From the Society for Vascular Surgery

Outcomes of endovascular aneurysm repair with contemporary volume-dependent sac embolization in patients at risk for type II endoleak

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Objective: **The aim of this study was to evaluate outcomes of intraoperative aneurysm sac embolization during endovascular aneurysm repair (EVAR) in patients considered at risk for type II endoleak (EII), using a sac volume-dependent dose of fibrin glue and coils.**
Methods: **Between January 2012 and December 2014, 126 patients underwent EVAR. Based on preoperative computed tomography evaluation of anatomic criteria, 107 patients (85%) were defined as at risk for EII and assigned to randomization for standard EVAR (group A; n = 55, 44%) or EVAR with intraoperative sac embolization (group B; n = 52, 42%); the remaining 19 patients (15%) were defined as at low risk for EII and excluded from the randomization (group C). Computed tomography scans were evaluated with OsiriX Pro 4.0 software to obtain aneurysm sac volume. Freedom from EII, freedom from EII-related reintervention, and aneurysm sac volume shrinkage at 6, 12, and 24 months were compared by Kaplan-Meier estimates. Patients in group C underwent the same follow-up protocol as groups A and B.**
Results: **Patient characteristics, Society for Vascular Surgery comorbidity scores (0.99 ± 0.50 vs 0.95 ± 0.55; $P = .70$), and operative time (149 ± 50 minutes vs 157 ± 39 minutes; $P = .63$) were similar for groups A and B. Freedom from EII was significantly lower for group A compared with group B at 3 months (58% vs 80%; $P = .002$), 6 months (68% vs 85%; $P = .04$), and 12 months (70% vs 87%; $P = .04$) but not statistically significant at 24 months (85% vs 87%; $P = .57$). Freedom from EII-related reintervention at 24 months was significantly lower for group A compared with group B (82% vs 96%; $P = .04$). Patients in group B showed a significantly overall mean difference in aneurysm sac volume shrinkage compared with group A at 6 months (-11 ± 17 cm^3 vs -2 ± 14 cm^3; $P < .01$), 12 months (-18 ± 26 cm^3 vs -3 ± 32 cm^3; $P = .02$), and 24 months (-27 ± 25 cm^3 vs -5 ± 26 cm^3; $P < .01$). Patients in group C had the lowest EII rate compared with groups A and B (6 months, 5%; 12 months, 6%; 24 months, 0%) and no EII-related reintervention.**
Conclusions: **This randomized study confirms that sac embolization during EVAR, using a sac volume-dependent dose of fibrin glue and coils, is a valid method to significantly reduce EII and its complications during early and midterm follow-up in patients considered at risk. Although further confirmatory studies are needed, the faster aneurysm sac volume shrinkage over time in patients who underwent embolization compared with standard EVAR may be a positive aspect influencing the lower EII rate also during long-term follow-up. (J Vasc Surg 2016;63:32-8.)**

Type II endoleak (EII) is the cause of reintervention for about 10% of endovascular aneurysm repair (EVAR) cases[1,2]; however, the success rate of these secondary procedures is about 45%,[3] and multiple accesses may be required over time. The extra medical expenses incurred for these additional procedures as well as the increased exposure of patients to radiation and contrast agents during follow-up represent a limitation to EVAR and occasionally can lead to a waste of its advantages in terms of costs[4] and clinical success.[5] In this scenario, prevention of EII formation could be a valid strategy. Previous experiences with aneurysm sac embolization during EVAR using variable doses of materials have already demonstrated its efficacy.[6]

In a previous study,[7] we showed a significantly reduced incidence of EII-related complications during midterm follow-up with the routine injection of a standard dose of fibrin glue in association with coils into the aneurysmal sac during EVAR compared with those patients who underwent standard EVAR. However, results obtained from this experience suggested that this procedure may be optimized by the injection of a tapered dose of material based on aneurysm sac dimension rather than a standard dose. Furthermore, to reduce costs, its use should not be routine but limited to those patients at risk of EII.

The purpose of this study was to evaluate early and midterm outcomes of this procedure with a randomized single-center study comparing standard EVAR vs EVAR

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and contemporary aneurysm sac embolization (embo-EVAR) in patients at risk for EII. The dose of material injected during embolization was tapered to the preoperative aneurysm sac volume dimension.

Furthermore, we investigated the effect of embo-EVAR on aneurysm sac volumetric variation during follow-up compared with standard EVAR.

METHODS

Patients. Between January 2012 and December 2014, all patients admitted to the Clinic of Vascular and Endovascular Surgery of Padova University who underwent EVAR for infrarenal abdominal aortic aneurysms were prospectively recorded in a dedicated database. This study was approved by the Ethics Committee of our institution. All patients enrolled in the study gave their consent.

