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Endovascular Repair of Abdominal Aortic Aneurysms

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Executive Summary

Abdominal aortic aneurysms (AAA) constitute a significant source of morbidity and mortality. Endovascular repair (EVAR) provides a minimally invasive procedure that reduces morbidity, hospital stay, and promotes an early return to function. The four currently available endografts include the Medtronic AneuRx®, the Gore Excluder®, the Cook Zenith®, and the Endologix Powerlink®. Eligibility for EVAR revolves around anatomic limitations, where short, angulated, or wide necks and severe tortuosity can lead to suboptimal outcomes. Endovascular graft leak constitutes the major complication associated with EVAR. Other complications include kinking, perforation, separation, fracture, migration, and erosion. The largest randomized clinical trial to date, EVAR-1, demonstrated comparability of the first-generation EVAR to open surgical repair. Two non-industry trials continue to enroll patients for elective repair. Preliminary evidence suggests that EVAR may also be useful in patients with ruptured AAA. Because the procedural-related mortality of EVAR is currently in the 1-2% range, treating smaller aneurysms (4-5.5cm) may someday prove to be beneficial.

Introduction

Abdominal aortic aneurysms (AAA) constitute a significant source of morbidity and mortality. An estimated one million Americans have AAAs, of which only 15% are diagnosed, and 6% are treated, one-third of those by endovascular aortic repair (EVAR) ([1]). The risk of rupture increases non-linearly. For example, a 4-5cm aneurysm has an annual risk of rupture of 0.5%-5.0%, whereas a 6-7cm aneurysm has a 10-20% annual risk of rupture ([2]). The decision to operate prophylactically on asymptomatic patients involves consideration of the risk of operative mortality and life expectancy compared to the risk of rupture. Generally, patients will experience a survival benefit from open repair if their AAA exceeds 5-5.5cm. The surgical mortality for open repair is 2-5% in randomized trials; major morbidity includes pseudoaneurysm (1.3%), erectile dysfunction (≈5%), aortoenteric fistula (0.9%), graft infection (0.4%), and bowel ischemia (0.3%); and recovery time ranges from 6- 24 weeks ([3]). Decade-old data from a series of 154 consecutive ambulatory patients at a single center found an operative mortality of 4% and a mean hospital stay of 10.7 days. A third of patients did not experience complete recovery at a mean of 34 months. Remarkably, 18% of patients said they would not undergo the repair again knowing the extended recovery process involved ([4]). EVAR provides a minimally invasive procedure that reduces morbidity, hospital stay, and promotes an early return to function.

Endovascular Repair and Complications

The EVAR Procedure

The four endografts currently available in the United States include the *Medtronic AneuRx®*, the *Gore Excluder®*, the *Cook Zenith®*, and the *Endologix Powerlink®*. The grafts vary in outer diameter from 18-23F and in graft material (polytetrafluoroethylene or woven polyester) (Figure 1). A brief description of the EVAR procedure provides insight into the potential anatomical challenges of the procedure. First, the patient is anesthetized with general endotracheal anesthesia, spinal epidural, or conscious sedation, depending on

Figure 1 **Available US Endografts for Abdominal Aortic Aneurysm Repair**

patient comorbidities and anesthesia preference. Femoral artery access is obtained with either percutaneous access (with percutaneous closure device established) or femoral artery cut down. Large 24F sheaths are placed on the side of the main body, and 18F sheaths on the contralateral side. A diagnostic aortogram with a marker catheter confirms the length measurements obtained off-line by CT angiogram for the renal arteries to the iliac bifurcation and the origin of the hypogastric (aka internal iliac artery) arteries. The angiographic measurement allows for adjustment of the off-line measurements to take into account tortuousity, bends, turns, and angulations. The device is introduced just below the renal arteries and deployed, and the contralateral limb is subsequently accessed from the contralateral iliac artery. The contralateral limb graft is subsequently deployed. The interventionalist assesses whether further length is required, and final balloon inflations are used to seal the proximal and distal zones as well as each of the overlapping stent junctions. Aortography is repeated to confirm the absence of leaks. The groin is closed or repaired with a total procedural time of approximately 2 hours.

Eligibility for EVAR revolves around anatomic limitations. The proximal neck must have a landing zone length of 15mm, and the device diameter must exceed the aortic diameter by 10-20% to seal the proximal and distal edges, and to reduce the possibility of leaks in terms of graft implantation, stability, or seal. Short, angulated, or wide necks and severe AAA tortuosity can lead to suboptimal outcomes. The common femoral artery and iliac arteries must accommodate the 18-24F delivery systems and have a distal landing zone. In addition, up to two-thirds of all AAAs have aneurysmal involvement of the iliac arteries. While iliac aneurysmal involvement extending to the hypogastric artery bifurcation can complicate distal landing zone considerations, it does not preclude the application of EVAR technology. Anatomic limitations assessment occurs with preoperative imaging using CT angiography.

