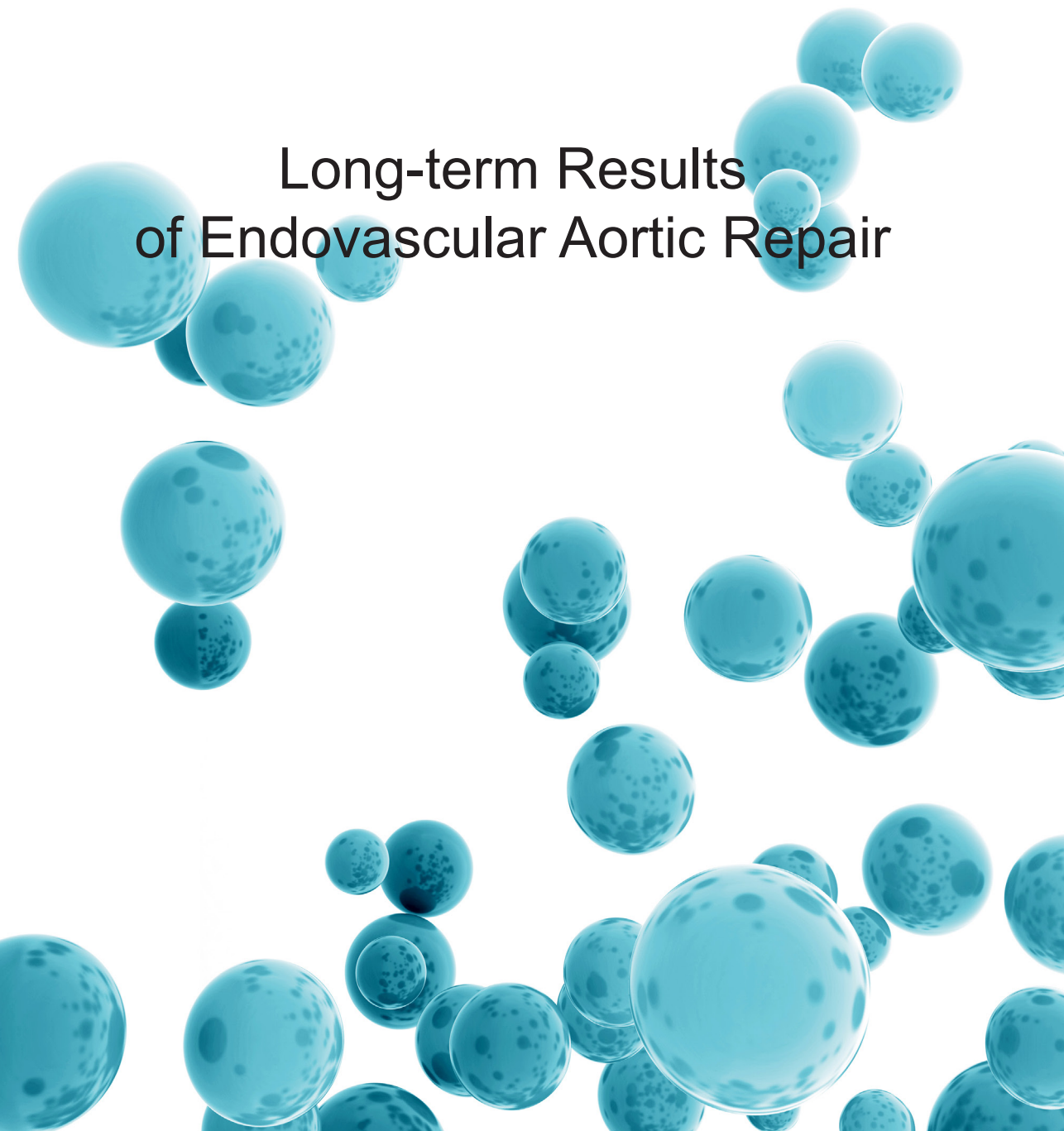


SUVI VÄÄRÄMÄKI

# Long-term Results of Endovascular Aortic Repair





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Long-term Results  
of Endovascular Aortic Repair



ACADEMIC DISSERTATION

To be presented, with the permission of  
the Board of the School of Medicine of the University of Tampere,  
for public discussion in the small auditorium of building M,  
Pirkanmaa Hospital District, Teiskontie 35, Tampere,  
on 9 September 2016, at 12 o'clock.

