Elective endovascular stent-grafting of abdominal aortic aneurysms

Hobo, R.

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CHAPTER 9

General discussion and final considerations

Introduction

Endovascular repair is an alternative to open aortic resection in the prophylactic treatment of non-ruptured abdominal aortic aneurysms. This minimal invasive method exerts less stress on the patient's physical well-being. In addition, its considerable short-term benefits include a decrease in perioperative complications and a reduction in ICU and hospital admission time.[1,2] However, long-term durability remains a subject of concern. Device-related complications are not uncommon and frequently require secondary interventions.[3,4] As well as technical improvements, proper selection of patients may enhance initial technical success and reduce long-term complications and the need for reintervention. Understanding of possible risk factors concerning adverse anatomy or procedural factors is necessary for proper patient selection. Therefore, the goal of this thesis was to assess procedural, patient and anatomical factors and their impact on the effectiveness of endovascular abdominal aortic aneurysm repair.

Risk factors related to adverse anatomy

Inflammatory abdominal aortic aneurysms

Approximately 5 to 10% of abdominal aortic aneurysms have an inflammatory component (IAAA). Conventional surgery of IAAA patients is associated with longer operating time, higher mortality and morbidity rates and an increased need for blood transfusions.[5] For these reasons, EVAR may be a valuable treatment option in these patients. Since EVAR in IAAA patients is still controversial, the goal was to investigate the outcome of EVAR in patients with IAAA and to compare it with EVAR in patients with non-inflammatory AAA.

Out of 3665 patients, 52 (1.4%) had IAAA which was diagnosed by computed tomography (CT). These patients were relatively younger, had a better cardiac condition, but were more frequently smokers than patients without IAAA. Technical success was comparable in both groups of patients. Similar mortality and morbidity rates were observed up to four years of follow-up. There were no differences in the incidences of type I, II, and III endoleaks, device migration, kinking, stenosis, or thrombosis.

In conclusion: The results following EVAR in patients with IAAA and patients with non-inflammatory AAA were largely similar with regard to early and mid-term results. EVAR is a feasible method of excluding the IAAA from the circulation. Although perianeurysmal fibrosis did not regress in a considerable proportion of patients, clinical outcome was favourable.

Severe infrarenal aortic neck angulation

Proper selection of patients is essential to minimize the risk of post-EVAR complications as not all patients are eligible for EVAR owing to aortoiliac morphology. Aortic morphology, especially related to the proximal neck, often complicates the endovascular procedure, or increases the risk of device-related complications. Moreover, severe angulation of the infrarenal aortic neck is thought to be a predictor of adverse outcome in EVAR.[6] Therefore, the goal was to examine the influence of severe neck angulation on proximal type I endoleak, infrarenal aortic neck dilatation, proximal stent-graft migration, and eventually rupture of the aneurysm following EVAR.

In a group of 5183 patients, severe infrarenal neck angulation was associated with proximal type I endoleak seen on the completion angiogram and stent-graft migration before discharge. Late adverse events included proximal neck dilation $\geq$4 mm, proximal type I endoleak, and the need for secondary interventions. Mortality and rupture rates were similar in patients both with and without severe neck angulation.

There were only minimal differences between the three most frequently used stent-graft brands that were assessed. Infrarenal neck angulation was associated with proximal endoleak seen on completion angiogram in patients who received an Excluder or a Zenith stent-graft, and associated with early proximal migration in Zenith stent-grafts. Late proximal neck dilation was associated with infrarenal neck angulation in patients with an Excluder or a Talent stent-graft. Patients with a Talent stent-graft and severe neck angulation were also more prone to late proximal endoleaks and more frequently required secondary interventions.

In conclusion: Severe infrarenal aortic neck angulation was clearly associated with proximal type I endoleak, while the relationship with stent-graft migration was not clear. Excluder, Zenith, and Talent stent-grafts performed well in patients with severe neck angulation, with only minor differences between these devices.

Concomitant common iliac artery aneurysms

In approximately 15 to 40% of AAA patients, the aneurysm extends into at least one common iliac artery (CIA).[7] Since coexistence of a CIA aneurysm frequently complicates the procedure, special technical expertise may be required. Technical and anatomical considerations have been focused upon, while less has been reported on mid-term success rates.[8] Therefore, the aim was to investigate the influence of simultaneous CIA aneurysm exclusion on mid-term outcome of EVAR.