Study design. This is a single-center prospective randomized study designed to evaluate the efficacy of EVAR and contemporary aneurysm sac embolization with a sac volume-dependent dose of coils and fibrin glue in the prevention of EII and its complications.

Only patients who underwent elective EVAR were considered. All commercially available aortobifurcated endografts were included in this study, whereas aortouniiliac and tubular grafts were not included. Only patients considered at risk of EII were included in the randomization and were randomized to standard EVAR (group A) or embo-EVAR (group B). Patients considered at low risk for EII were not randomized; these cases (group C) underwent standard EVAR and received the same follow-up protocol as groups A and B.

The end points of the study were to compare EII rate, freedom from EII-related reinterventions, and aneurysm sac volume variation during follow-up between patients undergoing the two different interventions.

Treatment and definitions. Aneurysm sac embolization in group B was performed using coils (Tornado MReye embolization coil, IMWCE-35-10-20 mm; Cook Medical, Limerick, Ireland) with fibrin glue (Tissucol; Baxter Hyland Immuno AG, Vienna, Austria). The Tornado MReye coils were preferred because they are not accountable for scatter artifacts on computed tomography angiography (CTA) and guarantee a better detection of an eventual endoleak during follow-up. In our previous retrospective study,[7] we performed this approach using a standard dose of coils (N = 3) and glue (5 mL), which was effective in the prevention of EII only for aneurysms with a preoperative sac volume ≤ 125 cm^3, whereas a higher volume was an independent predictor of EII after EVAR. Thus, we decided to use a volume-dependent dose of embolizing material. In particular, the fibrin glue dose was maintained at 5 mL if the calculated preoperative CTA aneurysm volume was ≤ 125 cm^3 and 10 mL if it was >125 cm^3. Similarly, we maintained three coils if the aneurysm volume was ≤ 125 cm^3, whereas one additional coil was added for every 50 cm^3 of volume in aneurysm sacs >125 cm^3.

The patients' preoperative demographics, cardiovascular risk factors, and medical therapy were registered; the Society for Vascular Surgery comorbidity grading system[8] and the American Society of Anesthesiologists score were used to assess the operative comorbidity risk.

The definition for risk of EII was not previously standardized but based on anatomic criteria extracted from the available literature.[9,10] The anatomic characteristics identified at preoperative CTA were (1) patency of the inferior mesenteric artery (IMA), with a luminal diameter at the origin ≥ 3 mm; and (2) patency of at least three pairs of lumbar arteries, or two pairs of lumbar arteries and a sacral artery or an accessory renal artery, or any diameter (also <3 mm) patent IMA. Patients who did not match these criteria were considered at low risk for EII.

Surgical outcomes were defined in accordance with the current standard report for EVAR.[11]

Aneurysm sac volume was calculated on 1-mm-thin CTA slices using OsiriX Pro 4.0 software. Aneurysm sac volume variation between preoperative and follow-up CTA scans was measured for all randomized patients to evaluate the effect of EII on sac shrinkage within the two groups.

The follow-up was performed in all patients (groups A, B, and C) by contrast-enhanced CTA at approximately 3, 6, and 12 months and then yearly after that. Overall average length of follow-up was 16 months (range, 1-36 months), with a mean follow-up period of 16 months for both group A (15.9 $\pm$ 9.9 months) and group B (16.4 $\pm$ 10.7 months). Indications for EII-related reintervention were an increase of >5 mm in maximum diameter within two consecutive CTA studies and persistent EII (EII on three or more consecutive CTA studies during follow-up) with any increase in aneurysm sac diameter. The definition of freedom from reintervention was applied to those patients who during their follow-up did not have an EII or had an EII that did not require additional procedures.

All the endovascular procedures were performed by those surgeons who routinely perform EVAR (three operators) at our institution. The operative technique of embo-EVAR has been previously described in detail.[7] Briefly, as for standard EVAR, bilateral placement of a 10F sheath in the common femoral artery was obtained over the wire. A second unilateral puncture in the side of the contralateral limb was made just below the 10F sheath, and a 23-cm-long 5F Brite Tip introducer (Cordis, Bridgewater, NJ) was advanced over the wire and left in the abdominal aortic aneurysm sac. The extra time needed for placement of the 5F introducer is usually brief (1 or 2 minutes). At this point, a standard EVAR was performed over the wires placed through the 10F sheaths on both common femoral arteries.

