# Updating Our Understanding of EVAR

Have the results shown a significant improvement in outcomes with a new generation of devices?

BY FREDERICO BASTOS GONÇALVES, MD; SANDER TEN RAA, MD, PHD; DANIËL EEFTING, MD, PHD; ELLEN V. ROUWET, MD, PHD; JOHANNA M. HENDRIKS, MD, PHD; AND HENCE J.M. VERHAGEN, MD, PHD

Endovascular aneurysm repair (EVAR) has largely become the preferred technique for elective treatment of infrarenal abdominal aortic aneurysms (AAAs). Since its introduction in 1991, when Volodos et al and Parodi et al independently demonstrated the feasibility of transfemoral graft placement to exclude the aneurysm sac from circulation,[1,2] we have been treading a steep and restless path of evolution. During the last 2 decades, we have come from cumbersome homemade devices to off-the-shelf, user-friendly designs featuring countless technological advances. The growing proportion of AAA repair using EVAR across the globe is a clear indicator that this method has gained wide acceptance from physicians and patients.

Despite all of the experience acquired to date, it remains unclear what results can be expected, mainly because of the gradual improvement of devices and understanding of postoperative findings. The three largest randomized controlled trials comparing EVAR and open repair have now published their long-term data, and their results are strikingly similar.[3-5] However reassuring these results may be, we must bear in mind that the endografts used during the study intervals of these randomized controlled trials have been either significantly modified or discontinued, and much has changed in the management of postoperative complications. These facts cast doubt on the clinical applicability of the findings.

Since the introduction of EVAR, technical improvements have been coupled with expanding anatomical limits. This phenomenon adds to the number of available devices and also combines with the technological turnover of endografts, which complicates the math for risk estimation. However, results are always dependent on a combination of three strongly associated factors: (1) device improvements, (2) accumulated experience and centralization, and (3) evolution in instructions for use (IFU).

> Despite the expansion of treatment to patients with more adverse anatomy, it is clear that the results of standard elective EVAR continue to improve.

## DEVICE IMPROVEMENTS

Long-term results, although still sparse, generally support the idea that EVAR offers safe and lasting prevention of aneurysm-related death. This is true despite high, yet steadily decreasing, secondary intervention rates and the burden associated with lifelong follow-up. Taking as

an example the recently published long-term outcomes from the UK EVAR trials, one must bear in mind that recruitment for these trials lasted from 1999 to 2004, meaning that none of the endografts used are still commercially available. All have been significantly revised to resolve proven faults and reduce early and late complications, and some have been discontinued.

The paradigmatic example is the Excluder AAA endoprosthesis (Gore & Associates, Flagstaff, AZ). The change in the fabric porosity, undertaken in 2004, significantly reduced the rate of aneurysm expansion after treatment and, as a consequence, the need for secondary interventions;[6,7] however, the more permeable generation of the device was used in the UK EVAR trials. In patients treated with this latter generation of device who have adequate seal and absence of endoleaks on the first postoperative CT angiography, 5-year freedom from aneurysm-related adverse events may be as high as 98% (Figure 1).

As another example, in a publication on EVAR with neck thrombus from our group, migration was observed in 9.8% of patients, with significant differences according to the implanted endoprosthesis.[8] Active proximal fixation (suprarenal or infrarenal) was the important determinant for preventing migration. Because the suprarenal aorta is usually free of thrombus, we currently prefer nitinol-based devices with suprarenal active fixation to treat this group of patients, with very positive results.

These findings are in line with the larger sample size of the EUROSTAR study, which in 2005 reported a total of 1,579 patients in whom this graft was implanted.[9] The investigators found that, compared to the Zenith device (Cook Medical, Bloomington, IN), the Talent stent graft (Medtronic, Inc., Minneapolis, MN) was more likely to migrate (odds ratio, 3.61; 95% confidence interval, 2.1–6.4) and more often required conversion to open repair (odds ratio, 3.5; 95% confidence interval, 1.9–6.3). All major devices that are currently commercially available offer active proximal fixation, but this was not so at the time of these studies.

