	SD	N	Mean Diameter (cm)	SD	
Ascending	116	4.0	0.4	104	3.4	0.4	<0.001
Descending	116	3.2	0.3	114	2.8	0.3	<0.001
Supraceliac	115	3.0	0.3	113	2.7	0.3	<0.001
Suprarenal	116	2.8	0.3	114	2.7	0.3	0.004
Infrarenal	117	2.4	0.5	114	2.2	0.3	<0.001
Bifurcation	113	2.3	0.3	112	2.0	0.2	<0.001

SD, standard deviation.

*Independent sample *t* test.

From Wanhainen A, et al. Thoracic and abdominal aortic dimension in 70-year-old men and women: a population-based whole-body MRI study. *J Vasc Surg*. 2008;47:504–512.

TABLE 71.2

Definition of Aneurysm at Various Aortic Segments: Size and Ratio to Normal

Aortic Segment	MEN		WOMEN	
	Diameter (cm)	Ratio to Normal	Diameter (cm)	Ratio to Normal
Ascending	4.7	1.8	4.2	1.7
Descending	3.7	1.5	3.3	1.3
Infrarenal	3.0	1.1	2.7	1.0

From Wanhainen A, et al. Thoracic and abdominal aortic dimension in 70-year-old men and women: a population-based whole-body MRI study. *J Vasc Surg*. 2008;47:504–512.

Peripheral

Iliac, popliteal, and femoral aneurysms follow aortic aneurysms in frequency and are often coexistent with aortic aneurysms. Aneurysms throughout the rest of the peripheral vascular system, usually degenerative in nature, may be related to other pathologic processes, such as arteritis, infection, and connective tissue disorders. The “normal” diameters of a variety of peripheral arteries, as determined from imaging studies, are listed in Table 71.3.

True vs. False Aneurysms

The distinction of true or false aneurysm (also termed “pseudoaneurysm”) is dependent on the vascular wall, since a “true aneurysm” has all layers of the wall incorporating or outside the dilated area, while a pseudoaneurysm has part of the wall containing connective tissue or contained hematoma (see Ch. 50, Anastomotic Aneurysms). Many peripheral pseudoaneurysms are the result of iatrogenic peripheral arterial access required for imaging or therapy (Fig. 71.1). These pseudoaneurysms often have a “neck” or narrow conduit between the affected artery and the main pseudoaneurysm cavity. When this morphology exists, therapy directed at inducing aneurysm thrombosis is often effective in treating the aneurysm.

Another frequent cause of pseudoaneurysms is the loss of anastomotic integrity at the site of a prior surgical anastomosis.

TABLE 71.3

Normal Diameters of Peripheral Arteries

	Normal Diameter (cm)
Celiac	0.5
Superior mesenteric	0.6
Common femoral	0.8
Popliteal	0.9
Tibial	0.3

Modified from Johnston KW, et al. Subcommittee on Reporting Standards for Arterial Aneurysms, Ad Hoc Committee on Reporting Standards, Society for Vascular Surgery and North American Chapter, International Society for Cardiovascular Surgery: Suggested standards for reporting on arterial aneurysms. *J Vasc Surg*. 1991;13:452–458.

These peri-anastomotic pseudoaneurysms represent dehiscence of the original suture line from the graft to the vessel (Fig. 71.2). Endovascular techniques have greatly simplified the repair of these lesions in many cases.

Location and Extent

Aneurysms are classified by their location (e.g., aortic, splenic) and their extent. *Ectasia* refers to an intermediate stage of enlargement, when an artery is abnormally large, but less than 50% greater than normal, whereas *arteriomegaly* refers to diffuse, continuous enlargement of multiple arterial segments, dilated to greater than 50% of normal. Arteriomegaly is a descriptive term rather than representative of a specific diagnosis. Both aneurysms and arteriomegaly are associated with an increased risk of aneurysmal disease in first-degree relatives.^{12,13} The term *aneurysmosis* is often used to describe multiple aneurysms in several anatomic locations, or the combination of aneurysmal degeneration in the setting of arteriomegaly.¹⁴

Morphology

The shape of aneurysms is typically described as fusiform or saccular. Fusiform aneurysms represent a generalized increase in the entire diameter of the affected vessel while saccular

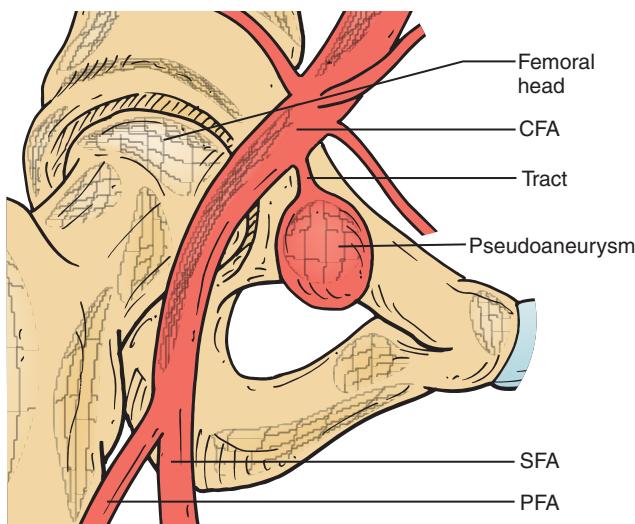


Figure 71.1 Iatrogenic femoral false aneurysm or pseudoaneurysm after percutaneous femoral arterial puncture. *CFA*, common femoral artery; *PFA*, profunda femoris artery; *SFA*, superficial femoral artery. (From Kronzon I. Diagnosis and treatment of iatrogenic femoral artery pseudoaneurysm: a review. *J Am Soc Echocardiogr*. 1997;10:236–245.)

aneurysms are localized, eccentric defects arising from a focal ulcer or weakness in the arterial wall, often as a result of trauma or infection (Fig. 71.3).

Most peripheral arterial aneurysms are associated with atherosclerotic degeneration of the entire wall, and a resultant fusiform or concentric saccular morphology. Some aneurysms routinely have eccentric saccular morphology, such as renal artery and cerebral aneurysms. Whereas fusiform aneurysms result from a generalized weakening of the entire circumference of the affected vessel, saccular aneurysms result from a focal weakness. Intrinsic causes associated with saccular aneurysms generally involve a focal “tear” or partial disruption of the arterial wall. Penetrating atherosclerotic ulcers and intramural hematomas are two such examples (see Ch. 84, Penetrating Aortic Ulcers). These entities have become distinguished from true aneurysms, and relatively straightforward endovascular techniques are often effective in covering these focal lesions.^{15,16}

The risk of rupture is well characterized for fusiform aneurysms, but is less well understood for saccular lesions. Saccular morphology is often used as a factor in advising intervention at a diameter less than that for fusiform aneurysms. However,

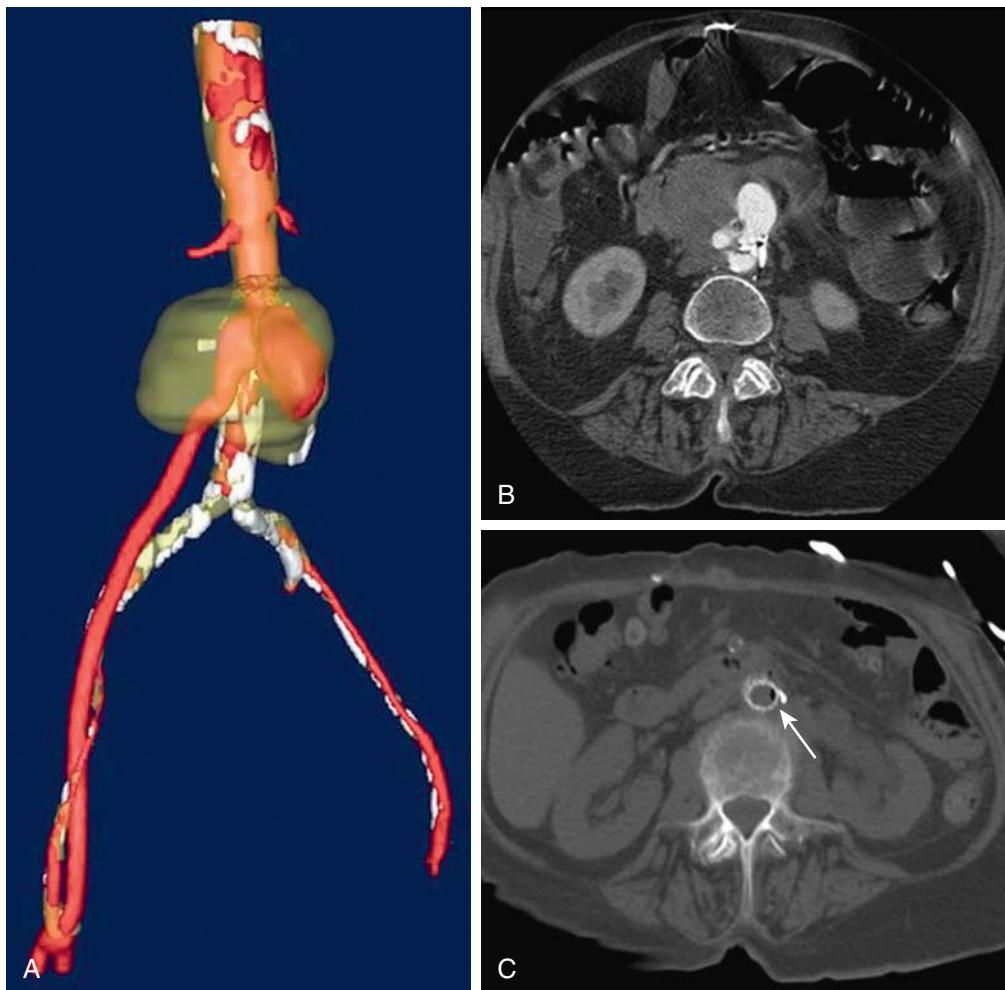


Figure 71.2 Three-dimensional reconstruction (A) and axial computed tomography imaging (B, C) of a proximal infected anastomotic pseudoaneurysm in an aortofemoral bypass graft. Arrow shows gas formed by infecting bacteria. (From Lew WK, et al. Endovascular management of mycotic aortic aneurysms and associated aortoenteric fistulas. *Ann Vasc Surg*. 2009;23:81–89.)

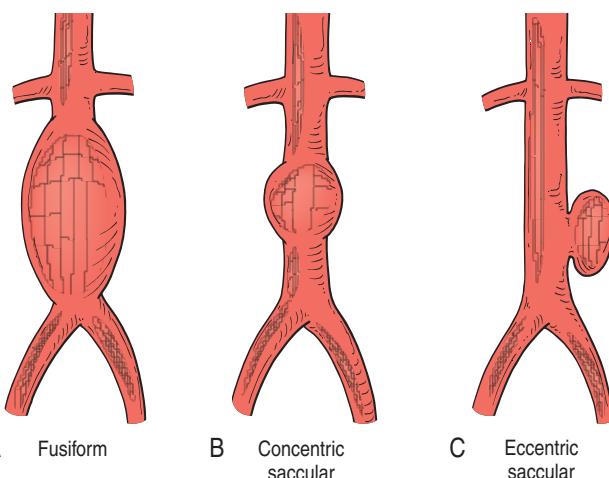


Figure 71.3 (A) Fusiform; (B) concentric saccular; and (C) eccentric saccular aneurysm morphology.

data suggesting that saccular aneurysms are more prone to rupture are lacking. Symptoms, size, growth rate, and amenability to repair are still the most important factors used in the decision to repair these unusual lesions.

Etiology

Degenerative

The terms *degenerative* and *atherosclerotic* are often used to describe the most common type of aneurysm. Some authors prefer the term *degenerative* to *atherosclerotic* in describing the common form of aneurysm, as there is no proven causative relationship between aneurysms and atherosclerosis. The role of atherosclerosis in aneurysm formation is likely complex. Specific factors associated with degenerative aneurysms include the presence of abnormal levels of metalloproteinases in the media of aneurysm specimens.^{17,18} In addition, there is evidence of deficits in antiproteolytic enzymes that inhibit metalloproteinases, specifically tissue inhibitor metalloproteinase-1.¹⁹

Smoking is the most significant risk factor for the development and growth of degenerative aneurysms²⁰ and represents the most attractive target for risk reduction. In addition, inflammation has been closely linked to aneurysm presence and growth and is discussed in detail in other chapters.

Inflammatory

The term *inflammatory* refers to an aneurysm with an exaggerated inflammatory component, which incites a fibrotic reaction around the aneurysm. The infrarenal abdominal aorta is most often affected by this inflammatory process and has the appearance on axial imaging of a thick inflammatory “rind” around the exterior of the affected vessel, which may envelop adjacent structures such as the ureters, leading to obstruction (Fig. 71.4).

Efforts to determine a genetic susceptibility for inflammatory aneurysm formation have yielded only similarities, rather than differences, in the genetic background of degenerative versus inflammatory aneurysms.²¹ Detailed studies of the

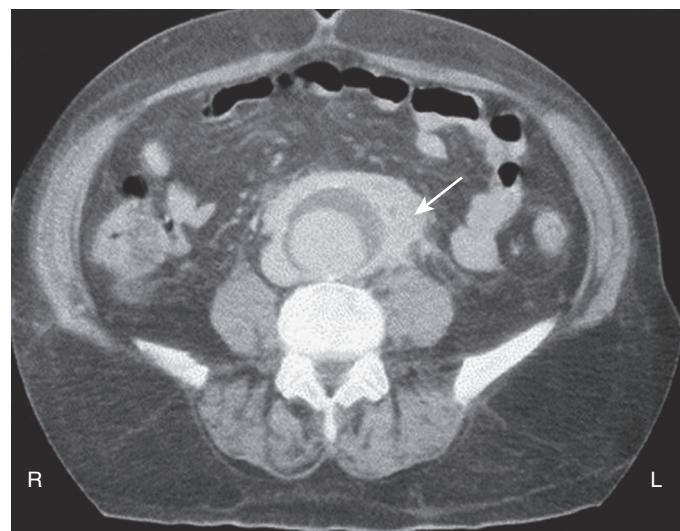


Figure 71.4 Typical appearance of inflammatory aortic aneurysm on computed tomography with thick periaortic fibrotic process. (From Speziale F, et al. Inflammatory aneurysms of the abdominal aorta involving the ureters: is combined treatment really necessary? *J Urol*. 2001;165:27–31.)

cellular infiltrate and cytokine profiles documented in patients with inflammatory aneurysms may eventually lead to a better understanding of this difficult and enigmatic disease state.²² The primary surgical challenge of these lesions is dissecting surrounding structures safely during open repair. The complications associated with traditional open surgery have included duodenal perforation and ureteral injury. Endovascular repair of inflammatory aneurysms has been reported to result in regression of the perianeurysmal inflammation and fibrosis.²³

Takayasu arteritis, giant cell arteritis, polyarteritis nodosa, Behçet disease, Cogan syndrome, and cystic medial necrosis represent other inflammatory arterial conditions associated with aneurysmal degeneration (see Ch. 138, Vasculitis and Other Arteriopathies). The location, severity and management of these lesions are related to the ability to control the primary inflammatory process with medical therapy.

Aneurysms Associated with Arterial Dissection

Spontaneous arterial dissection most often occurs in the aorta, but it can also occur in peripheral arteries. Dissection describes a spontaneous tear of the intima and the subsequent propagation of that tear along the anatomic plane within the media (see Ch. 83, Aortic Dissection: Epidemiology, Pathophysiology, Clinical Presentation, and Medical and Surgical Management). The failure of the initial intimal tear to propagate may result in a penetrating aortic ulcer or intramural hematoma, as discussed above. Arterial pressure and acute arterial distension as the result of mural delamination are the driving forces behind the propagation of the dissection. The most common symptomatic presentation of this process is dissection in either the ascending or descending portion, or both. Since the structural integrity of arteries is dependent on a three-layer structure, the primary morbidities associated with arterial dissection are acute occlusion and aneurysm formation. Aneurysmal degeneration resulting from dissection can cause acute rupture or

a more gradual dilatation over time, similar to that seen with degenerative aneurysms. Chronic aneurysms due to dissection are generally treated by the same guidelines for size, growth, and symptoms that are used for the management of degenerative aneurysms.

Traumatic

Aneurysms that result from trauma are pseudoaneurysms, due to perforation of an artery that results in local containment of hemorrhage, rather than uncontrolled bleeding. The location of these aneurysms parallels the most common sites of trauma or iatrogenic injury.

Developmental and Congenital Anomalies

Aneurysms associated with anomalous arterial and cardiac structures are not uncommon but are highly variable, depending on the nature of the primary structural defect. These lesions are clinical representations of the embryologic defect that resulted in the primary arterial or cardiac anomaly. One such embryologic arterial anomaly is the persistent sciatic artery; more than 40% of these patients will develop aneurysmal degeneration. Kommerell diverticulum is another aneurysmal degeneration, located at the origin of an aberrant right subclavian artery, which can intensify the esophageal obstruction associated with aberrant right subclavian artery (*dysphagia lusoria*).²² Congenital abdominal aortic aneurysms have also been reported in young patients, such as those with tuberous sclerosis, but without other known connective tissue disorders, and are thought to represent a congenital defect in the aorta itself.²⁴ Although it is not strictly a congenital disorder, aortic aneurysm increases in incidence from approximately 5% in the general population to approximately 20% to 30% in male siblings of an aneurysm patient, suggesting a significant genetic linkage.²⁵

Infectious

Aneurysms may result from primary infection of the arterial wall from blood-borne seeding or the extension of an adjacent infectious process that primarily infects the arterial tissue (Fig. 71.5). Most primary infected arterial aneurysms, as opposed to secondary infection of a pre-existing aneurysm, have a saccular shape, and all saccular-shaped aneurysms should be evaluated for an infectious etiology. A wide variety of organisms, including many strains of bacteria²⁶ and fungi (e.g., *Candida*, *Aspergillus*), tuberculosis, and syphilis have been documented to be causative. Infected aneurysms can occur in essentially any vessel, and their incidence is increased in locations where illicit drugs are injected, and patient populations that are severely immunosuppressed (e.g., transplant recipients, patients with HIV, etc.)²⁷ (see Ch. 145, Infected Arterial Aneurysms).

Repair of infected aneurysms is difficult because prosthetic material is usually contraindicated and there are limited durable autogenous substitutes available. In addition, the open approach to these lesions is made more difficult by the inflammatory response to the infected tissue, making tissues friable and tissue planes difficult to define. Work with antibiotic-impregnated prosthetics, cryopreserved allograft,

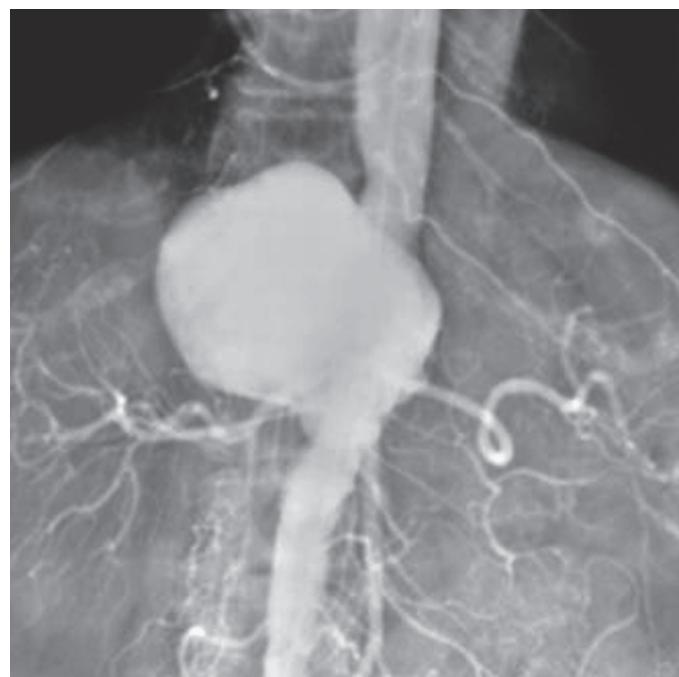


Figure 71.5 An infected aortic eccentric saccular aneurysm. (From Macedo TA, et al. Infected aortic aneurysms: imaging findings. *Radiology*. 2004;231:250–257.)

and primary endografting in these cases continues, although the complications and mortality of patients with infected aneurysms is high.

SPECIFIC ARTERIES

Arterial aneurysms occur throughout the vasculature from a wide variety of causes. Their prognosis and therapy are largely dependent on their anatomic location. Aneurysms located in circulatory beds that have robust collateral circuits can often be embolized or excluded from the circulation by ligation or other means. Aneurysms in critical locations of the circulatory system require replacement of that arterial segment with an adequate substitute, in the form of an autogenous or prosthetic graft. Key information for specific artery aneurysms is presented here and discussed in detail in subsequent chapters in this section.

Aortic

Aneurysms occur throughout the length of the aorta, with the preponderance occurring in the infrarenal segment. Aneurysms occurring in the ascending aorta are typically degenerative or the sequelae of aortic dissection; the arch and descending aorta are similarly affected in their predilection for aneurysmal disease. Isolated thoracic aneurysms were found in 0.9% of autopsies in Sweden²⁸ and represent 3% of repairs in the United States.²⁹ The infrarenal location is by far the most common for aortic aneurysms; abdominal aortic aneurysms are at least nine times more common than thoracic aneurysms.³⁰ Approximately 1.7% of women and 5% of men older than 65 years have an infrarenal aortic diameter greater than 3 cm, and the incidence of aortic aneurysm increases by about 6% for each decade after

that age.³¹ Aneurysms involving the thoracic and abdominal aorta, thoracoabdominal aneurysms, are less frequent than either isolated thoracic or isolated abdominal aortic aneurysms, but represent some of the most formidable challenges for repair in vascular surgery (see Ch. 78, Thoracic and Thoracoabdominal Aortic Aneurysms: Etiology, Epidemiology, Natural History, Medical Management and Decision Making).

Iliac

Aneurysms are most frequently found in the common iliac artery, often in the presence of a concomitant infrarenal aortic aneurysm. A review of patients with iliac aneurysms revealed that only 11% presented without a concomitant aortic aneurysm.²⁹ Internal iliac aneurysms are the next most frequent lesion in this circulatory bed, although they are also often found in association with common iliac aneurysms. Isolated internal iliac artery aneurysms present with rupture in 40% of patients and are associated with a 31% death rate.³² Isolated internal iliac aneurysms are less frequently diagnosed when asymptomatic and are more difficult to control when ruptured; these are two reasons for the elevated rates of rupture and death. External iliac aneurysms are very rare and usually associated with traumatic lesions or other nondegenerative causes (see Ch. 77, Isolated Iliac Artery Aneurysms and their Management).

Femoral

The incidence of true aneurysms of the femoral artery is relatively low, likely on the order of 5/100,000 patients.³³ True degenerative femoral artery aneurysms do occur, and a recent study suggests that these lesions typically do not cause complications unless they are greater than 3.5 cm or contain thrombus. These aneurysms are frequently bilateral (26%) and 88% of patients have a synchronous aneurysm at another site (Fig. 71.6).

The most serious and high-risk femoral aneurysms are infected pseudoaneurysms from illicit injection drug abuse,³⁴ while femoral pseudoaneurysms most often result as a complication of percutaneous femoral access or disruption of surgical bypass anastomoses. These lesions can be challenging to repair and are often not amenable to endovascular techniques.

Popliteal

The most common peripheral arterial aneurysm, popliteal aneurysm, occurs in approximately 1% of men aged 65 to 80 years.³⁵ Popliteal aneurysms are frequently bilateral and often occur concomitantly with aortic aneurysms,³³ making investigations for their presence an important part of the examination of any patient with an abdominal aortic aneurysm. As opposed to rupture of aortic aneurysms, the primary morbidity associated with popliteal aneurysms is acute thrombosis, ischemia, and limb loss.³⁶

Visceral

The incidence of aneurysms occurring in the trunk or branches of the celiac and superior mesenteric arteries vary, but a

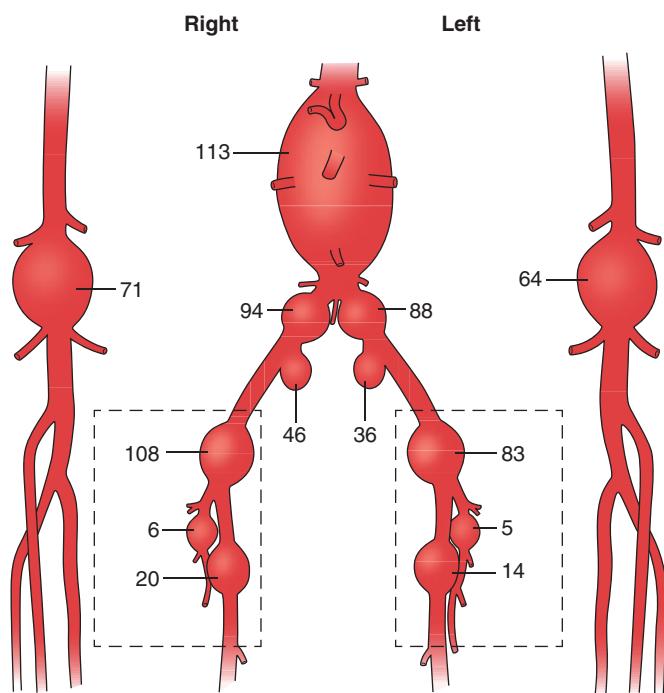


Figure 71.6 The locations and distribution are shown of degenerative femoral artery aneurysms (FAAs; dotted boxes) and additional synchronous and metachronous aneurysms. Forty-seven patients (26%) had bilateral degenerative FAAs. (From Lawrence PF, Hartlander-Locke MP, Oderich GS, et al. The current management of isolated degenerative femoral artery aneurysms is too aggressive for their natural history. *J Vasc Surg*. 2014;59(2):343–349.)

reasonable estimate is that these aneurysms occur in ~1% of the population, based on postmortem series.³⁷ Splenic artery aneurysms lag behind only the aortoiliac segment as the second most common aneurysm in the abdominal cavity and account for approximately 60% of all visceral or splanchnic aneurysms.³⁷ Splenic aneurysms occur more frequently in women and are also associated with portal hypertension. Pregnancy is a specific risk factor for rupture. Many visceral aneurysms can be managed with endovascular techniques of endografting or embolization. In the case of splenic artery aneurysms involving the hilum, splenectomy can also be performed for treatment.

Renal

The renal circulatory bed is characterized by its low resistance and high flow characteristics, and the high flow is an explanation for the location and frequency of renal aneurysms. Renal aneurysms occur in ~0.1% of the population.³⁸ Renal artery aneurysms are often saccular rather than fusiform and are often occur in association with fibromuscular dysplasia. Renal aneurysms can also result from the full spectrum of associated aneurysmal causes, including connective tissue disorders, arteritides, trauma, and spontaneous dissection. The morbid sequelae of renal aneurysms include thrombotic and embolic events, poorly controlled hypertension, and rupture. While rupture is rare, the risk is particularly elevated in the third trimester of pregnancy, with maternal and fetal mortality rates of 70% and 100%, respectively.³⁹ Current recommendations for

repair include size greater than 2–3 cm, lesions occurring in woman of child-bearing years, refractory hypertension, flank pain, and hematuria. However, the size criteria are not based on rigorous data, and this may be too aggressive an approach.⁴⁰ Both endovascular and open surgical reconstruction play a significant role in the treatment of these lesions.

Cerebrovascular

Whereas intracranial aneurysms are relatively common and represent a major challenge for neurosurgeons and neuroradiologists, extracranial cerebral arteries are rarely affected by aneurysmal degeneration. The few aneurysms that do occur in the carotid are in the internal, common, and external segments, in order of decreasing frequency. Dissection, which may occur after trauma, can lead to both internal carotid and vertebral artery late aneurysmal degeneration⁴¹ (see Ch. 97, Carotid Artery Aneurysms).

Upper Extremity

Subclavian artery aneurysms can result from the repetitive trauma associated with thoracic outlet syndrome.⁴² Iatrogenic brachial pseudoaneurysms, which occur after percutaneous access, are the only other upper extremity aneurysms that occur with any frequency (see Ch. 86, Upper Extremity Aneurysms).

MULTIPLE ANEURYSMS

Aortic

The fact that patients with a diagnosis of an infrarenal aortic aneurysm are more often found to have a concurrent thoracic aortic aneurysm or popliteal aneurysm has been known for many years. Crawford noted that more than 50% of patients with thoracic aneurysms also had abdominal aneurysms and that 12% of patients with abdominal aneurysms had thoracic aneurysms.⁴³ In a report from the Mayo Clinic managing patients with multiple aneurysms during a two-decade period in 1990, this group represented only 3.4% of all aneurysm procedures performed⁴⁴ (Fig. 71.7). Patients with connective tissue disorders or other systemic conditions that predispose to aneurysmal degeneration, such as Marfan syndrome or Ehlers–Danlos syndrome have a significantly higher incidence of multiple aneurysms and recurrent aneurysm disease. These patients must be monitored closely throughout their lives for aneurysms in typical and atypical locations (see Ch. 141, Aneurysms Caused by Connective Tissue Abnormalities).

Peripheral

Popliteal aneurysm is the most frequently occurring peripheral aneurysm and is the most common aneurysm to be bilateral; synchronous and metachronous aneurysms in other sites are also common. Galland reviewed a 17-year experience with popliteal aneurysms and noted that 59% of the patients had

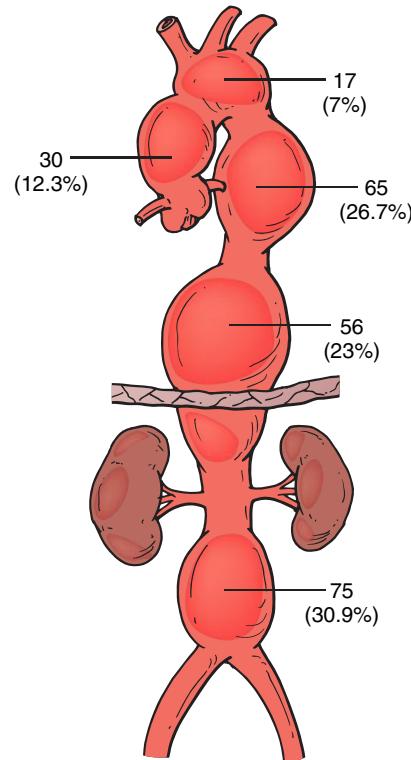


Figure 71.7 Incidence and location of 243 aneurysms in 102 patients with multiple aortic aneurysms. (From Gloviczki P, et al. Multiple aortic aneurysms: the results of surgical management. *J Vasc Surg*. 1990;11:19–27.)

bilateral aneurysms and 49% had coexisting abdominal aortic aneurysms.⁴⁵ Other peripheral aneurysms can occur in multiple locations, but their incidence is far less, so they do not warrant a heightened suspicion for synchronous disease, as occurs with popliteal and infrarenal aortic aneurysms.

Familial

Patients with a family history of aneurysm disease have a 30% increased risk of having an aneurysm, although the specific genetic explanation for this susceptibility has not been elucidated.⁴⁶ This is true for abdominal aortic aneurysms discovered outside the context of a diagnosed congenital disorder or connective tissue disorder. Although it is not completely understood, this is the most common familial risk factor for aneurysm disease and warrants screening of siblings and children of affected patients.

Connective Tissue Disorders

Connective tissue disorders are primary causes of familial aneurysmal disease and require genetic characterization and counseling. As the technology to completely delineate a single individual's genetic code becomes a clinical reality, this area of diagnosis and management is very likely to see significant changes in the coming years. Familial inheritance of aneurysmal disease includes Ehlers–Danlos, Marfan, and Loeys–Dietz syndromes and a variety of less common connective tissue defects.

Cystic Medial Degeneration

A familial pattern of thoracic aortic aneurysm has been termed *familial thoracic aortic aneurysm syndrome*. Whereas no overt connective tissue disorder has been recognized in these patients, they do share the characteristic of cystic medial degeneration.⁴⁷ Bicuspid aortic valve has also been associated with a high incidence of ascending aortic aneurysm, and cystic medial degeneration has been proved by tissue biopsy in 75% of these patients.⁴⁸ Turner syndrome is also associated with ascending aortic aneurysm, aortic dissection, and bicuspid aortic valve.⁴⁹

CURRENT ANEURYSM MANAGEMENT

There have been many recent advances in the management of aneurysms, owing mostly to a better understanding of their natural history and indications for treatment, better risk factor modification, improved diagnostic tools, more accurate classification, more options for treatment and better and more specific endograft design. In addition, once treated, there is a better understanding and options for follow-up, better classification systems for complications, and indications for re-treatment, all of which have been published. Given the enormous literature related to aneurysms, which are managed by multiple specialties, reporting standards, practice guidelines, best practices, and appropriate use criteria have been published about many specific aneurysms, including thoracic endovascular aneurysm repair (TEVAR), fenestrated endovascular aneurysm repair (FEVAR), visceral, and AAA.^{50–53} As an example the Practice Guidelines on the Treatment of AAA include 29 recommendations regarding AAA supported by level 1A evidence. The Society for Vascular Surgery has been the leader in publishing these documents in the *Journal of Vascular Surgery*, using the best available evidence on each aspect of aneurysm management. In addition, there are an increasing number of patient-oriented manuals that summarize the current information on aneurysms, helping patients to understand their disease and to advise them about the best option for their specific aneurysm.

SELECTED KEY REFERENCES

Chaikof EL, Brewster DC, Dalman RL, et al. Society for Vascular Surgery: The care of patients with abdominal aortic aneurysm: the Society for Vascular Surgery practice guidelines. *J Vasc Surg*. 2009;50(Suppl):S2–S49.

The most recent comprehensive clinical practice guidelines for patients with abdominal aortic aneurysm.

Friedman S. *Evolution of aortic surgery. A history of vascular surgery*. Malden, MA: Blackwell Futura; 2007:74–88.

A comprehensive description of the history and evolution of aortic surgery. Important information regarding early approaches with rigid tubes, sutureless anastomoses, and a variety of other techniques that ultimately gave way to fabric prostheses and sutured anastomoses.

Lederle FA, Nelson DB, Joseph AM. Smokers' relative risk for aortic aneurysm compared with other smoking-related diseases: a systematic review. *J Vasc Surg*. 2003;38:329–334.

Reviews the data regarding smoking and its association with aortic aneurysms and a variety of other atherosclerotic vascular conditions as well as chronic obstructive pulmonary disease. Documents the powerful risk factor that smoking is for development of aortic aneurysms.

Moll FL, Powell JT, Fraedrich G, et al. European Society for Vascular Surgery: Management of abdominal aortic aneurysms clinical practice guidelines of the European society for vascular surgery. *Eur J Vasc Endovasc Surg*. 2011;41(Suppl 1):S1–S58.

The most recent clinical practice guidelines for the management of aortic aneurysm from the European Society of Vascular Surgery.

Perry MO. John Hunter – triumph and tragedy. *J Vasc Surg*. 1993;17:7–14.

An excellent article about John Hunter, the father of modern surgery and the first to approach arterial aneurysms surgically in the modern era.

Wanhainen A, Themudo R, Ahlström H, Lind L, Johansson L. Thoracic and abdominal aortic dimension in 70-year-old men and women: a population-based whole-body MRI study. *J Vasc Surg*. 2008;47:504–512.

An excellent population-based study that objectively looks at the prevalence of aneurysmal disease in a single Scandinavian country and documents the statistically meaningful definitions of “normal” aortic diameter in men and women at various aortic loci.

A complete reference list can be found online at www.expertconsult.com.

REFERENCES

1. Centers for Disease Control and Prevention, National Center for Health Statistics. *Underlying Cause of Death*, 1999–2017.
2. Slaney G. A history of aneurysm surgery. In: Greenhalgh RM, et al., ed. *The Cause and Management of Aneurysms*. Philadelphia: WB Saunders; 1990:1–18.
3. Crowe SJ. *Halsted of Johns Hopkins: the man and his men*. Springfield, IL: Charles C Thomas; 1957.
4. Perry MO. John Hunter—triumph and tragedy. *J Vasc Surg*. 1993;17:7–14.
5. Matas R. Traumatic aneurysm of the left brachial artery. Incision and partial excision of the sac—recovery. *Med News NY*. 1888;53:462–466.
6. Matas R. An operation for the radical cure of aneurysm based upon arteriorrhaphy. *Ann Surg*. 1903;37:161–196.
7. Matas R. Ligation of the abdominal aorta. *Ann Surg*. 1925;81:457–464.
8. Friedman S. *Evolution of aortic surgery: A history of vascular surgery*. Malden, MA: Blackwell Futura; 2007:74–88.
9. Voorhees Jr AB, et al. The use of tubes constructed from Vinyon “N” cloth in bridging arterial defects. *Ann Surg*. 1952;135:332–336.
10. DeBakey ME, et al. Clinical application of a new flexible knitted Dacron arterial substitute. *Am Surg*. 1958;24:862–869.
11. Johnston KW, et al. Subcommittee on Reporting Standards for Arterial Aneurysms, Ad Hoc Committee on Reporting Standards, Society for Vascular Surgery and North American Chapter, International Society for Cardiovascular Surgery: Suggested standards for reporting on arterial aneurysms. *J Vasc Surg*. 1991;13:452–458.
12. Lawrence PF, et al. Peripheral aneurysms and arteriomegaly: is there a familial pattern? *J Vasc Surg*. 1998;28:599–605.
13. Belardi P, et al. Type I aneurysmosis: complementary index for diagnosis. *Vascular*. 2005;13:11–15.
14. Batt M, et al. Penetrating atherosclerotic ulcers of the infrarenal aorta: life-threatening lesions. *Eur J Vasc Endovasc Surg*. 2005;29:35–42.
15. Eggebrecht H, et al. Intramural hematoma and penetrating ulcers: indications to endovascular treatment. *Eur J Vasc Endovasc Surg*. 2009;38:659–665.
16. Lijnen HR. Metalloproteinases in development and progression of vascular disease. *Pathophysiol Haemost Thromb*. 2003;33:275–281.
17. Sierevogel MJ, et al. Matrix metalloproteinases: a therapeutic target in cardiovascular disease. *Curr Pharm Des*. 2003;9:1033–1040.
18. Brophy CM, et al. Decreased tissue inhibitor of metalloproteinases (TIMP) in abdominal aortic aneurysm tissue: a preliminary report. *J Surg Res*. 1991;50:653–657.
19. Lederle FA, et al. Smokers’ relative risk for aortic aneurysm compared with other smoking-related diseases: a systematic review. *J Vasc Surg*. 2003;38:329–334.
20. Rasmussen TE, et al. Genetic similarity in inflammatory and degenerative abdominal aortic aneurysms: a study of human leukocyte antigen class II disease risk genes. *J Vasc Surg*. 2001;34:84–89.
21. Eagleton MJ. Inflammation in abdominal aortic aneurysms: cellular infiltrate and cytokine profiles. *Vascular*. 2012;20:278–283.
22. Williams LR, et al. Persistent sciatic artery. Clinical aspects and operative management. *Am J Surg*. 1983;145:687–693.
23. Rehring TF, et al. Regression of perianeurysmal fibrosis and ureteral dilation following endovascular repair of inflammatory abdominal aortic aneurysm. *Ann Vasc Surg*. 2001;15:591–593.
24. Sterpetti AV, et al. Congenital abdominal aortic aneurysms in the young. Case report and review of the literature. *J Vasc Surg*. 1988;7:763–769.
25. Baird PA, et al. Sibling risks of abdominal aortic aneurysm. *Lancet*. 1995;346:601–604.
26. Brown SL, et al. Bacteriologic and surgical determinants of survival in patients with mycotic aneurysms. *J Vasc Surg*. 1984;1:541–547.
27. Nair R, et al. Arterial aneurysms in patients infected with human immunodeficiency virus: a distinct clinicopathology entity? *J Vasc Surg*. 1999;29:600–607.
28. Svensjo S, et al. Thoracic and thoracoabdominal aortic aneurysm and dissection: an investigation based on autopsy. *Br J Surg*. 1996;83:68–71.
29. Lawrence PF, et al. The epidemiology of surgically repaired aneurysms in the United States. *J Vasc Surg*. 1999;30:632–640.
30. Kuivaniemi H, et al. Opportunities in abdominal aortic aneurysm research: epidemiology, genetics, and pathophysiology. *Ann Vasc Surg*. 2012;26:862–870.
31. Scott RA, et al. Abdominal aortic aneurysm in 4237 screened patients: prevalence, development and management over 6 years. *Br J Surg*. 1991;78:1122–1125.
32. Dix FP, et al. The isolated internal iliac artery aneurysm—a review. *Eur J Vasc Endovasc Surg*. 2005;30:119–129.
33. Diwan A, et al. Incidence of femoral and popliteal artery aneurysms in patients with abdominal aortic aneurysms. *J Vasc Surg*. 2000;31:863–869.
34. Coughlin PA, et al. Arterial consequences of recreational drug use. *Eur J Vasc Endovasc Surg*. 2006;32:389–396.
35. Trickett JP, et al. Screening and management of asymptomatic popliteal aneurysms. *J Med Screen*. 2002;9:92–93.
36. Ravn H, et al. Swedish Vascular Registry: Nationwide study of the outcome of popliteal artery aneurysms treated surgically. *Br J Surg*. 2007;94:970–977.
37. Panayiotopoulos YP, et al. Aneurysms of the visceral and renal arteries. *Ann R Coll Surg Engl*. 1996;78:412–419.
38. Stanley JC, et al. Renal artery aneurysms. Significance of macroaneurysms exclusive of dissections and fibrodyplastic mural dilations. *Arch Surg*. 1975;110:1327–1333.
39. Cohen JR, et al. Ruptured renal artery aneurysms during pregnancy. *J Vasc Surg*. 1987;6:51–59.
40. Coleman DM, Stanley JC. Renal artery aneurysms. *J Vasc Surg*. 2015;62(3):779–785.
41. Pham MH, et al. Endovascular stenting of extracranial carotid and vertebral artery dissections: a systematic review of the literature. *Neurosurgery*. 2011;68:856–866.
42. Davidovic L, et al. Ruptured abdominal aortic aneurysms: factors influencing early survival. *Ann Vasc Surg*. 2005;19:29–34.
43. Crawford ES, et al. Aortic aneurysm: a multifocal disease. Presidential address. *Arch Surg*. 1982;117:1393–1400.
44. Gloviczki P, et al. Multiple aortic aneurysms: the results of surgical management. *J Vasc Surg*. 1990;11:19–27; discussion 27–28.
45. Galland RB. Popliteal aneurysms: from John Hunter to the 21st century. *Ann R Coll Surg Engl*. 2007;89:466–471.
46. Frydman G, et al. The value of screening in siblings of patients with abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg*. 2003;26:396–400.
47. Albornoz G, et al. Familial thoracic aortic aneurysms and dissections—incidence, modes of inheritance, and phenotypic patterns. *Ann Thorac Surg*. 2006;82:1400–1405.
48. de Sa M, et al. Histologic abnormalities of the ascending aorta and pulmonary trunk in patients with bicuspid aortic valve disease: clinical relevance to the Ross procedure. *J Thorac Cardiovasc Surg*. 1999;118:588–594.
49. Elsheikh M, et al. Hypertension is a major risk factor for aortic root dilatation in women with Turner’s syndrome. *Clin Endocrinol (Oxf)*. 2001;54:69–73.
50. Upchurch Jr GR, et al. Society for Vascular Surgery Clinical Practice Guidelines for Thoracic Endovascular Aneurysm Repair (TEVAR). *J Vasc Surg*. 2020;3:S0741-5214(20)31521-4.
51. Oderich G, et al. Reporting Standards for endovascular aortic repair of aneurysms involving the renal-mesenteric arteries. *J Vasc Surg*. 2021;73(1S):4S–52S.
52. Chaer R, et al. The Society for Vascular Surgery Clinical practice guidelines on the management of visceral aneurysms. *J Vasc Surg*. 2020;72(1S):3S–39S.
53. Chaikof EL, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg*. 2018;67(1):2–77.e2.



Aortoiliac Aneurysms: Evaluation, Decision Making, and Medical Management

RISHI A. ROY, ERIC YATES PRUITT, and
GILBERT R. UPCHURCH JR.

INTRODUCTION 914

DEFINITIONS 914

EPIDEMIOLOGY 915

 Associated Aneurysms 915

 Rupture Risk 916

PATHOPHYSIOLOGY 916

DIAGNOSIS 918

 History 918

 Physical Examination 918

 Ultrasound 918

Computed Tomography 919

Magnetic Resonance Imaging 919

Angiography 919

SCREENING AND SURVEILLANCE

RECOMMENDATIONS 919

MEDICAL THERAPY 921

INDICATIONS FOR INTERVENTION 921

 Risk Calculator 922

FUTURE DIRECTIONS 922

CHAPTER ALGORITHM 923

INTRODUCTION

Ancient Egyptians were the first to recognize aortic aneurysms as early as 1550 BCE, and Antyllus was the first to attempt treatment of aneurysms through ligation of the vessels, but this was met with poor results.^{1,2} Through time our understanding of the anatomy, and pathophysiology of abdominal aortic aneurysms (AAA) has progressed and great advances have been made in the management of this complex disease. The 20th century marked a period of rapid advances in the open surgical management of aortic aneurysms by proximal ligation or obliteration (Cooper, 1817; Matas, 1888), extra-arterial wrapping (Poppe, 1946), and direct reconstruction with autologous (Carrel, 1948; Dubost, 1951) or synthetic (Voorhees, 1952) material.^{3–7} Vast improvements in the management and outcomes of AAA came with the work performed by DeBakey and Cooley in the 1950s.⁵ However, operative techniques remained relatively stagnant until 1990 when Juan Parodi performed the first endovascular stent of an infrarenal AAA.^{6,7} Since the US Food and Drug Administration (FDA) approved the first stent grafts for use in repair of infrarenal aortic aneurysms in 1999, endovascular techniques

have overtaken traditional open repair as the most common approach to the elective and emergent management of this condition (see Ch. 75, Aortoiliac Aneurysms: Endovascular Treatment).

DEFINITIONS

Arterial aneurysms are defined as an increase in arterial diameter by 1.5 times the normal diameter with involvement of all three anatomic layers. For the infrarenal aorta, an aneurysm is defined as greater than 3 cm or 50% larger than a normal proximal segment measured in either the anteroposterior or transverse dimension in a plane perpendicular to the longitudinal axis of the aorta. The original definition of a median aortic size of 2.2 to 2.3 cm is based from analysis of 70-year-old Caucasian subjects, but it is now known that there are variations in mean aortic diameter based on sex and race. However, the Aneurysm Detection and Management (ADAM) Veterans Affairs Cooperative Study Group concluded that these differences in average aortic size are not significant enough to change the previous definition of an aneurysm.^{8,9} Pseudoaneurysms and

penetrating aortic ulcers can result in focal increases in arterial diameter, but the pathophysiology of these diseases differs from that of aneurysms.

EPIDEMIOLOGY

Aortic aneurysms can form anywhere along the aorta, but approximately 30% of aneurysms are found in the infrarenal aorta.¹⁰ Inferences regarding the affected patient cohorts, incidence, and prevalence of AAAs are drawn from autopsy and screening studies designed to target groups thought to be at increased risk for aneurysm, primarily based on age or sex (Table 72.1).^{11–17} In the United States, the prevalence of AAA as defined by an aortic diameter >3 cm was found to be 1.4% among those between the ages of 50 and 84 years.⁹ Age has been determined to be the most significant risk factor for the development of AAA. This risk is increased in the age ranges of 65 to 69, with an odds ratio of 5.4, and 75–79 with an odds ratio of 14.5.⁹ Caucasian race and male sex are also additional risk factors for development with aneurysm incidence in women peaking later than in men.^{8–11}

Smoking has been shown to be the single biggest modifiable risk factor in the development of AAA with a direct correlation to smoking duration. In fact, a smoking history of <0.5 pack per day for 10 years increases the risk of AAA. This has been shown to be dose-dependent with risk increasing by 12-fold when smoking more than one pack a day for over 35 years.⁹ Interestingly as smoking prevalence in the United States has decreased, so too has aneurysm prevalence.¹⁸

Family history is not commonly reported in those with AAA, but when present it increases the risk of AAA development by 20%.^{19,20} Additional risk factors with less strong associations include increased salt intake, atherosclerotic disease, history of myocardial infarction, peripheral vascular disease, cerebrovascular disease and hypertension.^{8,21} Negative risk factors include female sex, African American race, and diabetes.^{8,21} Between 7% and 11% of patients with chronic obstructive pulmonary disease (COPD) have an AAA.²² Overall, risk is diminished with smoking cessation, well-controlled diabetes mellitus, eating fruits and vegetables more than three times a week, and exercise more than once a week.⁹

Associated Aneurysms

Adjacent arterial segments are often involved in aneurysmal dilation of the infrarenal aorta, with 5%–15% extending to the juxta- or suprarenal aorta and 10%–25% involving the iliac arteries.²³ Synchronous thoracic aneurysms are present in 12% of cases,²⁴ while femoral or popliteal aneurysms are present in 14% of male patients.¹² However, AAAs have been reported in 62% of patients with popliteal artery aneurysms and in 85% of those with femoral artery aneurysms (see Ch. 85, Lower Extremity Aneurysms).^{25,26}

Iliac artery aneurysms (IAAs) most commonly occur in the common iliac artery (CIA) (70%), typically in conjunction with AAA. The largest series of CIA aneurysms noted that 86% presented with AAA or had been treated for one in the past.²⁷ Only 6.4% of patients will have isolated CIA aneurysms, and one-quarter of those will have bilateral CIA aneurysms. Internal iliac artery aneurysms (IIAAs) are quite rare, accounting for 0.04% of all aortoiliac aneurysms.²⁸ Again, aneurysms of these vessels are defined as 1.5 times the normal vessel diameter (>1.85 cm in males or 1.5 cm in females).²⁹ The prevalence of IAAs in patients with clinically relevant AAAs varies from 15% to 40%. Although most IAAs are degenerative in nature, injury from penetrating trauma or iatrogenic injury from operative intervention in the area of the iliac arteries may also play a role in their development. There is also an association of IAAs with vasculitides, such as Behcet disease, fibromuscular dysplasia, Takayasu arteritis and connective tissue disorders. There have been reports of mycotic IAAs, but these are very rare^{30,31} (see Ch. 141, Aneurysms Caused by Connective Tissue Abnormalities).

The natural history of IAA, particularly those occurring in isolation, is less well understood but deserves special mention. The Mayo Clinic group reported a median expansion rate in CIA aneurysms of 0.29 cm per year and reported no ruptures at less than 3.8 cm.³² A recent review of the literature on IIAs noted that these aneurysms are quite large when they initially present, likely due to an anatomic location that precludes detection on physical examination unless the aneurysm impinges on surrounding anatomic structures sufficiently to produce symptoms associated with the compression of nerves or urogenital/colorectal structures. Asymptomatic aneurysms,

TABLE 72.1 Prevalence of Abdominal Aortic Aneurysm by Age and Gender

Study Location	Lederle, USA ¹¹	Chichester, UK ¹²	Viborg, Denmark ¹³	Western Australia ¹⁴	MASS UK ¹⁵	Rotterdam, Netherlands ¹⁶	Tromso, Norway ¹⁷
N	73,451	15,775	12,629	41,000	67,800	5419	6386
Gender	Men and women	Men and women	Men	Men	Men	Men and women	Men and women
Age (years)	50–79	65–80	65–73	65–79	65–74	>55	55–74
Sampling dates	1992–1995	1988–1990	1994–1998	1996–1998	1997–1999	1994–1995	1994–1995
Date published	1997	1995	2005	2004	2002	1995	2001
Aneurysm prevalence	1.4% (1.4% in men, 0.2% in women)	4.0% (7.6% in men, 1.3% in women)	4.0%	7.2%	4.9%	4.1% men, 0.7% women	8.9% men, 2.2% women

discovered by physical examination or incidentally through imaging, averaged 5.1 cm in diameter, whereas nonruptured and ruptured symptomatic aneurysms averaged 7.6 and 8.3 cm, respectively³³ (see Ch. 77, Isolated Iliac Artery Aneurysms and their Management).

Rupture Risk

Rupture risk for AAA is stratified by the diameter of the aneurysm, with larger aneurysms conferring increased risk (Table 72.2). Studies have shown that the rupture risk is less than 2% when the aneurysm is less than 4 cm and increases significantly when aneurysm diameter increases beyond 5 cm.^{34,35} The UK Small Aneurysm Study also found that the risk of rupture was independently associated with female sex, larger AAA diameter at the time of initial diagnosis, smoking, lower FEV1, and higher mean arterial pressure. Risk of rupture was not associated with age, BMI, serum cholesterol or ankle/brachial index. Of note, females were shown to have a three-fold increased risk of rupture compared with males with similar aortic diameters. Modifiable risk factors shown to decrease the risk of rupture were control of hypertension and smoking cessation.³⁵

Other aneurysm characteristics also appear to predict rupture risk. Saccular aneurysms carry increased risk of rupture when compared to fusiform aneurysms.³⁶ This is due to the increased wall stress seen in asymmetric aneurysms.^{37,38} Imaging characteristics that increase rupture risk are the presence of dissection, mural thrombus, or peripheral calcifications of the aneurysm sac.³⁹ The UK Morphology of Ruptured AAA study reported that the most likely site for rupture is the middle third of the aneurysm at the point of greatest diameter.⁴⁰

Growth rate must be considered when discussing the progression of AAA. Unfortunately, evidence notes a high degree of variation in AAA diameter assessment when followed by ultrasound due to technician differences. A Canadian study showed that this variability decreased significantly when a measured change in diameter was greater than 0.78 cm.⁴¹ Growth rate is reported as 2.2 mm/year and is not different between men or women. Smoking and the presence of a larger aneurysm, however, increased the rate of growth while presence of diabetes decreased growth rate.^{42–44} Currently, intervention is indicated for AAA with a growth rate greater than or equal to 10 mm in a 12-month period.⁴⁵

TABLE 72.2

12-Month Risk of Rupture Based on Abdominal Aortic Aneurysm Diameter

AAA Diameter (cm)	Rupture Risk (%)
3.0–3.9	0.3
4.0–4.9	0.5–1.5
5.0–5.9	1–11
6.0–6.9	11–22
>7	>30

AAA, abdominal aortic aneurysms.

Overall, death from AAA rupture has declined in estimates, this can likely be attributed to decline in smoking, increased public awareness, improved operative outcomes, and improvement in overall cardiovascular health. This is further supported by the fact that in countries where cigarette usage has not declined, aneurysm-related mortality continues to increase⁹ (see Ch. 76, Ruptured Aortoiliac Aneurysms and their Management).

PATHOPHYSIOLOGY

The descending thoracic and abdominal aortas are formed through embryonic fusion of the paired dorsal aortas, which communicate with the developing heart via the aortic arches. The wall of the mature aorta is composed of three layers: the intima, with its single layer of endothelial cells; the media, made up of smooth muscle cells within a structural protein matrix; and the adventitia, a tough layer of collagen fiber and fibroblasts (see Ch. 2, Embryology and Developmental Anatomy).

The embryologic process appears to give rise to regional heterogeneity in different parts of the aorta, with variation in the response of neural crest-derived smooth muscle cells of the thoracic aorta versus mesoderm-derived smooth muscle cells in the abdominal aorta. This regional variation clearly affects the secretion of and susceptibility to various cytokines and growth factors thought to be implicated in aneurysm development. This heterogeneity is also reflected in the tissue characteristics of the aortic media within different anatomic segments. In the thoracic aorta, the media contains 55 to 60 lamellar units, with adventitial vasa vasorum penetrating the vascular zone of the outer layers, whereas there are 28 to 32 lamellar units in the abdominal aortic media. This makes the abdominal aorta relatively avascular compared with the more proximal aorta, relying more on the transintimal diffusion of oxygen and nutrients.^{24,46}

Inflammation has been implicated as a key component of aneurysmal degeneration of aortic tissue. Analysis of circulating biomarkers has been extensively studied in those with AAA. Specifically, fibrinogen, WBC, fibrinogen, D-dimer, NT-proBNP, and cTnT levels are elevated.⁴⁷ There has also been a linear correlation found between levels of C-reactive protein and aortic diameter.⁴⁸ Currently, none of these markers have the sensitivity, specificity, or validation to provide diagnostic prognosis for rupture risk.^{47,49}

AAA are the result of the media thinning due to destruction of smooth muscle cells and elastin, inflammatory cell infiltration, neovascularization and collagen deposition.^{50–53} Several factors play a role in the inflammatory component of aneurysmal degeneration. The accumulation of intramural thrombus (ILT) is one such component. It is thought that this effect is mediated through a cascade of platelet activation, ultimately leading to increased oxidative stress and proteolytic injury. Mural thrombus recovered from human AAA samples are notable for recruitment of inflammatory cells such as neutrophils and inflammatory cytokines.⁵⁴ The thrombus itself is laminated, progressing from an initial luminal layer with fresh thrombus and cross-linked fibrin to an outer layer in contact

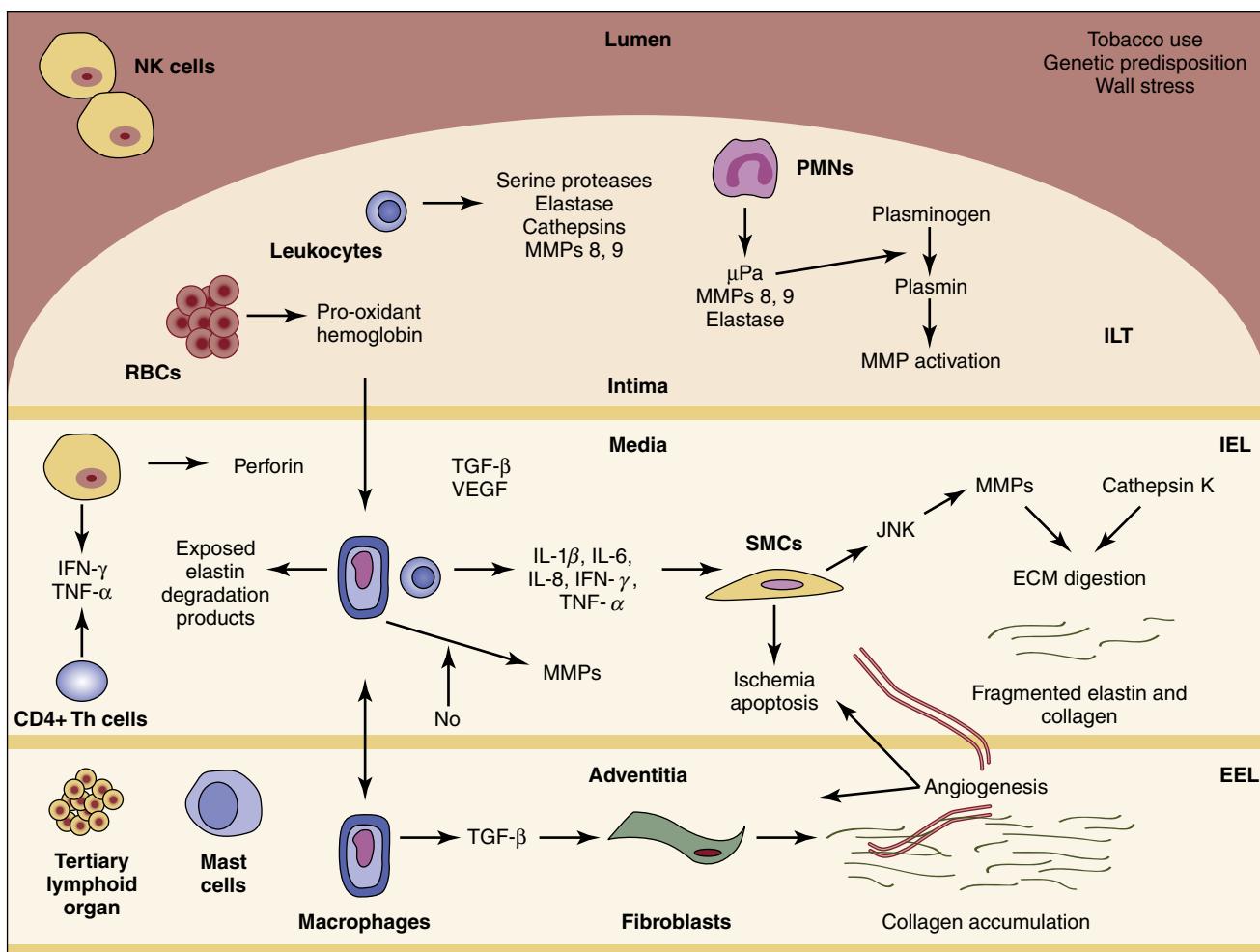


Figure 72.1 Schematic Diagram Demonstrating the Complexity of Abdominal Aortic Aneurysm Pathogenesis.⁴⁶ *ECM*, extracellular matrix; *EEL*, external elastic lamina; *IEL*, internal elastic lamina; *IFN- γ* , interferon- γ ; *IL*, interleukin; *ILT*, intraluminal thrombus; *JNK*, c-Jun N-terminal kinase; *MMP*, matrix metalloproteinase; *NK*, natural killer cell; *NO*, nitric oxide; *PMN*, polymorphonuclear cell; *RBC*, red blood cell; *SMC*, smooth muscle cell; *TGF- β* , transforming growth factor- β ; *Tb*, T-helper cell; *TNF- α* , tumor necrosis factor- α ; *uPa*, urokinase-type plasminogen activator; *VEGF*, vascular endothelial growth factor. (From English SJ, Upchurch GR Jr. Pathogenesis of abdominal aortic aneurysms. In: Stanley JC, Veith FJ, Wakefield TW, eds. *Current Therapy in Vascular and Endovascular Surgery*. 5th ed. Philadelphia, PA: Elsevier; 2014:203–206, with permission.)

with the aortic wall, the latter being characterized by advanced fibrinolysis. At this level, plasmin serves to activate matrix metalloproteinases (MMPs) and TGF- β and participates directly in matrix protein degeneration. The predominant MMPs are MMP 9, MMP2 and MMP12.^{50,55–57} The importance of the biologic activity of the ILT is underscored by the observation that increased thrombus burden is associated with an increased AAA growth rate. Wall thinning, medial loss of smooth muscle cells, elastin degradation, and adventitial inflammation have all been associated with the presence of ILT (Fig. 72.1). It has been suggested that the impact of thrombus burden may also be associated with aortic wall hypoxia.^{54,58}

Although much attention has been focused on medial degeneration, marked changes in the adventitia have also been observed in AAAs. Inflammation – in the form of extensive periaortic and adventitial infiltration by lymphocytes, macrophages, and mast cells – is noted histologically. Adventitial

degeneration is also characterized by extensive fibrosis. This fibrosis, driven by macrophage/TGF- β -mediated fibroblast proliferation and activation, may provide some degree of protection from rupture, but it may also be associated with pathologic retroperitoneal fibrosis, with adherence to and injury of adjacent retroperitoneal structures. Neoangiogenesis, typically limited to the adventitia and outer media, is also observed in AAAs.⁵⁹

There is also a clear genetic role in the development of AAA, with heritability estimated as high as 70%.⁶⁰ If a patient has a first-degree relative with an AAA, their chance of developing an AAA is approximately doubled irrespective of the presence of a connective tissue disorder.^{60,61} Further evidence is emerging that there are genetic risks for AAA development that do not fall into the spectrum of named connective tissue disorders. Large genome-wide association studies have recognized several novel gene loci that confer increased risk of AAA development

TABLE 72.3 Connective Tissue Syndromes Associated with Abdominal Aortic Aneurysms

Syndrome	Gene	Defect	Inheritance Pattern
Marfan syndrome	<i>FBN1</i>	Defect in Fibrillin-1	Autosomal dominant pattern
Loeys–Dietz syndrome	<i>TGFB1</i> gene mutations cause type I, <i>TGFB2</i> gene mutations cause type II, <i>SMAD3</i> gene mutations cause type III, <i>TGFB2</i> gene mutations cause type IV, and <i>TGFB3</i> gene mutations cause type V	Overactive TGF-β pathway	Autosomal dominant pattern
Ehlers–Danlos vascular type (formerly type IV)	<i>COL3A1</i>	Defect in collagen type III	Autosomal dominant pattern
Familial abdominal aortic aneurysm ^{50–52}	Not specifically identified	ECM Defect in DAB2 interacting protein (DAB2IP) Defect in low-density receptor-related protein (LRP1)	Unknown

ECM, extracellular matrix; TGF, transforming growth factor.

regardless of family history.⁶² In addition to the novel genetic loci, several named connective tissue disorders confer increased risk for AAA development and subsequent rupture, and these are listed in Table 72.3.

Frank bacterial infection of the aortic wall is also clearly associated with the development of mycotic aortic aneurysms (MAA). MAA are also known to be rapidly expanding and associated with high mortality.⁶³ Fortunately, MAA only make up 0.6%–2% of all AAA.⁶³ It has been proposed that bacterial colonization of either the aortic wall or ILT may contribute to AAA formation and progression either directly or indirectly through alteration of the immunologic milieu. Published literature indicates that the most commonly isolated species are *Salmonella*, followed by *Staphylococcus* species, *Streptococcus* species and *E. coli*.⁶³

DIAGNOSIS

History

Patients with AAAs are typically asymptomatic. Those who are symptomatic and previously undiagnosed often present with diffuse nonspecific abdominal and/or lower back pain. This pain is usually described as unique and different from their standard chronic abdominal or lower back pain. Patients may also state that they can feel pulsations in their abdomen. Those who are thin may state that they can see a pulsatile mass in their abdomen. Certainly, there is a high probability that these patients have as part of their medical history hypertension, atherosclerotic disease, and tobacco use.

Physical Examination

AAAs may be detected on physical examination as a palpable pulsatile (expansile) mass, most commonly supraumbilical and in the midline. The location, however, may be variable, as aortic tortuosity can result in a lateral and/or infraumbilical location. The sensitivity of physical examination depends

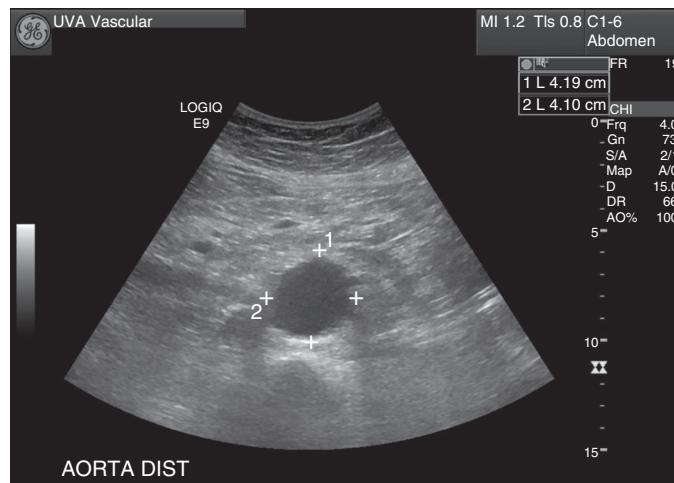


Figure 72.2 Ultrasound of the abdominal aorta documents an abdominal aortic aneurysm noted with maximal measurement of 4.19 × 4.10 cm in the anteroposterior and transverse dimensions.

on the aneurysm's size and the patient's habitus. Owing to the previously mentioned high probability of concomitant femoral artery aneurysms and PAAs, these areas should also undergo examination and imaging.⁹

Ultrasound

The detection and characterization of aneurysms is greatly aided by modern imaging techniques. Ultrasound (US) examination has been demonstrated to afford excellent sensitivity and specificity (Fig. 72.2). US may be limited by patient habitus or bowel gas, but, importantly, it avoids the complications associated with more invasive testing, radiation, and exposure to a contrast medium. US is an excellent choice for screening and evaluation of diameter and as such is currently the recommended screening modality.⁹ It must also be noted that US is not an ideal method for detecting rupture, as it is unable to image all portions of the aortic wall. In addition,



Figure 72.3 Computed tomographic angiogram of the abdomen and pelvis showing an infrarenal abdominal aortic aneurysm measuring approximately 5.6 × 6.5 cm.

in the non-fasting emergently examined patient, ideal image acquisition may be precluded. It has been estimated that US may fail to detect up to 50% of aneurysm ruptures (see Ch. 22, Vascular Laboratory: Arterial Duplex Scanning).

Computed Tomography

Computed tomography (CT) provides excellent imaging of AAAs, with greater reproducibility of diameter measurements than US. CT, particularly with the adjunctive use of iodinated contrast to perform a CT angiogram (CTA), provides a wealth of anatomic information, including defects in vessel calcification, thrombus, and concurrent arterial occlusive disease. CTA also permits invaluable multiplanar and three-dimensional reconstruction and analysis for operative planning (Fig. 72.3). Drawbacks associated with CTA include substantial exposure to radiation, particularly in the setting of serial examinations, and the use of iodinated contrast media is problematic in a population with a high incidence of associated kidney disease (see Ch. 29, Computed Tomography).

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) are, like CT, quite sensitive in the detection of AAAs (Fig. 72.4). Unlike CT, MRI does not demonstrate aortic wall calcification, which may be quite important in operative planning. Although the study does not require the use of iodinated contrast, MRA utilizes gadolinium, which has been associated with the development of nephrogenic systemic fibrosis in patients with a low GFR. The availability of MRI



Figure 72.4 Magnetic resonance (MR) angiogram of the abdomen and pelvis performed on a 3 Tesla MR scanner with contrast. Imaging shows an infrarenal abdominal aortic aneurysm measuring 7.8 × 7.8 cm.

may also be limited by the presence of incompatible metallic implants or foreign bodies. However, the ability to acquire dynamic images throughout the cardiac cycle may ultimately prove clinically useful (see Ch. 30, Magnetic Resonance Imaging and Arteriography).⁶⁴

Angiography

Due to its invasive nature, contrast angiography is not the preferred method for screening or surveillance for AAAs. Typically, per the imaging guidelines developed by the American College of Radiology, it is reserved for cases where further detailed characterization of an aneurysm is required or for intervention, as in the case of preoperative embolization of an accessory renal artery prior to endovascular aneurysm repair⁶⁵ (see Ch. 27, Arteriography).

SCREENING AND SURVEILLANCE RECOMMENDATIONS

Screening and surveillance guidelines for AAA are generated by a variety of organizations and vary slightly between various countries. The guidelines that follow are based on several key population-based screening studies and their final recommendations are informed by a range of considerations, including quality of evidence characteristic of the screening modality and cost.⁶⁶

Initial screening has been a topic of much debate centered around the age at which someone should be screened, what risk factors should be considered, and the appropriateness of screening for women. As such, various societies have different

TABLE 72.4 Screening and Surveillance Recommendations

Year	Organization	Initial Screening	Referral for Treatment	Surveillance	Repeat Screening
2018	Society for Vascular Surgery ⁹	US for men and women aged 65–75 years who have ever smoked US for first-degree relatives of those with AAA who are between 65 and 75 years of age or in those older than 75 years and in good health. US if healthy 75-year-old men and women who have ever smoked and have not undergone screening before	Symptomatic aneurysm Fusiform aneurysms ≥5.5 cm in otherwise healthy male patients Women with saccular aneurysms Woman with an aneurysm between 5.0 and 5.4 cm	Imaging at 3-year intervals for AAA between 3.0 and 3.9 cm Imaging yearly for AAA 4–4.9 cm Imaging every 6 months for AAA 5.0–5.4 cm	None
2010	European Society for Vascular Surgery ^{66,102}	Men should be screened with a single US at age 65 Population screening of older female smokers does not reduce incidence of rupture	Men should be considered for intervention when maximal diameter reaches 5.5 cm		
2009	Society for Vascular Surgery ¹⁰³	One-time US screening for men aged ≥65 Screening recommended for first-degree relatives of patients with AAA	Smoking cessation is recommended to reduce risk of AAA growth and rupture Elective repair is recommended for patients with a fusiform AAA ≥5.5 cm in maximal diameter		
2007	National Screening Committee (UK) ¹⁰²	US screening available for all men aged ≥65			
2007	Canadian Society for Vascular Surgery ¹⁰⁴	All men aged from 65 to 75 to be screened Individual selective screening for those at high risk: women aged >65 with high risk secondary to smoking, cerebrovascular disease, and family history Men aged <65 with positive family history			
2005	American College of Cardiology/American Heart Association ¹⁰⁵	Screening for men aged ≥65 Screening for women aged 60–85 with a family history of AAA	Intervention is not recommended for asymptomatic infrarenal or juxtarenal AAAs if they measure less than 5.0 cm in diameter in men or <4.5 cm in diameter in women	Patients with infrarenal or juxtarenal AAAs measuring 4–5.4 cm in diameter should be monitored by ultrasound or computed tomographic scans every 6–12 months to detect expansion	
2004	Society for Vascular Surgery/American Association for Vascular Surgery/Society for Vascular Medicine and Biology ¹⁰⁶	Screening for all men aged 60–85 Screening for women aged 60–85 with a family history of AAA			

AAA, abdominal aortic aneurysm; US, ultrasound.

screening criteria (Table 72.4) and until recently, screening for women was not recommended in the United States.

Screening of women for AAA has been controversial due to few women being included in the initial screening trials so

the incidence of rupture could not be identified.⁹ Current evidence, however, indicates that despite the lower incidence of AAA in women, the rate of rupture is higher and the overall life expectancy is longer. These findings suggest that it may be

more cost-effective to screen women than previously thought.⁶⁷ Taking these considerations into account, currently the Society for Vascular Surgery (SVS) recommends screening for men and women 65–75 years old who have ever smoked, with different thresholds for treatment based on gender (Table 72.4).⁹ A recent retrospective analysis that found that aneurysm diameter indexed to body size (aortic size index = aneurysm diameter [cm]/body surface area [m^2]) represents a superior prediction model for rupture risk in women, which may further improve screening guidelines for women in the future.⁶⁸

For those who are found to have an AAA either incidentally or on screening ultrasound, there has been much controversy over screening intervals. The incidence of AAAs exceeding 4 cm following “negative” initial screening is lower than that after initial screening, but both the ADAM trial and others have demonstrated that a subset of patients deemed “normal” at a first screening will go on to develop aneurysms susceptible to rupture.^{8,21} A recent meta-analysis has stratified patients with different-sized AAA seen on initial screening into groups based upon rupture risk with different screening interval recommendations based upon the size of the aneurysms.⁶⁹ These recommendations have been adopted in the current SVS Guidelines, but the level of recommendation remains weak (Table 72.4).⁹

MEDICAL THERAPY

The current approach to the medical management of infrarenal aortic aneurysms focuses mainly on small aneurysms. Although multiple agents – including statins, angiotensin-converting enzyme (ACE) inhibitors, β -blockers, and antibiotics including tetracycline and doxycycline – have been shown in animal models to slow aneurysm progression, effectiveness has not been clearly demonstrated in humans. The only interventions that have been shown to reduce AAA progression to rupture are smoking cessation and blood pressure control; this is particularly true in females.^{9,54}

Successful experimental targets, in animal models, for pharmaceutical AAA stabilization include anti-inflammatory, protease inhibition, oxidative stress, blood pressure lowering, lipid metabolism, cell therapy, matrix/morphogens, metabolism, neutraceuticals, and sex hormones.^{54,70} Additional targeted mechanisms for potential medical management include the inhibition of immune function, dyslipidemia, hypertension, connective tissue degradation, oxidative stress, and vascular smooth muscle degradation.

It has also been proposed that increasing aortic blood flow through exercise may slow the growth of aortic aneurysms. However, this has not been proven in human modeling. It has been shown that patients with small aneurysms tolerated exercise programs well for the 3 years of the study. Concurrently, this same study showed that there was no significant increase in the size of AAAs during that time period.⁷¹ Moderate physical activity does not increase aneurysm growth rate or rupture, and patients should be encouraged to continue with activity.

Beta-blockers have been shown in animal models to be effective in stopping the expansion of AAAs.^{72,73} Some earlier small randomized human trials supported this claim. However,

more recently conducted large randomized controlled trials did not find a significant reduction in growth of AAAs in patients on beta-blocker therapy.^{74,75} Hemodynamic control, specifically with propranolol, has not been shown to decrease AAA expansion.⁷⁴

Other antihypertensive medications have also been studied to determine their effectiveness in inhibiting AAA growth.^{75–78} ACE inhibitors were reviewed with initial reports from small, retrospective studies resulting in positive effects in helping slow the growth of small aneurysms.⁷⁹ Again, further investigation in larger retrospective studies refuted these early claims and showed no demonstrable effect.^{80,81} In fact, the UK small aneurysm trial indicated an increase in the growth rate of aneurysms in patients taking ACE inhibitors.³⁵ Although ACE inhibitors themselves have not been shown to significantly affect aneurysm growth, overall control of hypertension and initiation of statin therapy have a positive effect on the perioperative risk of those who will later undergo operative intervention.

Doxycycline has been the subject of many trials, as it inhibits the activity of multiple MMPs. Although doxycycline has been shown to be effective in multiple animal models,^{82–85} this finding has not yet translated into humans. A recent randomized clinical trial which compared patients with small aneurysms treated with either a placebo or 100 mg doxycycline orally twice daily, showed that doxycycline compared to placebo did not significantly reduce growth of AAA.⁸⁶

Statin therapy has also been shown in animal models to slow the expansion of AAAs, but once again it has not clearly been shown to be effective by any randomized controlled trials in humans.^{81,87,88} The UK Heart Protection Study showed that the requirement for AAA repair was unaffected by statin therapy. This same trial, however, showed a relative reduction of 22% in major adverse cardiovascular events.⁸⁹

The use of antiplatelet agents to reduce thrombus burden has been proposed as a mechanism to slow aneurysm expansion. In rat models, antiplatelet agents were shown to reduce AAA expansion.^{90,91} However, no randomized control trials have shown direct correlation of reduction of AAA expansion with the use of antiplatelet therapy in humans. In summary, to date, there is no definitive evidence to suggest any specific medical management strategy slows the growth rate of AAAs.⁹² The lack of translation from animal models to human research is likely due to inadequate animal models, lack of understanding of progression of human disease, and poorly designed and underpowered trials.⁹³ With the continued research in bettering large animal models, translation to human efficacy may be identified in the near future.

INDICATIONS FOR INTERVENTION

In general, the size criterion for elective repair is 5.5 cm for men and 5 cm for women.^{9,94} Both the UK small aneurysm trial and the ADAM trial documented that surveillance of aneurysms between 4 and 5.5 cm is safe with compliant patients. However, in the ADAM trial, over 80% of patients with aneurysms between 5 and 5.4 cm underwent eventual repair. Additionally, over 60% of patients initially assigned to the

surveillance groups in both trials eventually underwent repair. With 10-year follow-up in the UK small aneurysm trial, this percentage increased to 74%. Additional indications for elective or early intervention included saccular aneurysms, dissection of mural thrombus, or fracture of saccular calcification. It has been shown that elective repair of asymptomatic AAAs less than 5.5 cm in diameter provides no survival benefit as compared with surveillance and elective repair once the AAA has reached traditional size criteria.⁹⁵

For those patients who are symptomatic or have suffered rupture, there is no specific size criterion for repair. However, while ruptured AAA should be repaired urgently, symptomatic patients may be medically optimized in the ICU prior to urgent repair.⁹⁶ For patients who can tolerate repair, whether endovascular or open, intervention should be offered (see Chapter Algorithm).

The difficulty in the overall consideration of operative intervention is that early intervention in certain patients may be beneficial, especially when operative risk is less than rupture risk and/or potential mortality due to rupture. Factors that impact aortic rupture risk include the initial maximal aneurysm diameter, rate of growth, and morphology. One should also consider elective operative mortality risk, life expectancy, and patient preference before proceeding with AAA repair.

A secondary consideration is the decision to pursue open versus endovascular intervention. It has been shown that long-term mortality is equivalent at approximately the 2-year mark whether open or endovascular repair is performed. However, endovascular intervention offers a three-fold reduction in perioperative mortality, particularly in patients with significant comorbidities.^{97,98} Despite this, there remains a clear role for open repair of AAA. In young, otherwise healthy patients, open repair may be preferred due to longer durability. Patients who may require re-intervention due to anatomic features may also benefit from open repair. Lastly, patients with connective tissue disorders are prone to long-term complications from endovascular repairs due to progression of their disease, and an open repair may be a more durable option in these patients⁹⁴ (see Ch. 73, Abdominal Aortic Aneurysms: Open Surgical Treatment).

Risk Calculator

With increasing sophistication of outcomes research, including the establishment of high-quality prospective registries, risk calculators have been developed enabling more patient-specific determination of risk when operative intervention is under consideration. The provision of more risk-specific information for patients with particular comorbidities is quickly becoming the standard of care, and it is recommended by the Centers for Medicare & Medicaid Services as a discussion point during the informed consent process. Risk calculators are easily found on the Internet and are available in downloadable applications for a tablet or mobile phone. Bertges et al. reported the Vascular Study Group of New England (VSGNE) risk index specifically for patients undergoing carotid endarterectomy, lower extremity bypass, and endovascular or open repair of infrarenal AAAs.⁹⁹ As compared with previously used risk calculators,

this one, explicitly derived for particular vascular interventions, was better at predicting the actual rates of postoperative cardiac events. It has been shown that risk calculators that were not vascular-specific clearly underestimated the number of postoperative cardiac events in vascular patients.¹⁰⁰ This specific risk calculator has been validated by the Vascular Quality Initiative database and is recommended for use (Level of recommendation: 2 Weak/Quality of evidence: C Low) by the SVS practice guidelines on the care of patients with an abdominal aortic aneurysm.⁹

The SVS provides online access to this risk calculator for intervention-specific events. For open AAA repair, the calculator considers the following patient and procedural variables: serum creatinine, the presence of chronic obstructive pulmonary disease, the anticipated level of distal anastomosis, planned proximal aortic clamp position, BMI, race, previous coronary artery bypass graft or percutaneous coronary intervention, results of patient's stress test within past 2 years, history of congestive heart failure, and age.¹⁰⁰

FUTURE DIRECTIONS

Endograft technology continues to evolve to improve outcomes and broaden current indications for use. Similarly, advances in our understanding of the genetic and molecular pathophysiology of aneurysm formation, growth, and rupture will drive the next round of advances in diagnosis and therapy. Better characterization of the serologic/proteomic/transcriptomic profile during aneurysm growth and particularly around the time of rupture may yield opportunities to develop biomarker screening for existing aneurysms and for evidence of active progression and impending rupture. As an example, future care of the AAA patients may involve measurement of circulating plasma levels of peptides associated with collagen and elastin degeneration during proteolysis of the extracellular matrix (ECM).¹⁰¹

With the help of precision and genomic medicine, earlier identification of patients at risk of aneurysm development or rupture may be feasible. As the cost of genomic sequencing has decreased, so too has the capacity for pre-emptive genotyping which can allow for identification of at-risk populations. Through the use of complex models and genome-wide association studies, gene loci associated with AAA development are being identified and polygenic risk calculators have already been developed.⁶² Integration into clinical practice is yet to be seen but is likely in the near future.