Once the endograft was completely deployed and the aneurysm excluded, the coils were advanced into the sac through a 5F catheter by the 5F introducer and nonselectively released. Subsequently, the catheter was exchanged with a 35-cm-long Duplocath catheter (Baxter International,

Deerfield, Ill) connected to a Duploject syringe clip; this was fed into the introducer until it reached the aneurysm sac. At this point, to prevent distal embolization of the fibrin glue, two noncompliant balloons were inflated on both iliac graft branches, and the glue was injected into the aneurysm sac through the two-way catheter. After approximately 40 seconds, the balloons were deflated, the Duplocath catheter was removed, and the final angiogram was obtained to verify sac thrombosis and to document eventual residual endoleak; the time needed to complete the nonselective embolization after complete deployment of the endograft was about 7 or 8 minutes.

Intraoperative and postoperative therapy was the same for all patients; 5000 USP heparin units were given by endovenous infusion during the procedure, and single antiplatelet therapy was administered from the day after surgery.

Statistical analysis. The randomization scheme was obtained by using sealed opaque envelopes containing the indication to EVAR or embo-EVAR that were put into a container in blocks of 50 (25 EVAR, 25 embo-EVAR). The envelopes were extracted by an operator blinded to the study the day before the procedure was planned. Considering the literature-reported prevalence of EII ranging from 10% to 30% of patients[12,13] and the EII rate at our institution,[7] the sample size was calculated to be 50 patients per group, assuming a type I error probability $\alpha = .05$ and a power $1 - \beta = .80$.

Continuous data are expressed as mean ± standard deviation, categorical data as number and percentage. Two-sample *t*-test was used to compare continuous data; χ^2 and Fisher exact tests were used for the analysis of categorical variables. The Kaplan-Meier method was used to estimate freedom from EII-related reintervention; the log-rank test was used to compare two procedures. All the statistical analyses were performed using the R 3.1.2 software (R Foundation for Statistical Computing, Vienna, Austria), and a *P* value $< .05$ was considered to be statistically significant.

RESULTS

During the study period, 158 patients underwent EVAR at our institution. The flow chart in Fig 1 describes the selection to randomization.

No significant differences were found between groups A and B in terms of demographics, cardiovascular risk factors, and perioperative risk assessment (Table I) or anatomic characteristics (Table II).

Interestingly, operative data showed that there were no statistically significant differences in the mean operative time between the two groups (149.4 ± 50.7 minutes in group A and 156.8 ± 39.6 minutes in group B; $P = .10$). Also, there were no differences in the types of endograft used and in the number of additional endovascular procedures. The number of EIIs detected at final intraoperative angiography was equal in the two groups (20.0% vs 20.0%; $P = 1.00$; Table III).

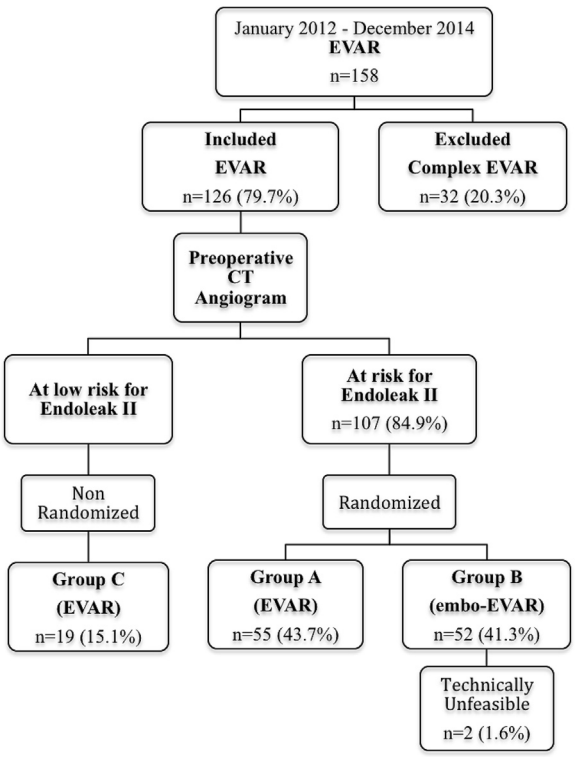

Fig 1. Inclusion and randomization of patients. *CT,* Computed tomography; *EVAR,* endovascular aneurysm repair; *embo-EVAR,* EVAR with aneurysm sac embolization.

No differences were reported between the two groups in terms of major medical or surgical complications within 30 days. Technical success was achieved in 100% of cases in both groups, and no aneurysm ruptures or deaths were reported. There were three cases of early reintervention: one in group A (due to arterial femoral access complication) and two in group B (one femoral access complication and one limb ischemia; $P = .60$).

The descriptive analysis of freedom from EII illustrated in Fig 2 shows that during follow-up, the EII rate was significantly higher in group A than in group B at 3 months (41% vs 20%; $P = .02$), 6 months (31% vs 15%; $P = .04$), and 12 months (30% vs 14%; $P = .04$) but not any longer at 24 months (16% vs 13%; $P = .57$). Interestingly, group C (low EII risk) showed the lowest rate of EII (one case) during the whole follow-up period; this patient had EII detected at 3 months, and it spontaneously resolved after 1 year from EVAR with no need for reintervention.

