Elective endovascular stent-grafting of abdominal aortic aneurysms
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Citation for published version (APA):
CHAPTER 1

General introduction
Abdominal Aortic Aneurysms

An abdominal aortic aneurysm (AAA) is a pathological arterial focal dilatation that can be defined as an irreversible increase in aortic diameter of at least 50% of normal size.\(^1\) Aneurysms can develop anywhere in the arterial system, but predominantly occur at arches, side-branches or bifurcations. The normal size of the infrarenal aorta is 17 mm in men and 15 mm in women.\(^2\) Commonly, an aortic diameter greater than 30 mm is regarded as aneurysmatically dilated. Rupture of an aneurysm is the most severe complication of AAA, leading to massive haemorrhage and eventually death if left untreated.

Aneurysms predominantly affect elderly men (>65 years of age), and are responsible for approximately 1-2% of deaths.\(^3\) Although women are less frequently affected, rupture and mortality rates are higher in women with AAA than in men.\(^4\) The incidence of AAA increased rapidly in the second half of the twentieth century, which may be attributed to the aging population.\(^5,6\)

Risk factors for AAA include advanced age, male gender, Caucasian race, tobacco smoking, elevated serum cholesterol, hypertension and family history.\(^7-10\) Non-ruptured AAAs rarely cause symptoms and diagnosis is usually made coincidentally at abdominal imaging assessment for other reasons. Ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) all are sensitive imaging techniques for detecting abdominal aneurysms.\(^5,11\)

The classic triad of rupture is severe hypotensive shock, a pulsatile abdominal mass and non-colic abdominal or lower back pain.\(^12\) Ruptured AAAs should be treated as a matter of urgency. Postponing treatment decreases survival. Even after optimal surgery and postoperative care, the thirty-day mortality is around 50%. The overall mortality rate following acute rupture of the aorta including patients treated surgically, and those who died outside the hospital, is as high as 80-90%.\(^13\)

Rupture of the aneurysm depends on the diameter and expansion rate of the AAA.\(^14,15\) The risk of AAA rupture means that continuing attempts have been made to develop prophylactic surgical therapy.\(^16\) Aneurysm resection and replacement with a prosthetic-graft has become the standard treatment of choice for large AAAs.\(^17\)

Endovascular Repair

In the early nineteen-nineties, Juan C. Parodi introduced the minimally invasive catheter-based surgical technique of intraluminal grafting as an alternative to open aortic repair.\(^18\) This technique excludes the aneurysm
from the systemic circulation by delivering a stent-graft into the aneurysmal aorta without the need to open the abdominal cavity, thus avoiding aortic cross-clamping. The stent-graft consists of a stainless steel or nitinol stent-frame which is covered by an impervious Dacron fabric or polytetrafluoroethylene (PTFE) layer. The procedure is best performed in a well-equipped operating room, suited to handle possible complications or unexpected laparotomy in the event of conversion to open surgical repair. Because a prosthetic graft is placed intraluminally, operating room conditions have to conform to the highest standards. The procedure can be performed under general, spinal or local anaesthesia according to the preferences of the patient and the surgeon. Intravenous heparin is routinely administered to prevent intraluminal coagulation. Access to one or both femoral arteries is achieved by a longitudinal or suprainguinal oblique incision in the groin. After a guidewire and subsequently a catheter are inserted, angiography is performed to assess the arterial anatomy and the site for proximal anchoring of the stent. The sheath containing the device, the delivery system, is then advanced into the aneurysm. By pulling back the sheath, the self-expanding stent is deployed. Older systems, no longer in use, were expanded by inflating a balloon. Following deployment, a completion angiogram is done to verify whether deployment has been successful and to see if there is any systemic blood flow in the aneurysmal cavity, i.e. an endoleak. Nowadays, percutaneous access is gaining in popularity and may replace surgical arteriotomy in the future.