Recent data from the latest devices available also suggest a significant decrease in the rates of migration, type I endoleaks, and postimplant ruptures, although long-term data are obviously missing, which stands in striking contrast to the results of first-generation[10,11] and second-generation[12,13] endoprostheses. In a recent publication, Holt et al, taking only patients treated from 2004 onward, report much lower aneurysm-related mortality (0.9 deaths per 100 person-years) and primary sac expansion rates (6.7 per 100 person-years) than those reported in earlier trials and image repository studies.[14]

To further illustrate this point, we can look back to the results on 1,190 patients treated with a Stentor (Min-Tec,

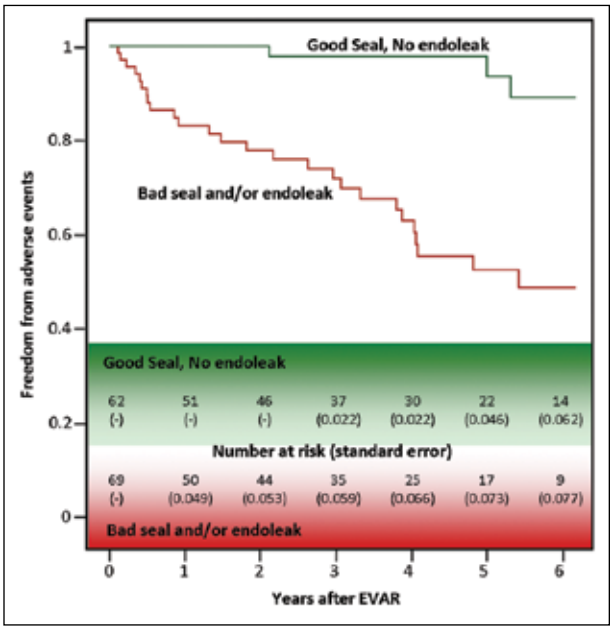


**Figure 1. Adverse event rates for patients with and without good seals and endoleaks on the first postoperative CT angiogram. Adapted from Bastos Gonçalves F, van de Lujitgaarden KM, Hoeks SE, et al. Adequate seal and no endoleak on the first postoperative computed tomography as criteria for no additional imaging up to 5 years after endovascular aneurysm repair. *J Vasc Surg*. In press.**

Freeport, Grand Bahama, The Bahamas) or Vanguard (Boston Scientific Corporation, Natick, MA) endograft, as reported by Leurs et al.[15] Despite a 9.3% intraoperative complication rate, the 30-day mortality rate was only 2.9%. However, at 4 years, 7% of patients died from AAA-related causes, and at 8 years, this number doubled. Patients with larger aneurysms were at a particular risk of complications, with cumulative rates of conversion or rupture of 60% at 8 years.

## EVOLUTION IN IFU

Patients' anatomical characteristics greatly influence EVAR results, and these limitations are roughly reflected in manufacturers' IFU. These IFU, in turn, are based on clinical identification of risk factors, as well as engineers' expectations resulting from benchmark testing. Although it is logical that treatment within the IFU generally offers better results (Table 1), it is obvious that opinions differ when it comes to acceptable risk, which is consequently reflected between institutions in the varying proportions of EVARs performed outside the IFU. Some manufacturer recommendations are not arguable (such as maximum neck diameter), whereas others may be considered to be within acceptable risk, depending on

**TABLE 1. CONTEMPORARY REGULATORY STUDIES (ALL PATIENTS WITHIN IFU)**

| Graft | Year of Publication | N | Follow-Up (Months) | Technical Success, N (%) | Clinical Success | Secondary Intervention | Type I/III Endoleaks | Ruptures | Migration | Sac Growth |
|---|---|---|---|---|---|---|---|---|---|---|
| Endurant[16] | 2012 | 150 | 12 | 99.3% | 93.3% | 15% | 0.7% | 0 | 0% | 0% |
| Powerlink[17] | 2009 | 192 | 49 | 97.9% | NS | 13.5% | 1.6% | 0 | 4.2% | 10.3% |
| Cook Zenith[18] | 2008 | 739 | 30 | NS | NS | 19% | 1.3% | 0.1% | 0.4% | NS |

*Abbreviations: NS, nonsignificant.*

the institution's experience, the device that is used, and the patient's comorbidities.