Spontaneous EII resolution occurred in 33% vs 30% of patients after 6 months, 62% vs 65% after 12 months, and 66% vs 65% after 24 months, respectively, in group A and group B ($P = .96$). The number of persistent EIIs was eight (14.5%) in group A and three (6.0%) in group B ($P = .13$). During the follow-up, there were four cases (7.2%) in group A and three cases (6.0%) in group B of new-onset EII ($P = .55$) in patients without any previous sign of endoleak at CTA. Interestingly, anticoagulant and

Table I. Demographics, cardiovascular risk factors, and perioperative risk assessment in the 105 patients who underwent standard endovascular aneurysm repair (EVAR; *group A*) and EVAR with aneurysm sac embolization (*group B*)

Variable[a]	*Group A (n = 55)*	*Group B (n = 50)*	P
Demographics			
Age, years	75.9 ± 7.1	74.8 ± 8.3	.75
Male gender	52 (94.5)	48 (96.0)	1.00
Cardiovascular risk factors			
Hypertension	50 (90.9)	44 (88.0)	.75
Diabetes	9 (16.4)	7 (14.0)	.79
Smoking[b]	35 (63.6)	32 (64.0)	1.00
Ischemic heart disease	22 (40.0)	14 (28.0)	.22
Arrhythmia[c]	16 (29.1)	15 (30.0)	1.00
CRI (creatinine >1.5 mg/dL)	4 (7.3)	5 (10.0)	.73
COPD[d]	9 (16.4)	9 (18.0)	1.00
Medical therapy			
None	7 (12.7)	8 (16.0)	.78
Antiplatelet	32 (58.2)	26 (52.0)	.56
Dual antiplatelet	3 (5.5)	5 (10.0)	.47
Anticoagulant	11 (20.0)	8 (16.0)	.62
Antiplatelet and anticoagulant	2 (3.6)	3 (6.0)	.67
Perioperative risk assessment			
ASA score	2.7 ± 0.5	2.6 ± 0.4	.26
SVS cardiac score	1.27 ± 1.07	1.08 ± 0.99	.35
SVS pulmonary score	0.40 ± 0.85	0.40 ± 0.78	1.00
SVS renal score	0.08 ± 0.14	0.10 ± 0.30	.66
SVS sum score	0.99 ± 0.50	0.95 ± 0.55	.70

ASA, American Society of Anesthesiologists; *COPD,* chronic obstructive pulmonary disease; *CRI,* chronic renal insufficiency; *SVS,* Society for Vascular Surgery.
[a]Data are presented as the mean ± standard deviation or number (%).
[b]Includes current and former smokers.
[c]Symptomatic arrhythmia or treatment requiring arrhythmia.
[d]Requiring medications.

Table II. Preoperative aneurysm sac characteristics and anatomic spectrum for the 105 patients with abdominal aortic aneurysm who underwent standard endovascular aneurysm repair (EVAR; *group A*) and EVAR with aneurysm sac embolization (*group B*)

Variable[a]	*Group A (n = 55)*	*Group B (n = 50)*	P
Aneurysm sac characteristics			
Volume, cm^3	120.6 ± 51.0	129.6 ± 72.1	.45
Diameter, cm	5.3 ± 0.86	5.6 ± 0.90	.08
Anatomical spectrum			
Patent IMA	44 (80.0)	38 (76.0)	.64
Patent lumbar artery pairs			
2	2 (3.6)	4 (8.0)	.42
3	32 (58.2)	28 (56.0)	.85
≥4	21 (38.2)	18 (36.0)	.84
Accessory renal arteries[b]	13 (23.6)	14 (28.0)	.66
Percentage of thrombus volume			
0%-25%	13 (23.6)	11 (22.0)	1.00
25%-50%	30 (54.5)	25 (50.0)	.70
50%-75%	12 (21.8)	14 (28.0)	.50
Thrombus position			
Absent	10 (18.2)	5 (10.0)	.27
Anterior	11 (20.0)	13 (26.0)	.49
Posterior	6 (10.9)	5 (10.0)	1.00
Circumferential	10 (18.2)	8 (16.0)	.80
Other concomitant aneurysms			
Monolateral iliac aneurysm	7 (12.7)	1 (2.0)	.07
Bilateral iliac aneurysm	1 (1.8)	2 (4.0)	.60
Mean iliac aneurysm diameter, cm	3.1 ± 1.16	3.4 ± 1.82	.31

IMA, Inferior mesenteric artery.
[a]Data are presented as the mean ± standard deviation or number (%).
[b]Accessory renal arteries arising from the aneurysm or required to be covered by the endograft.

antiplatelet therapy did not have an impact on EII, but this result may be related to the small number of events (type II error).