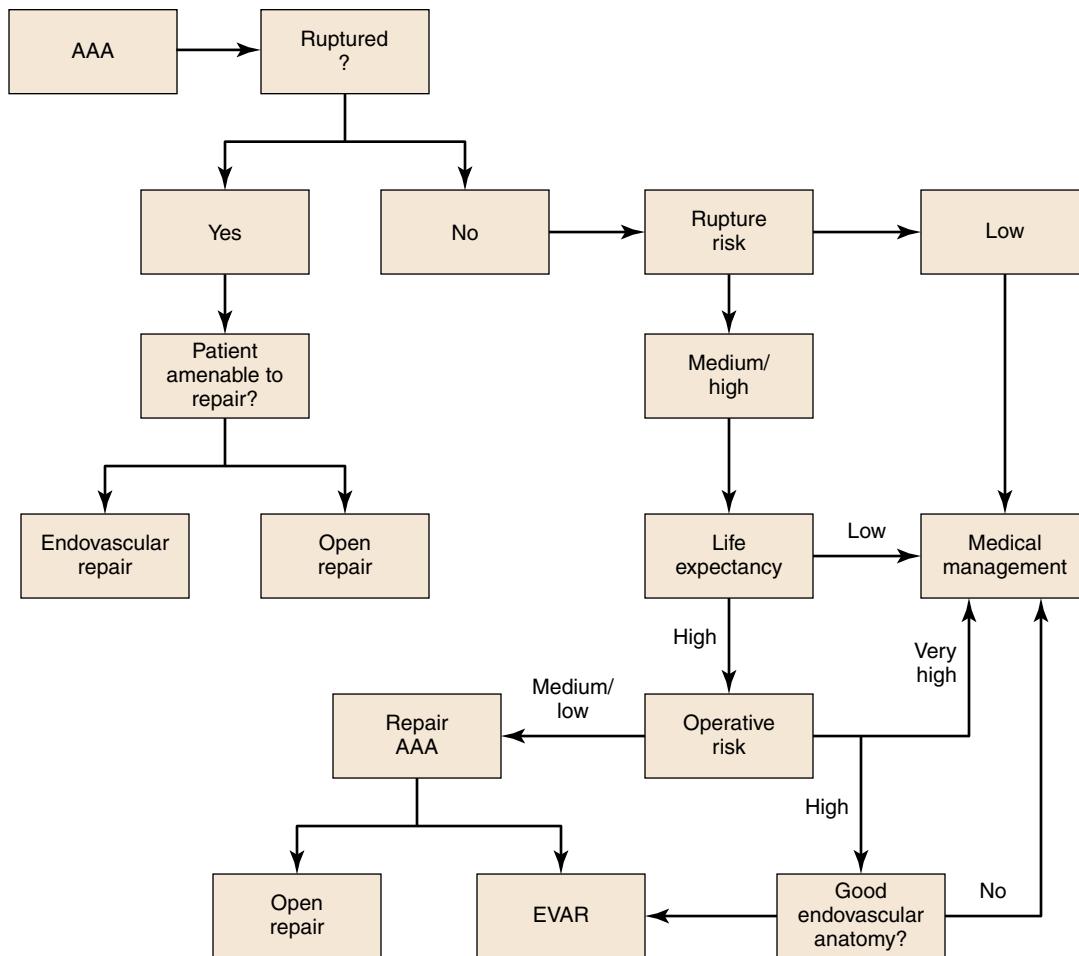
Imaging interpretation and technology may also help with advancements in dealing with AAAs. At its most basic level, this may simply reflect the incorporation of observed characteristics of aneurysms into the interpretation of existing imaging technology to provide the clinician parameters for consideration beyond simple maximal aneurysm diameter and gross morphology. Disruption of the ILT by fresh hemorrhage, yielding a "crescent sign" on CT or three-dimensional ultrasonographic imaging, may be used to suggest impending rupture. As calcification of the external media has been observed to be protective against growth, improved characterization of the degree and properties of observed calcification may also be used to inform imaging interpretation and individual patient risk.

Better definition of the characteristics of aortic ILT and wall inflammation may also lead to the assessment of inflammatory cell activity using MRI, scintigraphy, or radionucleotide scans.

The most ambitious goal, however, remains the translation of the growing body of knowledge regarding the biologic mechanisms of aneurysm formation, growth, and rupture into effective medical therapy. Beneficiaries of these advances will include patients with small aneurysms as well as those with

larger aneurysms who are medically ineligible for repair. Promising current targets include: (1) interruption of the inflammatory cascade leading to the degeneration of medial smooth muscle and ECM through MMPs 2, 8, and 9 as well as inflammatory cytokines, including TNFs and interleukins IL-1 β , IL-4, IL-6, and IL-8; (2) suppressing neoangiogenesis, which characterizes adventitial changes; and (3) minimizing the oxidative injury associated with ILT.

CHAPTER ALGORITHM



(A simple algorithm for the management of patients with abdominal aortic aneurysms (AAAs). EVAR, endovascular aneurysm repair.)

SELECTED KEY REFERENCES

Baxter BT, Terrin MC, Dalman RL. Medical management of small abdominal aortic aneurysms. *Circulation*. 2008;117:1883–1889.

Comprehensive and up-to-date review of state-of-the-art medical management of small AAAs.

Holt PJE, Poloniecki JD, Gerrard D, et al. Meta-analysis and systematic review of the relationship between volume and outcome in abdominal aortic aneurysm surgery. *Br J Surg*. 2007;94:395–403.

Large-scale meta-analysis of 500,000 patients who underwent aneurysm repair demonstrating a significant reduction in perioperative mortality when surgery was performed in hospitals performing a large number of cases per year.

Lederle FA, Freischlag JA, Kyriakides TC, et al. Long-term comparison of endovascular and open repair of abdominal aortic aneurysm. *N Engl J Med*. 2012;367:1988–1997.

Key randomized trial of EVAR versus open AAA repair. No differences were seen in the overall death or reintervention rates between open repair and endovascular aneurysm repair in long-term follow-up in this large-scale randomized controlled trial.

Lederle FA, Johnson GR, Wilson SE, et al. Rupture rate of large abdominal aortic aneurysms in patients refusing or unfit for elective repair. *JAMA*. 2002;287:2968–2972.

The largest study to date of patients with “large” (>5.5 cm) aneurysms who refused or were unfit for elective repair. A high percentage had autopsy studies performed and most did not undergo surgery, thus demonstrating the natural history of these patients in a controlled environment.

Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med.* 2002;346:1437–1444.

Classic U.S. randomized trial comparing open AAA repair and surveillance with selected repair; similar results (mostly in men) were demonstrated despite a lower mortality rate for open repair in this study.

Lindholt JS, Norman P. Screening for abdominal aortic aneurysm reduces overall mortality in men. A meta-analysis of the mid- and long-term effects of screening for abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg.* 2008;36:167–171.

Largest accumulation of AAA screening study results yet published (>125,000 patients) that includes long-term follow-up from the screening studies; a significant reduction in aneurysm-related and all-cause long-term mortality was demonstrated.

Powell JT, Brown LC, Forbes JF, et al. Final 12-year follow-up of surgery versus surveillance in the UK Small Aneurysm Trial. *Br J Surg.* 2007;94:702–708.

Long-term follow-up on the seminal randomized trial comparing open AAA repair and surveillance with selected repair.

Powell JT, Sweeting MJ, Brown LC, et al. Systematic review and meta-analysis of growth rates of small abdominal aortic aneurysms. *Br J Surg.* 2011;98:609–618.

Detailed literature review of studies discussing growth rates of small AAAs. More detailed estimates of aneurysm growth by initial aneurysm size were gained, along with determinants of growth rate.

Schermerhorn ML, O’Malley AJ, Jhaveri A, et al. Endovascular vs. open repair of abdominal aortic aneurysms in the Medicare population. *N Engl J Med.* 2008;358:464–474.

Largest comparison of “matched” open and endovascular AAA repair cases to date, with more than 22,000 patients in each group. This is the first study to quantify the secondary procedures and hospitalizations related to the open abdominal incision (bowel obstruction and hernia repair), not just aorta-related interventions. It also captures the rate of discharge to skilled nursing facilities.

Sweeting MJ, Thompson SG, Brown LC, Powell JT. RESCAN collaborators. Meta-analysis of individual patient data to examine factors affecting growth and rupture of small abdominal aortic aneurysms. *Br J Surg.* 2012;99(5):655–665.

Individual patient data meta-analysis of 15,000 patients over 18 trials of aneurysm surveillance versus early repair. The influence of covariates, including demographics, medical, and drug history on aneurysm growth and rupture rates, were determined.

Thompson SG, Ashton HA, Gao L, et al. on behalf of the Multicentre Aneurysm Screening Study (MASS) Group. Final follow-up of the Multicentre Aneurysm Screening Study (MASS) randomized trial of abdominal aortic aneurysm screening. *Br J Surg.* 2012;99:1649–1656.

Final results of the largest randomized trial on AAA screening, demonstrating a reduction in aneurysm-related and all-cause mortality.

A complete reference list can be found online at www.expertconsult.com.

REFERENCES

1. Lytton DG, Resuhr LM. Galen on abnormal swellings. *J Hist Med All Sci.* 1978;XXXIII:531–549.
2. Stehbens WE. History of aneurysms. *Med Hist.* 1958;2:274–280.
3. Matas R. Aneurysm of the abdominal aorta at its bifurcation into the common iliac arteries. *Ann Surg.* 1940;112:909–922.
4. Volodos NL, et al. Clinical experience of the use of self-fixing synthetic prostheses for remote endoprosthetics of the thoracic and the abdominal aorta and iliac arteries through the femoral artery and as intraoperative endoprosthesis for aorta reconstruction. *Vasa Suppl.* 1991;33:93–95.
5. DeBakey ME, Cooley DA, Crawford ES, Morris GC. Clinical application of a new flexible knitted dacron arterial substitute. *AMA Arch Surg.* 1958;77:713–724.
6. Parodi JC. Endoluminal treatment of arterial diseases using a stent-graft combination: reflections 20 years after the initial concept. *J Endovasc Surg.* 1997;4:3–4.
7. Parodi JC, Barone A, Piraino R, Schonholz C. Endovascular treatment of abdominal aortic aneurysms: lessons learned. *J Endovascular Ther.* 1997;4:102–110.
8. Lederle FA, et al. The Aneurysm Detection and Management Study Screening Program: Validation Cohort and Final Results. *Arch Intern Med.* 2000;160:1425–1430.
9. Chaikof EL, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg.* 2018;67:2–77.e2.
10. Głowiczki P, et al. Multiple aortic aneurysms: The results of surgical management. *J Vasc Surg.* 1990;11:19–28.
11. Lederle FA, et al. Prevalence and associations of abdominal aortic aneurysm detected through screening. *Ann Intern Med.* 1997;126:441.
12. Scott RA, Wilson NM, Ashton HA, Kay DN. Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study. *Br J Surg.* 1995;82:1066–1070.
13. Lindholt JS, Juul S, Fasting H, et al. Screening for abdominal aortic aneurysms: single centre randomized controlled trial. *BMJ.* 2005;330:750.
14. Norman PE, Jamrozik K, Lawrence-Brown MM, et al. Population based randomized controlled trial on impact of screening on mortality from abdominal aortic aneurysm. *BMJ.* 2004;329:1259.
15. Ashton HA, Buxton MJ, Day NE, et al. Multicentre Aneurysm Screening Study Group. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomized controlled trial. *Lancet.* 2002;360:1531.
16. Pleumeekers HJ, Hoes AW, van der Does E, et al. Aneurysms of the abdominal aorta in older adults: The Rotterdam Study. *Am J Epidemiol.* 1995;142:1291.
17. Singh K, Bønaa KH, Jacobsen BK, et al. Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study: The Tromsø Study. *Am J Epidemiol.* 2001;154(3):236–244.
18. Lederle FA. The rise and fall of abdominal aortic aneurysm. *Circulation.* 2011;124:1097–1099.
19. Keulen CJ, van V, Pals G, Rauwerda JA. Familial abdominal aortic aneurysm: a systematic review of a genetic background. *Eur J Vasc Endovasc.* 2002;24:105–116.
20. Luijten KM, van de, et al. Lower atherosclerotic burden in familial abdominal aortic aneurysm. *J Vasc Surg.* 2014;59:589–593.
21. Cornuz J, Pinto CS, Tevaarai H, Egger M. Risk factors for asymptomatic abdominal aortic aneurysmSystematic review and meta-analysis of population-based screening studies. *Eur J Public Health.* 2004;14:343–349.
22. Brown LC, Powell JT. Risk factors for aneurysm rupture in patients kept under ultrasound surveillance. *Ann Surg.* 1999;230:289.
23. Pleumeekers HJCM, et al. Aneurysms of the abdominal aorta in older adults. *Am J Epidemiol.* 1995;142:1291–1299.
24. Ruddy JM, Jones JA, Spinale FG, Ikonomidis JS. Regional heterogeneity within the aorta: Relevance to aneurysm disease. *J Thorac Cardiovasc Surg.* 2008;136:1123–1130.
25. Graham LM, et al. Clinical significance of arteriosclerotic femoral artery aneurysms. *Arch Surg.* 1980;115:502–507.
26. Whitehouse WM, et al. Limb-threatening potential of arteriosclerotic popliteal artery aneurysms. *Surgery.* 1983;93:694–699.
27. Huang Y, et al. Common iliac artery aneurysm: Expansion rate and results of open surgical and endovascular repair. *J Vasc Surg.* 2008;47:1203–1211.e2.
28. Parry DJ, Kessel D, Scott DJ. Simplifying the internal iliac artery aneurysm. *Ann Roy Coll Surg.* 2001;83:302–308.
29. Subcommittee on Reporting Standards for Arterial Aneurysms, Ad Hoc Committee on Reporting Standards, Society for Vascular Surgery and North American Chapter, International Society for Cardiovascular Surgery. Suggested standards for reporting on arterial aneurysms. *J Vasc Surg.* 1991;13:452–458.
30. Kretz B, et al. Mycotic aneurysm of both internal iliac arteries due to *Candida albicans*. *Ann Vasc Surg.* 2014;28:738.e11–4.
31. Polat KY, et al. Spontaneous mycotic external iliac artery aneurysm rupture after perforated acute appendicitis in a renal allograft recipient. *Exp Clin Transplant Official.* 2011;9:211–213.
32. Huang Y, et al. Common iliac artery aneurysm: Expansion rate and results of open surgical and endovascular repair. *J Vasc Surg.* 2008;47:1203–1211.e2.
33. Wilhelm BJ, Sakharpe A, Ibrahim G, Baccaro LM, Fisher J. The 100-year evolution of the isolated internal iliac artery aneurysm. *Ann Vasc Surg.* 2014;28:1070–1077.
34. Lederle FA, et al. Rupture rate of large abdominal aortic aneurysms in patients refusing or unfit for elective repair. *JAMA.* 2002;287:2968–2972.
35. The UK Small Aneurysm Trial Participants. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet.* 1998;352:1649–1655.
36. Taylor BV, Kalman PG. Saccular aortic aneurysms. *Ann Vasc Surg.* 1999;13:555–559.
37. Vorp DA, Raghavan ML, Webster MW. Mechanical wall stress in abdominal aortic aneurysm: Influence of diameter and asymmetry. *J Vasc Surg.* 1998;27:632–639.
38. Fillinger MF, et al. Anatomic characteristics of ruptured abdominal aortic aneurysm on conventional CT scans: implications for rupture risk. *J Vasc Surg.* 2004;39:1243–1252.
39. Schurink GWH, Baalen JM, van Visser MJT, Bockel JH van. Thrombus within an aortic aneurysm does not reduce pressure on the aneurysmal wall. *J Vasc Surg.* 2000;31:501–506.
40. Golledge J, Abrokwa J, Shenoy KN, Armour RH. Morphology of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc.* 1999;18:96–104.
41. Schmidt MH, Mitchell JR, Downey DB. Sonographic surveillance of abdominal aortic aneurysms: what is the smallest change in measured diameter that reliably reflects aneurysm growth? *Can Assoc Radiologists J.* 1999;50:241–246.
42. Sweeting MJ, Thompson SG, Brown LC, RESCAN collaborators. Meta-analysis of individual patient data to examine factors affecting growth and rupture of small abdominal aortic aneurysms. *J Vasc Surg.* 2012;56:1473.
43. RESCAN Collaborators, et al. Surveillance intervals for small abdominal aortic aneurysms: a meta-analysis. *JAMA.* 2013;309:806–813.
44. Brady AR, Thompson SG, Fowkes FGR, Greenhalgh RM, Powell JT. Abdominal aortic aneurysm expansion. *Circulation.* 2004;110:16–21.
45. Erbel R, et al. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). *Eur Heart J.* 2014;35:2873–2926.
46. Kuivaniemi H, Ryer EJ, Elmore JR, Tromp G. Understanding the pathogenesis of abdominal aortic aneurysms. *Expert Rev Cardiovasc Ther.* 2015;13:975–987.
47. Folsom AR, et al. Circulating biomarkers and abdominal aortic aneurysm incidence. *Circulation.* 2015;132:578–585.

48. Stather PW, et al. Meta-analysis and meta-regression analysis of biomarkers for abdominal aortic aneurysm. *Br J Surg.* 2014;101:1358–1372.
49. Htun NM, Peter K. Biomarkers for AAA: Encouraging steps but clinical relevance still to be delivered. *Proteomics Clin Appl.* 2014;8:732–734.
50. Ailawadi G, Eliason JL, Upchurch Jr GR. Current concepts in the pathogenesis of abdominal aortic aneurysm. *J Vasc Surg.* 2003;38:584–588.
51. Lopez-Candales A, et al. Decreased vascular smooth muscle cell density in medial degeneration of human abdominal aortic aneurysms. *Am J Pathol.* 1997;150:993–1007.
52. Pan JH, et al. Macrophage migration inhibitory factor is associated with aneurysmal expansion. *J Vasc Surg.* 2003;37:628–635.
53. Nordon IM, Hinchliffe RJ, Loftus IM, Thompson MM. Pathophysiology and epidemiology of abdominal aortic aneurysms. *Nat Rev Cardiol.* 2011;8:92–102.
54. Golledge J. Abdominal aortic aneurysm: update on pathogenesis and medical treatments. *Nat Rev Cardiol.* 2019;16:225–242.
55. Annabi B, et al. Differential regulation of matrix metalloproteinase activities in abdominal aortic aneurysms. *J Vasc Surg.* 2002;35:539–546.
56. Li T, Lv Z, Jing JJ, Yang J, Yuan Y. Matrix metalloproteinase family polymorphisms and the risk of aortic aneurysmal diseases: A systematic review and meta-analysis. *Clin Genet.* 2017;93:15–32.
57. Longo GM, et al. Matrix metalloproteinases 2 and 9 work in concert to produce aortic aneurysms. *J Clin Investig.* 2002;110:625–632.
58. Parr A, et al. Thrombus volume is associated with cardiovascular events and aneurysm growth in patients who have abdominal aortic aneurysms. *J Vasc Surg.* 2011;53:28–35.
59. Mäyränpää MI, et al. Mast cells associate with neovessels in the media and adventitia of abdominal aortic aneurysms. *J Vasc Surg.* 2009;50:388–395.
60. Wahlgren CM, Larsson E, vascular PMJ. Genetic and environmental contributions to abdominal aortic aneurysm development in a twin population. *Atherosclerosis.* 2010;51:3–7.
61. Larsson E, Granath F, Swedenborg J, Hultgren R. A population-based case-control study of the familial risk of abdominal aortic aneurysm. *J Vasc Surg.* 2009;49:47–51.
62. Klarin D, et al. Genetic architecture of abdominal aortic aneurysm in the Million Veteran Program. *Circulation.* 2020;142(17):1633–1646.
63. Sörelius K, Budtz-Lilly J. Systematic review of the management of mycotic aortic aneurysms. *Atherosclerosis.* 2019;58:426–435.
64. Engellau L, et al. Measurements before endovascular repair of abdominal aortic aneurysms. *Acta Radiol.* 2003;44:177–184.
65. Radiology EP on VI and I, et al. ACR Appropriateness Criteria® Abdominal Aortic Aneurysm: Interventional Planning and Follow-Up. *J Am Coll Radiol.* 2018;15:S2–S12.
66. Moll FL, et al. Management of Abdominal Aortic Aneurysms Clinical Practice Guidelines of the European Society for Vascular Surgery. *Eur J Vasc Endovasc.* 2011;41:S1–S58.
67. Wanhainen A, Lundkvist J, Bergqvist D, Björck M. Cost-effectiveness of screening women for abdominal aortic aneurysm. *J Vasc Surg.* 2006;43:908–914.
68. Lo RC, et al. Relative importance of aneurysm diameter and body size for predicting abdominal aortic aneurysm rupture in men and women. *J Vasc Surg.* 2014;59:1209–1216.
69. Thompson S, et al. Systematic review and meta-analysis of the growth and rupture rates of small abdominal aortic aneurysms: implications for surveillance intervals and their cost-effectiveness. *Health Technol Assess.* 2013;17:1–118.
70. Makrygiannis G, et al. Sex differences in abdominal aortic aneurysm: the role of sex hormones. *Ann Vasc Surg.* 2014;28:1946–1958.
71. Myers J, et al. A randomized trial of exercise training in abdominal aortic aneurysm disease. *Med Sci Sports Exerc.* 2014;46:2–9.
72. Slaiby JM, Ricci MA, Gadowski GR, Hendley ED, Pilcher DB. Expansion of aortic aneurysms is reduced by propranolol in a hypertensive rat model. *J Vasc Surg.* 1994;20:178–183.
73. Moursi MM, Beebe HG, Messina LM, et al. Inhibition of aortic aneurysm development in blotchy mice by beta adrenergic blockade independent of altered lysyl oxidase activity. *J Vasc Surg.* 1995;21:792–800.
74. Wilmink ABM, Hubbard CSFF, Day NE, Quick CRG. Effect of propanolol on the expansion of abdominal aortic aneurysms: a randomized study. *Br J Surg.* 2000;87:499–499.
75. Wilmink ABM, et al. Are antihypertensive drugs associated with abdominal aortic aneurysms? *J Vasc Surg.* 2002;36:751–757.
76. Gadowski GR, Pilcher DB, Ricci MA, Burlington F. University of Vermont College of Medicine. Abdominal aortic aneurysm expansion rate: effect of size and beta-adrenergic blockade. *J Vasc Surg.* 1994;19:727–731.
77. Leach SD, Toole AL, Stern H, et al. Effect of β-adrenergic blockade on the growth rate of abdominal aortic aneurysms. *Arch Surg.* 1988;123:606–609.
78. Hackam DG, Thiruchelvam D, Redelmeier DA. Angiotensin-converting enzyme inhibitors and aortic rupture: a population-based case-control study. *Lancet.* 2006;368:659–665.
79. Kortekaas KE, et al. ACE inhibitors potently reduce vascular inflammation, results of an open proof-of-concept study in the abdominal aortic aneurysm. *PLoS One.* 2014;9:e111952.
80. Thompson AR, Cooper JA, Ashton HA, Hafez H. Growth rates of small abdominal aortic aneurysms correlate with clinical events. *Br J Surg.* 2010;97:37–44.
81. Sweeting MJ, Thompson SG, Brown LC, et al. Use of angiotensin converting enzyme inhibitors is associated with increased growth rate of abdominal aortic aneurysms. *J Vasc Surg.* 2010;52:1–4.
82. Pyo R, et al. Targeted gene disruption of matrix metalloproteinase-9 (gelatinase B) suppresses development of experimental abdominal aortic aneurysms. *J Clin Invest.* 2000;105:1641–1649.
83. Manning MW, Cassis LA, Daugherty A. Differential effects of doxycycline, a broad-spectrum matrix metalloproteinase inhibitor, on angiotensin II-induced atherosclerosis and abdominal aortic aneurysms. *Arterioscler Thromb Vasc Biol.* 2003;23:483–488.
84. Bartoli MA, et al. Localized administration of doxycycline suppresses aortic dilatation in an experimental mouse model of abdominal aortic aneurysm. *Ann Vasc Surg.* 2006;20:228.
85. Chung AWY, Yang HHC, Radomski MW, van Breemen C. Long-term doxycycline is more effective than atenolol to prevent thoracic aortic aneurysm in Marfan syndrome through the inhibition of matrix metalloproteinase-2 and -9. *Circ Res.* 2008;102:e73–e85.
86. Baxter BT, et al. Effect of doxycycline on aneurysm growth among patients with small infrarenal abdominal aortic aneurysms. *JAMA.* 2020;323:2029–2038.
87. Thompson A, et al. An analysis of drug modulation of abdominal aortic aneurysm growth through 25 years of surveillance. *J Vasc Surg.* 2010;52:55–61.e2.
88. Ferguson CD, et al. Association of statin prescription with small abdominal aortic aneurysm progression. *Am Heart J.* 2010;159:307–313.
89. Heart Protection Study Collaborative Group. Randomized trial of the effects of cholesterol-lowering with simvastatin on peripheral vascular and other major vascular outcomes in 20,536 people with peripheral arterial disease and other high-risk conditions. *J Vasc Surg.* 2007;45:645–654.e1.
90. Dai J, Louedec L, Philippe M, et al. Effect of blocking platelet activation with AZD6140 on development of abdominal aortic aneurysm in a rat aneurysmal model. *J Vasc Surg.* 2009;49:719–727.
91. Touat Z, et al. Renewal of mural thrombus releases plasma markers and is involved in aortic abdominal aneurysm evolution. *Am J Pathology.* 2006;168:1022–1030.
92. Golledge J, Powell JT. Medical management of abdominal aortic aneurysm. *Eur J Vasc Endovasc.* 2007;34:267–273.
93. Lindeman JH, Matsumura JS. Pharmacologic management of aneurysms. *Circ Res.* 2019;124:631–646.
94. Swerdlow NJ, Wu WW, Schermerhorn ML. Open and endovascular management of aortic aneurysms. *Circ Res.* 2019;124:647–661.
95. Lederle FA, Wilson AE, Johnson GR, et al. Aneurysm Detection and Management Veterans Affairs Cooperative Study Group. Immediate

- repair compared with surveillance of small abdominal aortic aneurysms. *Acc Curr J Rev.* 2002;11:87–88.
96. Bosch JAT, et al. Symptomatic abdominal aortic aneurysm repair: to wait or not to wait. *J Cardiovasc Surg.* 2013;57:830–838.
 97. Siracuse JJ, et al. Comparative safety of endovascular and open surgical repair of abdominal aortic aneurysms in low-risk male patients. *J Vasc Surg.* 2014;60:1154–1158.
 98. Hicks CW, et al. Hospital-level factors associated with mortality after endovascular and open abdominal aortic aneurysm repair. *JAMA Surg.* 2015;150:632–636.
 99. Bertges DJ, et al. The Vascular Study Group of New England Cardiac Risk Index (VSG-CRI) predicts cardiac complications more accurately than the Revised Cardiac Risk Index in vascular surgery patients. *J Vasc Surg.* 2010;52:674–683.e3.
 100. Eslami MH, et al. Comparison of a Vascular Study Group of New England risk prediction model with established risk prediction models of in-hospital mortality after elective abdominal aortic aneurysm repair. *J Vasc Surg.* 2015;62:1125–1133.e2.
 101. Golledge J, Tsao PS, Dalman RL, Norman PE. Circulating markers of abdominal aortic aneurysm presence and progression. *Circulation.* 2008;118:2382–2392.
 102. Davis M, Harris M, Earnshaw JJ. Implementation of the National Health Service Abdominal Aortic Aneurysm Screening Program in England. *J Vasc Surg.* 2013;57:1440–1445.
 103. Chaikof EL, et al. SVS practice guidelines for the care of patients with an abdominal aortic aneurysm: Executive summary. *J Vasc Surg.* 2009;50:880–896.
 104. Mastracci TM, Cinà CS, Canadian Society for Vascular Surgery. Screening for abdominal aortic aneurysm in Canada: Review and position statement of the Canadian Society for Vascular Surgery. *J Vasc Surg.* 2007;45:1268–1276.e5.
 105. Smith SC, et al. AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and Other Atherosclerotic Vascular Disease: 2011 Update. *Circulation.* 2011;124:2458–2473.
 106. Kent KC, et al. Screening for abdominal aortic aneurysm: A consensus statement. *J Vasc Surg.* 2004;39:267–269.

Abdominal Aortic Aneurysms: Open Surgical Treatment

MEL J. SHARAFUDDIN

Based on a previous edition chapter by Edward Y. Woo and Scott M. Damrauer

INTRODUCTION	925
EVOLVING ROLES OF OAR AND EVAR	926
IMPACT OF OAR VOLUMES ON OUTCOMES AND TRAINING	927
CURRENT INDICATIONS FOR OPEN AORTIC REPAIR	927
Patient Age, State of Health, and Preference	928
Underlying Genetic Vascular Syndrome or Connective Tissue Disorder	928
PREOPERATIVE ASSESSMENT AND PLANNING	929
Preoperative Imaging	929
Computed Tomography	929
Magnetic Resonance Angiography	929
OPERATIVE TECHNIQUE	929
TRANSPERITONEAL EXPOSURE	931
Pararenal Aorta	931
Supraceliac Aorta	932
MEDIAL VISCERAL ROTATION	932
AORTIC RECONSTRUCTION	934
Closure	934
RETROPERITONEAL EXPOSURE	935
Closure	936
ANATOMIC CONSIDERATIONS IN ABDOMINAL AORTIC SURGERY	937
Management of the Inferior Mesenteric Artery	937
Renovascular Variants	938
Venous Abnormalities	939

INTRAOOPERATIVE PRINCIPLES IN ABDOMINAL AORTIC SURGERY	939
Aortic Clamping	939
Intraoperative Renal Protection	939
POSTOPERATIVE COMPLICATIONS	939
Myocardial Ischemia	940
Respiratory Complications	940
Acute Kidney Injury	941
Visceral Ischemia	941
Colonic Ischemia	941
Lower Extremity Ischemia	941
Spinal Cord Ischemia	941
Postoperative Surveillance	942
SPECIAL SURGICAL CONSIDERATIONS AND VARIATIONS	942
Open Conversion of EVAR	942
Technical Considerations in OC and Endograft Explantation	942
INFECTED ABDOMINAL AORTIC ANEURYSMS	943
Primary Mycotic Aortic Aneurysm/Pseudoaneurysm	943
Secondary AAA Infection/Secondary Mycotic Aortic Aneurysm	944
Aortic Graft/Endograft Infection	944
INFLAMMATORY ABDOMINAL AORTIC ANEURYSMS	944
OAR versus EVAR in IAAA	946
CHAPTER ALGORITHM	946

INTRODUCTION

Abdominal aortic aneurysm (AAA) is a common disorder with an estimated incidence of 4%–7% in western countries.^{1–5} It is the 13th-leading cause of death in the United States, with 15,000 deaths yearly. Ruptured AAA (RAAA) continues to carry an operative mortality of 40%–70% and overall mortality

of 80%–90%, which have not improved much over the past four decades despite major advances in surgical care and the introduction of endovascular aortic aneurysm repair (EVAR).^{6–11} However, there appears to be a recent favorable trend in aneurysm-related mortality which may reflect increased eligibility to screening programs and sustained survival benefits from increasing use of an EVAR-first strategy in RAAA in patients

TABLE 73.1 Early Mortality in Population-Based and Database-Derived Series

Series	Study Period	Number of Patients	Mortality	Data Source
Bradbury et al. ²³	1976–1996	842	7.5%	Royal Edinburgh Infirmary Database
Heller et al. ¹¹	1979–1999	358,521	5.6%	National (US) Hospital Discharge Survey
Johnston et al. ³⁰	1986	666	4.8%	Canadian Society for Vascular Surgery
Lawrence et al. ³²	1990–1994	32,389	8.4%	National (US) Hospital Discharge Survey
Galland ²⁷	1990–1995	2680	4.8%	British Joint Vascular Research Group
Dardik ²⁵	1990–1995	2335	3.5%	Maryland Health Service Cost Review
Akkersdijk et al. ²⁰	1990	1289	6.8%	Dutch National Medical Registration
Kazmers et al. ³¹	1991–1993	3687	4.9%	(US) Veterans Affairs Medical Centers
Bush et al. ²⁴	1991–2008	14,232	4.4%	US NSQIP-VA
Lee et al. ³³	2001	4607	3.8%	National (US) Inpatient Sample
Huber et al. ²⁹	1994–1996	16,450	4.2%	National (US) Inpatient Sample
Rigberg et al. ³⁴	1995–1999	9778	3.8%	California Statewide
Dimick et al. ²⁶	1996–1997	7980	3.8%	National (US) Inpatient Sample
Anderson et al. ²¹	2000–2002	3064	3.9%	New York (US) Statewide
Schermerhorn et al. ¹⁹	2001–2004	22,830	4.8%	Medicare (US) Beneficiaries
Schwarze et al. ²⁸²	2001–2006	75,222	3.0%	National (US) Inpatient Sample
Davenport and Xenos ²⁸³	2005–2009	3967	3.4%	US NSQIP
De la Motte et al. ³⁵	2007–2010	1176	3.3%	Danish nationwide cohort
Hicks et al. ³⁶	2007–2011	34,535	3.8%	Medicare (US) Beneficiaries
Grant et al. ²⁸	2008–2010	48,593	4.7%	UK National Vascular Database
Teixeira et al. ¹⁸	2003–2014	3530	2.7%	Society for Vascular Surgery (SVS) Vascular Quality Initiative (VQI)

with adequate imaging and suitable anatomy.^{7,12–14} In contrast to RAAA, modern outcomes with open aortic repair (OAR) for intact AAA are excellent. Historically in the 5% to 8% range, early mortality of OAR in most population-based registries, carefully controlled trials, and high volume centers of excellence now approaches 3% (Table 73.1).^{7,11,15–37} Early detection of AAA through screening and timely elective repair is the most reliable strategy for preventing aneurysm-related death with several randomized studies demonstrating 50% reduction in AAA rupture rate and overall AAA-related mortality.^{38–41}

EVOLVING ROLES OF OAR AND EVAR

The landscape of AAA repair changed drastically in 1999 following approval by the FDA of two EVAR devices for commercial use. This minimally invasive therapy offered lower operative mortality compared to OAR with fast recovery and return to normal daily life and activities (see Ch. 75, Aortoiliac Aneurysms: Endovascular Treatment).^{42–45} Within a decade, several high-quality randomized controlled trials had been conducted demonstrating better short-term and equivalent intermediate-term outcomes with EVAR compared to OAR.^{46–49} This helped propel EVAR to become the primary mode of therapy for the majority of patients with AAA, with OAR reserved for patients with increasingly complex anatomies or contraindications to

EVAR.^{50–52} A study of Medicare recipients' data from 2003 to 2013 illustrated the disruptive impact of EVAR on OAR, with a 76% decrease in OAR volume while EVAR volume nearly doubled.⁵³ Continued growth of EVAR adoption also reflects introduction of newer generation devices and evolution of newer innovative complex EVAR techniques, notably fenestrated EVAR (FEVAR) and chimney EVAR (Ch-EVAR), enabling more minimally invasive treatment options for juxtarenal and pararenal AAAs.^{53–55} OAR is currently mostly offered to patients not amenable to EVAR, and as a result has become increasingly complex with requirement of suprarenal or supraceliac aortic cross-clamping in 30%–50% of cases, and a frequent need for additional reconstruction of concomitant aortoiliac occlusive disease.^{50,51,56} Despite the growing popularity of EVAR, OAR has maintained its status as time-tested standard of care in AAA treatment, owing to its versatility and established safety and efficacy.^{15,17,57,58} A meta-analysis of case series comparing the outcomes of elective OAR (1575 patients) and FEVAR (751 patients) for juxtarenal AAA showed a similar perioperative mortality of 4.1%, although FEVAR was associated with higher rates of secondary reintervention and renal impairment during follow-up.⁵⁹ A propensity-matched comparison of the outcomes of FEVAR and OAR in complex AAA of comparable anatomy showed higher morbidity and mortality with FEVAR,⁶⁰ reaffirming the value of OAR as the

gold standard and the need for further progress in endovascular approaches.

Despite growing complexity of OAR procedures, it is remarkable that the mortality rate of OAR has not increased accordingly. When examining contemporary series of juxtarenal and suprarenal AAAs and extent IV thoracoabdominal aortic aneurysms, the outcomes are quite comparable to those seen in infrarenal AAA (Tables 73.2 and 73.3).^{61–67} A relatively recent analysis of Vascular Study Group of New England (VSGNE) registry data compared OAR outcomes in 443 complex AAA (suprarenal clamp in 340, supraceliac clamp in 103) and 1432 infrarenal AAA, demonstrating an early mortality rate of 3.6% for complex AAA repair compared to 1.2% for routine infrarenal AAA repairs.⁶⁸

IMPACT OF OAR VOLUMES ON OUTCOMES AND TRAINING

A strong association has been repeatedly observed between hospital and operator volume of OAR procedures and perioperative adverse events and mortality.^{57,69–72} Although outcomes with EVAR are less dependent of the surgeon's case volume, worse EVAR outcomes are more likely to occur in low-volume facilities.⁷³ However, the shift towards EVAR, along with the

recent apparent decrease in AAA incidence in western countries, have lowered the exposure of vascular surgical trainees to OAR, raising concerns about maintenance of competency and highlighting a need for new training paradigms and assessment tools.^{74,75}

The argument for retaining open operative skills is important and will likely be addressed in the future by the creation of dedicated open aortic surgical training pathways and/or centralization of complex aortic care to higher volume centers.^{72,76,77} Sequestration of high-end operator skills and large operative volume into a smaller number of centers has been proposed as an option to provide ideal training opportunities in those facilities.^{69,70,78}

CURRENT INDICATIONS FOR OPEN AORTIC REPAIR

Widespread adoption of EVAR has permanently changed the landscape of AAA treatment, with EVAR becoming the preferred treatment modality in most patients meeting the indications for repair.⁷⁹ However, even in the current "EVAR era," several scenarios remain in which OAR is preferable to EVAR and newer complex endovascular aortic interventions (Box 73.1).

TABLE 73.2

Major Contemporary Abdominal and Type IV Thoracoabdominal Aortic Aneurysm Series – Mortality and Clamping Level

	Publication Year	Patients	Early Mortality	Long-Term Survival
Suprarenal Clamp				
Chong et al. ^{284,a}	2009	171	1.8%	67.7% at 5 years
Landry et al. ^{285,a}	2009	82	6.1%	NR
Knott et al. ^{286,a}	2008	126	0.8%	63.8% at 5 years
Chiesa et al. ²⁸⁷	2006	85	3.5%	NR
Nathan et al. ⁶³	2011	97	3.4%	69.1% at 5 years
Tsai et al. ^{62,a}	2012	199	2.5%	74% at 5 years
Supraceliac Clamp				
Martin et al. ⁶⁶	2000	57	1.8%	NR
Martin et al. ^{66,b}	2000	53	11.0%	NR
Coselli et al. ^{64,b}	2007	329	3.60%	65.3% at 5 years
Chiesa et al. ²⁸⁷	2006	34	2.9%	NR
Kieffer et al. ^{65,b}	2008	171	13.4%	NR
Richards et al. ^{67,a,b}	2010	53	6.0%	78% at 3 years
Nathan et al. ⁶³	2011	108	5.4%	52.9% at 5 years
Nathan et al. ^{63,b}	2011	83	5.6%	50% at 5 years
Patel et al. ^{61,b}	2011	179	2.8%	62% at 5 years
Tshomba et al. ^{288,b}	2015	222	4.9%	NR

^aElective.

^bType IV TAAA.

NR, not reported.

Modified from Nathan DP, Brinster CJ, Jackson BM, et al. Predictors of decreased short- and long-term survival following open abdominal aortic aneurysm repair. *J Vasc Surg*. 2011;54:1237–1243.

TABLE 73.3 Results of Major Randomized Endovascular Aneurysm Repair Trials

Trial	Recruitment Period	Publication Year	Follow-up (Years)	N	OAR ARM		EVAR ARM		
					30-Day Mortality	Long-term All-Cause Mortality	N	30-Day Mortality	Long-Term All-Cause Mortality
DREAM ^{47,278}	2000–2003	2004, 2010	6	178	4.6%	70%	173	1.2%	69%
OVER ^{49,279,280}	2002–2008	2009, 2019	9	437	2.5%	70%	444	0.5%	68%
EVAR-1 ^{80,281}	1999–2004	2010, 2018	15	626	6.2%	68%	626	2.1%	73%
ACE ⁴⁶	2005–2008	2011	3	149	1.3%	54%	150	0.7%	53%

BOX 73.1**Current Indications for Open Aortic Repair**

- Unfavorable anatomy for EVAR or FEVAR (unmet IFU requirements for current approved devices)
- Need to preserve patency of IMA (hypertrophied vessel, occluded SMA/CA or bilateral hypogastric arteries, or prior hemicolectomy)
- Renovascular variants (horseshoe kidney, renal ectopia, multiple small renal arteries arising across the abdominal aorta, etc.)
- Inability to preserve at least one hypogastric with EVAR
- Symptomatic or ruptured juxtarenal AAA (inability to await construction of a custom-built FEVAR device)
- Any prohibitive access issues such as excessive aortoiliac tortuosity and/or small access vessels and/or iliofemoral occlusive disease not amenable to staged optimization
- Strong patient preference, with no prohibitive risk factors for OAR
- Prolonged life expectancy (younger than 65 years)

* Delayed open conversion with partial or total explantation.

** Treatment of choice consists of oversewing of back-bleeding branches, obliterative endoaneurysmorrhaphy with stent graft preservation.

*** EVAR may be considered in those instances as a bridge option prior to definitive OAS after stabilization and/or infection source control.

- Known connective tissue disorder or genetic vascular syndrome
- Likely non-compliance with required follow-up requirements of EVAR, in the absence of prohibitive risk factors for OAR
- Open conversion:
 - Infection of prior EVAR/FEVAR
 - Failure after prior EVAR, F/B-EVAR not amenable to endovascular rescue. Usually due to type 1 or 3 endoleak, device migration*
 - Prior EVAR with type 2 endoleak and sac growth, refractory to endovascular treatment**
 - Failure after prior OAR, not amenable to endovascular rescue
 - Inflammatory AAA
 - Mycotic AAA
 - Infection or aortoenteric fistula***

Patient Age, State of Health, and Preference

The age and general health of a patient plays an important role in procedure choice. Reports on suboptimal long-term results of EVAR suggest that younger patients with long life expectancy and low perioperative risk may benefit more from open repair. Recent evidence from randomized trials and population-based studies suggests significant increase in cancer deaths in patients who underwent EVAR, raising concern for the impact of radiation exposure from lengthy complex endovascular procedures and reinterventions as well as numerous CTA studies.^{80,81} This, in addition to personal preference, could impact procedure choice in favor of OAR, especially in patients with prolonged life expectancy.

Underlying Genetic Vascular Syndrome or Connective Tissue Disorder

Although classic cardiovascular risk factors are the leading cause of AAA, diagnosis of AAA in patients younger than 60 years should prompt evaluation for underlying genetic and/or connective tissue disorders, especially in the presence of a family history. There is a list of more than 30 inheritable conditions that can potentially manifest with aortic aneurysm.

Although these are commonly associated with thoracic aortic aneurysms, they can also affect the abdominal aorta, albeit to a lesser extent. These include Marfan syndrome (MFS), vascular Ehlers–Danlos syndrome (VED), Loeys–Dietz syndrome (LDS), arterial tortuosity syndrome (ATS), and aneurysm osteoarthritis syndrome (AOS) (see Ch. 141, Aneurysms Caused by Connective Tissue Abnormalities).^{82–84} Mutations in genes encoding for extracellular matrix components are associated with increased risk of abdominal aortic pathology and aneurysm formation. However, considerable variability exists in clinical presentations. Clinical decision making is quite complex in those disorders. For example, the risk of rupture in LDS and AOS is higher at smaller aortic diameters than in MFS. Also, OAR is more challenging in VED than in MFS owing to increased arterial wall fragility. Although small series have been published on the selective use of EVAR in certain connective tissue disorders such as MFS,⁸⁵ there is generally profound lack of knowledge on which of these syndromes, if any, would be amenable to EVAR.

OAR is the procedure of choice with these syndromes. The operative technique differs in that an attempt should be made at excluding all ectatic segments because of the propensity of future deterioration. Reinforcement of suture line with felt, and secondary reinforcement with tissue glue should be done

routinely. Reimplantation of visceral side branches to the main aortic graft using *in situ* inclusion or Carrel patch technique should be avoided because of the risk of progressive aneurysmal degeneration or suture line disruption. Instead, visceral branch reconstruction is focused on the use of multi-branched synthetic graft (Coselli Thoracoabdominal Graft, Terumo Aortic, Sunrise, FL), with branch limb anastomoses performed endo-aortically onto the ostia of corresponding visceral branches.^{86–88}

PREOPERATIVE ASSESSMENT AND PLANNING

Careful patient selection and preparation is critical for optimal outcomes. Because of the physiologic derangements that occur as a result of the hemodynamic stress of aortic cross-clamping, a detailed understanding of the patient's cardiac, pulmonary, and renal function is necessary to determine who is a candidate for OAR. Preoperative assessment of frailty cannot be overstated in open aortic surgery, given its known association with postoperative mortality and adverse outcomes.⁸⁹ Frailty is a multidimensional syndrome of loss of reserves (energy, physical ability, cognition, health) that gives rise to vulnerability to adverse events. Preoperative identification of high-risk patients may help mitigate procedural and long-term outcomes and improve shared decision-making regarding AAA repair.⁹⁰ Several preoperative frailty and nutritional parameters such as nutritional status and psoas muscle sarcopenia have been suggested to help identify high-risk patients for OAR so that endovascular aneurysm repair or no intervention can be recommended.^{91–93} The modified frailty index (mFI) score is a commonly used measure derived from comorbidity and preoperative functional status data that can be used as a predictive tool to aid in surgical planning of patients undergoing elective AAA repair.⁹⁴ Similarly, in individuals with diminished physiologic reserve or compromised baseline functional status, it must be determined whether the patient's current and anticipated postoperative quality of life are sufficient. This is especially pertinent in the elderly, where postoperative complications may condemn the patient to long-term skilled nursing care and permanent loss of independent functional status.

Preoperative Imaging

Computed Tomography

American College of Radiology appropriateness criteria suggests CTA as the optimal choice for detailed characterization of AAA, with MR angiography (MRA) to be considered if CT cannot be performed (see Ch. 29, Computed Tomography).^{95–98} CTA data processing on modern workstation enables comprehensive assessment of vascular anatomy including geometric measures, angulation, tortuosity, underlying occlusive disease, extent of wall calcification, mural thrombus and shaggy aorta,⁹⁹ which are crucial for planning the best approach including preoperative choice of clamp site (and endovascular treatment)^{99–101} (Fig. 73.1). This can yield

valuable preoperative planning information and has become a standard of care that most vascular surgeons are well versed in.^{99–101} CTA can also accurately assess for involvement of the visceral aortic segment and branches with the aneurysmal process or occlusive disease.^{102,103} Preoperative information derived from CTA is crucial for determining if suprarenal or supraceliac clamping is anticipated and potential clamp placement sites can be examined for heavy or circumferential calcification or thrombus. Concomitant occlusive disease of the visceral vessels and aortoiliac segment is also readily apparent on CTA, allowing decisions regarding the need for endarterectomy or complex reconstruction to be made pre-operatively.^{104–106} CTA also provides valuable information about variant anatomy that might alter the operative plan, such as retro-aortic or circumferential renal vein, multiple renal arteries or a horseshoe kidney. Concomitant distal stenotic, occlusive, or aneurysmal disease will influence the site of distal reconstruction, as well as the need for additional procedures. Numerous advances have occurred in CTA technology such as lower radiation dose, time-resolved dynamic imaging, and ability to perform comprehensive aortic imaging using a much smaller amount of iodinated contrast using dual energy beam CT technology.¹⁰⁷

Magnetic Resonance Angiography

Magnetic resonance angiography (MRA) can be used for assessment of aneurysm extent, size and for preoperative planning (see Ch. 30, Magnetic Resonance Imaging and Arteriography).^{108,109} It can replace CTA for planning in patients for whom iodinated contrast is contraindicated. One major drawback is poor visualization of calcification and propensity to artifacts that can degrade diagnostic quality.¹⁰⁹ However, MRA can better delineate the pathologic process in inflammatory AAA, or extent of phlegmon in mycotic aneurysms especially those related to direct spread from an adjacent source such as infectious spondylitis.¹¹⁰ Noncontrast MRA sequences for comprehensive evaluation of AAA in patients who cannot receive gadolinium are also becoming increasingly available.^{111,112}

OPERATIVE TECHNIQUE

There are two widely practiced approaches to open aneurysm repair: transperitoneal and retroperitoneal, dependent on surgeon's preference and patient-specific anatomic requirements or comorbidities (see Ch. 56, Abdominal Vascular Exposures). The transperitoneal approach offers rapid access to the infrarenal aorta with straightforward positioning and allows higher flexibility in terms of accessing the entire aortoiliac segments including the hypogastric arteries and all aortic visceral branches, albeit with additional expanded exposures which can be technically demanding. It is ideal for use in emergencies. While the retroperitoneal approach requires a more involved positioning process, it allows excellent exposure of the visceral aorta that can be easily extended into the distal thoracic aorta. In addition, the retroperitoneal approach is invaluable in patients with a hostile abdomen due to prior abdominal surgery, obese patients, and arguably in patients with poor cardiopulmonary



Figure 73.1 A 71-year-old male patient presenting with a 5.0-cm left common iliac artery aneurysm and a 4.8-cm juxtarenal AAA. He has anomalous renovascular anatomy with a small accessory right renal artery and left renal ectopia (pelvic) with a single artery arising from the distal abdominal aorta. (A) CTA was reviewed using segmented reconstruction on a 3D workstation, allowing the complex anatomy to be better visualized. The patient underwent open repair with 24 × 12 mm bifurcated PTFE graft with reimplantation of the pelvic kidney artery onto the proximal right limb. A brief period of suprarenal clamping was needed for the proximal anastomosis after which the clamp was transferred to the main body of the graft, allowing the right kidney to be reperfused. We then promptly proceeded with revascularization of the left pelvic kidney. Upon examining the repair configuration and the orientation of left renal artery, it was reimplanted onto the proximal right limb of the graft, which was in turn anastomosed to the proximal right common iliac artery. Lastly, the left limb of the graft was anastomosed to the left common iliac bifurcation. The patient had an uncomplicated postoperative course. (B) Follow-up CTA 2 years later shows the repair and left renal artery reconstruction to be widely patent.

reserve.^{113,114} New SVS guidelines also favor a retroperitoneal approach for open repair of IAAA.¹¹⁵ Main drawbacks of the retroperitoneal approach include limited exposure of the

distal right iliac artery and its branches. It can also be difficult to obtain adequate visualization of right renal artery beyond its proximal-most segment. Advocates of the retroperitoneal

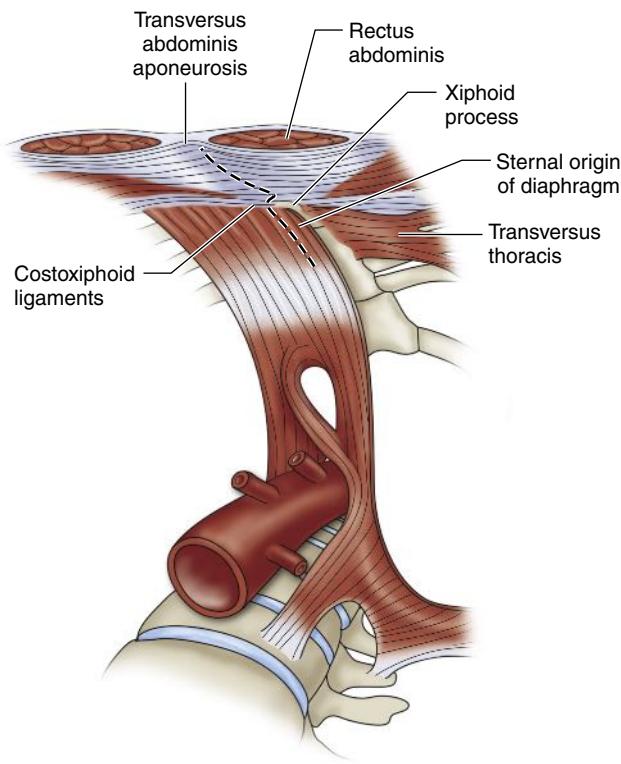


Figure 73.2 The lynchpin of upper aortic exposure. When using a midline incision, it is imperative to extend cephalad along the xiphoid process. This maneuver allows transection of the transverse thoracis, anterior diaphragmatic fibers, ventral and dorsal costoxiphoid ligaments, rectus abdominis, and aponeuroses of abdominal muscles. Attention to this detail of the upper incision allows much better cranial exposure facilitating exposure of the paravisceral aorta as well as easier and wider retraction.

approach cite decreased postoperative fluid requirements, pulmonary edema, pneumonia, respiratory failure, postoperative ileus, shorter length of intensive care unit and overall hospital stays, shorter time to full recovery, and less cost,^{18,114,116,117} although other studies disputed those advantages.^{113,118} A recent study compared the two approaches in 1282 patients from the VQI national database, showing the transabdominal approach to be associated with higher rates of late reintervention and readmission.¹¹⁹

TRANSPERITONEAL EXPOSURE

The transperitoneal approach can be performed through a variety of incisions (midline, transverse, and bilateral subcostal with many other variants) depending on the surgeon's preference and patient habitus. Surface anatomy and body habitus of the patient play an important role in planning the type of incision.

When a midline incision is used in a patient where visceral aortic exposure is required, an important detail is to extend its proximal extent alongside the xiphoid process. This simple maneuver allows the release of several attachments, ligaments and aponeuroses, appropriately referred to as the "lynchpin of proximal aortic exposure." By enhancing the mobility of the

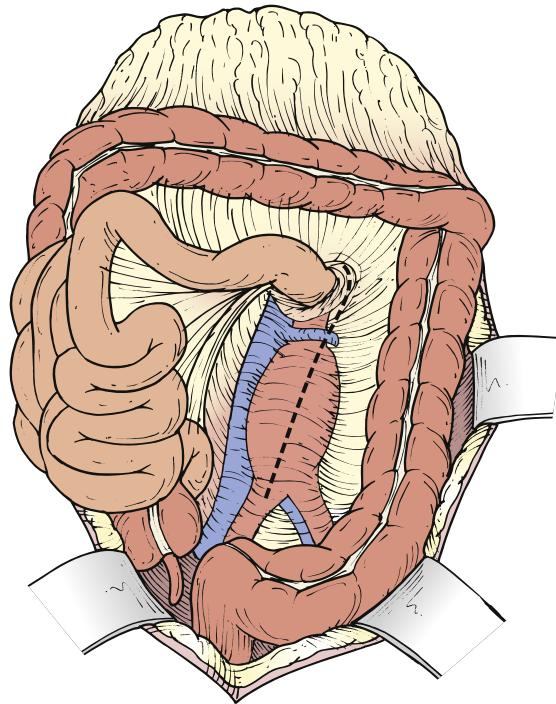


Figure 73.3 The aorta is exposed by incising the overlying posterior peritoneum.

lower costal margin this extension allows wider retraction and greatly facilitates exposure of the paravisceral and celiac aorta (Fig. 73.2).¹²⁰ The omentum and transverse colon are retracted cephalad, and the small bowel is packed in the right hemiabdomen. A self-retaining retractor, such as the Omni (Omni-Tract, St. Paul, MN) or Thompson (Thompson Surgical Instruments, Traverse City, MI), greatly facilitates exposure and should be set up at this point. The ligament of Treitz is divided, the third and fourth portions of the duodenum are reflected to the patient's right, and the periaortic lymphatic and connective tissue is ligated and divided (Fig. 73.3). The inferior mesenteric vein can be divided to facilitate exposure. The incision in the posterior peritoneum is then continued caudally in this plane to expose the entire infrarenal aorta. Although starting to the left of the aorta at the ligament of Treitz, the incision in the posterior peritoneum should course to the right of the aortic midline to prevent injury to the IMA, sigmoid mesentery, and autonomic nervous plexus at the bifurcation (Fig. 73.4). In cases where tube graft reconstruction is planned with distal anastomosis to the aorta itself, the dissection does not need to proceed beyond what is necessary to obtain distal control at the level of the bilateral proximal common iliac arteries. In certain cases where external clamping is to be avoided as when the common iliac arteries are heavily calcified, endoluminal clamping can be used with a Foley catheter or large Fogarty balloon (Fig. 73.5).

Pararenal Aorta

A growing proportion of patients requiring OAR have aneurysms with short or no infrarenal neck.⁵⁰ Juxtarenal aneurysms often require suprarenal clamping, which necessitates

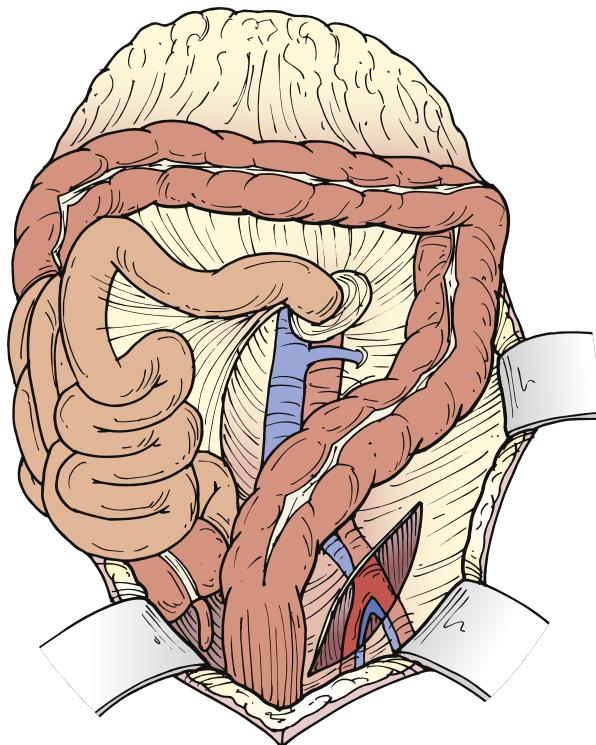


Figure 73.4 The left iliac artery can be accessed by mobilizing the sigmoid colon medially and incising the posterior peritoneum at its base.

additional proximal aortic exposure. To do so, the posterior peritoneum is opened cephalad to the level of the left renal vein. Location of the left renal vein should always be ascertained on the preoperative CT scan. It can be mobilized to gain more proximal aortic exposure by dividing some of the tethering branches (gonadal, adrenal, and lumbar branches) (Fig. 73.6A). Alternatively, the left renal vein can be divided safely, albeit an increased risk of transient azotemia has been reported.^{121–124} In order to preserve its drainage through side branches, the division point should be as close to the inferior vena cava as possible (Fig. 73.6B). The decision to divide the left renal vein needs to be made before proceeding with aggressive mobilization, because adequate renal venous drainage once it is divided requires patency of most side branches. If there is concern for compromised renal venous drainage after renal vein division, an end-to-end reanastomosis can be readily performed after completion of the aortic reconstruction.¹²⁴ If a retro-aortic or circumferential left renal vein is present, care must be taken to avoid injuring the vein.

Supraceliac Aorta

The supraceliac aorta is exposed separately (non-continuous with the primary infrramesocolic exposure) by dividing the lesser omentum or gastrohepatic ligament. The aorta is identified by palpation, and the overlying fibers of the right crus of the diaphragm are divided. Mobilization of the left lobe of the liver by dividing the left triangular and coronary ligaments, as well as the falciform ligament, can assist with exposure but is

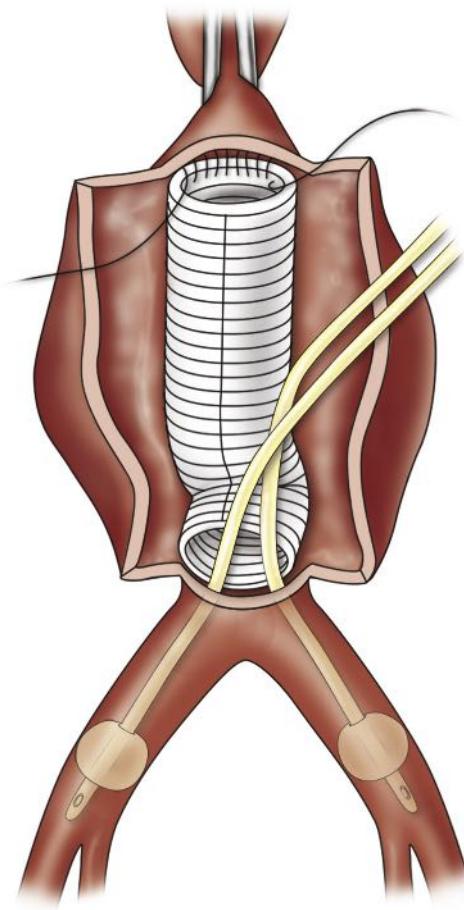


Figure 73.5 Technique of endoluminal control of common iliac arteries. Foley catheters are inserted under direct visualization and inflated enough to arrest back-bleeding.

often not necessary. A nasogastric tube is helpful for identifying and protecting the esophagus, which is retracted to the left. The aorta can be dissected anteriorly down to the level of the celiac axis, although care must be taken to avoid injury to the pancreas as one proceeds caudally.

An important technique for rapid supraceliac aortic control is blind digital dissection and incision of the right diaphragmatic crus to allow clamp application¹²⁵ (Fig. 73.7). Another helpful rapid proximal control technique is introduction of occlusion balloon through a small sac aortotomy. Supraceliac control can also be achieved endovascularly through a transfemoral approach using a variety of tools and devices, akin to the approaches used in EVAR or vascular trauma.^{126–128} These maneuvers can be lifesaving when faced with rapid exsanguination until secure proximal aortic control approach is established.

MEDIAL VISCERAL ROTATION

Suprarenal aneurysms are best approached using a retroperitoneal exposure. However, the visceral segment of the aorta can be accessed transperitoneally using a left medial visceral rotation (Fig. 73.8A). The left colon is mobilized by incising

the posterior peritoneum just lateral to the line of Toldt. This incision is carried cephalad through the phrenicocolic ligament and then medially toward the aortic hiatus along the underside of the diaphragm. The plane separating the

posterior aspect of Gerota's fascia and posterior abdominal wall is developed, allowing the colon, pancreas, spleen, and left kidney to be reflected medially *en bloc* (Fig. 73.8B). As the kidney is mobilized, the lumbar branch of the left renal

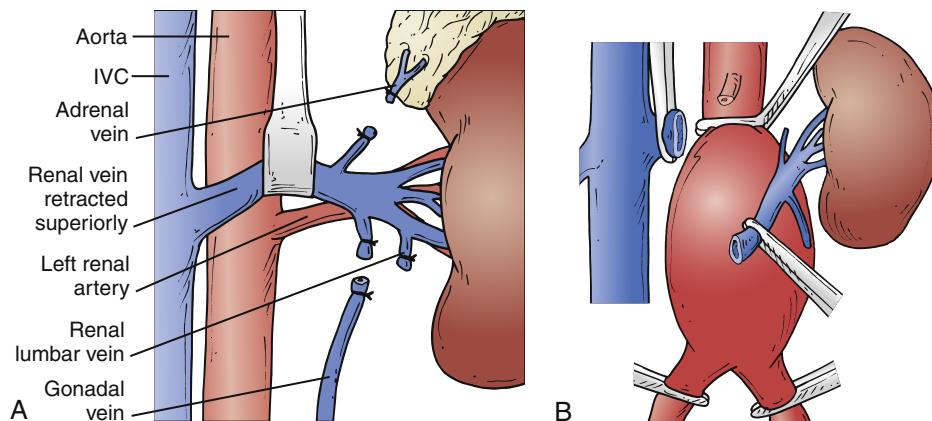


Figure 73.6 The renal vein can be mobilized by dividing its side branches (A) or simply divided close to the inferior vena cava (IVC) (B).

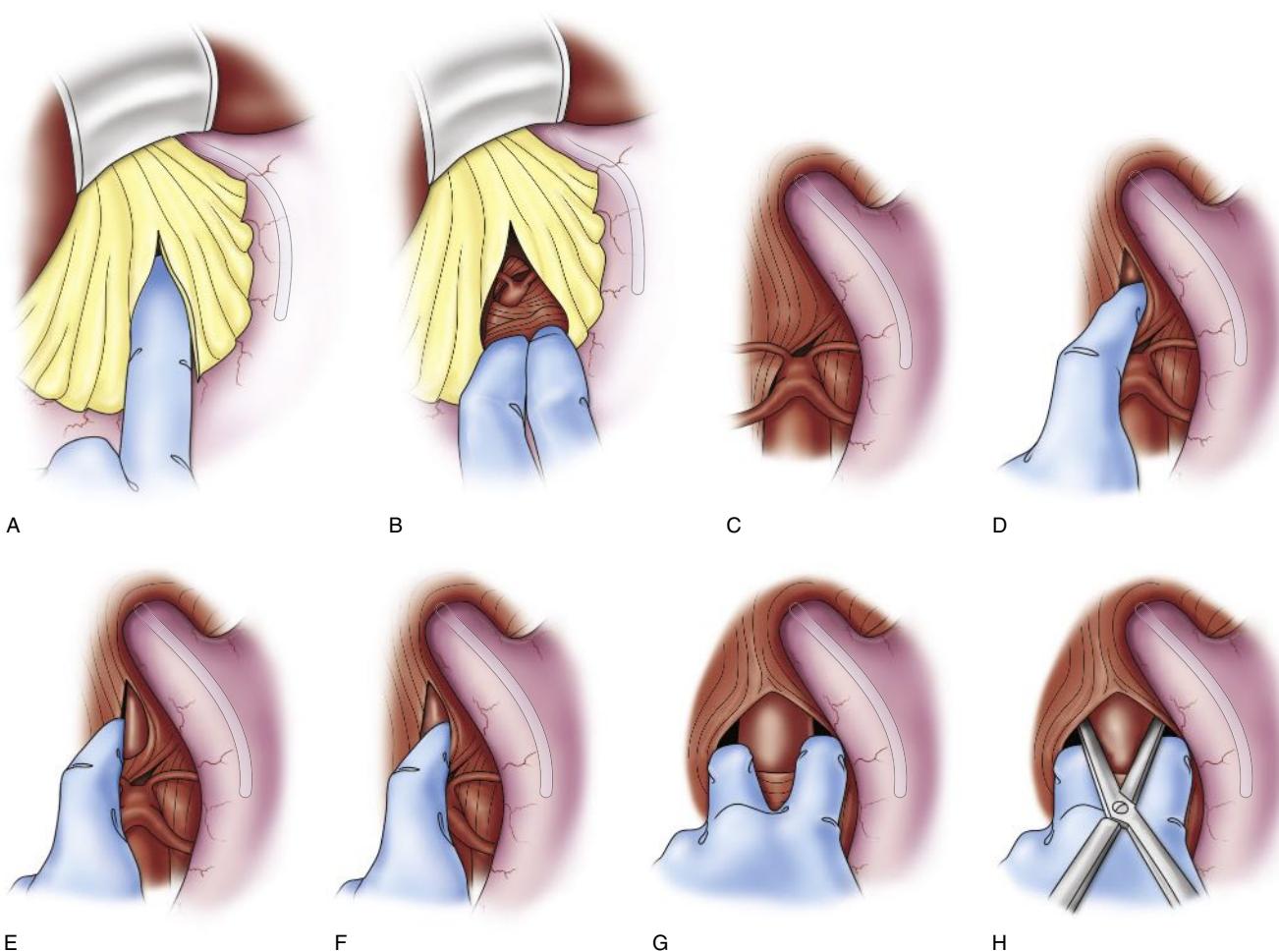


Figure 73.7 Technique of blind digital control and clamping of the supraceliac aorta. The nasogastric tube both protects the esophagus from injury and facilitates peri-aortic dissection in the presence of a collapsed aorta in a hypotensive patient. (A,B) The gastrohepatic omentum underneath the left lobe of the liver is opened bluntly with the digit. (C) The esophagus is palpated with the nasogastric tube in place and displaced to the left. (D) The right crus of the diaphragm is incised digitally using repeated longitudinal sweeps with the digit to expose the anterior surface of the aorta, which may or may not be pulsate dependent on the patient's hemodynamic condition. (D-F) Additional controlled blunt finger dissection is used to free up the anterior and lateral surfaces of the aorta. (G,H) The clamp is guided over two fingers against the anterior aspect of the vertebral bodies and the aorta can then be clamped.

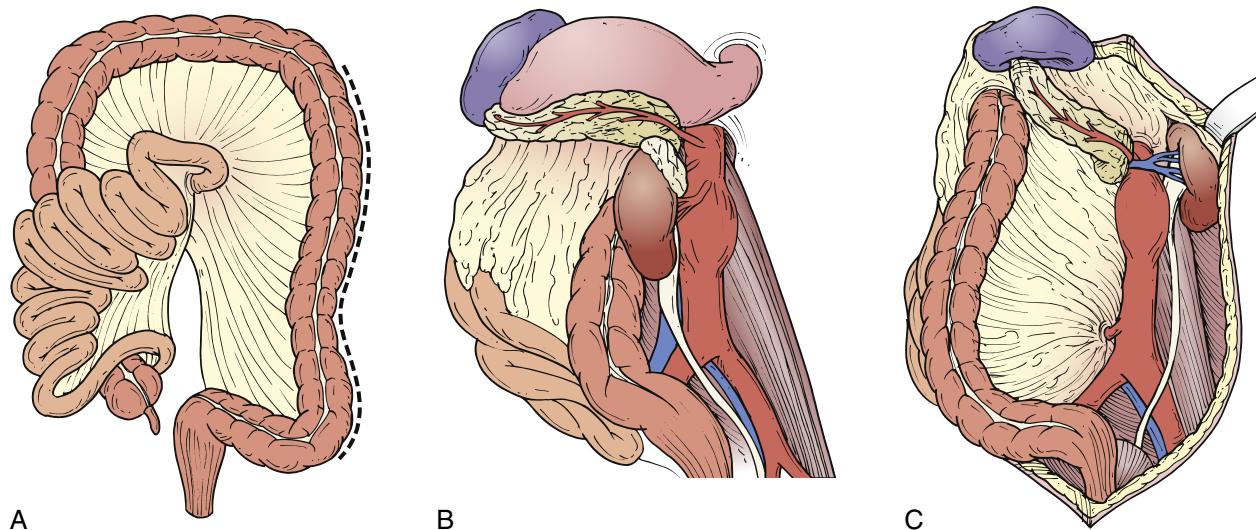


Figure 73.8 When using the transperitoneal approach, a left medial visceral rotation facilitates access to the visceral segment of the aorta. The peritoneum is incised along the line of Toldt (A) and the left colon, pancreas, and spleen are mobilized medially. The kidney can be mobilized *en bloc* (B) or left in the renal fossa (C).

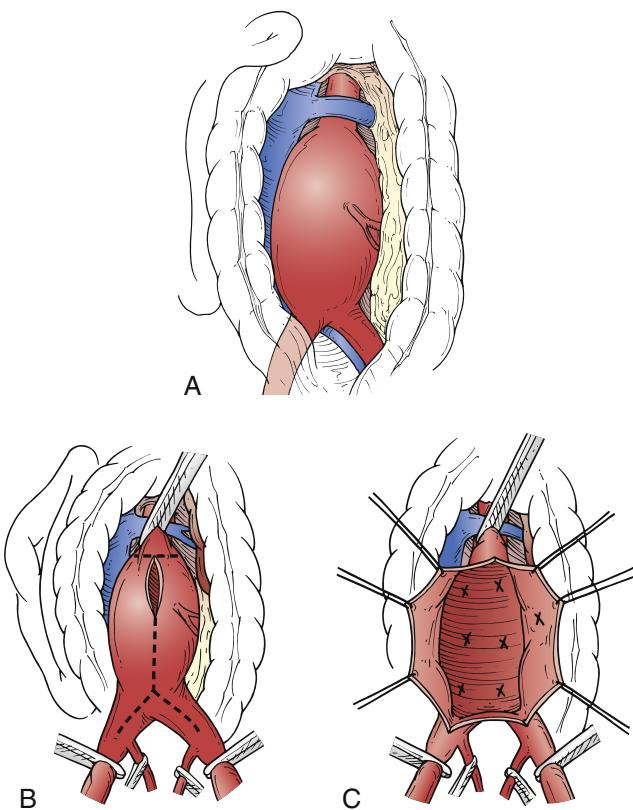


Figure 73.9 The aneurysm (A) is opened with a T-shaped (B) incision. Aortic retention sutures (C) can be used to help facilitate exposure.

vein should be identified and ligated to prevent avulsion. Alternatively, the kidney can be left in the renal fossa, which requires dividing the linorenal and linophrenic ligaments and developing a plane between the anterior surface of Gerota's fascia and the posterior surface of the colonic mesentery and pancreas (Fig. 73.8C).

AORTIC RECONSTRUCTION

Once the appropriate aortic segments and relevant side branches are exposed, proximal and distal clamping sites are identified. Thorough assessment of the aortic neck prior to clamping is important, to avoid thrombo-atheromatous embolic events. Clamping and unclamping sequences should also be kept to a minimum (preferably one). Circumferential control of the aorta and iliac arteries or their encirclement is not necessary and may increase the risk of injury to posterior structures, especially the iliac veins. Only enough exposure to apply a clamp is needed. The patient is heparinized and distal clamps are applied first to prevent distal embolization during application of the proximal clamp. The aneurysm is opened via a longitudinal aortotomy, which is T-ed off proximally and distally to facilitate anastomosis (Fig. 73.9). The proximal anastomotic site is cleared of thrombus and calcium, and an end-to-end anastomosis is performed using a running polypropylene suture. Laminated thrombus should be cleared from the remainder of the aneurysm sac, and back-bleeding lumbar vessels are identified and suture ligated. The distal reconstruction is performed in a similar fashion (Fig. 73.10). Forward flushing of the graft and back-bleeding of the distal vessels is done before completing the anastomosis.

Closure

After hemostasis has been obtained, the redundant aneurysm wall is snugly imbricated over the graft in using a running absorbable suture. The posterior peritoneum is also gently approximated to form a second closure layer over the graft (Fig. 73.11). This helps exclude the bowel from the retroperitoneum and avoids contact with the graft, minimizing the risk of aortoenteric fistula formation. If the sac or retroperitoneum could not be fully approximated over the graft, a flap of greater omentum should be brought down to cover the graft. The anterior abdominal wall is closed according to surgeon preference.

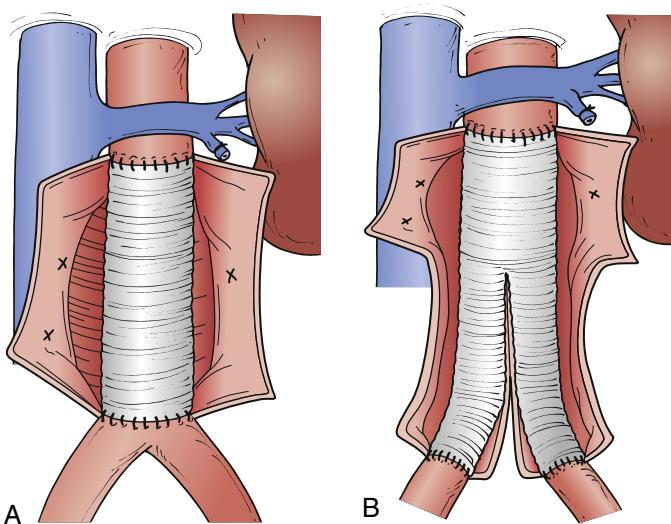


Figure 73.10 Completed repair with either a tube graft (A) or a bifurcated graft (B).

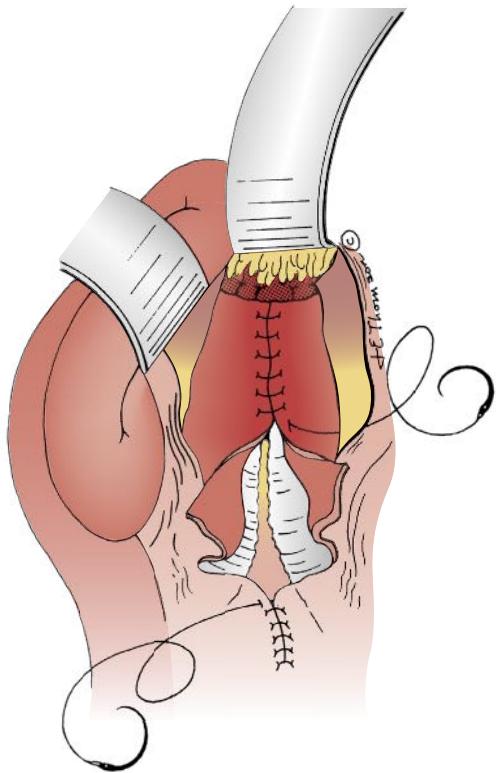


Figure 73.11 The aneurysm sac and posterior peritoneum are closed over the graft.

RETROPERITONEAL EXPOSURE

The patient is placed in the right lateral decubitus position with the hips rotated towards the neural position as much as possible without losing the upper torso rotation. The left arm is placed on an arm rest and a pad is placed to protect the right axilla. The table break is centered at the iliac crest and the table is maximally flexed, with the left knee bent to relax

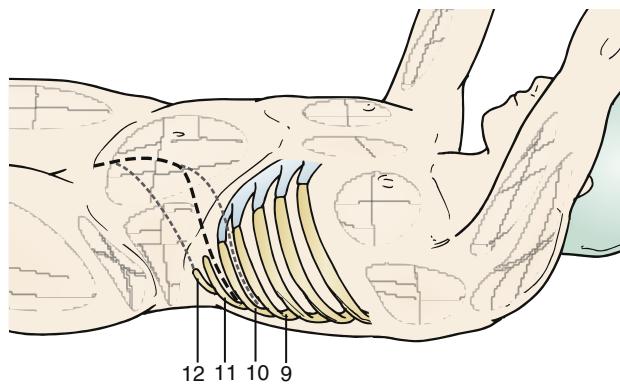


Figure 73.12 Incision (heavy line) for retroperitoneal aortic exposure. Alternate incisions are shown as dashed gray lines. In our experience, the lower incision coursing towards the 12th rib, sometimes augmented by 12th rib resection, often provides sufficient exposure in most infrarenal and juxtarenal aneurysms.

the psoas muscle. A beanbag positioner is used to secure the patient in this position. The chest and abdomen and left groin are prepped and draped in the standard fashion. Access to the right groin can be obtained, if needed, by flexing the hips further posteriorly.

Location of the retroperitoneal incision varies depending on the most cephalad required level of exposure. Although most infrarenal and juxtarenal exposures can be easily accomplished through an incision along the left 11th intercostal space, a 10th interspace incision can enable more optimal exposure of the visceral and supraceliac aorta (Fig. 73.12). The incision starts at the posterior axillary line and is carried onto the lateral border of the left rectus muscle and a level below the umbilicus determined by the intended distal extent of the reconstruction. The external oblique, internal oblique, and transversus abdominis muscles are sequentially opened with care taken not to violate the peritoneum. The peritoneum is bluntly swept off the abdominal wall and diaphragm. Exposure can be enhanced by dividing 2 to 3 cm of the diaphragm. The left psoas muscle is identified, and the peritoneal and retroperitoneal contents are swept anteromedially throughout the length of the wound, as well as off the inferior surface of the diaphragm, enabling exposure of the entire intraabdominal aorta. At this stage, the left ureter should be identified and protected, because it runs anterior to the aorta and left common iliac artery. There are two planes of dissection in the retroperitoneal approach (Fig. 73.13). The retrorenal plane, where dissection is carried behind left kidney and ureter, is preferred in most reconstructions owing to its ability to offer uninterrupted access to the aorta and the visceral branches. In the less commonly used anterenal retroperitoneal approach, the plane of exposure is carried anterior to the left kidney (which is left *in situ*) and posterior to the pancreas. This modified approach can be necessary for exposure of proximal portion of SMA (first 6 to 8 cm), as when SMA or pararenal aortic endarterectomy is contemplated. It is also preferred in the presence of a retro-aortic left renal vein. The Omni retractor is positioned to assist with the exposure. The intercostal incision can be better maintained using a **Finochietto rib retractor**. Further mobilization of the

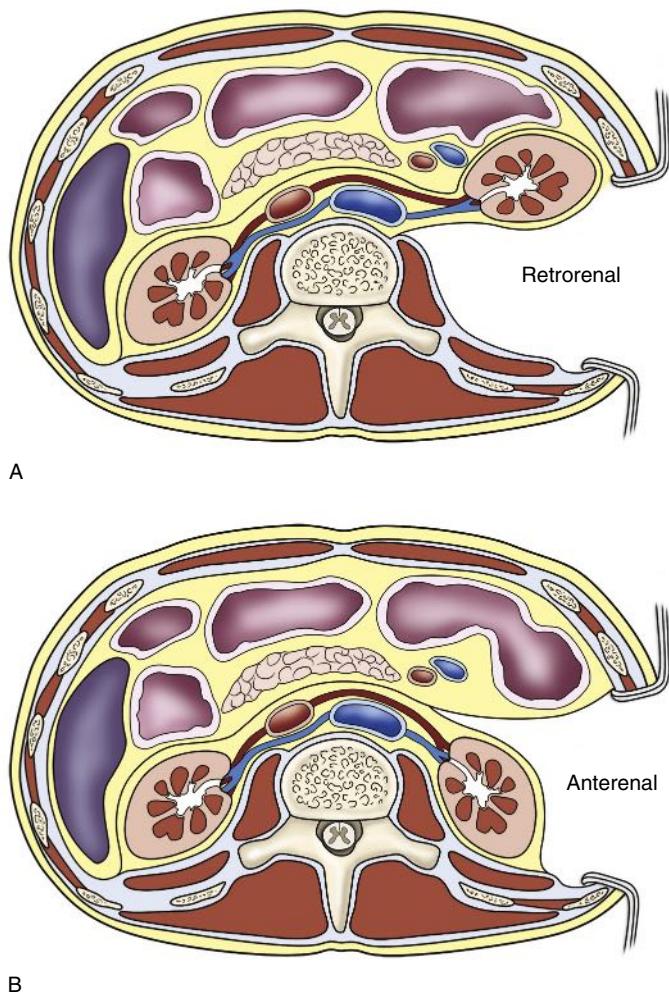


Figure 73.13 Cross-sectional views of the two main planes of dissection in the left retroperitoneal approach. (A) The retrorenal plane is used in many exposures. (B) The anterrenal plane can be a helpful variation in certain anatomic variations or disease patterns such as presence of a retro-aortic left renal vein or when a need is anticipated to expose the proximal segment of the superior mesenteric artery.

peritoneal sac, at times with detachment of the inferior mesenteric pedicle, can help enhance distal exposure of the right common iliac artery.