The first grafts to be implanted consisted of a single tube and were only suitable for aneurysms with a distal landing zone above the aortic bifurcation. However, this type of condition only occurs in 6 to 11% of patients. Later, tapered aortouniiliac stent-grafts were developed that could be deployed distally in a common iliac artery. To maintain contralateral perfusion, a cross-over femorofemoral bypass was fashioned and the contralateral iliac artery was closed with an occluding stent. Nowadays, most endografts have a bifurcated configuration congruous with the anatomical situation, with antegrade blood flow to both iliac arteries. An endograft device can be custom-made to meet individual patient needs, however, most companies only manufacture fixed size ranges of the individual components (main body and iliac limbs). Several types of endograft device have been developed, each having specific characteristics. Although differences exist in the applicability and performance of various types and makes of endograft, no one type can be considered as the single best choice. It has been documented that the new, improved generation of endografts gives better results than earlier generations.
Early reports demonstrated the feasibility of endovascular aneurysm repair (EVAR),\textsuperscript{28-31} even in high-risk patients.\textsuperscript{32} The endovascular technique has several advantages over conventional open repair which means that often patients who were denied open aortic repair because of severe comorbidities, can still be treated. The procedure exerts less physical stress on the patient’s physical well-being. Fewer major postoperative complications, especially cardiac sequelae, have been observed.\textsuperscript{33-35} The need for admission to an intensive care unit has declined and hospital admission has been reduced to only a few days.\textsuperscript{29,30,34} Most notably, two randomized-controlled clinical trials, the British EVAR-1 trial and the Dutch DREAM-trial, reported a significant decrease in 30-day mortality rate to approximately one-third of that in patients undergoing conventional open aortic repair.\textsuperscript{36,37} Although, in this study the difference in aneurysm-related mortality was sustained over a postoperative follow-up period of four years, all-cause mortality rates of endovascular vs. open repair converged after the first postoperative year.\textsuperscript{38,39} As an explanation, EVAR may only postpone death in patients who are highly likely to die from non-aneurysm related causes.

Endovascular abdominal aortic aneurysm exclusion was initially aimed at treating patients unfit for conventional open repair. However, current opinions diverge on whether patients with severe comorbidities will benefit from EVAR or whether no interventional treatment is preferable. Sicard et al. reported EVAR to be a safe form of treatment in patients who would otherwise be at high risk from open surgery, and that it prevented AAA-related mortality.\textsuperscript{40} In contrast, other reports demonstrated that both early and late mortality rates were substantially increased in patients considered unfit for open repair when compared with patients with a normal operative risk.\textsuperscript{41} Moreover, when compared with watchful waiting, the EVAR-2 trial reported no improvement in survival in patients unfit for open repair.\textsuperscript{42} Therefore, surveillance may be the best option in patients with a short life expectancy.

Although EVAR seems to offer an attractive alternative to open repair, there is much dispute about its ultimate role. The long-term durability of the reconstruction (stent-graft and device fixation) is still unclear and permanent aneurysm exclusion can not be ascertained. Continuous follow-up regimens are necessary because a continued need for secondary interventions has been reported.\textsuperscript{43-45} Late graft-related complications including migration, device kinking and endoleakage, have been observed in a considerable proportion of patients.\textsuperscript{44,46} An endoleak is defined as persistent blood flow into the aneurysmal sac, resulting in further pressurisation and strain on the aneurysmal wall. This may lead to further aneurysmal dilatation and ultimately rupture.\textsuperscript{47} Four different types of endoleak can be distinguished.\textsuperscript{48} A Type I endoleak is a leak at the proximal or distal attach-
ment site i.e. endoleakage at the landing zone. A Type II endoleak is reperfusion from arterial branches including the lumbar, inferior mesenteric and hypogastric arteries. A Type III endoleak is a mid-graft leak from holes in the fabric and incomplete sealing of junctions between the body and limbs of modular endografts. A Type IV endoleak originates from blushing associated with the porosity of the fabric of the device. These complications often require repair by reintervention either by endovascular or open surgery. For these reasons, many authors recommend lifelong surveillance.\textsuperscript{44-46,49} Several aspects of surveillance are still the subject of debate. For instance, the frequency of surveillance, the method that should be used, and whether every patient needs regular surveillance. Morphological characteristics of the aneurysm, the patient's age and medical condition may cause the physician to reduce the frequency, or even omit surveillance.