Overall survival at 24 months was 96% for group A and 91% for group B ($P = .57$), and there were no aneurysm-related deaths. The Kaplan-Meier estimates of freedom from EII-related reinterventions showed a significantly higher rate of reintervention in group A than in group B after 24 months (82% vs 96%; $P = .04$; Fig 3). All the six reinterventions in group A consisted of the endovascular embolization of the feeding vessels causing the endoleak; in one case, a secondary reintervention was required. In group B, only one patient underwent retrograde selective IMA embolization and aneurysm sac filling with ethylene vinyl alcohol copolymer (Onyx; Covidien ev3, Plymouth, Minn) 18 months after EVAR. Conversely, there were no reinterventions in group C.

In our institution, the cost for a single patient embolization during EVAR with this technique is calculated to be ≈ €600 ($800), whereas the institutional reimbursement expenses for a secondary reintervention for embolization with coils of an EII after EVAR is ≈ €9000 ($11,800). Considering that during follow-up, seven reinterventions were performed in group A and sac embolization in all 50 patients and reintervention only in one patient in group B, the total costs were ≈ €63,000 ($70,750) for group A and €39,000 ($43,800) for group B; these different expenses was significantly lower overall in group B compared with group A ($P = .0001$).

Over time, group A showed a lower shrinkage rate compared with group B, and this was significant after 6 months (-2.2 ± 14.2 cm^3 vs -10.6 ± 17.1 cm^3; $P = .007$), 12 months (-2.9 ± 32.2 cm^3 vs -18.9 ± 26.6 cm^3; $P = .02$), and 24 months (-4.6 ± 25.9 cm^3 vs -27.3 ± 24.7 cm^3; $P = .008$; Table IV).

The same analysis was performed after stratification for those cases with EII within the two groups; in particular, even if not statistically significant, the overall sac volume in group B tended to decrease compared with group A, in which the overall sac volume increased both at 12 months (-6.1 ± 19.7 cm^3 vs 16.8 ± 37.3 cm^3; $P = .24$) and at 24 months (-2.5 ± 10.6 cm^3 vs 13.5 ± 37.1 cm^3; $P = .59$)

DISCUSSION

Most EIIs are innocuous and resolve spontaneously after a variable period, but those with a mechanism of

Table III. General operative and procedural information by standard endovascular aneurysm repair (EVAR; *group A*) and EVAR with aneurysm sac embolization (*group B*)

Variable[a]	*Group A (n = 55)*	*Group B (n = 50)*	P
Operative data			
General anesthesia	44 (80.0)	46 (92.0)	.10
Operative time, minutes	149.4 ± 50.7	156.8 ± 39.6	.63
Radiation exposure, minutes	22.1 ± 6.5	23.5 ± 7.0	.29
Contrast dye, mL	83.2 ± 10.9	85.4 ± 9.9	.28
Length of stay, days	3.9 ± 2.2	4.2 ± 3.6	.60
Procedural data			
Type of endograft			
Cook Zenith	24 (43.6)	21 (42.0)	1.00
Gore Excluder	11 (20.0)	12 (24.0)	.64
Medtronic Endurant	17 (30.9)	15 (30.0)	1.00
Endologix AFX	1 (1.8)	0 (—)	1.00
Lombard Medical Aorfix	2 (3.6)	0 (—)	.49
Vascutek Anaconda	0 (—)	2 (4.0)	.22
Additional endovascular procedures			
Proximal cuff	5 (9.0)	2 (4.0)	.44
Distal iliac extension	9 (16.4)	5 (10.0)	.40
EII at final angiography	11 (20.0)	10 (20.0)	1.00

EII, Type II endoleak.
[a]Data are presented as the mean ± standard deviation or number (%).

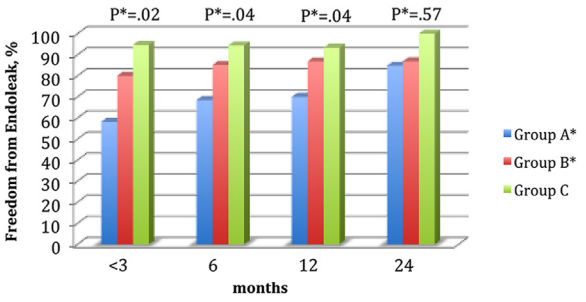

Fig 2. Descriptive analysis of freedom from type II endoleaks (EIIs) during early and midterm follow-up in groups A, B, and C.