The retroperitoneal exposure provides excellent access to the entire visceral aorta and at least 5 cm of the supraceliac aorta, after dividing the left crus of the diaphragm (Fig. 73.14). Once a suitable spot for clamping is identified, the aorta is bluntly dissected along its anterior and posterior surfaces. Care must be taken to avoid avulsing any lumbar arteries or veins that run posteriorly. Again, it is unnecessary to attempt to fully encircle the aorta or iliac arteries, which can pose a risk for injury to adjacent structures. The left renal artery is identified and dissected back to its origin so that it is not compromised during aortotomy.

Arterial reconstruction for infrarenal or juxtarenal aneurysms proceeds in a similar manner to the transperitoneal approach described above. However, the retroperitoneal is also ideal for reconstruction of pararenal and suprarenal AAA,

given easy access to distal thoracic aortic and visceral abdominal aorta (Figs. 73.15 and 73.16). In the case of Crawford extent IV aneurysm involving all visceral branches, the aneurysm is opened longitudinally to the level of normal proximal aorta, and the left renal artery is excised from the aortic aneurysm with a small cuff of surrounding wall and retracted out of the immediate field. Visceral revascularization is traditionally accomplished through an inclusion patch containing the ostia of the right RA, SMA and CA, which are often clustered closely to allow inclusion in one island. The left renal artery is then detached and attached directly on the opposite side of the graft or alternatively to a sidearm interposition graft. At times, if the right RA, SMA and CA are clustered closely adjacent to nonaneurysmal aorta, the proximal end of the aortic graft is beveled to incorporate these three vessels behind the proximal anastomosis using a running polypropylene suture (Fig. 73.15 B and C). The supraceliac clamp is then transferred caudad to the proximal graft allowing reperfusion of the viscera and right kidney. The left kidney is now revascularized by reimplantation of the left RA patch on the aortic graft or a sidearm branch. Minimizing ischemic time during visceral revascularization is paramount; thus, proper conduct of the operation and attention to technique is critical. During the revascularization process, cold crystalloid perfusate can be administered to the non-perfused kidneys through Pruitt canulae connected to a cooled circuit. The distal aortic anastomosis proceeds in a similar manner to the transabdominal approach.

The downside of inclusion revascularization techniques is residual potentially diseased aortic wall that could be prone to further degeneration and subsequent aneurysmal dilation, referred to as visceral aortic patch (VAP) aneurysm.¹²⁹ A more robust option is use of a multibranched thoracoabdominal graft, allowing branch anastomoses to be performed sequentially onto the ostia of the corresponding visceral artery (Fig. 73.16).^{86–88} Sutureless hybrid aortic debranching, commonly known as VORTEC (Viabahn Open Revascularization Technique), is a hybrid approach to visceral branch revascularization that can be applied during open treatment of TAAA and pararenal AAA.^{130–134} It enables visceral revascularization without extensive exposures or prolonged clamping during visceral anastomosis¹³⁵ (Fig. 73.17). VORTEC was made easier by introduction of the Gore hybrid vascular graft (GHVG; W.L. Gore, Flagstaff, AZ),¹³¹ although its recent removal from the market has necessitated adoption of surgeon-made variants.^{136,137}

Closure

After obtaining hemostasis, the self-retaining retractor system is removed, and the peritoneal sac is returned to its normal anatomic configuration. Because the peritoneum has not been violated, the graft remains separate from the peritoneal contents, and the aneurysm sac does not need to be closed at the conclusion of the repair. Any rents in the peritoneum, however, should be closed; this can be accomplished with running absorbable suture. The flex is taken out of the operating table to remove tension on the wound during closure and the flank

incision is closed in multiple layers. The ribs and diaphragm can be incorporated into the closure of the transversus abdominis and internal oblique muscles in a single layer of running absorbable suture. Great care must be taken to avoid inadvertent colonic injury during closure. Wide-based mobilization of the peritoneal sac is crucial to ensure ample free edges during closure. The external oblique, with its associated fascia, is closed over this in an interrupted manner because it provides the strength for the closure.

ANATOMIC CONSIDERATIONS IN ABDOMINAL AORTIC SURGERY

Several anatomic situations exist that can complicate open aneurysm repair and require additional planning to address. Fortunately, the vast majority of these should be detected on the

preoperative CTA and plans can be made to address them in a proactive manner.

Management of the Inferior Mesenteric Artery

Note should be made on the preoperative CTA as to the patency of the IMA. If it is thrombosed, then no further consideration is needed. However, if there is significant SMA disease, bilateral hypogastric artery occlusions, a large IMA, or prior colectomy, IMA preservation may be indicated. Intraoperatively, sluggish back-bleeding from the IMA orifice has been long considered an indication to preimplant, whereas vigorous back-bleeding or IMA stump pressure to systemic pressure ratio >0.4 indicates it would be safe to oversew.¹³⁸ When needed, IMA revascularization can be accomplished either by reimplantation of the IMA into the graft using a small Carrel cuff or in an end-to-end fashion from a sidearm interposition graft.

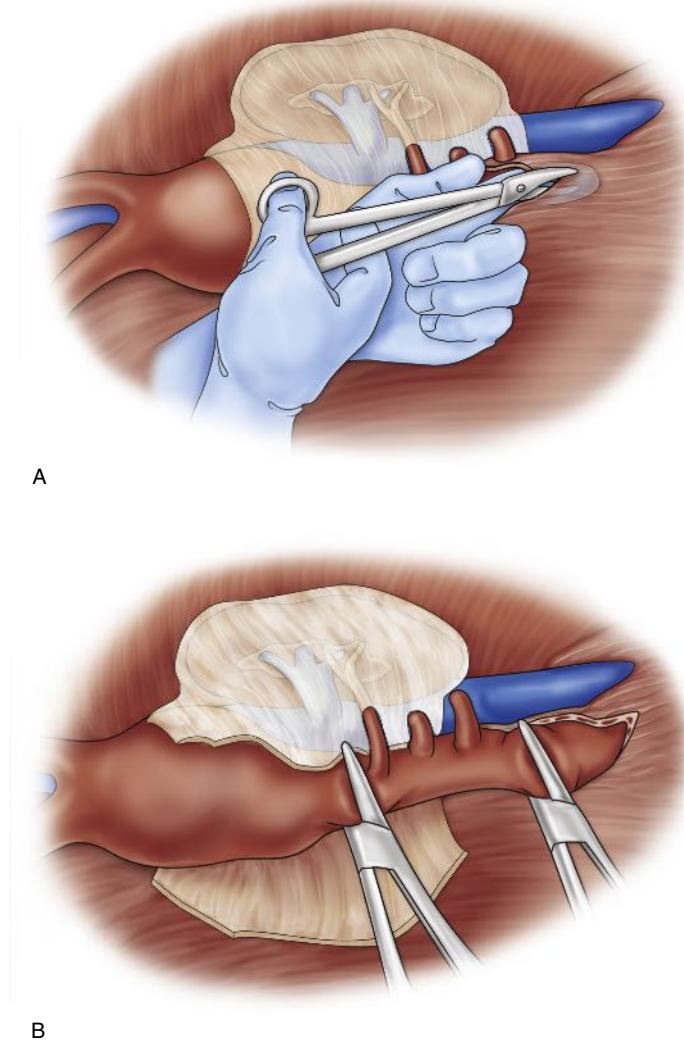


Figure 73.14 Cephalad exposure in the retroperitoneal approach is enhanced by division of the diaphragmatic crus (A), enabling unhindered exposure of the entire visceral aorta in addition to up to 10 cm of the distal thoracic aorta (B).

Renovascular Variants

Horseshoe kidney, ectopic kidney, cross-fused ectopia, and pancake kidney are the most frequent urological congenital

anomalies, occurring in 0.25% of the general population.^{139–142} Relevance to OAR relates to presence of multiple renal arteries arising across the abdominal aorta and common iliac arteries occurring in up to 30% of all patients and possibility of an

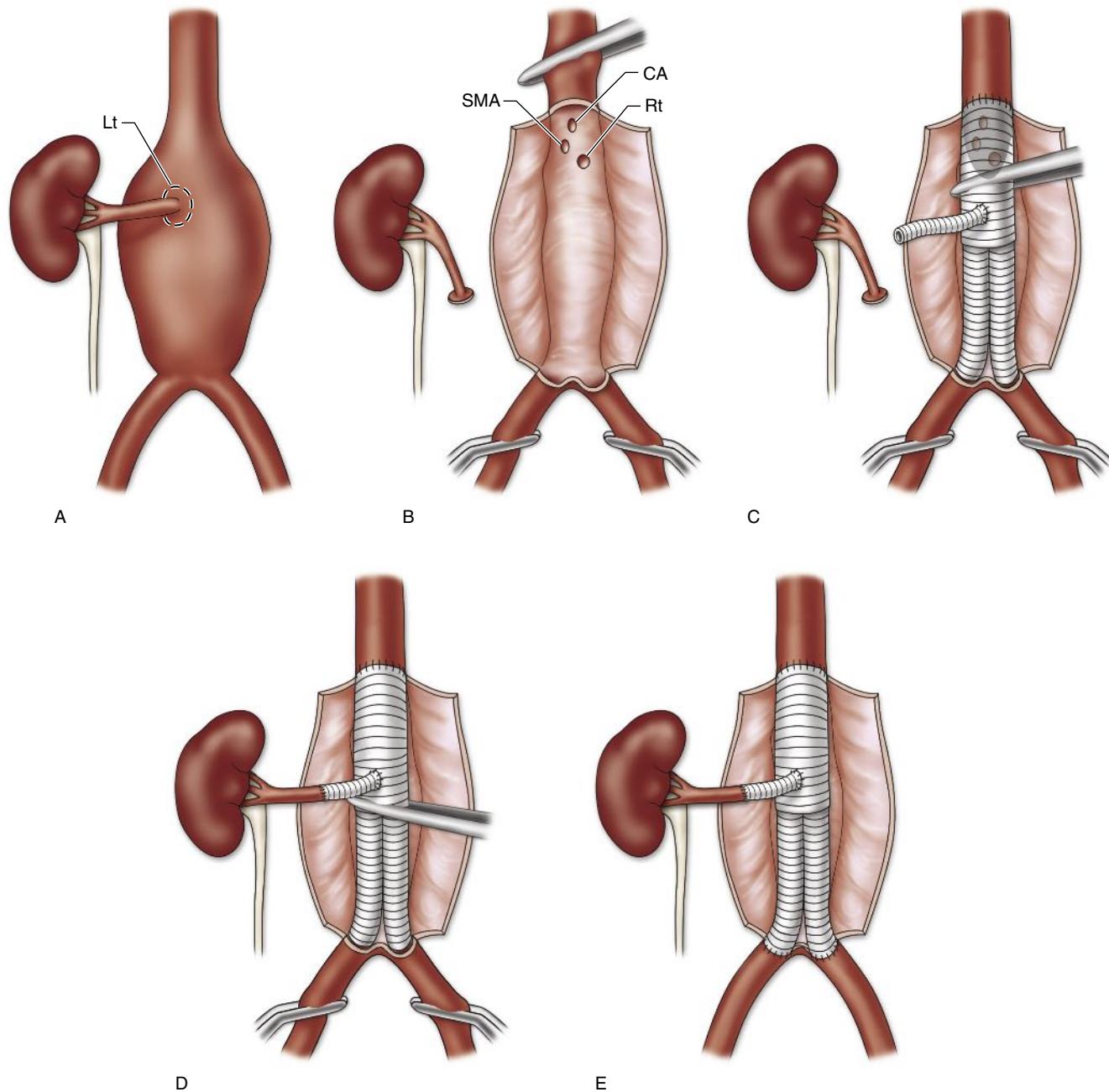


Figure 73.15 Reconstruction of type IV thoracoabdominal aortic aneurysm using a beveled anastomosis (CA, SMA and Rt RA) with left renal artery reattachment. After distal and proximal clamping, the aorta is opened and the left renal artery is detached (**A,B**). The proximal graft is beveled to accommodate an anastomosis incorporating the visceral segment and right RA (shown as gray shaded area). The clamp is then advanced distal to the anastomosis (**C**). The left renal artery is bypassed with a presewn side arm from the graft (**D**). The distal anastomosis is completed, and the clamp removed (**E**). Alternatively, if the CA, SMA and Rt RA are closely clustered, standard proximal anastomosis of the aortic graft is constructed to the normal distal thoracic aorta, with visceral revascularization accomplished using the inclusion technique of an aortic island containing the CA, SMA and Rt RA ostia before separate reattachment of the left renal artery. CA, celiac artery; RA, renal artery; SMA, superior mesenteric artery.

inter-renal isthmus that needs to be divided to gain access to the aorta.^{143,144} Management of AAA in the setting of a horseshoe kidney is difficult because of the technical challenges in exposure and revascularization, and longer aortic cross-clamp times required in those repairs.¹⁴⁵ The presence of a horseshoe kidney with multiple renal arteries originating from the aorta and iliac arteries will often render endovascular repair inappropriate, without risking the loss of significant renal function.¹⁴⁶ Careful review of preoperative imaging is essential to better plan the operative approach and need for revascularization (see Fig. 73.1).

Venous Abnormalities

Significant venous abnormalities of the renal veins and IVC are present in between 1% and 10% of the population, respectively.^{147–150} Retroaortic left renal vein, circumaortic left renal vein, left-sided IVC, and duplicated IVC can pose significant

challenges with regard to aortic exposure, clamp placement and if unrecognized a risk for major bleeding.^{150–152}

INTRAOPERATIVE PRINCIPLES IN ABDOMINAL AORTIC SURGERY

Aortic Clamping

The dramatic effect of aortic cross-clamping on the patient's physiology must be managed in real time by the anesthesia team. Effort must be directed at maintaining adequate blood pressure and perfusion while avoiding excessive hypertension. Care must be taken to optimize preload and afterload to minimize the effects of cross-clamping on myocardial oxygen demand. Mean arterial pressure must also be reduced before application of the cross-clamp. This must all be done in a way that anticipates the ultimate need to remove the aortic cross-clamp and the ensuing hypotension. Accordingly, clear and direct communication between the surgeon and anesthesiologist is crucial around the time of the application and removal of the cross-clamp, so that the physiology can be managed appropriately. Advance notice is given to the anesthesiologist of the approximate duration of cross-clamping before proceeding and again prior to unclamping. A dedicated anesthesia team for these procedures likely results in the best outcomes.

Intraoperative Renal Protection

A number of agents have been utilized to offer renal protection during aortic cross-clamping, including furosemide, mannitol, dopamine, and acetylcysteine; these benefits have not been borne out in clinical experience, and these interventions are not without risk and adverse effects.^{153–156} Fenoldopam, a selective dopamine receptor antagonist, was thought to hold promise for renal protection based on its ability to augment renal blood flow in normotensive human volunteers¹⁵⁷ as well as the results of two small studies on patients undergoing aortic surgery.^{158,159} Selective renal perfusion using cold hyperosmolar crystalloid, histidine–tryptophan–ketoglutarate (HTK) solution, or saline with mannitol and methylprednisolone have been associated with improved renal outcomes following the repair of juxtarenal AAA requiring suprarenal clamping and in extent IV TAAA.^{61,62,160–164} Other groups have obtained similarly excellent results without using intraoperative adjuncts and focusing on minimizing aortic cross-clamp time.^{63,165} Ultimately, reducing ischemic time to the kidneys likely has the greatest beneficial effects on renal protection. Maneuvers such as beveling the proximal anastomosis to include the right renal artery and reimplantation of the left renal artery are useful in this regard.

POSTOPERATIVE COMPLICATIONS

Although advances in intraoperative and postoperative care have been credited with improving outcome of OAR over the past 3 decades,¹¹³ perioperative adverse events are not uncommon following open aneurysm repair.¹⁷ Lifeline registry data of

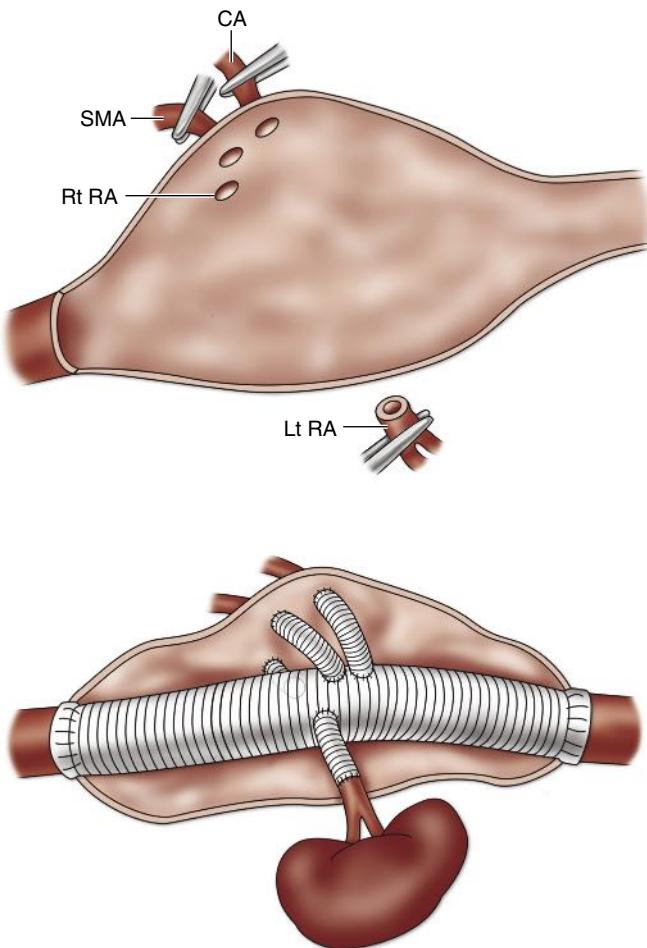


Figure 73.16 Use of the multibranched thoracoabdominal graft can facilitate revascularization of multiple side branches arising from an extent IV TAAA when the inclusion patch is not feasible. It should also be used preferentially in patients with connective tissue disorders. Anastomosis to the SMA is constructed first, followed by the renal arteries. Cold perfuse infusion into the renal arteries during clamping enhances renal protection.

patients who underwent open repair of intact infrarenal aortic aneurysms in the setting of randomized device trials demonstrated 71% overall, 26% serious, and 11% major adverse event rates in the perioperative period. Moreover, data from single centers, the National Surgical Quality Improvement Program (NSQIP), and the Vascular Study Group of New England (VS-GNE) suggest that as procedure complexity increases, the rate of overall complication also increases.^{68,166} Dedicated cardiovascular intensive care units, daily involvement of a critical care physician¹⁶⁷ and a high nurse-to-patient ratio¹⁶⁸ have all been shown to significantly improve outcomes.

Myocardial Ischemia

Aortic cross-clamping causes significant hemodynamic perturbations increasing demand on the heart, increasing the rate of

perioperative cardiac complications. Perioperative myocardial infarction occurs in up to 10% of patients in the perioperative period.¹⁹ The use of perioperative beta blockade for patients undergoing major noncardiac surgery has been shown to reduce cardiovascular events and in-hospital mortality in large retrospective population studies¹⁶⁹ and prospective randomized trials.^{106,170,171} A smaller observational trial focused on patients undergoing AAA repair similarly showed that the administration of beta blockers reduces in-hospital mortality (see Ch. 44, Systemic Complications: Cardiac).¹⁷²

Respiratory Complications

Postoperative pulmonary complications are associated with lower long-term survival.¹⁷³ Patients who undergo complex aortic repairs with prolonged suprarenal clamping often

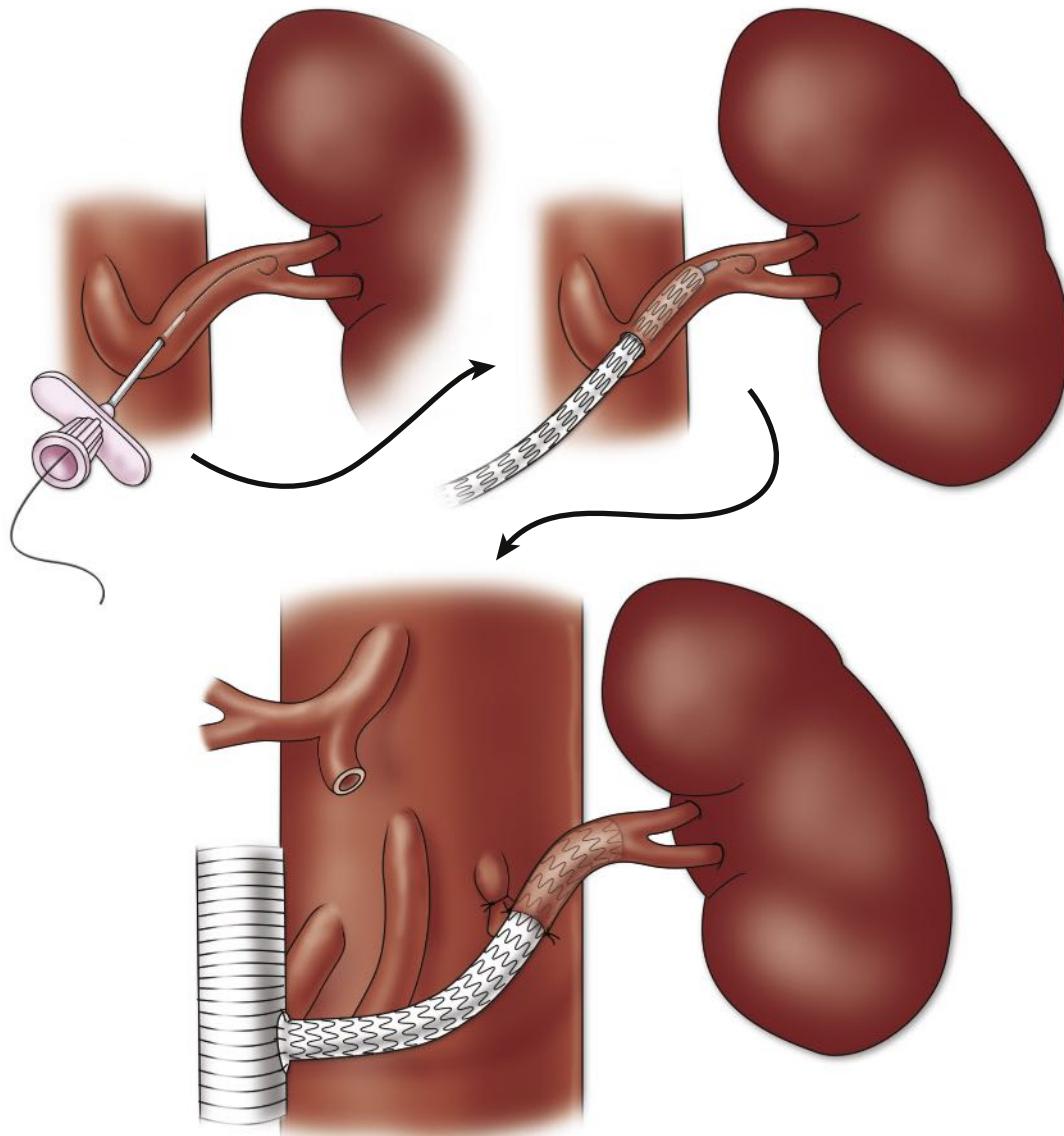


Figure 73.17 Sutureless visceral branch revascularization can be rapidly accomplished using VORTEC (Viabahn Open Rebranching technique). Viabahn stent graft is deployed into the visceral branch and secured with two simple polypropylene sutures. It is then trimmed to length and sewn onto the main prosthetic conduit or into a side branch.

require ongoing fluid resuscitation. Once this stabilizes and requirement for pressor support has ended it is generally safe to proceed with extubation using standard criteria. Despite relative success in avoiding prolonged intubation, pulmonary complications remain common, with postoperative pneumonia occurring in up to 17% of patients (see Ch. 45, Systemic Complications: Respiratory).¹⁹

Acute Kidney Injury

The risk of acute kidney injury (AKI) is closely related to the level and duration of aortic clamping. Another factor may be embolization during pararenal or paravisceral aortic mobilization and cross clamping when mural thrombus or atheroma are present.^{174,175} It is therefore crucial to occlude the renal arteries during application and release of a perirenal clamp to protect against embolic events. If excessive disease is present in that segment, then avoidance of the paravisceral aorta altogether in favor of supraceliac clamping is recommended. A meta-analysis of patients undergoing open elective pararenal aortic aneurysm repair demonstrated postoperative renal insufficiency in 15% to 20% of the patients, but dialysis-dependent renal failure in only 3.5%.¹⁷⁶ A recent large study from VQI evaluated factors associated with postoperative renal dysfunction after OAR for juxtarenal AAA in 2635 patients and noted a 24% incidence of AKI, with 2.2% requiring temporary dialysis and an additional 1.7% progressing to permanent dialysis. Postoperative renal dysfunction, even when mild, was associated with increased perioperative and long-term mortality. Minimization of suprarenal clamping time and use of renal protection adjuncts such as cold perfusion are important considerations during OAR. Likewise, close attention to blood loss, volume status and the liberal use of intravenous fluids and colloid throughout the perioperative period are key in preventing cumulative kidney injury. The use of cold renal perfusion was associated with lower risk of AKI when suprarenal cross-clamping times exceeded 25 minutes (see Ch. 46, Systemic Complications: Renal).¹⁷⁷

Visceral Ischemia

The most common type of visceral ischemia during OAR is renal ischemia. It can be due to hypoperfusion, thrombosis, thrombo-atheroembolism especially if the renal artery is not protected during application of suprarenal or juxtarenal clamp, mechanical lumen compromise due to faulty suture line, occlusive flap during endarterectomy of an ostial renal artery lesion or the aortic segment bearing the renal arteries. SMA ischemia due to atheroembolism is uncommon in OAR unless a supramesenteric clamp is applied. Another cause of SMA ischemia is crush injury from aggressive retraction of the small bowel during exposure of the retroperitoneum. This can often be recognized by dusky discoloration of the bowel and loss of pulse in the SMA. Ischemia of the colon can also be recognized during surgery. Dusky discoloration of the colon should prompt assessment of the SMA and hypogastric arteries (where pertinent), and consideration of IMA reimplantation.

Colonic Ischemia

Colonic ischemia (CI) occurs more commonly in OAR than EVAR and is more common in ruptured AAA.^{138,178–180} Post-operative CI following OAR occurs at a rate of 0.5% to 5%, but carries mortality risk as high as 39%.^{17,138,178,179,181–184} Ligation of a large IMA, inadvertent ligation of important collaterals in the retroperitoneum, failure to revascularize the hypogastric arteries, pre-existing iliofemoral occlusive disease, SMA stenosis, atheroembolism, mechanical retractor injury, previous colonic resection, perioperative hypotension, intraoperative blood loss and perioperative hypovolemia, and excessive use of vasopressors postoperatively can all contribute to colonic ischemia. Although some advocate for routine implantation of the IMA,¹⁸⁵ others described no protective effect against ischemic colitis and higher complications rate.¹⁸⁶

Postoperative CI can present in various ways including early postoperative diarrhea, melena, hematochezia, abdominal pain or peritonitis, fever and leukocytosis.^{182,183} When suspected, further diagnostic testing is done to rule out colorectal ischemia. Flexible sigmoidoscopy or colonoscopy are sensitive to even early partial mucosal ischemic changes and can be quickly and safely done at the bedside.¹⁸⁷ Contrast-enhanced CT is another helpful diagnostic tool.¹⁸⁸ When CI is clinically suspected, aggressive volume resuscitation and broad-spectrum intravenous antibiotics should be immediately instituted before further evaluation. Patients with disease limited to the mucosa, or submucosa without evidence of systemic derangement, can be managed conservatively, whereas those with full-thickness involvement especially with evidence of perforation of organ failure require emergent exploratory laparotomy (see Ch. 133, Acute Mesenteric Ischemia: Epidemiology, Pathophysiology, Clinical Evaluation, and Management).^{183,189}

Lower Extremity Ischemia

In a recent analysis of the NSQIP database, lower extremity ischemia occurred in 2% of patients undergoing OAR and was associated with significantly higher early mortality and other severe adverse events including CI and major adverse cardiac events (MACE).^{190,191} As a rule, robust distal back-bleeding should be ensured before completion of the distal anastomosis. Distal perfusion should also be checked before reversal of anticoagulation or retroperitoneal closure, and before leaving the operating room. Lower extremity ischemia complicating OAR can be the result of technical anastomotic complications, twisting or kinking of tunneled limb in a bifurcated graft, clamp injury, acute thrombosis, or embolization of mural thrombus at the clamp site or aneurysmal content during manipulation. Careful clamp site location and adherence to proper clamping/unclamping sequence during and after completion of the anastomoses, as well as ensuring adequate systemic anticoagulation, are crucial.

Spinal Cord Ischemia

Spinal cord ischemia (SCI) following open AAA repair is a very rare event. Reported rates of SCI in the literature are

generally less than 1%, even in suprarenal aortic aneurysm repairs.^{166,173,189} However a higher incidence can be anticipated in extent IV TAAA repair. The extent of intercostal artery debranching in the distal thoracic aorta is likely a major risk factor; however, other considerations such as previous thoracic aortic procedures, aortic cross-clamp location and time, patency of the internal iliac arteries, and occurrence of profound intraoperative or postoperative hypovolemia and hypotension all likely play a role.^{6,189,192}

Postoperative Surveillance

Surveillance imaging is needed after OAR, albeit not nearly at the frequency required after EVAR. The goal is to rule out delayed anastomotic failures and other operative complications. Although sac diameter is easily assessed by ultrasound (US), aortic neck dilatation, which is known to occur after both OAR and EVAR, is best assessed by CTA.¹⁹³ CTA should be obtained within 6 months of OAR to ensure baseline integrity of the repair. Afterwards, CT imaging is repeated every 5 years, per SVS guidelines.¹¹⁵ If not done before, CTA of the chest should also be obtained at least once given the high rate of metachronous thoracic aneurysms in this population.⁶

SPECIAL SURGICAL CONSIDERATIONS AND VARIATIONS

Open Conversion of EVAR

Open conversion (OC) refers to conversion from EVAR to an open procedure to exclude the aneurysm, usually with complete or partial explantation of the endograft. There has been a dramatic increase in OC in the recent years, reflective of the increased reliance on EVAR outside IFU constraints; as a result, the number of patients with failed EVAR and no options for endovascular salvage is growing. Analysis of VQI national data for patients who underwent elective OAR from 2002 to 2014, showed that 4% (159 procedures) of all open repairs consisted of OC of a prior failed EVAR.¹⁹⁴ Another study examining the NSQIP database from 2005 and 2013 showed a similar 4% prevalence of OC repairs (300 of 7488 OAR). A recent meta-analysis of 26 studies, with 641 patients who underwent delayed OC from 1991 to 2014, confirmed the rising numbers, with a cumulative single center OC rate of 3.7%, and mean delay from the index EVAR procedure of 38.5 months.¹⁹⁵

OC falls into two categories: acute (AOC) and elective (EOC). Reported mortality rates for late conversion among contemporary series range from 0% to 22%. Given the likely decompensated status of patients presenting acutely, AOC carries up to tenfold increase in 30-day mortality compared with EOC.¹⁹⁴⁻²⁰¹ Although still technically demanding, EOC is associated with low procedure-related mortality, with outcomes comparable to elective juxtarenal OAR.^{194,195,199,200,202}

Device incorporation and inflammation, especially when interval procedures had been performed for endoleak management, can render explantation much more difficult.^{115,203} In a

meta-analysis, median delay of AOC from index EVAR procedure was 38.5 months.¹⁹⁵ Rarely, immediate AOC is needed during the index procedure: (1) non-rescuable device failure or deformation resulting in hemorrhage or flow compromise; (2) iatrogenic aortic or iliac artery perforation; (3) high-risk type 1 or 3 endoleak; (4) compromised flow to viscera or lower extremities. Indications for late AOC are rupture, infection, or aortoenteric fistula.^{194,204,205} Cause of rupture in delayed presentations is usually type 1 or 3 endoleak, although rupture can also occur in the context of a longstanding type 2 endoleak with progressive sac enlargement. Device thrombosis, migration or component separation are seldom seen with modern devices.

Technical Considerations in OC and Endograft Explantation

Open conversion for a failed endograft is a complex undertaking. For devices with suprarenal fixation, supraceliac clamping is often necessary even if infrarenal reconstruction is planned. Furthermore, extensive inflammation of the periaortic tissue planes render dissection of the aortic neck challenging. Once proximal and distal control is achieved the aneurysm sac is opened. At this point additional control can be achieved by clamping the iliac limbs of the endograft. If needed, the endograft can be divided or its component detached allowing additional endoluminal control with balloon catheters. If the graft is being explanted for infectious reasons, all prosthetic material needs to be removed. This is usually not difficult given lack of incorporation in an infected field. Otherwise, leaving portions of the endograft that are judged risky to remove without compromising the reconstruction may be a safer approach and was not associated with adverse effects in a series of 22 patients.²⁰⁶ Removal of an endograft with suprarenal fixation can be particularly difficult given incorporation of metal wire and full-thickness penetration of barbs into the aortic wall. If removed forcefully, extensive damage to the suprarenal aorta can occur with possible compromise of visceral branches. Various approaches have been described to facilitate this task²⁰⁷ (Fig. 73.18), of which the simplest is to leave the suprarenal stent in place and detach the fabric-bearing segments. The proximal anastomosis suture line could include the bare metal remnants along every other bite along with the aortic tissue being approximated to the graft. We prefer to include a Teflon felt or bovine pericardium ribbon to the anastomosis to reinforce the anastomosis. Distally, if the iliac limbs are well incorporated, they can be left *in situ*. If configuration lends itself to a tube repair and the limbs can be removed, the distal anastomosis is constructed in the usual manner after endoluminal control of the iliac arteries using balloon catheters (see Fig. 73.5). Otherwise, the replacement graft is sewn distally to the proximal edge of the residual trunk of the endograft, with either felt reinforcement or incorporation of adjacent aortic sac into the suture line. It is important to evacuate all content from the aneurysm sac and oversew any back-bleeding from the IMA or lumbar arteries.

The remainder of the operation is conducted as in any standard OAR.

INFECTED ABDOMINAL AORTIC ANEURYSMS

Infected or mycotic aortic aneurysms (MAA) account for only 1%–2% of all aortic aneurysms.^{208–211} Three categories of infected AAA can be recognized, as described below.^{211–215}

Primary Mycotic Aortic Aneurysm/ Pseudoaneurysm

Sometimes referred to as true or primary mycotic aortic aneurysms, mycotic aortic pseudoaneurysms are usually the result of hematogenous seeding of a non-aneurysmal aortic wall from endocarditis in a normal or atherosclerotic aorta. The resulting usually saccular infected pseudoaneurysm occurs from focal destruction of the aortic wall. This can also occur from direct spread into the aortic wall from an adjacent infectious process.

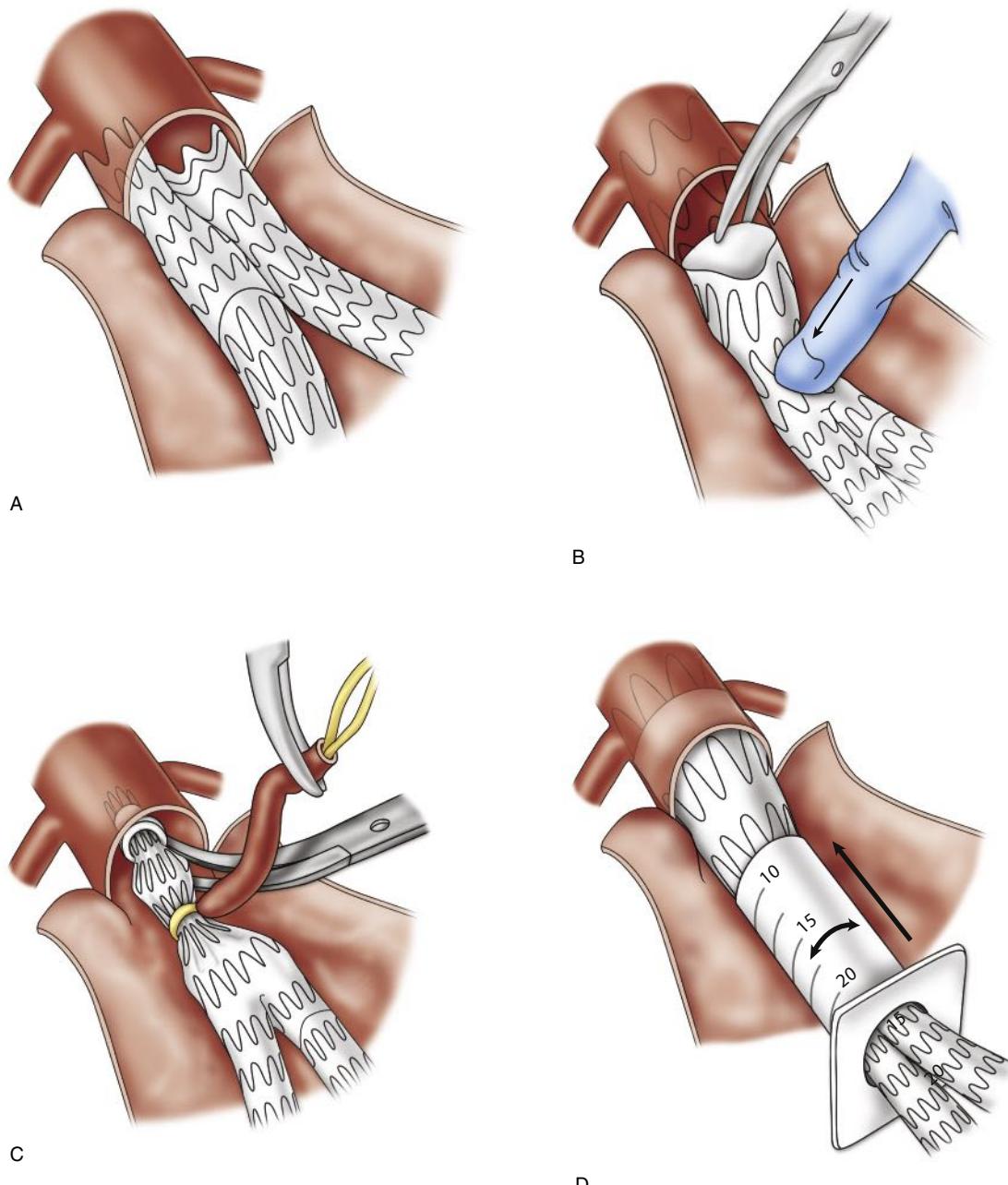


Figure 73.18 Various options and techniques helpful in aortic endograft explantation. (A) Graft infolding technique most useful for endografts with infrarenal fixation. (B) Excision of all fabric-bearing components, leaving the usually adherent suprarenal component *in situ*. (C) Rumel tourniquet is applied to the top sealing stent, enabling partial collapse of the suprarenal component which is then retrieved with an angled clamp. (D) Extraction of the endograft including the suprarenal fixation stent by withdrawing it into the barrel of a 20-mL syringe.

Secondary AAA Infection/Secondary Mycotic Aortic Aneurysm

This category represents secondary infection of a pre-existing AAA, usually as a result of hematogenous seeding. Secondary infection of a native AAA can also occur due to extension from an adjacent infectious process such as spondylitis or diverticulitis.

Aortic Graft/Endograft Infection

This represents infection of either an open surgical conduit or endograft in a previously repaired AAA. Multiple possible etiologies for AGI were described including breach-contamination during the initial repair which, depending on the bacterial load and virulence of the bacterial species, may have a considerable delay before presentation. Infection can also occur as a result of seeding from an episode of bacteremia, or as a localized extension from an adjacent infectious process (Fig. 73.19). Another important and lethal variety of AGI represents a manifestation of aortoenteric fistula (AEF), which most commonly occurs from the duodenum, usually at the level of the proximal anastomosis of an open surgical graft that was not optimally covered during the initial operation, or the proximal fixation segment of a usually oversized endograft (see Ch. 49, Graft Infection).

Diagnosis of an infected aortic aneurysm is confirmed based on patient history, clinical findings, laboratory tests including inflammatory markers and blood cultures, and imaging. CT angiography will demonstrate either a fusiform in case of secondary MAA, or a saccular aneurysm in primary MAA, the shape of which depends on its phase of evolution. Additional suggestive findings include irregular edema of aortic wall, variable enhancement, periaortic stranding of fat planes, discrete periaortic fluid collection, phlegmon, or contained rupture.^{208,209,216–218} Endoscopy and isotope-tagged WBC scanning are useful in confirming and localizing the infection and plays an important role in the modern management algorithm of mycotic aortic aneurysms (see Fig. 73.19B).²¹⁹ EVAR can serve as an initial bridge therapy in MAA presenting with rupture or at high risk of rupture, enabling the patient to be optimized for an eventual definitive open repair.^{214,220,221} Definitive management of AEF is similar to MAA with the additional requirement of duodenal repair.²²² However, selective use of EVAR in high-risk patients with AEF or to temporize those presenting with GI bleeding has been suggested.^{223,224} EVAR or F/BEVAR with lifelong suppressive antibiotics can be offered as definitive therapy for MAA, after sterilization with adequate course of IV antibiotics and demonstration of active infection resolution through negative blood cultures and normal WBC isotope scanning.^{225–228}

Before definitive management of any type of aortic infection, the patient's physiologic status is optimized in preparation for surgery. Intravenous antibiotics targeting the offending organism to lower the septic burden and reduce inflammation and tissue friability. In patients with uncontrolled sepsis, percutaneous or open drainage of infected collections

may be required.^{229,230} This is followed by prompt surgical repair. Components of infected AAA surgery include: (1) selection of adequate operative exposure allowing proximal, distal and branch vessel control; (2) excision of all prosthetic material^{230,231}; (3) aggressive debridement of all devitalized or infected tissue; (4) copious irrigation; (5) revascularization preferably via *in situ* reconstruction using an infection-resistant conduit (cryopreserved allograft, autologous femoral vein graft, rifampin-soaked or silver-coated prosthetic conduit)^{208–210,218,223,232–241}; (6) if *in situ* reconstruction is not feasible, extra-anatomic revascularization with excision of the involved aortic segment, vascular staple or double-layered suture closure of proximal and distal stumps and coverage with healthy tissue^{242,243}; and (7) complete coverage of the graft and anastomoses with healthy omentum.

A recent analysis of open repair of MAA comparing various approaches found the best short- and long-term outcomes to be for *in situ* reconstruction compared with extra-anatomic reconstruction, and for prosthetic grafts compared with autogenous vein or allografts, although the highest rate of infection recurrence was in prosthetic grafts.²⁴⁴ The advantage of *in situ* reconstruction over extra-anatomic bypass is avoidance of blind stumps at the edges of the excised infected aortic segment, which may be prone to thrombosis or blow-out.²⁴⁵

INFLAMMATORY ABDOMINAL AORTIC ANEURYSMS

Inflammatory AAAs (IAAAs) account for 4%–7% of all AAAs. Typical presentation is pain, constitutional symptoms, elevated inflammatory markers, and distinguishing findings on imaging including thick, enhancing aortic wall (mantle sign).^{246–249} Intraoperatively, it displays fibrotic reaction in the adjacent retroperitoneum seen as smooth, glistening white adherent layer, with dense adhesions to adjacent structures, notably the duodenum and ureters.^{247,250–252} Although frequently symptomatic, there is a lower risk of rupture compared to a similar size common variety AAA.²⁵² IAAAs are classified into IgG4-related and IgG4-nonrelated variants.^{253,254} The IgG4-related variety accounts for more than half of cases, displays aggressive periaortic fibrosis and is characterized by steroid sensitivity and low incidence of rupture.

Nonoperative medical management with corticosteroids is recommended in a symptomatic patient with AAA diameter below the threshold for repair.^{115,255} Other immunosuppressive agents such as azathioprine, methotrexate and tamoxifen have been used as steroid-sparing agents.^{256,257} Immunosuppressive therapy is also recommended prior to invasive treatment to reduce periaortic inflammation thus lowering the risk of operative complications.^{258,259} Although the lifetime risk of rupture with IAAA is low (<5%),²⁶⁰ the same threshold for repair as for common AAA is indicated according to recent SVS and EVS guidelines.^{115,255} Another indication for repair is refractory symptoms in spite of medical treatment, where the intervention goal is to control the inflammatory process.²⁴⁸ Since the response of perianeurysmal inflammation to either

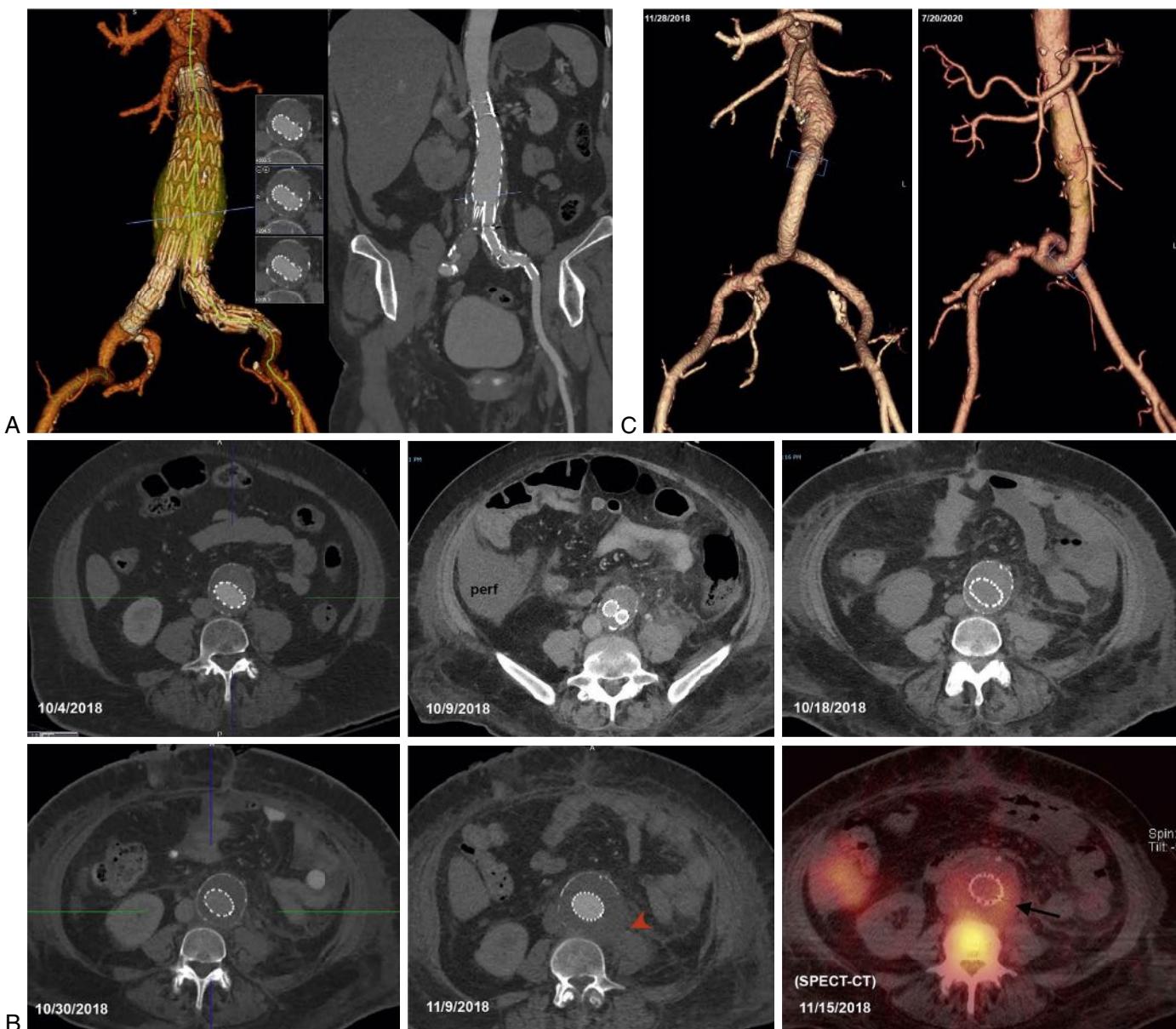


Figure 73.19 A 63-year-old female patient who underwent an EVAR for a 5.2-cm infrarenal AAA using a Zenith Flex device (Cook, Bloomington, IN). She had an ectatic left common iliac artery necessitating coverage of the hypogastric artery and extension into the external iliac artery. (A) CTA on postoperative day 1 after development of low abdominal pain. Endoscopic diagnosis of ischemic proctocolitis, initially managed conservatively until she developed perforation requiring hemicolectomy with colostomy. Her course was also complicated by *Clostridium difficile* colitis and bacteremia on multiple blood cultures. (B) Serial CT examinations demonstrating progressive sac enlargement, with periaortic fatty stranding evolving into a discrete periaortic phlegmon, eventually with loss of left posterolateral aortic wall integrity (red arrowhead). The last panel demonstrates increased isotopic uptake in the sac on a tagged-WBC scan using SPECT-CT fusion (black arrow). She was taken to the operating room 40 days after the initial EVAR, where she underwent complete explantation of the device (including the suprarenal fixation stent). Extensive debridement of all infected and necrotic tissue was performed. *In situ* reconstruction was performed using a cryopreserved allograft anastomosed distally to the right common iliac bifurcation and left external iliac artery. (C) Follow-up CTA, 2 years later, shows the reconstruction to be widely patent, with resolution of pelvic inflammation. Note the remodeling resulted in ventral tortuosity that has occurred with subsequent healing (compared to CTA performed 10 days after the repair).

open or endovascular repair is highly variable,^{249,261} maintenance immunosuppressive therapy may be required in addition to continued surveillance for development of progressive aortic dilatation, hydronephrosis and AEF.^{249,262} Perfusion

CT and FDG-PET have been used to assess disease activity and guide decisions about initiation or modification of therapy, and to quantitate periaortic inflammation response to both immunosuppression and invasive therapy.^{261,263,264}

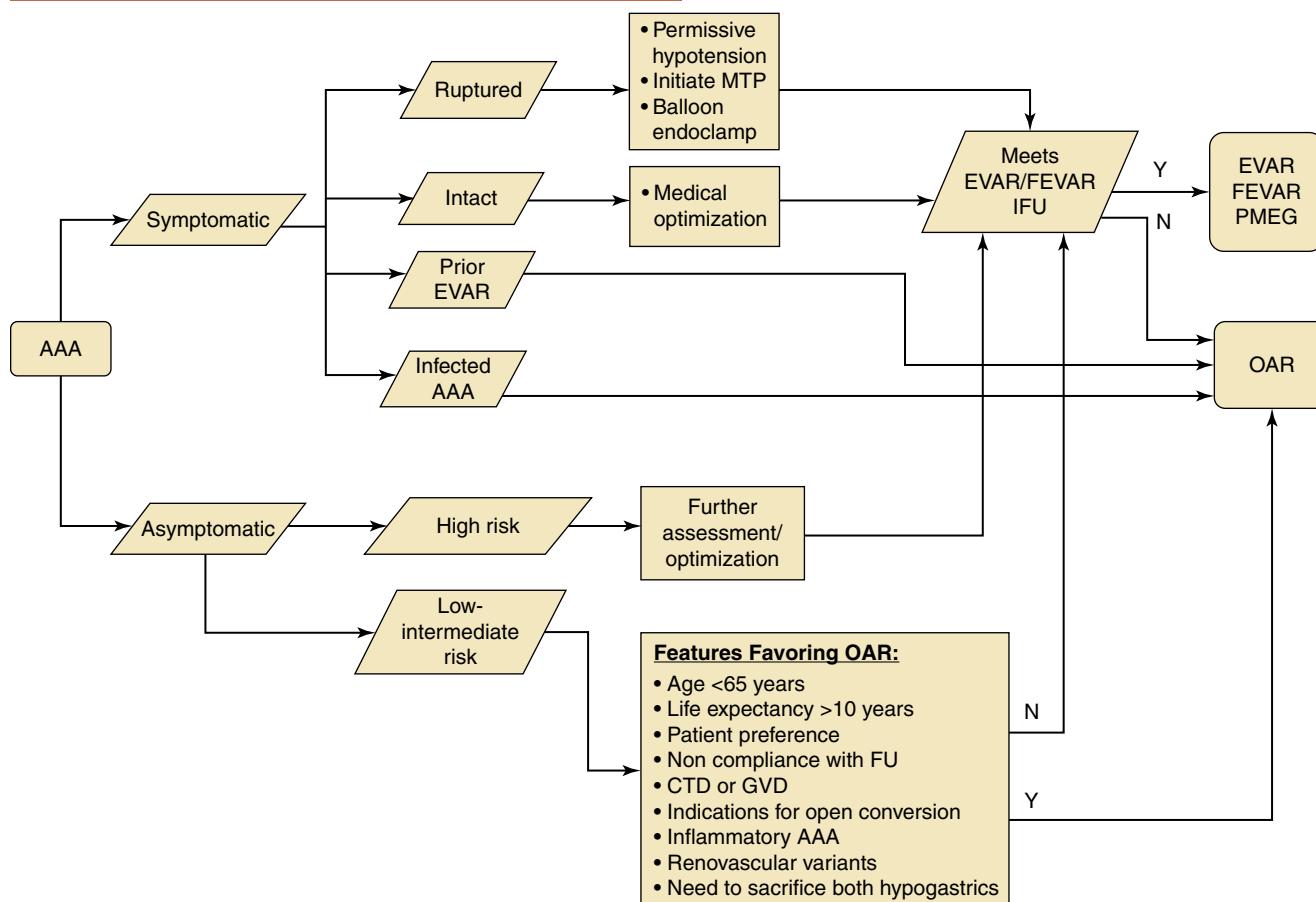
OAR versus EVAR in IAAA

The rationale for performing EVAR in IAAA is avoidance of dissection in the inflamed, fibrotic retroperitoneum. There has been debate as to the regression of the inflammatory process after EVAR compared to OAR. Several studies have shown the safety of EVAR in IAAA, especially in patients at high risk for OAR,^{265–271} with 30-day mortality of 2%–3% compared to 4%–11% with OAR, and an equally low rate of morbidities. However, periaortic fibrosis and hydronephrosis persisted in half of the patients after EVAR. A recent study of IgG4-positive IAAA patients treated with EVAR showed a high rate of persistent symptoms, elevated IgG4 levels, periaortic inflammatory thickening on CT, and lack of regression of aortic sac diameter.²⁷² Hydronephrosis and periaortic fibrosis may persist and even progress after EVAR.^{268,269} Therefore, continued immunosuppressive therapy^{257,273} and close postoperative surveillance may be indicated to control periaortic inflammation. Occasionally ureteral stents, nephrostomy, or open surgical ureteral lysis may also be required. Therefore, OAR remains the procedure of choice in IAAA and should be preferentially offered in patients with IAAA who also have severe hydronephrosis or high-grade inflammation on

quantitative or biologic imaging and are deemed at low operative risk.²⁶⁹

Operative strategy in OAR of IAAA differs from common aneurysms in that dissection should be kept to a minimum. Although transperitoneal approach has been more commonly used historically,^{248,249,271,274–276} recent SVS guidelines strongly recommend a retroperitoneal approach, mostly to avoid dissection of the duodenum.¹¹⁵ If a transperitoneal approach is chosen, dissection of the proximal neck should be limited, leaving the duodenum attached to the thickened peel. Proximal control necessitates suprarenal or supraceliac clamp position in nearly 40% of procedures.^{248,249,260,269,275,276} The aneurysm sac should be entered from the left anterolateral side and little to no attempt should be made to dissect away adjacent structures. The ureters are frequently involved in the inflammatory process as well, and ureteral stents can be protective. Anastomoses should also be constructed carefully, because of fragility of the often-inflamed aortic wall, with a frequent need for reinforcement with pledges. When strict safeguards are adopted, OAR can be performed safely in IAAA with acceptable operative mortality and morbidity and long-term outcomes,^{248,249,265,275–277} although mortality rates (6%–11%) remain higher than historic rates for common variety AAA.^{246,248,269,274}

CHAPTER ALGORITHM



Decision Making in Abdominal Aortic Aneurysm: Open Versus Endovascular Repair. CTD, connective tissue disorder; EVAR, endovascular aortic repair; FEVAR, fenestrated EVAR; GVD, genetic vascular disorder; MTP, massive transfusion protocol; OAR, open aortic repair; PMEG, physician-modified endograft.

SELECTED KEY REFERENCES

Chaikof EL, Dalman RL, Eskandari MK, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg.* 2018;67(1):2–77.e2.

Comprehensive up-to-date recommendations on diagnosis, treatment, and follow-up of AAA from the Society for Vascular Surgery.

Deery SE, Zettervall SL, O'Donnell TFX, et al. Transabdominal open abdominal aortic aneurysm repair is associated with higher rates of late re-intervention and readmission compared with the retroperitoneal approach. *J Vasc Surg.* 2020;71(1):39–45.e1.

Modern comparison of retroperitoneal versus transperitoneal exposure.

Hicks CW, Canner JK, Arhuidese I, et al. Comprehensive assessment of factors associated with in-hospital mortality after elective abdominal aortic aneurysm repair. *JAMA Surg.* 2016;151(9):838–845.

Useful review of factors contributing to mortality after open and endovascular aneurysm repair.

Scali ST, Beck AW, Chang CK, et al. Defining risk and identifying predictors of mortality for open conversion after endovascular aortic aneurysm repair. *J Vasc Surg.* 2016;63(4):873–881.e1.

In-depth analysis of risk factor modeling in open conversion of EVAR.

Wanhainen A, Verzini F, Van Herzele I, et al. European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms (vol 57, pg 8, 2019). *Eur J Vasc Endovasc Surg.* 2020;59(3):494.

Comprehensive up-to-date recommendations on diagnosis, treatment, and follow-up of AAA from the European Society for Vascular Surgery.

A complete reference list can be found online at www.expertconsult.com.

REFERENCES

1. Gillum RF. Epidemiology of aortic aneurysm in the United States. *J Clin Epidemiol.* 1995;48(11):1289–1298.
2. Melton III LJ, Bickerstaff LK, Hollier LH, et al. Changing incidence of abdominal aortic aneurysms: a population-based study. *Am J Epidemiol.* 1984;120(3):379–386.
3. Svensjö S, Björck M, Wanhainen A. Update on screening for abdominal aortic aneurysm: a topical review. *Eur J Vasc Endovasc Surg.* 2014;48(6):659–667.
4. Kostun ZW, Malik RK. Screening for abdominal aortic aneurysms. *Clin Imaging.* 2016;40(2):321–324.
5. Ulug P, Powell J, Sweeting M, et al. Meta-analysis of the current prevalence of screen-detected abdominal aortic aneurysm in women. *Br J Surg.* 2016;103(9):1097.
6. Hoornweg LL, Storm-Versloot MN, Ubbink DT, et al. Meta analysis on mortality of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg.* 2008;35(5):558–570.
7. Kontopodis N, Taylas E, Ioannou CV, et al. Systematic review and meta-analysis of outcomes of open and endovascular repair of ruptured abdominal aortic aneurysm in patients with hostile vs. friendly aortic anatomy. *Eur J Vasc Endovasc Surg.* 2020;59(5):717–728.
8. Bown MJ, Sutton AJ, Bell PRF, Sayers RD. A meta-analysis of 50 years of ruptured abdominal aortic aneurysm repair. *Br J Surg.* 2002;89(6):714–730.
9. Robinson WP, Schanzer A, Li Y, et al. Derivation and validation of a practical risk score for prediction of mortality after open repair of ruptured abdominal aortic aneurysms in a U.S. regional cohort and comparison to existing scoring systems. *J Vasc Surg.* 2013;57(2):354–361.
10. Salata K, Hussain MA, de Mestral C, et al. Population-based long-term outcomes of open versus endovascular aortic repair of ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2020;71(6):1867–1878.e8.
11. Heller JA, Weinberg A, Arons R, et al. Two decades of abdominal aortic aneurysm repair: have we made any progress? *J Vasc Surg.* 2000;32(6):1091–1100.
12. Abdulameer H, Al Taii H, Al-Kindi SG, Milner R. Epidemiology of fatal ruptured aortic aneurysms in the United States (1999–2016). *J Vasc Surg.* 2019;69(2):378–384.e2.
13. Bartek MA, Kessler LG, Talbott JM, et al. Washington State abdominal aortic aneurysm-related mortality shows a steady decline between 1996 and 2016. *J Vasc Surg.* 2019;70(4):1115–1122.
14. D’Oria M, Hanson KT, Shermerhorn M, et al. Editor’s Choice – Short Term and Long Term Outcomes After Endovascular or Open Repair for Ruptured Infrarenal Abdominal Aortic Aneurysms in the Vascular Quality Initiative. *Eur J Vasc Endovasc Surg.* 2020;59(5):703–716.
15. Lee H-G, Clair DG, Ouriel K. Ten-year comparison of all-cause mortality after endovascular or open repair of abdominal aortic aneurysms: a propensity score analysis. *World J Surg.* 2013;37(3):680–687.
16. Dangas G, O’Connor D, Firwana B, et al. Open versus endovascular stent graft repair of abdominal aortic aneurysms: a meta-analysis of randomized trials. *JACC Cardiovasc Intervent.* 2012;5(10):1071–1080.
17. Zwolak RM, Sidawy AN, Greenberg RK, et al. Lifeline registry of endovascular aneurysm repair: open repair surgical controls in clinical trials. *J Vasc Surg.* 2008;48(3):511–518.
18. Teixeira PG, Woo K, Abou-Zamzam AM, et al. The impact of exposure technique on perioperative complications in patients undergoing elective open abdominal aortic aneurysm repair. *J Vasc Surg.* 2016;63(5):1141–1146.
19. Schermerhorn ML, O’Malley AJ, Jhaveri A, et al. Endovascular vs. open repair of abdominal aortic aneurysms in the Medicare population. *N Engl J Med.* 2008;358(5):464–474.
20. Akkersdijk G, Van der Graaf Y, Van Bockel J, et al. Mortality rates associated with operative treatment of infrarenal abdominal aortic aneurysm in The Netherlands. *Br J Surg.* 1994;81(5):706–709.
21. Anderson PL, Arons RR, Moskowitz AJ, et al. A statewide experience with endovascular abdominal aortic aneurysm repair: rapid diffusion with excellent early results. *J Vasc Surg.* 2004;39(1):10–18.
22. Bayly P, Matthews J, Dobson P, et al. In-hospital mortality from abdominal aortic surgery in Great Britain and Ireland: Vascular Anaesthesia Society audit. *Br J Surg.* 2001;88(5):687–692.
23. Bradbury A, Adam D, Makhdoomi K, et al. A 21-year experience of abdominal aortic aneurysm operations in Edinburgh. *Br J Surg.* 1998;85(5):645–647.
24. Bush RL, DePalma RG, Itani KM, et al. Outcomes of care of abdominal aortic aneurysm in Veterans Health Administration facilities: results from the National Surgical Quality Improvement Program. *Am J Surg.* 2009;198(5):S41–S48.
25. Dardik A, Lin JW, Gordon TA, et al. Results of elective abdominal aortic aneurysm repair in the 1990s: a population-based analysis of 2335 cases. *J Vasc Surg.* 1999;30(6):985–995.
26. Dimick JB, Stanley JC, Axelrod DA, et al. Variation in death rate after abdominal aortic aneurysmectomy in the United States: impact of hospital volume, gender, and age. *Ann Surg.* 2002;235(4):579.
27. Galland R. Mortality following elective infrarenal aortic reconstruction: a Joint Vascular Research Group study. *Br J Surg.* 1998;85(5):633–636.
28. Grant S, Grayson A, Mitchell D, McCollum C. Evaluation of five risk prediction models for elective abdominal aortic aneurysm repair using the UK National Vascular Database. *Br J Surg.* 2012;99(5):673–679.
29. Huber TS, Wang JG, Derrow AE, et al. Experience in the United States with intact abdominal aortic aneurysm repair. *J Vasc Surg.* 2001;33(2):304–311.
30. Johnston KW, Scobie TK. Multicenter prospective study of nonruptured abdominal aortic aneurysms. I. Population and operative management. *J Vasc Surg.* 1988;7(1):69–81.
31. Kazmers A, Jacobs L, Perkins A, et al. Abdominal aortic aneurysm repair in Veterans Affairs medical centers. *J Vasc Surg.* 1996;23(2):191–200.
32. Lawrence PF, Gazak C, Bhirangi L, et al. The epidemiology of surgically repaired aneurysms in the United States. *J Vasc Surg.* 1999;30(4):632–640.
33. Lee WA, Carter JW, Upchurch G, et al. Perioperative outcomes after open and endovascular repair of intact abdominal aortic aneurysms in the United States during 2001. *J Vasc Surg.* 2004;39(3):491–496.
34. Rigberg DA, Zingmond DS, McGory ML, et al. Age stratified, perioperative, and one-year mortality after abdominal aortic aneurysm repair: a statewide experience. *J Vasc Surg.* 2006;43(2):224–229.
35. De La Motte L, Jensen L, Vogt K, et al. Outcomes after elective aortic aneurysm repair: a nationwide Danish cohort study 2007–2010. *Eur J Vasc Endovasc Surg.* 2013;46(1):57–64.
36. Hicks CW, Canner JK, Arhuidese I, et al. Comprehensive assessment of factors associated with in-hospital mortality after elective abdominal aortic aneurysm repair. *JAMA Surg.* 2016;151(9):838–845.
37. Liu Y, Yang Y, Zhao J, et al. Systematic review and meta-analysis of sex differences in outcomes after endovascular aneurysm repair for infrarenal abdominal aortic aneurysm. *J Vasc Surg.* 2020;71(1):283–296.e4.
38. Scott R, Wilson N, Ashton H, Kay D. Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study. *Br J Surg.* 1995;82(8):1066–1070.
39. Scott R, Group MASS. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. *Lancet.* 2002;360(9345):1531–1539.
40. Schermerhorn M. Updated US Preventive Services Task Force Recommendations for Abdominal Aortic Aneurysm-Are We Really Up to Date? *JAMA Surg.* 2020;155(2):101–103.
41. O’Donnell TFX, Schermerhorn ML. Abdominal aortic aneurysm screening guidelines: United States Preventative Services Task Force and Society for Vascular Surgery. *J Vasc Surg.* 2020;71(5):1457–1458.
42. Jordan Jr WD, Moore Jr WM, Melton JG, et al. Secure fixation following EVAR with the Powerlink XL System in wide aortic necks: results of a prospective, multicenter trial. *J Vasc Surg.* 2009;50(5):979–986.e1.
43. Turnbull IC, Criado FJ, Sanchez L, et al. Five-year results for the Talent enhanced Low Profile System abdominal stent graft pivotal trial including early and long-term safety and efficacy. *J Vasc Surg.* 2010;51(3):537–544.e2.

44. Rouwet E, Torsello G, de Vries J-P, et al. Final results of the prospective European trial of the Endurant stent graft for endovascular abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg.* 2011;42(4):489–497.
45. Levin DC, Rao VM, Parker L, et al. Endovascular repair vs open surgical repair of abdominal aortic aneurysms: comparative utilization trends from 2001 to 2006. *J Am Coll Radiol.* 2009;6(7):506–509.
46. Bocquemin J-P, Pillet J-C, Lescalie F, et al. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low-to moderate-risk patients. *J Vasc Surg.* 2011;53(5):1167–1173.e1.
47. De Bruin JL, Baas AF, Bath J, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1881–1889.
48. United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, et al. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1863–1871.
49. Lederle FA, Freischlag JA, Kyriakides TC, et al. Long-term comparison of endovascular and open repair of abdominal aortic aneurysm. *N Engl J Med.* 2012;367:1988–1997.
50. Albuquerque Jr FC, Tonnessen BH, Noll Jr RE, et al. Paradigm shifts in the treatment of abdominal aortic aneurysm: trends in 721 patients between 1996 and 2008. *J Vasc Surg.* 2010;51(6):1348–1353.
51. Costin JA, Watson DR, Duff SB, et al. Evaluation of the complexity of open abdominal aneurysm repair in the era of endovascular stent grafting. *J Vasc Surg.* 2006;43(5):915–920.
52. Joels CS, Langan EM, Daley CA, et al. Changing indications and outcomes for open abdominal aortic aneurysm repair since the advent of endovascular repair. *Am Surg.* 2009;75(8):665–670.
53. Suckow BD, Goodney PP, Columbo JA, et al. National trends in open surgical, endovascular, and branched-fenestrated endovascular aortic aneurysm repair in Medicare patients. *J Vasc Surg.* 2018;67(6):1690–1697.e1.
54. Varkevisser RRB, O'Donnell TFX, Swerdlow NJ, et al. Fenestrated endovascular aneurysm repair is associated with lower perioperative morbidity and mortality compared with open repair for complex abdominal aortic aneurysms. *J Vasc Surg.* 2019;69(6):1670–1678.
55. Pitoulis GA, Donas KP, Schulte S, et al. Two-dimensional versus three-dimensional CT angiography in analysis of anatomical suitability for stentgraft repair of abdominal aortic aneurysms. *Acta Radiologica.* 2011;52(3):317–323.
56. Barshe NR, McPhee J, Ozaki CK, et al. Increasing complexity in the open surgical repair of abdominal aortic aneurysms. *Ann Vasc Surg.* 2012;26(1):10–17.
57. Landon BE, O'Malley AJ, Giles K, et al. Volume-outcome relationships and abdominal aortic aneurysm repair. *Circulation.* 2010;122(13):1290–1297.
58. Martin MC, Giles KA, Pomposelli FB, et al. National outcomes after open repair of abdominal aortic aneurysms with visceral or renal bypass. *Ann Vasc Surg.* 2010;24(1):106–112.
59. Rao R, Lane TRA, Franklin IJ, Davies AH. Open repair versus fenestrated endovascular aneurysm repair of juxtarenal aneurysms. *J Vasc Surg.* 2015;61(1):242–255.e5.
60. Raux M, Patel VI, Cochenne F, et al. A propensity-matched comparison of outcomes for fenestrated endovascular aneurysm repair and open surgical repair of complex abdominal aortic aneurysms. *J Vasc Surg.* 2014;60(4):858–864.
61. Patel VI, Ergul E, Conrad MF, et al. Continued favorable results with open surgical repair of type IV thoracoabdominal aortic aneurysms. *J Vasc Surg.* 2011;53(6):1492–1498.
62. Tsai S, Conrad MF, Patel VI, et al. Durability of open repair of juxtarenal abdominal aortic aneurysms. *J Vasc Surg.* 2012;56(1):2–7.
63. Nathan DP, Brinster CJ, Woo EY, et al. Predictors of early and late mortality following open extent IV thoracoabdominal aortic aneurysm repair in a large contemporary single-center experience. *J Vasc Surg.* 2011;53(2):299–306.
64. Coselli JS, Bozinovski J, LeMaire SA. Open surgical repair of 2286 thoracoabdominal aortic aneurysms. *Ann Thor Surg.* 2007;83(2):S862–S864.
65. Kieffer E, Chiche L, Godet G, et al. Type IV thoracoabdominal aneurysm repair: predictors of postoperative mortality, spinal cord injury, and acute intestinal ischemia. *Ann Vasc Surg.* 2008;22(6):822–828.
66. Martin GH, O'Hara PJ, Hertzler NR, et al. Surgical repair of aneurysms involving the suprarenal, visceral, and lower thoracic aortic segments: early results and late outcome. *J Vasc Surg.* 2000;31(5):851–862.
67. Richards J, Nimmo A, Moores C, et al. Contemporary results for open repair of suprarenal and type IV thoracoabdominal aortic aneurysms. *Br J Surg.* 2010;97(1):45–49.
68. Deery SE, Lancaster RT, Baril DT, et al. Contemporary outcomes of open complex abdominal aortic aneurysm repair. *J Vasc Surg.* 2016;63(5):1195–1200.
69. Scali ST, Beck AW, Sedrakyan A, et al. Hospital volume association with abdominal aortic aneurysm repair mortality. *Circulation.* 2019;140(15):1285–1287.
70. Sawang M, Paravastu SCV, Liu Z, et al. The relationship between aortic aneurysm surgery volume and peri-operative mortality in Australia. *Eur J Vasc Endovasc Surg.* 2019;57(4):510–519.
71. Zetttervall SL, Schermerhorn ML, Soden PA, et al. The effect of surgeon and hospital volume on mortality after open and endovascular repair of abdominal aortic aneurysms. *J Vasc Surg.* 2017;65(3):626–634.
72. Arnaoutakis DJ, Scali ST, Neal D, et al. Surgeon experience association with patient selection and outcomes after open abdominal aortic aneurysm repair. *J Vasc Surg.* 2020;72(4):1325–1336.e2.
73. Meltzer AJ, Connolly PH, Schneider DB, Sedrakyan A. Impact of surgeon and hospital experience on outcomes of abdominal aortic aneurysm repair in New York State. *J Vasc Surg.* 2017;66(3):728–734.e2.
74. Lilja F, Mani K, Wanhainen A. Editor's Choice – Trend-break in Abdominal Aortic Aneurysm Repair With Decreasing Surgical Workload. *Eur J Vasc Endovasc Surg.* 2017;53(6):811–819.
75. Nayahangan LJ, Lawaetz J, Strøm M, et al. Ensuring competency in open aortic aneurysm repair – development and validation of a new assessment tool. *Eur J Vasc Endovasc Surg.* 2020;59(5):767–774.
76. Greenleaf EK, Hollenbeak CS, Aziz F. Outcomes after ruptured abdominal aortic aneurysm repair in the era of centralized care. *J Vasc Surg.* 2020;71(4):1148–1161.
77. El-Arousy H, Lim S, Batagini NC, et al. Open aortic surgery volume experience at a regionalized referral center and impact on Accreditation Council for Graduate Medical Education trainees. *J Vasc Surg.* 2019;70(3):921–926.
78. Davidovic LB, Maksic M, Koncar I, et al. Open repair of AAA in a high volume center. *World J Surg.* 2017;41(3):884–891.
79. Schermerhorn ML, Bensley RP, Giles KA, et al. Changes in abdominal aortic aneurysm rupture and short-term mortality, 1995–2008: a retrospective observational study. *Ann Surg.* 2012;256(4):651–658.
80. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. *Lancet.* 2016;388(10058):2366–2374.
81. Markar SR, Vidal-Diez A, Sounderahaj V, et al. A population-based cohort study examining the risk of abdominal cancer after endovascular abdominal aortic aneurysm repair. *J Vasc Surg.* 2019;69(6):1776–1785.e2.
82. Mangum KD, Farber MA. Genetic and epigenetic regulation of abdominal aortic aneurysms. *Clin Genet.* 2020;97(6):815–826.
83. Roscher AA, Dieter RA, Raabe TD. Genetics of aortic diseases. In: Dieter RS, Dieter RA Jr, Dieter RA III, eds. *Diseases of the Aorta.* Cham: Springer International Publishing; 2019:55–84.
84. Pinard A, Jones GT, Milewicz DM. Genetics of thoracic and abdominal aortic diseases: aneurysms, dissections, and ruptures. *Circ res.* 2019;124(4):588–606.
85. Conway AM, Qato K, Anand G, et al. Endovascular abdominal aortic aneurysm repair in patients with Marfan syndrome. *Vascular.* 2020;28(1):48–52.
86. de la Cruz KI, LeMaire SA, Weldon SA, Coselli JS. Thoracoabdominal aortic aneurysm repair with a branched graft. *Ann Cardiothorac Surg.* 2012;1(3):381–393.

87. Glebova NO, Hicks CW, Alam R, et al. Technical aspects of branched graft aortic reconstruction in patients with connective tissue disorders. *J Vasc Surg.* 2016;64(2):520–525.
88. Hicks CW, Lue J, Glebova NO, et al. A 10-year institutional experience with open branched graft reconstruction of aortic aneurysms in connective tissue disorders versus degenerative disease. *J Vasc Surg.* 2017;66(5):1406–1416.
89. Kraiss LW. Moving frailty assessment beyond knowing it when you see it. *J Vasc Surg.* 2020;71(1):307–308.
90. George EL, Chen R, Trickey AW, et al. Variation in center-level frailty burden and the impact of frailty on long-term survival in patients undergoing elective repair for abdominal aortic aneurysms. *J Vasc Surg.* 2020;71(1):46–55.e4.
91. Drudi LM, Phung K, Ades M, et al. Psoas muscle area predicts all-cause mortality after endovascular and open aortic aneurysm repair. *Eur J Vasc Endovasc Surg.* 2016;52(6):764–769.
92. Kodama A, Takahashi N, Sugimoto M, et al. Associations of nutritional status and muscle size with mortality after open aortic aneurysm repair. *J Vasc Surg.* 2019;70(5):1585–1593.
93. Cheng BT, Soult MC, Helenowski IB, et al. Sarcopenia predicts mortality and adverse outcomes after endovascular aneurysm repair and can be used to risk stratify patients. *J Vasc Surg.* 2019;70(5):1576–1584.
94. Barbey SM, Scali ST, Kubilis P, et al. Interaction between frailty and sex on mortality after elective abdominal aortic aneurysm repair. *J Vasc Surg.* 2019;70(6):1831–1843.
95. Beebe HG, Kritpracha B. Computed tomography scanning for endograft planning: evolving toward three-dimensional, single source imaging. *Semin Vasc Surg.* 2004;17(2):126–134.
96. Sprouse LR 2nd, Meier GH 3rd, Parent FN, et al. Is three-dimensional computed tomography reconstruction justified before endovascular aortic aneurysm repair? *J Vasc Surg.* 2004;40(3):443–447.
97. Velazquez OC, Woo EY, Carpenter JP, et al. Decreased use of iliac extensions and reduced graft junctions with software-assisted centerline measurements in selection of endograft components for endovascular aneurysm repair. *J Vasc Surg.* 2004;40(2):222–227.
98. Reis SP, Majdalany BS, AbuRahma AF, et al. ACR appropriateness criteria® pulsatile abdominal mass suspected abdominal aortic aneurysm. *J Am Coll Radiol.* 2017;14(5):S258–S265.
99. Ding Y, Shan Y, Zhou M, et al. Amount of intraluminal thrombus correlates with severe adverse events in abdominal aortic aneurysms after endovascular aneurysm repair. *Ann Vasc Surg.* 2020;67:254–264.
100. Wu J, Taylor RJ, Li G, et al. *Cloud-based medical image processing system with tracking capability*. Google Patents; 2018.
101. Macía I, Legarreta JH, López-Linares K, et al. Chapter 15 – Preoperative planning of endovascular procedures in aortic aneurysms. In: Balocco S, Zuluaga MA, Zahnd G, et al., eds. *Computing and Visualization for Intravascular Imaging and Computer-Assisted Stenting*. Academic Press; 2017:413–444.
102. Hagspiel KD, Norton PT. *Computed Tomography Angiography (CTA). Imaging in Peripheral Arterial Disease*. Springer; 2020:45–61.
103. Picel AC, Kansal N. Essentials of endovascular abdominal aortic aneurysm repair imaging: preprocedural assessment. *Am J Roentgenol.* 2014;203(4):W347–W357.
104. Cikrit DF, Harris VJ, Hemmer CG, et al. Comparison of spiral CT scan and arteriography for evaluation of renal and visceral arteries. *Ann vasc Surg.* 1996;10(2):109–116.
105. Errington M, Ferguson J, Gillespie I, et al. Complete pre-operative imaging assessment of abdominal aortic aneurysm with spiral CT angiography. *Clin Radiol.* 1997;52(5):369–377.
106. Qanadli SD, Mesurolle Bt, Coggia M, et al. Abdominal aortic aneurysm: pretherapy assessment with dual-slice helical CT angiography. *Am J Roentgenol.* 2000;174(1):181–187.
107. Horinouchi H, Sofue K, Nishii T, et al. CT angiography with 15 mL contrast material injection on time-resolved imaging for endovascular abdominal aortic aneurysm repair. *Eur J Radiol.* 2020;126:108861.
108. François CJ. Abdominal Magnetic Resonance Angiography. *Magnetic Resonance Imaging Clinics.* 2020;28(3):395–405.
109. Tatli S, Yucel EK. *MRA of the Aorta and Peripheral Arteries. Cardiovascular Magnetic Resonance Imaging*. New York: Springer; 2019:381–405.
110. Tennant WG, Hartnell GG, Baird RN, Horrocks M. Radiologic investigation of abdominal aortic aneurysm disease: comparison of three modalities in staging and the detection of inflammatory change. *J Vasc Surg.* 1993;17(4):703–709.
111. Edelman RR, Koktzoglou I. Noncontrast MR angiography: An update. *J Magn Res Imaging.* 2019;49(2):355–373.
112. Salehi Ravesh M, Langguth P, Pfarr JA, et al. Non-contrast-enhanced magnetic resonance imaging for visualization and quantification of endovascular aortic prosthesis, their endoleaks and aneurysm sacs at 1.5 T. *Magnet Res Imaging.* 2019;60:164–172.
113. Cambria RP, Brewster DC, Abbott WM, et al. Transperitoneal versus retroperitoneal approach for aortic reconstruction: a randomized prospective study. *J Vasc Surg.* 1990;11(2):314–325.
114. Sicard GA, Reilly JM, Rubin BG, et al. Transabdominal versus retroperitoneal incision for abdominal aortic surgery: report of a prospective randomized trial. *J Vasc Surg.* 1995;21(2):174–183.
115. Chaikof EL, Dalman RL, Eskandari MK, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg.* 2018;67(1):2–77.e2.
116. Arko FR, Bohannon WT, Mettauer M, et al. Retroperitoneal approach for aortic surgery: is it worth it? *Cardiovasc Surg.* 2001;9(1):20–26.
117. Borkon MJ, Zaydfudim V, Carey CD, et al. Retroperitoneal repair of abdominal aortic aneurysms offers postoperative benefits to male patients in the Veterans Affairs Health System. *Ann Vasc Surg.* 2010;24(6):728–732.
118. Sieunarine K, Lawrence-Brown M, Goodman M. Comparison of transperitoneal and retroperitoneal approaches for infrarenal aortic surgery: early and late results. *Cardiovasc Surg.* 1997;5(1):71–76.
119. Deery SE, Zettervall SL, O'Donnell TFX, et al. Transabdominal open abdominal aortic aneurysm repair is associated with higher rates of late reintervention and readmission compared with the retroperitoneal approach. *J Vas Surg.* 2020;71(1):39–45.e1.
120. Bower TC. Techniques of open mesenteric reconstructions. In: Oderich GS, ed. *Mesenteric Vascular Disease: Current Therapy*. New York: Springer; 2015:145–156.
121. Chung BH, Kang JH, Heo SH, et al. The effect of left renal vein division on renal function following open abdominal aortic surgery using propensity score matching analysis. *Ann Vasc Surg.* 2020;62:232–237.
122. Mehta T, Wade RG, Clarke JM. Is it safe to ligate the left renal vein during open abdominal aortic aneurysm repair? *Ann Vasc Surg.* 2010;24(6):758–761.
123. West CA, Noel AA, Bower TC, et al. Factors affecting outcomes of open surgical repair of pararenal aortic aneurysms: A 10-year experience. *J Vasc Surg.* 2006;43(5):921–928.e1.
124. Samson RH, Lepore MR, Showalter DP, et al. Long-term safety of left renal vein division and ligation to expedite complex abdominal aortic surgery. *J Vasc Surg.* 2009;50(3):500–504.
125. Veith F, Gupta S, Daly V. Technique for occluding the supraceliac aorta through the abdomen. *Surg gynecol obstet.* 1980;151(3):426–428.
126. Malina M, Veith F, Ivancev K, Sonesson B. Balloon occlusion of the aorta during endovascular repair of ruptured abdominal aortic aneurysm. *J Endovasc Ther.* 2005;12(5):556–559.
127. Berland TL, Veith FJ, Cayne NS, et al. Technique of supraceliac balloon control of the aorta during endovascular repair of ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2013;57(1):272–275.
128. Brenner M, Teeter W, Hoehn M, et al. Use of resuscitative endovascular balloon occlusion of the aorta for proximal aortic control in patients with severe hemorrhage and arrest. *JAMA Surg.* 2018;153(2):130–135.
129. Dardik A, Perler BA, Roseborough GS, Williams GM. Aneurysmal expansion of the visceral patch after thoracoabdominal aortic replacement: an argument for limiting patch size? *J Vasc Surg.* 2001;34(3):405–410.
130. Lachat M, Mayer D, Criado FJ, et al. New technique to facilitate renal revascularization with use of telescoping self-expanding stent grafts: VORTEC. *Vascular.* 2008;16(2):69–72.