In contrast to other endoleaks, the type II endoleak is non-device related and reintervention is not necessary. Most type II endoleaks can be treated by watchful waiting, particularly in the event of a decreasing or stable aneurysmal sac diameter.\textsuperscript{50} The general consensus is that type II endoleaks should only be repaired if the aneurysmal sac is expanding.\textsuperscript{48,51} Sometimes aneurysmal growth is observed in excluded aneurysms without evident endoleak. This phenomenon is characterised by persistent or recurrent pressurisation of the aneurysmal sac and is called endotension.\textsuperscript{52,53} Its cause is most likely a very low flow endoleak that cannot be seen on imaging. The blood may clot at the source of the leakage, the thrombus closes the leak, but the pressure is conducted through the thrombus. In patients with endotension but no evidence of endoleak, the risk of rupture is larger than in patients without endotension or endoleak and therefore, require treatment similar to patients with endoleaks.

At EVAR follow-up, CT angiography is the method of choice for detecting endoleak or migration although this imaging technique is currently being challenged by duplex ultrasound. Ultrasonography is less expensive and does not require the use of iodinated contrast with its small but inherent risk of nephrotoxicity, but is not as accurate as CT imaging.\textsuperscript{54} However, ultrasound examination may be used to replace CT angiography if initial follow-up CT examinations do not reveal endoleaks and sealing zones are solid.

Not all AAA patients are suitable for EVAR. Anatomical limitations restrict the applicability of EVAR. The unaffected infrarenal aortic neck should be 1.0 to 1.5 cm long to provide a landing zone for proximal anchoring of the device. The iliac arteries need to be of sufficient diameter to allow the passage of the sheath. Tortuosity of the iliac vessels may complicate unhindered passage of the guidewires. Nevertheless, continuing technical
improvements are increasing the suitability of EVAR even in patients with complex arterial anatomy. Ancillary procedures can be employed to facilitate passage through the iliac arteries or stent fixation. Endografts can be extended to above the renal arteries using a bare proximal anchoring stent-ring to improve fixation. More recently, fenestrated stent-grafts have come into use. These grafts are connected by covered or bare stents that constitute a bridge between the aortic stent-graft and the renal and superior mesenteric arteries and celiac trunk, and are increasingly being used in patients with juxta- or suprarenal AAA.

Before stent-graft treatment of the aneurysm is undertaken, accurate preoperative imaging assessment should be done. Inaccurate or inadequate measuring can lead to incomplete aneurysm exclusion or to a higher incidence of device-related complications. Spiral CT is the method of choice to take morphological measurements in order to select optimal endograft size. Conversely, it has been suggested that spiral CT alone may not be adequate for predicting the suitability for endovascular treatment and additional angiographic examination is required. Currently, image data processing allows the calculation and visualisation of centre stream lines and stretched images of tortuous segments, thus obviating the need for preoperative angiograms.

Early elective open surgical repair of small abdominal aortic aneurysms (40-55 mm) has been demonstrated not to be clinically effective, with an overall mortality rate after 10 years comparable to patients who were randomised to a strategy of surveillance until the aneurysm had grown or became symptomatic. Moreover, costs were lower in the surveillance only study group. The advent of EVAR with its reduced operative mortality may be associated with a different outcome. Indeed, patients with small aneurysms have quite low mortality, and this has led some to expect that EVAR in this category may compare more favourably with surveillance only. A clinical randomised trial (CAESAR - Comparison of Surveillance vs. Aortic Endografting for Small Aneurysm Repair) was conducted which aimed to demonstrate improved survival in EVAR in patients with a small aneurysm. Later, doubts were cast on this improved outcome, as an Australian audit has demonstrated EVAR in small AAAs to be inappropriate.