Concomitant CIA aneurysm was present in about 17% of a cohort of 7554 AAA patients. These patients were less physically fit (more frequently unfit for open repair and/or classified as ASA III or IV) and had more complex aneurysms (larger AAA diameter and infrarenal necks, more frequently hypogastric artery occlusion, and severe angulation of the aortic neck or common iliac arteries) than patients without CIA aneurysms. These patients had higher 5-year cumulative incidences of distal type I endoleak, iliac limb occlusion, secondary transfemoral intervention, and aneurysm rupture, but had mortality rates similar to AAA patients without concomitant iliac aneurysms.

In conclusion: Patients with CIA aneurysms have more advanced aneurysmatic disease and comorbidity. The incidence of device-related complications was increased which warrants caution with EVAR in these patients.

Procedural factors

Adjuvant procedures

Nowadays, a larger proportion of patients with AAA (in some institutions over seventy percent of those presenting) are being treated by EVAR than in the nineteen-nineties. Co-morbidities and complex aneurysmal anatomy means that adjuvant procedures to obtain successful aneurysm repair are frequently required.[9] Moreover, adjuvant procedures are performed to resolve intraoperative pitfalls e.g. gaining access to the aneurysm, anchoring the device, or preserving peripheral blood flow. Thus, adjuvant procedures enable the surgeon or interventional radiologist to provide EVAR to patients who would otherwise not be eligible. The success of these techniques has not been thoroughly investigated. Therefore, our purpose was to compare the outcome of EVAR with adjuvant procedures with unassisted EVAR. Examples of adjuvant procedures are the use of an iliac artery conduit for access, balloon angioplasty or bare stents to improve iliac limb flow, and large bare stents to assist fixation at the infrarenal neck. Surgical procedures may include endarterectomy, patch plasty of access arteries, or banding procedures to resolve type I proximal or distal endoleak.

In a group of 4631 patients, 29.2% required adjuvant procedures of which the majority were endovascular (78.1%). The remainder comprised surgical procedures via the groin or abdomen which were associated with a higher 30-day mortality rate than in patients who underwent unassisted EVAR. Complication and mortality rates beyond the operative period were similar to those in AAA patients in whom these ancillary techniques were not carried out.

In conclusion: The 30-day mortality rate was increased in patients requiring groin and abdominal surgical procedures. EVAR should be recommended with caution when these procedures are anticipated.

Aortic cuffs and iliac limb extensions

Complete exclusion of the aneurysm cannot always be obtained with the basic endograft components (body and uni- or bilateral iliac limb). Inaccurate preoperative size or length measurement, primary endoleaks, or extended iliac aneurysmal disease may necessitate the use of aortic cuffs or iliac limb extensions, to achieve complete proximal and distal sealing of the aneurysm. These extensions, deployed during the initial intervention are presumably associated with a greater risk of procedure-related complications.[10] This may either be caused by the use of the device extension or by the underlying abnormality. Therefore, the objective was to assess whether the use of endograft extensions influenced early or late outcomes of EVAR.

Aortic cuffs were used in approximately 4% and iliac limb extensions in 22% of 6668 AAA patients. Patients in whom aortic cuffs were deployed had larger aneurysms, and shorter and more frequently angulated proximal infrarenal necks. Patients in whom iliac limb extensions were deployed had larger aneurysms and more frequently aneurysmatic, occluded or angulated iliac arteries. Both types of extensions yielded comparable technical success in AAA patients who did not have any endograft extensions. Additional graft junctions did not lead to an increased incidence of type III or any other endoleaks. Aortic cuffs were not associated with any late adverse events, whereas iliac limb extensions were associated with an increased incidence of device kinking and secondary transfemoral interventions.

In conclusion: Despite an increased incidence of device kinking and secondary interventions in patients treated with iliac limb extensions, it is reassuring to find that EVAR still gives satisfactory results even if extensions are required. However, graft extensions should be used only when there is a clear indication for them, because single-component devices are potentially less vulnerable to late device failure. Accurate pre- or intraoperative assessment of the aortoiliac morphological configuration helps avoid unnecessary extensions.

Secondary interventions

The long-term durability of EVAR remains a subject of concern, despite generally reported favourable short- and mid-term outcomes. Currently there is consensus that life-long surveillance is necessary to monitor endo-

graft function.[11] Device-related complications are frequently observed. The EUROSTAR analysis showed that overall 9% of patients with EVAR required a secondary procedure. The most severe events included migration, aneurysmal growth, type I or III endoleak, bleeding and graft infection; these constituted the indication for reintervention in 60%. As these complications are generally considered to be associated with an increased risk for aneurysm rupture, early identification and repair by secondary intervention is required to obviate poor outcome.[12,13] Because previous studies investigating secondary interventions primarily assessed first generation stent-grafts, our purpose was to provide an assessment of the need for secondary intervention in a cohort treated with currently available stent-grafts.