131. Schneider F, Dubourg AP, Ricco J-B. Use of VIABAHN Open Revascularisation TECHnique (VORTEC) for Iliofemoral Bypass. *EJVES Short Rep.* 2018;39:50–53.
132. Bornak A, Goldstein LJ, Rey J, et al. Aortic aneurysmal repair with sutureless visceral revascularization using novel hybrid vascular graft and a gradual funneling technique. *Vasc Endovasc Surg.* 2012;46(3):258–261.
133. Winklehner A, Nguyen-Kim TDL, Pfammatter T, et al. Graft patency in long-term survivors after renovisceral debranching with VORTEC. *Cardiovasc Intervent Radiol.* 2015;38(3):606–612.
134. Kahlberg A, Bossi M, Mascia D, et al. Renal and visceral sutureless anastomosis during thoracoabdominal aortic repair. In: Tshomba Y, Baccellieri D, Chiesa R, eds. *Visceral Vessels and Aortic Repair: Challenges and Difficult Cases*. Cham: Springer International Publishing; 2019:213–223.
135. Oderich G, Mendes B, Gloviczki P, et al. Current role and future directions of hybrid repair of thoracoabdominal aortic aneurysms. *Perspect Vasc Surg Endovasc Ther.* 2012;24:14–22.
136. Tsai M-T, Tseng C-C, Kan C-D. Transaortic modification of the Viabahn Open Revascularization Technique (VORTEC) to facilitate renal artery revascularization in a hybrid EVAR procedure. *J Endovasc Ther.* 2013;20(5):647–651.
137. Bonvini S, Ricotta JJ, Piazza M, et al. ViPS technique as a novel concept for a sutureless vascular anastomosis. *J Vasc Surg.* 2011;54(3):889–892.
138. Moghadamyeghaneh Z, Sgroi MD, Chen SL, et al. Risk factors and outcomes of postoperative ischemic colitis in contemporary open and endovascular abdominal aortic aneurysm repair. *J Vasc Surg.* 2016;63(4):866–872.
139. Jorgensen MS, Farres H, Almerez T, et al. Complex repair of juxtarenal abdominal aortic aneurysm with an anatomical variant of the renal arteries. *Ann Vasc Surg.* 2019;58:377.e5–e8.
140. Mudoni A, Caccetta F, Caroppo M, et al. Crossed fused renal ectopia: case report and review of the literature. *J Ultrasound.* 2017;20(4):333–337.
141. Tinelli G, Sica S, Minelli F, et al. Horseshoe kidney protection with histidine–tryptophan–ketoglutarate solution during surgical abdominal aortic aneurysm repair. *Ann Vasc Surg.* 2020;63:459.e5–e8.
142. Lomoro P, Simonetti I, Vinci G, et al. Pancake kidney, a rare and often misdiagnosed malformation: a case report and radiological differential diagnosis. *J Ultrasound.* 2019;22(2):207–213.
143. Beregi JP, Mauroy B, Willoteaux S, et al. Anatomic variation in the origin of the main renal arteries: spiral CTA evaluation. *Eur Radiol.* 1999;9(7):1330–1334.
144. Gulas E, Wysiadecki G, Cecot T, et al. Accessory (multiple) renal arteries – Differences in frequency according to population, visualizing techniques and stage of morphological development. *Vascular.* 2016;24(5):531–537.
145. Göksel O, Çınar B, Kömürcü G, Ahin S, Eren T. Surgical treatment of abdominal aortic aneurysms associated with horseshoe kidney. *Vascular.* 2006;14(1):27–31.
146. Ruppert V, Umscheid T, Rieger J, et al. Endovascular aneurysm repair: Treatment of choice for abdominal aortic aneurysm coincident with horseshoe kidney? Three case reports and review of literature. *J Vasc Surg.* 2004;40(2):367–370.
147. Aljabri B, MacDonald P, Satin R, et al. Incidence of major venous and renal anomalies relevant to aortoiliac surgery as demonstrated by computed tomography. *Ann Vasc Surg.* 2001;15(6):615–618.
148. Dilli A, Ayaz UY, Kaplanoglu H, et al. Evaluation of the left renal vein variations and inferior vena cava variations by means of helical computed tomography. *Clin Imaging.* 2013;37(3):530–535.
149. Trigaux J-P, Vandrogenbroek S, De Wispelaere J-F, et al. Congenital anomalies of the inferior vena cava and left renal vein: evaluation with spiral CT. *J Vasc Intervent Radiol.* 1998;9(2):339–345.
150. Truty MJ, Bower TC. Congenital anomalies of the inferior vena cava and left renal vein: Implications during open abdominal aortic aneurysm reconstruction. *Ann Vasc Surg.* 2007;21(2):186–197.
151. Bartle EJ, Pearce WH, Sun JH, Rutherford RB. Infrarenal venous anomalies and aortic surgery: avoiding vascular injury. *J Vasc Surg.* 1987;6(6):590–593.
152. Giordano JM, Trout III HH. Anomalies of the inferior vena cava. *J Vasc Surg.* 1986;3(6):924–928.
153. Hersey P, Poullis M. Does the administration of mannitol prevent renal failure in open abdominal aortic aneurysm surgery? *Inter Cardiovasc Thor Surg.* 2008;7(5):906–909.
154. Hynninen MS, Niemi TT, Pöyhönen R, et al. N-acetylcysteine for the prevention of kidney injury in abdominal aortic surgery: a randomized, double-blind, placebo-controlled trial. *Anesthesia Analgesia.* 2006;102(6):1638–1645.
155. Macedo E, Abdulkader R, Castro I, et al. Lack of protection of N-acetylcysteine (NAC) in acute renal failure related to elective aortic aneurysm repair—a randomized controlled trial. *Nephrol Dial Transplant.* 2006;21(7):1863–1869.
156. Schoenwald PK. Intraoperative management of renal function in the surgical patient at risk: Focus on aortic surgery. *Anesthesiol Clin North Am.* 2000;18(4):719–737.
157. Mathur VS, Swan SK, Lambrecht LJ, et al. The effects of fenoldopam, a selective dopamine receptor agonist, on systemic and renal hemodynamics in normotensive subjects. *Crit Care Med.* 1999;27(9):1832–1837.
158. Gilbert TB, Ju Hasnain, Flinn WR, et al. Fenoldopam infusion associated with preserving renal function after aortic cross-clamping for aneurysm repair. *J Cardiovasc Pharmacol Therapeut.* 2001;6(1):31–36.
159. Halpenny M, Rushe C, Breen P, et al. The effects of fenoldopam on renal function in patients undergoing elective aortic surgery. *Eur J Anaesthesiol.* 2002;19(1):32–39.
160. Crawford ES, Crawford JL, Safi HJ, et al. Thoracoabdominal aortic aneurysms: preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. *J Vasc Surg.* 1986;3(3):389–404.
161. Ochsner J, Mills N, Gardner P. A technique for renal preservation during suprarenal abdominal aortic operations. *Surg Gynecol Obst.* 1984;159(4):388–390.
162. Schmitt JD, Fatehpur S, Tezval H, et al. Hypothermic renal protection using cold histidine–tryptophan–ketoglutarate solution perfusion in suprarenal aortic surgery. *Ann Vasc Surg.* 2008;22(4):520–524.
163. Yeung K, Jongkind V, Coveliers H, et al. Routine continuous cold perfusion of the kidneys during elective juxtarenal aortic aneurysm repair. *Eur J Vasc Endovasc Surg.* 2008;35(4):446–451.
164. Bhamidipati CM, Coselli JS, LeMaire SA. Perfusion techniques for renal protection during thoracoabdominal aortic surgery. *J Ex Corp Technol.* 2012;44(1):P31–7.
165. Kasahara H, Shimizu H, Yozu R. Postoperative renal function after juxtarenal aortic aneurysm repair with simple cross-clamping. *Ann Vasc Surg.* 2013;27(3):291–298.
166. Patel VI, Lancaster RT, Conrad MF, et al. Comparable mortality with open repair of complex and infrarenal aortic aneurysm. *J Vasc Surg.* 2011;54(4):952–959.
167. Pronovost PJ, Jenckes MW, Dorman T, et al. Organizational characteristics of intensive care units related to outcomes of abdominal aortic surgery. *JAMA.* 1999;281(14):1310–1317.
168. Pronovost PJ, Dang D, Dorman T, et al. Intensive care unit nurse staffing and the risk for complications after abdominal aortic surgery. *Eff Clin Pract.* 2001;4(5):199–206.
169. Lindenauer PK, Pekow P, Wang K, et al. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. *N Engl J Med.* 2005;353(4):349–361.
170. Mangano DT, Layug EL, Wallace A, Tateo I. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. *N Engl J Med.* 1996;335(23):1713–1721.
171. Poldermans D, Boersma E, Bax JJ, et al. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. *N Engl J Med.* 1999;341(24):1789–1794.
172. Kurzencwyg D, Filion KB, Pilote L, et al. Cardiac medical therapy among patients undergoing abdominal aortic aneurysm repair. *Ann Vasc Surg.* 2006;20(5):569–576.
173. Nathan DP, Brinster CJ, Jackson BM, et al. Predictors of decreased short-and long-term survival following open abdominal aortic aneurysm repair. *J Vasc Surg.* 2011;54(5):1237–1243.

174. Green RM, Ricotta JJ, Ouriel K, DeWeese JA. Results of supraceliac aortic clamping in the difficult elective resection of infrarenal abdominal aortic aneurysm. *J Vasc Surg.* 1989;9(1):124–134.
175. Allen BT, Anderson CB, Rubin BG, et al. Preservation of renal function in juxtarenal and suprarenal abdominal aortic aneurysm repair. *J Vasc Surg.* 1993;17(5):948–959.
176. Tallarita T, Sobreira ML, Oderich GS. Results of open pararenal abdominal aortic aneurysm repair: tabular review of the literature. *Ann Vasc Surg.* 2011;25(1):143–149.
177. O'Donnell TFX, Boitano LT, Deery SE, et al. Factors associated with postoperative renal dysfunction and the subsequent impact on survival after open juxtarenal abdominal aortic aneurysm repair. *J Vasc Surg.* 2019;69(5):1421–1428.
178. Gurakar M, Locham S, Alshaikh HN, Malas MB. Risk factors and outcomes for bowel ischemia after open and endovascular abdominal aortic aneurysm repair. *J Vasc Surg.* 2019;70(3):869–881.
179. Ultee KH, Zettervall SL, Soden PA, et al. Incidence of and risk factors for bowel ischemia after abdominal aortic aneurysm repair. *J Vasc Surg.* 2016;64(5):1384–1391.
180. Williamson JS, Ambler GK, Twine CP, et al. Elective repair of abdominal aortic aneurysm and the risk of colonic ischaemia: systematic review and meta-analysis. *Eur J Vasc Endovasc Surg.* 2018;56(1):31–39.
181. Björck M, Troeng T, Bergqvist D. Risk factors for intestinal ischaemia after aortoiliac surgery: a combined cohort and case-control study of 2824 operations. *Eur J Vasc Endovasc Surg.* 1997;13(6):531–539.
182. Brewster D, Franklin D, Cambria R, et al. Intestinal ischemia complicating abdominal aortic surgery. *Surgery.* 1991;109(4):447–454.
183. Longo WE, Lee TC, Barnett MG, et al. Ischemic colitis complicating abdominal aortic aneurysm surgery in the US veteran. *J Surg Res.* 1996;60(2):351–354.
184. Becquemin JP, Majewski M, Fermani N, et al. Colon ischemia following abdominal aortic aneurysm repair in the era of endovascular abdominal aortic repair. *J Vasc Surg.* 2008;47(2):258–263.
185. Jayaram A, DeMartino RR, Bower TC, et al. Outcomes following inferior mesenteric artery reimplantation during elective aortic aneurysm surgery. *Ann Vasc Surg.* 2020;66:65–69.
186. Lee KB, Lu J, Macsata RA, et al. Inferior mesenteric artery re plantation does not decrease the risk of ischemic colitis after open infrarenal abdominal aortic aneurysm repair. *J Vasc Surg.* 2019;69(6):1825–1830.
187. Jalalzadeh H, van Schaik TG, Duin JJ, et al. The value of sigmoidoscopy to detect colonic ischaemia after ruptured abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg.* 2019;57(2):229–237.
188. Cruz C, Abujudeh HH, Nazarian RM, Thrall JH. Ischemic colitis: spectrum of CT findings, sites of involvement and severity. *Emerg Radiol.* 2015;22(4):357–365.
189. Menegaux F, Tréallet C, Kieffer E, et al. Aggressive management of nonocclusive ischemic colitis following aortic reconstruction. *Arch Surg.* 2006;141(7):678–682.
190. Behrendt C-A, Dayama A, Debus ES, et al. Lower extremity ischemia after abdominal aortic aneurysm repair. *Ann Vasc Surg.* 2017;45:206–212.
191. Deery SE, O'Donnell TFX, Bodewes TCF, et al. Early reintervention after open and endovascular abdominal aortic aneurysm repair is associated with high mortality. *J Vasc Surg.* 2018;67(2):433–440.e1.
192. Rosenthal D. Spinal cord ischemia after abdominal aortic operation: is it preventable? *J Vasc Surg.* 1999;30(3):391–399.
193. Oberhuber A, Buecken M, Hoffmann M, et al. Comparison of aortic neck dilatation after open and endovascular repair of abdominal aortic aneurysm. *J Vasc Surg.* 2012;55(4):929–934.
194. Scali ST, Beck AW, Chang CK, et al. Defining risk and identifying predictors of mortality for open conversion after endovascular aortic aneurysm repair. *J Vasc Surg.* 2016;63(4):873–881.e1.
195. Kouvelos G, Koutsoumpelis A, Lazaris A, Matsagkas M. Late open conversion after endovascular abdominal aortic aneurysm repair. *J Vasc Surg.* 2015;61(5):1350–1356.
196. Ultee KHJ, Soden PA, Zettervall SL, et al. Conversion from endovascular to open abdominal aortic aneurysm repair. *J Vasc Surg.* 2016;64(1):76–82.
197. Goudeketting SR, Fung Kon Jin PHP, Ünlü Ç, de Vries JPPM. Systematic review and meta-analysis of elective and urgent late open conversion after failed endovascular aneurysm repair. *J Vasc Surg.* 2019;70(2):615–628.e7.
198. Perini P, Bianchini Massoni C, Mariani E, et al. Systematic review and meta-analysis of the outcome of different treatments for type 1a endoleak after EVAR. *Ann Vasc Surg.* 2019;60:435–446.e1.
199. Brinster CJ, Fairman RM, Woo EY, et al. Late open conversion and explantation of abdominal aortic stent grafts. *J Vasc Surg.* 2011;54(1):42–46.
200. Perini P, Gargiulo M, Silingardi R, et al. Twenty-two year multicentre experience of late open conversions after endovascular abdominal aneurysm repair. *Eur J Vasc Endovasc Surg.* 2020;59(5):757–765.
201. Lyden SP, McNamara JM, Sternbach Y, et al. Technical considerations for late removal of aortic endografts. *J Vasc Surg.* 2002;36(4):674–678.
202. Kelso RL, Lyden SP, Butler B, et al. Late conversion of aortic stent grafts. *J Vasc Surg.* 2009;49(3):589–595.
203. Mehta M, Paty PSK, Roddy SP, et al. Treatment options for delayed AAA rupture following endovascular repair. *J Vasc Surg.* 2011;53(1):14–20.
204. Phade SV, Keldahl ML, Morasch MD, et al. Late abdominal aortic endograft explants: Indications and outcomes. *Surgery.* 2011;150(4):788–795.
205. Perini P, Gargiulo M, Silingardi R, et al. Late open conversions after endovascular abdominal aneurysm repair in an urgent setting. *J Vasc Surg.* 2019;69(2):423–431.
206. Steenberge SP, Lyden SP, Turney EJ, et al. Outcomes after partial endograft explantation. *Ann Vasc Surg.* 2016;31:1–7.
207. Usatii A, Payne W, Santilli S. Removal of an infected aortic endograft and open aortic reconstruction: technical remarks. *Ann Vasc Surg.* 2013;27(5):679–683.
208. Müller BT, Wegener OR, Grabitz K, et al. Mycotic aneurysms of the thoracic and abdominal aorta and iliac arteries: experience with anatomic and extra-anatomic repair in 33 cases. *J Vasc Surg.* 2001;33(1):106–113.
209. Oderich GS, Panneton JM, Bower TC, et al. Infected aortic aneurysms: aggressive presentation, complicated early outcome, but durable results. *J Vasc Surg.* 2001;34(5):900–908.
210. Reddy DJ, Shepard AD, Evans JR, et al. Management of infected aortoiliac aneurysms. *Arch Surg.* 1991;126(7):873–879.
211. Shiraei T, Barrett S, Heywood S, et al. Incidence, management, and outcomes of aortic graft infection. *Ann Vasc Surg.* 2019;59:73–83.
212. Sörelius K, Budtz-Lilly J, Mani K, Wanhainen A. Systematic review of the management of mycotic aortic aneurysms. *Eur J Vasc Endovasc Surg.* 2019;58(3):426–435.
213. Vallejo N, Picardo NE, Bourke P, et al. The changing management of primary mycotic aortic aneurysms. *J Vasc Surg.* 2011;54(2):334–340.
214. Cullen JM, Booth AT, Mehaffey JH, et al. Clinical characteristics and longitudinal outcomes of primary mycotic aortic aneurysms. *Angiology.* 2019;70(10):947–951.
215. Laohapensang K, Rutherford RB, Arworn S. Infected aneurysm. *Ann Vasc Dis.* 2010;3(1):16–23.
216. Macedo TA, Stanson AW, Oderich GS, et al. Infected aortic aneurysms: imaging findings. *Radiology.* 2004;231(1):250–257.
217. Brossier J, Lesprit P, Marzelle J, et al. New bacteriological patterns in primary infected aorto-iliac aneurysms: a single-centre experience. *Eur J Vasc Endovasc Surg.* 2010;40(5):582–588.
218. Dubois M, Daenens K, Houthoofd S, et al. Treatment of mycotic aneurysms with involvement of the abdominal aorta: single-centre experience in 44 consecutive cases. *Eur J Vasc Endovasc Surg.* 2010;40(4):450–456.
219. Puges M, Bérard X, Ruiz J-B, et al. Retrospective study comparing WBC scan and 18F-FDG PET/CT in patients with suspected prosthetic vascular graft infection. *Eur J Vasc Endovasc Surg.* 2019;57(6):876–884.
220. Clough R, Black S, Lyons O, et al. Is endovascular repair of mycotic aortic aneurysms a durable treatment option? *Eur J Vasc Endovasc Surg.* 2009;37(4):407–412.
221. Setacci C, de Donato G, Setacci F. Endografts for the treatment of aortic infection. *Sem Vasc Surg.* 2011;24(4):242–249.

222. Dias AP, Farivar BS, Steenberge SP, et al. Management of failed endovascular aortic aneurysm repair with explantation or fenestrated-branched endovascular aortic aneurysm repair. *J Vasc Surg.* 2018;68(6):1676–1687.e3.
223. Batt M, Jean-Baptiste E, O'Connor S, et al. Early and late results of contemporary management of 37 secondary aortoenteric fistulae. *Eur J Vasc Endovasc Surg.* 2011;41(6):748–757.
224. Rodrigues dos Santos C, Casaca R, Mendes de Almeida JC, Mendes-Pedro L. Enteric Repair in Aortoduodenal Fistulas: A Forgotten but Often Lethal Player. *Ann Vasc Surg.* 2014;28(3):756–762.
225. Durgin JM, Arous EJ, Kumar S, et al. Complete regression of a symptomatic, mycotic juxtarenal abdominal aortic aneurysm after treatment with fenestrated endovascular aneurysm repair. *J Vasc Surg.* 2016;64(3):803–806.
226. Berchtold C, Eibl C, Seelig MH, et al. Endovascular treatment and complete regression of an infected abdominal aortic aneurysm. *J Endovasc Ther.* 2002;9(4):543–548.
227. Kinney EV, Kaebnick HW, Mitchell RA, Jung MT. Repair of mycotic paravisceral aneurysm with a fenestrated stent-graft. *J Endovasc Ther.* 2000;7(3):192–197.
228. Kan C-D, Yen H-T, Kan C-B, Yang Y-J. The feasibility of endovascular aortic repair strategy in treating infected aortic aneurysms. *J Vasc Surg.* 2012;55(1):55–60.
229. Chino S, Kato N, Noda Y, et al. Treatment of infected aneurysms of the abdominal aorta and iliac artery with endovascular aneurysm repair and percutaneous drainage. *Ann Vasc Surg.* 2016;36:289.e11–289.e15.
230. Fatima J, Duncan AA, de Grandis E, et al. Treatment strategies and outcomes in patients with infected aortic endografts. *J Vasc Surg.* 2013;58(2):371–379.
231. Davila VJ, Stone W, Duncan AA, Wood E, Jordan WD, Zea N, et al. A multicenter experience with the surgical treatment of infected abdominal aortic endografts. *J Vasc Surg.* 2015;62(4):877–883.
232. Dorweiler B, Neufang A, Chaban R, et al. Use and durability of femoral vein for autologous reconstruction with infection of the aortoilio-femoral axis. *J Vasc Surg.* 2014;59(3):675–683.
233. Escobar GA, Eliason JL, Hurie J, et al. Rifampin soaking Dacron-based endografts for implantation in infected aortic aneurysms—new application of a time-tested principle. *Ann Vasc Surg.* 2014;28(3):744–748.
234. Vogt PR. Arterial allografts in treating aortic graft infections: something old, something new. *Sem Vasc Surg.* 2011;24(4):227–233.
235. Pupka A, Skora J, Janczak D, et al. In situ revascularisation with silver-coated polyester prostheses and arterial homografts in patients with aortic graft infection – a prospective, comparative, single-centre study. *Eur J Vasc Endovasc Surg.* 2011;41(1):61–67.
236. Oderich GS, Bower TC, Hofer J, et al. In situ rifampin-soaked grafts with omental coverage and antibiotic suppression are durable with low reinfection rates in patients with aortic graft enteric erosion or fistula. *J Vasc Surg.* 2011;53(1):99–107.e7.
237. Goéau-Brissonnière O, Javerlat I, Koskas F, et al. Rifampin-bonded vascular grafts and postoperative infections. *Ann Vasc Surg.* 2011;25(1):134–142.
238. Wilson WR, Bower TC, Creager MA, et al. Vascular Graft Infections, Mycotic Aneurysms, and Endovascular Infections: A Scientific Statement From the American Heart Association. *Circulation.* 2016;134(20):e412–e460.
239. Harlander-Locke MP, Harmon LK, Lawrence PF, et al. The use of cryopreserved aortoiliac allograft for aortic reconstruction in the United States. *J Vasc Surg.* 2014;59(3):669–674.e1.
240. Lew W, Moore W. Antibiotic-impregnated grafts for aortic reconstruction. *Sem Vasc Surg.* 2011;24(4):211–219.
241. Lee C-H, Hsieh H-C, Ko P-J, et al. In situ versus extra-anatomic reconstruction for primary infected infrarenal abdominal aortic aneurysms. *J Vasc Surg.* 2011;54(1):64–70.
242. Berger P, Moll FL. Aortic graft infections: is there still a role for axillobifemoral reconstruction? *Sem Vasc Surg.* 2011;24(4):205–210.
243. Sharp WJ, Hoballah JJ, Mohan CR, et al. The management of the infected aortic prosthesis: A current decade of experience. *J Vasc Surg.* 1994;19(5):844–850.
244. Post ICJH, Vos CG. Systematic review and meta-analysis on the management of open abdominal aortic graft infections. *Eur J Vasc Endovasc Surg.* 2019;58(2):258–281.
245. Lehnert T, Gruber H-P, Maeder N, Allenberg J-R. Management of primary aortic graft infection by extra-anatomic bypass reconstruction. *Eur J Vasc Surg.* 1993;7(3):301–307.
246. Tang T, Boyle J, Dixon A, Varty K. Inflammatory abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg.* 2005;29(4):353–362.
247. Stella A, Gargiulo M, Fagioli GL, et al. Postoperative course of inflammatory abdominal aortic aneurysms. *Ann Vasc Surg.* 1993;7(3):229–238.
248. Lindblad B, Almgren B, Bergqvist D, et al. Abdominal aortic aneurysm with periareolar fibrosis: Experience from 11 Swedish vascular centers. *J Vasc Surg.* 1991;13(2):231–239.
249. Wicker CM, von Stein P, Bianchini Massoni C, et al. Long-term results after open repair of inflammatory infrarenal aortic aneurysms. *J Vasc Surg.* 2019;69(2):440–447.
250. Walker D, Bloor K, Williams G, Gillie I. Inflammatory aneurysms of the abdominal aorta. *Br J Surg.* 1972;59(8):609–614.
251. Nitecki SS, Hallett Jr JW, Stanson AW, et al. Inflammatory abdominal aortic aneurysms: a case-control study. *J Vasc Surg.* 1996;23(5):860–869.
252. Hellmann DB, Grand DJ, Freischlag JA. Inflammatory abdominal aortic aneurysm. *JAMA.* 2007;297(4):395–400.
253. Kasahima S, Zen Y, Kawashima A, et al. A new clinicopathological entity of IgG4-related inflammatory abdominal aortic aneurysm. *J Vasc Surg.* 2009;49(5):1264–1271.
254. Stone JH, Zen Y, Deshpande V. IgG4-related disease. *N Engl J Med.* 2012;366(6):539–551.
255. Wanhainen A, Verzini F, Van Herzele I, et al. European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms (vol 57, pg 8, 2019). *Eur J Vasc Endovasc Surg.* 2020;59(3):494.
256. van der Bilt FE, Hendriks TR, van der Meijden WAG, et al. Outcome in patients with idiopathic retroperitoneal fibrosis treated with corticosteroid or tamoxifen monotherapy. *Clin Kidney J.* 2016;9(2):184–191.
257. van Bommel EF, van der Veer SJ, Hendriks TR, Bleumink GS. Persistent chronic peri-aortitis ('inflammatory aneurysm') after abdominal aortic aneurysm repair: systematic review of the literature. *Vasc Med.* 2008;13(4):293–303.
258. Sasaki S, Sakuma M, Kunihara T, et al. Efficacy of steroid therapy in the treatment of inflammatory abdominal aortic aneurysms. *Int J Angiol.* 1997;6(4):234–236.
259. Baskerville P, Blakeney C, Young A, Browne N. The diagnosis and treatment of peri-aortic fibrosis ('inflammatory'aneurysms). *Br J Surg.* 1983;70(6):381–385.
260. Pennell RC, Hollier LH, Lie J, et al. Inflammatory abdominal aortic aneurysms: a thirty-year review. *J Vasc Surg.* 1985;2(6):859–869.
261. Bier G, Henes J, Eulenbruch C, et al. Perfusion-based assessment of disease activity in untreated and treated patients with aortitis and chronic periaortitis: correlation with CT morphological, clinical and serological data. *Br J Radiol.* 2015;88(1056):20150526.
262. Mizushima I, Inoue D, Yamamoto M, et al. Clinical course after corticosteroid therapy in IgG4-related aortitis/periaortitis and periaortitis: a retrospective multicenter study. *Arthritis Res Therapy.* 2014;16(4):R156.
263. Cistaro A, Penna D, Pelosi E, et al. 18F-FDG PET/CT in management of retroperitoneal fibrosis: A promising tool. *J Nucl Med.* 2012;53(suppl 1):2145.
264. Bier G, Kurucay M, Henes J, et al. Monitoring disease activity in patients with aortitis and chronic periaortitis undergoing immunosuppressive therapy by perfusion CT. *Acad Radiol.* 2017;24(4):470–477.
265. Santos Á Duque, Reyes Valdivia A, Romero Lozano MA, et al. Outcomes of open and endovascular repair of inflammatory abdominal aortic aneurysms. *Vascular.* 2018;26(2):203–208.
266. Stone WM, Fankhauser GT, Bower TC, et al. Comparison of open and endovascular repair of inflammatory aortic aneurysms. *J Vasc Surg.* 2012;56(4):951–956.
267. Cardaci MB, Destraix R, Van Houte B, Vazquez C. Endovascular repair of inflammatory aortic aneurysms: experience in a single center. *Ann Vasc Surg.* 2019;58:255–260.

268. Bianchini Massoni C, Stein Pv, Schernthaler M, et al. Endovascular treatment of inflammatory infrarenal aortic aneurysms. *Vasc Endovasc Surg.* 2016;50(1):21–28.
269. Paravastu SC, Ghosh J, Murray D, et al. A systematic review of open versus endovascular repair of inflammatory abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg.* 2009;38(3):291–297.
270. Maeda H, Umezawa H, Hattori T, et al. Early and late outcomes of inflammatory abdominal aortic aneurysms: comparison with the outcomes after open surgical and endovascular aneurysm repair in literature reviews. *Int Angiol.* 2013;32(1):67–73.
271. Nuellari E, Prifti E, Esposito G, Kapedani E. Surgical treatment of inflammatory abdominal aortic aneurysms: outcome and predictors analysis. *Med Arch.* 2014;68(4):244–248.
272. Sakai K, Watanabe T, Yoshida T. Endovascular treatment of immunoglobulin G4-related inflammatory abdominal aortic aneurysm. *J Vasc Surg Cases Innov Tech.* 2018;4(3):189–192.
273. Vaglio A, Palmisano A, Alberici F, et al. Prednisone versus tamoxifen in patients with idiopathic retroperitoneal fibrosis: an open-label randomised controlled trial. *Lancet.* 2011;378(9788):338–346.
274. Sultan S, Duffy S, Madhavan P, et al. Fifteen-year experience of transperitoneal management of inflammatory abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg.* 1999;18(6):510–514.
275. Igari K, Kudo T, Toyofuku T, Inoue Y. Open surgical repair for inflammatory abdominal aortic and iliac artery aneurysms. *Ann Vasc Surg.* 2017;39:105–110.
276. Cvetkovic S, Koncar I, Ducic S, et al. Early and long-term results of open repair of inflammatory abdominal aortic aneurysms: Comparison with a propensity score-matched cohort. *J Vasc Surg.* 2020;72(3):910–917.
277. Chisci E, Pigozzi C, Guidotti A, et al. IP033. Contemporary management of inflammatory abdominal aortic aneurysm repair: lesson learned after 117 consecutive cases. *J Vasc Surg.* 2018;67(6):e97–e98.
278. Prinsen M, Verhoeven ELG, Buth J, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med.* 2004;351(16):1607–1618.
279. Lederle FA, Freischlag JA, Kyriakides TC, et al. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. *Jama.* 2009;302(14):1535–1542.
280. Lederle FA, Kyriakides TC, Stroupe KT, Freischlag JA, Padberg FT Jr, Matsumura JS, et al. Open versus endovascular repair of abdominal aortic aneurysm. *N Engl J Med.* 2019;380(22):2126–2135.
281. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1863–1871.
282. Schwarze ML, Shen Y, Hemmerich J, Dale W. Age-related trends in utilization and outcome of open and endovascular repair for abdominal aortic aneurysm in the United States, 2001–2006. *J Vasc Surg.* 2009;50(4):722–729.e2.
283. Davenport DL, Xenos ES. Deep venous thrombosis after repair of non-ruptured abdominal aneurysm. *J Vasc Surg.* 2013;57(3):678–683.e1.
284. Chong T, et al. Suprarenal aortic cross-clamp position: a reappraisal of its effects on outcomes for open abdominal aortic aneurysm repair. *J Vasc Surg.* 2009;49:873–880.
285. Landry G, et al. Open abdominal aortic aneurysm repair in the endovascular era: effect of clamp site on outcomes. *Arch Surg.* 2009;144:811–816.
286. Knott AW, et al. Open repair of juxtarenal aortic aneurysms (JAA) remains a safe option in the era of fenestrated endografts. *J Vasc Surg.* 2008;47:695–701.
287. Chiesa R, et al. Open repair of pararenal aortic aneurysms: operative management, early results, and risk factor analysis. *Ann Vasc Surg.* 2006;20:739–746.
288. Tshomba Y, Baccellieri D, Mascia D, et al. Open treatment of extent IV thoracoabdominal aortic aneurysms. *J Cardiovasc Surg.* 2015;56(5):687–697.

Endovascular Aneurysm Repair Techniques

CLAYTON J. BRINSTER and W. CHARLES STERNBERGH III

INTRODUCTION	948
FIXATION	948
Positive Fixation, Column Support, and Friction	949
Infrarenal Versus Suprarenal Fixation	949
SEALING	949
ILIAC LIMBS	949
SIZING	949
GRAFT MATERIAL	949
RADIOOPACITY	949
DEPLOYMENT PRECISION AND EASE OF USE	950
GRAFT SELECTION AND PRIMARY DEVICE CHARACTERISTICS	950
Endograft Configurations	950
Preoperative Sizing and Planning	951
PREOPERATIVE IMAGING	951
Computed Tomography Arteriography	951
Alternative Imaging	951
ENDOGRAFT SIZING	951
Aortic Neck Diameter	951
Sizing the Conical Aortic Neck	953
Length Measurements	953

Iliac Diameters	954
PATIENT SELECTION	954
ANESTHESIA, ACCESS, AND IMAGING	954
Anesthesia	954
Vascular Access	954
Percutaneous Access	954
Open Surgical Access	954
Iliac Occlusive Disease	955
Iliac Conduit Placement	955
Imaging	955
Equipment	955
Gantry Positioning	955
EVAR DEPLOYMENT	955
Wire Placement	955
Delivery of the Main Device	956
Proximal Endograft Deployment	956
Accessory Renal Artery Management	956
Contralateral Gate Cannulation	956
Limb Deployment	957
Completion Arteriography	958
EVAR TROUBLESHOOTING	959

INTRODUCTION

Current commercially available systems have a wide variety of configurations that are capable of treating the majority of infrarenal aortoiliac aneurysms. Various options exist for stent-graft fixation, sealing, patency, sizing, and durable exclusion of aortic aneurysms. Radiopacity, deployment precision, ease of use, and sheath size and flexibility are additionally important characteristics. Current commercially available infrarenal endografts and their respective US Food and Drug Administration (FDA) approval dates can be seen in Table 74.1.

FIXATION

An essential feature of all stent grafts is a method of fixation to the surrounding aortic intima to inhibit distal migration from the intended seal zone after deployment, as systolic blood flow delivers constant force against the stent graft. In tortuous aortic anatomy, augmented vector forces increase the risk of component separation and migration of graft components. Aortic remodeling after endovascular aneurysm repair (EVAR) can also result in morphologic changes of the excluded aorta, resulting in loss of seal, stent graft migration, component separation, and limb kinking or thrombosis.

TABLE 74.1

Current Commercially Available FDA-Approved Infrarenal Aortic Stent Graft Devices

Device	Manufacturer	FDA Approval Date	Implants Worldwide (Approx.)
Excluder	Gore	2002	350,000
Zenith Flex	Cook	2003	200,000
Endurant	Medtronic	2010	400,000
AFX	Endologix	2011	83,000
Ovation	Trivascular	2011	15,000
Aorfix	Lombard	2013	N/A*
Treo	Terumo	2020	9000

*Updated implant number undisclosed by Lombard Medical.

FDA, Food and Drug Administration.

Positive Fixation, Column Support, and Friction

Multiple endograft features are designed to prevent graft migration and consequent complications. *Positive fixation* describes the use of metal hooks, barbs, anchors, or supplemental staples to attach the graft to the aortic wall and prevent migration. In endografts designed to straddle the aortic bifurcation with proximal extension of graft components, *columnar support* helps maintain the position of the cranial aspect of the device with buttressed support from the bifurcation component. The outward radial force of the stents themselves creates *friction* with the vessel wall that reduces the risk of migration. Increased risks of long-term migration in first generation devices without active fixation have led to near universal incorporation of active fixation in current endograft designs. Some devices have polyester fuzz or other prosthetic material that induces a fibrotic reaction in the aortic neck and aids in graft fixation, and several devices include a combination of these characteristics.

Infrarenal Versus Suprarenal Fixation

Infrarenal fixation describes active sealing at the proximal most aspect of the endograft in the infrarenal aortic neck. Endografts with suprarenal fixation employ a bare metal stent that is separated from the sealing component of the infrarenal portion of the stent graft, extending the fixation component into the pararenal and suprarenal aorta. The suprarenal aortic neck is typically more uniform and resistant to late dilation, and long-term fixation with this suprarenal fixation may be improved. If open conversion and complete graft explantation become necessary, removal of endografts with suprarenal fixation requires a comparatively more complex surgical approach, and a variety of techniques have been utilized in this situation.

SEALING

Currently approved endografts are designed to seal aortic aneurysms with ideal infrarenal aortic morphology, which includes a straight, cylindrical, 10 to 15 mm long neck without significant

thrombus or calcification. Seal zone adjuncts include anchoring screws or endoanchors, covered flares that expand beyond the nominal diameter of the main graft, polyester fuzz, sealing cuffs, and off-label stent utilization. The basic stent pattern of the proximal portion of the device impacts sealing and conformability, both critical factors for treating angulated or shorter necks.

ILIAC LIMBS

The unsupported limbs of first generation EVAR devices were often plagued by kinking and limb occlusion, which prompted frequent off-label use of additional stents within the originally unsupported limbs to maintain adequate patency. Late fabric erosion with subsequent type III endoleak and aneurysm enlargement or rupture is one complication of this approach that illustrates a late pitfall of off-label component use. Although most current, fully supported endograft limbs provide excellent long-term patency, there is sufficient space between stents or stent rings in some devices to allow potential limb kinking, compression, and occlusion in cases with challenging anatomy. Concomitant iliac arterial injury during EVAR, heavy circumferential distal aortic or iliac calcification, severe iliac tortuosity, and excessive graft limb oversizing are additional factors that increase the degree of difficulty and associated risk of limb occlusion with EVAR.

SIZING

Currently approved aortic stent grafts come in a wide range of aortic diameters, iliac limb diameters, and graft lengths that are labeled for varying anatomic configurations. The complexity of case planning varies with each system due to variability in respective indications for use (IFU), differences in sizing windows, techniques, tapering zones, and usable seal zones.

GRAFT MATERIAL

Widely used polyester or polytetrafluoroethylene (PTFE) graft material is similar to that used for open surgical repair. In contrast to surgical grafts that become incorporated in fibrous retroperitoneal tissue, stent grafts are suspended in aortic thrombus and may develop transudates or microfistulations that do not close. The graft material may abrade with constant wear against metallic stent components or may be subject to weave deformation by attachment sutures. Sutures themselves may wear or break, causing subsequent increased abrasion. Some stent grafts are sutured only at the ends of the stent, whereas others use a composite bonding process without sutures.

RADIOOPACITY

Endograft components are visible with widely available, high-quality fluoroscopy systems; however, accurate visualization with portable C-arms, particularly in obese patients, can be challenging. Respective delivery systems and endografts have a variety of radiopaque markers to facilitate rotational orientation, deployment, and gate cannulation. Such markers vary with each specific device, and not all are positioned in the same orientation with respect to the graft's fabric edge, which

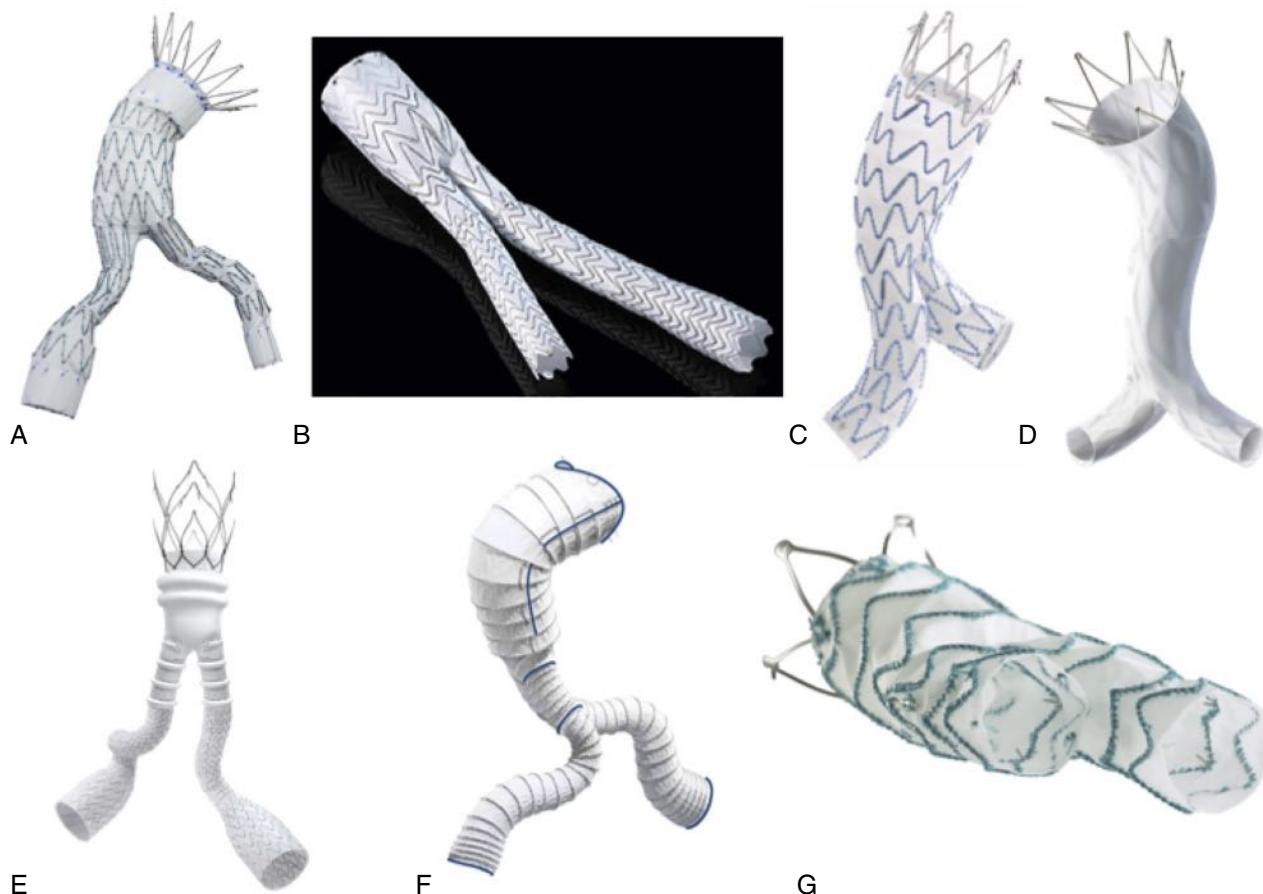


Figure 74.1 Commercially Available Endografts. (A) Cook Zenith Flex; (B) Gore Excluder; (C) Medtronic Endurant II; (D) Endologix AFX; (E) Trivascular Ovation; (F) Lombard Aorfix; (G) Terumo Treo.

is typically not radiopaque at commonly used magnifications. Some markers are circumferential, whereas others are positioned intermittently around the circumference of the device.

DEPLOYMENT PRECISION AND EASE OF USE

Deployment components vary in flexibility, trackability, valve function, outer diameter of the ipsilateral and contralateral sheaths, sheath exchange requirements, and deployment precision. The labeling, torque responsiveness, need for exchange-length wires, difficulty in cannulation of the contralateral gate, and other attributes all contribute to the relative complexity of the deployment sequence with each respective graft. Ease of deployment is thus only one aspect of a device's performance.

GRAFT SELECTION AND PRIMARY DEVICE CHARACTERISTICS

Detailed knowledge of sizing, deployment techniques, failure modes, expected outcomes, and reintervention techniques is essential to provide a durable endovascular result. There are a few anatomic situations in which one particular device may

be preferred, although even in these situations a surgeon with mastery of a single specific device could probably make that device work for challenging cases (Fig. 74.1). Difficult iliac anatomy can often be treated with smaller systems or those featuring deployment systems with a higher degree of flexibility and trackability. Short lengths from the lower renal artery to the aortic bifurcation can be better treated with some respective devices. Severely angulated, short aortic necks are not well treated with any approved system except the Aorfix, but more flexible investigational devices (Conformable Excluder, W.L. Gore) and off-label aortic stents can potentially overcome challenging proximal necks. Less angulated short necks may be addressed with branched endografts, fenestrated devices or parallel graft adjuncts (see Ch. 82, Fenestrated and Branched Endograft Treatment of Juxtarenal, Paravisceral, Thoracoabdominal, and Aortic Arch Aneurysms: Device Selection and Technical Considerations).

Endograft Configurations

Bifurcated devices are currently utilized in greater than 95% of EVAR in the treatment of infrarenal aortic aneurysms. These are either modular (Endurant, Excluder, Ovation, Zenith, Aorfix, Treo) or unibody (AFX [Endologix]). While there are no commercially available devices for isolated saccular aneurysms

BOX 74.1**Relative Indications for Aorto-Uni-Iliac Endograft Configuration**

- Very small (<15 mm) terminal aorta (which would not accommodate a bifurcated device)
- Severe unilateral iliac occlusive disease
- Secondary treatment of migration of a short-body endograft

or penetrating aortic ulcers of the infrarenal aorta, off-label use of “stacked” aortic cuffs, larger iliac components, or small diameter thoracic extensions can be utilized for this purpose when sufficient proximal and distal landing zones are present. Aorto-uni-iliac endografts (ReNu, Endurant) can be utilized in conjunction with a contralateral iliac occlusion device and a femoral–femoral bypass. The relative indications for use of this configuration are listed in **Box 74.1**. Branched and fenestrated endografts and chimney or snorkel grafts can be utilized in juxta- or pararenal aneurysms with inadequate normal aorta to achieve a durable proximal seal.

Preoperative Sizing and Planning

Precise sizing and meticulous preoperative planning are essential for successful initial and long-term outcome after EVAR.

PREOPERATIVE IMAGING

Computed Tomography Arteriography

Computed tomography arteriography (CTA) is the cornerstone of preoperative imaging for EVAR (see **Ch. 29**, Computed Tomography). The maximum recommended slice diameter is 2.5 mm for standard devices, while sizing for fenestrated or branched devices requires finer cuts. Intravenous contrast should be routinely used unless the patient has severe renal insufficiency. The axial, coronal, sagittal, and three-dimensional (3D) reconstructions (**Fig. 74.2A**) should all be reviewed. Post-processing software allows further image interrogation by generating centerline reconstructions, which aid in precise length, diameter, and angle measurements. Access to dedicated software that allows sophisticated post-processing, manipulation, and analysis of images is recommended. Standard digital subtraction arteriography (DSA) has little utility in the standard preoperative evaluation for EVAR and should not be routinely employed.

Patients with significant renal insufficiency present challenges in preoperative imaging prior to EVAR. Frequently, noncontrast computed tomography (CT) scanning provides enough basic anatomic information to proceed with standard, infrarenal EVAR, especially in emergent settings. Diameter and length measurements can be made from such a study, and if the anatomy appears uncomplicated and there is no clinical suspicion of associated occlusive disease, it may be reasonable to proceed. Potentially important anatomic information can be missed, however, including: (1) the presence of laminated thrombus in the aortic neck; (2) patency of important side branches such as the hypogastric arteries; and (3) potential

occlusive disease in the common or external iliac arteries. Significant calcification, particularly the common and external iliac arteries, should make the operator suspicious that associated prohibitive occlusive disease may be present. In this setting, the femoral pulse examination is essential.

Alternative Imaging

In the patient with severe renal insufficiency who needs further delineation of pertinent anatomy prior to EVAR, intravascular ultrasound (IVUS) can be used to size the aortic and iliac seal zones, evaluate for potential aortic neck eccentric thrombus, and interrogate the external iliac arteries for potential occlusive disease. Direct angiographic imaging can be obtained using carbon dioxide (CO₂) as the contrast agent with relatively good visualization, especially with modern imaging systems. An additional option is to place a catheter for direct aortic injection of contrast for CTA rather than intravenous dye. Our preferred approach involves right transradial access and placement of an angiographic catheter in the proximal aortic arch. On-table CTA or transport to a radiology/CT suite with subsequent CTA is performed. We prefer to use 30 cc of contrast mixed with 70 cc of saline, injected at 4 cc/second with an 8 to 10 second delay. This can provide excellent imaging with a 75% reduction in contrast dye use.

ENDOGRAFT SIZING

Aortic Neck Diameter

Measurement of the aortic neck diameter should be taken proximally at the level of the lower renal artery and extend 15 mm caudally in 5 mm increments. These measurements should be made from the *minor axis*, or shortest transverse diameter, of axial cuts, or ideally from reformatted slices that allow a plane perpendicular to the centerline. The key here is not to overestimate diameter based on oblique CTA cuts of the tortuous aortic neck utilizing the major axis. Using electronic calipers, these measurements are generally made from adventitia to adventitia to size the aortic neck for most devices. Intima-to-intima measurements were used in the US pivotal studies of the Excluder endograft (W.L. Gore) and are recommended for use with this device.

Endografts should be oversized 10% to 20% in comparison to the aortic neck. In practical terms, this usually translates into an endograft diameter that is 3 to 4 mm larger than the aortic neck. Currently, EVAR devices range from diameters of 18 to 36 mm and can accommodate aortic diameters of 16 to 32 mm (**Table 74.2**).

If full apposition of the endograft to the aortic wall is not achieved, the risk of a type IA endoleak is substantial. The risks of excessive oversizing are less obvious, however. Bench testing has demonstrated that oversizing greater than 20% can create pleats in the fabric (**Fig. 74.3**). This pleating of the fabric decreases flush apposition of fabric to aortic intima, jeopardizes proximal seal, and contributes to an increased risk of a type IA endoleak and decreased fixation regardless of the endograft used.



Figure 74.2 (A) Computed tomographic angiography reconstruction of a 6.3-cm abdominal aortic aneurysm (AAA). (B) Angiogram demonstrating the same AAA. (C) Immediate post-endovascular aneurysm repair angiogram demonstrating exclusion of the AAA without endoleak.

TABLE 74.2 Notable Characteristics of Current Commercially Available Infrarenal Aortic Stent Graft Devices, Including their Graft and Stent Material Design, the Sizes of Aneurysms Appropriate for Treatment with Each Respective Device, the Delivery System Profile, Proximal Fixation Level, and Other Unique Features

Device	Graft Material	Stent Material	Treatable Aortic Neck Diameter (mm)	Minimum Aortic Neck Length (mm)	Maximum Treatable Aortic Neck Angle	Treatable Iliac Artery Range (mm)	OD Delivery Sheath Main Body/Limb (Fr)	Proximal Fixation	Unique Features
Excluder	ePTFE	Nitinol	19–32	15	<60°	8–25	16–18/12–15	Infrarenal	Repositionable delivery system allows multiple attempts to achieve accurate proximal landing
Zenith Flex	Polyester	Stainless Steel	18–32	15	<60°	7.5–20	18–22/14–16	Suprarenal	Shortened Z-stents of main body and limbs inhibit migration and kinking
Endurant II/IIs	Polyester	Nitinol	19–32	10	<60°	8–25	18–20/14–16	Suprarenal	Three-piece system allows flexible <i>in situ</i> length sizing, approved to treat 10 mm proximal neck length
AFX	ePTFE	Cobalt Chromium Alloy	18–32	15	<60°	10–23	19/9	Infrarenal or Suprarenal	Unibody component provides anatomic fixation on aortic bifurcation
Ovation	ePTFE	Nitinol	16–30	10	<60°	8–25	14–15/12–15	Suprarenal	Smallest delivery sheath profile (14F OD), proximal sealing ring expanded with polymer <i>in vivo</i>
Aorfix	Polyester	Nitinol	19–29	15	<90°	9–19	22/20	Infrarenal	Approval to treat aortic necks with 60°–90° angulation
Treo	Polyester	Nitinol	17–32	15	<60°	8–20	18–19/12–14	Suprarenal and Infrarenal	Two levels of active proximal fixation; limb locking system reduces risk of modular disconnection

ePTFE, expanded polytetrafluoroethylene.

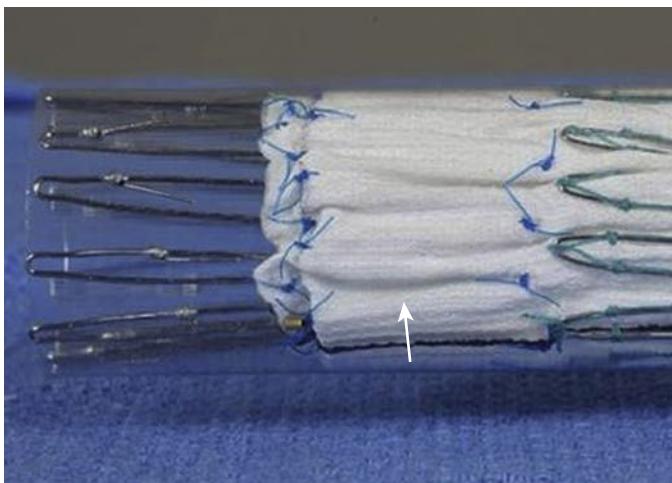


Figure 74.3 Oversizing causes pleating of the fabric (arrow). This is a 28-mm Zenith endograft in a 22-mm tube (27% oversize). Such pleating increases the risk of type I endoleak and migration.

Sizing the Conical Aortic Neck

Patients with conical necks, meaning those with more than a 10% change (2 to 3 mm) in neck diameter over the first 15 mm length of aortic neck length, pose an interesting sizing conundrum. In a patient with an aortic neck diameter of 20 mm at the renal arteries that dilates to 24 mm at a position 15 mm caudal, sizing to the larger diameter would suggest the use of a 28 mm endograft. However, this would correspond to a proximal oversizing of 40%. Conversely, sizing to the smaller diameter, such as a 24 mm endograft in a 20 mm neck, would result in inadequate oversizing in a larger area caudally. In these situations, it is prudent to “split the difference,” so as to give at least a minimum 10% oversizing in the larger segment and a less than 30% oversizing in the smaller segment. If the degree of size mismatch does not allow such sizing, for example in a situation where there is more than a 3 to 4 mm conical change in first 15 mm of neck, EVAR is not advisable. In either circumstance, extension into the pararenal segment of the aorta with fenestrated or parallel endograft techniques may offer a more durable solution.

Length Measurements

Accurate length measurement between proximal and distal landing zones is critical in selecting the correct endograft components. For EVAR, utilization of axial, coronal and/or sagittal CTA reconstructions is accurate when calculating the distance between the lower renal artery and the aortic bifurcation in the absence of significant tortuosity or aortic neck angulation. These measurements alone will underestimate the length between the aortic bifurcation and the hypogastric arteries, especially with tortuous vessels. Conversely, length measurements based on centerline calculations with EVAR will occasionally overestimate the true length needed. Knowledge of anatomic patterns and respective graft component behavior aids in accurate preoperative planning.



Figure 74.4 “Balleting” or Intentional Crossing of Iliac Limbs. This technique can facilitate cannulation of the contralateral gate of short-bodied modular endografts. A longer contralateral iliac limb is frequently required.

Situations that typically require longer iliac limbs than the measurements suggest include the presence of extreme iliac tortuosity, cases that require crossing or “balleting” of the iliac limbs (Endurant and Excluder, Fig. 74.4), and when extension of the limbs to the external iliac arteries is necessary. In these anatomic circumstances, it is wise to choose a longer length if in doubt.

Modular devices with variable body lengths, such as the Cook Zenith system, give additional flexibility in sizing by allowing adjustment of the amount of overlap between the components. With this device, the contralateral iliac gate is ideally positioned 1 to 2 cm from the aortic bifurcation. Unlike the iliac components, when there is doubt about the correct main body length, the shorter length should generally be chosen. Other scenarios that would call for a shorter body length include patients with a narrow (<20 mm) distal aortic neck or those with an eccentric calcific “reef” in the terminal aorta. In these instances, after opening the ipsilateral limb, there may be inadequate room for the contralateral gate to open, making cannulation difficult. Of note, the Medtronic Endurant IIIs, approved by the FDA in 2014, aim to address and simplify the main body and limb length issues. This stent graft features the shortest available ipsilateral and contralateral main body covered length at 103 and 80 mm, respectively. All main body limb diameters are fixed, allowing any limb to be used on either side. Limb length can therefore be determined during the procedure, offering a potential advantage in emergent cases.

Iliac Diameters

Limbs for the iliac arteries should be sized 10% to 20% greater than their respective minor axis diameter. For nonectatic iliac arteries, this generally translates into an iliac limb diameter 1 to 3 mm larger than the native vessel. Particular care should be made to correctly size the iliac limb if extension to the external iliac is required. Excessive oversizing in this scenario may increase the risk of limb kinking and thrombosis. When extending to the external iliac artery, the limb should ideally land proximal to or greater than 15 to 20 mm distal to points of major angulation in order to avoid kinking and possible limb thrombosis. At least 2 to 3 cm length of distal seal is recommended in patients with large or tortuous common iliac aneurysms that may undergo significant conformational changes with aneurysmal degeneration. In patients with large common iliac aneurysms (>25 mm), branched iliac endograft devices should be considered.

PATIENT SELECTION

Proper patient selection for EVAR is dependent on detailed preoperative evaluation of each respective patient's anatomy. The major anatomic factor in predicting success with EVAR is the suitability of the infrarenal aortic neck, including the length, diameter, angulation and morphology. The IFU for most current devices suggest a minimum neck length of 10 to 15 mm and angulation of less than 60 degrees. The Endurant device (Medtronic) has an IFU approved neck length of 4 mm to 10 mm when adjunctive endoanchors are also employed. An exception to the limitations on neck angulation is found with the Aorfix device (Lombard), which is FDA-approved for aortic neck angles ≤90 degrees. Considering proper oversizing and available endograft sizes, aortic neck diameters up to 32 mm can be accommodated by currently approved devices.

The ideal native anatomic configuration is a parallel aortic neck without eccentric laminated thrombus or heavy calcification. Patients with irregularly shaped necks have a greater risk of inadequate seal and subsequent endoleak. In addition to patients with conical and reverse conical necks, the occasional patient will have a localized posterior bulge in the neck, the so-called double-bubble, which can compromise the seal zone.

While a patient with a single adverse aortic anatomic variable can frequently be treated effectively with standard infrarenal EVAR, those patients who have aortic necks with multiple compromising anatomic features are more problematic. Although highly angulated necks are associated with inferior outcomes, if the neck length is greater than 2 cm and the morphology uniform, the patient may be a reasonable EVAR candidate. Patients with neck lengths of 10 to 15 mm can frequently attain a good initial outcome in the absence of other anatomic compromise. However, the risk of late neck degeneration and a subsequent type IA endoleak may be increased, particularly in the setting of a larger aortic neck diameter or significant angulation. All devices will have compromised outcomes if the anatomic constraints are profoundly exceeded

and cases are performed outside respective IFU. Patients with aortic necks less than 10 mm in length should be considered for open surgical repair, fenestrated EVAR, or EVAR with parallel grafts.

ANESTHESIA, ACCESS, AND IMAGING

Anesthesia

The choice of anesthetic technique can be tailored to the patient's comorbidities and body habitus. In all situations, it is ideal to control the patient's respirations, either by vocal instruction or by control with the ventilator. Although general endotracheal anesthesia is common, the use of local anesthetic infiltration and intravenous sedation is possible and may be preferred in some clinical scenarios such as aneurysm rupture. When utilizing open surgical exposure for vascular access, a regional (spinal or epidural) or general anesthetic is favored by most operators. In a patient who may need an iliofemoral conduit, general anesthesia is clearly the appropriate choice.

Vascular Access

Access to the femoral vessels can be achieved in an open surgical or percutaneous fashion.

Percutaneous Access

The popularity of percutaneous access for EVAR and thoracic endovascular aortic repair (TEVAR) has increased markedly over the last 10 years (see Ch. 75, Aortoiliac Aneurysms: Endovascular Treatment). Box 74.2 lists the relative contraindications for this procedure.

Open Surgical Access

With open access, either a vertical or oblique skin incision can be utilized. The advantages of a traditional vertical incision include the ease of gaining additional exposure of the iliac and femoral vessels. Postoperative wound problems can be minimized by keeping the incision above the femoral crease, which is possible in most patients. However, an oblique skin exposure is favored by many operators because wound problems are generally less frequent with this exposure. This technique of open exposure may be particularly useful in the morbidly obese patient. If the angle into the femoral vessel is too acute, a small counter incision can be made inferior to the skin incision to facilitate sheath insertion.

BOX 74.2

Relative Contraindications to Percutaneous Access for Endovascular Aneurysm Repair

- Severely scarred groin
- High femoral bifurcation
- Need for frequent introducer sheath changes
- Significant proximal iliac occlusive disease
- Small iliofemoral arteries
- Anterior calcific femoral disease

Iliac Occlusive Disease

The iliac vessels should be carefully studied preoperatively with CTA so any potential difficulties in access can be anticipated. Focal iliac occlusive disease can be treated with balloon angioplasty immediately prior to endograft insertion. If possible, bare metal stents should not be placed initially, however, as the large sheaths required for endograft placement would need to be advanced through them, increasing the possibility of stent migration or arterial injury. If an iliac lesion warrants stent placement and is not covered by the distal extent of the endograft, the additional stent can be placed at the completion of the EVAR.

Hydrophilic dilators can be effective in dilating longer segments of occlusive disease, and may also alert the operator to potential issues with device tracking. These dilators should only be placed over very stiff wires to avoid wire kinking and arterial trauma. Maintenance of wire access across a diseased, narrowed, or angulated segment during device and sheath removal is essential to allow potential endovascular salvage of life-threatening arterial injury. Confirmatory angiography after device or sheath removal is recommended.

There are other potential approaches to obtaining access in the setting of small iliac arteries. It is possible to create an “internal endoconduit” by placing a covered stent in the external iliac vessel, which is then aggressively angioplastied to the required diameter of 7 to 9 mm. The covered stent will protect against the extensive dissection and/or free rupture of the native vessel which can be caused by aggressive angioplasty. Clearly, there must be a sufficient proximal and distal seal zone for the covered stent. From a practical point of view, however, such ideal landing zones are not routinely present. As with other anatomic variations, prudent patient selection is critical. While these techniques have been anecdotally reported with successful outcomes, larger series are needed to establish the safety of these adjunct access procedures prior to broader utilization.

Iliac Conduit Placement

The potential use of a surgically placed conduit should be in the “toolbox” of all operators performing endovascular aortic aneurysm repair. While the need for a surgical conduit is unusual with current, lower profile devices, patients with diffusely calcified and very small external iliac arteries may require an iliac artery conduit for appropriate EVAR access. Careful review of the preoperative CTA or direct intraoperative visual inspection of the common femoral and terminal external iliac artery with open exposure can aid decision making regarding placement of an external or common iliac artery conduit in equivocal cases.

An iliac conduit is performed through a right or left low retroperitoneal incision. We favor a standard end-to-side anastomosis at the level of the distal common iliac artery. A 10-mm prosthetic conduit (Dacron or PTFE) will accommodate the largest required sheath. The conduit should be tunneled under the inguinal ligament through a femoral counter incision. The distal end of the conduit is then clamped to the drapes and

accessed in the usual fashion. After the EVAR is completed, most operators elect to anastomose the distal end of the conduit to the common femoral artery in an end-to-side fashion. Alternately, the conduit can be removed, leaving a small “stump” on the common iliac artery that is oversewn in layers with prolene suture.

Imaging

Equipment

High-quality fluoroscopy and angiographic equipment is essential to successful EVAR. A contemporary fixed-imaging unit as part of a “hybrid” operating room (OR) is increasingly utilized in many institutions. The performance of fenestrated or branched EVAR mandates this level of imaging.

Gantry Positioning

The precision of proximal endograft deployment with EVAR is considerably enhanced by adjusting the gantry of the fluoroscope to be perpendicular to the axis of the aortic neck. A large percentage of infrarenal aortic necks have a modest amount of anterior angulation, which should be adjusted for by adding an appropriate amount of cranial tilt to the fluoroscopy unit. The angulation required can be estimated by review of the preoperative CTA. The majority of infrarenal aortic necks have 5 to 15 degrees of cranial angulation, but this increases to as much as 30 to 40 degrees in highly angulated necks. Adjusting the left/right obliquity is also helpful in precisely locating the origin of the lower renal artery. An appropriate amount of left anterior oblique (LAO) will give the proper orientation to the renal arteries in most cases. Frequently, this translates to approximately 10 to 20 degrees of LAO. These adjustments are particularly important in patients with short or angulated aortic necks.

EVAR DEPLOYMENT

Wire Placement

After bilateral open or percutaneous femoral access is achieved, a floppy 0.035 J-wire should be placed in the proximal thoracic aorta and catheter-exchanged for a stiff guide wire (Lunderquist, Amplatz Super Stiff, or Meier). Care should be taken not to cross the aortic arch with careless or imprecise wire manipulation, as this amount of proximal wire access is unnecessary for standard EVAR. In addition, failure to routinely visualize the location of these stiff wires in the thoracic aorta increases the risk of inadvertent cannulation of an arch vessel, aortic or branch vessel trauma, plaque disruption and stroke. After the stiff wire is placed, the distal end of the wire should be marked clearly on the operative drape so that a stable position is ensured throughout the procedure. Through the contralateral femoral access, a pigtail catheter is then placed just above the renal arteries, which is usually between the L1 and L2 vertebral bodies. If there is concern about iliac occlusive disease, a hand-injection retrograde angiogram from the femoral access or power angiogram at the

aortic bifurcation should be performed and the occlusive disease treated as detailed previously. If there is uncertainty regarding the correct main body length to select, an aortogram with a 1-cm graded marker catheter can be performed to confirm the distance between the lowest renal artery and the ipsilateral hypogastric artery origin. Otherwise, arteriography should not be performed until the undeployed main component is advanced into the pararenal aorta. Particularly in patients with significant iliac or aortic neck tortuosity, placement of the undeployed endograft in the pararenal aorta may alter the relative position of the renal arteries as the aorta accommodates to the hardware over a stiff wire, making pre-insertion arteriography inaccurate.

Delivery of the Main Device

To ensure proper main body and contralateral gait orientation, the endograft is commonly examined and rotated *ex vivo* under fluoroscopy to acclimate the operator with graft markers. The contralateral gate or limb of the main device should be appropriately oriented prior to insertion. This orientation should be confirmed as the device is advanced and during any rotational adjustments to eliminate friction-associated iliac injury. In addition, attempts to rotate the device statically may not translate to the entire device, particularly in tortuous or small iliac arteries. Rotation of the graft is safer as the graft is advanced or withdrawn longitudinally over a stiff wire, which reduces the acquired torque in the device prior to deployment. Failure to follow these principles can cause a relative twist and misdeployment of the endograft or injury to the aorta or iliac arteries.

If the endograft is not advancing smoothly, the first step is to change to an extra stiff guide wire such as a Lunderquist. Using this wire in combination with the current generation of trackable, lower profile devices, it is uncommon to fail to deliver the endograft to the desired location. Unexpected iliac occlusive disease may contribute to the inability to advance the endograft, and confirmation of iliac anatomy is suggested in these circumstances. If these maneuvers are not successful, use of a “buddy wire” can be considered. A second extra stiff wire can be placed through the iliac helping to further straighten the tortuous segment.

Proximal Endograft Deployment

After the main device is positioned in the proximal infrarenal aorta and the contralateral gate/limb position is satisfactory, the gantry position of the fluoroscopy unit is adjusted with the appropriate amount of cranial and oblique angulation as detailed previously. A magnified view should be utilized, with the lower renal artery in the center of the screen and proximal graft marker position verified to minimize parallax errors. Using a power contrast injector, a short-burst injection using a high rate to small volume ratio will allow good visualization of the renal arteries with a small amount of contrast. A 20-cc/s injection rate with a total of 7 to 15 cc of contrast is

usually sufficient, depending on the equipment and patient’s body habitus. It is essential to visualize both renal arteries. If the lower renal artery is not close to the center of the image, the table or fluoroscopy unit should be adjusted and the image repeated.

With devices that are designed for a slow, step-wise deployment (Endurant, Excluder, Zenith), initial deployment should begin approximately 1 cm above the intended proximal position. The endograft should then slowly be pulled caudally until the proximal extent of the device fabric sits immediately below the lower renal artery. After the initial proximal deployment, the gantry position may be adjusted further to ensure a perfectly perpendicular alignment with the aortic neck. The anterior and posterior aspects of the endograft should appear superimposed if the gantry position is parallel to the aortic neck. If they do not superimpose, the degree of cranial tilt can be adjusted, and the arteriogram repeated. The goal is to place the endograft within 2 mm of the caudal aspect of the lower renal artery orifice. Maximal overlap of the graft within the aortic neck will increase the seal zone, reducing the likelihood of a type IA endoleak and late migration.

After the proximal landing zone of the endograft is established, deployment of the endograft continues until the contralateral gate is freed. Many operators will then recheck the position of the endograft relative to the renal arteries at this time. Deployment of a bare suprarenal stent is now generally performed with devices that have this feature. After deployment of the bare suprarenal stent, no further movement of the main device is possible. An exception to this principle is found with the C3 Excluder endograft (W.L. Gore), which has no suprarenal stent and can be reconstrained and repositioned twice if the initial position is not ideal.

Accessory Renal Artery Management

In patients with normal renal function, it is generally safe to cover such an accessory renal artery with the endograft. Embolization of the vessel prior to coverage is not generally performed. Patients with significantly impaired renal function pose a more difficult situation. Further reduction in a patient’s renal function by coverage of an accessory renal artery is far from ideal. However, alternate approaches, including a fenestrated endograft or open surgical repair, have markedly elevated morbidity and mortality in the patient with significant renal insufficiency.

Contralateral Gate Cannulation

For modular devices, the next step is cannulation of the contralateral iliac gate. This step is obviated if a unibody device such as the AFX Endologix is utilized. Retrograde cannulation of the gate should be possible in greater than 95% of cases. Several technical adjuncts will facilitate this maneuver. Perhaps the most important step is planning appropriate gate orientation for favorable cannulation prior to endograft deployment based on aortoiliac angles as visualized on preoperative CTA

reconstructions. Deployment of the gate in a slightly anterolateral position will usually complement the angle of the contralateral common iliac artery at the aortic bifurcation and allow straightforward access.

With short body devices such as the Endurant and Excluder, it is sometimes easier to rotate the contralateral gate ipsilateral to the main limb, thus crossing or “balleting” the limbs. This maneuver is particularly helpful if the angle of a respective proximal common iliac artery is splayed laterally, there is a large aortic sac, or the anterior–posterior diameter of the aortic bifurcation is significantly less than the left–right diameter. This decision can be made intraoperatively after bilateral wire access is obtained – if the wires from each respective femoral artery access sheath cross with heavy angulation at the aortic bifurcation, gate cannulation is usually more favorable with limb crossing. This maneuver may also lessen the risk of limb kinking and thrombosis postoperatively. With a long body device such as Zenith, the contralateral gate should be within 1 to 2 cm of the iliac artery, and thus crossing the iliac limbs is inadvisable. In cases where one common iliac has significantly more lateral angulation than the other, placing the main device in the *more* tortuous side will facilitate the contralateral gate cannulation.

Several maneuvers will speed cannulation of the gate:

1. After retrieving the pigtail or other angiographic catheter, avoid pulling the wire back into the iliac artery. If there is severe tortuosity or a narrow distal aortic neck it can occasionally be challenging to regain access to the aneurysm sac. Sheath support across the angulation is sometimes helpful to maintain adequate access.
2. Choose a steerable wire such as an angled Glidewire and an appropriately angled catheter for more challenging cannulation if attempts with standard catheter fail, such as a DAV/Bernstein, C2, or Van Schie 5.
3. Position the contralateral sheath (8 Fr × 25 cm or similar) at the bifurcation just proximal to the respective common iliac orifice for increased catheter support.
4. Oblique the fluoroscopic views to maximally “open” the gate. Using both the catheter and wire to steer, attempt to place the wire into the gate. If the wire first appears to be in the appropriate orientation with the gate but ultimately is not, then the operator knows that the wire is either anterior or posterior. In such a case, by changing the obliquity of the fluoroscopic image with the wire in place, it will then become clear whether anterior or posterior deflection is needed. If the wire is seen to transiently engage the gate fabric but not cannulate successfully, subtle, controlled movements of the catheter tip to slightly change the angle of the wire should follow until the gate is accessed. Occasionally a different-shaped catheter will facilitate cannulation.
5. Use of a steerable, deflectable tip support sheath, now available from several companies in various lengths and diameters, will facilitate challenging gate cannulation when other techniques fail. In addition, a steerable sheath can also be used in cases of extreme difficulty to advance a wire over the flow divider across the contralateral gate in retrograde fashion after the ipsilateral limb is deployed. This wire can

then be snared from the contralateral femoral access sheath, externalized, and a catheter advanced over this wire into the main body. The indwelling reversed wire is then maneuvered into the thoracic aorta proximally, a catheter advanced, and the reversed wire removed and replaced.

Confirmation of proper gate cannulation is essential and can be done with angiography or by spinning the pigtail catheter in the area of the aortic neck. Some operators utilize a 12- or 14-mm balloon inflated in the gate while the gantry is rotated to confirm appropriate positioning. Failure to routinely confirm the wire position can result in deployment of the limb outside of the gate, requiring complex endovascular salvage or open conversion.

Rarely, the contralateral gate cannot be cannulated in a retrograde fashion despite utilization of the above maneuvers. Failure to cannulate is usually the result of the gate not opening adequately because of a small (<20 mm) distal aortic neck, an eccentric calcific distal aortic “reef” (long body devices) or extreme tortuosity (short body devices). In such situations, the gate can be cannulated with the steerable sheath technique described above or in antegrade fashion via brachial or radial access. Once a wire is negotiated through the gate in an antegrade fashion from above, it is snared in the respective iliac artery and withdrawn through the corresponding femoral access sheath. Then, over a catheter, the wire can be exchanged for typical retrograde deployment. An alternate method of antegrade cannulation is to approach the gate by going “up-and-over” the flow divider with an appropriately shaped catheter, such as a Simmons 1, or SOS. However, our experience has been that the anatomic issues that made retrograde cannulation impossible also make this approach problematic and frequently unsuccessful.

If all attempts at gate cannulation are unsuccessful, the final bailout technique is conversion of the bifurcated device into an aorto-uni-iliac configuration. This maneuver should be needed in extremely rare circumstances. With the Zenith device, this is accomplished with a specifically made converter endograft that is deployed within the main body, excluding the contralateral gate. A similar configuration can be accomplished with other modular devices by either the use of stacked aortic/iliac cuffs, an aortounibody graft, or deploying a second main body device within the existing main body device with the contralateral gate oriented 180 degrees opposite the existing contralateral gate. After conversion to such a configuration, an occluder must be placed in the contralateral common iliac artery, and contralateral limb perfusion re-established with a femoral–femoral bypass.

Limb Deployment

Once contralateral gate cannulation is confirmed, the distal landing zone in the iliac artery is established with a retrograde arteriogram shot through the previously placed contralateral sheath. The image intensifier should be positioned with complimentary, contralateral obliquity to best visualize the take-off of the respective hypogastric artery; this is typically 20 degrees LAO for the right iliac artery and RAO for the left

iliac artery. Caudal angulation of 5 to 10 degrees is often beneficial. Appropriate angulation should be determined during evaluation of the preoperative images and reconstructions. A marker catheter placed over the wire is recommended to accurately determine desired coverage length. Ideally, more iliac overlap is preferred over less. The absolute minimum overlap into the iliac artery (common or external) is 2 cm in a patient with nontortuous vessels and a less than 6 cm AAA. Patients with larger AAA and/or tortuous anatomy should receive longer iliac coverage, if possible. These patients may have greater conformational changes as the AAA sac thromboses and shrinks in the postoperative period, putting increased axial strain on the device components. This scenario can produce migration of the iliac limb with a subsequent type IB endoleak, graft kinking, and limb thrombosis, or component separation. The same principle applies to recommended overlap if multiple limbs are required.

In patients with extremely tortuous iliac arteries, landing the distal end of the device within 1 cm of an acute angle should be avoided. Any kinking or stenosis of the endograft limbs should be treated aggressively with angioplasty, usually with a compliant balloon (Coda, Reliant). If any significant residual stenosis persists, one should consider the placement of a self-expanding stent within the endograft. Occasionally a narrow distal aortic neck compresses both iliac limbs. Use of simultaneous, conventional, noncompliant angioplasty balloons will usually resolve this issue. If there is significant recoil, the use of bilateral balloon-expandable or self-expanding stents in this location should be considered.

A compliant molding balloon (Coda, Reliant, P50) may be utilized at the aortic neck, iliac gates, and distal iliac limb to optimize seal (Fig. 74.5). It is important not to overinflate this balloon outside the proximal or distal aspect of the endograft. Rupture of the pararenal aorta and iliac arteries has been reported after overly aggressive inflation of these compliant balloons.

Completion Arteriography

After endograft placement is completed, a completion arteriogram is performed through an angiographic catheter placed in the pararenal aorta (see Fig. 74.2C). Use of a power injector with an injection rate of 15 cc/s and a total contrast volume of 30 cc is recommended. Because the large sheath size of devices will frequently reduce iliac flow, these should be routinely aspirated with 20 cc syringes during the injection. Image acquisition should continue for a minimum of 5 sec after the contrast in the iliac arteries has washed out to allow visualization of late type II endoleaks (Box 74.3). The completion arteriogram should be systematically and carefully studied in the following manner:

1. Confirm patency of the renal and hypogastric arteries.
2. Assess the precision of the proximal and distal endograft landing zone apposition. The proximal extent of the endograft should be ideally within 2–3 mm of the lowest renal artery. If this distance is considerably greater, and the residual seal zone is less than 10 to 15 mm,

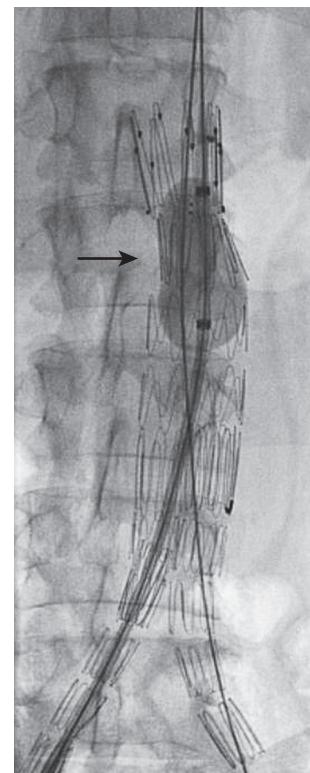


Figure 74.5 Use of a compliant molding balloon (Coda) on the aortic neck to optimize the seal (arrow).

BOX 74.3

Treatment Options for Type II Endoleak

Coil or glue embolization

Transarterial

- Via branch vessel
- Behind graft limb

Translumbar

Transcaval

Laparoscopic IMA clipping

Open surgical

- Ligation of lumbars or IMA
- Open conversion

IMA, inferior mesenteric artery.

placement of an aortic cuff should be considered, even in the absence of a type IA endoleak. Likewise, iliac extensions should be placed if there is inadequate overlap with the iliac artery or if a type IB endoleak persists after balloon dilation.

3. Evaluate for unsuspected occlusive external iliac disease. If significant tortuosity in the iliac vessels exists, the stiff wires in place for the endograft deployment should be exchanged for flexible wires prior to the final arteriogram. Stiff wires will occasionally cause the tortuous iliac artery to in-fold or “accordion,” giving the radiographic appearance of severe stenosis (Fig. 74.6). These pseudo-lesions will disappear with removal of the stiff wire. True occlusive lesions should be treated accordingly.
4. Assess for endoleak.