Despite differences in conception, materials, and design, most currently marketed devices follow roughly similar recommendations for anatomy-based patient selection. However, somewhat subtle differences often point out the strong points of each device. Because the IFU frequently change with each innovation introduced, studies that use them as selection criteria may become no longer relevant in a relatively short period of time. Perhaps the most limiting adverse neck characteristic is neck length, as adequate proximal seal is an essential condition for success. Due to the fact that deployment mechanisms have become increasingly accurate and device fixation has improved, most manufacturers gradually reduced the recommended minimum from 20 mm to 10 or 15 mm. This will obscure the results of improved seal and fixation technology.

Proximal neck diameter was also a common limitation of patients undergoing EVAR, because most devices were not produced in large enough proximal diameters. Several studies suggest that large aortic neck diameters are associated with worse prognosis, more frequent and rapid dilatation of the neck, greater likelihood of type IA endoleaks and reintervention, and a more rapid decline in renal function after EVAR.[19-22] Still, endograft diameters gradually evolved to diameters of 34 to 36 mm for all major brands. Many argue that a 32-mm neck is already aneurysmal and that implantation of an endograft in an aneurysmal neck will result in inevitable loss of seal and consequent failure to exclude the sac from circulation. A wide neck is, therefore, a great example of how expanding indications may result in less-pronounced benefits from latter-generation endografts.

Iliac tortuosity, stenosis, calcifications, thrombus, or dilatations are generally considered as less-favorable conditions for EVAR. Low-profile delivery systems (≤ 18 F) with hydrophilic coatings are becoming the standard today, as these markedly reduce failure to deploy and introduction-related complications, such as iliac rupture. The inevitable expansion of EVAR to patients with adverse iliac anatomy is the most plausible explanation for persistent rates of graft occlusion, ranging from 1% to 4% with most devices.

## DEVICE-RELATED ADVANCES

The general trends in newer endovascular devices for AAA are lower-profile and more hydrophilic delivery sheaths, user-friendly mechanisms, a more compliant structure that better adapts to underlying anatomy, and two-step proximal deployment with tip capture (or repositionable, as in the case of the Excluder AAA endoprosthesis with C3 delivery system [Gore & Associates]). Out of all of the newer-generation endoprostheses, the Endurant AAA stent graft system (Medtronic, Inc.) has received the greatest scrutiny in peer-reviewed literature; generally, results have corresponded to expectations. Our group has published on a series of 45 patients with extreme angulation of the proximal neck treated by EVAR using the Endurant stent graft.[23] These were compared to matched controls (n = 65) with angulations within the IFU. Angulated necks up to 125° (mean, 80.8°) were treated, reflecting the severity of angulation in that group of patients.

During a median follow-up of 3 years, no differences were found in clinical success rates compared to the control group ($P$ = .79). Two post-EVAR ruptures occurred, one in each group. No differences were found in the rate or type of reinterventions. Neck dilatation > 2 mm occurred in 45% of patients versus 43% in the control group ($P$ = .23) despite similar oversizing. Mean angulation changes in the study group were $\alpha$ -16° ± 18° and $\beta$ -29° ± 23°. From these results, we concluded that severe proximal neck angulation had no influence on midterm results when using the Endurant endograft. Device conformability resulted in minor changes in neck angulation over time, reducing the risk of complications (Figure 2).

ENGAGE registry results are starting to emerge, as inclusion was concluded in April 2011. Of the 1,266