UNIVERSITY OF TAMPERE

SUVI VÄÄRÄMÄKI

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of Endovascular Aortic Repair

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# CONTENTS

Abstract .....	7
Tiivistelmä .....	9
List of original publications .....	11
Abbreviations .....	12
1 Introduction .....	13
2 Review of the Literature .....	15
2.1 Aortic aneurysms .....	15
2.1.1 Types of aortic aneurysm .....	15
2.1.2 Epidemiology .....	16
2.1.3 Aetiology, risk factors and pathophysiology .....	16
2.1.4 Rupture risk .....	17
2.1.5 Diagnosis and treatment .....	19
2.2 Aortic dissection .....	20
2.2.1 Classification .....	20
2.2.2 Epidemiology .....	21
2.2.3 Aetiology, risk factors and pathophysiology .....	21
2.2.4 Complication risk .....	22
2.2.5 Diagnosis and treatment .....	22
2.3 Endovascular aneurysm repair (EVAR) .....	24
2.3.1 Technique .....	24
2.3.2 First-generation stent-graft Vanguard® .....	25
2.3.3 Second-generation stent-graft Zenith® .....	26
2.3.4 Follow-up .....	27
2.3.5 Graft-related complications .....	28
2.3.6 EUROSTAR Registry and randomized EVAR trials .....	30
2.3.6.1 Short-term results .....	32
2.3.6.2 Mid- and long-term results .....	32
2.3.7 REVAR .....	34
2.4 Thoracic endovascular aortic repair (TEVAR) .....	34
2.4.1 Technique .....	34
2.4.2 Complications .....	36
2.4.3 Follow-up .....	36
2.4.4 Short-term results .....	36
2.4.5 Mid- and long-term results .....	37

2.5	Hybrid repair of a thoracoabdominal aortic aneurysm .....	39
2.6	The chimney, sandwich, FEVAR and BEVAR techniques .....	40
3	Aims of the Study .....	43
4	Materials And Methods .....	44
4.1	Study population .....	44
4.2	Methods .....	45
4.2.1	Indication for treatment .....	45
4.2.2	Operative technique .....	45
4.2.3	Follow-up .....	46
4.2.4	Primary outcome measures .....	46
4.2.5	Secondary outcome measures .....	47
4.2.6	Statistical methods .....	47
5	Results .....	48
5.1	Long-term results of EVAR using the first-generation Vanguard® stent-graft (I) .....	48
5.1.1	Operative and 30-day results .....	48
5.1.2	Long-term results .....	49
5.1.2.1	Late survival .....	49
5.1.2.2	Complications .....	49
5.1.2.3	Secondary interventions .....	50
5.2	Long-term results of EVAR using the second-generation Zenith® stent-graft (II) .....	51
5.2.1	Operative details and 30-day results .....	51
5.2.2	Long-term results .....	52
5.2.2.1	Late survival .....	52
5.2.2.2	Complications .....	54
5.2.2.3	Secondary interventions .....	55
5.3	Long-term results of TEVAR .....	56
5.3.1	Operative details and technical success .....	56
5.3.2	30-day outcomes .....	59
5.3.3	Long-term results .....	60
5.3.3.1	Late survival .....	60
5.3.3.2	Complications .....	62
5.3.3.3	Secondary interventions .....	63
5.4	Results of hybrid repair for thoracoabdominal aortic aneurysm .....	63
5.4.1	Operative details and 30-day outcomes .....	63
5.4.2	Long-term results .....	65
5.4.2.1	Late survival .....	65
5.4.2.2	Complications and secondary interventions .....	65