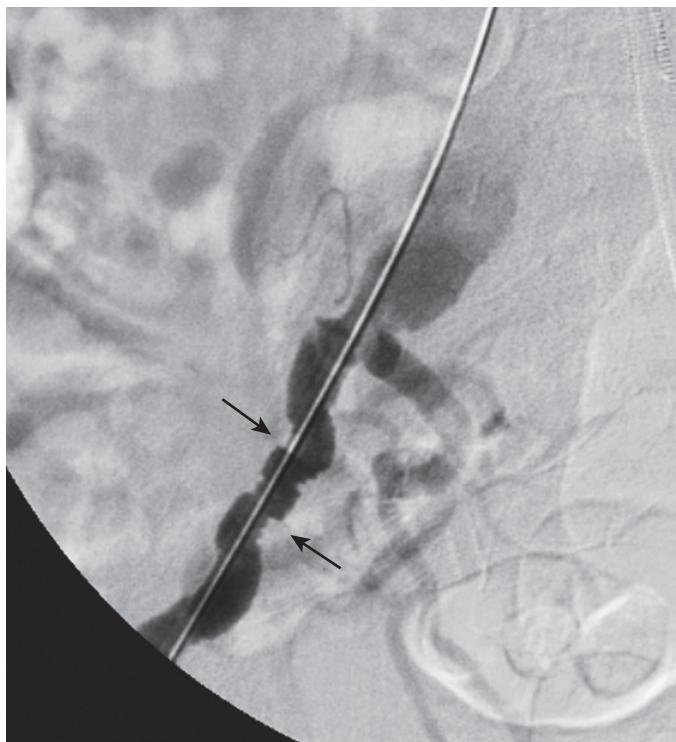


Figure 74.6 “Pseudolesion” of the external iliac artery (arrows). This is caused by placement of a super-stiff wire in a tortuous vessel, causing it to “accordion” around the wire. Removal of the stiff wire corrects the stenosis without adjunctive measures.

EVAR TROUBLESHOOTING

Despite optimal planning and conduct of an EVAR procedure the vascular surgeon may be faced with intraoperative and/or postoperative issues that will require attention and treatment (see Ch. 75, Aortoiliac Aneurysms: Endovascular Treatment).

SELECTED KEY REFERENCES

Baxter RD, Hansen SK, Gable CE, et al. Outcomes of open versus percutaneous access for patients enrolled in the GREAT Registry. *Ann Vasc Surg.* 2021;70:370–377.

Excellent overview of percutaneous access for EVAR.

Howard DPJ, Marron CD, Sides E, et al. Editor’s Choice – Influence of Proximal Aortic Neck Diameter on Durability of Aneurysm Sealing and Overall Survival in Patients Undergoing Endovascular Aneurysm Repair. Real World Data from the Gore Global Registry for Endovascular Aortic Treatment (GREAT). *Eur J Vasc Endovasc Surg.* 2018;56(2):189–199.

A total of 3166 consecutive patients from 78 global centers undergoing EVAR for infrarenal AAA between 2011 and 2017 were analyzed.

Muhs BE, Jordan W, Ouriel K, et al. Matched cohort comparison of endovascular abdominal aortic aneurysm repair with and without EndoAnchors. *J Vasc Surg.* 2018;67:1699–1707.

Cohort-matched analysis of patients treated with an endovascular repair and their outcomes related to residual aneurysm sac behavior at 2 years showing a significant difference in the residual aneurysm sac behavior – patients with EndoAnchor implants had a significant reduction in aneurysm sac size.

Schermerhorn ML, Buck DB, O’Malley AJ, et al. Long-term outcomes of abdominal aortic aneurysm in the medicare population. *N Engl J Med.* 2015;373(4):328–338.

Large population-based study concluding EVAR, as compared with open repair, was associated with an early survival advantage that gradually decreased over time and that the rate of late rupture was significantly higher after endovascular repair than after open repair.

Singh M, Fairman R, Anain P, et al. Final results of the Endurant Stent Graft System in the United States regulatory trial. *J Vasc Surg.* 2016;64(1):55–62.

Five-year results of the Pivotal Trial demonstrating limited adverse events, and suggesting increased durability and reliability of second generation devices.

Aortoiliac Aneurysms: Endovascular Treatment

ANDRES SCHANZER and KIMBERLY T. MALKA

Based on a previous edition chapter by Ronald M. Fairman and Grace J. Wang

GRAFT TYPES	960
PERCUTANEOUS TECHNIQUE	962
RANDOMIZED TRIALS OF ENDOVASCULAR ANEURYSM REPAIR VERSUS OPEN REPAIR	963
Perioperative Outcomes	963
Long-Term Outcomes	963
Population-Based Results	963
ENDOVASCULAR ANEURYSM REPAIR COMPARED WITH MEDICAL MANAGEMENT	964
ENDOVASCULAR ANEURYSM REPAIR IN RUPTURED ABDOMINAL AORTIC ANEURYSMS	964
COMPLICATIONS OF ENDOVASCULAR ANEURYSMS REPAIR	964
Endoleak	964
Type I	964
Type II	966
Type III	966
Type IV	967
Type V	967
Endoleak Detection	967
Migration	968
Graft Limb Occlusion	968
Renal Artery Occlusion	968
Neck Dilatation	968
Stent-Graft Infection	969
Pelvic Ischemia	969
Stent-Graft Fatigue	969
FOLLOW-UP	969
Computed Tomography Scans and Ultrasound	970
Re-intervention Rates	970
ENDOVASCULAR REPAIR OF THE JUXTARENAL AORTA	970
Encroachment Technique	970
Snorkel Technique	970
Results	971
Fenestrated Endografts	971
ENDOVASCULAR REPAIR OF COMMON ILIAC AND INTERNAL ILIAC ARTERY ANEURYSMS	971
Common Iliac Artery Aneurysms	971
Internal Iliac Artery Aneurysms	971
COST OF ENDOVASCULAR ANEURYSM REPAIR	971
SUMMARY	974
CHAPTER ALGORITHM	974

The first stent-based endoprosthesis with aortoiliac fixation was used in a human in May of 1985 to treat iliac artery stenosis.¹ This technology was then used to treat aneurysmal disease in March of 1987, when a stent graft was delivered through the femoral artery to treat a post-traumatic pseudoaneurysm in the thoracic aorta.² Four years later in 1991, Juan Parodi published his experience with deployment of a stent-anchored, Dacron prosthetic through the femoral arteries for treatment of abdominal aortic aneurysms.³ From that point on, the endovascular aneurysm repair (EVAR) revolution commenced. This chapter focuses on the outcomes of EVAR and their comparison with open surgical repair outcomes.

960

GRAFT TYPES

The initial aortic endografts were constructed by suturing a balloon-expandable stent to a standard Dacron tube graft.³ These grafts were limited to treatment of patients who had proximal and distal seal zones within the aorta. Different strategies were developed to treat aneurysms extending to the aortic bifurcation. Yusuf et al. described the use of an aorto-uni-iliac graft sutured to self-expanding stents in combination with a femoral-femoral bypass and occlusion of the contralateral iliac artery.⁴ In 1993, the unibody bifurcated aorto-bi-iliac stent was developed⁵ and the modular bifurcated design quickly followed.⁶ Early studies investigating these methods concluded

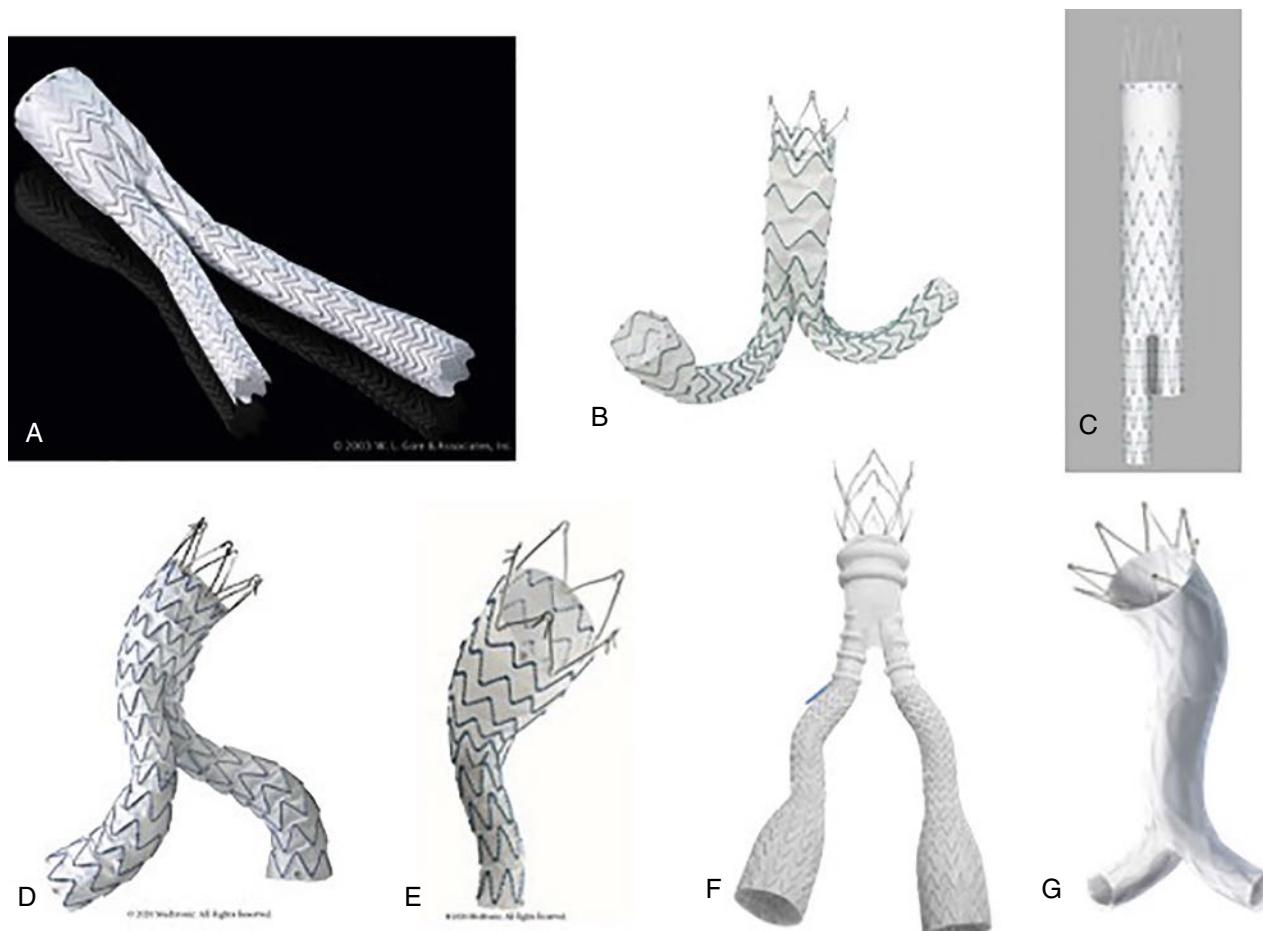


Figure 75.1 (A) Gore Excluder stent graft. (B) Terumo Treo stent graft. (C) Cook Zenith stent graft. (D) Medtronic Endurant stent graft. (E) Metronic Endurant AUI stent graft. (F) Endologix Alto stent graft. (G) Endologix AFX2 stent graft.

that the aorto-uni-iliac and bifurcated configurations had a lower incidence of both early and late endoleaks when compared with tubular aortic configurations.⁷ These modular configurations rapidly became the design of choice for modern endografts. Regulatory approval for the abdominal aortic stent graft occurred in 1996 in Europe and subsequently in the United States in 1999. Early graft designs brought with them notable problems with the emerging technology. In September of 1999, the FDA approved two grafts for the treatment of AAA, the Guidant Ancure device (Indianapolis, IN) and the Medtronic AneuRx graft (Minneapolis, MN). The Guidant Ancure consisted of a Dacron graft supported only at the proximal and distal fixation sites.⁸ While there was early success with this device, notable problems were observed with both the delivery system as well as with attachment site hook fractures.^{9,10} A high incidence of iliac limb stenoses and occlusions were also seen and attributed to the graft limbs being unsupported by stents.¹¹

The original AneuRx graft (Medtronic, Minneapolis, MN), although well received because of its innovative ease of deployment and smaller profile, was plagued with a higher migration rate.^{12–14} This endograft underwent a series of

modifications but was ultimately discontinued in favor of newer grafts. Early grafts were also prone to type IV endoleaks for a variety of reasons, including fabric tears caused by fatigue erosion of the stents against the material.¹⁵ This observation led to the secure suturing of stents to the fabric to prevent excessive motion over time. The initial Excluder graft (W.L. Gore, Flagstaff, AZ) had a propensity for type IV endoleak due to fabric porosity, resulting in development of their next generation low-porosity fabric which was used in future designs and resulted in an improved rate of aneurysm sac shrinkage.¹⁶ Failures in early endografts led to improvement in all areas of graft design including graft material, delivery systems, stent design and composition, and method of securing the stent to the graft material.

The modern version of stent-graft design is a bifurcated graft, most commonly using a modular system to allow for the most flexibility with regard to patient anatomy. Currently, seven FDA-approved endografts are commercially available for the treatment of infrarenal AAAs in the United States (Fig. 75.1, Table 75.1). Each device has some unique features that are intended to result in improved outcomes. Most current stent-graft designs have favored suprarenal

TABLE 75.1 Device Characteristics of Current Stent Grafts

Device Name	Company	Proximal Neck IFU	Iliac IFU	Fabric	Metal	Active Fixation	Notes
AFX2	Endologix	Length: 15 mm Diameter: 18–32 mm	Length: 15 mm Diameter: 10–23 mm	Duraply	Cobalt chromium alloy	Deployment at aortic bifurcation	
Alto	Endologix	Length: 7 mm Diameter: 16–30 mm	Length: 10 mm Diameter: 8–25 mm	ePTFE	Nitinol	Suprarenal stent with barbs and infrarenal sealing rings	Custom sealing polymer ring
Endurant II/ Endurant IIs	Medtronic	Length: 10 mm* Diameter: 19–32 mm	Length: 15 mm Diameter: 8–25 mm	Woven Polyester	Nitinol	Suprarenal stent with barbs	*Indicated for 4 mm neck with the use of endoanchors
Endurant II AUI <i>Aorto-uni-iliac</i>	Medtronic	Length: 10 mm* Diameter: 19–32 mm	Length: 15 mm Diameter: 8–25 mm	Woven Polyester	Nitinol	Suprarenal stent with barbs	*Indicated for 4 mm neck with the use of endoanchors, Aorto-uni-iliac device
Excluder	Gore	Length: 15 mm Diameter: 19–32 mm	Length: 10 mm Diameter: 8–25 mm	ePTFE	Nitinol	Infrarenal barbs	
Incraft	Cordis	Length: 10 mm Diameter: 17–31 mm	Length: 15 mm Diameter: 7–22 mm	PET	Nitinol	Suprarenal stent with barbs	Not currently marketed in the US
Treo	Terumo Aortic	Length: 10 mm (<60° angle and diameters 17–32 mm) Length: 15 mm (60–75° angle and diameters 16–30 mm)	Length: 10 mm (diameters 8–13 mm) Length: 15 mm (diameters 13–20 mm)	Woven Polyester	Nitinol	Suprarenal stent	
ZenithFlex	Cook	Length: 15 mm Diameter: 18–32 mm	Length: 10 mm Diameter: 7.5–20 mm	Woven Polyester	Stainless steel Cook-Z® stent	Suprarenal with barbs	

stents to inhibit downward migration, the development of type I endoleak, and endograft failure. The AFX device is the only one that touts passive fixation, whereby the flow divider of the stent graft sits directly on the aortic bifurcation. Most devices require at least 10 mm of proximal seal zone. However, the Endurant II and IIs grafts are approved for treatment of 4 mm neck lengths with the use of the Heli-FX™ EndoAnchor™ system. The C3 delivery system for the Gore Excluder graft allows for the ability to reposition the graft through the use of a constraining dial which allows for proximal trunk reconstraining and reopening. The only current FDA approved aorto-uni-iliac device for the treatment of infrarenal AAA is the Endurant II AUI device. The Zenith Renu is an aorto-uni-iliac device indicated for treatment of patients who have undergone prior EVAR but have an inadequate proximal seal. The two newest FDA-approved devices are the Ovation Alto (Endologix, approved March 2020) and the Treo (Terumo Aortic, approved May 2020). The Ovation Alto offers several design changes on the original Ovation, including relocation of the sealing ring closer to the edge of the fabric.¹⁷

PERCUTANEOUS TECHNIQUE

With the advent of smaller delivery systems, percutaneous technique has been used, decreasing the morbidity of the procedure even further. The most common vascular closure device used for percutaneous EVAR is the Perclose Proglide (Abbott, Abbott Park, IL) which consists of a pre-tied Prolene suture, and can accommodate a 5- to 8-Fr arteriotomy with one suture and an 8.5- to 24-Fr arteriotomy with two sutures. For arteriotomies greater than 8 Fr in size, the “preclose technique” is required. The vast diameters treatable with the Perclose Proglide make it a popular choice in performing percutaneous EVAR. The predictors for failure of the technique include small access vessel diameter and anterior wall calcification.¹ Therefore, the role of ultrasound-guided access when contemplating the use of vascular closure devices is crucial. The use of this technique has a 94% success rate with only 1.6% of the complications requiring open surgery.¹⁸ Additionally, the use of this technique has resulted in a decreased complication rate and hospital length of stay, making it an extraordinarily useful technique given appropriate anatomy.¹¹

RANDOMIZED TRIALS OF ENDOVASCULAR ANEURYSM REPAIR VERSUS OPEN REPAIR

Perioperative Outcomes

EVAR-1 was a randomized prospective UK study including 1082 patients that compared EVAR with open AAA repair in patients who were fit enough to undergo open surgical repair from 1999 to 2003.¹⁹ The 30-day mortality rate was reduced in the EVAR group (1.7% vs. 4.7%), although secondary interventions were more common (9.8% vs. 5.8%). The **DREAM** trial was a multicenter randomized trial (enrolling from 2000 to 2003) that compared open repair with EVAR in 345 patients,²⁰ and found a reduction in operative mortality in EVAR patients (1.2% vs. 4.6%) as well as reduction in the combined rate of operative mortality and severe complications (4.7% vs. 9.8%). The **Open Versus Endovascular Repair (OVER)** trial including 881 patients from 42 VA centers randomized to either EVAR or open repair²¹ demonstrated that perioperative mortality was improved in the EVAR group (0.5% vs. 3.0%), yet no difference was seen in mortality at 2 years (7.0% vs. 9.8%). The **Anevrisme de l'aorte abdominal: Chirurgie versus Endoprosthesis (ACE)** trial compared EVAR with open surgical repair in low- to moderate-risk patients. In-hospital mortality and the incidence of postoperative complications were not statistically different. In addition, with a median follow-up of 3 years, no difference was observed in survival or the incidence of major events.²²

Long-Term Outcomes

Although the results from the **EVAR-1**, **DREAM**, and **OVER** trials rather conclusively demonstrate the improved perioperative morbidity and mortality profile of EVAR compared with open aortic aneurysm repair, concerns remain over the long-term durability and survival benefit of EVAR.²³ The **OVER** trial long-term results revealed that, although the perioperative advantage of EVAR was still realized at 3 years, survival was similar between groups beyond this time.²⁴ **EVAR-1** trial 15-year outcomes demonstrate that, after 8 years, open repair has both a lower all-cause and aneurysm-related mortality than EVAR.²⁵ The **DREAM** trial showed no difference in mortality between the EVAR and open groups during 12 years of follow-up, although the freedom from re-intervention was higher in the open group when compared to EVAR (78.9% vs 62.2%).²⁶ Evaluation of 15-year outcomes from the **EVAR-1** trial demonstrate that, after 8 years, open repair has both a lower all-cause and aneurysm-related mortality than EVAR.²⁵

Although long-term outcomes do not seem as favorable as the perioperative outcomes when comparing EVAR to open repair, it is important to remember that there have been many advances in stent-graft technologies since the early trials. A comparison between newer stent grafts and those that are off the market reveals a striking difference regarding rates of migration, rupture, conversion, and re-intervention.^{27,28} A recent meta-analysis demonstrated higher all-cause mortality,

secondary rupture, and re-intervention in EVAR when compared to open repair at 5–9 years; however, subanalysis of more recent studies demonstrated no difference in long-term mortality.²⁹

The success of EVAR is highly dependent on the patient's anatomic suitability for the procedure. Factors that determine anatomic suitability include neck diameter, neck length, and angulation. A US-based study of 10,228 patients who underwent EVAR from 1999 through 2008 demonstrated that only 42% of patients met the most stringent criteria for instructions for use, whereas 69% met a more liberal definition of instructions for use, and that the 5-year rate of sac enlargement after EVAR was 41%.³⁰ A single-center retrospective cohort study shows a 43.8% rate of adherence to IFU in a population of patients requiring late conversion to open surgery after EVAR, compared to a 79% rate of adherence to IFU in the overall cohort.³¹ Furthermore, long-term follow-up of EVAR patients has been inconsistent,³² a cause for concern given the not infrequent need for secondary interventions in the mid to long term. A study of 19,962 Medicare beneficiaries undergoing EVAR from 2001 to 2008 showed that 50% of patients were lost to annual imaging follow-up at 5 years after surgery.¹²

Population-Based Results

In general, institutional series are reported by academic centers with a high level of expertise and controlled, prospective, multicenter studies reflect the beneficial effects of rigorous patient and investigator selection. Therefore, statewide and nationwide audits may provide a more accurate clinical picture, although procedure-specific information may be sparse because the study is usually based on administrative data. Studies of this kind have confirmed the short-term advantages of EVAR over open AAA repair.^{33,34} This was further examined in a study of late survival with re-interventions and readmission after open and EVAR.³⁵ Re-intervention and readmissions were more frequent after EVAR than after open repair (7.56 vs. 6.96/100 person-years), but the majority of these re-interventions were minor endovascular interventions. Notably, rupture was five times more common after EVAR compared with open repair, but with a relatively low rate overall. In the open repair group, as expected, laparotomy-associated re-interventions were more common and were associated with a mortality rate of 12.2%. The study concluded that survival was negatively impacted by re-intervention or readmission after EVAR or open surgery, which contributed to the loss of survival benefit of EVAR over time. Looking specifically at patients over the age of 65, a study of Medicare beneficiaries from 2003 to 2007 showed that open repair was associated with an increased risk of all-cause mortality and AAA-related mortality over a follow-up period of 5.7 years.³⁶ Both short- and long-term mortality outcomes, as well as the higher re-intervention rate after EVAR, have been confirmed in more recent population-based studies.³⁷ In an analysis of Medicare data from 2001 to 2008, the overall perioperative mortality rate was 1.6% for EVAR and 5.2% for propensity score-matched open surgical controls.³⁸ However, late survival was similar between the two groups, although the

survival curves did not converge until after 3 years. By 8 years, the EVAR group had more aneurysm-related interventions as well as a higher rate of aneurysm rupture while the open repair group had a higher rate of laparotomy-associated complications.

ENDOVASCULAR ANEURYSM REPAIR COMPARED WITH MEDICAL MANAGEMENT

To date, there have been no medical therapies that have been effective in slowing the rate of AAA growth or preventing rupture. Therefore, most studies comparing EVAR to medical management have looked at patients with high operative risk. This question was addressed by the EVAR-2 trial, in which 338 patients who were unfit for an open repair were randomized to either EVAR or medical management.³⁹ The aneurysm-related mortality and all-cause mortality rates were no different between groups. The 30-day mortality rate for EVAR was 9%, although 3.6% of these deaths were from rupture while awaiting EVAR, because the median time to intervention was 57 days. Furthermore, 25% of patients assigned to medical management eventually underwent EVAR either because of patient preference or surgeon preference, with a strikingly low mortality rate. Given the number of AAA ruptures in the EVAR group while awaiting surgery, as well as crossover of the medically treated patients to the treatment group, it is perhaps not surprising that no difference was seen in aneurysm-related or overall mortality between groups at 4 years. Long-term follow-up from the EVAR-2 trial shows no difference in life expectancy between EVAR and medical management, but a significantly lower aneurysm related mortality in the EVAR group.⁴⁰ Despite its shortcomings, EVAR-2 correctly underscores the fact that very-high-risk patients may not benefit from AAA repair because they often die from other causes before a benefit can be realized. However, it appears that EVAR can be performed safely by experienced surgeons in carefully selected high-risk patients.

Although EVAR-2 is the only randomized controlled trial comparing EVAR to medical management in high-risk patients, other studies provide data on performing EVAR in high-risk patients. A retrospective study comparing high-risk and normal-risk patients undergoing EVAR from 2006 to 2013 found no difference in perioperative mortality or early complication rates, although the high-risk group had lower long-term survival rates, which was expected.⁴¹ Data from the Department of Veterans Affairs National Surgical Quality Improvement Program on high-risk veterans undergoing EVAR showed a 30-day mortality rate of 3.4% and a 1-year mortality rate of 9.5%, which was significantly reduced compared with open repair (5.2% and 12.4%, respectively).⁴² The Veterans Affairs large aneurysm study, which was an observational study of surgically unfit patients, showed a 1-year rupture rate of 9.4% for aneurysms measuring 5.5 to 5.9 cm, 10.2% for aneurysms 6.0 to 6.9 cm, and 32.5% for aneurysms measuring 7.0 cm or greater.⁴³ A more recent literature review found yearly rupture

rates of 3.5% for aneurysms 5.5 to 6 cm, 4.1% for aneurysms 6.1 to 7 cm, and 6.3% for aneurysms >7 cm, although this study was not limited to high-risk patients.⁴⁴ Taken together, these data demonstrate that EVAR may be safely performed in patients who are deemed unfit for open repair, but may not offer a survival benefit. Decisions should be made on a case-by-case basis after extensive discussion with the patient.

ENDOVASCULAR ANEURYSM REPAIR IN RUPTURED ABDOMINAL AORTIC ANEURYSMS

Three separate multicenter randomized controlled trials have failed to show a mortality benefit for EVAR compared to open repair in ruptured AAA. The IMPROVE trial is a multicenter randomized clinical trial comparing EVAR to open repair in ruptured AAAs. Interestingly, there was no significant difference in 30-day mortality between EVAR and open repair groups (35.7% vs. 39.3%), although there was a fourfold decrease in mortality in the EVAR group amongst patients who received local anesthesia compared to those who received general anesthesia.⁴⁵ Similar results were found in another randomized trial from Amsterdam (AJAX) with a 30-day mortality rate of 21% for EVAR and 25% for open repair,⁴⁶ as well as one from France (ECAR) with a 30-day mortality rate of 18% for EVAR and 24% for open repair.⁴⁷ All three studies have been criticized, with the AJAX and ECAR trials having small numbers and excluding high-risk patients, and the IMPROVE trial having a large amount of crossover between groups after randomization.⁴⁸ A meta-analysis of studies comparing EVAR and open repair for ruptured AAA found improved mortality rates in EVAR in both hemodynamically stable (18.9% vs. 28.2%) and hemodynamically unstable (36.8% vs. 61.7%) patients.⁴⁹ Additionally, a review of surgical registries from 11 countries has demonstrated a mortality benefit for EVAR over open repair in ruptured AAAs.⁵⁰ Current SVS guidelines recommend the use of EVAR first in anatomically suitable candidates who present with ruptured AAA⁵¹ (see Ch. 76, Ruptured Aortoiliac Aneurysms and their Management).

COMPLICATIONS OF ENDOVASCULAR ANEURYSMS REPAIR

Endoleak

An endoleak is defined as persistent blood flow in the aneurysm sac following stent grafting. Endoleaks are categorized into five different types, which differ in etiology as well as treatment (Fig. 75.2).⁵²⁻⁵⁸

Type I - Early vs Late

Type I endoleak is defined as persistent blood flow into the sac either from around the graft proximally (type IA) or distally (type IB). When recognized in the operating room, type I endoleaks are typically addressed by performing proximal device extension and/or bare metal stent deployment to buttress radial

①

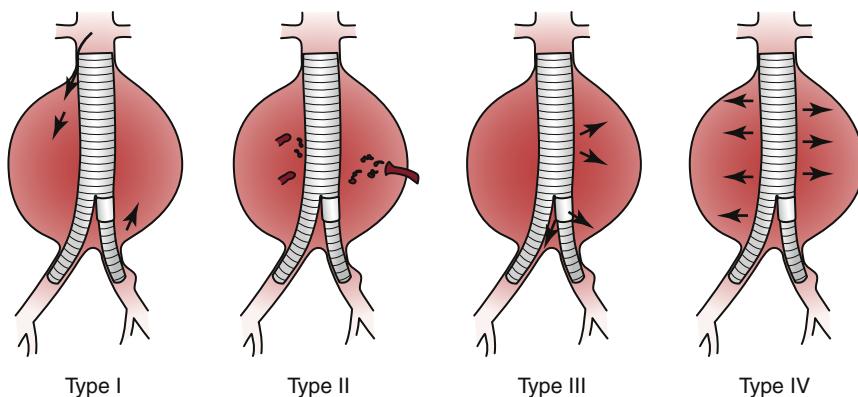


Figure 75.2 A *Type I* endoleak (periprosthetic) occurs at the proximal or distal attachment zones (or at both). A *Type II* endoleak is caused by retrograde flow from patent lumbar or inferior mesenteric arteries. A *Type III* endoleak arises from a defect in the graft fabric, an inadequate seal, or disconnection of modular graft components. A *Type IV* endoleak is due to graft fabric porosity, which often results in a generalized mild blush of contrast material within the aneurysm sac. (From White GH, May J, Waugh RC, et al. Type III and Type IV endoleak: toward a complete definition of blood flow in the sac after endoluminal AAA repair. *J Endovasc Surg*. 1998;5:305–309.)

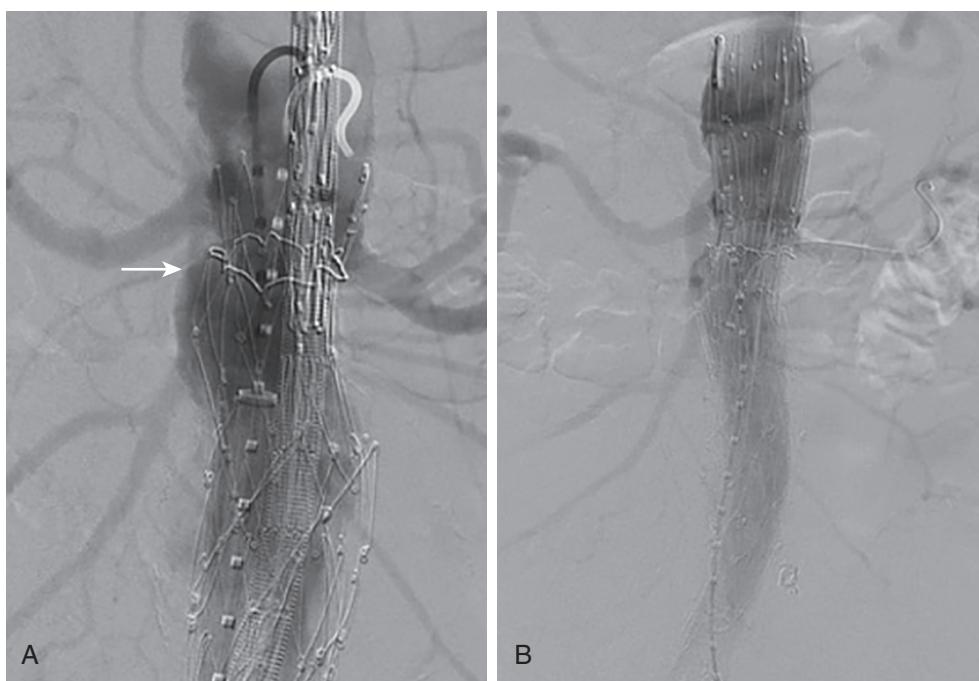


Figure 75.3 (A) Example of delayed type I endoleak secondary to proximal neck degeneration (arrow). (B) Treatment consisted of proximal extension with a Zenith fenestrated endograft.

support in the neck, with or without renal artery snorkel/encroachment techniques to preserve renal artery blood flow.⁵⁹ The Aptus EndoStapling System (Heli-FX, Aortic Securement System, Sunnyvale, CA), which uses screws to secure the stent graft to the aortic wall, may also be used to enhance the proximal seal. If the main body or trunk of the prior stent graft is too short for the deployment of a proximal extension, an aorto-uni-iliac device may be used, necessitating a femoral-femoral artery bypass and embolization of the contralateral proximal iliac artery with an occlusion device. The patency rate of femoral to femoral artery bypass done with aorto-uni-iliac stent grafting for treatment of aortic aneurysmal disease is high, with a primary patency at 54 months of 90.9% and assisted primary and

secondary patency rates of 97.7% and 100% at 66 months.⁶⁰ When type I endoleak is detected late, it is typically secondary to caudad migration of the stent graft or continued dilatation of the neck. A proximal extension may be deployed to achieve a proximal seal. If type I endoleak continues after proximal stent-graft extension or bare metal stent placement, embolization with glue and/or coils has been shown to be a useful adjunct in treating persistent type I endoleak in a few small series.^{61–63} A fenestrated graft may also be used to extend the seal zone to the juxtarenal and suprarenal aorta⁶⁴ (Fig. 75.3) (see Ch. 82, Fenestrated and Branched Endograft Treatment of Juxtarenal, Paravisceral, Thoracoabdominal, and Aortic Arch Aneurysms: Device Selection and Technical Considerations).

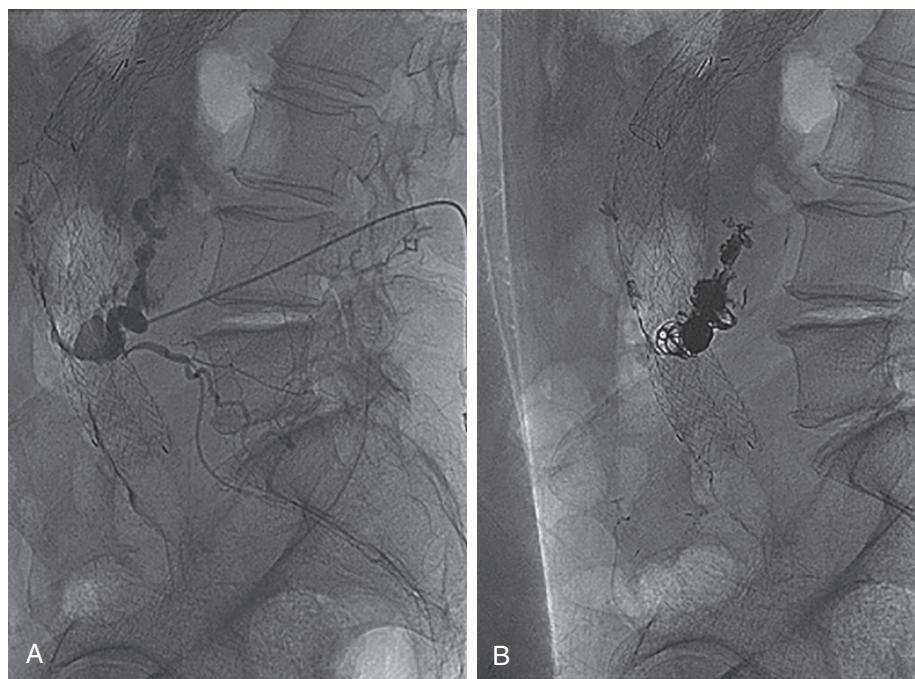


Figure 75.4 (A) A type II endoleak is visible on translumbar angiography. (B) Coils were delivered via the same approach to embolize the lumbar arteries contributing to the endoleak.

Some authors have described open surgeries without complete graft explant in the treatment of proximal type I endoleaks including an external wrap of the neck or an interposition graft from the infrarenal aortic neck to the endograft, although these techniques are not widely studied.^{65,66} Distal common iliac artery dilatation with type IB endoleak can be treated with hypogastric artery occlusion and extension of distal seal to the external iliac artery or by use of a branched iliac device (Zenith or Gore). If the previously described maneuvers are not successful in fixing the endoleak, operative explant of the stent graft is necessary because of the high risk of rupture associated with type I endoleak.

Type II

Type II endoleak is defined as persistent sac filling from back-bleeding side branches (i.e., the inferior mesenteric artery, lumbar arteries, or middle sacral artery). Postoperative CT scans show type II endoleak in 10% to 20% of patients following EVAR.^{52-54,67} In comparison with type I and type III endoleaks, type II endoleaks can have a relatively benign course, with as many as 80% resolving spontaneously within 6 to 12 months of stent-graft repair.²⁷ Furthermore, the risk of aneurysm rupture due to a type II endoleak is small but has been shown to occur in certain cases. Multivariate analysis of the EUROSTAR data showed no association between type II endoleak and risk of aneurysm rupture or need for surgical conversion.⁵⁴ A recent meta-analysis likewise demonstrated the rarity of aneurysm rupture with isolated type II endoleak.⁶⁸ Therefore, typically type II endoleaks are not treated unless aneurysm sac enlargement is documented. Persistent type II endoleaks are usually associated with a large endoleak cavity,⁶⁹

flow between inflow and outflow arteries,⁷⁰ and large, patent inferior mesenteric and lumbar arteries.⁷¹ Embolization can be performed using coils or N-butyl cyanoacrylate glue. The transarterial approach can be undertaken to embolize the inferior mesenteric artery through the superior mesenteric artery via the marginal artery of Drummond. The transcaval approach has also been described, during which the aneurysm sac is punctured through the IVC using a TIPS needle to inject coils or thrombin into the aneurysm sac or the vessels causing the type II endoleak.⁷² The translumbar approach uses CT and fluoroscopy to directly puncture the aneurysm sac (Fig. 75.4).⁷³ Regardless of the approach, type II endoleaks physiologically behave like AV malformations, and embolization of the nidus of the endoleak alone is usually inadequate for complete treatment. It is critically important to ensure that flow is obliterated in the inflow and outflow vessels. Retroperitoneal endoscopic ligation of the lumbar arteries has also been described.⁷⁴ If the previous interventions fail to be successful, and the aneurysm sac continues to enlarge, operative explant or direct ligation of the back-bleeding vessel via sacotomy is required. The Nellix Endograft (Endologix, Inc, Irvine, CA) was developed to combat type II endoleaks by using polymer to fill the aneurysm sac. Data from the first stage of the device trial revealed a high rate of migration, leading to a change in the IFU.⁷⁵ The device is currently still undergoing investigational trials in the US.

Type III

A type III endoleak results from fabric erosion or a leak between stent-graft components. Only modular grafts are at risk for component separation, but all devices are at risk for graft failure. Rates of type III endoleak range from 0% to 1.5%.^{54,76}

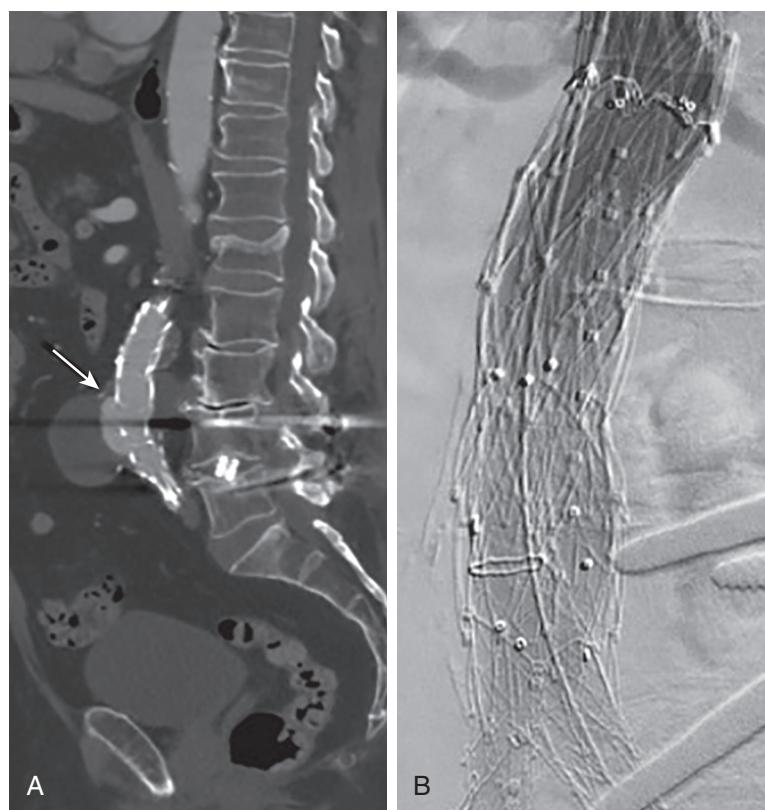


Figure 75.5 (A) Type III endoleak resulting from component separation after an EVAR (arrow). (B) The endoleak was treated by re-lining the graft with an additional bifurcated device.

Type III endoleak from fabric erosion or component separation can be effectively treated with stent-graft relining or bridging of components to effectively seal the defect (Fig. 75.5). In cases in which the device pieces are particularly separated in space due to excessive tortuosity, obtaining wire access through both components may be challenging, and transbrachial or transradial access with a snare may be useful in this situation. While in the operating room, arteriography with the pigtail catheter in the main body of the stent graft and below the proximal fixation site can help to distinguish a type I from a type III endoleak.

Type IV

Type IV endoleaks are related to porosity of the graft fabric, occur less frequently with current-generation stent grafts, and are usually noted within 30 days of graft implantation. They usually resolve after graft interstices thrombose. No treatment is usually required because they are short-lived and resolve on their own. However, high graft porosity, as demonstrated by the earlier-generation Excluder graft, can lead to sac growth in the absence of demonstrable endoleak.¹⁶

Type V

Type V endoleak, or “endotension,” is defined as elevated sac aneurysm pressure without a demonstrable endoleak. It is generally believed that the etiology is an undetected endoleak or transmission of systemic pressure through thrombus. Endotension is typically detected as continued sac enlargement on

CT scan but can also be detected by direct aneurysm sac pressure sensors (Cardiomems, Atlanta, GA; no longer commercially available). After thorough evaluation with delayed phase contrast-enhanced CT angiogram and contrast arteriography, relining with proximal and/or distal extension may be initially performed. If this is not successful, operative explant is necessary in the setting of continued AAA enlargement.

Endoleak Detection

Contrast-enhanced CT scan is the “gold standard” for detection of endoleaks using unenhanced, early, and delayed phases. The unenhanced scan shows mural calcium, which can be distinguished from contrast on subsequent series. Types I and III endoleaks are best detected on arterial phase images, whereas type II endoleaks are best detected on delayed phase images. The location of the endoleak may give an indicator as to its origin. For example, a ventrally oriented leak is likely to be emanating from the inferior mesenteric artery, whereas a dorsally oriented endoleak is more likely to be supplied by the iliolumbar arteries.⁵⁶ If the endoleak is not demonstrated on three-dimensionally reconstructed CT images, arteriography is warranted. Alternative imaging modalities include magnetic resonance imaging (MRI)^{77,78} and duplex ultrasound.^{79–81} MRI is an expensive imaging modality and, while there may be some benefit in avoiding the use of iodinated contrast agents in patients with renal insufficiency, there is a small risk of nephrogenic systemic fibrosis with gadolinium exposure in patients with a glomerular filtration rate less than 30.⁸² Duplex

ultrasound does not require contrast administration and is not associated with radiation exposure, but its success depends greatly on the technologist and it can be challenged by patient factors such as morbid obesity or presence of bowel gas. A recent meta-analysis revealed a pooled sensitivity of 0.83 and a pooled specificity of 1.00 for duplex ultrasound detection of type I and type III endoleaks.⁶⁸ Data from a relatively large study revealed that, although duplex ultrasound yielded only a sensitivity of 67% compared with CT scan, no type I endoleaks or endoleaks requiring intervention were missed.⁸⁰

Migration

Migration refers to caudal movement of the stent graft, which may lead to loss of proximal fixation and result in type IA endoleak. Cephalad migration of iliac limbs occurs less frequently, and rarely a stent graft can migrate proximally to encroach on the renal arteries. Proximal neck diameter and length as well as degree of infrarenal aortic neck angulation are all associated with proximal stent-graft migration.⁸³ Postprocedural causes for stent-graft migration include aortic neck dilatation, sac shrinkage with concomitant sac shortening, and displacement of the stent graft from external compression.^{65,84,85} The most important planning strategy is adherence to the instructions for use, as much as possible. Preprocedurally, a proximal neck fixation length of 10–15 mm is typically recommended, depending on angulation and endograft-specific IFU. Data from early devices suggest that a seal can be established in short necks, at least in the short term;^{86,87} however, long-term follow-up of EVARs placed outside of IFU show an increased incidence of type I endoleaks in patients with short necks.⁸⁸ In addition, avoiding angulation greater than 60 degrees between the infrarenal neck and the longitudinal axis of the aortic aneurysm is associated with less migration. To avoid migration in patients with short and angulated necks, several manufacturers have modified their original devices to make them more flexible. In addition, most endografts also offer active fixation with the use of barbs, which are an integral part of the device and become embedded in the aortic wall. The AFX2 stent graft (Endologix) provides passive fixation via its “anatomic” seating on the aortic bifurcation. It is designed to allow for aortic extensions to be added proximally, which is ideal in the presence of a highly angulated neck. For patients with short necks who are not candidates for open surgery, there are currently two commercially available devices that are approved for necks as short as 4 mm, the Zenith Fenestrated endograft (Cook) and the Endurant (Medtronic) with the use of endoanchors.

Graft Limb Occlusion

Stent-graft limb occlusion occurs after 3% to 7% of EVAR procedures,^{89,90} usually within the first 6 months following EVAR, but can occur at any timepoint during follow-up. It occurs more frequently in patients who have aortoiliac occlusive disease,^② a small distal aorta (<14 mm),^③ tortuous iliacs, or if those who require external iliac artery landing.^④ Earlier stent grafts were associated with a higher rate of limb occlusion than

current-generation stent grafts (18.7% vs. 4.3%).⁹⁰ During the conduct of the operation, it is important at the completion of the endovascular stent-graft repair to remove stiff wires before performing the completion arteriogram. This provides the ability to detect any occult kinks that may be straightened by the presence of a stiff wire.⁹¹ Most patients with limb occlusion present with either buttock, thigh, and/or calf claudication; rest pain is infrequently encountered.⁹⁰ Usually the limb can be recanalized with either thrombolysis or surgical thrombectomy techniques^② with adjunctive iliac stenting as needed. When a kink is identified and treated with a stent, patency rates are quite high. Arteriography with oblique orientation can be helpful in providing views to identify the problem. In addition, intravascular ultrasound (IVUS) and measurement of pullback pressures may help identify graft infolding, which may not be appreciated on arteriography.⁹² In those patients in whom the limb cannot be reopened^③ femoral-femoral bypass or axillofemoral bypass is performed to revascularize the affected leg.

Renal Artery Occlusion

Renal artery occlusion occurs either from inadvertent stent-graft coverage of the renal artery origins or from embolization. Stent-graft coverage most often occurs procedurally; delayed upward migration of the stent graft after EVAR is extremely uncommon.⁹³ During the procedure, under systemic heparinization, graft impingement on the renal artery orifice may not be readily apparent. In some endografts, the fabric can extend above the radiopaque markers; thus, the radiopaque stent struts must be placed to ensure that the fabric does not cover the renal artery origin. Appropriate positioning of the C-arm to avoid parallax and to ensure that the origin of the renal artery is appreciated is paramount. When detected in the operating room, rescue renal stenting can be attempted via the femoral or brachial approach to preserve renal artery flow. When detected late, renal artery stenting may still be possible; however, open hepatorenal or splenorenal bypass may be required.⁹⁴ In a single-institution study investigating suprarenal versus infrarenal fixation, suprarenal fixation did not cause a decrease in renal function or increase the need for dialysis.⁹⁵ Embolization to the renal arteries can be a cause of early or delayed renal insufficiency. This is especially true if thrombus is present in the area of aortic fixation. A recent study showed that the presence of thrombus in the neck in combination with suprarenal fixation was associated with an increase in thromboembolic complications.⁹⁶

Neck Dilatation

The juxtarenal portion of the aorta is not as prone to dilatation as is the infrarenal aorta, but this region can dilate following EVAR,⁹⁷ resulting in migration and/or type I endoleak and risk of rupture.¹³ In a study of 230 patients, the predictors for neck dilatation were large AAA diameter, large aortic neck size, and circumferential neck thrombus.⁹⁸ It is interesting to note that the type of proximal fixation does not appear to significantly affect neck dilation.⁹⁹ Indeed, a study evaluating the neck

following endovascular and open repair found similar increases in neck diameter over time, suggesting that the dilatation is a sign of progression of disease rather than the radial force of a stent graft that is larger than the aortic neck.¹⁰⁰ However, generous oversizing of the stent graft should be avoided as excessive oversizing was associated with higher migration, aneurysm expansion risk, and early neck dilation.^{101,102}

Stent-Graft Infection

Infection of the aortic stent graft is a rare event, with small case series reporting an incidence of 0.2% to 0.7%.¹⁰³ The Vascular Low-Frequency Disease Consortium reviewed a multi-institutional database to characterize patients who presented with aortic endograft infection. Most patients were treated with *in situ* aortic replacement with cryopreserved allograft, neoaortoiliac system, or prosthetic graft (most antibiotic-soaked); while others underwent axillary–femoral bypass. This study demonstrated a 30-day mortality of 11% in the operative group, while 6/9 patients died after conservative management after an average of 56 days.¹⁰⁴ In this study, 19 out of 197 replacement grafts also required explant, with the largest risk factors being prosthetic graft material not soaked in antibiotic and extra-anatomic bypass. In the largest case series to date, nine patients presented with infected EVAR at a tertiary referral center.¹⁰⁵ All patients underwent complete explants of the stent graft. Seven patients survived to discharge, and the mean follow-up of the surviving patients was 11 months. In this series the presence of a concomitant aortoenteric fistula was particularly virulent. Two of the three patients with aortoenteric fistula died before discharge. A recent meta-analysis identified the causal organism as *Staphylococcus* (30.1%), *Streptococcus* (14.8%), or fungus (9.2%) in a majority of cases, with 27% of cases having negative cultures.¹⁰⁶ In this review, 10% of patients underwent conservative treatment with a mortality rate of 58% while 90% of patients underwent operative treatment with a mortality rate of 33%. Other studies have shown improved outcomes with conservative management, with a retrospective study of EVAR and TEVAR graft infections showing an overall mortality of 25% but no difference in outcome in surgical patients vs. those treated with antibiotics alone.¹⁰⁷ Bias in the first study may result from patients who have more comorbidities not being offered surgical intervention while the small sample size in the second study may result in type II error. The general consensus is for complete removal of the infected endograft with anatomic or extra-anatomic reconstruction; however, long-term antibiotic therapy as a palliative measure can be attempted in patients who are not operative candidates.

Pelvic Ischemia

The incidence after EVAR varies in the literature, but pelvic ischemia is a known complication of EVAR and typically occurs as a consequence of occlusion of one or both internal iliac arteries in the presence of a common iliac or internal artery aneurysm. Pelvic ischemia can manifest as buttock claudication, buttock necrosis, spinal cord ischemia, colorectal ischemia, and

erectile dysfunction.^{108–110} In a review that included data from 18 studies detailing internal iliac artery embolization before EVAR, buttock claudication occurred in 55% of patients overall, with 52% occurring after unilateral embolization and 63% occurring after bilateral embolizations.¹⁰⁹ Other studies similarly found that bilateral embolization was associated with an increase in pelvic ischemic complications.¹¹⁰ Although relatively common initially, buttock claudication appears to improve in most patients. In a study in which bilateral internal iliac arteries were occluded, buttock claudication occurred in 31% of patients but persisted beyond 1 year in only 9% of patients.¹¹¹ In addition, multiple studies have shown that embolization of the internal iliac artery proximal to its bifurcation is associated with a lower incidence of buttock claudication than if more distal branches are occluded, because this allows more pelvic collateral flow via internal iliac branches.^{111,112} Colonic ischemia is relatively rare following internal iliac artery embolization and EVAR, with an incidence of 0.9% in standard EVAR patients and of 2.6% in patients also undergoing internal iliac artery embolization.¹¹³ Spinal cord ischemia is also a rare complication following EVAR. In a small series that examined the incidence of complications following bilateral internal iliac artery embolization before EVAR, the incidence was 3% and was characterized as paraparesis.¹¹¹ A systematic review identified difficult anatomy, prolonged procedure time, performance of additional procedures, and extensive intravascular handling as risk factors for the development of spinal cord ischemia after EVAR.¹¹⁴

Stent-Graft Fatigue

The aortic stent graft is under constant mechanical stress during the cardiac cycle, which can cause fracture of barbs and stent struts. With the exception of the original Zenith stent (stainless steel), most stent grafts are composed of nitinol, which is an ideal material given its flexibility and conformability. However, nitinol can be associated with surface irregularities, which serve as foci for stress and strain and can predispose to wire fracture. This problem has been lessened with electropolishing chemical etching techniques. Strut and stent fractures have been reported in multiple older-generation devices,^{115–120} although newer devices are not free from this finding. Not all stent failures require intervention as many will not be associated with any clinical significance; however, barb separation or disruption associated with migration and endoleak formation or stent fracture associated with graft disruption must be treated as outlined earlier for type I endoleak and type III endoleak, respectively.

FOLLOW-UP

Postoperative follow-up is important for ensuring continued success of EVAR. Postoperative surveillance allows for detection of endoleaks, aneurysm sac expansion, stent fracture, limb kinking, and material fatigue. Unequivocally, life-long follow-up is a key component of EVAR.

Computed Tomography Scans and Ultrasound

Initial protocols were adopted from early FDA-sponsored pivotal trials;¹²¹ however, the frequent use of CT scanning has raised concerns related to the added cost of these studies, as well as cumulative radiation exposure^{122,123} and use of nephrotoxic agents. Although ultrasound/duplex avoids radiation exposure and the use of contrast, concerns have been raised in the past regarding its variable sensitivity in detecting endoleaks.⁸¹ Based on recent reports, some investigators have proposed that follow-up with duplex as the sole imaging modality is appropriate, provided no endoleak or sac enlargement is documented on the first annual CT scan.¹²⁴ The Society for Vascular Surgery (SVS) practice guidelines currently recommend contrast-enhanced CT scanning and color duplex ultrasound at 1 month after EVAR, with either contrast-enhanced CT or duplex ultrasound repeated at 12 months and then annually if no endoleak is seen on the first postoperative scan.⁵¹ Detection of an endoleak at 1 month would prompt another CT scan at 6 months to evaluate the need for intervention. An algorithm is provided summarizing the current strategy for follow-up imaging after EVAR according to current SVS recommendations.

Re-intervention Rates

Long-term data is now available from the EVAR-1 and EVAR-2 studies which demonstrate a re-intervention rate of 4.1 per 100 person-years.¹²⁵ However, it is important to remember that the long-term data from these trials are for devices that are now largely off the market. Long-term outcomes of the Zenith endograft (Cook) show freedom from re-intervention rates of 98%, 87.7%, 75.7%, and 69.9% at 1, 5, 10, and 14 years, respectively.¹²⁶ The effect of re-interventions and readmissions following EVAR versus open aneurysm repair was also examined in Medicare beneficiaries.³⁵ Survival was found to be negatively affected by readmission or re-intervention in both groups. However, the majority of secondary interventions after EVAR were minor in nature, with a relatively low 30-day mortality.

ENDOVASCULAR REPAIR OF THE JUXTARENAL AORTA

For some patients with a proximal infrarenal neck length less than 10 to 15 mm (the traditional desired neck length for EVAR), partial renal artery coverage with adjunctive renal artery stenting can be performed.⁵⁹

Encroachment Technique

This technique is used when partial renal artery coverage is needed to achieve a seal (Fig. 75.6A). The aortic stent graft is deployed in the usual fashion, with careful attention paid to the relationship between the top of the stent-graft fabric and the lowest renal artery. The optimal degree of angulation and rotation for visualizing the take-off of the renal artery is determined based off of the preoperative CT angiogram. Catheter and wire access of the renal artery can usually be obtained transfemorally. If a device with a suprarenal stent is used, care is taken to access the base of the triangular stent rather than in between the triangular stents. A combination of a Rosen wire (Cook Medical) and a guide catheter system are used to serve as a platform for performing the renal stent. Balloon-expandable stents are favored in this location because the increased radial force is essential to push the superior margin of the stent graft inferiorly to preserve renal artery flow.

Snorkel Technique

This technique is used when complete coverage of the renal artery origin is required to achieve a seal (see Fig. 75.6B). Upper extremity access is key because the snorkel maneuver is often used when more extensive coverage of the renal artery is required, and the stent is required to be positioned alongside the aortic main body stent graft before entering the orifice of the artery. A combination of a Rosen wire and a long sheath are used as the platform. The renal stent comes to lie entirely outside the aortic stent graft, parallel to it, until it enters the renal artery orifice. A covered stent is preferred for this purpose. The length of the renal stent is usually longer because of the distance along the aortic stent graft, which needs to be traversed before reaching the origin of the renal artery. It is important to maintain balloon support of the renal stent while ballooning

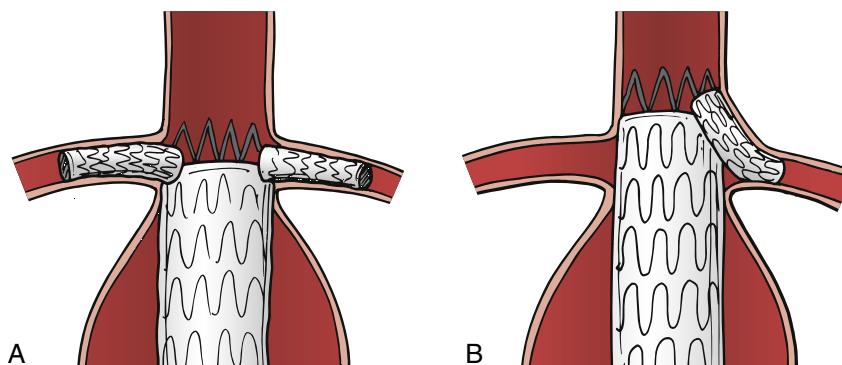


Figure 75.6 (A) The encroachment bilateral renal stenting technique. (B) The snorkel technique. (From Chaikof E, Cambria R. *Atlas of Vascular Surgery and Endovascular Therapy*. Philadelphia: Elsevier; 2012.)

the aortic graft, because compression of the stent can occur with this maneuver.

T.e. Bising

Results

Using either the encroachment or snorkel technique, a case series showed that sealing of the aneurysm was possible with a primary assisted patency of renal artery stents of 100% at a median follow-up of 12.5 months.⁵⁹ A review of other studies demonstrates technical success rates of 98.2%–100%, patency rates >95%, and rates of endoleak ranging from 14%–25%.^{127–129}

Fenestrated Endografts

The Zenith Fenestrated endograft (Cook Medical) was FDA approved in 2012 for the treatment of juxtarenal abdominal aortic aneurysms with a 4 mm neck. These devices are custom-made to suit a specific patient's anatomy and can incorporate the renal arteries using large (8–12 mm) or small (6–8 mm) fenestrations as well as a scallop, which can also incorporate the superior mesenteric artery. Results from a prospective study demonstrate a 100% technical success rate, 1.5% 30-day mortality rate, and no ruptures with an average follow-up of 37 months.¹³⁰ This study also demonstrated a 3% rate of renal artery occlusion and 9% rate of renal artery stenosis. Evaluation of mid-term outcomes for patients undergoing juxtarenal AAA repair with the Zenith fenestrated device who had a neck diameter <60° demonstrates AAA sac shrinkage in 65% of patients, no cases of AAA sac enlargement, no type I or III endoleaks, and no occlusion of target vessels with an average follow-up of 25 months.¹³¹

ENDOVASCULAR REPAIR OF COMMON ILIAC AND INTERNAL ILIAC ARTERY ANEURYSMS

Common Iliac Artery Aneurysms

Current stent-graft technology allows for treatment of iliac artery aneurysms with a seal zone diameter of up to 25 mm at the common iliac artery bifurcation. When the diameter of the seal zone is greater than 25 mm or the aneurysmal disease extends to the origin of the external iliac artery, the endograft can be extended into the external iliac artery, with coil embolization or plug occlusion (Amplatzer vascular plug, St. Jude Medical, Inc., St. Paul, MN) of the proximal internal iliac artery to prevent a type II endoleak.¹³² To preserve internal iliac artery flow, an external to internal iliac artery bypass can be performed with proximal ligation of the internal iliac artery to effectively "re-position" the iliac bifurcation more distally. In one series of 22 patients, all bypasses remained patent at a mean follow-up of 15 months, with only mild buttock claudication occurring in two patients ipsilateral to the site of coil embolization.¹³³ Another series showed similar excellent internal iliac bypass patency rates of 91%, as well as freedom from ischemic symptoms.¹³⁴

The Gore Excluder Iliac Branch Endoprosthesis (IBE) was FDA approved in March 2016 and is designed to achieve a more stable seal in those with ectatic or aneurysmal iliac

arteries. The device is also intended to preserve important pelvic collaterals to decrease the likelihood of buttock claudication and to reduce the complications of spinal cord ischemia should more extensive aortic repair be required (Fig. 75.7). A prospective trial of 63 patients demonstrated a 95.2% technical success rate, and 95.1% patency of the internal iliac limb at 6 months with freedom from new-onset buttock claudication being 100%.¹³⁵ A second study looking at early outcomes of this endograft demonstrates similar results with a 93.5% procedural success rate, and a 6-month primary patency of the internal component of 94%.¹³⁶

Internal Iliac Artery Aneurysms

Internal iliac artery aneurysms are typically managed with endovascular coiling/plug occlusion with stent-graft coverage of the origin, although an iliac branch device solution could be considered if anatomy is suitable. If the proximal landing zone is compromised, a chimney/snorkel can be deployed extending into either the common or external iliac artery,¹³⁷ or the "sandwich technique" may be used (Fig. 75.8).¹³⁸ A hybrid technique has also been described. An aorto-uni-iliac endograft with a femoral-to-femoral artery bypass can be performed with a covered stent deployed from the contralateral external to the internal iliac artery in a "reverse U" fashion (Fig. 75.9)¹³⁹ (see Ch. 77, Isolated Iliac Artery Aneurysms and their Management).

COST OF ENDOVASCULAR ANEURYSM REPAIR

In 2019, a comparison of EVAR performed via percutaneous or open femoral access showed an average cost of \$16,628.50 for percutaneous EVAR versus \$21,705.80 for EVAR performed via open femoral exposure.¹⁴⁰ A 2020 study found that the cost of the index surgery was an average of \$25,924 for EVAR and \$31,442 for open surgery; however, over time, patients who underwent EVAR had an average disease-related spending of \$7322 through 5 years of follow-up while patients who underwent open repair had an average disease-related spending of \$2076 in the same time period.¹⁴¹ In a study investigating the cost of long-term surveillance and secondary procedures, the cumulative post-placement cost of EVAR for all patients at 5 years was \$11,351.¹⁴² When these patients are separated into groups based on those who required secondary interventions, massive cost differences were noted (\$31,696 for patients undergoing secondary intervention compared with \$3668 for those not requiring secondary intervention). The 5-year cost for patients with endoleak was \$26,739 compared with \$5,706 for those without endoleak. In the OVER trial,²⁴ the probability of EVAR being less costly and more effective was 71% for life-years and 51% for quality-adjusted life years (QALYs). A cost-utility model based on a meta-analysis of patients treated with EVAR or open repair of ruptured aneurysms was performed. EVAR was less costly compared with open repair (\$26,133 vs. \$28,395).²² The mean QALY was higher for EVAR compared with open repair (3.09 vs. 2.49). EVAR was thus cost-effective compared with open repair at a threshold of \$30,000 to \$45,000/QALY.

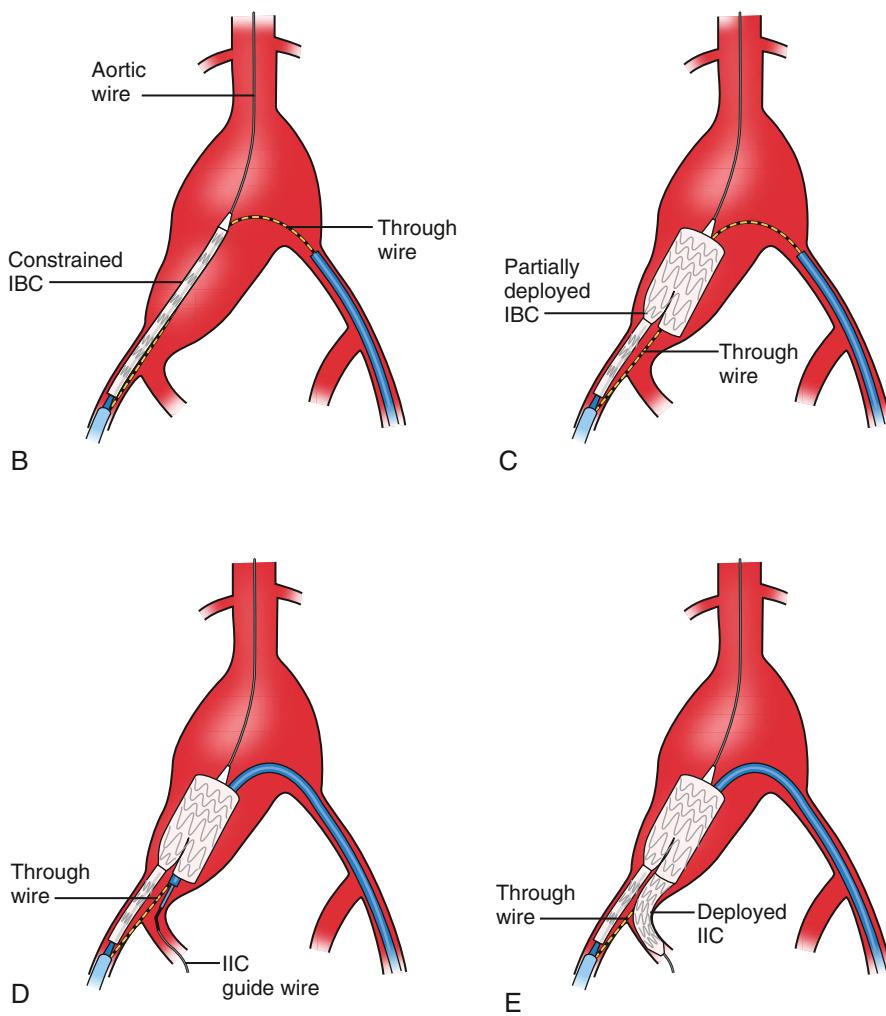
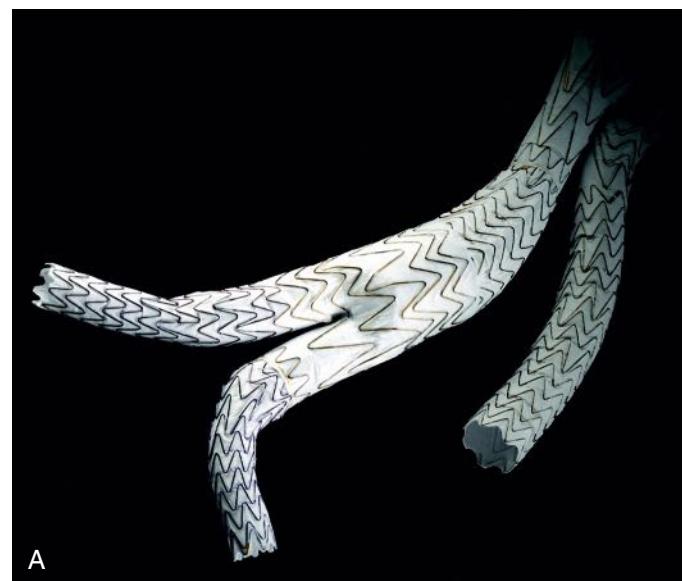


Figure 75.7 (A) Gore iliac branch component. (B) Aortic wire, constrained iliac branch component (IBC), through wire. The guide wire is passed through the sheath and snared from the contralateral groin. (C) Partially deployed IBC, through wire. The aortic wire is passed through the IBC and the through wire is passed through the branch and the IBC is advanced into common iliac artery and partially deployed. (D) Through guide wire, internal iliac component (IIC) guide wire. The wire is advanced into the internal iliac artery. (E) Through wire, deployed internal iliac component. The internal iliac stent is deployed. (GORE® EXCLUDER® Iliac Branch Endoprosthesis. ©2021.)

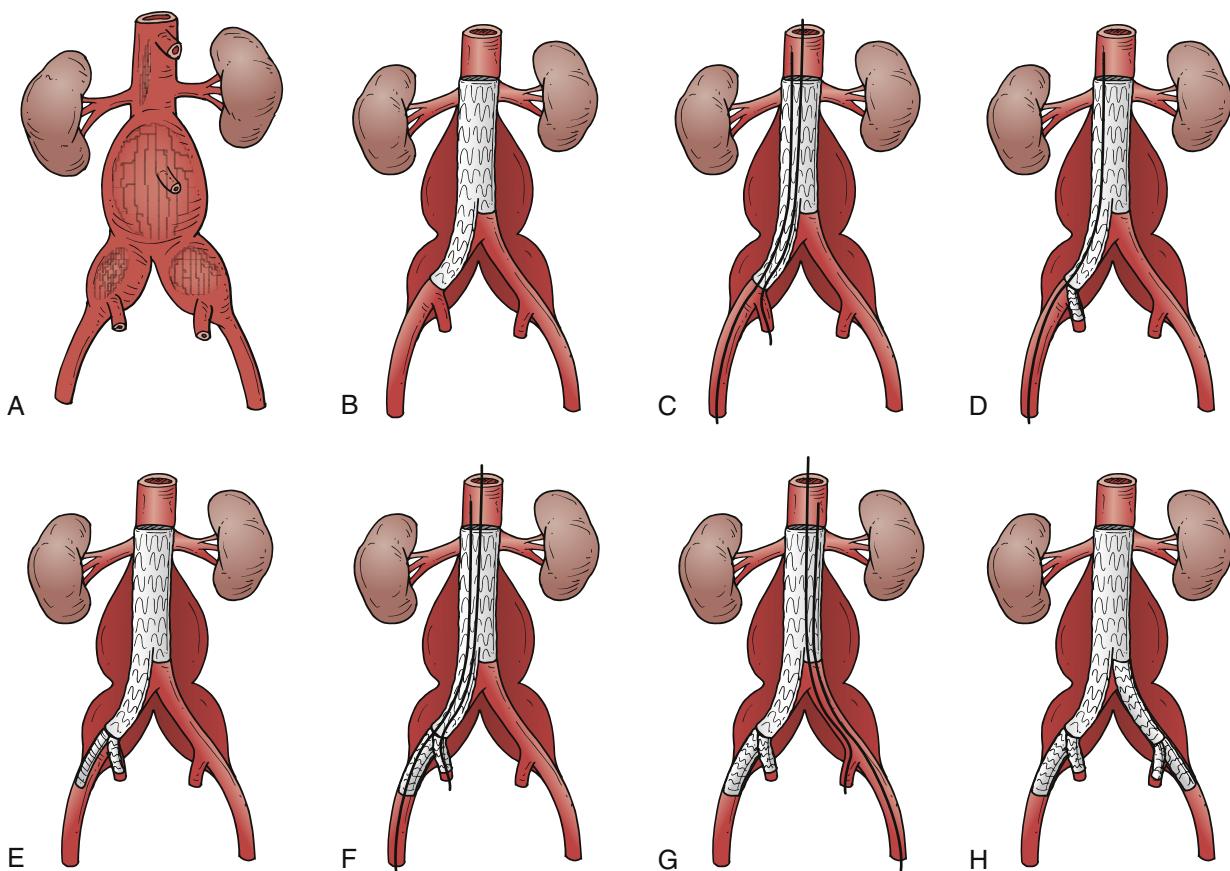


Figure 75.8 (A) Aortoiliac aneurysm extending to the internal iliac artery (IIA). (B) Deploy the main body of the bifurcated stent graft. (C) Cannulate the ipsilateral IIA using left brachial access. (D) Deploy the covered stent inside the nondiseased IIA with 5 cm overlapping into the iliac limb extension. (E) Position the iliac limb extension with the proximal end distal to the IIA stent. (F) Deploy the iliac limb extension and then the internal iliac artery stent. (G) For bilateral sandwich repair, deploy the contralateral iliac limb stent graft, then cannulate the remaining IIA, using left brachial access. (H) Deploy the iliac limb extension followed by the internal iliac artery stent. (From Lobato AC, Camacho-Lobato L. The sandwich technique to treat complex aortoiliac or isolated iliac aneurysms: results of midterm follow-up. *J Vasc Surg*. 2013;57:28S.)

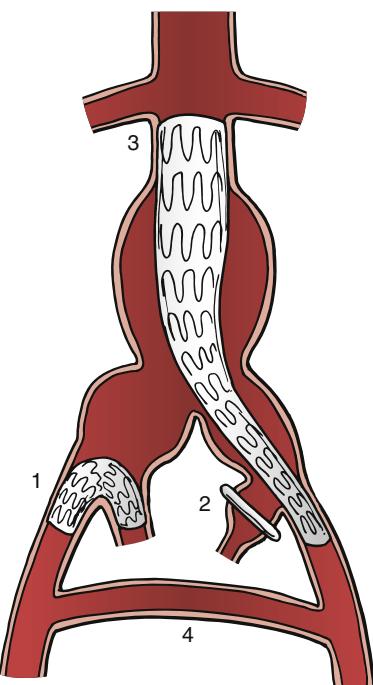


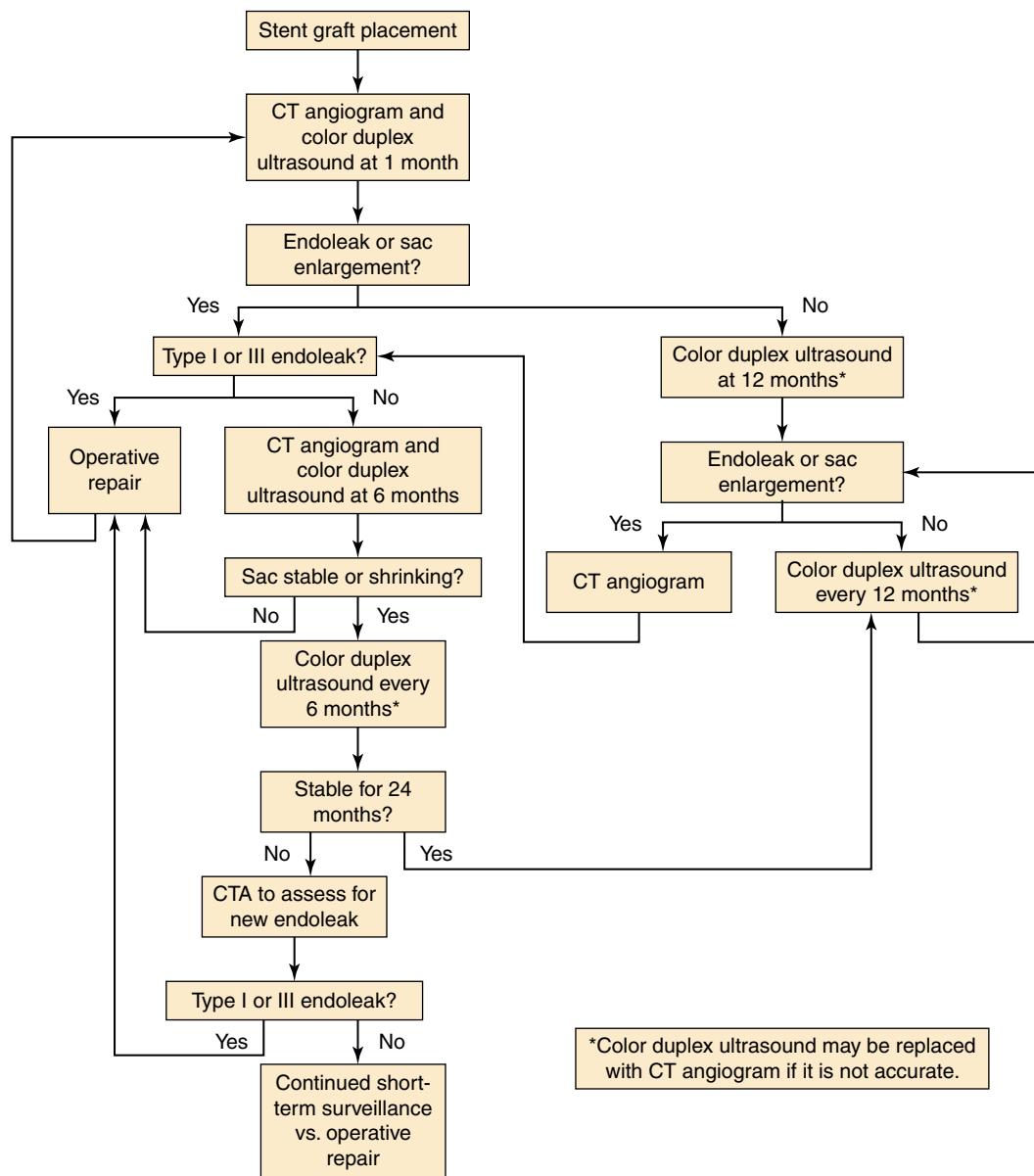
Figure 75.9 Diagram of external-to-internal iliac artery stent (1) and contralateral internal iliac artery occlusion (2). Aorto-uni-iliac device (3) and femoral-femoral artery bypass (4). (From Ghosh J, Murray D, Paravastu S, et al. Contemporary management of aorto-iliac aneurysms in the endovascular era. *Eur J Vasc Endovasc Surg*. 2009;37:184.)

SUMMARY

In summary, over the last three decades, vascular specialists have successfully introduced and embraced a new, minimally invasive approach to the treatment of abdominal aortic aneurysms. Countless patients have benefitted from EVAR and it should be noted that in an exceptionally brief span of time, vascular providers have developed and implemented the necessary skill set required to provide EVAR to patients safely, with extremely low perioperative mortality. We now find ourselves at a critical moment that requires a rigorous assessment of the advantages and disadvantages of EVAR, as

it has become the mainstay for AAA treatment. Device development with a focus on durability to prevent late AAA sac enlargement and rupture is an imperative. While next generation EVAR devices, such as the highly promising branched and fenestrated solutions currently undergoing investigation, will expand the anatomic boundary conditions suitable for successful EVAR, current technology makes careful patient selection critical. Caution should be exercised when patients selected for EVAR do not meet device instructions for use and, most importantly, each patient and treating physician must commit to life-long follow-up incorporating careful endograft imaging surveillance.

CHAPTER ALGORITHM



Surveillance strategy following endovascular repair of an abdominal aortic aneurysm.

SELECTED KEY REFERENCES

EVAR trial participants. Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): randomised controlled trial. *Lancet.* 2005;365:2187–2192.

This study remains the only source of level 1 data on the relative mortality of EVAR and observation in patients considered unfit for surgical repair, but there are methodologic concerns, as discussed in this chapter.

Giles KA, Landon BE, Cotterill P, et al. Thirty-day mortality and late survival with reinterventions and readmissions after open and endovascular aortic aneurysm repair in Medicare beneficiaries. *J Vasc Surg.* 2011;53(1):6–12. 13e1.

This large review of Medicare beneficiaries examined the effect of reinterventions and readmission following EVAR and open aortic aneurysm repair.

Greenhalgh RM, Brown LC, Kwong GP, et al. EVAR trial participants: comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomized controlled trial. *Lancet.* 2004;364:843–848.

This large prospective randomized study compares the results of open surgery with the results of EVAR in good-risk patients. It is one of the few sources of level 1 data on the subject.

Lederle FA, Freischlag JA, Kyriakides TC, et al. Long-term comparison of endovascular and open repair of abdominal aortic aneurysm. *N Engl J Med.* 2012;367(21):1988–1997.

A randomized controlled study comparing EVAR with open repair over a mean 5.2-year follow-up period in the veteran population.

Lederle FA, Freischlag JA, Kyriakides TC, et al. Outcomes following endovascular versus open repair of abdominal aortic aneurysm: a randomized trial. *JAMA.* 2009;302(14):1535–1542.

A randomized controlled study comparing EVAR with open repair over a 2-year period in the veteran population.

Schermerhorn ML, O’Malley AJ, Jhaveri A, et al. Endovascular versus open repair of abdominal aortic aneurysms in the Medicare population. *N Engl J Med.* 2008;358:464–474.

This retrospective analysis is one of the few sources of data on the late complications of open surgical aortic aneurysm repair.

UK EVAR Trial Investigators, Greenhalgh RM, Brown LC, et al. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1863–1871.

Long-term follow-up study of EVAR-1.

van Marrewijk C, Buth J, Harris PL, et al. Significance of endoleaks after endovascular repair of abdominal aortic aneurysms: The EUROSTAR experience. *J Vasc Surg.* 2002;35:461–473.

This review of registry data examines the relationship between endoleak type, failure mode, and outcome. It provides a sound basis for the interpretation of postoperative CT findings.

van Marrewijk CJ, Leurs LJ, Vallabhaneni SR, et al. Risk-adjusted outcome analysis of endovascular abdominal aortic aneurysm repair. *J Endovasc Ther.* 2005;12:417–429.

This analysis of EUROSTAR registry data gives the device-specific risks for various late complications of EVAR.

A complete reference list can be found online at www.expertconsult.com.