Complications

Endovascular graft leak constitutes the major complication associated with EVAR (Figure 2). Classification includes Type I leak (leak around the proximal and distal attachment site), Type II leak (leak inside the aneurysm by a feeder vessel circuit), Type III leaks (leak due to graft fabric tear or disconnection), and Type IV leaks (leak through the graft itself). Because leaks often are asymptomatic, a CT angiogram or abdominal ultrasound follow-up is recommended at 1 month, 6 months, 12 months, and then annually thereafter. Alternatively, the implanted CardioMEMS Endosure™ AAA Pressure Measurement System can be used to assess for increase in endotension. This device, placed endovascularly in the aneurysm sac at the time of graft placement, allows for remote measurement of pressure within the excluded sac (5). Endotension and the CardioMEMS Endosure™ is awaiting validation as a predictor of aneurysm exclusion/endoleak detection.

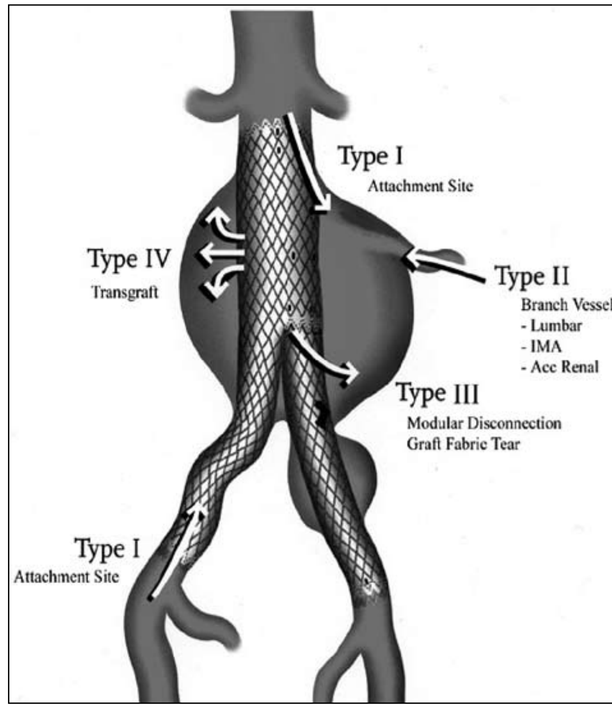

Figure 2 **Types of Endoleaks**
IMA = inferior mesenteric artery, Acc Renal = accessory renal

Other complications of EVAR include stent graft failure, namely kinking, perforation, separation, fracture, migration, and erosion. Stent graft failure is being addressed with next generation of endografts, which have improved durability, deliverability, and applicability.

Trial Data

The largest randomized clinical trial to date (conducted from 1999-2003), EVAR-1, demonstrated comparability of the first-generation EVAR to open surgical repair (6). EVAR-1 randomized 1082 patients with aneurysms of at least 5.5cm to undergo EVAR or surgical repair. The 30-day operative mortality was significantly lower in the endovascular arm (1.7% vs. 4.7%, p=0.009, odds ratio [OR] 0.35, 95% confidence interval [CI] 0.16–0.77). The trade off was a higher rate of secondary interventions with 9.8% of EVAR-assigned patients requiring secondary interventions compared to 5.8% of surgical patients. Of the EVAR patients that required reintervention, 36% were for repair of endoleaks and 20% had conversion to open repair. At four years, there remained a statistically significant absolute

3% aneurysm-related mortality benefit with EVAR, however reintervention occurred in 41% of EVAR patients compared to 9% of open repair patients, resulting in an overall cost increase of £3311 (approximately $6,572) per patient ([7]). Most of the reintervention took place in the first month of EVAR. Contemporary rates of reintervention are estimated to be significantly lower.

More recent registry data confirms the applicability of EVAR for AAA. The Lifeline registry is a US-based trial comparing 2664 patients who underwent EVAR to an historical control of 334 patients who underwent surgical repair. At six years, the EVAR group was found to have a 99% freedom from rupture, a 98% freedom from aneurysm-related death, and a 95% freedom from surgical conversion ([8]). The surgical arm had a low periprocedural mortality rate, and at 4 years there was no difference in survival between the two arms. This data demonstrated that there is no increase in late rupture or secondary interventions with EVAR, a concern that arose from earlier data using the first generation stent grafts.