6	Discussion .....	69
6.1	General aspects .....	69
6.2	Long-term results of EVAR using the first-generation Vanguard® stent-graft .....	69
6.3	Long-term results of EVAR using the second-generation Zenith® stent-graft .....	71
6.4	Long-term results of TEVAR in TAAs and type B dissections .....	73
6.5	Results of hybrid repair .....	76
6.6	Future prospects .....	77
6.7	Limitations of the present study .....	78
7	Summary And Conclusions .....	79
	Acknowledgements .....	80
	References .....	82
	Original Publications .....	103





# ABSTRACT

Endovascular aneurysm repair (EVAR) was introduced in 1991 by Parodi as a minimally invasive procedure compared to traditional open surgery in the treatment of abdominal aortic aneurysm (AAA). Due to good short-term results, the technique was extended to thoracic endovascular aortic repair (TEVAR). Further, there was enthusiasm to also extend the application to thoracoabdominal aortic aneurysms (TAAAs), and the so-called hybrid approach, including open revascularization of the visceral arteries, followed by stent-graft exclusion of the aneurysm, was later invented. Furthermore, total endovascular aortic repair has been introduced, but the method is still under development.

The aim of this thesis was to evaluate the long-term results of endovascular aortic repair in patients treated at Tampere University Hospital (TAUH). At first, patients with an AAA who were treated with the first-generation stent-graft Vanguard® and, later, patients who were treated with the second-generation stent-graft Zenith® were analyzed. The long-term results of TEVAR were evaluated in patients with a thoracic aortic aneurysm (TAA) or type B dissection treated with an endovascular technique in both elective and emergency settings. Furthermore, the long-term success of TAAA treatment with a hybrid procedure was assessed.

The first-generation stent-graft Vanguard® was used in 48 AAA patients between 1997 and 1999. The stent-graft was associated with good short-term results, but poor mid- and long-term results. There were three (6%) AAA ruptures and ten (21%) late conversions to open repair during the follow-up. Technique-related complications were encountered in 90% of the patients, and 81% required an additional procedure. Similar problems were reported internationally, and the Vanguard® stent-graft was withdrawn from the market in 1999. Compared to similar studies, complications were mostly treated endovascularly rather than with direct open conversion at Tampere University Hospital (TAUH).

A total of 282 patients underwent elective AAA repair with the second-generation stent-graft Zenith® between 2000 and 2010. This stent-graft yielded good short-, mid- and long-term results as there were only two (0.7%) aneurysm-related deaths and one (0.4%) late conversion to open repair during the surveillance. Graft-related complications occurred in 38% of the patients, and 13% required a secondary procedure. The most common complication was an endoleak, but there was no significant association between aneurysm-

related factors and endoleaks. Unique to our study was that most of the complications (87%) appeared during the first three years of follow-up and no events occurred after six years of follow-up. Furthermore, most of the additional procedures (82%) were performed within the first four years of surveillance and none after six years. This finding suggests that the commonly preferred life-long surveillance may not be necessary for all patients.

TEVAR was performed in 78 patients due to a TAA (N=51) or type B dissection (N=27) between 1998 and 2013. Of these, 24 were emergency cases. Seven different stent-grafts were used for repair. Left subclavian artery (LSA) coverage was necessary in 41% of the cases and it was not routinely revascularized. A cerebrovascular event (CVE) was suffered by 7.7% of the patients and 2.6% developed spinal cord ischaemia (SCI) resulting in permanent paraparesis. There was also another two cases of SCI that resolved with spinal fluid drainage. CVE was more frequent in the emergency than the elective setting ( $p=0.048$ ), and LSA did not significantly increase the risk of SCI or CVE ( $p=0.79$  and  $p=0.18$ ). There was one aneurysm rupture in long-term follow-up. The most common complication was a type I endoleak, but no significant predictive factors were found for its development. Overall, 24% of the patients required an additional procedure in follow-up, including one late conversion to open repair.

