6-month group. Overall, fatal and nonfatal VTE during and after treatment occurred in 8% of those receiving 3 months of anticoagulation (n = 31) and in 8% of those receiving 6 months anticoagulation (n = 29; $P = .80$; 95% confidence interval [CI] difference, –3.1% to 4.7%). No patients in either group had a fatal hemorrhage during treatment, but there were eight major hemorrhages in those treated for 6 months and none in those treated for 3 months ($P = .008$; 95% CI, –3.5% to –0.7%). Adverse events occurred in 8% of the patients receiving 3 months of anticoagulation (n = 31) and in 9% of the patients receiving 6 months of anticoagulation (n = 35; $P = .79$, 95% CI –4.9% to 3.2%).

Comment: The data with regard to the hard end points in this study—death from VTE or major hemorrhage—are likely reliable. The data with respect to recurrence, extension, or failure to resolve VTE are likely highly unreliable because they were derived from review forms completed by clinicians at each individual site, without specific requirements for imaging during follow-up. Indeed, the idea that the DVT resolved in >95% of the patients treated with oral anticoagulation is completely disparate with regard to the findings of serial imaging studies in patients with DVT. The authors also provide no information about possible postphlebitic syndrome in their patients. Follow-up is too short for such an analysis. Overall, the study indicates no difference in death from VTE with 3 or 6 months of anticoagulation in a patient with VTE and unidentified risk factors. The data are not sufficient to conclude that there is no difference in recurrence of VTE with the two treatment paradigms.

Heritability of Platelet Responsiveness to Aspirin in Activation Pathways Directly and Indirectly Related to Cyclooxygenase-1

Faraday N, Yanek LR, Mathias R, et al. Circulation 2007;115:2490-6.

Conclusion: There is a genetic basis to variability in residual platelet function after aspirin exposure.

Summary: It is known that the inability of aspirin to suppress platelet function can be associated with future risk of myocardial infarction, stroke, and cardiovascular death. The authors sought to determine if there was genetic variation that could be linked to insufficient aspirin responsiveness.

Aspirin responsiveness was assessed in 1880 asymptomatic patients. The mean age was 44 ± 13 years, and 58% were women. Patients were recruited from 309 white and 208 black families with premature coronary heart disease. Platelet function was determined ex vivo before and after ingestion of aspirin (81 mg/d for 2 weeks). Platelet function was determined with a panel of tests assessing platelet activation in pathways indirectly and directly related to cyclooxygenase-1 (COX-1). Multivariable regression analysis was also used to determine the proportion of phenotypic variance related to coronary heart disease risk factor covariates.

Arachidonic acid–induced thromboxane B_2 production was inhibited by >99% with aspirin ($P < .0001$). Platelet activation by pathways indirectly related to COX-1 and inhibition of urinary thromboxane excretion was more variable, with inhibition rates varying from 0% to 100%. Covariates contributed somewhat to variability in aspirin responsiveness ($r^2 = 0.001$-0.133). Direct COX-1 phenotypes were not heritable across races. Phenotypes indirectly related to COX-1 were consistently and strongly heritable across races ($r^2 = 0.266$-0.762; $P < .01$).

Comment: This is the first study to demonstrate that responsiveness to aspirin is highly heritable. This applies particularly to phenotypic responses in activation pathways that are indirectly related to COX-1. The study is also the first to demonstrate that heritable factors contribute more strongly than traditional cardiac risk factors to individual variability in residual platelet function after aspirin exposure. It may be that inadequate response to aspirin therapy runs in families.

Mid-term Survival After Abdominal Aortic Aneurysm Surgery Predicted by Cardiopulmonary Exercise Testing

Carlisle J, Swart M. Br J Surg 2007;94:966-9.

Conclusion: Cardiopulmonary exercise (CPX) testing, in combination with comorbidity scoring, identifies patients unlikely to survive in the mid-term after successful abdominal aortic aneurysm (AAA) repair.

Summary: The purpose of AAA repair is to prevent aneurysm-related death. Patients at high risk of death from other causes are unlikely to benefit overall from AAA repair. A number of risk factors found on history and physical examinations correlate with survival after surgery. CPX testing identifies patients at increase risk of dying after surgery (Chest 1999;116: 355-62). In this study the authors sought to determine whether preoperative CPX testing could predict survival after elective open AAA repair. Patients were also assessed with the Simplified Acute Physiology Score (SAPS) II, the Acute Physiology and Chronic Health Evaluation (APACHE) II score, and the Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM). CPX fitness was determined with equipment measuring ventilatory minute volume, oxygen consumption, and carbon dioxide while subjects pedaled an exercise bicycle. Four variables were derived from CPX exercise measurements: anaerobic threshold, peak oxygen consumption ($\dot{V}O_2$ peak), and ventilatory equivalents for oxygen ($\dot{V}E/\dot{V}O_2$) and carbon dioxide ($\dot{V}E/\dot{V}CO_2$). The Revised Cardiac Risk Index (RCRI) was also determined for each patient, with one point assigned for AAA repair, history of ischemic heart disease, history of heart failure, cerebrovascular disease, insulin-dependent diabetes, and a preoperative serum creatinine concentration of about 177 μmol/L.