Two non-industry trials continue to enroll patients to evaluate the role of EVAR compared to open surgery in elective patients with AAA. The first is the ACE trial, by Assistance Publique-Hôpitaux de Paris, which is randomizing 600 patients to EVAR or open surgery. The second trial, sponsored by the Department of Veterans Affairs, is the Open Versus Endovascular Repair (OVER) Trial for Abdominal Aortic Aneurysms. This trial is randomizing 900 patients to EVAR versus open surgery, and expects to complete enrollment in 2011.

The EVAR-2 study enrolled 338 patients ineligible for open repair due to excessive operative risk from active coronary disease, severe pulmonary disease, or renal dysfunction, and randomized them to either EVAR or medical therapy. The procedural mortality was 9%, while the medical therapy arm had a rupture rate of 9 per 100 patient-years. At the end of 4 years, the overall mortality was 64%, with no difference in either arm, but EVAR-treated patients had a high risk of both complications (33%) and reintervention (18%). Although the authors concluded that EVAR was of limited utility in this high-risk patient population, a recent VA observational retrospective study found that EVAR treated high-risk patients have a significantly improved mortality compared to those patients who underwent open treatment, providing greater optimism for high-risk patients [9]. Patients with high American Society of Anesthesiology scores and comorbid conditions underwent EVAR (788 patients) or open repair (1580 patients). Both 30-day (3.4% vs. 5.2%, p=0.047) and 1-year all-cause mortality (9.5% vs. 12.4%, p=0.038) were significantly lower in the EVAR group. This promising data suggests that therapeutic options that improve mortality may be available in high-risk surgical populations.

Preliminary evidence suggests that EVAR may be useful in patients with ruptured AAA. One observational, single center study found that patients with ruptured AAA and anatomic suitability had improved survival when treated with EVAR compared to surgical repair ([10]). Another observational study found similar 1-year survival rates for EVAR and surgical repair ([11]). These studies are limited by their small size and observational nature, and await randomized trial confirmation.

Because the procedural related mortality of EVAR is in the range of 1-2%, it may become beneficial in the future to treat smaller aneurysms (4-5.5cm). A Veteran's Administration trial randomized patients with aneurysms of this size to surgery versus observation. At 4.9 years, there was no difference in mortality, although at 8 years the surgical arm had a statistically significant reduction in mortality ([12]). To evaluate whether prophylactic treatment of aneurysms 4-5cm is beneficial, the PIVOTAL trial is randomizing 1050 patients to EVAR or continued follow-up. Patients must have AAAs that are double the size of the reference aorta and must meet criteria for the Medtronic AneuRx® device. Crossover will be allowed for patients whose aneurysm becomes symptomatic, exceeds 5cm, or is experiencing rapid growth. Cook Zenith® is enrolling 740 patients in a similar Phase IV trial, and expects to complete its study in 2011.

New Devices

Endovascular repair technology has been further extended and modified in order to address the major limitation excluding patients from this therapy, specifically involvement of branch vessels (either renal, mesenteric, or hypogastric). Additional advances include the fenestrated and branched endografts. These grafts, not presently available in the US, allow for side branch stenting of important arteries (eg, the renal arteries), while still excluding the aneurysm ([13]). To expand the patient population that may be eligible for endovascular repair, Lombard Medical is testing the Aorfix™ Stent Grafts in patients with a neck angulation of 60-90°. Other groups are attempting to address endovascular leaks. A French trial sponsored by Medtronic is in Phase II testing of an autologous, platelet-rich thrombin seal for endovascular devices to prevent Type I leaks. An independent fixation method has also been developed to give added security against EVAR migration, and is still in the investigational stages. A truly percutaneous endograft allowing for small, 12-14F, sheath sizes has been hindered by material durability, and awaits further advances.

Conclusion

Endovascular repair of AAA is becoming the preferred option in appropriate patients. The devices are getting smaller and easier to use. Stent migration and stent fracture are being addressed by technical improvements, including active fixation, and better patient selection. Endoleak remains a cause of repeat intervention, although this is decreasing. Long-term "sac watch" may improve with alternative methods to CT angiography (eg, CardioMEMS implantable pressure sensors). Randomized trials and observational data comparing EVAR to open surgery have found favorable intermediate-term results for EVAR. Applicability (currently ~50%-60%) and durability is improving with the development of larger neck devices with suprarenal fixation and bifurcated/fenestrated grafts. Assuming current investigations are confirmatory, it is likely a greater number of endografts will be implanted, including in smaller aneurysms.

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