The EUROSTAR registry

Because of promising favourable short-term advantages and unclear long-term durability, the need for further assessment of endovascular AAA treatment became apparent when this technique became available at a wider group of institutions. In order to provide quick answers to questions concerning procedural factors and long-term effects, a registry was initiated by...
the European collaborators on Stent-graft Techniques for Abdominal aortic aneurysm Repair (EUROSTAR). This voluntary multi-centre registry was established in 1996. A major advantage of organized collaboration is the ability to gather a large amount of data in a reduced time span. Furthermore, ongoing analysis of improved or new devices provides updated knowledge and enables questions arising from previous investigations to be addressed. The goal of EUROSTAR was the commercially unbiased, scientifically reliable collation and analysis of data of AAA endografts, and publication of treatment outcome. Obviously, voluntary registries are subject to a certain bias. Data, especially related to follow-up, is frequently incomplete. Therefore, voluntary registries can supplement but not replace randomized clinical trials.

Several brands of stent-grafts that have been developed over the years were included in the EUROSTAR registry. These commercially available stent-grafts include Anaconda (Sulzer Vascutek, Austin, Texas), AneuRx (Medtronic Corp., Sunnyvale, Calif), EVT/Ancure (Guidant Endovascular Technologies, Menlo Park, Calif), Excluder (W.L. Gore Inc., Flagstaff, Ariz), Fortron (Cordis/Johnson & Johnson, Fort Lauderdale, Fla), Lifepath (Edwards Lifesciences, Irvine, Calif), Powerlink (Endologix, Irvine, Calif), Stentor (MinTec, La Ciotat, France), Talent (World Medical Manufacturing, Sunrise, Fla), Vanguard (Boston Scientific Corporation, Oakland, New Jersey) and Zenith (Cook Inc., Bloomington, Indiana). Over time several of these grafts have been withdrawn from the device market. The EUROSTAR registry was financially supported by endograft companies in exchange for biannual brand-specific progress reports. It must be emphasized that the EUROSTAR Steering Group, who was overseeing the scientific output, was independent from any commercial company regarding data collection, analysis and publication. The steering committee consisted of vascular surgeons and interventional radiologists from across Europe, and was responsible for establishing the EUROSTAR protocol, designing standardized case record forms (CRF) and supervising the data registry centre and publication of papers (See Appendix for a list of participating hospitals - the collaborators -, and members of the Steering Group).

Patients with a non-ruptured, asymptomatic AAA, who underwent endovascular prophylactic surgery were prospectively enrolled in the registry after giving informed consent. Findings at follow-up examination were recorded at 1, 3, 6, 12, 18 and 24 months following the procedure, and annually thereafter. Data on a relatively small group of patients treated before the commencement of the registry (October 1996) were retrospectively collected and thereafter prospectively. A data entry secretary was responsible for entering the returned forms into the database. Data managers were
responsible for data verification and analysis, encouraging compliance and communication with participating collaborators. The EUROSTAR registry was maintained in an online database from 2002 until December 2006 (www.eurostar-online.org). This site offered password protected data entry facilities and 24 hour up-to-date descriptive statistics to participating physicians (KIKA Medical, Nancy, France). In addition, endograft companies were granted access to device-specific global statistics. Alternatively, collaborators were able to submit completed CRFs to the data registry centre.

Outline of this thesis

This thesis aims to assess patient, anatomical and procedural factors and their impact on the effectiveness of endovascular abdominal aortic aneurysm repair.

Chapter 1 includes a general introduction to endovascular aneurysm repair and the EUROSTAR registry.

The first section (Chapters 2-4) addresses risk factors related to adverse anatomy. In Chapter 2, the results of EVAR in patients with inflammatory aneurysms are reported. In Chapter 3, the influence of severe infrarenal neck angulation on procedural outcome is investigated. In Chapter 4, the endovascular repair of AAA with concomitant common iliac artery aneurysms is discussed.

In the second section (Chapters 5-6), procedural factors and their influence on the outcome of the procedure are assessed. In Chapter 5, the influence of adjuvant procedures performed during EVAR, on the outcome of the procedure is investigated. In Chapter 6, the influence of aortic cuffs and iliac limb extensions on the outcome of EVAR is assessed.

In Chapter 7 the need for and outcome of secondary interventions that became necessary during long-term follow-up is reported.

Chapter 8 deals with survival prediction following EVAR using the Glasgow Aneurysm Score.

Chapter 9 comprises a general discussion and final considerations.
References


Chapter 1