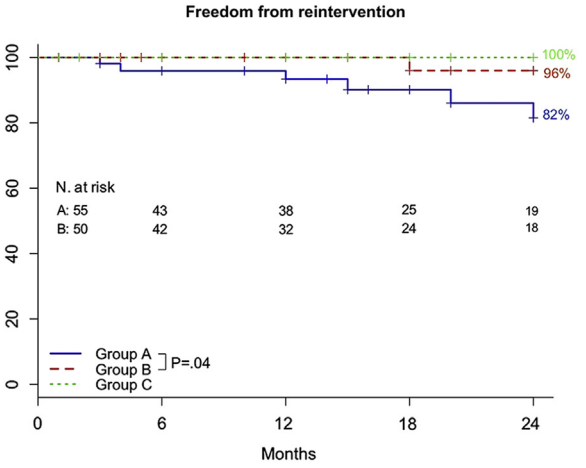

Fig 3. Kaplan-Meier curve for freedom from type II endoleak (EII)-related reintervention during early and midterm follow-up in groups A, B, and C. Standard error <10%.

inflow-outflow between patent branches and the sac can cause sac enlargement or be persistent and expose the patient to a higher risk of adverse outcomes.[13,14] In these cases, the primary approach is usually endovascular, with selective embolization of feeding branches.[15] Several authors recently developed the concept of prevention rather than treatment, using selective embolization of feeding branches with different methods and materials before EVAR. Alerci et al[16] used microcoils, whereas Burbelko et al[17] used vascular plug; even if it is effective, this approach could be a waste of advantages for the patient who needs to undergo two different procedures, and health care costs are increased. Muthu et al[18] have described routine intraoperative selective IMA embolization and thrombin injection into the aneurysm sac just before EVAR. This last approach has the advantage of exposing the patient to a single procedure; on the other hand, selective IMA embolization may require longer operative time and injection of a higher dose of contrast material compared with standard EVAR.

To be clarified also is that the objective of these reported experiences with preventive embolization is often to reduce the incidence of EII in the patient identified preoperatively as at high risk, not to reduce the overall incidence of EII complications in the population of patients undergoing EVAR. In this regard, we agree with the conclusion of Cieri et al[19] that EII is an enigmatic and unpredictable marker of worse outcome after EVAR, and any adjunctive preventive procedure to avoid EII complications in patients at high risk may be a waste of resources over time.

As we agree with this concept, prevention may be effective only if the entire EVAR cohort is routinely exposed to a protocol and the procedure does not have to modify the advantages of EVAR itself in terms of exposure of the patient to radiation and contrast agents, operative time, and costs. Furthermore, this procedure needs to be reproducible and standardized.

The technique used at our institution to prevent EII after EVAR was similar to that reported by Ronsivalle et al,[20] in which they used routine nonselective sac embolization during EVAR with variable doses of fibrin glue in association with coil embolization.

Our previous experience,[7] however, was performed using a "standard dose" of fibrin glue and coils; the results of this retrospective study demonstrated a significantly lower freedom from related reintervention at 18 months in those who underwent embolization compared with standard EVAR (93% vs 99%; $P = .03$). To be emphasized is that the use of a standard dose of material was effective to a sac volume of 125 cm^3 (about 5.8 cm in diameter), whereas higher preoperative sac volumes (>125 cm^3) were an independent predictor of EII (odds ratio, 4.0; 95% confidence interval, 1.5-10.5; $P = .005$).

This method is not based on the traditional concept of selective occlusion of the target feeding branches; the

Table IV. Aneurysm sac volume variation compared with the preoperative volume

Variable[a]	*Group A*	*Group B*	P
CTA ≤3 months			
Volume variation			
cm^3	+2.7 ± 12.8	−1.2 ± 5.8	.05
%	+2.3 ± 11.1	−0.9 ± 4.3	.05
CTA at 6 months			
Volume variation			
cm^3	−2.2 ± 14.2	−10.6 ± 17.1	.007[b]
%	−1.7 ± 15.3	−7.5 ± 10.6	.02[b]
CTA at 12 months			
Volume variation			
cm^3	−2.9 ± 32.2	−18.9 ± 26.6	.02[b]
%	−2.1 ± 26.8	−14.2 ± 16.7	.02[b]
CTA at 24 months			
Volume variation			
cm^3	−4.6 ± 25.9	−27.3 ± 24.7	.008[b]
%	−2.9 ± 21.5	−21.6 ± 17.2	.005[b]

CTA, Computed tomography angiography.
[a]Data are presented as the mean ± standard deviation (cm^3 and %).
[b]Statistically significant.

purpose is to facilitate sac thrombosis at the time of endograft implantation and to avoid the formation of the mechanism that maintains EII (through-and-through or stable backflow from large collaterals). When the EII is established, intervention to treat it may be challenging (presence of an endograft) and has a reported success rate of about 43%. The advantage of embo-EVAR is that nonselective embolization allows the procedure to be easy and fast, with no differences in operative time ($P = .63$), exposure to contrast material ($P = .28$), and radiation exposure ($P = .43$) compared with standard EVAR. On the other hand, routine embolization may cause an overtreatment in all those EVAR patients who really are at low risk for EII.