REFERENCES

1. Volodos NL, Shekhanin VE, Karpovich IP, et al. [A self-fixing synthetic blood vessel endoprostheses]. *Vestn Khir Im I I Grek.* 1986;137:123–125.
2. Volodos NL, Karpovich IP, Shekhanin VE, et al. [A case of distant transfemoral endoprosthesis of the thoracic artery using a self-fixing synthetic prosthesis in traumatic aneurysm]. *Grudn Khir.* 1988;84:86.
3. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. *Ann Vasc Surg.* 1991;5:491–499.
4. Yusuf SW, Whitaker SC, Chuter TA, et al. Early results of endovascular aortic aneurysm surgery with aortouniliac graft, contralateral iliac occlusion, and femorofemoral bypass. *J Vasc Surg.* 1997;25:165–172.
5. Chuter TA, Donayre C, Wendt G. Bifurcated stent-grafts for endovascular repair of abdominal aortic aneurysm. Preliminary case reports. *Surg Endosc.* 1994;8:800–802.
6. Blum U, Voshage G, Lammer J, et al. Endoluminal stent-grafts for infrarenal abdominal aortic aneurysms. *N Engl J Med.* 1997;336:13–20.
7. May J, White GH, Yu W, et al. Importance of graft configuration in outcome of endoluminal aortic aneurysm repair: a 5-year analysis by the life table method. *Eur J Vasc Endovasc Surg.* 1998;15:406–411.
8. Moore WS, Matsumura JS, Makaroun MS, et al. EVT/Guidant Investigators. Five-year interim comparison of the Guidant bifurcated endograft with open repair of abdominal aortic aneurysm. *J Vasc Surg.* 2003;38:46–55.
9. Problems with endovascular grafts for treatment of abdominal aortic aneurysm (AAA). *J Vasc Surg.* 2001;33:1361–1362.
10. Moore WS, Rutherford RB. Transfemoral endovascular repair of abdominal aortic aneurysm: results of the North American EVT phase 1 trial. EVT Investigators. *J Vasc Surg.* 1996;23:543–553.
11. Parent 3rd FN, Godzichvili V, Meier 3rd GH, et al. Endograft limb occlusion and stenosis after ANCURE endovascular abdominal aneurysm repair. *J Vasc Surg.* 2002;35:686–690.
12. Tonnissen BH, Sternbergh 3rd WC, Money SR. Mid- and long-term device migration after endovascular abdominal aortic aneurysm repair: a comparison of AneuRx and Zenith endografts. *J Vasc Surg.* 2005;42:392–400; discussion 400–401.
13. Cao P, Verzini F, Zannetti S, et al. Device migration after endoluminal abdominal aortic aneurysm repair: analysis of 113 cases with a minimum follow-up period of 2 years. *J Vasc Surg.* 2002;35:229–235.
14. Conners 3rd MS, Sternbergh 3rd WC, Carter G, et al. Endograft migration one to four years after endovascular abdominal aortic aneurysm repair with the AneuRx device: a cautionary note. *J Vasc Surg.* 2002;36:476–484.
15. Leurs LJ, Buth J, Laheij RJ. Long-term results of endovascular abdominal aortic aneurysm treatment with the first generation of commercially available stent grafts. *Arch Surg.* 2007;142:33–41; discussion 42.
16. Haider SE, Najjar SF, Cho JS, et al. Sac behavior after aneurysm treatment with the Gore Excluder low-permeability aortic endoprostheses: 12-month comparison to the original Excluder device. *J Vasc Surg.* 2006;44:694–700.
17. Holden A, Lyden S. Initial experience with polymer endovascular aneurysm repair using the Alto stent graft. *J Vasc Surg Cases Innov Tech.* 2020;6:6–11.
18. Jaffan AA, Prince EA, Hampson CO, Murphy TP. The preclose technique in percutaneous endovascular aortic repair: a systematic literature review and meta-analysis. *Cardiovasc Interv Radiol.* 2013;36:567–577.
19. Greenhalgh RM, Brown LC, Kwong GP, et al. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet.* 2004;364:843–848.
20. Prinsen M, Verhoeven EL, Buth J, et al. Dutch Randomized Endovascular Aneurysm Management (DREAM) Trial Group. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med.* 2004;351:1607–1618.
21. Lederle FA, Freischlag JA, Kyriakides TC, Open Versus, et al. Endovascular Repair Veterans Affairs Cooperative Study Group. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. *JAMA.* 2009;302:1535–1542.
22. Becquemin JP, Pillet JC, Lescalie F, ACE trialists, et al. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients. *J Vasc Surg.* 2011;53:1167–1173.e1.
23. Ohki T, Veith FJ, Shaw P, et al. Increasing incidence of midterm and long-term complications after endovascular graft repair of abdominal aortic aneurysms: a note of caution based on a 9-year experience. *Ann Surg.* 2001;234:323–334; discussion 334–335.
24. Stroupe KT, Lederle FA, Matsumura JS, Open Versus, et al. Endovascular Repair Veterans Affairs Cooperative Study Group. Cost-effectiveness of open versus endovascular repair of abdominal aortic aneurysm in the OVER trial. *J Vasc Surg.* 2012;56:901–909 e2.
25. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM, EVAR Trial investigators. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. *Lancet.* 2016;388:2366–2374.
26. van Schaik TG, Yeung KK, Verhagen HJ, DREAM Trial participants. Long-term survival and secondary procedures after open or endovascular repair of abdominal aortic aneurysms. *J Vasc Surg.* 2017;66:1379–1389.
27. Brewster DC, Jones JE, Chung TK, et al. Long-term outcomes after endovascular abdominal aortic aneurysm repair: the first decade. *Ann Surg.* 2006;244:426–438.
28. Torella F. Effect of improved endograft design on outcome of endovascular aneurysm repair. *J Vasc Surg.* 2004;40:216–221.
29. Li B, Khan S, Salata K, et al. A systematic review and meta-analysis of the long-term outcomes of endovascular versus open repair of abdominal aortic aneurysm. *J Vasc Surg.* 2019;70:954–969. e30.
30. Schanzer A, Greenberg RK, Hevelone N, et al. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. *Circulation.* 2011;123:2848–2855.
31. 's Choice – Late Open Surgical Conversion after Endovascular Abdominal Aortic Aneurysm Repair. Kansal V, Nagpal S, Jetty P, eds. *Eur J Vasc Endovasc Surg.* 2018;55:163–169.
32. Schanzer A, Messina LM, Ghosh K, et al. Follow-up compliance after endovascular abdominal aortic aneurysm repair in Medicare beneficiaries. *J Vasc Surg.* 2015;61:16–22. e1.
33. Anderson PL, Arons RR, Moskowitz AJ, et al. A statewide experience with endovascular abdominal aortic aneurysm repair: rapid diffusion with excellent early results. *J Vasc Surg.* 2004;39:10–19.
34. Lee WA, Carter JW, Upchurch G, et al. Perioperative outcomes after open and endovascular repair of intact abdominal aortic aneurysms in the United States during 2001. *J Vasc Surg.* 2004;39:491–496.
35. Giles KA, Landon BE, Cotterill P, et al. Thirty-day mortality and late survival with reinterventions and readmissions after open and endovascular aortic aneurysm repair in Medicare beneficiaries. *J Vasc Surg.* 2011;53(6–12):13.e1.
36. Jackson RS, Chang DC, Freischlag JA. Comparison of long-term survival after open vs endovascular repair of intact abdominal aortic aneurysm among Medicare beneficiaries. *JAMA.* 2012;307:1621–1628.
37. Williams CR, Brooke BS. Effectiveness of open versus endovascular abdominal aortic aneurysm repair in population settings: A systematic review of statewide databases. *Surgery.* 2017;162:707–720.
38. Schermerhorn ML, Buck DB, O'Malley AJ, et al. Long-term outcomes of abdominal aortic aneurysm in the Medicare population. *N Engl J Med.* 2015;373:328–338.
39. EVAR trial participants. Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): randomised controlled trial. *Lancet.* 2005;365:2187–2192.
40. Sweeting MJ, Patel R, Powell JT, Greenhalgh RM, EVAR Trial Investigators. Endovascular repair of abdominal aortic aneurysm in patients physically ineligible for open repair: very long-term follow-up in the EVAR-2 randomized controlled trial. *Ann Surg.* 2017;266:713–719.

41. Lim S, Halandras PM, Park T, et al. Outcomes of endovascular abdominal aortic aneurysm repair in high-risk patients. *J Vasc Surg.* 2015;61:862–868.
42. Bush RL, Johnson ML, Hedayati N, et al. Performance of endovascular aortic aneurysm repair in high-risk patients: results from the Veterans Affairs National Surgical Quality Improvement Program. *J Vasc Surg.* 2007;45:227–233; discussion 233–235.
43. Lederle FA, Johnson GR, Wilson SE, Veterans Affairs Cooperative Study #, et al. 417 Investigators. Rupture rate of large abdominal aortic aneurysms in patients refusing or unfit for elective repair. *JAMA.* 2002;287:2968–2972.
44. Parkinson F, Ferguson S, Lewis P, South East Wales Vascular Network, et al. Rupture rates of untreated large abdominal aortic aneurysms in patients unfit for elective repair. *J Vasc Surg.* 2015;61:1606–1612.
45. IMPROVE trial investigators, Powell JT, Hinchliffe RJ, Thompson MM, et al. Observations from the IMPROVE trial concerning the clinical care of patients with ruptured abdominal aortic aneurysm. *Br J Surg.* 2014;101:216–224; discussion 224.
46. Reimerink JJ, van der Laan MJ, Koelemay MJ, et al. Systematic review and meta-analysis of population-based mortality from ruptured abdominal aortic aneurysm. *Br J Surg.* 2013;100:1405–1413.
47. Desgranges P, Kobeiter H, Katsahian S, Investigators ECAR, et al. Editor's Choice - ECAR (Endovasculaire ou Chirurgie dans les Anevrismes aorto-iliaques Rompus): a French randomized controlled trial of endovascular versus open surgical repair of ruptured aorto-iliac aneurysms. *Eur J Vasc Endovasc Surg.* 2015;50:303–310.
48. Veith FJ, Rockman CB. The recent randomized trials of EVAR versus open repair for ruptured abdominal aortic aneurysms are misleading. *Vascular.* 2015;23:217–219.
49. Zhang S, Feng J, Li H, et al. Open surgery (OS) versus endovascular aneurysm repair (EVAR) for hemodynamically stable and unstable ruptured abdominal aortic aneurysm (rAAA). *Heart Vessels.* 2016;31:1291–1302.
50. Budtz-Lilly J, Bjorck M, Venermo M, et al. Editor's Choice – The impact of centralisation and endovascular aneurysm repair on treatment of ruptured abdominal aortic aneurysms based on international registries. *Eur J Vasc Endovasc Surg.* 2018;56:181–188.
51. Chaikof EL, Dalman RL, Eskandari MK, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg.* 2018;67:2–77.e2.
52. Chuter TA, Faruqi RM, Sawhney R, et al. Endoleak after endovascular repair of abdominal aortic aneurysm. *J Vasc Surg.* 2001;34:98–105.
53. Buth J, Harris PL, van Marrewijk C, Fransen G. The significance and management of different types of endoleaks. *Semin Vasc Surg.* 2003;16:95–102.
54. van Marrewijk C, Buth J, Harris PL, et al. Significance of endoleaks after endovascular repair of abdominal aortic aneurysms: The EUROSTAR experience. *J Vasc Surg.* 2002;35:461–473.
55. Resch T, Ivancev K, Lindh M, et al. Persistent collateral perfusion of abdominal aortic aneurysm after endovascular repair does not lead to progressive change in aneurysm diameter. *J Vasc Surg.* 1998;28:242–249.
56. Gorich J, Rilinger N, Sokiranski R, et al. Leakages after endovascular repair of aortic aneurysms: classification based on findings at CT, angiography, and radiography. *Radiology.* 1999;213:767–772.
57. Gorich J, Rilinger N, Sokiranski R, et al. Treatment of leaks after endovascular repair of aortic aneurysms. *Radiology.* 2000;215:414–420.
58. Baum RA, Carpenter JP, Golden MA, et al. Treatment of type 2 endoleaks after endovascular repair of abdominal aortic aneurysms: comparison of transarterial and translumbar techniques. *J Vasc Surg.* 2002;35:23–29.
59. Hiramoto JS, Chang CK, Reilly LM, et al. Outcome of renal stenting for renal artery coverage during endovascular aortic aneurysm repair. *J Vasc Surg.* 2009;49:1100–1106.
60. Heredero AF, Stefanov S, del Moral LR, et al. Long-term results of femoro-femoral crossover bypass after endovascular aortouniliac repair of abdominal aortic and aortoiliac aneurysms. *Vasc Endovascular Surg.* 2008;42:420–426.
61. Choi SY, Lee DY, Lee KH, et al. Treatment of type I endoleaks after endovascular aneurysm repair of infrarenal abdominal aortic aneurysm: usefulness of N-butyl cyanoacrylate embolization in cases of failed secondary endovascular intervention. *J Vasc Interv Radiol.* 2011;22:155–162.
62. Eberhardt KM, Sadeghi-Azandaryani M, Worlicek S, et al. Treatment of type I endoleaks using transcatheter embolization with onyx. *J Endovasc Ther.* 2014;21:162–171.
63. Ameli-Renani S, Pavlidis V, Morgan RA. Early and midterm outcomes after transcatheter embolization of type I endoleaks in 25 patients. *J Vasc Surg.* 2017;65:346–355.
64. Schanzer A, Beck AW, Eagleton M, U.S., et al. Multicenter Fenestrated/ Branched Aortic Research Consortium. Results of fenestrated and branched endovascular aortic aneurysm repair after failed infrarenal endovascular aortic aneurysm repair. *J Vasc Surg.* 2020;72(3):849–858.
65. Ghouri M, Kraicer Z. Endoluminal abdominal aortic aneurysm repair: the latest advances in prevention of distal endograft migration and type 1 endoleak. *Tex Heart Inst J.* 2010;37:19–24.
66. Nabi D, Murphy EH, Pak J, Zarins CK. Open surgical repair after failed endovascular aneurysm repair: is endograft removal necessary? *J Vasc Surg.* 2009;50:714–721.
67. Sheehan MK, Ouriel K, Greenberg R, et al. Are type II endoleaks after endovascular aneurysm repair endograft dependent? *J Vasc Surg.* 2006;43:657–661.
68. Karthikesalingam A, Al-Jundi W, Jackson D, et al. Systematic review and meta-analysis of duplex ultrasonography, contrast-enhanced ultrasound or computed tomography for surveillance after endovascular aneurysm repair. *Br J Surg.* 2012;99:1514–1523.
69. Timaran CH, Ohki T, Rhee SJ, et al. Predicting aneurysm enlargement in patients with persistent type II endoleaks. *J Vasc Surg.* 2004;39:1157–1162.
70. Arko FR, Filis KA, Siedel SA, et al. Intrasac flow velocities predict sealing of type II endoleaks after endovascular abdominal aortic aneurysm repair. *J Vasc Surg.* 2003;37:8–15.
71. Arko FR, Rubin GD, Johnson BL, et al. Type-II endoleaks following endovascular AAA repair: preoperative predictors and long-term effects. *J Endovasc Ther.* 2001;8:503–510.
72. Scali ST, Vlada A, Chang CK, Beck AW. Transcaval embolization as an alternative technique for the treatment of type II endoleak after endovascular aortic aneurysm repair. *J Vasc Surg.* 2013;57:869–874.
73. Rhee R, Oderich G, Hertault A, et al. Multicenter experience in trans-lumbar type II endoleak treatment in the hybrid room with needle trajectory planning and fusion guidance. *J Vasc Surg.* 2020;72(3):1043–1049.
74. Wisselink W, Cuesta MA, Berends FJ, et al. Retroperitoneal endoscopic ligation of lumbar and inferior mesenteric arteries as a treatment of persistent endoleak after endoluminal aortic aneurysm repair. *J Vasc Surg.* 2000;31:1240–1244.
75. Carpenter JP, Lane 3rd JS, Trani J, et al. Refinement of anatomic indications for the Nellix System for endovascular aneurysm sealing based on 2-year outcomes from the EVAS FORWARD IDE trial. *J Vasc Surg.* 2018;68:720–730.e1.
76. Hiramoto JS, Reilly LM, Schneider DB, et al. Long-term outcome and reintervention after endovascular abdominal aortic aneurysm repair using the Zenith stent graft. *J Vasc Surg.* 2007;45:461–465; discussion 465–466.
77. Pitton MB, Schweitzer H, Herber S, et al. MRI versus helical CT for endoleak detection after endovascular aneurysm repair. *AJR Am J Roentgenol.* 2005;185:1275–1281.
78. van der Laan MJ, Bartels LW, Viergever MA, Blankenstein JD. Computed tomography versus magnetic resonance imaging of endoleaks after EVAR. *Eur J Vasc Endovasc Surg.* 2006;32:361–365.
79. Manning BJ, O'Neill SM, Haider SN, et al. Duplex ultrasound in aneurysm surveillance following endovascular aneurysm repair: a comparison with computed tomography aortography. *J Vasc Surg.* 2009;49:60–65.
80. Sandford RM, Bown MJ, Fishwick G, et al. Duplex ultrasound scanning is reliable in the detection of endoleak following endovascular aneurysm repair. *Eur J Vasc Endovasc Surg.* 2006;32:537–541.

81. AbuRahma AF, Welch CA, Mullins BB, Dyer B. Computed tomography versus color duplex ultrasound for surveillance of abdominal aortic stent-grafts. *J Endovasc Ther.* 2005;12:568–573.
82. Kanal E, Barkovich AJ, Bell C, et al. ACR Blue Ribbon Panel on MR Safety. ACR guidance document for safe MR practices. 2007 *AJR Am J Roentgenol.* 2007;188:1447–1474.
83. Asenbaum U, Schoder M, Schwartz E, et al. Stent-graft surface movement after endovascular aneurysm repair: baseline parameters for prediction, and association with migration and stent-graft-related endoleaks. *Eur Radiol.* 2019;29:6385–6395.
84. Resch T, Ivancev K, Brunkwall J, et al. Distal migration of stent-grafts after endovascular repair of abdominal aortic aneurysms. *J Vasc Interv Radiol.* 1999;10:257–264; discussion 265–266.
85. Wolf YG, Hill BB, Lee WA, et al. Eccentric stent graft compression: an indicator of insecure proximal fixation of aortic stent graft. *J Vasc Surg.* 2001;33:481–487.
86. Greenberg R, Fairman R, Srivastava S, Criado F, Green R. Endovascular grafting in patients with short proximal necks: an analysis of short-term results. *Cardiovasc Surg.* 2000;8:350–354.
87. Stanley BM, Semmens JB, Mai Q, et al. Evaluation of patient selection guidelines for endoluminal AAA repair with the Zenith Stent-Graft: the Australasian experience. *J Endovasc Ther.* 2001;8:457–464.
88. Oliveira-Pinto J, Oliveira N, Bastos-Goncalves F, et al. Long-term results of outside “instructions for use” EVAR. *J Cardiovasc Surg (Torino).* 2017;58:252–260.
89. Carroccio A, Faries PL, Morrissey NJ, et al. Predicting iliac limb occlusions after bifurcated aortic stent grafting: anatomic and device-related causes. *J Vasc Surg.* 2002;36:679–684.
90. Cochenne F, Becquemin JP, Desgranges P, et al. Limb graft occlusion following EVAR: clinical pattern, outcomes and predictive factors of occurrence. *Eur J Vasc Endovasc Surg.* 2007;34:59–65.
91. Fairman RM, Baum RA, Carpenter JP, et al. Phase II EVT Investigators. Limb interventions in patients undergoing treatment with an unsupported bifurcated aortic endograft system: a review of the Phase II EVT Trial. *J Vasc Surg.* 2002;36:118–126.
92. Woody JD, Makaroun MS. Endovascular graft limb occlusion. *Semin Vasc Surg.* 2004;17:262–267.
93. Ishibashi H, Ishiguchi T, Ohta T, et al. Late events and mid-term results after endovascular aneurysm repair. *Surg Today.* 2014;44:50–54.
94. Adu J, Cheshire NJ, Riga CV, et al. Strategies to tackle unrecognized bilateral renal artery occlusion after endovascular aneurysm repair. *Ann Vasc Surg.* 2012;26:1127.e1–7.
95. Mehta M, Cayne N, Veith FJ, et al. Relationship of proximal fixation to renal dysfunction in patients undergoing endovascular aneurysm repair. *J Cardiovasc Surg (Torino).* 2004;45:367–374.
96. Shintani T, Mitsuoka H, Atsuta K, et al. Thromboembolic complications after endovascular repair of abdominal aortic aneurysm with neck thrombus. *Vasc Endovascular Surg.* 2013;47:172–178.
97. Wever JJ, de Nie AJ, Blankensteijn JD, et al. Dilatation of the proximal neck of infrarenal aortic aneurysms after endovascular AAA repair. *Eur J Vasc Endovasc Surg.* 2000;19:197–201.
98. Cao P, Verzini F, Parlani G, et al. Predictive factors and clinical consequences of proximal aortic neck dilatation in 230 patients undergoing abdominal aorta aneurysm repair with self-expandable stent-grafts. *J Vasc Surg.* 2003;37:1200–1205.
99. Kapetanios D, Banafshe R, Jerkku T, et al. Current evidence on aortic remodeling after endovascular repair. *J Cardiovasc Surg (Torino).* 2019;60:186–190.
100. Oberhuber A, Buecken M, Hoffmann M, et al. Comparison of aortic neck dilatation after open and endovascular repair of abdominal aortic aneurysm. *J Vasc Surg.* 2012;55:929–934.
101. Sternbergh 3rd WC, Money SR, Greenberg RK, et al. Influence of endograft oversizing on device migration, endoleak, aneurysm shrinkage, and aortic neck dilation: results from the Zenith Multicenter Trial. *J Vasc Surg.* 2004;39:20–26.
102. Sampaio SM, Panneton JM, Mozes G, et al. AneuRx device migration: incidence, risk factors, and consequences. *Ann Vasc Surg.* 2005;19:178–185.
103. Hobbs SD, Kumar S, Gilling-Smith GL. Epidemiology and diagnosis of endograft infection. *J Cardiovasc Surg (Torino).* 2010;51:5–14.
104. Smeds MR, Duncan AA, Harlander-Locke MP, et al. Vascular Low-Frequency Disease Consortium. Treatment and outcomes of aortic endograft infection. *J Vasc Surg.* 2016;63:332–340.
105. Laser A, Baker N, Rectenwald J, et al. Graft infection after endovascular abdominal aortic aneurysm repair. *J Vasc Surg.* 2011;54:58–63.
106. Li HL, Chan YC, Cheng SW. Current evidence on management of aortic stent-graft infection: a systematic review and meta-analysis. *Ann Vasc Surg.* 2018;51:306–313.
107. Cernohorsky P, Reijnen MM, Tiellu IF, et al. The relevance of aortic endograft prosthetic infection. *J Vasc Surg.* 2011;54:327–333.
108. Maldonado TS, Rockman CB, Riles E, et al. Ischemic complications after endovascular abdominal aortic aneurysm repair. *J Vasc Surg.* 2004;40:703–709; discussion 709–710.
109. Rayt HS, Bown MJ, Lambert KV, et al. Buttock claudication and erectile dysfunction after internal iliac artery embolization in patients prior to endovascular aortic aneurysm repair. *Cardiovasc Interv Radiol.* 2008;31:728–734.
110. Lin PH, Bush RL, Chaikof EL, et al. A prospective evaluation of hypogastric artery embolization in endovascular aortoiliac aneurysm repair. *J Vasc Surg.* 2002;36:500–506.
111. Bratby MJ, Munneke GM, Belli AM, et al. How safe is bilateral internal iliac artery embolization prior to EVAR? *Cardiovasc Interv Radiol.* 2008;31:246–253.
112. Cynamon J, Lerer D, Veith FJ, et al. Hypogastric artery coil embolization prior to endoluminal repair of aneurysms and fistulas: buttock claudication, a recognized but possibly preventable complication. *J Vasc Interv Radiol.* 2000;11:573–577.
113. Farivar BS, Kalsi R, Drucker CB, et al. Implications of concomitant hypogastric artery embolization with endovascular repair of infrarenal abdominal aortic aneurysms. *J Vasc Surg.* 2017;66:95–101.
114. Moulakakis KG, Alexiou VG, Karaolanis G, et al. Spinal cord ischemia following elective endovascular repair of infrarenal aortic aneurysms: a systematic review. *Ann Vasc Surg.* 2018;52:280–291.
115. Najibi S, Steinberg J, Katzen BT, et al. Detection of isolated hook fractures 36 months after implantation of the Ancure endograft: a cautionary note. *J Vasc Surg.* 2001;34:353–356.
116. Zarins CK, Arko FR, Crabtree T, et al. Explant analysis of AneuRx stent grafts: relationship between structural findings and clinical outcome. *J Vasc Surg.* 2004;40:1–11.
117. Beebe HG, Cronenwett JL, Katzen BT, et al. Vanguard Endograft Trial Investigators. Results of an aortic endograft trial: impact of device failure beyond 12 months. *J Vasc Surg.* 2001;33: S55–63.
118. Carpenter JP, Anderson WN, Brewster DC, et al. Lifepath Investigators. Multicenter pivotal trial results of the Lifepath System for endovascular aortic aneurysm repair. *J Vasc Surg.* 2004;39:34–43.
119. Dias NV, Ivancev K, Malina M, et al. Strut failure in the body of the Zenith abdominal endoprosthesis. *Eur J Vasc Endovasc Surg.* 2007;33:507.
120. Roos JE, Hellinger JC, Hallet R, et al. Detection of endograft fractures with multidetector row computed tomography. *J Vasc Surg.* 2005;42:1002–1006.
121. Chaikof EL, Brewster DC, Dalman RL, et al. SVS practice guidelines for the care of patients with an abdominal aortic aneurysm: executive summary. *J Vasc Surg.* 2009;50:880–896.
122. Brenner DJ, Hall EJ. Computed tomography—an increasing source of radiation exposure. *N Engl J Med.* 2007;357:2277–2284.
123. Zhou W. Radiation exposure of vascular surgery patients beyond endovascular procedures. *J Vasc Surg.* 2011;53:39S–43S.
124. Sternbergh 3rd WC, Greenberg RK, Chuter TA, et al. Redefining post-operative surveillance after endovascular aneurysm repair: recommendations based on 5-year follow-up in the US Zenith multicenter trial. *J Vasc Surg.* 2008;48:278–284; discussion 284–285.
125. Patel R, Powell JT, Sweeting MJ, et al. The UK EndoVascular Aneurysm Repair (EVAR) randomised controlled trials: long-term follow-up and cost-effectiveness analysis. *Health Technol Assess.* 2018;22:1–132.

126. Verzini F, Romano L, Parlani G, et al. Fourteen-year outcomes of abdominal aortic endovascular repair with the Zenith stent graft. *J Vasc Surg.* 2017;65:318–329.
127. Lee JT, Greenberg JI, Dalman RL. Early experience with the snorkel technique for juxtarenal aneurysms. *J Vasc Surg.* 2012;55:935–946; discussion 945–946.
128. Moulakakis KG, Mylonas SN, Avgerinos E, et al. The chimney graft technique for preserving visceral vessels during endovascular treatment of aortic pathologies. *J Vasc Surg.* 2012;55:1497–1503.
129. Usai MV, Torsello G, Donas KP. Current evidence regarding chimney graft occlusions in the endovascular treatment of pararenal aortic pathologies: a systematic review with pooled data analysis. *J Endovasc Ther.* 2015;22:396–400.
130. Oderich GS, Greenberg RK, Farber M, Zenith Fenestrated Study Investigators, et al. Results of the United States multicenter prospective study evaluating the Zenith fenestrated endovascular graft for treatment of juxtarenal abdominal aortic aneurysms. *J Vasc Surg.* 2014;60:1420–1428. e1–5.
131. Gallitto E, Gargiulo M, Freyrie A, et al. The endovascular treatment of juxta-renal abdominal aortic aneurysm using fenestrated endograft: early and mid-term results. *J Cardiovasc Surg (Torino).* 2019;60:237–244.
132. Ryer EJ, Garvin RP, Webb TP, et al. Comparison of outcomes with coils versus vascular plug embolization of the internal iliac artery for endovascular aortoiliac aneurysm repair. *J Vasc Surg.* 2012;56:1239–1245.
133. Hosaka A, Kato M, Kato I, et al. Outcome after concomitant unilateral embolization of the internal iliac artery and contralateral external-to-internal iliac artery bypass grafting during endovascular aneurysm repair. *J Vasc Surg.* 2011;54:960–964.
134. Lee WA, Nelson PR, Berceli SA, et al. Outcome after hypogastric artery bypass and embolization during endovascular aneurysm repair. *J Vasc Surg.* 2006;44:1162–1168; discussion 1168–1169.
135. Schneider DB, Matsumura JS, Lee JT, et al. Prospective, multicenter study of endovascular repair of aortoiliac and iliac aneurysms using the Gore Iliac Branch Endoprosthesis. *J Vasc Surg.* 2017;66:775–785.
136. van Sterkenburg SM, Heyligers JM, van Bladel M, Dutch IBE Collaboration, et al. Experience with the GORE EXCLUDER iliac branch endoprosthesis for common iliac artery aneurysms. *J Vasc Surg.* 2016;63:1451–1457.
137. Friedman SG, Wun H. Hypogastric preservation with Viabahn stent graft during endovascular aneurysm repair. *J Vasc Surg.* 2011;54:504–506.
138. Lobato AC. Sandwich technique for aortoiliac aneurysms extending to the internal iliac artery or isolated common/internal iliac artery aneurysms: a new endovascular approach to preserve pelvic circulation. *J Endovasc Ther.* 2011;18:106–111.
139. Kotsis T, Tsanis A, Sfyroeras G, et al. Endovascular exclusion of symptomatic bilateral common iliac artery aneurysms with preservation of an aneurysmal internal iliac artery via a reverse-U stent-graft. *J Endovasc Ther.* 2006;13:158–163.
140. Thurston JS, Camara A, Alcasid N, et al. Outcomes and cost comparison of percutaneous endovascular aortic repair versus endovascular aortic repair with open femoral exposure. *J Surg Res.* 2019;240:124–129.
141. Trooboff SW, Wanken ZJ, Gladders B, et al. Longitudinal spending on endovascular and open abdominal aortic aneurysm repair. *Circ Cardiovasc Qual Outcomes.* 2020;13:e006249.
142. Noll Jr RE, Tonnessen BH, Mannava K, et al. Long-term postplacement cost after endovascular aneurysm repair. *J Vasc Surg.* 2007;46:9–15; discussion 15.



Ruptured Aortoiliac Aneurysms and their Management

KONRAD SALATA and THOMAS F. LINDSAY

INTRODUCTION	977
EPIDEMIOLOGY	977
Incidence	977
Mortality of Ruptured Abdominal Aortic Aneurysms and Repairs	978
PATHOPHYSIOLOGY OF AORTIC RUPTURE	978
Biomechanical Analysis and Predicting Aortic Rupture	978
Role of Aortic Thrombus/Inflammation	979
CLINICAL FEATURES	980
Signs and Symptoms	980
Differential Diagnosis	980
Diagnostic Evaluation	981
Plain Radiographs	981
Ultrasound	981
Computed Tomography	981
Is THERE TIME for a COMPUTED TOMOGRAPHY SCAN IN RUPTURED ABDOMINAL AORTIC ANEURYSM?	981
INITIAL MANAGEMENT STRATEGIES	982
Patient Triage and Inter-Hospital Transfer	982
Permissive Hypotension	982
Protocol-Based Approach	982
Anatomic Suitability for Endovascular Ruptured Aneurysm Repair	982
Operative Preparation and Setup	982
OPERATIVE STRATEGIES: ENDOVASCULAR REPAIR	982
Initial Management Technique	984
Arterial Access and Aortic Occlusion Balloon	984
Choice of Anesthesia and Approach	984
Bifurcated Versus Aorto-Uni-Iliac Stent Grafts	984
Conversion to Open Repair	984
OPERATIVE STRATEGIES: OPEN REPAIR	984
Transperitoneal Approach	984
Retroperitoneal Approach	985
Operative Technique	985
Aortocaval Fistula	986
Autotransfusion	986
Hypothermia	986
Abdominal Closure	986
COMPLICATIONS OF RUPTURED ABDOMINAL AORTIC ANEURYSM REPAIR	986
Local Complications	986
Colonic Ischemia	986
Assessment for Abdominal Compartment Syndrome	987
Spinal Ischemia	987
Systemic Complications	987
Cardiac Complications	987
Respiratory Failure	987
Renal Dysfunction	987
Liver Failure	988
Multisystem Organ Failure	988
OUTCOMES OF RUPTURED ABDOMINAL AORTIC ANEURYSM REPAIR	988
Randomized Trials	988
Meta-Analyses of Randomized Trials	988
Observational Studies	989
Preoperative Predictors of Mortality	991
Postoperative Estimates of Survival	991
Predictors of Late Survival	991
Late Reinterventions	992
Rupture After Endovascular Aneurysm Repair	992
QUALITY OF LIFE	992
CHAPTER ALGORITHM	993

INTRODUCTION

Rupture of an abdominal aortic aneurysm (RAAA) conveys a mortality risk 5- to 10-fold higher vs. elective repair.^{1–4} A major decline in RAAA incidence is now evident in both North America and Europe (Fig. 76.1).^{5,6–9} Despite improvements in perioperative management, service centralization, open RAAA survival rates have only marginally improved. However, ruptured endovascular repair (REVAR) has been associated with improved outcomes, with reductions in mortality, major adverse cardiac events and improved long-term mortality.^{4,10–17} RAAA is an abdominal aortic aneurysm (AAA) with extraluminal blood on computed tomography (CT) or noted clinically at the time of surgery. A contained rupture refers to blood outside the aneurysm sac confined to the retroperitoneal space. A free rupture refers to bleeding directly into the peritoneal cavity. A symptomatic, nonruptured AAA is one with back pain or tenderness over the aorta on deep palpation but with an intact aneurysm on CT and at surgery. The pain is thought to be due to acute wall expansion, intramural hemorrhage, wall degeneration, or bleeding into the thrombus and is considered

a prelude to rupture. Symptomatic aneurysms are not associated with hypotension, and survival is much better than for RAAA, but worse than after elective repair.¹⁸ Symptomatic aneurysms require rapid diagnosis and urgent management to prevent rupture. Inclusion within RAAs data can artificially improve outcomes.¹⁹

The first successful RAAA reconstruction was by Henry Bahnson with a homograft in 1953.²⁰ By 1954 Cooley and DeBakey had treated six RAAA patients, with a 50% survival rate.²¹ Just as elective open aneurysm reconstruction was rapidly applied to ruptures, so too was endovascular aneurysm repair (EVAR), with Yusuf et al. reporting the first REVAR in England in 1994²² (see Ch. 75, Aortoiliac Aneurysms: Endovascular Treatment).

EPIDEMIOLOGY

Incidence

The true incidence of RAAA has historically been difficult to quantify due to the inability to quantify death outside of

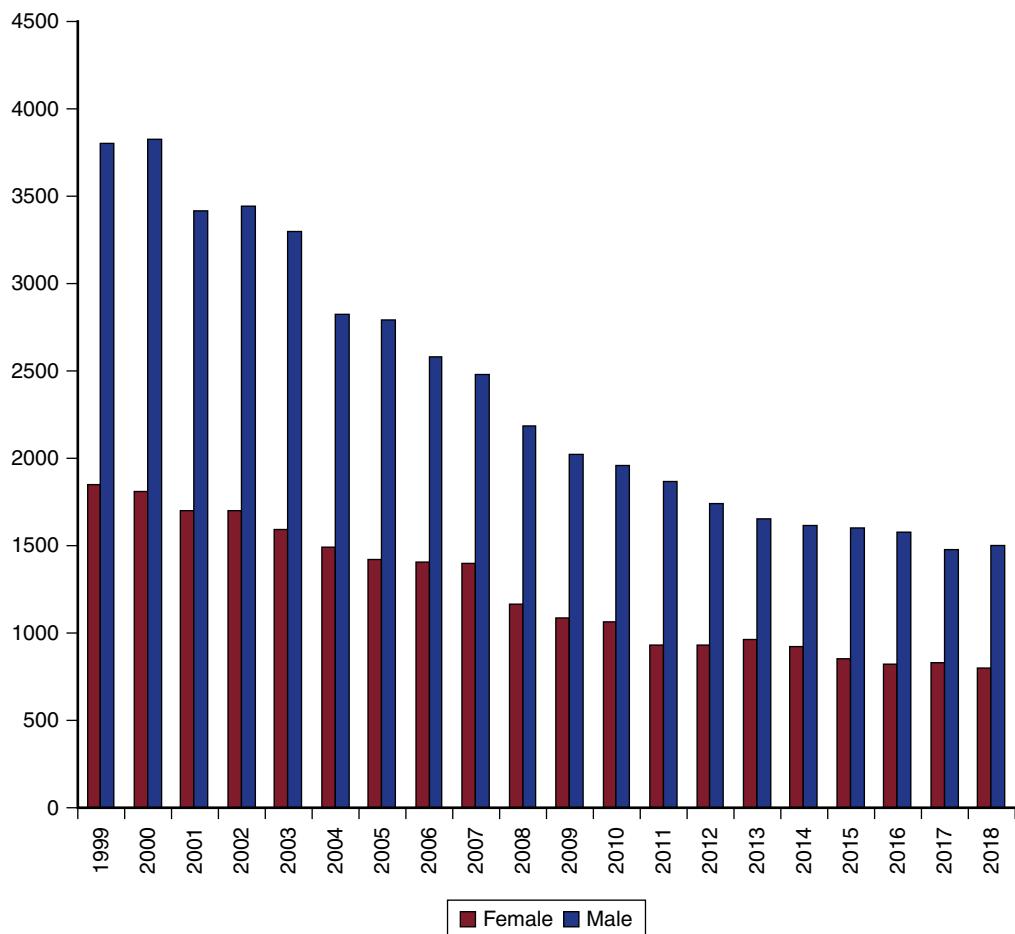


Figure 76.1 Ruptured abdominal aortic aneurysm (RAAA) death rates per 100,000 population between 1999 and 2018 in United States for men and women between the ages of 55 and 94 years. (From Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying Cause of Death 1999–2018 on CDC WONDER Online Database, released in 2020. Data are from the Multiple Cause of Death Files, 1999–2018, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Available at: <http://wonder.cdc.gov/ucd-icd10.html>)

hospital. The incidence of RAAA was thought to be increasing at the turn of the century based on English, Welsh and Swedish population-based studies.^{3,23} However, contemporary studies from the past two decades have shown a decline in the incidence of ruptured (and intact) AAA in most Western populations. In Germany, the decline in incidence of RAAA repair was 30% from 2005 to 2014.²⁴ A population-based analysis of the Swedvasc registry from 1994 to 2014 revealed a 25% decrease in RAAA repairs.²⁵ Analysis of data from the Swedish National Patient Registry revealed that lower socio-economic status and educational level were associated with higher odds for presentation with RAAA.²⁶ Population-based research using Canadian data demonstrated a 69% decrease in RAAA repairs from 2003 to 2016,²⁷ and confirmed significant decreases across all ages, in men,²⁸ and at non-teaching hospitals.²⁹ English Hospital Episode Statistics data from 2002 to 2015 confirmed these sex differences in RAAA repair rates.³⁰ In Medicare beneficiaries from 1995 to 2008, AAA-related deaths halved, with the greatest decline seen in patients older than 80 years.⁹ Data from the Centers for Disease Control and Prevention reported that in 1999–2018 deaths from RAAA dropped by 60% across all ages and in both sexes (Fig. 76.1). Similarly, data from the US National Vital Statistics Registry demonstrated a 70% decrease in incidence of deaths due to RAAA.³¹ Mortality varied significantly by geographic region both in Vital Statistics and VQI data.³² Deaths are more frequent in men compared with women and the peak age for females was older than for men.

Population screening has been shown to reduce AAA-related deaths,³³ but the decline in mortality due to RAAA began before widespread population screening. EVAR may have led to more elective AAA repairs in older and less fit patients, thereby reducing the at-risk population for RAAA.³⁴ The greatest absolute reduction in RAAA has come from a decline in the prevalence of intact AAA in the Swedish³⁵ and United Kingdom (UK) screening programs, where the detection rate was 1.7%, less than the 4% expected.³⁶ This has been attributed to decreased levels of smoking and improved control of cardiovascular risk factors.^{7,34,37,38}

Mortality of Ruptured Abdominal Aortic Aneurysms and Repairs

In two population-based series of RAAA, overall mortality rates were 89% and 86%.^{12,39} A recent population-based Swedish study reported a 76.5% overall mortality from 2011–2015, with a 36% repair rate.²⁶ The Danish national registry noted a decrease in operative mortality from 51% to 42% from 1994 to 2008, related to centralization of services and better pre-hospital care. Vascunet outcomes data for 7040 RAAA repairs noted a mortality rate of 31.6%, with the rate declining by 4.2% between 2005 and 2009 attributed to EVAR.⁴⁰ German population-based data examining more than 20,000 RAAA repairs from 2005 to 2014 noted operative mortality of 40%.²⁴ Data from 1994 to 2014 from the Swedvasc registry demonstrated a reduction in RAAA operative mortality from 38 to 28%.²⁵ Comparison of English and American databases from

2005 to 2010 noted that intervention for RAAA was offered to 80% in the US (21% EVAR) vs. only 58% in the UK (8.5% EVAR). Postintervention mortality was similar at 41.6% and 41.8%.¹⁵ A more recent study examining this comparison revealed intervention rates of 91% and 75% in the US and UK, with in-hospital mortalities of 45% and 35%, respectively.⁴¹ Other studies from the US have confirmed these reductions in operative morality for RAAA.

The high postoperative mortality after aortic rupture is related to a high incidence of myocardial infarction, colon ischemia, renal failure, and multiple organ failure (MOF). The synergistic effect of the total body ischemia caused by hemorrhagic shock and the lower torso ischemia that occurs during repair, followed by reperfusion secondary to resuscitation and aortic unclamping, has been proposed to explain the high incidence of MOF and mortality after repair.^{42,43} EVAR minimizes the ischemic insult induced by aortic clamping, and RAAAs anatomically suitable for EVAR have the lowest mortality and complication rates.^{44,45}

PATHOPHYSIOLOGY OF AORTIC RUPTURE

Aneurysm rupture represents failure of the aortic wall to bear the load of the blood pressure. Aneurysmal aortic wall is weaker than the normal structure (65 N/cm² vs. 121 N/cm² for aneurysmal vs. normal aortic wall).^{46,47} Laplace's law (wall tension is proportional to radius times pressure) relates wall tension to pressure and emphasizes the importance of aneurysm size but does not account for complex AAA geometry or for regional changes in wall strength that may be weakened secondary to localized inflammatory processes that are part of the pathophysiology of aneurysm formation. Approximately 10% of AAAs rupture below the repair threshold.⁴⁸

Biomechanical Analysis and Predicting Aortic Rupture

Finite element analysis has been applied to AAAs to estimate regional variations in peak wall stress (PWS) for many small segments of the entire aortic wall using CT scan data, and provides a visual representation of PWS variability. Early 3D representations of PWS noted that the posterior wall of the aorta had higher values corresponding to sites where clinical observations and autopsy studies document the rupture sites.^{49–53} Newer computational models include an analysis of flow, shear stress, growth and remodeling theory that allows evolving wall thickness, stiffness, regional heterogeneity, and fluid–structure interactions within the aneurysm sac to be analyzed.^{54,55} Areas of low shear stress and increased thrombus deposition have been identified at sites of aortic rupture⁵⁶ (Fig. 76.2). Recently both high and low fidelity models of peak wall rupture risk (PWRR) were found to be better than diameter alone in predicting rupture risk. While computational models have increased our understanding of biomechanical factors, they have yet to become routine in clinical practice.^{57,58}

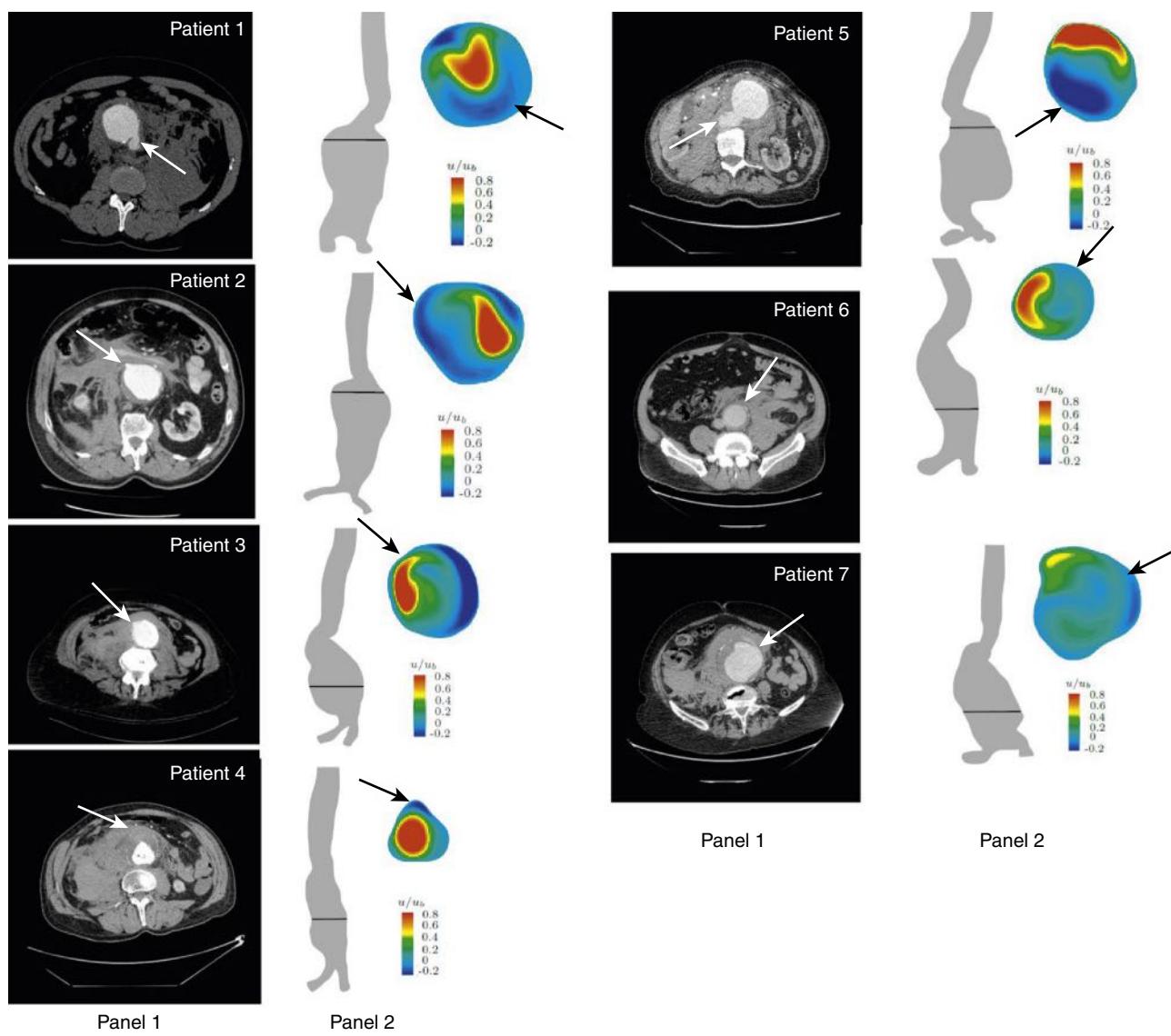


Figure 76.2 Panel 1: Axial computed tomography angiography (CTA) images of seven ruptured abdominal aortic aneurysms (RAAAs), indicating the location of rupture (white arrows). Panel 2: Anterior–posterior AAA flow channel silhouettes, indicating level of rupture (black line), and cross-sectional images of normalized velocity profiles, indicating the location of rupture (black arrows). (From Boyd AJ, Kuhn DC, Lozowy RJ, Kulbisky GP. Low wall shear stress predominates at sites of abdominal aortic aneurysm rupture. *J Vasc Surg*. 2016;63(6):1613–1619.)

Role of Aortic Thrombus/Inflammation

In 1965 Martin surmised that as an aneurysm develops, it becomes lined with thrombus, which weakens it by interfering with nutrition of that wall segment.⁵⁹ Schurink et al.⁶⁰ confirmed that intraluminal thrombus does not reduce pressure near the aneurysm wall, using a pressure transducer during open AAA repair. Vorp et al.⁶¹ noted localized hypoxia in regions of thicker thrombus leading to localized wall neovascularization, inflammation, and regional wall thinning. Hypoxia also affects the function of vascular smooth muscle cells, causing them to secrete more collagenase than in normoxic conditions, with less elastin and collagen production.^{50,52,53} Autopsy studies of patients who died of infrarenal RAAAs noted that 80% of ruptures occurred at the site of mural thrombus.⁶² CT studies of patients admitted

with rupture showed that most occurred through the thrombus or at its edge. Others argue that ruptures are caused by fissures in the intraluminal thrombus, due to proteolytic enzymes on the luminal surface of the clot.⁶³ A Dutch report,⁶³ although accepting a role for fissure formation, confirmed that intraluminal thrombus thickness was associated with vascular smooth muscle cell apoptosis (or cell death), elastin degradation, and high levels of matrix metalloproteinase 2 and correlated with aneurysm rupture. A prospective MRI study of infrarenal AAAs, identified a subset of patients with inflammatory activity noted on the MRI (Fig. 76.3). Those AAAs grew faster and were more likely to rupture compared to those where inflammatory activity was absent. The specific mechanisms that contributed to the activity observed have yet to be defined.^{5,64}

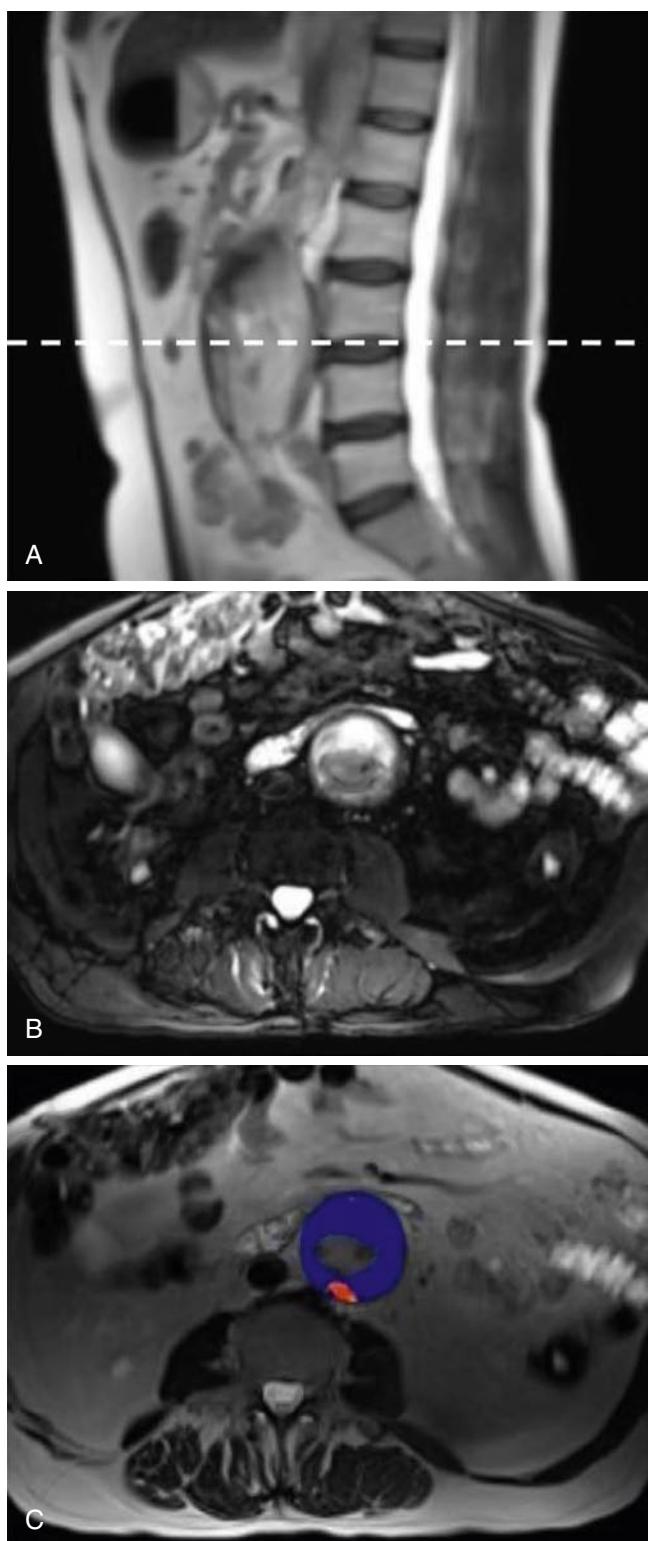


Figure 76.3 MRI of Abdominal Aortic Aneurysm. (A) T2-weighted HASTE (Half Fourier Acquisition Single Shot Turbo Spin Echo) sequence in the sagittal plane. (B) Cross-sectional image (dashed line in A) using a T2-weighted fat-saturated sequence to highlight intraluminal thrombus (white) within the aneurysm. (C) T2 map (blue) overlying the T2-weighted HASTE sequence (B), demonstrating enhancement of the posterior aneurysm wall with ultra-small super-paramagnetic particles of iron oxide (USPIO) (red). (From MA3RS Study Investigators, Newby D, Forsythe R, McBride O, et al. Aortic wall inflammation predicts abdominal aortic aneurysm expansion, rupture, and need for surgical repair. *Circulation.* 2017;136(9):787–797.)

CLINICAL FEATURES

Signs and Symptoms

The classic presentation of RAAA includes the triad of acute-onset abdominal/back pain, hypotension, and a pulsatile abdominal mass. Severe and unremitting back pain is caused by rupture of the aneurysm into the retroperitoneum. The pain may radiate to the back, testes, inguinal canal, or rectum. On examination, the patient is frequently pale, diaphoretic, and hypotensive with a tender, pulsatile abdominal mass. Flank ecchymosis is a late sign.

Differential Diagnosis

In patients older than 50 years with hypotension and/or syncope, consideration of RAAA is critical. The differential diagnosis may include renal colic, diverticulitis, pancreatitis, gastrointestinal hemorrhage, myocardial infarction, and perforated ulcer. The recognition of RAAA in the early stages can be difficult. Presentation can range from sudden onset pain and hypotension to slowly increasing pain over days as the AAA gradually stretches and ruptures. In this age group, chronic back problems are common and vertebral erosion from rupture can be mistaken for exacerbation of long-standing back problems.^{65–67}

Among those subsequently diagnosed with an RAAA, only 23% had a definitive and immediate diagnosis of RAAA made by the first examining physician.^{68,69} The rate of incorrect diagnosis ranges from 16% to 60%, and one study found misdiagnosis is associated with a median 4.8 hour delay to surgical intervention associated with misdiagnosis, but this did not result in excess mortality.^{70,71} The most common misdiagnoses were renal colic, perforated viscus, diverticulitis, gastrointestinal hemorrhage, and ischemic bowel. The initial manifestation of renal colic occurs infrequently in patients older than 60 years. The classic triad was present in only 9% of the misdiagnosed group compared with 34% of the correctly diagnosed group. The presence of a pulsatile mass was identified in 72% of those correctly diagnosed but in only 26% of the misdiagnosed patients. A recent study of Medicare beneficiaries from 2007 to 2014, including 17,963 with RAAA demonstrated a 3.4% missed diagnosis rate.⁷² Significant predictors of missed diagnosis with discharge home included female sex, Black ethnicity and emergency department discharges within 1 year of presentation, and comorbid end-stage renal disease (ESRD), dementia, depression, hypertension, coronary disease and chronic obstructive pulmonary disease (COPD) were associated with missed diagnosis.⁷³

Rare presentations include rupture into an adjacent structure. Acute gastrointestinal bleed can occur due to a primary aortoduodenal fistula. An aortocaval fistula presents as a pulsatile abdominal mass, machinery-like bruit, or thrill with elevated jugular venous pressure and new-onset acute congestive heart failure. Cauda equina syndrome,⁷⁴ lower extremity motor deficit,⁷⁵ incarcerated inguinal hernia,⁷⁶ and phlegmasia cerulea dolens⁷⁷ are other rare manifestations.

Diagnostic Evaluation

Plain Radiographs

Although the use of plain radiography is currently rare, a retrospective review of plain films of patients with RAAAs showed evidence of the diagnosis on 90% of the films.⁷⁸ Enlargement of a calcified aortic wall beyond normal limits was seen in 65%, and loss of a psoas shadow from retroperitoneal hemorrhage was identified in 75%.

Ultrasound

Bedside ultrasound in the emergency department by trained emergency physicians has led to its use in cases of suspected RAAA. Focused assessment with sonography in trauma (FAST) protocols can rapidly identify fluid collections and direct further trauma care.^{73,79} When ultrasound is used in patients with back pain, abdominal pain, or other indication of AAA, it can identify aortic aneurysms with high sensitivity, specificity, and positive and negative predictive values.^{80,81} No large prospective studies have been conducted, although with appropriate training the use of ultrasound to quickly assess patients for the presence of AAA is likely beneficial as it directs rapid investigation and therapy. It is not sufficiently accurate to exclude rupture,^{80,82} and is consistent with rupture in only 51% of cases.^{73,80,82}

Computed Tomography

The most accurate method for diagnosis of RAAA is CT. While non-contrast CT can identify retroperitoneal hemorrhage associated with RAAA, scanning with contrast enhancement is ideal to plan either open surgical repair (OSR) or EVAR (Fig. 76.4).

Proper timing of contrast injection reduces the contrast volume required, lessening its renal impact. Suspected RAAA patients going to CT should be accompanied and monitored for acute deterioration.

When evidence of retroperitoneal blood with an AAA is used as the “gold standard” for diagnosis of RAAA on CT, it is 77% sensitive and 100% specific.⁸³ Its positive and negative predictive values are 100% and 89%.⁸⁴ In the Amsterdam Acute Aneurysm (AJAX) study, agreement on CT diagnosis of RAAA was only moderate in five observers, agreement on suitability for EVAR was only fair in vascular surgeons and radiologists experienced in EVAR.⁸⁵

Is there time for a computed tomography scan in ruptured abdominal aortic aneurysm?

The delay between the initial manifestation of RAAA and the time to death has been studied to determine whether sufficient time exists to perform a CT scan and to evaluate patients’ suitability for EVAR. The time from onset of symptoms to death for patients managed conservatively was a median of 16 hours.⁸⁶ Only 13% died within 2 hours of hospital admission, suggesting that sufficient time exists for most patients to undergo CT scanning and evaluation for EVAR. For patients offered intervention, a door to intervention time of less than 90 minutes has not been shown to improve mortality.⁸⁷ A small number of patients in both the Immediate Management of the Patient with Rupture: Open Versus Endovascular Repair (IMPROVE) and the Amsterdam Acute Aneurysm randomized controlled trials (RCTs) were too unstable for CT scanning and required immediate transfer to the operating room.⁸⁸ Prospective data from the IMPROVE trial demonstrated that

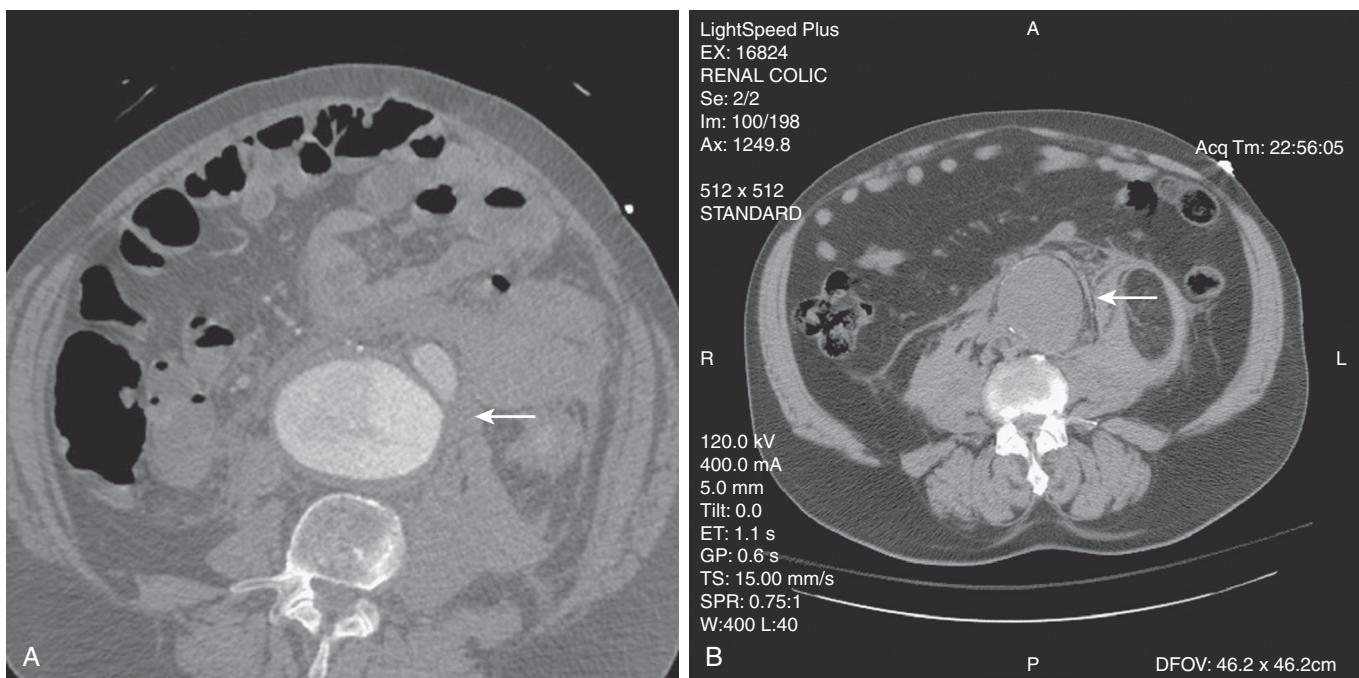


Figure 76.4 (A) Frank rupture of an infrarenal abdominal aortic aneurysm with contained extravasation (arrow).

(B) Computed tomography scan of a ruptured abdominal aortic aneurysm. Note the pattern of stranding of blood into the tissues (arrow). No contrast material was used, and the scan was performed for the diagnosis of renal colic.

90% to 97% of patients had a CT scan prior to intervention and the time to arrival at the operating room was 25 minutes shorter in the EVAR group vs. OSR despite the requirement for a contrast-enhanced CT scan.⁸⁹ Thus, for the majority of patients who are stable on arrival at a center where definitive care will be carried out, a prompt CT scan does not adversely affect mortality.^{86,90} A protocol for priority management of RAAA may significantly shorten the time to definitive therapy despite the CT scan requirement.^{91,92}

INITIAL MANAGEMENT STRATEGIES

Patient Triage and Inter-Hospital Transfer

RAAA is a surgical emergency, and when the diagnosis is being considered, immediate vascular surgery consultation is critical. Rural hospitals without vascular surgery expertise have a higher burden of RAAA patients and more commonly do not offer intervention.^{93,94} Interhospital patient transfer increases delays to the operating room, although most studies demonstrate that transferred patients do not have a higher but in fact lower mortality.^{90–92,94} VQI registry data showed no mortality difference in those with door to intervention times less than 90 minutes compared to those greater than 90 minutes. However, high-volume centers, teaching centers, and high bed capacity hospitals have significantly lower mortality for RAAA patients.^{15,93,94}

Permissive Hypotension

Preoperative resuscitation of RAAA patients with hypotension must be judicious.^{89,95–99} Large volumes of intravenous fluids raise blood pressure, causing further hemorrhage by overcoming the tamponade, result in hemodilution, coagulopathy, hypothermia, and acidosis, and further deterioration.¹⁰⁰ Protocols that restrict aggressive fluid resuscitation in hypotensive trauma patients with hemorrhagic shock improve survival so that permissive hypotension for RAAA patients is recommended.¹⁰¹ Fluid resuscitation should be sufficient to maintain consciousness, minimize organ ischemia, prevent ST depression, and maintain a systolic pressures of 70 to 80 mm Hg.^{96,102} Contemporary algorithms for management of RAAA patients include permissive hypotensive resuscitation.¹⁰⁰ Aggressive volume resuscitation before proximal aortic control is a predictor of increased postoperative mortality.^{98,99} The IMPROVE trial demonstrated that those with the lowest BP had the highest mortality and increasing SBP to greater than 70 mm Hg was beneficial.⁸⁹ Observational studies also suggest that increased fluid administration prior to aortic control increased mortality.¹⁰² Implementation of a controlled hypotension strategy in a regional ambulance service for patients with hypotension, in which only 27% had a final diagnosis of RAAA, demonstrated the overall risk of harm was low.⁹⁸ Evidence regarding resuscitation with blood vs. crystalloids is limited; if blood is available, it should accompany the patient during transfer and can be given to maintain consciousness.

Protocol-Based Approach

RAAA care begins with early identification by the emergency room staff, and rapid notification of the vascular surgeon/team^{91,102,103} (Fig. 76.5). While an ER ultrasound can identify an AAA and retroperitoneal hematoma, a fine cut, low contrast volume CT scan to assess neck diameter, angulation, and iliac size is of critical importance after blood work including a cross-match.¹⁰³ Hemodynamically unstable patients can be directly transferred to the operating room without a preoperative CT scan for balloon control with either an EVAR or conversion to OSR as needed.¹⁰² EVAR for RAAA requires a preoperative contrast CT scan. EVAR obstacles are anatomic suitability, availability of staff and equipment, feasibility of treating hemodynamically stable and unstable patients, and ability of the care team to manage unexpected scenarios under emergent circumstances. One key factor is awareness among the emergency department staff of the diagnosis of RAAA and early notification of the on-call vascular surgeon/team.^{16,92,103,104}

Anatomic Suitability for Endovascular Ruptured Aneurysm Repair

The proportion of RAAA patients suitable for EVAR varied from 47% to 67% in two meta-analyses.^{105,106} RAAs have larger infrarenal aortic diameters and shorter neck lengths, which impact the percentage suitable for EVAR.^{107,108} The success of EVAR on RAAA outcomes has been examined in patients with favorable vs. unfavorable aortic neck morphology.^{105,106,109,110} Data from the IMPROVE trial demonstrated that shorter neck lengths were associated with higher mortality in both open and EVAR patients.¹¹¹ For every 15-mm increase in neck length the mortality dropped by approximately 20%. A longer neck in RAAA facilitated both open (with an easier clamp site) and EVAR (improved proximal seal). The relationship between neck length and outcome may be a key variable that explains the discrepancy in RAAA outcomes between population-based data and randomized trials.¹¹¹

Operative Preparation and Setup

The operating room should be equipped for both EVAR and OSR. Anesthesia, nursing, and technical personnel can simultaneously and rapidly prepare the patient for intervention. Large-bore access, insertion of an arterial line, and placement of a Foley catheter can be done simultaneously. The patient is prepared and draped (including one brachial artery site) awake for both EVAR and open conversion. Local anesthesia can be infiltrated and ultrasound used to obtain percutaneous access for balloon control, then EVAR or open repair can proceed with agents designed to have minimal effect on blood pressure.

OPERATIVE STRATEGIES: ENDOVASCULAR REPAIR

The role of EVAR for the treatment of RAAA management is increasing, and is the preferred method of therapy for

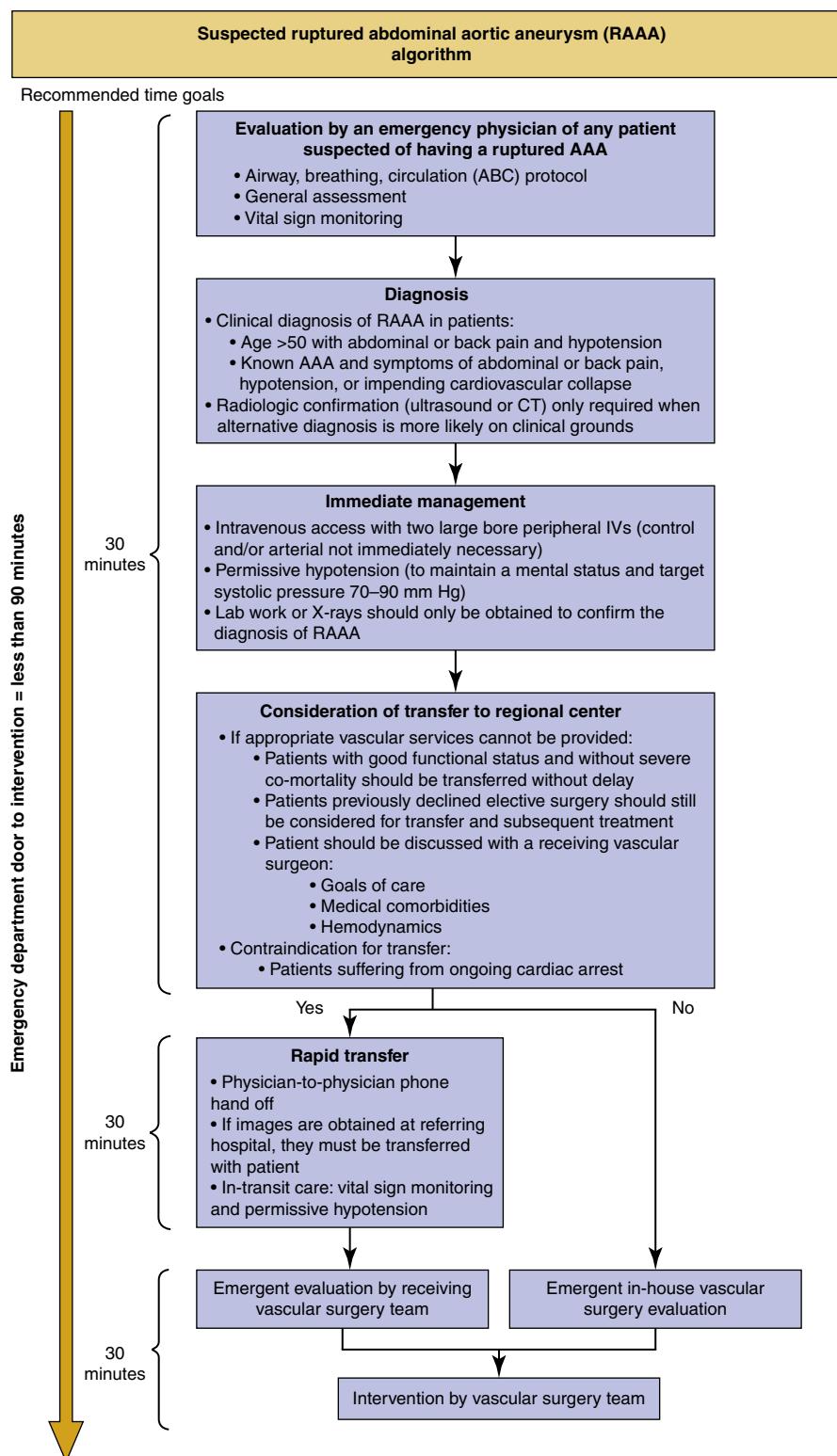


Figure 76.5 Algorithm for management of patients with suspected or confirmed ruptured abdominal aortic aneurysm. CT, computed tomography; IVs, intravenous lines. (From Chaikof EL, et al. The society for vascular surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg*. 2018;67(1):2–77.e2.)

appropriate anatomic candidates. Within the United States¹¹² and China,¹¹³ 55% of RAAAs were repaired by REVAR in 2015 and 2013, respectively.¹¹³ Uptake in other countries has been slower, with 30% of RAAA repairs conducted in

Sweden,²⁵ Canada,²⁹ Germany,²⁴ and Portugal¹¹⁴ done by EVAR. A population-based Canadian study has demonstrated higher uptake of REVAR among older patients and women, as well as statistically significant increases in EVAR uptake at

non-teaching hospitals from 2003 to 2016.²⁹ NIS data noted that EVAR was performed with higher percentages in teaching vs. urban vs. rural hospitals, and nonoperative therapy was highest in rural hospitals.⁹⁴ After age 80, the rate of OSR dropped and the rate of no intervention increased. A Canadian study has shown REVAR uptake to be highest among women, the elderly, and at non-teaching hospitals from 2003 to 2016.²⁹

Initial Management Technique

Arterial Access and Aortic Occlusion Balloon

A Cochrane meta-analysis of randomized studies has not shown any advantage of percutaneous femoral access over femoral cutdown for arterial access for elective EVAR.¹¹⁵ The access literature regarding access for REVAR is sparser than in the elective context. A single population based study of 502 patients identified from NSQIP data from 2011 to 2015 demonstrated no significant differences in mortality, wound complications, length of stay (LOS) or operative time between the two approaches.¹¹⁶ After local anesthesia and femoral access, a stiff ipsilateral wire is placed for device delivery. A 12–16 F by 45 cm sheath is advanced over the stiff wire and parked above the renal vessels (Fig. 76.6). In hemodynamically unstable patients a compliant aortic occlusion balloon can be partially or fully inflated as needed in the supraceliac abdominal aorta under fluoroscopic guidance.^{103,117,118} The sheath holds the balloon in place and needs to be secured by a team member. A retrospective single-center study of unstable RAAAs demonstrated that balloon occlusion reduced intraoperative mortality to 19% compared to 34% for conventional open cross-clamp; however, 30-day and in-hospital mortality rates were not significantly different (69% vs. 77%).¹¹⁹ The use of resuscitative endovascular balloon occlusion of the aorta (REBOA) for initial stabilization of RAAA patients has been the subject of some recent debate, but has not been well studied in the RAAA setting. A systematic review of the literature identified 50 non-randomized studies of which half were case series or case reports, and the remainder small cohort studies with small sample sizes and high risk of bias.¹²⁰ Pooled mortality among 396 REBOA patients was similar to that of conventional cross-clamp, at 39.1%. Iatrogenic aortic injury occurred in 6.4% of patients.

Choice of Anesthesia and Approach

Local anesthesia with conscious sedation allows maintenance of “sympathetic tone” in hemodynamically patients. Weak or absent femoral pulses can make percutaneous access difficult, but can be aided by ultrasound and micropuncture techniques. The advantages of local anesthesia must be balanced by the potential difficulties with incoherent and uncooperative patients.^{89,92} In hemodynamically unstable patients, the procedure can be started under local anesthesia, then converted to general anesthesia after REVAR for sheath removal and femoral repair.¹²¹ Local anesthesia for EVAR in the IMPROVE trial greatly reduced the 30-day mortality compared with general anesthesia (adjusted OR of 0.27).⁸⁹ This benefit has been confirmed by studies using NSQIP,^{122,123} VQI,¹²⁴ and the UK

National Vascular Registry data.¹²⁵ The most conservative adjusted hazard ratio from these studies was 0.70.¹²⁴ Patients >75 and unstable patients derived a smaller, but still statistically significant benefit.^{122,124}

Bifurcated Versus Aorto-Uni-Iliac Stent Grafts

Choice of stent graft is determined by the patient's aortoiliac morphology with no evidence to suggest superiority of one stent-graft manufacturer over another for REVAR.¹²⁶ An aorto-uni-iliac configuration with a fem-fem cross-over can be advantageous if the contralateral gate cannot be accessed expeditiously or significant unilateral occlusive disease or tortuosity exist. Maintaining pelvic perfusion with at least one internal iliac artery patent is recommended. Use of aorto-uni-iliac devices for EVAR of RAAA has similar outcomes to bifurcated stent grafts.^{127,128} However, hemodynamically stable patients may be better served with modular or bifurcated grafts.¹²⁹

Conversion to Open Repair

The IMPROVE trial reported a 2.67% conversion rate among patients in whom REVAR was started.¹³⁰ When OSR or conversion is needed, the aortic occlusion balloon is invaluable for hemodynamic stability. During laparotomy, it is crucial to maintain the position of the balloon and sheath to prevent prolapse into the AAA. Conversion after stent-graft deployment requires a tailored approach. For IA endoleaks, the suprarenal stent can be left in place to avoid aortic tearing. For IB endoleaks, an interposition graft can be sewn to the endograft.

OPERATIVE STRATEGIES: OPEN REPAIR

Transperitoneal Approach

This approach allows safe, rapid, and effective proximal aortic control at the supraceliac, suprarenal, or infrarenal aorta and distal control of the iliac or even femoral vessels (see Ch. 56, Abdominal Vascular Exposures).^{96,131} After supraceliac clamping, the infrarenal aortic neck is dissected and the clamp may be repositioned to the suprarenal or infrarenal aortic neck before or after the proximal anastomosis is completed, trying to minimize visceral ischemic time. Supraceliac clamping induces ischemic injuries to the liver, bowel, and kidneys, which, in addition to the injury induced by hemorrhagic shock, may contribute to the development of postoperative MOF.^{43,132} Supraceliac unclamping requires coordination with the anesthesia team to avoid sudden hypotension. Supraceliac control is beneficial for uncontrolled hemorrhage when immediate aortic control is needed, and it helps to avoid the renal and inferior mesenteric vein injuries that occur with blind retroperitoneal dissection in the face of large bleeding retroperitoneal hematoma.

For RAAA with clear CT evidence of suprarenal extension, a thoracoabdominal incision allows rapid access to the aorta above the diaphragm. Medial visceral rotation is carried out for visceral aortic exposure, and standard techniques are used to reconstruct the visceral segment.

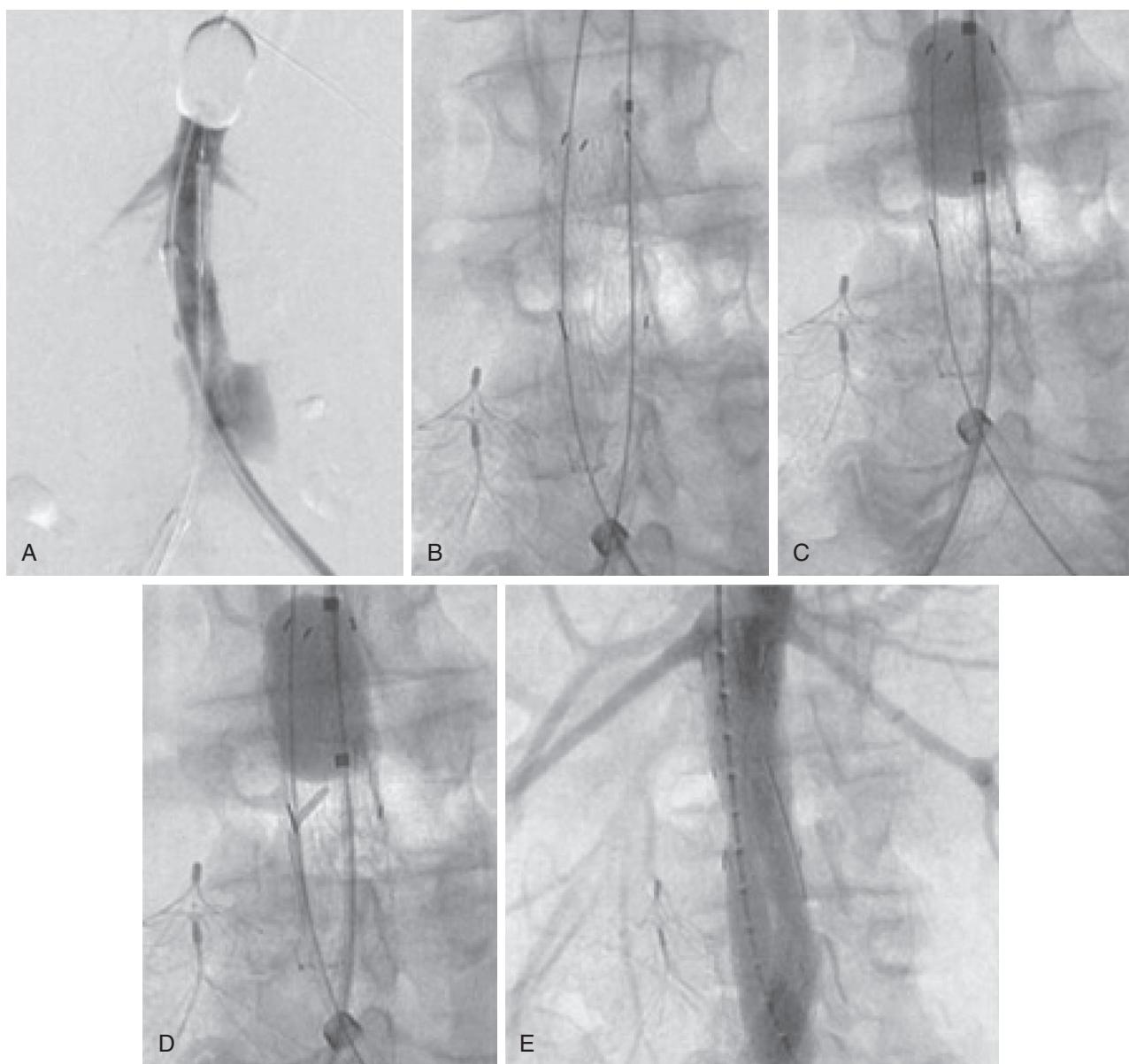


Figure 76.6 Managing the Aortic Occlusion Balloon During Stent-Graft Deployment. (A) The inflated suprarenal aortic occlusion balloon is advanced through the left femoral approach, the stent-graft main body is advanced through the right femoral approach, and arteriography is performed through the left femoral sheath supporting the occlusion balloon. (B) The aortic occlusion balloon is deflated and retracted from the aortic neck, and the stent-graft main body is subsequently deployed. This avoids trapping of the compliant aortic occlusion balloon between the aortic neck and the stent graft. (C) In hemodynamically unstable patients the occlusion balloon can be redirected into the infrarenal aortic neck within the stent-graft main body before contralateral gate cannulation. (D) After the occlusion balloon is reinflated in the stent-graft main body in hemodynamically unstable patients, the contralateral stent-graft gate can be cannulated, and contralateral stent-graft extensions are placed as needed. (E) After contralateral iliac extension and ruptured abdominal aortic aneurysm exclusion, the occlusion balloon can be removed, as shown in the completion arteriogram. (From Mehta M. Endovascular aneurysm repair for ruptured abdominal aortic aneurysm: the Albany Vascular Group approach. *J Vasc Surg.* 2010;52:1706–1712.)

Retroperitoneal Approach

This approach is suggested to expedite supraceliac exposure and control and is safe when performed by those facile with its use.^{133,134} It is particularly useful in the patient with challenging body habitus or hostile abdomen and has been associated with a reduction in postoperative mortality in one NSQIP study involving 404 patients from 2011 to 2014.¹³⁵

Operative Technique

After proximal control is achieved, one should allow the anesthesia team time for resuscitation, before the blood loss associated with aneurysm sac opening occurs. Controlling the IMA and iliac vessels can further limit this. Once the aneurysm is opened, balloon iliac occlusion, if required, and lumbar suture ligation are rapidly accomplished. With supraceliac aortic

control, bleeding from the proximal visceral arteries will require continuous suction during construction of the proximal anastomosis, preferably with a cell saver. Systemic heparin is generally avoided during RAAA repair, although it can be administered in a lower than usual dose just prior to clamp application. Alternatively, heparinized saline can be administered directly into the iliac arteries through occlusion balloons to attempt to reduce distal thrombosis. Aggressive retrograde flushing of the iliac arteries should be carried out before completing the distal anastomosis to remove any clot. Aortic repair is most rapidly accomplished with a tube graft. If bifurcated grafts are required, the easier of the two iliac (or femoral in aortobifemoral grafts) anastomoses is performed first to reduce lower torso ischemic time. Maintaining perfusion of one internal iliac artery is optimal to reduce pelvic and colon ischemia.