Secondary interventions were performed in 8.7% of 2846 AAA patients with at least twelve months of follow-up, corresponding with an annual rate of 4.6%. This rate was lower than in older studies suggesting the beneficial effect of better devices and greater surgical experience. The majority of secondary interventions consisted of transfemoral procedures, primarily indicated by type I or II endoleak, device limb stenosis, thrombosis, and device migration. Abdominal procedures (conversion to open repair or banding of sealing sites) were indicated by type I endoleaks, device migration, and aneurysm rupture, whereas extra-anatomical bypasses were indicated by graft limb thrombosis. Mortality rates were increased for abdominal and groin secondary procedures. Secondary transfemoral procedures had a mortality rate comparable with that of patients who did not need secondary intervention.

In conclusion: Although the incidence of secondary intervention following EVAR has decreased over recent years, transabdominal and extra-anatomical reinterventions were associated with an increased mortality risk and the continuing need for surveillance with regard to device-related complications is generally considered necessary. The quantitative effects of endovascular AAA repair, intensive surveillance, and subsequent secondary interventions on patient survival have been blurred by extensive competition from severe comorbidities in a heterogenous population, and are therefore incompletely known.

Glasgow Aneurysm Score

Although postoperative mortality after EVAR is low, the mortality risk in physically unfit patients may be considerable. In the UK EVAR II trial comprising unfit patients, the 30-day mortality was 9%. This emphasizes the importance of identifying patients at high risk for early postoperative death in two ways. First, to improve patient selection prior to endovascular inter-

vention, and second, to allow a more reliable comparative analysis of results from EVAR versus open repair. The Glasgow Aneurysm Score (GAS) has been demonstrated to be a good predictor of early postoperative death after elective open AAA repair.[14] The aim of this chapter was to evaluate the efficacy of this risk scoring method in predicting outcome following EVAR of asymptomatic, unruptured, infrarenal AAA.

Multivariate analysis demonstrated that GAS was an independent predictor of 30-day mortality following EVAR. The area under the curve in a receiver operating characteristic curve was 0.70 with a 95% confidence interval of 0.66 to 0.74 for predicting postoperative mortality. The 30-day mortality was 1.6% in AAA patients with a GAS less than its best cut-off value of 86.6 and 6.4% in patients with a higher score. Late survival was associated with GAS as well.

In conclusion: GAS is an effective risk scoring method in predicting 30-day mortality of AAA patients undergoing EVAR. Since, its efficacy has been demonstrated in elective open repair as well, GAS can be valuable in treatment decision-making.

Considerations

Overall, good clinical results with an acceptable incidence of complications were obtained in patients with AAA during endovascular repair even in anatomically challenging aneurysms including inflammatory AAA (*Chapter 2*), complicated angulated infrarenal aortic necks (*Chapter 3*), and concomitant iliac aneurysms (*Chapter 4*).

Endovascular repair may also be successful in complex procedures involving adjuvant procedures (*Chapter 5*) and/or the need for aortic cuffs or iliac extensions (*Chapter 6*). Nevertheless, lifelong surveillance remains necessary. Secondary procedures (*Chapter 7*) also yield satisfactory outcomes, but should be managed cautiously, as secondary open procedures may be more harmful to patients than initial open procedures.

As the risk of complications may be considerable, careful selection of patients is indicated, although the boundaries of aortoiliac morphological properties have not yet been fully explored. The Glasgow Aneurysm Score (*Chapter 8*) may help in predicting outcome following EVAR and has been demonstrated to be a strong predictor of 30-day mortality. However, the development of a predicting score especially designed for endovascular repair, may allow for a more accurate identification of AAA patients who have the most to gain with EVAR.

Registries

Voluntary registries of vascular interventions are an essential tool in the clinical evaluation of new technologies. These registries provide non-comparative data on the performance of new and unproven treatments. As endovascular techniques are constantly improving, data from vascular registries can be applied to monitor its feasibility and effectiveness. The EUROSTAR registry was established to quickly collate up-to-date scientifically reliable data on endovascular AAA repair. EUROSTAR has provided information on the pitfalls as well as the potential clinical benefits of EVAR in Europe since 1996.