In this scenario, to optimize the procedure, we applied two principal concepts. The first one is to treat not only those at high risk but all those at risk for EII and to exclude from treatment only those at low risk. Our definition of "at risk" was based primarily on the findings of Abularrage et al,[9] that IMA patency and increasing numbers of patent lumbar arteries predict persistent EII, and the findings of Marchiori et al,[10] in which increasing numbers of sac branches increase EII rate.

Applying as selection criteria the presence of a patent IMA and at least two pairs of lumbar arteries, many EVAR patients are at risk, whereas only those cases with circumferential thrombus and few small collaterals are not treated (low risk).

With this approach, the sensitivity in identifying EII was 96% at 2 years. In group C, the endoleak rate was the lowest (always <10%), with a progressive spontaneous decrease over time (2%-3% at 24 months); no patients in this subgroup needed secondary reintervention at 2 years. Furthermore, the exclusion of these patients reduced overall costs compared with our previous experience with systematic embolization ($P = .0001$ vs $P = .90$).[7]

The second concept is to taper the dose of material to be injected on the basis of the preoperative sac volume; it is our opinion that with this approach, the main factor affecting the outcome is the dose of material rather than the position. Different from standard embolization of feeding branches, in which it is crucial to deploy the material in a specific site, adequate sac filling surrounding the endograft is more important during embo-EVAR. This aspect is similar to that of new devices in commerce, such as the Nellix endograft (Endologix, Irvine, Calif), which employs a volume-dependent dose of a polymer injected in endobags surrounding the endograft; in the multicenter retrospective analysis of a consecutive series of 171 patients, an EII incidence of 2% was reported at 17 months.[21]

During follow-up, a significantly lower EII rate for group B compared with group A until 12 months ($P = .04$) was observed; after that period, even if the incidence of EII was lower in group B, this loses statistical significance ($P = .57$). On the other hand, freedom from reintervention at 24 months was significantly higher in group B than in group A (96% vs 82%; $P = .04$). Thus, we can assume that even if after 1 year there was a similar percentage of EIIs, patients who underwent embo-EVAR were more protected from the insidious evolution of EII, with sac expansion or endoleak persistence that usually requires additional intervention; even if not significant ($P = .13$), the number of persistent EIIs was higher in group A (n = 8; 14.5%) than in group B (n = 3; 6%).

This consideration is confirmed by the sac volume analysis performed overall within the two groups; this revealed a progressive significant sac volume reduction for group B compared with group A at 24 months ($P = .008$). However, when the same parameter was analyzed only for those patients with EII, this difference was maintained but was no longer significant at 24 months ($P = .59$); this may be related to the low number of events considered in the analysis.

Limitations of the study are related to the small cohort of patients enrolled and the limited follow-up as the time-dependent endoleak resolution compared with the intention-to-treat analysis. On the other hand, the randomization and the homogeneity of the two groups guarantee reliable findings.

CONCLUSIONS

To our knowledge, no other published study has compared in a randomized fashion aneurysm sac embolization during EVAR for patients at risk of EII using a sac volume-dependent dose of fibrin glue and coils with traditional EVAR. This technique is safe and effective in preventing EII-related complications during short-term and midterm follow-up after EVAR. Although further confirmatory studies are needed, the faster aneurysm sac volume shrinkage over time in patients who underwent embolization compared with standard EVAR may be a positive aspect influencing the lower EII rate also during long-term follow-up.

AUTHOR CONTRIBUTIONS

Conception and design: MP, MA
Analysis and interpretation: MP, FS
Data collection: FS, MZ
Writing the article: MP, FS
Critical revision of the article: MP, MM, JR, SL, FG, MA
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REFERENCES