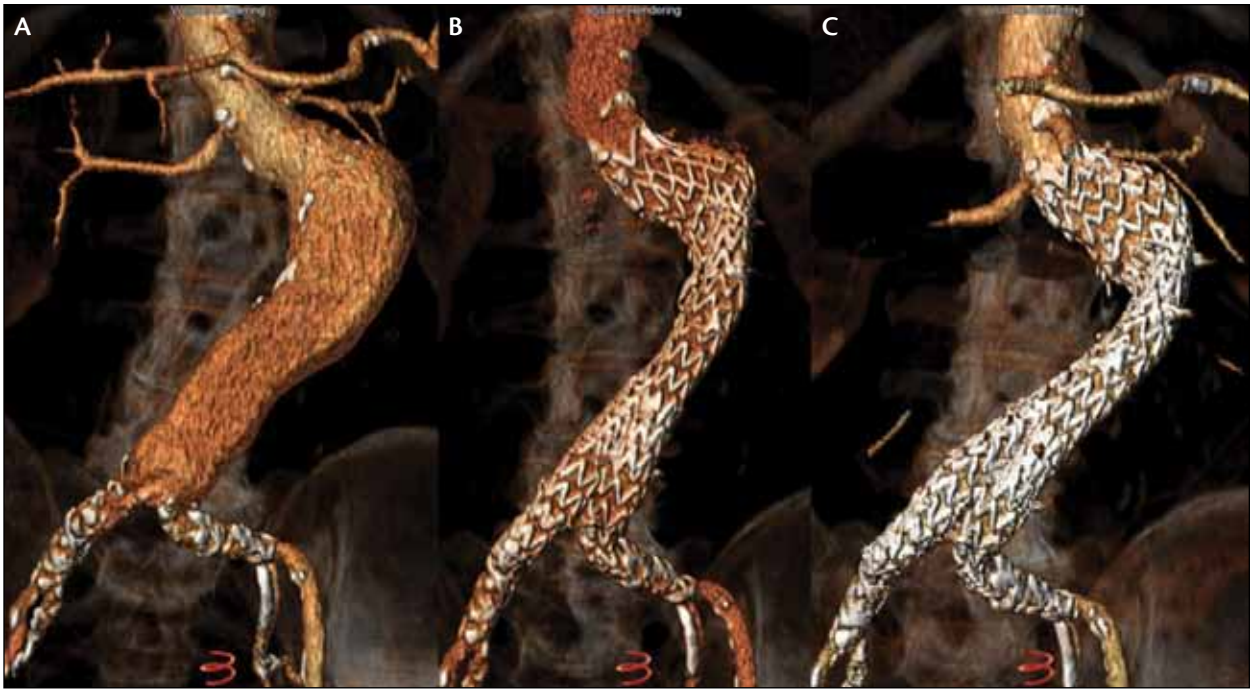


**Figure 2. Minor changes in anatomy after 2 years in very angulated anatomy using the Endurant device. Preoperative (A), first postoperative (B), and 2-year (C) three-dimensional volume-rendering reconstruction.**

patients included, 226 (17.9%) had devices implanted outside the IFU criteria. Even so, a recent publication on early results reports a technical success rate of 99%, and estimated overall survival, aneurysm-related survival, and freedom from secondary interventions at 1 year were 91.6%, 98.6%, and 95.1%, respectively. At 1 year, aneurysm size increased ≥ 5 mm in 2.8% and decreased ≥ 5 mm in 41.3% of cases. Although preliminary, these results suggest improvement from previous generations of endovascular devices.

The Powerlink stent graft (Endologix, Irvine, CA), with its anatomical fixation and rigid body concept, is the exception to the current trends of increased flexibility and conformability. Jordan et al have published results from the multicenter pivotal Powerlink trial using the Powerlink XL device (up to 36 mm) and reported very high success rates at 1 year.[24] The authors argue that columnar strength and anatomical fixation at the iliac bifurcation are ideal for very wide necks. However, early and midterm experience with the 36-mm Zenith device showed similar results to those for conventional EVAR, suggesting no significant adverse outcome with oversized necks.[25] Results from patients treated with other new-generation endografts, such as the Excluder AAA endoprosthesis with C3 delivery system and the Zenith Flex with Z-Trak (Cook Medical), are eagerly awaited.

## THE EFFECT OF ACCUMULATED EXPERIENCE AND CENTRALIZATION

As devices become better and indications are expanded, new learning curves are required, which can only be efficient in high-volume settings. Recently, we have shown the incidence and outcomes of post-EVAR occlusion in a large multicenter patient cohort using the Endurant device.[26] Data from 496 patients followed for a median of 1.7 years revealed a 4% occlusion rate. Most occurred within the first 2 months, and a technical error was considered to cause the occlusion in 60% of cases. A more liberal intraoperative and early postoperative strategy for intervention or reintervention may reduce the occlusion rates and improve outcomes. This is something we could only conclude by having sufficient volume to learn from a low-incidence complication.