The collaboration of well over 100 vascular centres throughout Europe has made it possible to gather data on a large number of patients in a reduced time-span. By the end of 2006, more than 10,000 patients with abdominal aortic aneurysms had been registered. Over the course of 10 years, several generations of endovascular devices have been used enabling ongoing analysis of current clinical practice. The inclusion of patients with a variety of aortoiliac morphological configurations and co-existing morbidities, and who have undergone adjuvant procedures, reflects common practice in European vascular centres. The large number of registered endovascular procedures created an opportunity to address research questions concerning small subpopulations such as patients with inflammatory aneurysms, which is harder to examine in trials or single-centre series.

The accuracy of the EUROSTAR database was enhanced by a requirement for prospective enrolment of newly-treated patients 24 hours before intervention. Data checks at regular intervals were performed by tracing inconsistencies between correlated data fields and by verifying electronic data with written data on CRFs and returned follow-up forms. Major inconsistencies or missing data were retrieved by contacting collaborating physicians. This process was conducted to ascertain absence of impossible or doubtful values as well as inconsistent interactions in the database. Nevertheless, data accuracy may be impaired by lack of double data entry and on-site monitoring, leading to underestimation of outcome results. Completeness of follow-up data was about 70%, which may also predispose to underestimation of outcome results.

Data were accessible to all participating vascular centres through a website maintained and hosted by KIKA Medical, Nancy, France. Global and centre-specific statistics could be requested to stimulate continuous patient enrolment.

Because a large variety of patients with differing risk profiles, aneurysmal dimensions, and co-morbidities was included, correction for possible confounders was deemed necessary. Almost all analyses were performed by

multivariate logistic regression or Cox proportional hazards model for censored data to obtain reliable results.

Since randomised controlled clinical trials (RCT) have been published in support of EVAR over conventional surgery for relatively fit patients, scientific evidence of a higher level has become available.[15,16] The question arises if an endovascular registry is still able to contribute to provision of information and improving knowledge on AAA repair. The value of registries could be enhanced considerably in the post-randomised trial era. There are three reasons for this:

First, there is a need for ongoing evaluation of endograft technology which is continuing to evolve. Evaluation of the performance of new iterations of stents, stent-grafts and other technical devices such as anti-embolism filters can be achieved only by continuous audit.

Secondly, there are applications of endovascular technologies that have not and will not be subjected to the test of randomised trials. EVAR of thoracic aneurysms, although an already well-established treatment, is unlikely to be subjected to a randomised controlled trial.[17] The perceived benefits over open repair in terms of lower operative mortality and morbidity are such that almost no clinician is left in any doubt about its advantages. Similarly, fenestrated and branched endografts for the treatment of complex juxtarenal and thoracoabdominal aneurysms or hybrid procedures for similar complex cases are extremely unlikely to be assessed in randomised trials. Thus, in a considerable number of procedures, where conditions are not uniform or application is less common, examination by RCTs is not expected. In the absence of level-1 evidence from RCTs, registries may be essential for careful monitoring outcomes of treatment.

Thirdly, the widespread use of EVAR as mainstream treatment in many vascular centres throughout Europe raises serious issues about quality control. Considering the small margin of advantage of EVAR over open repair, any relaxation of clinical standards, patient selection and technical performance of the procedure may easily result in a complete loss of advantage. Therefore, registries may continuously observe endovascular practice and monitor current treatment. In addition, there is a requirement for benchmarking and comparative audit as tools for quality control.

The EUROSTAR registry terminated its activities in 2007 after achieving the main targets set more than ten years before. Numerous scientific questions have been addressed and many peer-reviewed journal articles have been published. In addition, including the present one, three doctoral theses have been based on EUROSTAR data. Now EUROSTAR has ended, its role should be continued by the vascular community. For effective benchmarking of those institutions performing endovascular AAA repair, data collection needs to be both comprehensive and complete. Thus, all centres undertaking these procedures should be required to submit all relevant

data on all eligible patients. Compulsory data submission may be enhanced in nationwide registries under governmental or societal control.

Conclusion

For ten years, the EUROSTAR registry collected and analysed data on the outcome of EVAR. Many questions relevant to achieve optimal patient selection and to improve the endovascular procedure were addressed. EVAR has withstood the tests of extensive clinical assessment and scientific discourse well. Central data registries are needed to demonstrate the responsiveness of the vascular surgical profession to public demand for transparency in the provision of a higher quality care.

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