Multivariable analysis indicated that survival to 30 days and for the total observation period correlated best with $\dot{V}E/\dot{V}CO_2$. An increase in $\dot{V}E/\dot{V}CO_2$ by one unit increased the hazard ratio for death over the total observation period by 1.13 for each unit increase. RCRI was also associated with mid-term survival, as was anaerobic threshold.

Unfit patients were then defined as those with an RCRI >1 and a $\dot{V}E/\dot{V}CO_2$ of >42, and fit patients were then defined as those with an RCRI of 1 (and any $\dot{V}E/\dot{V}CO_2$), or an RCRI >1 but $\dot{V}E/\dot{V}CO_2$ <43. This definition provided 30 unfit patients and 100 fit patients for analysis. The 30 unfit patients were followed up for a total of 58 patient-years, and the 100 fit patients for a total of 278 patient-years. Two-year survival for the fit patients was 97%. Two-year survival for the unfit patients was 55% (95% confidence interval, 18%-65%; $P <178> .001$).

Comment: A significant problem with this study is that the distinction between fit and unfit patients was determined by observed mortality. Additional data based on prospective classification of patients undergoing open AAA repair is required to assess whether the retrospective analysis used to determine fit vs unfit potentially overestimated differences between groups. Nevertheless, it is unlikely that even patients with relatively large AAAs would experience a 55% rupture rate ≤2 years. The data suggest, as previously suggested by the Endovascular Aneurysm Repair II Trial (Lancet 2005;365:2187-92), that repair of AAAs in the marginally fit or unfit patient may be more about surgical technical skill than overall patient benefit.

Impact of Endoluminal Treatment on Small Abdominal Aortic Aneurysm: Aneurysm Sac Regression and Secondary Interventions With 5 Years of Follow-up

Hao Bui, Lujan R, Nguyen A, et al. Vasc Endovasc Surg 2007;41:294-300.

Conclusion: Endovascular intervention for small abdominal aortic aneurysms (AAAs) does not result in faster aneurysm sac regression or lower rates of secondary intervention.

Summary: It has been suggested endovascular repair be applied to small AAAs in an attempt to reduce secondary intervention rates associated with endovascular repair of larger AAAs. The authors reviewed 374 patients who underwent endovascular AAA repair between 1996 and 2006. Of these patients, 75 (20%) had a small AAA defined by an aneurysm sac diameter to aortic diameter ratio of <2 at the level of the renal arteries, and 299 patients had larger AAAs.

There were no significant differences in operative times or operative blood loss in patients undergoing endovascular repair for small AAAs vs those undergoing repair of larger AAAs. In the patients treated for small AAAs, 25.3% developed endoleaks compared with 36.1% of patients treated for larger AAAs ($P = .1$). Over a mean follow-up of 42 months (range, 1-109 months), 11 patients (14.7%) with small AAAs had secondary interventions. Of the patients with larger AAAs, 58 (19.4%) had secondary interventions ($P = .41$). At 5 years, small AAAs had a 2.5% regression in the aneurysm sac volume but a 3.0% increase in aneurysm diameter. Patients with large AAAs had slight increases in sac diameter (3.3%) at 1 month but steady decreases in sac volume (–13.4%) and aneurysm diameter (–8.8%) over 5 years.

Comment: The data argue against early intervention with endovascular techniques for small AAAs. Previous data from the University of Texas Southwestern Medical Center suggests waiting for small AAAs to enlarge to 5 to 5.5 cm does not reduce the applicability of endovascular techniques for their repair. Given those data, the relatively benign natural history of small AAAs, and the data presented here, it seems difficult to justify repair of small AAAs with endovascular techniques outside the context of a clinical trial.

Renal Insufficiency Following Contrast Media Administration Trial (REMEDIAL): A Randomized Comparison of 3 Preventive Strategies

Briguori C, Airoldi F, D'Andrea D, et al. Circulation 2007;115:1211-7.

Conclusion: A combination of volume supplementation by sodium bicarbonate plus N-acetylcysteine (NAC) provides better renal protection after contrast administration in patients with chronic kidney disease (CKD) than strategies of hydration with a combination of normal saline and NAC or the addition of ascorbic acid.

Summary: The optimal strategy for preventing contrast agent–induced nephrotoxicity (CIN) in patients with CKD is uncertain. Guidelines suggest volume expansion with saline, along with use of low or iso-osmolar contrast agents and limits on the volume of contrast agent (Kidney Int 2006;69:S51-3). Additional strategies focus on the use of antioxidants because reactive oxygen species are considered an important pathophysiologic cause of CIN (Kidney Int 2005;68:14-22). Both NAC and ascorbic acid have antioxidant properties.