Aortocaval Fistula

Continuous venous bleeding into the aortic open aneurysm sac after proximal and distal control have been achieved, suggests an aortocaval fistula. Direct digital pressure or the use of sponge sticks above and below the fistula is recommended. Suture of the fistula from within the aneurysm is recommended to avoid further additional venous injury, with care to avoid an air or aortic debris embolus during the repair.

Autotransfusion

The use of a cell saver device has proven beneficial in reducing mortality in RAAA patients undergoing OSR.¹³⁶ Red cell salvage reduces blood transfusions and is associated with reduced morbidity and mortality.¹³⁷ A retrospective review demonstrated that a ratio of autotransfusion/PRBC of greater than or equal to 1 was associated with lower mortality for open repair; however, liberal use of fresh frozen plasma did not decrease mortality.

Hypothermia

Hypothermia increases surgical bleeding, wound infections, and cardiac events and is associated with RAAA mortality.^{136,138} Current recommendations for hypothermic patients include the use of warmed anesthetic gases, intravenous fluids, and the use of forced-air warming devices.

Abdominal Closure

Primary abdominal closure after OSR is most common. However, in 25% to 30% of patients the abdomen cannot be closed primarily without significant tension secondary to swollen bowel, tissue edema, and retroperitoneal hematoma.¹³⁹ Patients who have severe preoperative anemia, prolonged shock, preoperative cardiac arrest, massive resuscitation, profound hypothermia, and severe acidosis may benefit from closure with mesh sewn to the fascia. Early mesh closure prevents abdominal compartment syndrome (ACS) and appears to reduce the incidence of MOF and may reduce mortality in

comparison to patients who eventually require return to the operating room for decompressive laparotomy and delayed mesh closure.¹³⁹ Vacuum-assisted closure systems are available but have not been proven useful, although do offer advantages in terms of high abdominal closure rates with a low incidence of complications in selected patients.^{139,140}

COMPLICATIONS OF RUPTURED ABDOMINAL AORTIC ANEURYSM REPAIR

Local Complications

After OSR and REVAR, limb ischemia can be due to graft limb thrombosis or distal embolism and requires rapid intervention. EVAR complications include access site bleeding and thrombosis ranging from 7% to 10%.¹⁶ Postoperative bleeding related to coagulopathy occurs in 12% to 14% of all RAAA patients.¹⁴¹ While INR, PT, fibrinogen levels and platelet counts have been used to direct replacement, newer and faster viscoelastic methods (VEM) and point of care platelet functional assays are increasingly used in trauma and cardiac surgery.¹⁰¹ These have yet to be tested in RAAA care but may likely have a role in rapid correction of coagulopathy.

Colonic Ischemia

Colonic ischemia remains a potential lethal consequence of AAA repair and occurs more frequently in RAAA. The etiology is a combination of ischemia secondary to IMA ligation, internal iliac occlusion, operative disruption of collaterals, embolization of debris, hypotension reduced perfusion, and splanchnic vasoconstriction due to shock and vasopressors. Prospective sigmoidoscopy studies noted an ischemic colitis incidence of 38% after OSR and 23% after REVAR ranging from patchy mucosal necrosis (grade I), to mucosal and muscularis involvement (grade II), to transmural necrosis, gangrene, and perforation (grade III).^{142–144} No blood test parameter was sufficiently discriminative to assist in diagnosis of colonic ischemia, so a high index of suspicion and routine sigmoidoscopy for RAAA patients is recommended.¹⁴²

A prospective analysis of RAAA patients who survived 24 hours demonstrated a 26% incidence of grades I and II ischemia and 10% incidence of grade III changes.¹⁴⁴ Only 11% of grade I or grade II changes progressed to grade III in 48 hours. Grade III changes have extensive sigmoid and rectal necrosis and a mortality rate of 55% despite aggressive surgical management. Factors determining the degree of colonic ischemia after RAAA repair include the degree and duration of hypotension, patency of the inferior mesenteric artery, and collateral supply between the superior mesenteric, inferior mesenteric, and internal iliac arteries. At the conclusion of OSR, careful bowel examination with Doppler evaluation of the mesenteric vessels should be routinely performed and reimplantation of the inferior mesenteric artery considered. The incidence of ischemic colitis differs with the type of repair: 4% for tube grafts, 2.7% for aortoiliac grafts vs. 22% for an aortobifemoral graft.

Colonic ischemia is also prevalent after EVAR of RAAA. After EVAR, prospective flexible sigmoidoscopy done 24 hours postoperatively noted a 22% incidence of ischemic changes, with 5% having segmental necrosis.^{142,143}

Assessment for Abdominal Compartment Syndrome

ACS was first described in RAAA and remains a common complication. Intraabdominal hypertension is graded on the basis of bladder pressures measured with 50 to 100 mL of instilled bladder fluid and zeroed at the pubic symphysis.¹⁴⁵ ACS is defined as a sustained intraabdominal pressure of more than 20 mm Hg that is associated with new organ dysfunction or failure.¹⁴⁶

After OSR the abdomen can be closed or left open with/without packing as the clinical situation dictates. Large retroperitoneal hematomas can be cautiously drained; however, postoperative oozing and tissue edema contribute to progressive increases in intraabdominal pressure. Clinical findings include a tense distended abdomen, progressive respiratory failure (elevated peak inspiratory pressures, decreased tidal volume, and elevated PCO_2), diminished cardiac output, and oliguria.^{145,147} Decompression laparotomy is recommended for intraabdominal hypertension greater than 25 mm Hg (grade III and grade IV) (see Chapter Algorithm, below).^{145,147}

ACS after both OSR and EVAR of RAAA is associated with use of an aortic occlusion balloon, massive blood transfusions, coagulopathy, and hemodynamic instability.^{145,148,149} A Swedish population-based study reported ACS developed in 6.8% after OSR vs. 6.9% after EVAR in RAAA, although 10.7% of OSR patients had the abdomen left open. The impact on 30-day mortality rate was significant (42.4% with ACS vs. 23.5% without); at 1 year it was 50.7% vs. 31.8%.¹⁵⁰ ACS requires prompt recognition and decompression laparotomy. Proactive abdominal decompression by percutaneous intraperitoneal blood removal or retroperitoneal hematoma evacuation after EVAR of RAAA has been successful.¹⁴⁹

Spinal Ischemia

Paraplegia and paraparesis are rare complications after RAAA repair with a risk for OSR of 1.2% compared with 0.5% to 11.5% for EVAR.^{151,152} Factors associated with spinal cord ischemic complications include interruption of the pelvic blood supply, prolonged aortic cross-clamping or balloon occlusion, preoperative and intraoperative hypotension, and embolization. Protective strategies include early recognition and institution of CSF drainage, maximizing spinal cord blood flow with MBP above 100, Hb >10 g/L and oxygen saturation of >92%. A role for hyperbaric oxygen therapy has been reported but evidence remains anecdotal at present.¹⁵³

Systemic Complications

Cardiac Complications

Myocardial infarction, arrhythmias, cardiac arrest, and congestive heart failure increase mortality after RAAA.¹⁴¹ Myocardial infarction develops secondary to the increased demand placed

on the heart in the setting of preexisting coronary artery disease. Preexisting coronary artery disease has been shown to increase the risk for MI and death after OSR of RAAA but not after EVAR.¹⁶ Cardiac arrest occurs in up to 20% of patients, with a mortality of 81% to 100%. Myocardial infarction develops in 37%–42% of OSR patients, with a mortality rate of 17% to 66%; arrhythmias and congestive heart failure develop in nearly 20% of patients, with a mortality approaching 40%.^{16,44,141} A recent RCT of remote ischemic preconditioning did not reduce the incidence of MI.¹⁵⁴ EVAR for RAAA has not been demonstrated to reduce the number of cardiac complications.⁴⁴ Postoperative measurement of cardiac-specific troponin has been shown to be elevated in up to 55% of RAAA patients. An elevated troponin and EKG changes were associated with significantly higher rates of CHF, cardiogenic shock, and in-hospital mortality (56.3% vs. 29.3%).¹⁵⁵ Elevation of troponin alone irrespective of the EKG changes was associated with an elevated mortality rate of 40.3% vs. 14.1% (see Ch. 44, Systemic Complications: Cardiac).

Respiratory Failure

Respiratory failure, pneumonia, and pulmonary complications develop in 36% to 41% of patients after OSR of RAAA and are predicted by preexisting chronic obstructive pulmonary disease (COPD)^{44,156} (see Ch. 45, Systemic Complications: Respiratory). Administration of large volumes of fluid and blood products, long cross-clamp times and COPD predisposes to the development of respiratory failure. REVAR significantly reduces postoperative lung dysfunction. Pneumonia, respiratory complications, including the need for tracheostomy are significantly lower after REVAR compared with OSR (28.5% vs. 35.9%, 4.6% vs. 9.9%, respectively; $P < 0.001$ for both).^{44,156}

Renal Dysfunction

Renal dysfunction after RAAA predicts mortality.^{44,141} It develops secondary to a combination of hypoperfusion secondary to hemorrhagic shock, ischemia from suprarenal clamping, renal vein ligation, contrast administration and preexisting renal disease. The incidence of renal dysfunction after elective AAA repair is low, but RAAA patients have an incidence of 26% to 45%.⁴⁴ Among RAAA patients who require dialysis (incidence 11%–40%), the mortality rate is between 76% and 89%.^{141,157} Renal dysfunction has been found to be increased in those with suprarenal cross-clamping, longer duration of cross-clamping, preexisting renal insufficiency, shock, and increased age.^{156–158} The US National Inpatient Sample (NIS) noted significantly less acute renal failure (ARF) for REVAR (12.1%) compared with 19.6% in OSR.⁹⁴ In Medicare patients, REVAR was associated with 33.4% incidence of ARF despite contrast administration vs. 45.4% for OSR. Coverage of a single renal artery was reported in 1.2% of REVAR cases in VQI and was bilateral in 0.8%. Single renal artery coverage significantly increased the odds of permanent dialysis (OR = 12.3) and combined permanent dialysis/30-day death (OR = 2.8). Bilateral renal coverage case outcomes were worse (in hospital mortality increased [OR = 5.7], permanent dialysis/30-day death [OR = 9.5], and permanent dialysis in

patients surviving to discharge [OR = 47.5]).¹⁵⁹ Coverage of accessory renal arteries does not increase the risk of dialysis (see Ch. 46, Systemic Complications: Renal).

Liver Failure

Hepatic failure is a late event after RAAA and is attributed to hypoxic hepatic injury.¹⁶⁰ Increased metabolic demands, hematoma reabsorption, and unrecognized preexisting hepatic dysfunction are risk factors and are associated with pulmonary, cardiac, and gastrointestinal dysfunction with a mortality rate of 83%.^{160,161}

Multisystem Organ Failure

The development of MOF depends upon the magnitude, number, and timing of inflammatory insults. Clinical RAAA data suggest that suprarenal clamp location, duration of clamping, and development of ACS are associated with higher rates of MOF and death.^{148,158} The incidence of MOF was noted to be 3.8% after elective AAA repair, 38% after urgent AAA repair, and 64% after OSR of RAAA.¹⁶² MOF after RAAA repair occurs more frequently after OSR than REVAR and has mortality rates of 64% to 93%.^{132,161,163}

The two-hit hypothesis of RAAA (hemorrhagic shock and ischemia secondary to temporary aortic clamping) initiating MOF may account for the persistently elevated mortality in patients undergoing RAAA repair and why REVAR reduces perioperative mortality.^{42,43,164,165} In a model of RAAA, hemorrhagic shock or aortic clamping alone were insufficient to result in the development of systemic organ injury. However, combining the insults resulted in a synergistic effect with systemic organ injury that resembled MOF.^{43,164,165} Hemorrhagic shock causes cardiac contractile dysfunction after resuscitation which further reduces tissue perfusion.¹⁶⁶ RAAA patients have neutrophils that are primed to respond to *ex vivo* stimulation on arrival to the ER and with further significant elevations in neutrophil oxidative burst postoperatively.¹⁶⁷ A significant relationship between the level of neutrophil oxidative bursts and the level of tissue oxidative injury products was identified. Both laboratory model and human subject data suggest that RAAA is a two-hit model of injury which may explain why REVAR reduces mortality, and why advances in perioperative management have not had a dramatic effect.

OUTCOMES OF RUPTURED ABDOMINAL AORTIC ANEURYSM REPAIR

The approach-specific results of RAAA repair have been described in single-center cohorts, national registries, RCTs, and meta-analyses.^{130,167–184} Major differences in outcomes exist between observational studies and the randomized trials. Population-based studies demonstrate a significant perioperative benefit of REVAR over open repair (Fig. 76.7).^{15,44,94} However, observational datasets often do not address confounding related to hemodynamics, neck length and anatomical suitability for REVAR. When hemodynamic stability is

accounted for, the results of OSR and EVAR are equivalent.¹⁸⁵ Aneurysm neck length is inversely associated with mortality and those with shorter, angulated necks and unfavorable EVAR anatomy are relegated to more technically challenging OSR in observational studies.⁸⁹ The randomized trials had different randomization strategies, criteria, and outcome measures.

Randomized Trials

The first RCT to evaluate REVAR vs. OSR was a pilot study that randomized 32 patients stable enough for CT and fit for OSR between 2002 and 2004.⁹¹ Thirty-day mortality was equivalent for REVAR and OSR (53%), but the trial showed the feasibility of RCTs for RAAA.

The Amsterdam Acute Aneurysm Trial (AJAX) trial evaluated 520 patients between 2004 and 2011.¹⁷⁶ Of these, 116 (22%) CT-confirmed RAAA patients deemed REVAR suitable by CT and clinically suitable for OSR were randomized to REVAR (57) or OSR (59). Mortality was 21% and 25% for REVAR and OSR. Rates of 30-day death or severe complications at were 42% and 47% ($P > 0.05$). Renal insufficiency was significantly reduced after REVAR.

The IMPROVE trial randomized 613 patients following the clinical diagnosis of RAAA.¹³⁰ Consequently, some symptomatic AAAs were randomized, some patients did not undergo repair, and treatment crossovers occurred. Following intention-to-treat analysis the 30-day mortality was 35.4% in REVAR vs. 37.4% for OSR, while 30-day mortality was 25% vs. 38% following as-treated analysis. Women had a significant mortality benefit from REVAR (37% to 57%; $P = 0.02$). The average aneurysm size was greater than 8 cm, and 64% of RAAAs were anatomically suitable for REVAR. There was no significant interaction with age or Hardman index. REVAR patients had shorter ICU stays, overall stays (14.4 days vs. 20.5 days) and a higher rate of direct discharge home (94% vs. 77%). Overall costs were not different at 30 days, but REVAR was more cost-effective and delivered more QALYs at 3 years (Fig. 76.10). There was no statistically significant difference in 3-year mortality (48 vs. 56%). However, all-cause mortality was lower for EVAR from 3 months to 3 years (HR 0.57).¹⁸⁶ Aneurysm neck length was inversely associated with mortality for both REVAR and OSR, and every 10 mm Hg increase in systolic BP improved survival odds 13%, while local anesthesia improved survival four-fold.⁸⁹

The Endovasculaire vs. Chirurgie dans les Anévrismes Rompus (ECAR) trial randomized patients with a systolic BP greater than 80 mm Hg after CT confirmation of rupture, and anatomic suitability for REVAR.¹⁵⁶ The 30-day and 1-year mortality rates were not different (30% EVAR vs. 35% OSR at 1 year). REVAR benefits were lower respiratory support time, pulmonary complications, blood transfusions, and duration of ICU stay.

Meta-Analyses of Randomized Trials

The pooled mortality in the three randomized trials demonstrated a nonsignificant mortality difference at 1 year of 38.5% for EVAR vs. 42.8% for open repair. Data for reinterventions could not be subject to meta-analysis.¹⁷⁹ When the analysis was redone including only those anatomically suitable for REVAR from

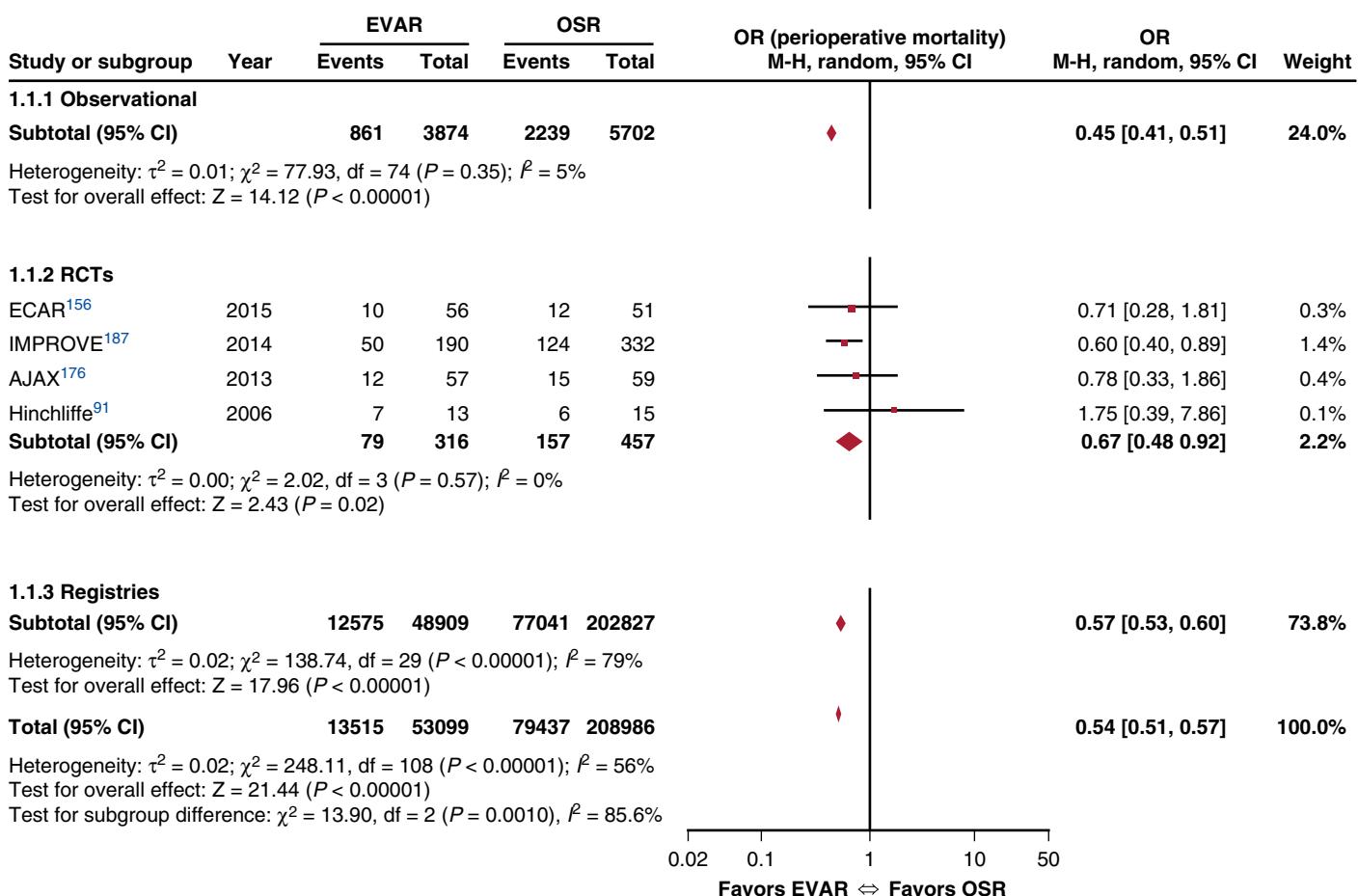


Figure 76.7 Perioperative outcomes of endovascular versus open ruptured abdominal aortic aneurysm repair from meta-analysis of randomized trial data for patients with confirmed rupture, and observational data. (Modified from Kontopoulos N, et al. Meta-analysis and meta-regression analysis of outcomes of endovascular and open repair for ruptured abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg*. 2020;59(3):399–410.)

the IMPROVE trial, the results were unchanged. The benefits of EVAR were shorter LOS, fewer pulmonary and renal complications, and lower costs. A Cochrane meta-analysis of all four RAAA trials demonstrated similar findings.¹⁸⁷ There was, no difference in 30-day mortality (OR 0.88). Myocardial infarction, stroke, composite cardiac complications, renal complications, severe bowel ischemia, spinal cord ischemia, reintervention, amputation, and respiratory failure were not amenable to meta-analysis. Assessment of outcomes beyond the perioperative period was not possible. In a meta-analysis of randomized and observational studies including more than 260,000 patients, REVAR was associated with a significant short-term survival benefit (OR 0.54).¹⁸⁸ Meta-regression demonstrated significant reductions in perioperative mortality among both REVAR and OSR over time; however, heterogeneity was found to be moderate to high, and a high likelihood of publication bias was found.

Observational Studies

A number of large observational studies examining RAAA repair outcomes have recently emerged. While Swedish and Japanese studies have not demonstrated any benefit of REVAR, North American studies have shown short-term mortality and

morbidity benefits.^{189,190} A 2001 to 2008 Medicare study of RAAA repairs demonstrated 33.8% vs. 47.7% mortality for REVAR and OSR, with significant differences for all ages.⁴⁴ Complications including pneumonia, renal and respiratory failure, venous thromboembolism, hemodialysis, and surgical complications were lower for REVAR. Hospital stay was 7 vs. 14 days for survivors, and discharge to home was 22% higher for REVAR. A significant long-term benefit for REVAR was seen in all ages which persisted for more than 4 years. At 36 months of follow-up, laparotomy-related complications were less after REVAR (1.8% vs. 6.2% for open; $P < 0.001$), but EVARs had higher endovascular AAA-related reinterventions (10.9% vs. 1.5%; $P < 0.001$). Data from other US databases have confirmed almost 50% reductions in short term mortality for REVAR patients.^{191–193} A Canadian population-based study of almost 3000 patients from 2003 to 2016 demonstrated significant early REVAR benefit with 50% lower hazards for mortality within 30 days of repair, but no differences thereafter (see Fig. 76.8). Analysis of VQI data of RAAA repair outcomes over time have revealed significant improvements in REVAR but not OSR mortality over time.¹⁹⁴ A comparison of UK ($n = 11,799$) with US data ($n = 23,828$) from 2005 to 2010 demonstrated lower OSR mortality, but

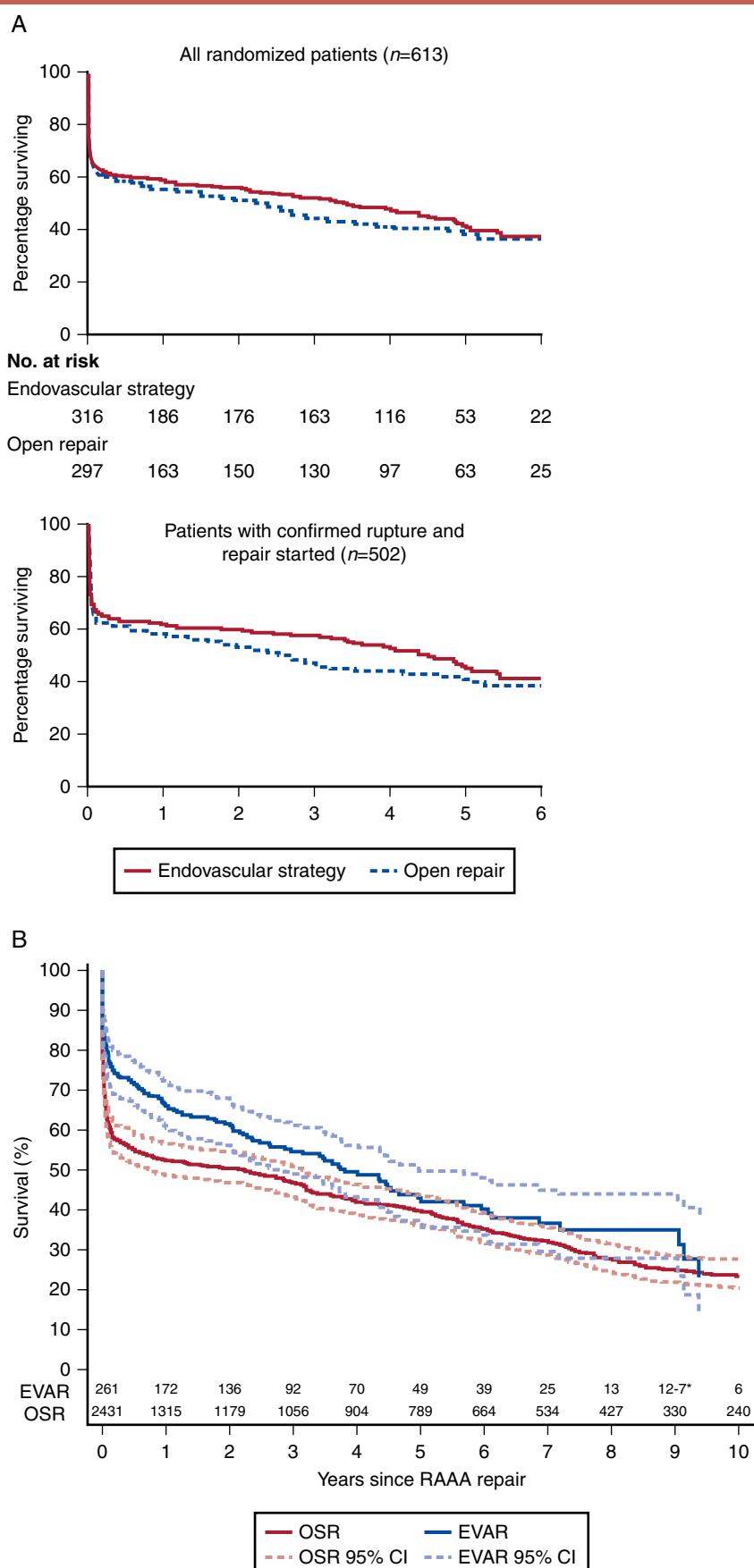


Figure 76.8 Outcomes of endovascular versus open repair of ruptured abdominal aortic aneurysm. (A) Kaplan-Meier estimates of long-term outcomes of REVAR versus open RAAA repair from the IMPROVE randomized trial. (B) Inverse probability of treatment weighted survival curves of long-term outcomes of REVAR versus open RAAA repair from Canadian population-based data. *Refers to a policy of the Institute for Clinical Evaluative Sciences where a value or difference between adjacent numbers at risk value of <6 occurs. Value presented is a range to eliminate risk of patient re-identification. (A, from IMPROVE Trial Investigators. Comparative clinical effectiveness and cost effectiveness of endovascular strategy v open repair for ruptured abdominal aortic aneurysm: Three year results of the IMPROVE randomised trial. *BMJ*. 2017;359:j4859. B, from Salata K, et al. Population-based long-term outcomes of open versus endovascular aortic repair of ruptured abdominal aortic aneurysms. *J Vasc Surg*. 2020;71:1867–1878.)

higher REVAR mortality in the UK. Overall postintervention mortality was not different (41.8% vs. 41.7%). UK survivors had longer LOS but were more commonly discharged to usual residence, whereas discharge to a skilled nursing facility was most common in the US. In both countries the overall, postintervention, and approach-specific mortality were significantly lower in teaching hospitals. In the UK, nonoperative therapy was more common on a weekend and at nonteaching hospitals. Weekend admission, interhospital transfer, and treatment at a nonteaching institution were significant predictors of mortality.

Preoperative Predictors of Mortality

RAAA scoring systems assess preoperative variables to predict postoperative outcomes before repair, including the Hardman index, Glasgow Aneurysm Score, VSGNE RAAA risk score, IMPROVE trial score and Neural Network scores, among others.^{195–202} None is sufficiently accurate to deny repair but can inform consent and risk estimation. Preoperative variables associated with a reduction in survival after OSR include loss of consciousness, cardiac arrest, congestive heart failure, renal insufficiency, age, female sex, nonwhite race, high APACHE II score, and low provider and hospital volume.^{15,141,157,162,195,198,203–211} Death after RAAA is most commonly associated with hypotension, advanced age, ischemic heart disease, cardiac arrest, low hemoglobin, and renal insufficiency.^{197,201,212–214} Several studies have investigated the effect of off-hour repair on RAAA outcomes. A German study demonstrated higher OSR mortality on weekends (OR 1.61), while a VQI study showed higher mortality only among patients requiring inter-hospital transfer on weekends.^{215,216} A meta-analysis of observational studies demonstrated an association between hostile anatomy and mortality following REVAR (HR 2.01).²¹⁷ Among REVAR patients, preoperative intubation, dependent functional status, COPD, and age are associated with postoperative mortality.²¹⁸ Other work has demonstrated no association between dependent functional status and RAAA repair outcomes after adjustment for age, sex, diabetes mellitus, preoperative dialysis, smoking and hypertension.²¹⁹ The VSGNE RAAA score identified age >76 (OR = 5.3), preoperative cardiac arrest (OR = 4.3), loss of consciousness (OR = 2.6), and suprarenal clamp (OR = 2.4) as predictors of mortality.^{200,208} Artificial neural networks could potentially assist in predicting RAAA outcomes by iterative computation as information becomes available in real time.²⁰⁹

The effects of age, sex, and centralization of care on RAAA outcomes have been a recent research focus. Swedish,²²⁰ the US²²¹ and Japanese¹⁹⁰ studies have shown similar mortality in octogenarians, and significant mortality benefits for REVAR in this age group. A meta-analysis of eight observational studies ($n = 7536$) confirmed similar perioperative mortality among octogenarians and younger patients with RAAA, and a significant two-fold risk reduction among octogenarians receiving REVAR.²²² Women with RAAA are 2 to 3 years older, have smaller AAA size, are offered repair less frequently, and have a higher mortality; they are also less likely to undergo REVAR despite a mortality benefit at 1 and 3 years.^{14,16,30,214,223–227}

A VQI study of 3700 RAAA repairs showed significant associations between female sex and 30-day mortality for both REVAR (OR 1.42) and OSR (OR 1.50). Women had significantly longer door to intervention times, despite nonsignificant pre-hospital delays.²²⁸ An inverse association between hospital aortic repair volume and perioperative mortality following open RAAA repair has been shown.^{188,229–232} No volume–outcome relationship existed when a supraceliac clamp was necessary, and for patients that underwent REVAR.^{229,232} While data suggests that RAAA care should be centralized, an absolute aortic repair volume threshold remains elusive.

Postoperative Estimates of Survival

At the conclusion of RAAA repair, the surgeon can review key variables to provide a prognosis. In a prospective Canadian study of OSR for RAAA, following adjustment for all preoperative, intraoperative, and postoperative variables, early survival was predicted by site of the aortic cross-clamp and occurrence of myocardial infarction, respiratory failure, kidney damage, and coagulopathy.¹⁴¹ Dialysis had a dramatic impact on survival, even in the absence of other complications. The development of two complications also has a dramatic impact on mortality, especially if one was a rise in creatinine concentration or dialysis requirement. Prolonged ICU stay is also associated with reduced 90 day and 1 year survival.²³³ Among REVAR patients, the need for laparotomy is associated with a six-fold increase in 30-day mortality.²¹⁸

Predictors of Late Survival

Three studies assessed late survival after OSR of an RAAA compared with elective OSR: US Veterans Affairs (VA) data, the Mayo Clinic, and the Canadian Aneurysm Study.^{205,209,234} The 5-year RAAA survival data were similar. For those alive 30 days postoperatively, 5-year survival was approximately 55% vs 70% for RAAA and elective AAA. Lower intraoperative urine output, respiratory failure, and myocardial infarction were associated with late mortality. The VA study also identified increasing age, illness severity, patient complexity, rupture, and aortic graft complications as independent predictors of late mortality.²³⁵ A UK study highlighted distance from hospital, operative duration, MOF, and creatinine as predictors of late mortality.²¹⁴ Late survival has been assessed in the US, UK, Sweden, and the Netherlands at 5 years and ranges between 38.6% in the UK and 50% in the US.^{203,207,235} The most common causes of late mortality were cardiovascular death (35% of cases) and cancer (29%, mostly lung and GI). Early mortality accounts for the largest drop in the RAAA patient's survival (Fig. 76.9).²⁰³

Multiple long-term RAAA outcomes analyses by repair approach have noted increasing usage of EVAR over time.^{27,207} After adjustment for confounding, EVAR did not independently demonstrate lower long-term mortality.^{11,207} However, EVAR was associated with improved survival.^{11,44} Primary predictors of 1- and 5-year mortality were patient comorbidities (home oxygen, dialysis, cerebrovascular disease, and ejection fraction <50%) and the indices of shock on admission (SBP <90, loss of consciousness, cardiac arrest).²⁰⁷

Late Reinterventions

In the IMPROVE trial at 3 years, a 28% aneurysm-related reintervention rate was noted, most of which occurred in the initial 3 months postoperatively.²³⁶ Bowel and limb ischemia were the

most common indications for reintervention within the first 3 months, while endograft-related problems including endoleak and migration were the commonest indications afterwards.

Rupture After Endovascular Aneurysm Repair

None of the currently available stent grafts is completely effective in preventing aneurysm rupture after EVAR.¹⁸⁴ Careful follow-up of REVAR patients is critical to prevent complications including repeat rupture.²³⁷ A meta-analysis of late reintervention for repeat RAAA following REVAR for RAAA demonstrated a rate similar to elective EVAR: 1.4% at 28 months, most commonly for type 1 endoleak.¹⁷⁹ Of those who ruptured after REVAR, 46.8% underwent intervention to treat the endoleak.

QUALITY OF LIFE

Quality of life (QoL) after RAAA repair has been assessed with several different instruments.²³⁸ The overall SF-36 scores compared favorably with those of the age- and sex-matched general population. Hospital survivors had 8.5 quality-adjusted life years, but physical functioning was significantly lower in RAAA repair survivors than in age- and sex-adjusted population controls. Major postoperative complications did not reduce the QoL in RAAA survivors. IMPROVE prospectively measured differences in QoL between EVAR and OSR survivors at 3 and 12 months. Mean utility scores were significantly higher for the EVAR group at 3 months but were not significant at 1 year.²³⁹ When mean cost was plotted vs. quality-adjusted life year differences, EVAR for RAAA delivered the best quality for the lowest costs (Fig. 76.10). The more rapid recovery from EVAR was likely reflected in these early differences which dissipated over time. Therefore, an aggressive approach to RAAA repair is justified as patients derive significant survival with good QoL following successful repair.

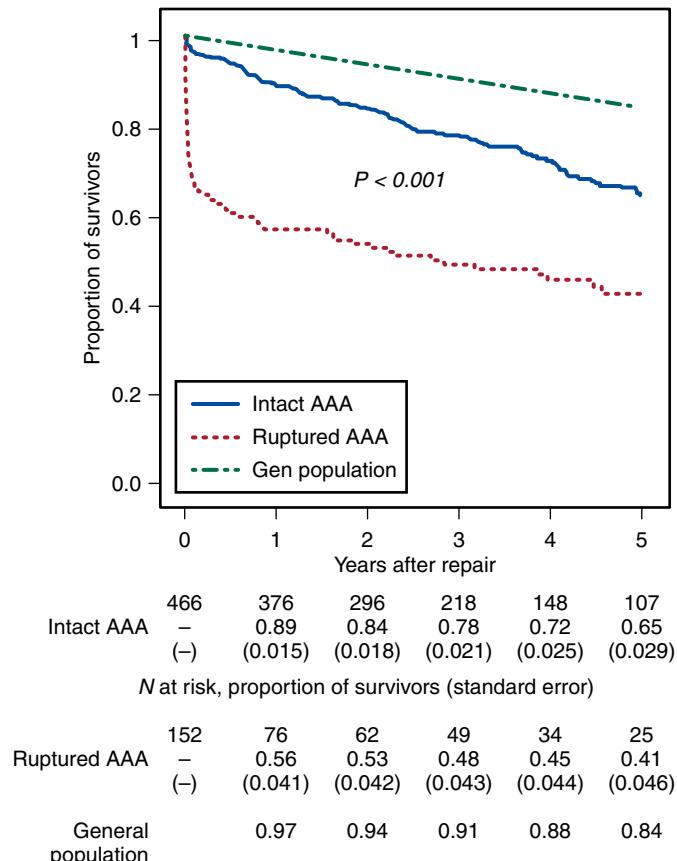


Figure 76.9 Kaplan-Meier survival estimates after abdominal aortic aneurysms (AAA) repair compared with an age and gender-matched general population.

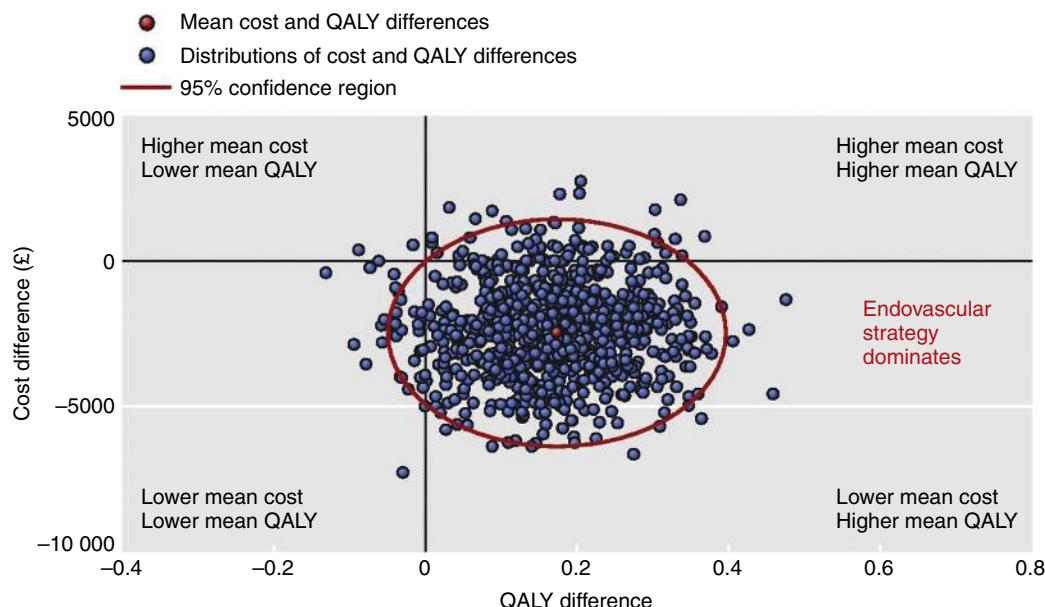
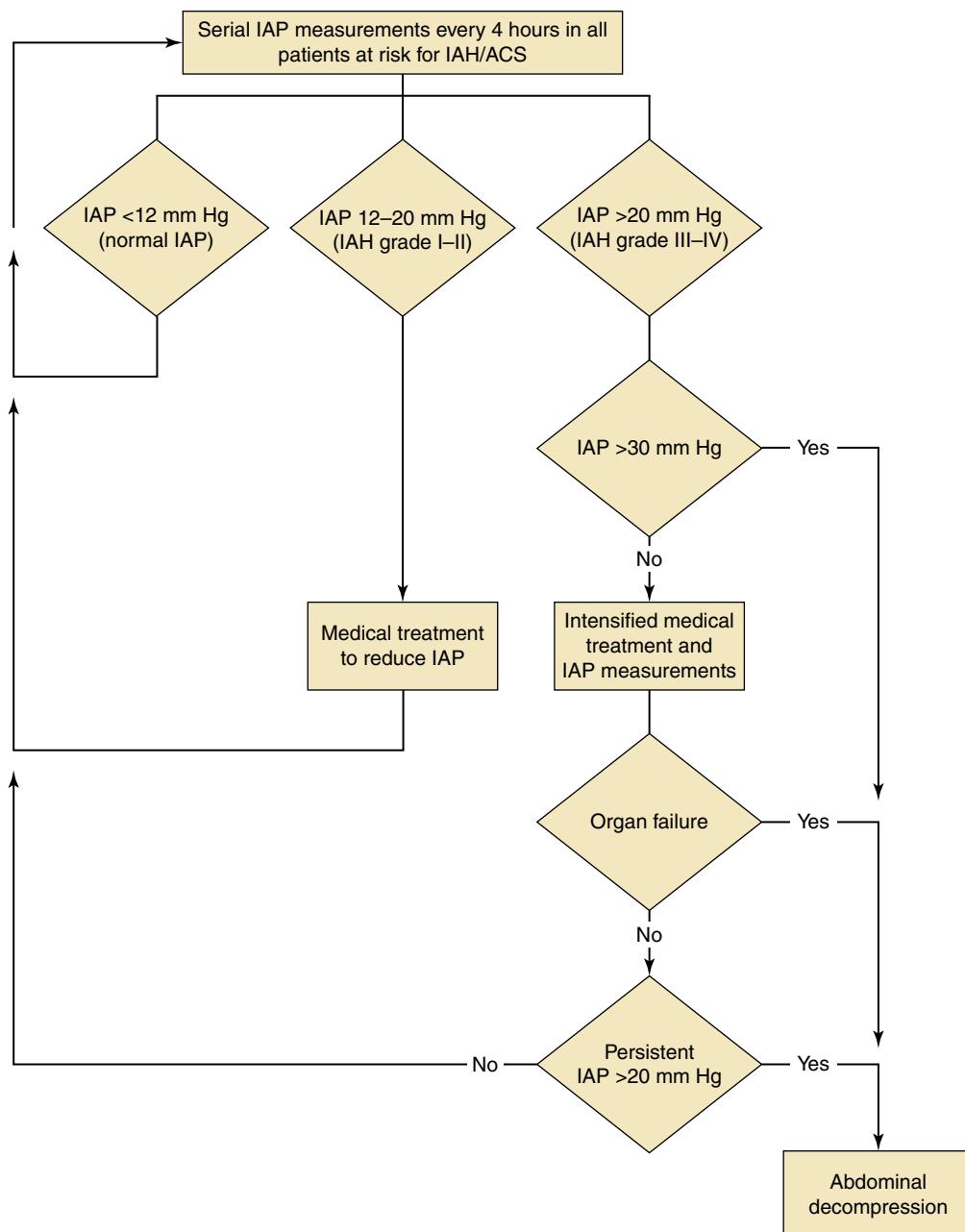


Figure 76.10 Uncertainty in mean cost (£) and quality-adjusted life year (QALY) differences and their joint distribution for endovascular strategy versus open repair for all 613 patients.

CHAPTER ALGORITHM



Algorithm for escalation of management of abdominal compartment syndrome (ACS) after endovascular repair of ruptured abdominal aortic aneurysms (RAAAs). *IAH*, intraabdominal hypertension; *IAP*, intraabdominal pressure. (From Karkos CD, et al. A systematic review and meta-analysis of abdominal compartment syndrome after endovascular repair of ruptured abdominal aortic aneurysms. *J Vasc Surg*. 2014;59(3):829–842.)

SELECTED KEY REFERENCES

Dick F, Erdoes G, Opfermann P, et al. Delayed volume resuscitation during initial management of ruptured abdominal aortic aneurysm. *J Vasc Surg*. 2013;57:943–950.

This study highlights the importance of appropriate volume resuscitation in patients with RAAA and its impact on patient survival.

IMPROVE Trial Investigators. Comparative clinical effectiveness and cost effectiveness of endovascular strategy v open repair for ruptured abdominal

aortic aneurysm: three-year results of the IMPROVE randomized trial. *BMJ*. 2017;359:j4859.

Excellent data on RAAA patients randomized to OSR vs. EVAR at 3 years.

Johnston KW. Ruptured abdominal aortic aneurysm: six-year follow-up results of a multicenter prospective study. Canadian Society for Vascular Surgery Aneurysm Study Group. *J Vasc Surg*. 1994;19:888–900.

This landmark study, one of the largest prospective OSR RAAA registries, highlights 6-year actuarial survival rates and determines the predictive variables that are associated with survival of patients.

Powell JT, et al. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ*. 2014;348:f7661.

Thirty-day mortality results for the largest randomized RAAA trial of OSR vs. EVAR.

Powell JT, et al. Observations from the IMPROVE trial concerning the clinical care of patients with ruptured abdominal aortic aneurysm. *Br J Surg*. 2014;101(3):216–224.

Detailed analysis of EVAR vs. OSR in the largest randomized trial with a rich dataset.

Sweeting MJ, et al. Ruptured aneurysm trials: the importance of longer-term outcomes and meta-analysis for 1-year mortality. *Eur J Vasc Endovasc Surg*. 2015;50(3):297–302.

This meta-analysis of three randomized RAAA EVAR vs. open repair trials results at 1 year.

A complete reference list can be found online at www.expertconsult.com.

REFERENCES

1. Reimerink JJ, et al. Systematic review and meta-analysis of population-based mortality from ruptured abdominal aortic aneurysm. *Br J Surg.* 2013;100(11):1405–1413.
2. Sarac TP, et al. Comparative predictors of mortality for endovascular and open repair of ruptured infrarenal abdominal aortic aneurysms. *Ann Vasc Surg.* 2011;25(4):461–468.
3. Cota AM, et al. Elective versus ruptured abdominal aortic aneurysm repair: A 1-year cost-effectiveness analysis. *Ann Vasc Surg.* 2005;19(6):858–861.
4. Hoornweg LL, et al. Meta analysis on mortality of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg.* 2008;35(5):558–570.
5. Schmitz-Rixen T, et al. Ruptured abdominal aortic aneurysm—epidemiology, predisposing factors, and biology. *Langenbecks Arch Surg.* 2016;401(3):275–288.
6. Choke E, et al. Changing epidemiology of abdominal aortic aneurysms in England and Wales: Older and more benign? *Circulation.* 2012;125(13):1617–1625.
7. Howard DP, et al. Age-specific incidence, risk factors and outcome of acute abdominal aortic aneurysms in a defined population. *Br J Surg.* 2015;102(8):907–915.
8. Norman PE, et al. Falling rates of hospitalization and mortality from abdominal aortic aneurysms in Australia. *J Vasc Surg.* 2011;53(2):274–277.
9. Schermerhorn ML, et al. Changes in abdominal aortic aneurysm rupture and short-term mortality, 1995–2008: A retrospective observational study. *Ann Surg.* 2012;256(4):651–658.
10. Bown MJ, et al. A meta-analysis of 50 years of ruptured abdominal aortic aneurysm repair. *Br J Surg.* 2002;89(6):714–730.
11. Salata K, et al. Population-based long-term outcomes of open versus endovascular aortic repair of ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2020;71:1867–1878.
12. Budd JS, et al. A study of the mortality from ruptured abdominal aortic aneurysms in a district community. *Eur J Vasc Surg.* 1989;3(4):351–354.
13. Holt PJ, et al. Aortic rupture and sac expansion after endovascular repair of abdominal aortic aneurysm. *Br J Surg.* 2012;99(12):1657–1664.
14. IMPROVE Trial Investigators. Endovascular strategy or open repair for ruptured abdominal aortic aneurysm: One-year outcomes from the IMPROVE randomized trial. *Eur Heart J.* 2015;36(31):2061–2069.
15. Karthikesalingam A, et al. Mortality from ruptured abdominal aortic aneurysms: Clinical lessons from a comparison of outcomes in England and the USA. *Lancet.* 2014;383(9921):963–969.
16. Mehta M, et al. Endovascular repair of ruptured infrarenal abdominal aortic aneurysm is associated with lower 30-day mortality and better 5-year survival rates than open surgical repair. *J Vasc Surg.* 2013;57(2):368–375.
17. Visser P, et al. In-hospital operative mortality of ruptured abdominal aortic aneurysm: A population-based analysis of 5593 patients in the Netherlands over a 10-year period. *Eur J Vasc Endovasc Surg.* 2005;30(4):359–364.
18. Nevala T, et al. Outcome of symptomatic, unruptured abdominal aortic aneurysms after endovascular repair with the Zenith stent-graft system. *Scand Cardiovasc J.* 2008;42(3):178–181.
19. Antonello M, et al. Glasgow aneurysm score predicts the outcome after emergency open repair of symptomatic, unruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg.* 2007;33(3):272–276.
20. Bahnsen HT. Treatment of abdominal aortic aneurysm by excision and replacement by homograft. *Circulation.* 1954;9(4):494–503.
21. Cooley DA, DeBakey ME. Ruptured aneurysms of abdominal aorta; excision and homograft replacement. *Postgrad Med.* 1954;16(4):334–342.
22. Yusuf SW, et al. Emergency endovascular repair of leaking aortic aneurysm. *Lancet.* 1994;344(8937):1645.
23. Acosta S, et al. Increasing incidence of ruptured abdominal aortic aneurysm: A population-based study. *J Vasc Surg.* 2006;44(2):237–243.
24. Kuhnl A, et al. Incidence, treatment and mortality in patients with abdominal aortic aneurysms. *Dtsch Arztebl Int.* 2017;114(22–23):391–398.
25. Lilja F, et al. Editor's choice - trend-break in abdominal aortic aneurysm repair with decreasing surgical workload. *Eur J Vasc Endovasc Surg.* 2017;53(6):811–819.
26. Zommorodi S, et al. Understanding abdominal aortic aneurysm epidemiology: Socioeconomic position affects outcome. *J Epidemiol Community Health.* 2018;72(10):904–910.
27. Salata K, et al. The impact of randomized trial results on abdominal aortic aneurysm repair rates from 2003 to 2016: A population-based time-series analysis. *Vascular.* 2019;27(4):417–426.
28. Salata K, et al. Prevalence of elective and ruptured abdominal aortic aneurysm repairs by age and sex from 2003 to 2016 in Ontario, Canada. *JAMA Network Open.* 2018;1(7):e185418.
29. Salata K, et al. Trends in elective and ruptured abdominal aortic aneurysm repair by practice setting in Ontario, Canada, from 2003 to 2016: A population-based time-series analysis. *CMAJ Open.* 2019;7(2):E379–E384.
30. Aber A, et al. Sex differences in national rates of repair of emergency abdominal aortic aneurysm. *Br J Surg.* 2019;106(1):82–89.
31. Abdulameer H, et al. Epidemiology of fatal ruptured aortic aneurysms in the United States (1999–2016). *J Vasc Surg.* 2019;69(2):378–384.e2.
32. Zettervall SL, et al. Significant regional variation exists in morbidity and mortality after repair of abdominal aortic aneurysm. *J Vasc Surg.* 2017;65(5):1305–1312.
33. Multicentre Aneurysm Screening Study Group. Multicentre aneurysm screening study (MASS): Cost effectiveness analysis of screening for abdominal aortic aneurysms based on four year results from randomised controlled trial. *BMJ.* 2002;325(7373):1135.
34. Anjum A, et al. Explaining the decrease in mortality from abdominal aortic aneurysm rupture. *Br J Surg.* 2012;99(5):637–645.
35. Svensjo S, et al. Low prevalence of abdominal aortic aneurysm among 65-year-old Swedish men indicates a change in the epidemiology of the disease. *Circulation.* 2011;124(10):1118–1123.
36. Earnshaw JJ. Triumphs and tribulations in a new national screening programme for abdominal aortic aneurysm. *Acta Chir Belg.* 2012;112(2):108–110.
37. Lederle FA. The rise and fall of abdominal aortic aneurysm. *Circulation.* 2011;124(10):1097–1099.
38. Otterhag SN, et al. Decreasing incidence of ruptured abdominal aortic aneurysm already before start of screening. *BMC Cardiovasc Disord.* 2016;16:44.
39. Heikkinen M, et al. Ruptured abdominal aortic aneurysm in a well-defined geographic area. *J Vasc Surg.* 2002;36(2):291–296.
40. Mani K, et al. Treatment of abdominal aortic aneurysm in nine countries 2005–2009: A vascunet report. *Eur J Vasc Endovasc Surg.* 2011;42(5):598–607.
41. Markar SR, et al. Comparison of surgical intervention and mortality for seven surgical emergencies in England and the United States. *Ann Surg.* 2019;270(5):806–812.
42. Lindsay TF, et al. Ruptured abdominal aortic aneurysm, a “two-hit” ischemia/reperfusion injury: Evidence from an analysis of oxidative products. *J Vasc Surg.* 1999;30(2):219–228.
43. Lindsay TF, et al. Acute pulmonary injury in a model of ruptured abdominal aortic aneurysm. *J Vasc Surg.* 1995;22(1):1–8.
44. Edwards ST, et al. Comparative effectiveness of endovascular versus open repair of ruptured abdominal aortic aneurysm in the medicare population. *J Vasc Surg.* 2014;59(3):575–582.
45. Portelli Tremont JN, et al. Endovascular repair for ruptured abdominal aortic aneurysms has improved outcomes compared to open surgical repair. *Vasc Endovascular Surg.* 2016;50(3):147–155.
46. Raghavan ML, et al. Ex vivo biomechanical behavior of abdominal aortic aneurysm: Assessment using a new mathematical model. *Ann Biomed Eng.* 1996;24(5):573–582.
47. Vorp DA, et al. Wall strength and stiffness of aneurysmal and nonaneurysmal abdominal aorta. *Ann NY Acad Sci.* 1996;800:274–276.
48. Bellamkonda KS, et al. Characteristics and outcomes of ruptured abdominal aortic aneurysms below the size threshold for elective repair. *J Vasc Surg.* 2020;72(1):e195–e196.

49. Fillinger MF, et al. In vivo analysis of mechanical wall stress and abdominal aortic aneurysm rupture risk. *J Vasc Surg.* 2002;36(3):589–597.
50. Raghavan ML, et al. Wall stress distribution on three-dimensionally reconstructed models of human abdominal aortic aneurysm. *J Vasc Surg.* 2000;31(4):760–769.
51. Raghavan ML, et al. Regional distribution of wall thickness and failure properties of human abdominal aortic aneurysm. *J Biomech.* 2006;39(16):3010–3016.
52. Vallabhaneni SR, et al. Heterogeneity of tensile strength and matrix metalloproteinase activity in the wall of abdominal aortic aneurysms. *J Endovasc Ther.* 2004;11(4):494–502.
53. Vande Geest JP, et al. The effects of aneurysm on the biaxial mechanical behavior of human abdominal aorta. *J Biomech.* 2006;39(7):1324–1334.
54. Bluestein D, et al. Intraluminal thrombus and risk of rupture in patient specific abdominal aortic aneurysm – FSI modelling. *Comput Methods Biomed Engin.* 2009;12(1):73–81.
55. Sheidaei A, et al. Simulation of abdominal aortic aneurysm growth with updating hemodynamic loads using a realistic geometry. *Med Eng Phys.* 2011;33(1):80–88.
56. Boyd AJ, et al. Low wall shear stress predominates at sites of abdominal aortic aneurysm rupture. *J Vasc Surg.* 2016;63(6):1613–1619.
57. Erhart P, et al. Prediction of rupture sites in abdominal aortic aneurysms after finite element analysis. *J Endovasc Ther.* 2016;23(1):115–120.
58. Polzer S, et al. Biomechanical indices are more sensitive than diameter in predicting rupture of asymptomatic abdominal aortic aneurysms. *J Vasc Surg.* 2020;71(2):617–626.e6.
59. Mower WR, et al. Effect of intraluminal thrombus on abdominal aortic aneurysm wall stress. *J Vasc Surg.* 1997;26(4):602–608.
60. Schurink GW, et al. Thrombus within an aortic aneurysm does not reduce pressure on the aneurysmal wall. *J Vasc Surg.* 2000;31(3):501–506.
61. Vorp DA, et al. Association of intraluminal thrombus in abdominal aortic aneurysm with local hypoxia and wall weakening. *J Vasc Surg.* 2001;34(2):291–299.
62. Simão da Silva E. Morphology and diameter of infrarenal aortic aneurysms: A prospective autopsy study. *Cardiovasc Surg.* 2000;8(7):526–532.
63. Polzer S, et al. The impact of intraluminal thrombus failure on the mechanical stress in the wall of abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg.* 2011;41(4):467–473.
64. Barwick TD, et al. 18F-FDG PET-CT uptake is a feature of both normal diameter and aneurysmal aortic wall and is not related to aneurysm size. *Eur J Nucl Med Mol Imaging.* 2014;41(12):2310–2318.
65. Li Y, et al. A contained ruptured abdominal aortic aneurysm presenting with vertebral erosion. *Ann Vasc Surg.* 2017;41:279. e13–e17.
66. Fonseca E, et al. The draped aorta sign of impending aortic aneurysm rupture. *Abdom Radiol (NY).* 2017;42(8):2190–2191.
67. Kakisis JD, et al. Vertebral erosion due to chronic contained rupture of the abdominal aorta. *Vasc Med.* 2017;22(1):70–71.
68. Marston WA, et al. Misdiagnosis of ruptured abdominal aortic aneurysms. *J Vasc Surg.* 1992;16(1):17–22.
69. Rose J, et al. Ruptured abdominal aortic aneurysms: Clinical presentation in Auckland 1993–1997. *ANZ J Surg.* 2001;71(6):341–344.
70. Akkersdijk GJ, et al. Ruptured abdominal aortic aneurysm: Initial misdiagnosis and the effect on treatment. *Eur J Surg.* 1998;164(1):29–34.
71. Smidfelt K, et al. The impact of initial misdiagnosis of ruptured abdominal aortic aneurysms on lead times, complication rate, and survival. *Eur J Vasc Endovasc Surg.* 2017;54(1):21–27.
72. Waxman DA, et al. Unrecognized cardiovascular emergencies among Medicare patients. *JAMA Intern Med.* 2018;178(4):477–484.
73. Korner M, et al. Current role of emergency us in patients with major trauma. *Radiographics.* 2008;28(1):225–242.
74. Engamba SA, et al. Contained ruptured abdominal aortic aneurysm presenting as cauda equina syndrome. *BMJ Case Rep.* 2017;bcr2016216602.
75. Aurelian SV, et al. Giant infrarenal aortic aneurysm rupture preceded by left lower limb motor deficit. *Ann Vasc Surg.* 2017;43:317.e11–317.e14.
76. Colpaert J, et al. Ruptured abdominal aneurysm disguised as an incarcerated inguinal hernia. *Acta Chir Belg.* 2017;117(6):398–400.
77. Ben Abdallah I, et al. Phlegmasia cerulea dolens as an unusual presentation of ruptured abdominal aortic aneurysm into the inferior vena cava. *Ann Vasc Surg.* 2017;40:298.e1–298.e4.
78. Loughran CF. A review of the plain abdominal radiograph in acute rupture of abdominal aortic aneurysms. *Clin Radiol.* 1986;37(4):383–387.
79. Shuman WP, et al. Suspected leaking abdominal aortic aneurysm: Use of sonography in the emergency room. *Radiology.* 1988;168(1):117–119.
80. Knaut AL, et al. Ultrasonographic measurement of aortic diameter by emergency physicians approximates results obtained by computed tomography. *J Emerg Med.* 2005;28(2):119–126.
81. Rubano E, et al. Systematic review: Emergency department bedside ultrasonography for diagnosing suspected abdominal aortic aneurysm. *Acad Emerg Med.* 2013;20(2):128–138.
82. Dent B, et al. Emergency ultrasound of the abdominal aorta by UK emergency physicians: A prospective cohort study. *Emerg Med J.* 2007;24(8):547–549.
83. Weinbaum FI, et al. The accuracy of computed tomography in the diagnosis of retroperitoneal blood in the presence of abdominal aortic aneurysm. *J Vasc Surg.* 1987;6(1):11–16.
84. Biancari F, et al. Diagnostic accuracy of computed tomography in patients with suspected abdominal aortic aneurysm rupture. *Eur J Vasc Endovasc Surg.* 2013;45(3):227–230.
85. Hoornweg LL, et al. Interobserver and intraobserver variability of interpretation of CT-angiography in patients with a suspected abdominal aortic aneurysm rupture. *Eur J Vasc Endovasc Surg.* 2008;35(3):295–300.
86. Lloyd GM, et al. Feasibility of preoperative computer tomography in patients with ruptured abdominal aortic aneurysm: A time-to-death study in patients without operation. *J Vasc Surg.* 2004;39(4):788–791.
87. Davis FM, et al. Variation in hospital door-to-intervention time for ruptured AAAs and its association with outcomes. *Ann Vasc Surg.* 2020;62:83–91.
88. Hoornweg LL, et al. The Amsterdam Acute Aneurysm Trial: Suitability and application rate for endovascular repair of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg.* 2007;33(6):679–683.
89. IMPROVE Trial Investigators. Observations from the improve trial concerning the clinical care of patients with ruptured abdominal aortic aneurysm. *Br J Surg.* 2014;101(3):216–224; discussion 224.
90. Boyle JR, et al. Existing delays following the presentation of ruptured abdominal aortic aneurysm allow sufficient time to assess patients for endovascular repair. *Eur J Vasc Endovasc Surg.* 2005;29(5):505–509.
91. Hincliffe RJ, et al. A randomised trial of endovascular and open surgery for ruptured abdominal aortic aneurysm - results of a pilot study and lessons learned for future studies. *Eur J Vasc Endovasc Surg.* 2006;32(5):506–513; discussion 14–15.
92. Mehta M, et al. Establishing a protocol for endovascular treatment of ruptured abdominal aortic aneurysms: Outcomes of a prospective analysis. *J Vasc Surg.* 2006;44(1):1–8; discussion 8.
93. Maybury RS, et al. Rural hospitals face a higher burden of ruptured abdominal aortic aneurysm and are more likely to transfer patients for emergent repair. *J Am Coll Surg.* 2011;212(6):1061–1067.
94. Park BD, et al. Trends in treatment of ruptured abdominal aortic aneurysm: Impact of endovascular repair and implications for future care. *J Vasc Surg.* 2013;216:745–754.
95. Bickell WH, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. *N Engl J Med.* 1994;331(17):1105–1109.
96. Crawford ES. Ruptured abdominal aortic aneurysm: An editorial. *J Vasc Surg.* 1991;13(2):348–350.
97. Johansson PI, et al. Proactive administration of platelets and plasma for patients with a ruptured abdominal aortic aneurysm: Evaluating a change in transfusion practice. *Transfusion.* 2007;47(4):593–598.

98. Reimerink JJ, et al. Controlled hypotension in patients suspected of a ruptured abdominal aortic aneurysm: Feasibility during transport by ambulance services and possible harm. *Eur J Vasc Endovasc Surg.* 2010;40(1):54–59.
99. Roberts K, et al. Hypotensive resuscitation in patients with ruptured abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg.* 2006;31(4):339–344.
100. Martini WZ. Coagulopathy by hypothermia and acidosis: Mechanisms of thrombin generation and fibrinogen availability. *J Trauma.* 2009;67(1):202–208; discussion 208–209.
101. Spahn DR, et al. The European guideline on management of major bleeding and coagulopathy following trauma: Fifth edition. *Crit Care.* 2019;23(1):98.
102. Dick F, et al. Delayed volume resuscitation during initial management of ruptured abdominal aortic aneurysm. *J Vasc Surg.* 2013;57(4):943–950.
103. Mehta M. Endovascular aneurysm repair for ruptured abdominal aortic aneurysm: The Albany Vascular Group approach. *J Vasc Surg.* 2010;52(6):1706–1712.
104. Peppelenbosch N, et al. Emergency treatment of acute symptomatic or ruptured abdominal aortic aneurysm. Outcome of a prospective intent-to-treat by EVAR protocol. *Eur J Vasc Endovasc Surg.* 2003;26(3):303–310.
105. Harkin DW, et al. Endovascular ruptured abdominal aortic aneurysm repair (EVRAR): A systematic review. *Eur J Vasc Endovasc Surg.* 2007;34(6):673–681.
106. Mastracci TM, et al. Endovascular repair of ruptured abdominal aortic aneurysms: A systematic review and meta-analysis. *J Vasc Surg.* 2008;47(1):214–221.
107. Badger SA, et al. Aortic necks of ruptured abdominal aneurysms dilate more than asymptomatic aneurysms after endovascular repair. *J Vasc Surg.* 2006;44(2):244–249.
108. Hincliffe RJ, et al. Comparison of morphologic features of intact and ruptured aneurysms of infrarenal abdominal aorta. *J Vasc Surg.* 2003;38(1):88–92.
109. Richards T, et al. The importance of anatomical suitability and fitness for the outcome of endovascular repair of ruptured abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg.* 2009;38(3):285–290.
110. Slater BJ, et al. Anatomic suitability of ruptured abdominal aortic aneurysms for endovascular repair. *Ann Vasc Surg.* 2008;22(6):716–722.
111. IMPROVE Trial Investigators. The effect of aortic morphology on perioperative mortality of ruptured abdominal aortic aneurysm. *Eur Heart J.* 2015;36(21):1328–1334.
112. Bath J, et al. Trends in management and outcomes of vascular emergencies in the nationwide inpatient sample. *Vasa.* 2020;49(2):99–105.
113. Tam G, et al. Epidemiology of abdominal aortic aneurysms in a Chinese population during introduction of endovascular repair, 1994 to 2013: A retrospective observational study. *Medicine.* 2018;97(9):e9740.
114. Dias-Neto M, et al. Nationwide analysis of ruptured abdominal aortic aneurysm in Portugal (2000–2015). *Eur J Vasc Endovasc Surg.* 2020;16:16.
115. Gimzewski M, et al. Totally percutaneous versus surgical cut-down femoral artery access for elective bifurcated abdominal endovascular aneurysm repair. *Cochrane Database Syst Rev.* 2017;2:CD010185.
116. Chen SL, et al. Comparison of percutaneous versus open femoral cut-down access for endovascular repair of ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2017;66(5):1364–1370.
117. Berland TL, et al. Technique of supraceliac balloon control of the aorta during endovascular repair of ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2013;57(1):272–275.
118. Najjar SF, et al. Percutaneous endovascular repair of ruptured abdominal aortic aneurysms. *Arch Surg.* 2007;142(11):1049–1052.
119. Raux M, et al. Endovascular balloon occlusion is associated with reduced intraoperative mortality of unstable patients with ruptured abdominal aortic aneurysm but fails to improve other outcomes. *J Vasc Surg.* 2015;61(2):304–308.
120. Borger van der Burg BLS, et al. A systematic review and meta-analysis of the use of resuscitative endovascular balloon occlusion of the aorta in the management of major exsanguination. *Eur J Trauma Emerg Surg.* 2018;44(4):535–550.
121. Starnes BW, et al. Management of ruptured abdominal aortic aneurysm in the endovascular era. *J Vasc Surg.* 2010;51(1):9–17; discussion 18.
122. Chen SL, et al. Locoregional anesthesia offers improved outcomes after endovascular repair of ruptured abdominal aortic aneurysms. *Ann Vasc Surg.* 2019;59:134–142.
123. Bennett KM, et al. Locoregional anesthesia is associated with lower 30-day mortality than general anesthesia in patients undergoing endovascular repair of ruptured abdominal aortic aneurysm. *J Vasc Surg.* 2019;70(6):1862–1867.e1.
124. Faizer R, et al. Decreased mortality with local versus general anesthesia in endovascular aneurysm repair for ruptured abdominal aortic aneurysm in the Vascular Quality Initiative database. *J Vasc Surg.* 2019;70(1):92–101.e1.
125. Mouton R, et al. Local anaesthesia for endovascular repair of ruptured abdominal aortic aneurysm. *Br J Surg.* 2019;106(1):74–81.
126. Kansal V, et al. The effect of endograft device on patient outcomes in endovascular repair of ruptured abdominal aortic aneurysms. *Vascular.* 2017;25(6):657–665.
127. Hincliffe RJ, et al. A modular aortouniliac endovascular stent-graft is a useful device for the treatment of symptomatic and ruptured infrarenal abdominal aortic aneurysms: One-year results from a multicentre study. *Eur J Vasc Endovasc Surg.* 2007;34(3):291–298.
128. Peppelenbosch N, et al. Endograft treatment of ruptured abdominal aortic aneurysms using the Talent aortouniliac system: An international multicenter study. *J Vasc Surg.* 2006;43(6):1111–1123; discussion 1123.
129. Gupta PK, et al. Outcomes after use of aortouniliac endoprosthesis versus modular or unibody bifurcated endoprostheses for endovascular repair of ruptured abdominal aortic aneurysms. *Vasc Endovasc Surg.* 2017;51(6):357–362.
130. IMPROVE Trial Investigators. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ.* 2014;348:f7661.
131. Nguyen AT, et al. Transperitoneal approach should be considered for suspected ruptured abdominal aortic aneurysms. *Ann Vasc Surg.* 2007;21(2):129–132.
132. Bown MJ, et al. The systemic inflammatory response syndrome, organ failure, and mortality after abdominal aortic aneurysm repair. *J Vasc Surg.* 2003;37(3):600–606.
133. Chang BB, et al. Selective use of retroperitoneal aortic exposure in the emergency treatment of ruptured and symptomatic abdominal aortic aneurysms. *Am J Surg.* 1988;156(2):108–110.
134. Darling 3rd C, et al. Current status of the use of retroperitoneal approach for reconstructions of the aorta and its branches. *Ann Surg.* 1996;224(4):501–506; discussion 506–508.
135. Siracuse JJ, et al. Contemporary open repair of ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2017;65(4):1023–1028.
136. Marty-Ané CH, et al. Ruptured abdominal aortic aneurysm: Influence of intraoperative management on surgical outcome. *J Vasc Surg.* 1995;22(6):780–786.
137. Serracino-Inglott F, et al. The use of a cell saver during repair of ruptured abdominal aortic aneurysms increases early survival. *Ann R Coll Surg Engl.* 2005;87(6):475.
138. Frank SM, et al. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. *JAMA.* 1997;277(14):1127–1134.
139. Rasmussen TE, et al. Early abdominal closure with mesh reduces multiple organ failure after ruptured abdominal aortic aneurysm repair: Guidelines from a 10-year case-control study. *J Vasc Surg.* 2002;35(2):246–253.
140. Acosta S, et al. Temporary abdominal closure after abdominal aortic aneurysm repair: A systematic review of contemporary observational studies. *Eur J Vasc Endovasc Surg.* 2016;51(3):371–378.
141. Johnston KW. Ruptured abdominal aortic aneurysm: Six-year follow-up results of a multicenter prospective study. Canadian Society for Vascular Surgery Aneurysm Study Group. *J Vasc Surg.* 1994;19(5):888–900.

142. Becquemin JP, et al. Colon ischemia following abdominal aortic aneurysm repair in the era of endovascular abdominal aortic repair. *J Vasc Surg.* 2008;47(2):258–263; discussion 263.
143. Champagne BJ, et al. Incidence of colonic ischemia after repair of ruptured abdominal aortic aneurysm with endograft. *J Am Coll Surg.* 2007;204(4):597–602.
144. Tottrup M, et al. The value of routine flexible sigmoidoscopy within 48 hours after surgical repair of ruptured abdominal aortic aneurysms. *Ann Vasc Surg.* 2013;27(6):714–718.
145. Loftus IM, et al. The abdominal compartment syndrome following aortic surgery. *Eur J Vasc Endovasc Surg.* 2003;25(2):97–109.
146. Kirkpatrick AW, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: Updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med.* 2013;39(7):1190–1206.
147. Meldrum DR, et al. Prospective characterization and selective management of the abdominal compartment syndrome. *Am J Surg.* 1997;174(6):667–672; discussion 672–673.
148. Mehta M, et al. Factors associated with abdominal compartment syndrome complicating endovascular repair of ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2005;42(6):1047–1051.
149. Horer T, et al. Tissue plasminogen activator-assisted hematoma evacuation to relieve abdominal compartment syndrome after endovascular repair of ruptured abdominal aortic aneurysm. *J Endovasc Ther.* 2012;19(2):144–148.
150. Ersryd S, et al. Editor's choice - abdominal compartment syndrome after surgery for abdominal aortic aneurysm: Subgroups, risk factors, and outcome. *Eur J Vasc Endovasc Surg.* 2019;58(5):671–679.
151. Peppelenbosch AG, et al. Open repair for ruptured abdominal aortic aneurysm and the risk of spinal cord ischemia: Review of the literature and risk-factor analysis. *Eur J Vasc Endovasc Surg.* 2010;40(5):589–595.
152. Peppelenbosch N, et al. Emergency endovascular treatment for ruptured abdominal aortic aneurysm and the risk of spinal cord ischemia. *J Vasc Surg.* 2005;42(4):608–614.
153. Parotto M, et al. Hyperbaric oxygen therapy for spinal cord ischaemia after complex aortic repair - a retrospective review. *Anaesthetist Intensive Ther.* 2018;50(2):103–109.
154. Pedersen TF, et al. Randomized clinical trial of remote ischaemic preconditioning versus no preconditioning in the prevention of perioperative myocardial infarction during open surgery for ruptured abdominal aortic aneurysm. *BJS Open.* 2018;2(3):112–118.
155. Kopolovic I, et al. Elevated cardiac troponin in the early post-operative period and mortality following ruptured abdominal aortic aneurysm: A retrospective population-based cohort study. *Crit Care.* 2012;16(4):R147.
156. Desgranges P, et al. Editor's choice - ECAR (Endovasculaire ou Chirurgie dans les Anevrismes aorto-iliaques Rompus): A French randomized controlled trial of endovascular versus open surgical repair of ruptured aorto-iliac aneurysms. *Eur J Vasc Endovasc Surg.* 2015;50(3):303–310.
157. Harris LM, et al. Ruptured abdominal aortic aneurysms: Factors affecting mortality rates. *J Vasc Surg.* 1991;14(6):812–818; discussion 819–820.
158. El-Sabour RA, et al. Suprarenal or supraceliac aortic clamping during repair of infrarenal abdominal aortic aneurysms. *Tex Heart Inst J.* 2001;28(4):254–264.
159. Tanius A, et al. Renal artery coverage during endovascular aneurysm repair for ruptured abdominal aortic aneurysm. *Ann Vasc Surg.* 2020;62:63–69.
160. Hermreck AS, et al. Severe jaundice after rupture of abdominal aortic aneurysm. *Am J Surg.* 1977;134(6):745–748.
161. Maziar DE, et al. The impact of multiple organ dysfunction on mortality following ruptured abdominal aortic aneurysm repair. *Ann Vasc Surg.* 1998;12(2):93–100.
162. Visser JJ, et al. Prediction of 30-day mortality after endovascular repair or open surgery in patients with ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2009;49(5):1093–1099.
163. Tilney NL, et al. Sequential system failure after rupture of abdominal aortic aneurysms: An unsolved problem in postoperative care. *Ann Surg.* 1973;178(2):117–122.
164. Forbes TL, et al. Leukocyte activity and tissue injury following ischemia-reperfusion in skeletal muscle. *Microvasc Res.* 1996;51(3):275–287.
165. Fan J, et al. Hemorrhagic shock primes for increased expression of cytokine-induced neutrophil chemoattractant in the lung: Role in pulmonary inflammation following lipopolysaccharide. *J Immunol.* 1998;161(1):440–447.
166. Shahani R, et al. Role of tnf-alpha in myocardial dysfunction after hemorrhagic shock and lower-torso ischemia. *Am J Physiol Heart Circ Physiol.* 2000;278(3):H942–950.
167. Sadat U, et al. An emergency evar service reduces mortality in ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg.* 2009;37(2):189–193.
168. Anain PM, et al. Early and mid-term results of ruptured abdominal aortic aneurysms in the endovascular era in a community hospital. *J Vasc Surg.* 2007;46(5):898–905.
169. Coppi G, et al. A single-center experience in open and endovascular treatment of hemodynamically unstable and stable patients with ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2006;44(6):1140–1147.
170. Holt PJ, et al. Propensity scored analysis of outcomes after ruptured abdominal aortic aneurysm. *Br J Surg.* 2010;97(4):496–503.
171. Mayer D, et al. Complete replacement of open repair for ruptured abdominal aortic aneurysms by endovascular aneurysm repair: A two-center 14-year experience. *Ann Surg.* 2012;256(5):688–695; discussion 695–696.
172. Mehta M, et al. The impact of hemodynamic status on outcomes of endovascular abdominal aortic aneurysm repair for rupture. *J Vasc Surg.* 2013;57(5):1255–1260.
173. Mehta M, et al. Treatment options for delayed AAA rupture following endovascular repair. *J Vasc Surg.* 2011;53(1):14–20.
174. Ockert S, et al. Early and midterm results after open and endovascular repair of ruptured abdominal aortic aneurysms in a comparative analysis. *J Endovasc Ther.* 2007;14(3):324–332.
175. Oranen BI, et al. Is emergency endovascular aneurysm repair associated with higher secondary intervention risk at mid-term follow-up? *J Vasc Surg.* 2006;44(6):1156–1161.
176. Reimerink JJ, et al. Endovascular repair versus open repair of ruptured abdominal aortic aneurysms: A multicenter randomized controlled trial. *Ann Surg.* 2013;258(2):248–256.
177. Sadat U, et al. Endovascular vs open repair of acute abdominal aortic aneurysms—a systematic review and meta-analysis. *J Vasc Surg.* 2008;48(1):227–236.
178. Saqib N, et al. Endovascular repair of ruptured abdominal aortic aneurysm does not confer survival benefits over open repair. *J Vasc Surg.* 2012;56(3):614–619.
179. Sweeting MJ, et al. Ruptured aneurysm trials: The importance of longer-term outcomes and meta-analysis for 1-year mortality. *Eur J Vasc Endovasc Surg.* 2015;50(3):297–302.
180. Ten Bosch JA, et al. Endovascular aneurysm repair is superior to open surgery for ruptured abdominal aortic aneurysms in EVAR-suitable patients. *J Vasc Surg.* 2010;52(1):13–18.
181. Veith FJ, et al. Collected world and single center experience with endovascular treatment of ruptured abdominal aortic aneurysms. *Ann Surg.* 2009;250(5):818–824.
182. Veith FJ, et al. Is a randomized trial necessary to determine whether endovascular repair is the preferred management strategy in patients with ruptured abdominal aortic aneurysms? *J Vasc Surg.* 2010;52(4):1087–1093.
183. Visser JJ, et al. Endovascular repair versus open surgery in patients with ruptured abdominal aortic aneurysms: Clinical outcomes with 1-year follow-up. *J Vasc Surg.* 2006;44(6):1148–1155.
184. Wyss TR, et al. Rate and predictability of graft rupture after endovascular and open abdominal aortic aneurysm repair: Data from the EVAR trials. *Ann Surg.* 2010;252(5):805–812.
185. Hill AB, et al. Health-related quality of life in survivors of open ruptured abdominal aortic aneurysm repair: A matched, controlled cohort study. *J Vasc Surg.* 2007;46(2):223–229.
186. IMPROVE Trial Investigators. Comparative clinical effectiveness and cost effectiveness of endovascular strategy v open repair for ruptured abdominal aortic aneurysm: Three year results of the improve randomised trial. *BMJ.* 2017;359:j4859.