There is much evidence to support centralization in vascular surgery.[27] For open AAA repair, annual surgeon volume has been associated with a nearly twofold difference in early mortality.[28] The unexpectedly high mortality rate for elective AAA repair that was found in the UK EVAR trials may also be largely explained by the many recruiting centers with very low volume. In a time of expanding indications (necessarily involving more complex anatomical characteristics) and of a wide range of endovascular devices, it appears logical to promote high-volume centers.

**TAKE-HOME POINTS**

- Although long-term results are limited at this time, EVAR is generally thought to be safe and to prevent aneurysm-related death.
- IFU are based on clinically identified patient risk factors and benchmark testing.
- The newest generation of endovascular devices to treat AAA have lower profiles, hydrophilic delivery sheaths, user-friendly mechanisms, and more compliant structures.
- As devices improve and indications are expanded, operators will face new learning curves, which are most efficiently overcome in high-volume settings.

## CONCLUSION

Despite the expansion of treatment to patients with more adverse anatomy, it is clear that the results of standard elective EVAR continue to improve. Essentially, this improvement results from effective device modifications and from growing expertise. We can no longer rely on results from studies in which outdated devices were used by largely inexperienced surgeons as a basis for our clinical decisions for elective AAA repair. Prospectively gathered data from large registries may provide more realistic outcome prediction, avoiding the publication bias of small retrospective studies. ■

*Frederico Bastos Gonçalves, MD, is with the Department of Vascular Surgery, Erasmus University Medical Centre in Rotterdam, The Netherlands. He has disclosed that he has no financial interests related to this article. Dr. Bastos Gonçalves may be reached at +31 107031810; f.bastosgoncalves@erasmusmc.nl.*

*Sander ten Raa, MD, PhD, is with the Department of Vascular Surgery, Erasmus University Medical Centre in Rotterdam, The Netherlands. He has disclosed that he has no financial interests related to this article. Dr. ten Raa may be reached at +31 107031810; s.tenraa@erasmusmc.nl.*

*Daniël Eefting, MD, PhD, is with the Department of Vascular Surgery, Erasmus University Medical Centre in Rotterdam, The Netherlands. He has disclosed that he has no financial interests related to this article. Dr. Eefting may be reached at +31 107031810; d.eefting@erasmusmc.nl.*

*Ellen V. Rouwet, MD, PhD, is with the Department of Vascular Surgery, Erasmus University Medical Centre in Rotterdam, The Netherlands. She has disclosed that she has no financial interests related to this article. Dr. Rouwet may be reached at +31 107031810; e.rouwet@erasmusmc.nl.*

*Johanna M. Hendriks, MD, PhD, is with the Department of Vascular Surgery, Erasmus University Medical Centre in Rotterdam, The Netherlands. She has disclosed that she has no financial interests related to this article. Dr. Hendriks may be reached at +31 107031810; j.m.hendriks@erasmusmc.nl.*

*Hence J.M. Verhagen, MD, PhD, is with the Department of Vascular Surgery, Erasmus University Medical Centre in Rotterdam, The Netherlands. He has disclosed that he is a consultant to Medtronic, Inc. and Gore & Associates. Dr. Verhagen may be reached at +31 107031810; h.verhagen@erasmusmc.nl.*

1. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. Ann Vasc Surg. 1991;5:491-499.
2. Volodos NL, Karpovich IP, Troyan VI, 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.
3. Lederle FA, Freischlag JA, Kyriakides TC, et al; OVER Veterans Affairs Cooperative Study Group. Long-term comparison of endovascular and open repair of abdominal aortic aneurysm. N Engl J Med. 2012;367:1988-1997.
4. Greenhalgh RM, Brown LC, Powell JT, et al; United Kingdom EVAR Trial Investigators. Endovascular versus open repair of abdominal aortic aneurysm. N Engl J Med. 2010;362:1863-1871.
5. De Bruin JL, Baas AF, Buth J, et al; DREAM Study Group. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. N Engl J Med. 2010;362:1881-1889.
6. Bastos Gonçalves F, Jairam A, Voute MT, et al. Clinical outcome and morphologic analysis after endovascular aneurysm repair using the Excluder endograft. J Vasc Surg. 2012;56:920-928.
7. Tanski W 3rd, Fillinger M. Outcomes of original and low-permeability Gore Excluder endoprosthesis for endovascular abdominal aortic aneurysm repair. J Vasc Surg. 2007;45:243-249.
8. Bastos Gonçalves F, Verhagen HJ, Chinsakchai K, et al. The influence of neck thrombus on clinical outcome and aneurysm morphology after endovascular aneurysm repair. J Vasc Surg. 2012;56:36-44.
9. van Marrewijk CJ, Leurs LJ, Vallabhaneni SR, et al; EUROSTAR collaborators. Risk-adjusted outcome analysis of endovascular abdominal aortic aneurysm repair in a large population: how do stent-grafts compare? J Endovasc Ther. 2005;12:417-429.
10. Jacobs T, Teodorescu V, Morrissey N, et al. The endovascular repair of abdominal aortic aneurysm: an update analysis of structural failure modes of endovascular stent grafts. Semin Vasc Surg. 2003;16:103-112.
11. 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.
12. Aburahma AF, Stone PA, Bates MC, et al. Endovascular repair of abdominal aortic aneurysms using 3 commercially available devices: midterm results. J Endovasc Ther. 2004;11:641-648.
13. Hobo R, Buth J; EUROSTAR collaborators. Secondary interventions following endovascular abdominal aortic aneurysm repair using current endografts. A EUROSTAR report. J Vasc Surg. 2006;43:896-902.
14. Holt PJ, Karthikesalingam A, Patterson BO, et al. Aortic rupture and sac expansion after endovascular repair of abdominal aortic aneurysm. Br J Surg. 2012;99:1657-1664.
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. Makaroun MS, Tuchek M, Massop D, et al; Endurant US Pivotal Trial Investigators. One year outcomes of the United States regulatory trial of the Endurant stent graft system. J Vasc Surg. 2011;54:601-608.
17. Wang GJ, Carpenter JP; Endologix Investigators. The Powerlink system for endovascular abdominal aortic aneurysm repair: six-year results. J Vasc Surg. 2008;48:535-545.
18. Sternbergh WC 3rd, Greenberg RK, Chuter TA, Tonnessen BH; Zenith Investigators. Redefining postoperative 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.
19. Brown LC, Brown EA, Greenhalgh RM, et al; UK EVAR Trial Participants. Renal function and abdominal aortic aneurysm (AAA): the impact of different management strategies on long-term renal function in the UK Endovascular Aneurysm Repair (EVAR) trials. Ann Surg. 2010;251:966-975.
20. Mohan IV, Laheij RJ, Harris PL; EUROSTAR collaborators. Risk factors for endoleak and the evidence for stent-graft oversizing in patients undergoing endovascular aneurysm repair. Eur J Vasc Endovasc Surg. 2001;21:344-349.
21. Schanzer A, Greenberg RK, Hevelone N, et al. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. Circulation. 2011;123:2848-2855.
22. Waasdorp EJ, de Vries JP, Hobo R, et al; EUROSTAR collaborators. Aneurysm diameter and proximal aortic neck diameter influence clinical outcome of endovascular abdominal aortic repair: a 4-year EUROSTAR experience. Ann Vasc Surg. 2005;19:755-761.
23. Bastos Gonçalves F, de Vries JP, van Keulen JW, et al. Severe proximal aneurysm neck angulation: early results using the Endurant stentgraft system. Eur J Vasc Endovasc Surg. 2011;41:193-200.
24. Jordan WD Jr, Moore WM Jr, Melton JG, et al; Endologix Investigators. Secure fixation following EVAR with the Powerlink XL system in wide aortic necks: results of a prospective, multicenter trial. J Vasc Surg. 2009;50:979-986.
25. Goodman M, Lawrence-Brown MM, Hartley D, et al. Treatment of infrarenal abdominal aortic aneurysms with oversized (36-mm) Zenith endografts. J Endovasc Ther. 2007;14:23-29.
26. van Zeggeren L, Bastos Gonçalves F, van Herwaarden JA, et al. Incidence and treatment results of Endurant endograft occlusion. J Vasc Surg. In press.
27. Karthikesalingam A, Hinchliffe RJ, Loftus IM, et al. Volume-outcome relationships in vascular surgery: the current status. J Endovasc Ther. 2010;17:356-365.
28. Birkmeyer JD, Stukel TA, Siewers AE, et al. Surgeon volume and operative mortality in the United States. N Engl J Med. 2003;349:2117-2127.