1. Faries PL, Cadot H, Agarwal G, Kent KC, Hollier LH, Marin ML. Management of endoleak after endovascular aneurysm repair: cuffs, coils, and conversion. J Vasc Surg 2003;37:1155-61.
2. Laheij RJ, Buth J, Harris PL, Moll FL, Stelter WJ, Verhoeven EL. Need for secondary interventions after endovascular repair of abdominal aortic aneurysms. Intermediate-term follow-up results of a European collaborative registry (EUROSTAR). Br J Surg 2000;87:1666-73.
3. Abularrage CJ, Patel V, Conrad MF, Schneider EB, Cambria RP, Kwolek CJ. Improved results using Onyx glue for the treatment of persistent type 2 endoleak after endovascular aneurysm repair. J Vasc Surg 2012;56:630-6.
4. Jouhannet C, Alsac JM, Julia P, Sapoval M, El Batti S, Di Primio M, et al. Reinterventions for type 2 endoleaks with enlargement of the aneurismal sac after endovascular treatment of abdominal aortic aneurysms. Ann Vasc Surg 2014;28:192-200.
5. Antonello M, Menegolo M, Piazza M, Bonfante L, Grego F, Frigatti P. Outcomes of endovascular aneurysm repair on renal function compared with open repair. J Vasc Surg 2013;58:886-93.
6. Pilon F, Tosato F, Danieli D, Campanile F, Zaramella M, Milite D. Intrasac fibrin glue injection after platinum coils placement: the efficacy of a simple intraoperative procedure in preventing type II endoleak after endovascular aneurysm repair. Interact Cardiovasc Thorac Surg 2010;11:78-82.
7. Piazza M, Frigatti P, Scrivere P, Bonvini S, Noventa F, Ricotta JJ 2nd, et al. Role of aneurysm sac embolization during endovascular aneurysm repair in the prevention of type II endoleak-related complications. J Vasc Surg 2013;57:934-41.
8. Chaikof EL, Fillinger MF, Matsumura JS, Rutherford RB, White GH, Blankensteijn JD, et al. Identifying and grading factors that modify the outcome of endovascular aortic aneurysm repair. J Vasc Surg 2002;35:1061-6.
9. Abularrage CJ, Crawford RS, Conrad MF, Lee H, Kwolek CJ, Brewster DC, et al. Preoperative variables predict persistent type 2 endoleak after endovascular aneurysm repair. J Vasc Surg 2010;52:19-24.
10. Marchiori A, von Ristow A, Guimaraes M, Schönholz C, Uflacker R. Predictive factors for the development of type II endoleaks. J Endovasc Ther 2011;18:299-305.
11. Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM, et al. Reporting standards for endovascular aortic aneurysm repair. J Vasc Surg 2002;35:1048-60.
12. Chuter TA, Faruqi RM, Sawhney R, Reilly LM, Kerlan RB, Canto CJ, et al. Endoleak after endovascular repair of abdominal aortic aneurysm. J Vasc Surg 2001;34:98-105.
13. Gelfand DV, White GH, Wilson SE. Clinical significance of type II endoleak after endovascular repair of abdominal aortic aneurysm. Ann Vasc Surg 2006;20:69-74.
14. Jones JE, Atkins MD, Brewster DC, Chung TK, Kwolek CJ, LaMuraglia GM, et al. Persistent type 2 endoleak after endovascular repair of abdominal aortic aneurysm is associated with adverse late outcomes. J Vasc Surg 2007;46:1-8.
15. Silverberg D, Baril DT, Ellozy SH, Carroccio A, Greyrose SE, Lookstein RA, et al. An 8-year experience with type II endoleaks: natural history suggests selective intervention is a safe approach. J Vasc Surg 2006;44:453-9.
16. Alerci M, Giamboni A, Wyttenbach R, Porretta AP, Antonucci F, Bogen M, et al. Endovascular abdominal aneurysm repair and impact of systematic preoperative embolization of collateral arteries: endoleak analysis and long-term follow-up. J Endovasc Ther 2013;20:663-71.
17. Burbelko M, Kalinowski M, Heverhagen JT, Piechowiak E, Kiessling A, Figiel J, et al. Prevention of type II endoleak using the AMPLATZER vascular plug before endovascular aneurysm repair. Eur J Vasc Endovasc Surg 2014;47:28-36.
18. Muthu C, Maani J, Plank LD, Holden A, Hill A. Strategies to reduce the rate of type II endoleaks: routine intraoperative embolization of the inferior mesenteric artery and thrombin injection into the aneurysm sac. J Endovasc Ther 2007;14:661-8.
19. Cieri E, De Rango P, Isernia G, Simonte G, Ciucci A, Parlani G, et al. Type II endoleak is an enigmatic and unpredictable marker of worse outcome after endovascular aneurysm repair. J Vasc Surg 2014;59:930-7.
20. Ronsivalle S, Faresin F, Franz F, Rettore C, Zanchetta M, Olivieri A. Aneurysm sac "thrombization" and stabilization in EVAR: a technique to reduce the risk of type II endoleak. J Endovasc Ther 2010;17:517-24.
21. Böckler D, Holden A, Thompson M, Hayes P, Krievins D, de Vries JP, et al. Multicenter Nellix EndoVascular Aneurysm Sealing system experience in aneurysm sac sealing. J Vasc Surg 2015;62:290-8.

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