187. Badger S, et al. Endovascular treatment for ruptured abdominal aortic aneurysm. *Cochrane Database Syst Rev.* 2017;5:CD005261.
188. Kontopoulos N, et al. Meta-analysis and meta-regression analysis of outcomes of endovascular and open repair for ruptured abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg.* 2020;59(3):399–410.
189. Lundgren F, et al. Treatment choice and survival after ruptured abdominal aortic aneurysm: A population-based study. *J Vasc Surg.* 2020;72:508–517.e11.
190. Yamaguchi T, et al. Impact of endovascular repair on the outcomes of octogenarians with ruptured abdominal aortic aneurysms: A nationwide Japanese study. *Eur J Vasc Endovasc Surg.* 2020;59(2):219–225.
191. Gupta AK, et al. Real-world evidence of superiority of endovascular repair in treating ruptured abdominal aortic aneurysm. *J Vasc Surg.* 2018;68(1):74–81.
192. D’Oria M, et al. Short term and long term outcomes after endovascular or open repair for ruptured infrarenal abdominal aortic aneurysms in the vascular quality initiative. *Eur J Vasc Endovasc Surg.* 2020;59(5):703–716.
193. Wang LJ, et al. Endovascular repair of ruptured abdominal aortic aneurysm is superior to open repair: Propensity-matched analysis in the vascular quality initiative. *J Vasc Surg.* 2020;72(2):498–507.
194. Varkevisser RRB, et al. Five-year survival following endovascular repair of ruptured abdominal aortic aneurysms is improving. *J Vasc Surg.* 2020;72(1):105–113.e4.
195. Acosta S, et al. The hardman index in patients operated on for ruptured abdominal aortic aneurysm: A systematic review. *J Vasc Surg.* 2006;44(5):949–954.
196. Tambbyraja AL, et al. Prognostic scoring in ruptured abdominal aortic aneurysm: A prospective evaluation. *J Vasc Surg.* 2008;47(2):282–286.
197. Tambbyraja AL, et al. Prediction of outcome after abdominal aortic aneurysm rupture. *J Vasc Surg.* 2008;47(1):222–230.
198. Kapma M, et al. Evaluation of risk prediction models, v-possum and gas, in patients with acute abdominal aortic rupture treated with evar or an open procedure. *J Cardiovasc Surg.* 2017;58(3):439–445.
199. Reite A, et al. Comparing the accuracy of four prognostic scoring systems in patients operated on for ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2017;65(3):609–615.
200. Neilson M, et al. External validation of a rapid ruptured abdominal aortic aneurysm score. *Ann Vasc Surg.* 2018;46:162–167.
201. von Meijenfeldt GC, et al. Development and external validation of a model predicting death after surgery in patients with a ruptured abdominal aortic aneurysm: The Dutch Aneurysm Score. *Eur J Vasc Endovasc Surg.* 2017;53(2):168–174.
202. Sweeting MJ, et al. Value of risk scores in the decision to palliate patients with ruptured abdominal aortic aneurysm. *Br J Surg.* 2018;105(9):1135–1144.
203. Bastos Goncalves F, et al. Life expectancy and causes of death after repair of intact and ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2016;63(3):610–616.
204. Boxer LK, et al. Payer status is related to differences in access and outcomes of abdominal aortic aneurysm repair in the United States. *Surgery.* 2003;134(2):142–145.
205. Cho J-S, et al. Long-term survival and late complications after repair of ruptured abdominal aortic aneurysms. *J Vasc Surg.* 1998;27(5):813–820.
206. Piper G, et al. Short-term predictors and long-term outcome after ruptured abdominal aortic aneurysm repair. *Am Surg.* 2003;69(8):703–709; discussion 709–710.
207. Robinson WP, et al. Endovascular repair of ruptured abdominal aortic aneurysms does not reduce later mortality compared with open repair. *J Vasc Surg.* 2016;63(3):617–624.
208. Robinson WP, et al. Derivation and validation of a practical risk score for prediction of mortality after open repair of ruptured abdominal aortic aneurysms in a US regional cohort and comparison to existing scoring systems. *J Vasc Surg.* 2013;57(2):354–361.
209. Wise ES, et al. Prediction of in-hospital mortality after ruptured abdominal aortic aneurysm repair using an artificial neural network. *J Vasc Surg.* 2015;62(1):8–15.
210. Meltzer AJ, et al. Impact of surgeon and hospital experience on outcomes of abdominal aortic aneurysm repair in New York state. *J Vasc Surg.* 2017;66(3):728–734.e2.
211. Phillips P, et al. Procedure volume and the association with short-term mortality following abdominal aortic aneurysm repair in European populations: A systematic review. *Eur J Vasc Endovasc Surg.* 2017;53(1):77–88.
212. Jang HN, et al. Evaluation of preoperative predictors of 30-day mortality in patients with ruptured abdominal aortic aneurysm. *Vasc Specialist International.* 2017;33(3):93–98.
213. Healey CT, et al. Predicting mortality of ruptured abdominal aortic aneurysms in the era of endovascular repair. *Ann Vasc Surg.* 2017;38:59–63.
214. Barakat HM, et al. Perioperative, postoperative, and long-term outcomes following open surgical repair of ruptured abdominal aortic aneurysm. *Angiology.* 2020;71(7):626–632.
215. Behrendt CA, et al. Impact of weekend treatment on short-term and long-term survival after urgent repair of ruptured aortic aneurysms in Germany. *J Vasc Surg.* 2019;69(3):792–799.e2.
216. O’Donnell TFX, et al. The weekend effect in AAA repair. *Ann Surg.* 2019;269(6):1170–1175.
217. Kontopoulos N, et al. Prognosis systematic review and meta-analysis of outcomes of open and endovascular repair of ruptured abdominal aortic aneurysm in patients with hostile vs. friendly aortic anatomy. *Eur J Vasc Endovasc Surg.* 2020;59(5):717–728.
218. Adkar SS, et al. Laparotomy during endovascular repair of ruptured abdominal aortic aneurysms increases mortality. *J Vasc Surg.* 2017;65(2):356–361.
219. Agrawal A, et al. Factors affecting patients’ functional status and their impact on outcomes of ruptured abdominal aortic aneurysms. *J Vasc Surg.* 2018;68(3):712–719.
220. Sonesson B, et al. Outcome after ruptured AAA repair in octo- and nonagenarians in Sweden 1994–2014. *Eur J Vasc Endovasc Surg.* 2017;53(5):656–662.
221. Tan TW, et al. Outcomes of endovascular and open surgical repair of ruptured abdominal aortic aneurysms in elderly patients. *J Vasc Surg.* 2017;66(1):46–70.
222. Roosendaal LC, et al. Outcome of ruptured abdominal aortic aneurysm repair in octogenarians: A systematic review and meta-analysis. *Eur J Vasc Endovasc Surg.* 2020;59(1):16–22.
223. Dillavou ED, et al. A decade of change in abdominal aortic aneurysm repair in the United States: Have we improved outcomes equally between men and women? *J Vasc Surg.* 2006;43(2):230–238; discussion 238.
224. McPhee JT, et al. The impact of gender on presentation, therapy, and mortality of abdominal aortic aneurysm in the United States, 2001–2004. *J Vasc Surg.* 2007;45(5):891–899.
225. Sidloff DA, et al. Sex differences in mortality after abdominal aortic aneurysm repair in the UK. *Br J Surg.* 2017;104(12):1656–1664.
226. Stuntz M, et al. Persisting disparities between sexes in outcomes of ruptured abdominal aortic aneurysm hospitalizations. *Sci Rep.* 2017;7(1):17994.
227. Zommorodi S, et al. Sex differences in repair rates and outcomes of patients with ruptured abdominal aortic aneurysm. *Br J Surg.* 2019;106(11):1480–1487.
228. Wang LJ, et al. Sex disparity in outcomes of ruptured abdominal aortic aneurysm repair driven by in-hospital treatment delays. *Ann Surg.* 2019;270(4):630–638.
229. Budtz-Lilly J, et al. Editor’s choice - the impact of centralisation and endovascular aneurysm repair on treatment of ruptured abdominal aortic aneurysms based on international registries. *Eur J Vasc Endovasc Surg.* 2018;56(2):181–188.
230. Trenner M, et al. Editor’s choice - high annual hospital volume is associated with decreased in hospital mortality and complication rates following treatment of abdominal aortic aneurysms: Secondary data analysis of the nationwide German DRG statistics from 2005 to 2013. *Eur J Vasc Endovasc Surg.* 2018;55(2):185–194.
231. Yamaguchi T, et al. The impact of institutional case volume on the prognosis of ruptured aortic aneurysms: A Japanese nationwide study. *Interactive Cardiovasc Thoracic Surg.* 2019;29(1):109–116.

232. Greenleaf EK, et al. Outcomes after ruptured abdominal aortic aneurysm repair in the era of centralized care. *J Vasc Surg.* 2020;71(4):1148–1161.
233. Gavali H, et al. Editor's choice - prolonged ICU length of stay after AAA repair: Analysis of time trends and long-term outcome. *Eur J Vasc Endovasc Surg.* 2017;54(2):157–163.
234. Kazmers A, et al. Aneurysm rupture is independently associated with increased late mortality in those surviving abdominal aortic aneurysm repair. *J Surg Res.* 2001;95(1):50–53.
235. Karthikesalingam A, et al. Comparison of long-term mortality after ruptured abdominal aortic aneurysm in England and Sweden. *Br J Surg.* 2016;103(3):199–206.
236. Powell JT, et al. Editor's choice - re-interventions after repair of ruptured abdominal aortic aneurysm: A report from the IMPROVE randomised trial. *Eur J Vasc Endovasc Surg.* 2018;55(5):625–632.
237. Skervin A, et al. Early and late aneurysm rupture after evar: A systematic review and meta-analysis. *Int J Surg.* 2015;23:S15–S134.
238. Hinterseher I, et al. Quality of life and long-term results after ruptured abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg.* 2004;28(3):262–269.
239. Laukontaus SJ, et al. Utility of surgery for ruptured abdominal aortic aneurysm. *Ann Vasc Surg.* 2006;20(1):42–48.

Isolated Iliac Artery Aneurysms and their Management

SHERNAZ S. DOSSABHOY and RONALD L. DALMAN

INTRODUCTION	995
PATHOGENESIS	995
NATURAL HISTORY	996
PRESENTATION	996
DIAGNOSIS	997
MANAGEMENT	997
Screening and Surveillance	997
Open Iliac Aneurysm Surgical Repair	999

Endovascular Repair of Common Iliac Artery Aneurysms	999
Endovascular Repair of Internal Iliac Artery Aneurysms	1002
Endovascular Repair Using Iliac Branch Devices	1003
CONCLUSIONS	1007
CHAPTER ALGORITHM	1008

INTRODUCTION

Iliac artery aneurysms (IAAs) commonly occur concurrently with more proximal arterial aneurysms. Isolated iliac aneurysms occur with an incidence of 0.4% to 1.9% in the general population.^{1,2} Aneurysmal degeneration typically involves the common iliac artery (CIA, 70%–90%) and internal iliac artery (IIA, 10%–30%), or both of these segments contiguously; external iliac artery (EIA) involvement is extremely rare.^{3,4} Bilateral common IAAs are present in at least 50% of affected patients.⁵

Iliac arteries are defined as aneurysmal when their diameter is 1.5 times greater than the “normal” or expected diameter. On physical examination, isolated asymptomatic iliac aneurysms are difficult to identify, mainly due to their anatomical location deep within the pelvis. Most commonly, IAAs are identified during abdominal aortic aneurysm (AAA) screening studies or recognized as incidental findings on abdominal and pelvic computed tomography (CT) imaging obtained for other purposes. However, when they do become symptomatic and rupture, isolated IAAs are associated with high mortality due to late and missed diagnosis or difficulty with exposure and control during open operative repair (reported mortality 0%–33% for elective surgery; 0%–75% for emergency surgery).^{1,4}

The operative approach to IAAs is guided by the anatomy, clinical stability, and the presence and severity of concomitant and proximal aortic disease. Like the experience with AAA repair, isolated IAA management has evolved toward an endovascular-first approach over the past two decades. The availability of dedicated iliac devices, including multiple branching stents, and the innovation of hybrid techniques have steadily improved the feasibility, ease, and durability of endovascular repair.

PATHOGENESIS

Mechanisms promoting IAA formation are multifactorial and involve both acquired and inherited risks (see Ch. 71, Arterial Aneurysms: Etiology, Epidemiology, and Natural History).^{6,7} Briefly, hypertension and cigarette smoking are the risk factors most prevalent in patients with iliac aneurysms.⁸ Other less common etiologies include previous trauma, iatrogenic injury, arteritis, connective tissue disorders, and infections. Historically, syphilis and tuberculosis were frequently associated with mycotic IAAs, but *Salmonella* is the most commonly identified pathogen today followed by *Staphylococcus*, a frequent culprit usually due to septic emboli.^{5,9–12} In a Chinese study of 18 patients with infected aortic and iliac aneurysms, the majority

(92%) were Gram-negative bacilli, including *Salmonella* species, *Klebsiella pneumoniae*, and *Escherichia coli*.¹³ Isolated case reports of *Candida* species have also been reported.¹⁴ It should be noted that in general for mycotic arterial aneurysms, *Staphylococcus* remains the most common pathologic species.

The proclivity for aneurysms to form in the common and internal iliac segments, sparing the external iliac artery, remains incompletely understood. Segments of the normal and aneurysmal adult aorta appear to have distinct DNA expression profiles, which may explain the site specificity and prevalence of various aneurysm phenotypes.^{11,15} The EIA may be resistant to aneurysm formation because of the distinct embryonic lineage of its vascular smooth muscle cells as compared to the aneurysm-prone common and internal iliac arteries.^{11,16} Immunobiological characteristics suggest phenotypical differences between the internal and external iliac arteries, emphasizing the concept that embryogenesis can influence the propensity of an artery to aneurysmal disease.^{11,16,17}

Disturbed or asymmetric iliac artery flow may also promote aneurysmal degeneration. In a series of 329 World War II veterans with unilateral above-the-knee amputations, amputees were five times more likely to develop abdominal aortic and iliac aneurysms than risk factor-matched controls.¹⁸ Further, AAA morphology was reproducibly related to which leg had been amputated, indicating that asymmetrical flow patterns in the aortoiliac system predisposed to pathological remodeling and aneurysmal degeneration.¹⁸ Iliac aneurysms may also form proximal to pelvic or femoral arteriovenous fistulae.

Recently three distinct morphologies of common iliac artery aneurysms (CIAs) have been identified: complex (involving a bifurcation), fusiform, and kinked (distal to a sharp bend or tortuosity in the CIA).¹⁹ Utilizing computational fluid dynamics, abnormal blood flow in the CIAA was observed to promote proximal aortic remodeling with resulting lateral deflection of the abdominal aorta towards the CIA side in most cases; these findings were confirmed in a validation cohort of 162 patients.²⁰

NATURAL HISTORY

There is a paucity of evidence regarding the true prevalence, natural history, and rupture potential of IAAs.⁷ Retrospective series have informed our understanding of this condition with regard to demographics, bilateral disease (found in 65% of patients in one series), and aneurysm expansion.^{21,22} In these series, the rate of diameter enlargement for IAAs under surveillance varied based on the baseline diameter present at the time of diagnosis; for IAA ≤ 3 cm, expansion rates averaged 0.05 to 0.15 cm/year, whereas aneurysms greater than 3 cm enlarged 0.26 to 0.29 cm/year; no differences in growth rates were noted between isolated IAAs and those present in patients with concomitant AAA.^{10,22}

IAAs are reportedly associated with a high propensity for rupture. They enlarge slowly over time, and are often first identified at the time of rupture.²³ In early reports, as many as 42% of IAAs were ruptured at the time of initial presentation, an event associated with significant mortality (range,

0%–56%).^{1,3,24} The mortality from emergent repair for rupture is approximately 28% (range, 0%–60%) as compared to a reported 5% mortality for elective IAA repair (range, 0%–50%).⁷ The mean size of ruptured IAAs varies in reports from 6 to 6.8 cm.²⁵ Though rare, in a series of 11 patients with isolated external iliac artery aneurysms (EIAs), four (36%) presented ruptured and one (9%) was symptomatic due to peripheral embolization. All ruptured EIAs were greater than 4 cm in diameter.²⁶ A literature review of internal iliac artery aneurysms (IIAs) identified 94 cases with 40% ruptured at presentation, median aneurysm size of 7.7 cm (range, 2–13 cm), and 31% mortality.²⁷ Thus, despite higher frequency and prevalence of imaging today, nearly half of IAAs in these series – common, external, and internal – still present ruptured.

In a report of 63 patients with ruptured IIAs across 28 European vascular centers, the majority (nearly 94%) ruptured at diameters greater than 4 cm with only one IIAA rupture occurring at less than 3 cm, and four occurring at less than 4 cm (6.3% of all ruptures).²⁸ Regarding anatomical distribution, isolated IIAs occurred in 30% of cases and were more typically present concurrent with aortic aneurysms (42%), common iliac aneurysms (65%), or both (37%).²⁸

Summarizing the existing evidence, uncomplicated IAAs <3.5 cm in diameter rarely rupture,^{27,28} supporting the generally accepted threshold of 3 to 3.5 cm for elective repair when asymptomatic (indications may vary between CIAs and IIAs). These recommendations vary based on anatomical location and complexity, rate of enlargement, presence of symptoms, and concomitant comorbid conditions. Symptomatic IAAs should be expeditiously repaired upon presentation at any diameter.

PRESENTATION

The anatomic location and proximity to adjacent pelvic structures including bowel, bladder, the urinary collecting system, nerve roots, and pelvic veins can obscure the diagnosis in the absence of a perceptible mass.³ Vague lower abdominal pain often results from compression or impingement of these neighboring structures. Patients may also complain of intermittent claudication or lower extremity pain secondary to embolic arterial occlusion, lower extremity paresis, sciatic neuralgia, lumbosacral pain, ureteral obstruction, tenesmus, or even constipation.¹⁰ Though rare, lower extremity deep venous thrombosis has been reported in case reports as the presenting symptom of isolated IIAs, due to the compression of the external iliac vein or the iliofemoral vein by the internal iliac artery.^{29,30}

Sudden abdominal, groin, or flank pain associated with hemorrhagic shock frequently portends rupture. Although frequently contained in the retroperitoneum at the outset, IAA rupture and resulting hemorrhage eventually leads to irreversible shock if not controlled. Delays in diagnosis contribute significantly to reported mortality, with or without emergent intervention.

In rare instances, IAAs can elicit thromboembolic symptoms and peripheral arterial insufficiency. In a single-center

retrospective review of 53 isolated IAAs over a 16-year period, intermittent claudication was identified in four cases due to iliac aneurysm thrombus causing stenosis, while ischemia was reported in three cases due to arterial embolism from the aneurysm.³¹ Distal embolization was the presenting symptom in 1 of 16 patients (9%) with symptomatic IAAs identified at a single institution over 6 years.⁸

DIAGNOSIS

As noted previously, physical examination frequently fails to identify even large IAAs.²³ Ultrasound represents the primary diagnostic and screening tool, especially in asymptomatic patients. Limitations may include user variability and suboptimal image resolution due to patient body habitus or the presence of intestinal gas. CT and magnetic resonance (MR) angiography imaging provide far more extensive detail of aortoiliac anatomy and improve diagnostic accuracy in challenging circumstances.³² However, the expense and risks of these techniques should be factored into the overall approach to the individual patient.⁷

Precise operative planning requires high-resolution, high-fidelity imaging, and in most circumstances, CT arteriography is optimal for this purpose. Using a combination of axial imaging and 3-D postprocessing, evaluation includes locations, diameters, and lengths of proximal and distal landing zones for endovascular grafting. Additionally, information regarding iliac artery tortuosity and angulation, the presence and severity of associated occlusive disease, ipsilateral and contralateral internal iliac artery patency, the status of the ipsilateral deep femoral artery, and concomitant abdominal or thoracic aortic pathology should be assessed.³³

MANAGEMENT

Iliac aneurysms are targeted for repair as they enlarge or become symptomatic (Fig. 77.1). Based on retrospective reviews and consensus statements, current recommendations favor elective repair for asymptomatic IAAs ≥ 3.5 cm in diameter in healthy patients (Table 77.1).^{7,34} Early and extensive application of CT imaging in the assessment of patients with abdominal pain has substantially reduced the historically high morbidity associated with delays in diagnosis of ruptured IAAs, but rupture

of previously unrecognized IAA still occurs, often presenting serious surgical management challenges.²⁷

Ruptured IAAs have been successfully treated using diverse endovascular techniques. In the case of ruptured CIAAs, an aortic occlusion balloon can be used to achieve proximal control of the infrarenal abdominal aorta together with coil embolization of the IIA and covered stenting of the CIA and EIA; this technique may be particularly useful in managing hemodynamically unstable patients (Fig. 77.2).³⁵ The newer iliac branch devices (IBDs; see section on Endovascular Repair Using Iliac Branch Devices) have been used to treat ruptured aortoiliac aneurysms while maintaining pelvic circulation with flow to the IIA with 100% primary assisted patency through three years and 25% secondary reintervention rate.³⁶ Finally, in the emergent setting, the Gore Excluder (Gore Contralateral Leg Endoprosthesis, W.L. Gore & Associates, Flagstaff, AZ) has been used as an inverted iliac limb endograft to successfully treat ruptured IIAAs.^{37,38} This off-label strategy involves removal of the device from its delivery shaft, reversal of the device for upside-down deployment, placement within a sheath, and use of a sheath dilator that has been modified as a pushing device to position and deploy the limb in a “pin and pull” technique.³⁷ While the latter two approaches may be useful in emergency situations, their long-term durability remains uncertain.

Screening and Surveillance

To date, no specific screening guidelines exist for isolated iliac artery aneurysms. The US Preventive Services Task Force (USPSTF) has recommended one-time screening for aortoiliac aneurysms with ultrasound for men aged 65 to 74 years who have ever smoked since 2005.³² The 2019 USPSTF guidelines include selective screening for men aged 65 to 75 years, who have never smoked; however, it recommended *against* routine screening of women aged 65 to 75 years, who have never smoked and without family history of AAA.³⁹ For women, who have ever smoked or have a family history of AAA, the “evidence is insufficient” to weigh the benefits and harms of screening.³⁹ However, the Society for Vascular Surgery (SVS) and others have argued for more liberal screening to prevent death from rupture.^{40,41}

As discussed above, asymptomatic IAAs less than 3 cm in diameter are best managed with serial surveillance imaging

TABLE 77.1

Proposed Protocol for CIAA Ultrasound Surveillance with Frequency of Scan Based on Size at Diagnosis and Predicted Rate of Expansion

CIAA diameter (cm)	Surveillance interval
1.5–2.0	3 years
2.1–2.5	2 years
2.6–3.0	1 year
3.1–3.5	6 months
>3.5	3 months

CIAA, common iliac artery aneurysm.

(Modified with permission from Dhanji A, Murray HE, Downing R. Ultrasound surveillance of common iliac artery aneurysms. *Ann Vasc Surg*. 2020;65:166–173.)

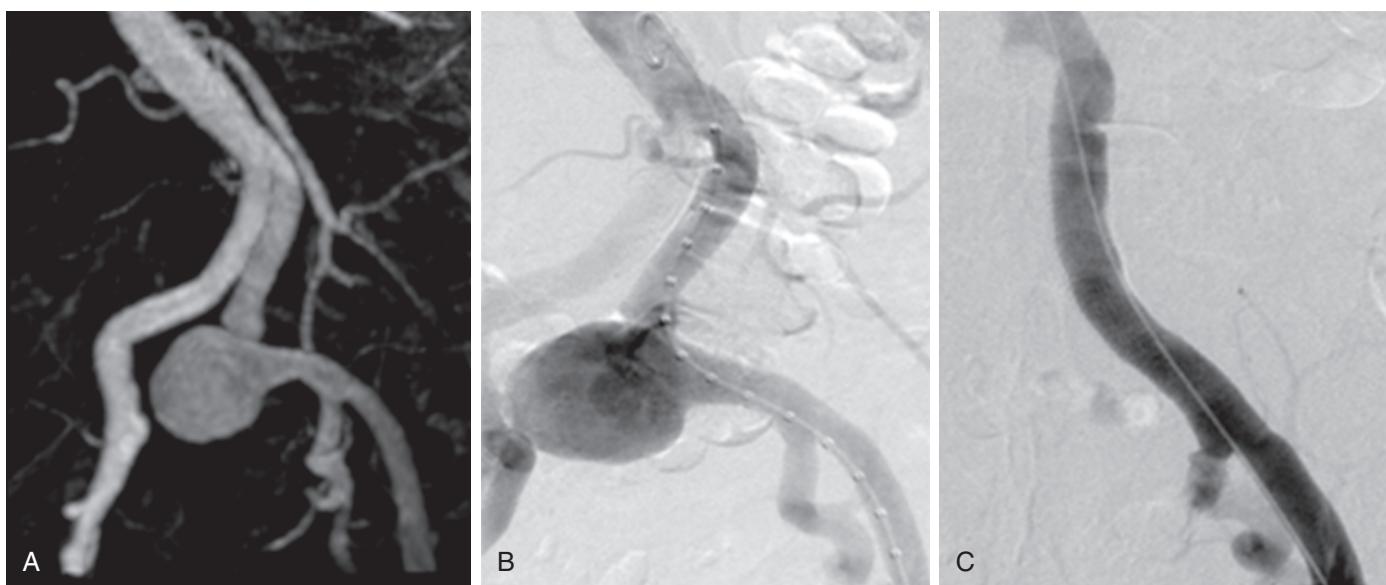


Figure 77.1 (A) MRI of isolated $3.8 \text{ cm} \times 3.5 \text{ cm}$ left CIA aneurysm, incidentally discovered. (B) Endovascular repair with sizing catheter placed ipsilateral. Angiogram demonstrating proximal and distal landing zones and iliac bifurcation. (C) Two covered stents deployed to seal and exclude aneurysm while preserving IIA. CIA, common iliac artery; IIA, internal iliac artery; MRI, magnetic resonance imaging.

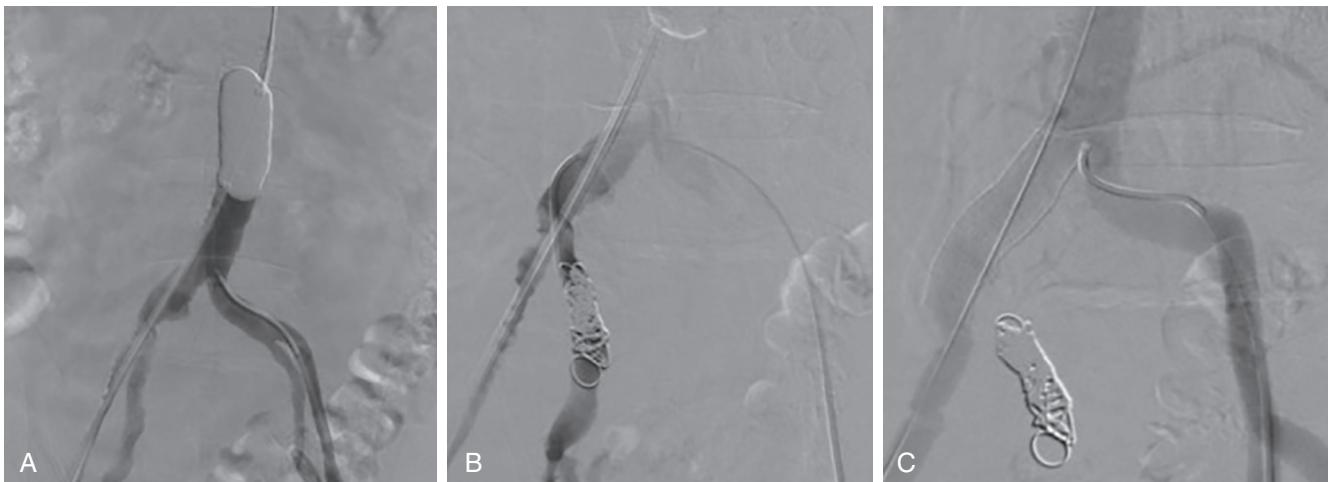


Figure 77.2 Management of a ruptured common iliac artery aneurysm with (A) proximal control of the abdominal aorta using an aortic occlusion balloon; (B) coil embolization of the right internal iliac artery; and (C) deployment of a covered stent graft. (From Kimura F, Ookubo R, Kobayashi D, et al. Successful endovascular repair of a ruptured isolated iliac artery aneurysm: A case report. *Clin Case Reports*. 2019;7(10):1880–1884.)

studies.²² Recent European society guidelines highlight the lack of data regarding appropriate follow-up intervals for IAAs and extrapolate recommendations based on AAA data, while the US guidelines make no specific recommendations regarding iliac aneurysm surveillance.^{34,40} Most recently, in a survey of 54 vascular laboratories within the United Kingdom's National Health Service, most centers began surveillance of CIAAs at 2.0–2.9 cm diameter. Growth was observed in 78% of CIAAs with an average growth rate of $1.5 \pm 0.3 \text{ mm/year}$. Unsurprisingly, a strong linear correlation was observed between CIAA diameter and time from diagnosis, whereby smaller diameter aneurysms ($< 3.0 \text{ cm}$) expanded more rapidly. Interestingly,

CIAAs with diameter $>3.0 \text{ cm}$ had an unpredictable growth trajectory with loss of linear growth. From these findings, the authors propose a protocol for ultrasound surveillance of CIAAs (Table 77.1).

Finally regarding surveillance after aneurysm treatment, in a series of 49 patients undergoing surgical or endovascular treatment of isolated IAA, despite adequate seal zone with successful aneurysm exclusion, the diameter of the proximal aorta was found to increase over time with no change or decrease in CIA diameters, thus underscoring the systemic nature of aneurysmal disease and the importance of long-term surveillance of both the aorta and iliac arteries after repair.⁴²

Open Iliac Aneurysm Surgical Repair

Due to the relatively inaccessible location of iliac aneurysms (situated deep in the pelvis), the presence of densely adherent pelvic veins, and the frequent co-occurrence of calcific occlusive disease, conventional surgical repair is challenging and carries risk of significant hemorrhage.⁴³ However, using standard open operative techniques, modern retractor systems, and patience, repair of isolated iliac aneurysms provides excellent long-term results and is generally well tolerated by low-risk patients.

The primary goal of surgical intervention is to maintain distal perfusion while preventing further aneurysmal degeneration and rupture.²³ The iliac artery may be approached from a midline, retroperitoneal, or transplant-type incision, depending on the extent of the aneurysm, the presence of unilateral or bilateral disease, and surgeon preference and experience (see Ch. 56, Abdominal Vascular Exposures). In general, large aneurysms that produce compressive symptoms require adequate exposure to effectively open and repair the aneurysm via standard endoaneurysmorrhaphy techniques. If an adequate portion of proximal CIA is nonaneurysmal, CIAs can be replaced with a prosthetic interposition graft. When the entire CIA is aneurysmal, however, control must be obtained on the aorta itself and the proximal graft must be anastomosed directly to the aorta; this usually requires transperitoneal or full retroperitoneal exposure (see Ch. 73, Aortoiliac Aneurysms: Open Surgical Treatment).

The quality of the artery will dictate the amount of exposure required for proximal vascular control. In terms of the distal extent, the graft can almost always be sewn to the bifurcation of the external and internal iliac arteries, thus preserving pelvic flow. In rare circumstances, with significant splaying of the external and internal iliac arteries or aneurysmal extension into the internal iliac artery, the distal extent of the graft must be sewn to more normal, distal arteries.

Direct open repair of the CIA also maintains collateral flow to the pelvis via the lumbar arteries and the inferior mesenteric artery, thus reducing the risk of postoperative colonic or pelvic ischemia.⁴⁴ As in the case of open AAA repair, resection of the aneurysm sac is not advised, because this increases the risk of bleeding and injury to adjacent adherent structures such as the iliac veins and the inferior vena cava. Preoperative placement of ureteral stents can reduce the risk of ureteral injury, particularly in advanced and inflammatory aneurysms.

Maintenance of antegrade IIA flow is essential for optimal outcomes, particularly in younger patients or those with contralateral internal iliac artery compromise or occlusion. Loss of IIA perfusion can lead to buttock claudication, impotence, and more rarely, colonic ischemia, gluteal necrosis, and spinal cord ischemia.^{45–50} In situations when both IIAs are affected, or if both are aneurysmal, it is advisable to use bypass grafting of at least one IIA to preserve antegrade flow.⁵ In their clinical experience with open repair of 715 iliac aneurysms in 438 patients, Huang et al. advised reimplantation of the inferior mesenteric artery to the aortic graft if both IIAs were occluded, though even adherence to that approach resulted in ischemic

colitis in two patients.²¹ When aneurysmal disease is limited to a single CIA, the ipsilateral IIA may be ligated without significant ischemic consequences. However, this strategy has other limitations, including a relatively high likelihood of progressive enlargement of residual IIAs distal to the ligature site. These may continue to be pressurized by retrograde branch artery flow, resulting in progressive enlargement, compressive symptoms, and a continued risk for late rupture.^{51–53}

Ultimately, in experienced hands, iliac artery aneurysmorrhaphy provides a durable repair with excellent outcomes. Mortality rates for elective procedures range from 0% to 5%, depending on the comorbidity profile and anatomic considerations.^{7,21,54,55} The overall incidence of perioperative complications ranges up to 22% including lower extremity ischemia from distal embolization or stenosis, visceral and pelvic wall ischemia from disruption of hypogastric flow, aneurysm reperfusion and rupture, arterioenteric fistulae, graft infection, and ureteral, neural, and venous injuries.^{3,7,56} Both early and late graft-specific complications are rare, and primary patency at 5 years approaches 100%.^{21,55}

Endovascular Repair of Common Iliac Artery Aneurysms

Treatment of concomitant aortoiliac aneurysmal disease has been preferentially endovascular since the advent of later-generation bifurcated AAA grafts.⁵⁷ Continued advancement of these technologies has shifted isolated IAA management to an endovascular-first approach as well. The most recently published European guidelines recommend endovascular repair of IAA as first-line therapy.³⁴ Endovascular repair reduces length of hospitalization, operative blood loss, the need for invasive monitoring and intensive care unit care postoperatively, and perioperative complications.⁵⁸ In a study of 33,161 patients with isolated IAA, derived from the National Inpatient Sample Database from 1988 to 2011, the total number of aneurysm repairs increased from 28 to 71 per 10 million US population following the introduction of endovascular aneurysm repair ($P < 0.001$).⁵⁹ In 2003, the annual number of endovascular iliac aneurysm repairs surpassed the number of open repairs, while death from rupture or repair of isolated IAA decreased from 4.4 to 2.3 per 10 million US population ($P < 0.001$) over a similar time period (see Ch. 74, Endovascular Aneurysm Repair Techniques and Ch. 75, Aortoiliac Aneurysms: Endovascular Treatment).³²

Single-center reports of endovascular repair of IAA demonstrate improvements in perioperative morbidity and mortality but with more frequent reinterventions than historically required following open repair. In a study of 72 patients with isolated IIAs (63 common, 21 internal, and 1 external iliac) undergoing endovascular repair from 1996 to 2015, mean aneurysm diameter was 5 cm and emergency repair was performed in 26% of patients due to rupture.⁶⁰ Overall primary technical success was 95.8% with rate of conversion to open 4.2%, in-hospital mortality 1.4%, and long-term overall mortality 30.6% with aneurysm-related mortality 2.8% (2 deaths). During mean follow-up of 4.3 years, the overall incidence of

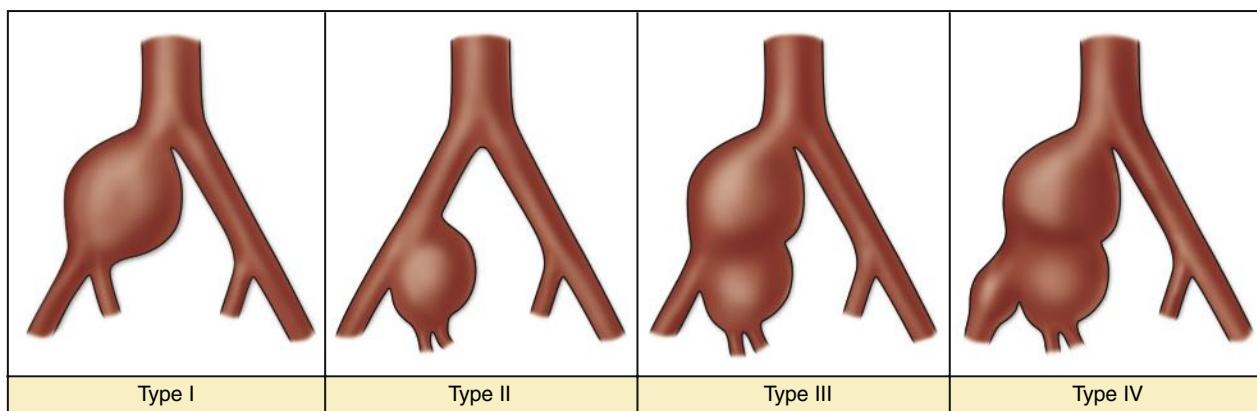


Figure 77.3 Anatomic Classification of Iliac Artery Aneurysms. (With permission from Wanhainen A, Verzini F, Van Herzele I, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *Eur J Vasc Endovasc Surg.* 2019;57(1):8–93; modified also with permission from the original by Reber PU, Brunner K, Hakki H, et al. Häufigkeit, Klassifikation und Therapie der isolierten Beckenarterienaneurysmen [Incidence, Classification and Therapy of Isolated Pelvic Artery Aneurysm]. *Chirurg.* 2001;72(4):419–424.)

endoleak was 25.8% (17 patients) with a relatively high rate of type I endoleaks (6 of 17). Ultimately 16.7% of patients required a reintervention.

In comparing outcomes of open versus endovascular repair of IAAs in 94 patients treated from 2004 to 2015, no differences were reported in 30-day morbidity, 30-day mortality, or overall survival between the two treatment modalities. However, undergoing endovascular repair or surgery for ruptured IAA increased the risk for reintervention substantially (HR 10.80 and 12.02, respectively; $P < 0.05$).⁶¹ In a recent meta-analysis, endovascular treatment was associated with higher risk of post-operative ischemic complications (including buttock claudication, bowel ischemia, and erectile dysfunction), lower risk of blood transfusion, and shorter hospital length of stay, while postoperative mortality and wound complications were similar between endovascular and open surgery groups.⁶² Importantly, primary patency and reintervention rates remained unclear due to the small number of studies ($n = 9$). Finally, in a series of 48 patients treated with percutaneous endovascular repair of IAAs, primary patency was 100% after 1 year and 87.6% after 4 years.⁶³

The primary goal of endovascular intervention is similar to that of open repair: exclude the aneurysm sac from the circulation, thereby minimizing risk for further expansion and rupture. Several classifications systems for isolated IAA have been proposed, mostly to standardize approaches to endovascular repair.^{25,64,65} The anatomic classification of IAAs put forth by Reber into type I to IV (Fig. 77.3) is simplified and can be applied regardless of operative strategy or device design.^{34,66}

Using standard techniques and devices, endovascular repair of isolated common IAAs requires approximately 2 cm of proximal and distal landing zone (see Fig. 77.1). In this case, the presence of a long common iliac artery (CIA) prior to the aneurysm allowed for creation of the proximal seal zone distal to the origin of the ipsilateral CIA. Lack of a proximal landing zone necessitates extension into the abdominal aorta to achieve seal.

In the latter circumstance, depending on the extent of aneurysmal involvement, a bifurcated aortic endograft is generally the most appropriate choice. For instance, when there is <70 mm proximal landing zone between the aortic bifurcation and a low renal artery branch, precluding the use of most off-the-shelf bifurcated aortic endografts, the “double-barrel”⁶⁷ or “double D” endograft technique can be used to deploy two limbs to each common iliac artery within an aortic cuff (Fig. 77.4).

Wide diameter distal common iliac arteries (>16 mm) have historically been treated with flared or bell-bottom iliac limbs to achieve aortoiliac aneurysm exclusion while preserving pelvic blood flow.⁶⁸ Although an initial seal may be obtained with these devices, long-term durability has been questioned due to the inherently diseased nature of the distal iliac artery.^{69,70} More recently, bell-bottom endovascular cuffs have been shown to be at risk for mid-term type Ib endoleak with any iliac limb >19 mm diameter prone to late failure.⁷¹ In a retrospective review of EVAR patients with CIA limbs ≥ 20 mm compared with those <20 mm, the rate of type Ib endoleak over 3 years was 3.9% (17 of 178) in the <20 mm iliac limb group versus 18% (11 of 61) in the ≥ 20 mm cohort. ROC curve analysis demonstrated a limb diameter >19 mm as a cutoff value for higher probability of type Ib endoleak. Moreover, in a direct comparison of treating CIAA with flared limbs versus the now widely available iliac branch devices (IBDs), Pini et al. reported better long-term outcomes with IBDs as compared to flared limbs with freedom from iliac complications at 5 years (100% vs. 78%, $P = 0.02$).⁷²

When the distal seal zone diameter is greater than 25 mm, or aneurysmal degeneration extends into the proximal IIA, the seal zone may be extended into the EIA; coil embolization or plug occlusion of the proximal internal iliac artery is generally employed to prevent retrograde flow into the common iliac aneurysm.⁷³ Because coil embolization of the internal iliac artery branches can be technically challenging, these adjuncts may be associated with increased operative time, contrast use, radiation



Figure 77.4 Postoperative CT after “double D” technique used to treat an isolated CIAA with a low branching right RA demonstrates (A) adequate blood flow to ectopic right RA and (B) double D shape of limbs within the aortic cuff. *CIAA*, common iliac artery aneurysm; *CT*, computed tomography; *RA*, renal artery. (From Date Y, Takano T, Fujii T, et al. Double D technique: an innovative modified bifurcated stent graft deployment strategy for an isolated common iliac artery aneurysm with a challenging renal artery anatomy. *Vasc Endovascular Surg.* 2019;53(7):613–616.)

time, and cost.⁷⁴ A hybrid approach including aorto-uni-iliac stent grafting from the distal aorta and extended into the EIA with coiling of the IIA and femorofemoral bypass to maintain perfusion to the contralateral limb has been employed to treat isolated large common iliac aneurysms for the last 20 years and remains in use today.⁷⁵ While requiring an additional step with extra-anatomic prosthetic graft, the long-term patency of femorofemoral bypass is acceptable in patients unsuitable for open aneurysm repair.

As an alternative, straightforward stent graft coverage of the IIA orifice without embolization can extend the distal sealing zone of the repair without significant complications. In a series of 137 patients undergoing endovascular aneurysm repair with stenting of the IIA ($n = 112$) or stenting with concomitant IIA coil embolization ($n = 25$), no significant differences were observed in incidence of postoperative buttock claudication (13.4% stenting alone, 12% stenting with coil embolization; $P = 0.852$), rates of secondary interventions, or cumulative survival at 4 years.⁷⁴ In another series of 79 patients undergoing CIAA repair without IIA coil embolization, the rate of type II endoleak arising from the covered IIA was low at 2.5%, however 26% of patients required reintervention and 28% of patients reported buttock claudication, persisting in 9.5% at one year; though no severe ischemic complications were reported, and no revascularizations were necessary.⁷⁶ Thus, covering the IIA without coil embolization may provide a safe alternative approach for some patients. However, failure to adequately seal the IIA in the process of CIA endografting may lead to long-term procedural failure secondary to persistent retrograde endoleak arising from the patent IIA. Furthermore, once the

IIA origin is covered, future percutaneous access is likely precluded, requiring open conversion or CT-guided transpsoas access directly to the internal iliac artery for later definitive management of aneurysm expansion. Ultimately, the decision to extend the repair to the EIA with or without IIA occlusion is highly dependent on the anatomy of the iliac bifurcation and presence or absence of aneurysmal degeneration involving the origin of the IIA itself (see Chapter Algorithm, below).

In patients with contralateral IIA occlusion or bilateral CIAAs, or those who are otherwise perceived to be at high risk for spinal cord ischemia, it is essential to preserve some degree of antegrade IIA flow. Current US and European society guidelines recommend preserving blood flow to at least one IIA during open and endovascular repair (Table 77.2).^{34,40} Typically, few patients experience prolonged or permanently debilitating symptoms following unilateral occlusion, and if bilateral IIA occlusion is deemed necessary, staged intervention to allow collateral flow development with close patient monitoring to detect symptom development is warranted. As an alternative to uni- or bilateral IIA occlusion, an external-to-internal iliac artery bypass may be performed in conjunction with proximal IIA ligation to effectively “move” the iliac bifurcation more distally.⁷⁷ Iliopoulos et al. examined the collateral arterial supply to the hypogastric arterial bed.⁷⁸ Using staged, sequential internal and external iliac artery occlusion techniques while measuring corresponding stump pressures, the authors demonstrated that the ipsilateral external iliac and femoral arterial systems actually provide more collateral internal iliac artery flow than does the contralateral internal iliac artery system. These findings emphasize the importance of maximizing ipsilateral

TABLE 77.2 Summary of Recent Practice Guidelines on Iliac Artery Aneurysm Repair.

	Recommendations	Level/Class of Recommendation ^a	Quality/Level of Evidence ^b
Society for Vascular Surgery (SVS), 2018	<ol style="list-style-type: none"> 1. We recommend preservation of flow to at least one internal iliac artery. 2. We recommend using FDA-approved branch endograft devices in anatomically suitable patients to maintain perfusion to at least one internal iliac artery. 3. We recommend staging bilateral internal iliac artery occlusion by at least 1 to 2 weeks if required for EVAR. 	1 1 1	A A A
European Society for Vascular and Endovascular Surgery (ESVS), 2019	<ol style="list-style-type: none"> 1. The threshold for elective repair of isolated iliac artery aneurysm (common iliac artery, internal iliac artery and external iliac artery, or combination thereof) may be considered at a minimum of 3.5 cm diameter. 2. In patients with iliac artery aneurysm, endovascular repair may be considered as first-line therapy. 3. Preserving blood flow to at least one internal iliac artery during open surgical and endovascular repair of iliac artery aneurysms is recommended. 4. In patients where internal iliac artery embolization or ligation is necessary, occlusion of the proximal main stem of the vessel is recommended if technically feasible, to preserve distal collateral circulation to the pelvis. 	IIb IIb I I	C B B C

^aLevel of recommendation from the SVS defined as 1 (strong) or 2 (weak); Class of recommendation from the ESVS defined as I (evidence that given treatment or procedure is beneficial, useful, effective); IIa (conflicting evidence with weight of evidence in favor of usefulness/efficacy); IIb (usefulness/efficacy less well established); or III (not useful/effective, may be harmful).

^bQuality of evidence from the SVS defined as A (high), B (moderate), or C (low). Level of evidence from the ESVS defined as A (data from multiple randomized clinical trials or meta-analyses); B (data from single randomized trial or large non-randomized studies); or C (consensus of expert opinion and/or small studies, retrospective studies, registries).

(Modified with permission from Chaikof EL, Dalman RL, Eskandari MK, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg*. 2018;67(1):2–77.e2; and Wanhainen A, Verzini F, Van Herzele I, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *Eur J Vasc Endovasc Surg*. 2019;57(1):8–93.)

external iliac and femoral arterial inflow and maintaining collaterals to compensate for an ipsilateral IIA occlusion and to minimize the risk for resulting pelvic ischemia. In one series of 22 patients, Hosaka et al. assessed the impact of performing endovascular aortoiliac stent grafting with concomitant unilateral internal iliac artery embolization and contralateral external-to-internal iliac artery bypass grafting, with both endograft limbs extended into the EIAs for distal seal.⁷⁹ During mean follow-up of 16 months, all bypasses remained patent without graft-related complications. Although there were no cases of sac enlargement or type I endoleak, persistent mild buttock claudication occurred in two patients (9%).⁷⁹

Innovation continues in the area of treating isolated iliac and aortoiliac aneurysms. In a series of four patients with isolated CIAAs undergoing total robotic laparoscopic repair with deployment of the Gore Hybrid Vascular Graft (GHVG; W. L. Gore & Associates, Flagstaff, AZ) for IIA preservation, technical success was 100% and patency of iliac artery grafts and GHVGs was 100% at 6 months⁸⁰ (see Ch. 64, Laparoscopic and Robotic Aortic Surgery).

Endovascular Repair of Internal Iliac Artery Aneurysms

Because of the multiple branches emanating from the internal iliac artery, preservation of flow in the presence of an IIAA is challenging. Maintaining pelvic perfusion helps to avoid the potential ischemic complications of IIA occlusion. A classification scheme for the severity of pelvic ischemia after intentional IIA occlusion during endovascular aortoiliac aneurysm repair has been developed: class 0, no symptoms; class I, nonlimiting claudication with exercise; class II, new onset impotence, with or without moderate to severe buttock pain, leading to physical limitation with exercise; class III, buttock rest pain, colonic ischemia, or both.⁸¹ In a series of 103 patients, following internal iliac artery occlusion, pelvic ischemic symptoms developed in 22 patients (21%) with 12 patients categorized in class I; 9 patients in class II; and 1 patient in class III.⁸¹ Furthermore, two unique preoperative angiographic findings were identified in 16 patients (16%) who ultimately developed chronic pelvic claudication: (1) stenosis of the remaining IIA origin greater

than 70% with nonopacification of more than three of the six typical IIA branches (63%); and (2) small-caliber, diseased or absent medial and lateral femoral circumflex arteries ipsilateral to the side of the IIA occlusion (25%).⁸¹ These findings emphasize the importance of preoperative evaluation of the pelvic circulation to aid in the safe planning of IIA embolization and identification of the need for revascularization procedures.

In a single-institution retrospective review of 46 patients with 55 IIAs treated in endovascular fashion with iliac branch devices (IBDs) or occlusion of IIA by ostium overage, the IIA coverage group had higher technical success (100% vs. 93.1%) and a lower rate of reintervention (4.3% vs. 13.8%), but a higher rate of gluteal claudication as compared with the IBD group (15.2% vs. 0%).⁸² Additionally, selective preservation of the superior gluteal artery (SGA) may be sufficient to reduce buttock claudication when treating isolated IIAs. In one series of 6 patients, covered self-expanding stent grafts were used to exclude the IIAs while preserving SGA flow while occluding the inferior gluteal artery (IGA) and other distal IIA branches with vascular plugs to prevent endoleak with 100% SGA graft patency and all patients free from buttock claudication at 1-month follow-up.⁸³ This technique requires choosing which branch of the IIA is most dominant (i.e. anterior or posterior trunk) based on preoperative imaging and preserving flow to the most relevant branch.

Novel endovascular or hybrid techniques may be utilized to preserve IIA flow, especially in emergent cases, with acceptable technical success and short-term outcomes. In general, direct stent graft repair is possible provided proximal and distal landing zones are present within the aneurysmal IIA. This may require landing the stent in the largest distal branch available following coil embolization of smaller branches feeding into the aneurysm sac. If the proximal landing zone is compromised, a “chimney” type graft can extend into the CIA or EIA,^{84,85} or the “sandwich” technique may be employed (Fig. 77.5).^{86,87} In the latter technique, the covered self-expanding stent within the IIA lies side by side with the iliac limb extender within the common iliac limb. This technique is one durable endovascular option to preserve IIA flow because it involves stenting into normal-sized arteries while excluding flow to the aneurysm itself. Alternatively, Wu et al. have described the crossover chimney technique, which consists of delivering the chimney graft across the aortic bifurcation outside the bifurcated stent graft to provide retrograde flow to the IIA in endovascular repair of iliac or aortoiliac aneurysms.^{88,89} Their midterm results were promising, with 100% initial technical success of IIA preservation without intraoperative endoleak. The crossover graft primary patency was 92.8% over a mean of 14.3 months (range, 6–21 months).⁸⁸ The “double-barrel” endograft technique has been used to treat aortoiliac aneurysms with preservation of bilateral IIAs, utilizing a bifurcated main body device followed by simultaneously deploying parallel endograft limbs into the EIA and IIA.⁶⁷ Another hybrid approach employs an aortouniiliac endograft with femorofemoral artery bypass along with a covered stent that is deployed retrograde from the “target” (distal) EIA into the ipsilateral internal iliac artery in a reverse U-shaped configuration (see Fig. 75.9).⁹⁰ This strategy,

also known as the “banana technique,” was reported to have 100% technical success at 30 days by Delpy et al. in a series of 17 patients, though nearly half of patients experienced complications by four-year follow-up.⁹¹ Experience has demonstrated, however, that it is difficult to maintain position and patency in the “U” endograft, which tends to dislodge, kink, or thrombose over time. Due to these durability concerns, and the need for adjunctive open femorofemoral bypass, this procedure has not gained widespread acceptance except in emergent settings. One hybrid approach to treating IIAs with heavily calcified iliac vessels includes first embolization and plugging the arteries distal to the aneurysm (internal iliac stem and anterior and posterior divisions), followed by a staged open surgical repair in which, after gaining only proximal control, the distal IIA is ligated and the aneurysm resected.⁹² In this case, calcification precluded the typical use of stent grafts, embolization of the internal iliac distal branches avoided pelvic dissection, reducing potential bleeding, and resection of the aneurysm sac avoids complications associated with compression of surrounding structures.⁹² On the other hand, in a series of 20 patients with isolated IIAs treated with embolization or coiling alone, no endoleaks or secondary aneurysm ruptures were observed through two-year follow-up, though 15% developed disabling buttock claudication that resolved in all but one patient.⁹³ Finally, gluteal blood flow can be preserved when treating distal IIAs with use of the intrahypogastric sandwich technique (Fig. 77.6).⁹⁴ While this technique may be used in anatomically suitable cases as an alternative to IIA embolization, its long-term durability is not well studied.

Endovascular Repair Using Iliac Branch Devices

The Gore Excluder iliac branch endoprosthesis (IBE; W.L. Gore & Associates, Flagstaff, AZ) is an iliac branch device designed to preserve IIA flow when treating common iliac or aortoiliac aneurysms (see Fig. 75.7A–C). After gaining U.S. Food and Drug Administration (FDA) approval in 2016, it remains the only commercially available device in the United States as of 2020. The Gore IBE device is composed of an iliac branch and a precannulated internal iliac component. The low profile (16-F) delivery system allows for repositioning and cannulation of the internal iliac vessels without need for brachial or axillary access. During the device’s feasibility study, Mendes et al. compared perioperative outcomes for the Gore Excluder IBE with the historical standard of open surgical repair in 67 consecutive patients (42 Gore IBE, 25 open) from 2014 to 2017. The Gore IBE group had significantly fewer blood transfusions and shorter ICU and hospital length of stay. Procedure-related reinterventions were lower in the Gore IBE group (4.7% vs. 20%, $P = 0.09$). The authors note cost-analysis and long-term follow-up is still needed to compare Gore IBE with longstanding standard of open repair.⁹⁵

Moreover, data from the Gore IBE 12-04 U.S. pivotal trial (prospective, 28 centers, $n = 63$ patients, 2013–2015) demonstrated 95.2% (60 of 63) technical success defined as lack of type I or III endoleak and 95.1% (58 of 61) internal iliac limb patency with 100% freedom from new buttock claudication

symptoms at 6-month follow-up.⁹⁶ The most recent midterm outcomes of the Gore IBE compare the U.S. investigational device exemption (IDE) trial (NCT01883999, 2013–2016, $n = 99$ patients) with the Global Registry for Endovascular Aortic Treatment (GREAT registry, 14 centers, 2013–2016, $n = 92$ patients).⁹⁷ Internal iliac branch patency was 93.6% at 12 and 24 months in the IDE group. Reintervention rates were similar between IDE and GREAT at 1 month (3% vs. 3.3%) and 6 months (5.1% vs. 5.4%), suggesting that the Gore IBE has performed well in both IDE and “real world” patients with aortoiliac or common iliac aneurysms. The 2019 SVS guidelines “recommend using FDA-approved branch endograft devices in

anatomically suitable patients to maintain perfusion to at least one internal iliac artery” (see Table 77.2).⁴⁰ Further long-term results are needed to fully evaluate the longer-term durability of this and other similar devices.

The Cook Zenith Branch Endovascular Graft – Iliac Bifurcation, also referred to as the Zenith Bifurcated Iliac Side (ZBIS; Cook Medical, Bloomington, IN), is a purpose-specific iliac branch device (IBD) that has been implanted in patients outside of the United States since 2006 (Fig. 77.7). The delivery system for this device comes with a preloaded curved catheter, which simplifies cannulation of the internal iliac artery from the contralateral groin. The Cook IBD is positioned

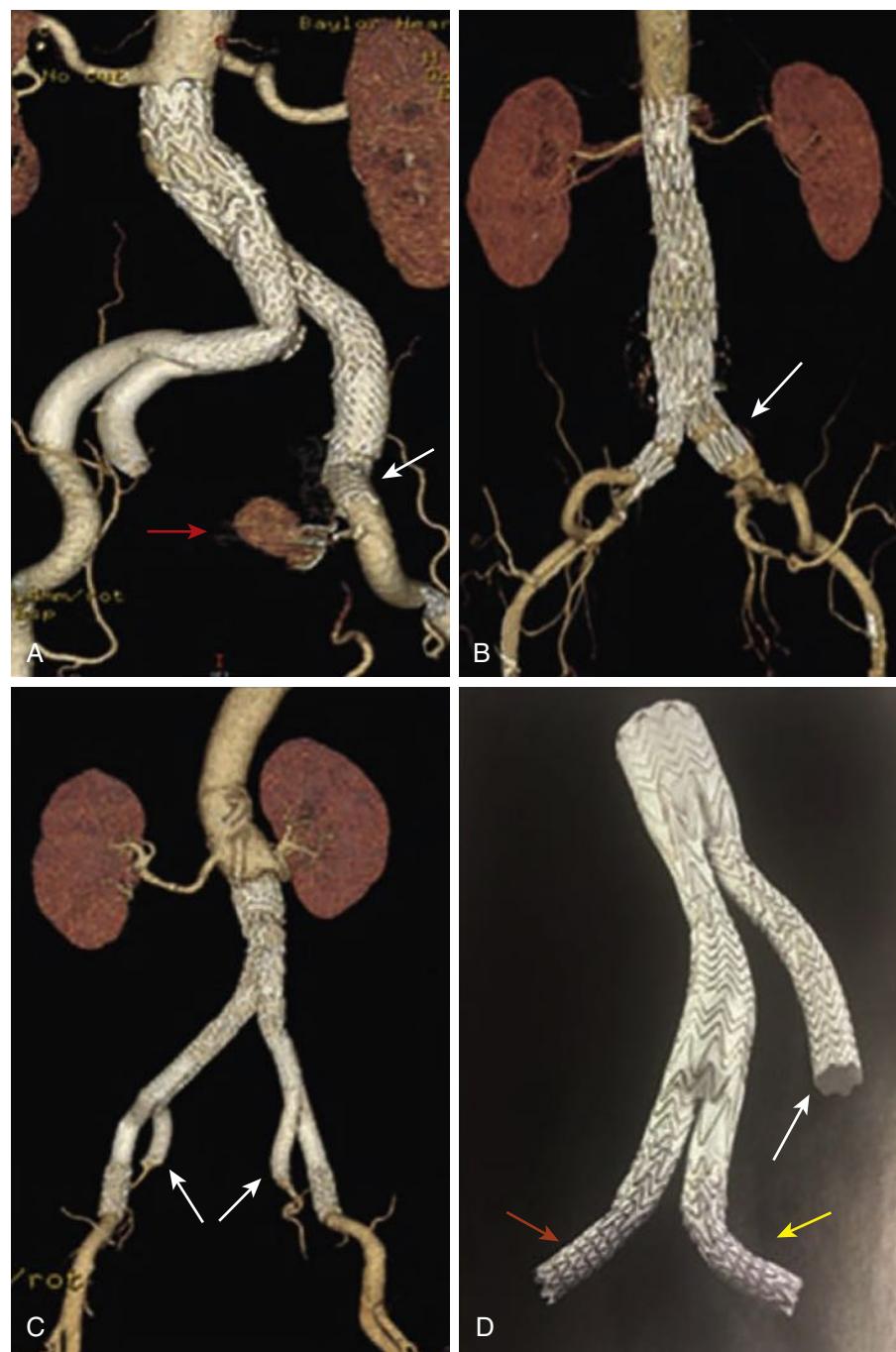


Figure 77.5 Endovascular techniques to preserve the internal iliac artery: (A) occlude and extend (red arrow: coil in IIA, white arrow: extension graft in EIA); (B) bell-bottom (arrow: large diameter extender); (C) sandwich graft (arrows: bilateral IIA); and (D) iliac branch graft (white arrow: left IA branch graft, red arrow: right EIA branch graft, yellow arrow: right IIA branch graft). *EIA*, external iliac artery; *IA*, iliac artery; *IIA*, internal iliac artery. (With permission from Shutze RA, Oglesby W, Lee A, et al. Results of repair of iliac artery aneurysms with the sandwich technique. *Baylor Univ Med Cent Proc*. 2017;30(1):7–10.)

over a stiff wire in typical fashion. Wire passage through the curved catheter is snared from the contralateral femoral artery. Following stiff wire exchange and partial deployment of the Cook IBD, a sheath is then introduced from the contralateral femoral artery into the internal iliac artery branch. A covered

bridging stent is then deployed after fully unsheathing the Cook IBD (Fig. 77.8). Depending on the anatomy, the standard bifurcated iliac stent configuration comes with a modular side-arm branch that can be short (~14 mm) and straight, or helical and elongated, to provide a longer sealing zone. The application of this device preserves internal iliac arterial flow and can also be used for complicated cases of concomitant common and internal IAAs.

In a series of 100 patients, IIA patency was 91.4% at 5 years, and cumulative Cook IBD side-branch patency was 87% at 60 months with 11% hypogastric side-branch occlusions occurring within the first year.⁹⁸ Extracting data from nine series using the Cook IBD in 196 patients, early technical success ranged from 85% to 100% with a collective postoperative IBD limb occlusion rate of 12%, and half of these patients developed buttock claudication.⁹⁹ The reported rate of combined type I or III endoleak was 1.5%, and the reintervention rate across all series was 6%.⁹⁹

More recently Simonte et al. reported their long-term experience with IBDs (134 Cook and 23 Gore devices) used in 149 patients over a 10-year period.¹⁰⁰ Initial technical success was 97.5%; however perioperative procedure failure occurred in seven patients, four during surgery and three within 30 days of the index procedure. In follow-up, freedom from IBD reintervention was 91.8% at 9 years and hypogastric patency was 90.4% at 10 years. Interestingly, the presence of ipsilateral hypogastric aneurysm ($P = 0.031$) and initial IBD use during the early “learning curve” period of the study ($P = 0.006$) were predictive of early failure on multivariate analysis.¹⁰⁰ In their 5-year experience, Parlani et al. also demonstrated that the presence of a hypogastric aneurysm was the only significant predictor of reintervention, with a hazard ratio of 5.9 (95% confidence interval 1.57–22.08; $P = 0.008$).⁹⁸ Based upon their reported experience, the authors now tend to avoid short distal necks, with more extensive distal landing

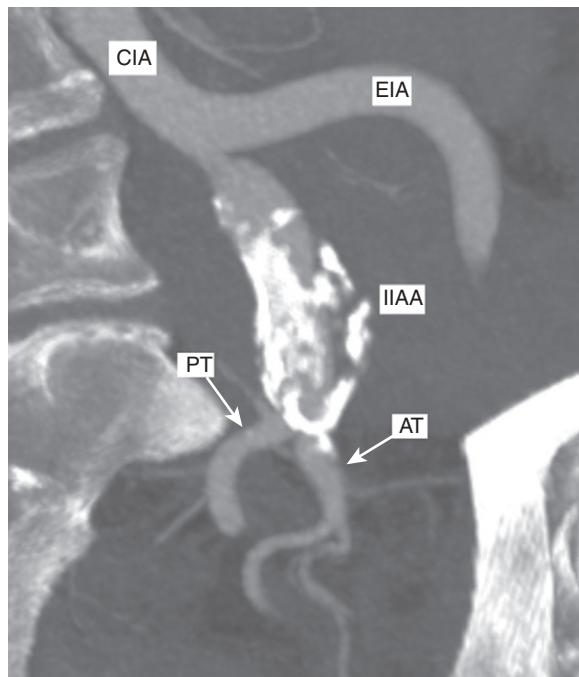


Figure 77.6 CT scan of a left isolated IIAA involving the anterior and posterior trunks. *AT*, anterior trunk (inferior gluteal artery, internal pudendal artery, medial rectal artery, obturator artery, superior and inferior vesical arteries); *CIA*, common iliac artery; *EIA*, external iliac artery; *IIAA*, internal iliac artery aneurysm; *PT*, posterior trunk (superior gluteal artery, lateral sacral arteries). (With permission from Garrido Espeja A, Andrés Navarro O, Roche Rebollo E, et al. Exclusively intrahypogastric sandwich technique to treat an isolated internal iliac artery aneurysm. *J Vasc Interv Radiol.* 2020;31(3):516–519.)

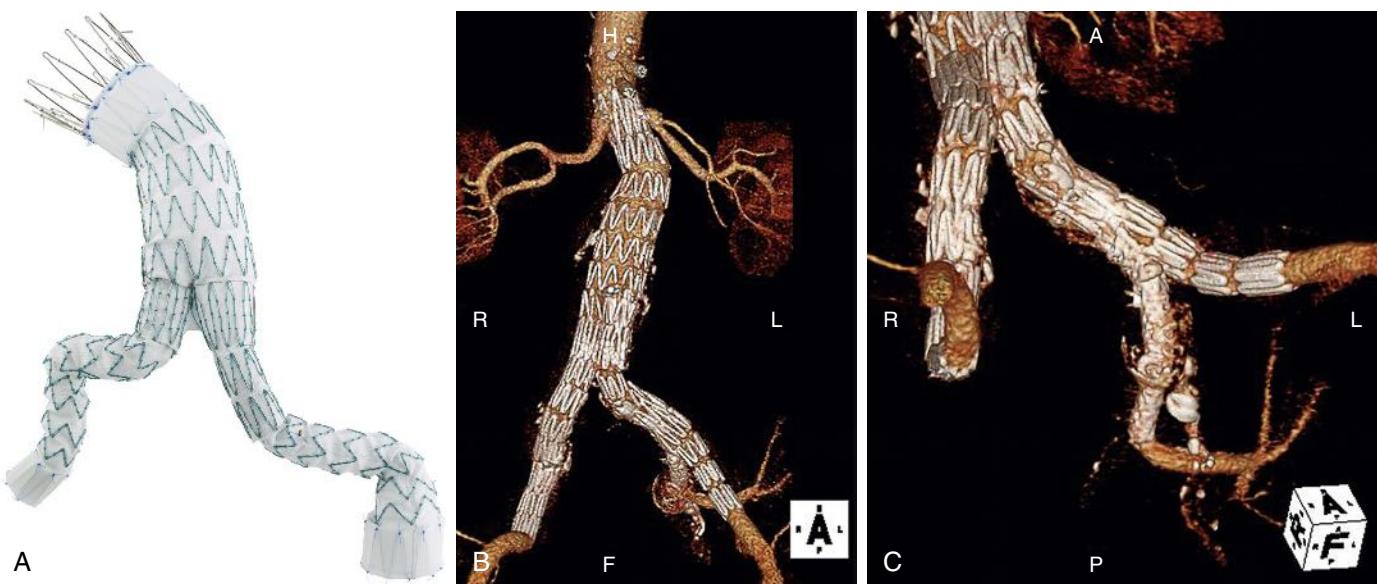


Figure 77.7 Zenith Iliac Branch Graft. (A) Picture of the iliac branch graft (Cook Medical, Bloomington, IN). (B) Computed tomographic angiography (CTA) of aortic stent graft and iliac branch graft. (C) CTA of iliac branch graft.

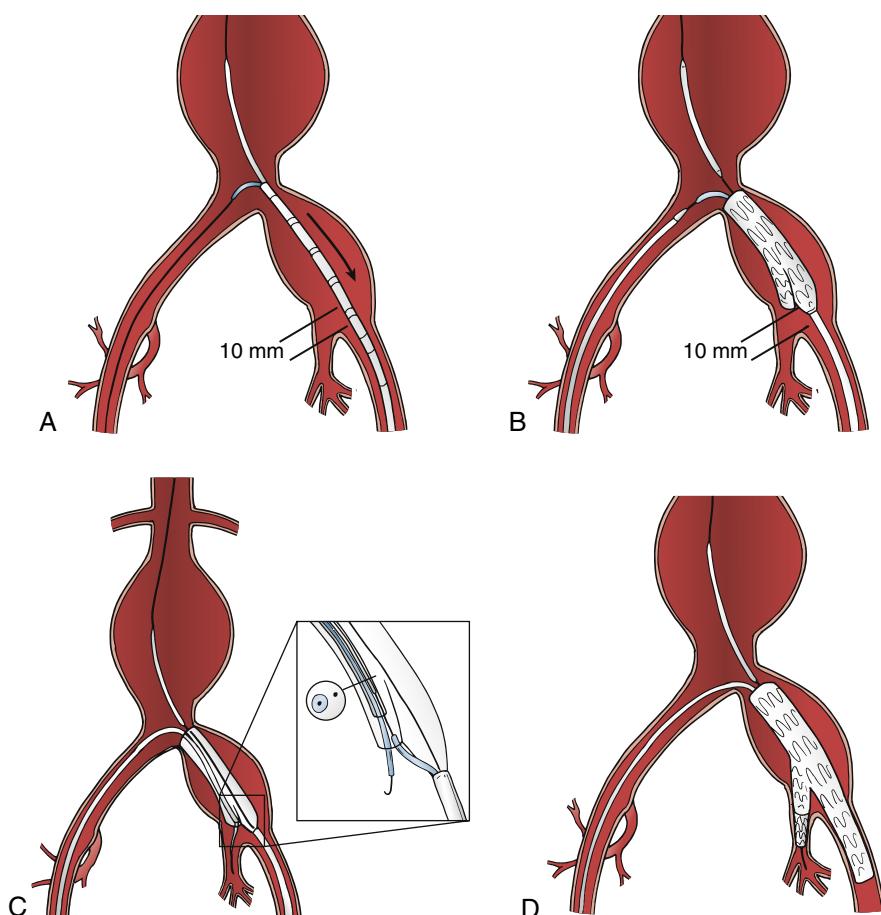


Figure 77.8 (A) The guide wire is passed through the curved catheter and snared from the contralateral groin. (B) The iliac-branched device (IBD) is partially deployed, and the sheath is advanced from the contralateral groin into the side branch of the IBD. (C) The wire is advanced into the internal iliac artery. (D) Following stiff-wire exchange, the covered stents are deployed after fully unsheathing the IBD. (From Serracino-Ingott F, Bray AE, Myers P. Endovascular abdominal aortic aneurysm repair in patients with common iliac artery aneurysms: Initial experience with the Zenith bifurcated iliac side branch device. *J Vasc Surg*. 2007;46:211–217.)

into the gluteal artery in case of extensive hypogastric aneurysmal involvement.^{98,100} Delay et al. treated 30 patients with CIAA with the Cook ZBIS device at two European centers. Technical success was 84% with notable 16% of cases having IIA thrombosis. Primary patency of IIA side branch was 84% at 1 year and 76% at 2 years. Freedom from reintervention was 89% at 1 and 2 years. Rate of endoleak was 3.3% for type III and 6.7% for type II. The authors note unanticipated procedural difficulty as a risk factor for perioperative failure, suggesting an important role for screening appropriateness of patients for the Cook IBD.¹⁰¹

Most recently, results from the pELVIS registry include 691 patients undergoing 747 elective endovascular repairs of aortoiliac ($n = 518$, 75%) or isolated iliac aneurysms ($n = 173$, 25%) with Cook IBDs ($n = 56$ bilateral) in nine European centers. Overall primary patency was 95.1% at 6 years and freedom from reintervention and conversion was 71% at 6 years. Of note, aneurysmal hypogastric and bilateral treatment were associated with increased late failure rate.¹⁰²

Along with the Gore IBE and Cook IBD, the JOTEC E-liac stent graft has been commercially available in Europe since 2014 (JOTEC GmbH, Hechingen, Germany). The E-liac device consists of self-expanding nitinol stents covered with woven polyester with a specially designed asymmetric spring

configuration, which results in high 3D flexibility and iliac artery conformability with a movable side branch for the internal iliac artery on a “squeeze to release” deployment system, allowing for a stepwise controlled release.¹⁰³ The PLIANT study was a European multicenter, prospective trial enrolling 97 patients treated with a JOTEC IBD from 2014 to 2016.¹⁰³ At 1 year, overall clinical success was 90% with internal iliac branch primary patency 98%, device-related reintervention rate 5%, and overall survival 100%. Four patients did not achieve technical success due to IIA occlusion on the E-liac device side ($n = 1$), infrarenal type Ia endoleak ($n = 1$), and type Ib endoleaks in the IIA ($n = 2$). Further results are awaited to confirm long-term efficacy and durability.

Although designed to be user friendly, both the Gore IBE and Cook IBD prostheses are less adaptable to complex anatomy, thus limiting their wider applicability especially when adhering to the instructions for use (IFU). Based on the current criteria for IBD use, up to 52% of patients may not be suitable for these devices.¹⁰⁴ Pearce et al. conducted a study from two centers and noted that by strictly complying with the manufacturer’s IFU, only 35% (35/99) of patients with IAAs treated over the past decade at those institutions would have been suitable for treatment with the Cook IBD or Gore IBE device while remaining strictly within the IFU.¹⁰⁵ In their

analysis, only 18.2% and 25.3% of patients fit the stringent inclusion criteria for the Cook and Gore IBDs, respectively.¹⁰⁵ The most common reason for exclusion for either device is the diameter of the internal iliac artery precluding an appropriate landing zone. A more recent study from a single institution in China found that of 102 patients, 14 were eligible for the Gore IBE, 10 for the Cook IBD, and 3 for both devices, with a total of 21 patients (20.6%) eligible for any type of IBD based on anatomic criteria.¹⁰⁶ Findings from the aforementioned GREAT registry also confirm the stringent criteria for IBDs with a slight majority of patients (55%, 51/92) receiving devices outside of IFU for one or more criteria; inadequate CIA diameter was the most common reason the Gore IBE could not be used.⁹⁷

Off-label use of Gore and Cook IBDs has been reported in the recent literature in both case reports and multicenter registries.^{107–109} In one case report, the Gore Excluder device was used to treat bilateral IIAs while maintaining pelvic perfusion without an aortoiliac component (off-label).¹¹⁰ Fargion et al. reported long-term results of off-label IBD for isolated CIA in 804 patients across nine high-volume European centers.¹⁰⁷ Patients were divided into two groups, with the first group treated with IBDs without proximal aortic extension and the second group treated by deploying a bifurcated aortic stent graft according to the IFU. There were no statistically significant differences between the two groups in terms of technical success, aneurysm-related early intervention, or 30-day mortality. Moreover, there was no observed difference in rate of IBD occlusion, target hypogastric artery occlusion, reintervention, or aneurysm-related death at 5 years between non-IFU and IFU groups. The authors advocate for single IBD placement as a safe and durable treatment option for isolated CIAA with suitable anatomy. Alternatively, in a small case series an aortic balloon-expandable covered stent (BeGraft, Bentley, Hechingen, Germany) was used as proximal extension for a Cook IBD to treat isolated common iliac artery aneurysms, allowing adequate seal in the CIA while simplifying the procedure with reduced procedure time, radiation exposure, contrast use, and cost.¹¹¹

In a single-center study, the *in vivo* anatomical conformability of the branched iliac stent grafts (13 Gore IBE vs. 9 Cook IBD) were compared when used in aortoiliac aneurysm repair.¹¹² Because the branched stent grafts rely on both the external and internal iliac axes, they are subjected to high tortuosity constraints that generate stiffness along the axes of repair, resulting in gradual shortening of the covered lengths.¹¹² This applied stress, in a setting of marked iliac tortuosity, can potentiate type Ib endoleaks, graft limb plication, and limb thromboses.^{112–115} After applying centerline software to compute and compare the index of tortuosity along the iliac axis, the authors found the Cook IBD stent graft more significantly modified the length and tortuosity of the iliac axis following implantation. The postoperative lengths along the internal iliac axis were not affected by either stent. Within

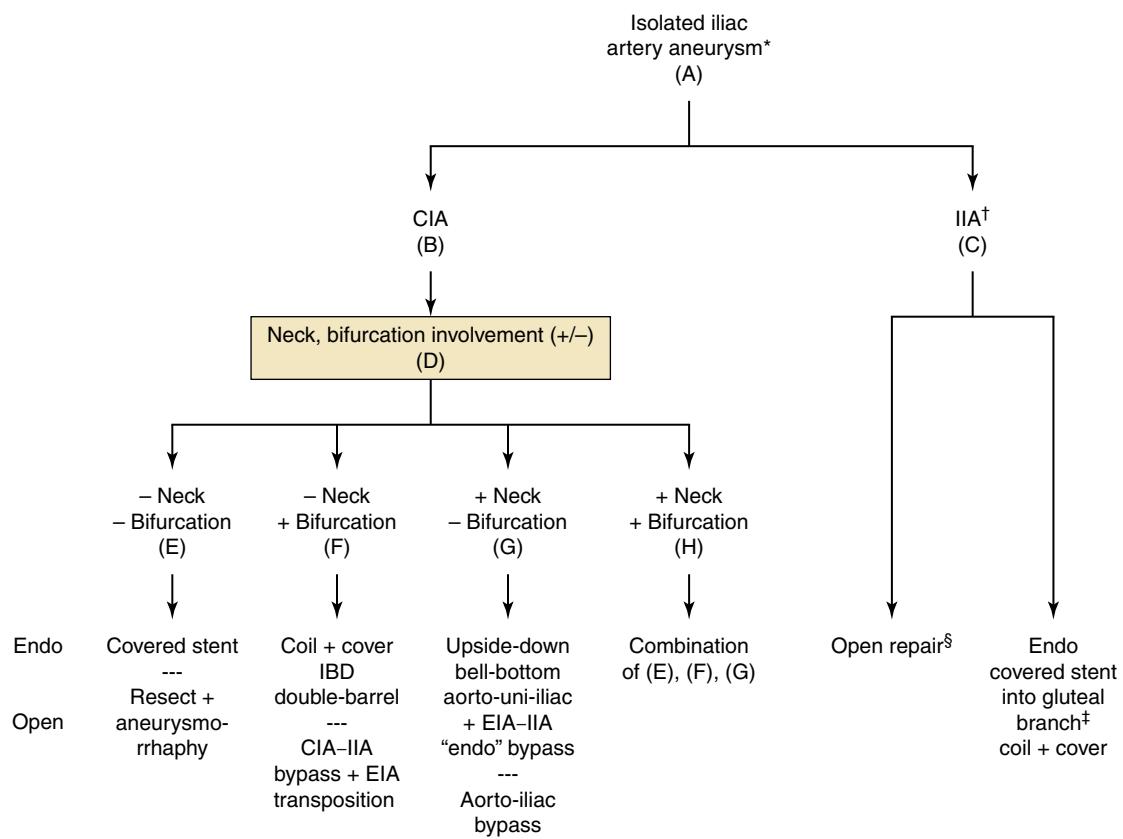
anatomical constraints, this finding appears to favor the use of the more conformable Gore IBE in cases of severe iliac tortuosity to minimize postoperative complications associated with stent malposition (type Ib or III endoleaks) or branch occlusion (pelvic ischemia). Moreover, in a multicenter European trial, Donas et al. evaluated secondary procedures after iliac branched device implantation with both Cook IBD (ZBIS) and Gore IBE in 525 patients.¹¹⁶ Overall, reintervention incidence was 7.3% over approximately 3 years, and the most common driver attributed to “short proximal sealing zone and poor conformability of the ZBIS device in elongated EIAs.” Finally, Mafeld et al. provided the first successful report of iliac aneurysm repair using customized manufactured devices with fenestrated iliac limbs.¹¹⁷ This novel technique may be useful for patients with challenging anatomy unsuitable for IBDs. Although the early and midterm results associated with iliac branch devices are promising for a limited number of patients meeting eligibility requirements, we will continue to see innovative hybrid techniques and custom-made devices fill an unmet need – for all these treatment options, long-term outcome data are still required.

CONCLUSIONS

While isolated iliac aneurysms are uncommon (<2%) in the general population, nearly 40% present ruptured, which has been associated with a high rate of mortality. The rest are usually recognized incidentally during imaging procedures indicated for other reasons. Symptomatic or large iliac aneurysms greater than 3.5 cm in diameter can be electively repaired safely with open, endovascular, or hybrid techniques. Surgical objectives are to repair and exclude the aneurysm with reconstruction or preservation of the internal iliac artery to minimize pelvic ischemia. Endovascular repair, with its associated reduced incidence of in-hospital morbidity and mortality along with reduced length of stay, has gained favor over open repair as the initial approach of choice for patients with suitable anatomy. Successful endovascular repair is highly dependent on precise, preoperative high-resolution cross-sectional imaging for detailed case planning.

Short- and mid-term outcomes for complete endovascular repair using newer iliac branch stent graft devices that maintain flow to both the external and internal iliac artery are promising, with acceptable initial technical success rates and durability as compared to techniques involving unilateral or bilateral internal iliac artery occlusion. Nevertheless, in situations where internal iliac artery patency is essential and a complex anatomy is not amenable to these devices, open surgical repair may be the preferred modality. Knowledge of all current devices and hybrid techniques allows for predictably excellent outcomes for almost any patient, regardless of anatomic limitations, when these are applied in a creative and innovative fashion.

CHAPTER ALGORITHM



CIA, common iliac artery; IIA, internal iliac artery; EIA, external iliac artery; IBD, iliac branch device.

*Defined as aneurysm of common, internal, or external iliac artery without aortic involvement and which may be unilateral (e.g., CIA, IIA, or EIA (rare)), bilateral (e.g., CIA+CIA or IIA+IIA), or in any combination (e.g., CIA+IIA)

†If symptomatic CIA aneurysm with bifurcation involvement or IIA aneurysm, bias toward coil and cover of IIA to minimize the steps required for repair

‡To exclude IIA aneurysm by this technique includes coil embolization of other distal branches

§Open repair includes resection with aneurysmorrhaphy, ligation of IIA alone or with EIA-IIA bypass

SELECTED KEY REFERENCES

Chakof EL, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg*. 2018;67(1):2–77.e2.

Most recent published guidelines from the Society for Vascular Surgery (SVS) on the management of aortic aneurysms, including three specific level I recommendations regarding the treatment of iliac artery aneurysms.

Dhanji A, et al. Ultrasound surveillance of common iliac artery aneurysms. *Ann Vasc Surg*. 2020;65:166–173.

Survey of 54 vascular laboratories within the United Kingdom's National Health Service, including 995 patients, to determine common iliac artery aneurysm growth rate and factors predisposing to aneurysm expansion with proposed guidelines for a dedicated ultrasound surveillance program of common iliac aneurysms.

Fargion AT, et al. Results of the multicenter pELVIS Registry for isolated common iliac aneurysms treated by the iliac branch device. *J Vasc Surg*. 2018;68(5):1367–1373.e1.

Multicenter report of off-label use of iliac branch devices for isolated CIA in 804 patients across nine high-volume European centers, demonstrating equivalence with devices used according to instructions for use (IFU) at 5 years.

Gray D, et al. EVAR with flared iliac limbs has a high risk of late type 1b endoleak. *Eur J Vasc Endovasc Surg*. 2017;54(2):170–176.

Definitive report indicating risk of mid-term type Ib endoleak with flared or bell-bottom endovascular limbs with iliac limb diameters >19 mm.

Huang Y, et al. Common iliac artery aneurysm: expansion rate and results of open surgical and endovascular repair. *J Vasc Surg*. 2008;47:1203–1210.

Retrospective single-institutional review from the Mayo Clinic reporting presentation, treatment and outcomes for 438 patients with 715 common iliac artery aneurysms.

Lee WA. Advanced aneurysm management techniques: management of internal iliac aneurysm disease. In: Dalman RL, et al., ed. *Operative Techniques in Vascular Surgery*. The Netherlands: Wolters Kluwer Health; 2015:2015–2023.

Contemporary resource with accompanying detailed images for reference – step by step.

Reber PU, et al. Häufigkeit, Klassifikation und Therapie der isolierten Beckenarterienaneurysmen [Incidence, Classification and Therapy of Isolated Pelvic Artery Aneurysm]. *Chirurg*. 2001;72(4):419–424.

Anatomic classification of iliac artery aneurysms recently adopted by the European Society for Vascular Surgery (ESVS) and included as a figure in this chapter.

Sandhu RS, et al. Isolated iliac artery aneurysms. *Semin Vasc Surg*. 2005;18:209–215.

Review with insight into natural history, workup and treatment modalities, including threshold for repair of 3.5 cm.

Schneider DB, et al. Prospective, multicenter study of endovascular repair of aortoiliac and iliac aneurysms using the Gore Iliac Branch Endoprosthesis. *J Vasc Surg*. 2017;66(3):775–785.

Two-year outcomes of the Gore iliac branch endoprostheses (IBE) 12-04 US pivotal clinical trial, which contributed to US FDA approval of the Gore IBE device in 2016.

Wanhainen A, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *Eur J Vasc Endovasc Surg*. 2019;57(1):8–93.

Most recent practice guidelines for abdominal and aorto-iliac aneurysms from the European Society for Vascular Surgery (ESVS) with four recommendations specific to iliac aneurysms, including minimum size threshold of 3.5 cm for elective repair, endovascular therapy as first-line treatment, and preservation of flow to at least one internal iliac artery.

Xiang Y, et al. Endovascular treatment versus open surgery for isolated iliac artery aneurysms: a systematic review and meta-analysis. *Vasc Endovascular Surg*. 2019;53(5):401–407.

Systematic review and meta-analysis, including nine observational studies, comparing perioperative outcomes and mortality for endovascular versus open surgery in treating isolated iliac aneurysms.

A complete reference list can be found online at www.expertconsult.com.