A total of ten patients with a TAAA were treated with a hybrid procedure between 2005 and 2013. The short-term results were good, with 0% 30-day mortality, one case of SCI (10%) and none of the patients requiring permanent dialysis. In the long-term follow-up, there was one graft occlusion, which was successfully thrombolysed. There were no aorta-related deaths. Complications were related to the early stages after primary treatment. In long-term surveillance the complications were sparse and treatable with endovascular means. The results support earlier findings on hybrid repair, suggesting that it is a good treatment choice in high-risk patients until total endovascular repair develops. Our last two studies highlight the importance of careful postoperative monitoring to watch for SCI when the coverage of the aorta becomes extensive or includes the aortic arch.

In conclusion, as the technique and stent-grafts have evolved, endovascular aortic repair has become an efficient treatment and shows good short- and long-term results in this demanding patient group.

# TIIVISTELMÄ

Vatsa-aortan aneurysman hoitona on 1950-luvulta lähtien käytetty avoleikkausta, jossa laajentunut aortan osuus korvataan verisuoni-istutteella eli proteesilla. Toimenpiteeseen liittyy kuitenkin jopa 10 %:n kuolleisuus etenkin iäkkäillä ja monisairailta potilailla. Leikkausriskien vähentämiseksi kehitettiin 1990-luvun alussa aortan endovaskulaarihoito (EVAR). Siinä laajentuneen aortan sisälle uitetaan nivusvaltimon kautta kasaan puristettu stenttiproteesi, joka avataan läpivalaisukontrollissa ja joka kiinnittyy terveeseen aortan osaan ylä- ja alaosaan. Lyhytaikaistulokset olivat hyviä: leikkauskuolleisuus oli pienempi ja potilaat toipuivat nopeammin kuin avoleikatut. Seurannassa tuli kuitenkin esiin stenttiproteesin kestävyysliittymiä ongelmia. Komplikaatioiden vuoksi tarvittiin toistuvia lisätoimenpiteitä ja jatkuvaa seurantaa radiologisin menetelmin. Sitten stenttiproteesit ovat kehittyneet nopeasti, mutta hoidon pitkäaikaistulokset ovat edelleen epäselviä hoitomuodon suuresta suosiosta huolimatta. Endovaskulaaritekniikka levisi nopeasti myös rinta-aortan sairauksien hoitoon (TEVAR). Myöhemmin kehitettiin myös ns. hybriditekniikka, jossa ensin aortasta lähtevät sisäelinvaltimot ohitetaan avoleikkauksella, minkä jälkeen aneurysmaattinen osuus peitetään stenttiproteesilla.

Väitöstutkimuksen aiheena oli selvittää aortan endovaskulaarisen hoidon pitkäaikaistuloksia Tampereen yliopistollisessa sairaalassa. Tutkimuksessa selvitettiin aluksi ensimmäisen polven Vanguard®-stenttiproteesilla vuosina 1997–1999 hoidetun 48 vatsa-aortan aneurysmapotilaan pitkäaikaistulokset. Lyhytaikaistulokset olivat hyviä, mutta pitkäaikaiseurannassa 90 %:lle potilaista kehittyi stenttiproteesiin liittyvä komplikaatio ja 81 %:lle täytyi tehdä lisätoimenpide. Suurin osa komplikaatioista voitiin hoitaa kuitenkin mini-invasiivisella suonensisäisellä tekniikalla. Seurantatulosten perusteella opittiin mahdollisista komplikaatioista, niiden hoidon tarpeellisuudesta ja hoitovaihtoehdoista.

Tutkimuksen toisessa vaiheessa selvitettiin toisen polven Zenith®-stenttiproteesilla vuosina 2000–2010 hoidetun 282 vatsa-aortan aneurysmapotilaan pitkäaikaistuloksia. Lyhytaikaistulokset olivat hyviä, ja pitkäaikaiseurannassa komplikaatioita oli vähemmän (38 %) ja vain 13 %:lle täytyi tehdä lisätoimenpide. Aneurysmakuolleisuus aineistossa oli 0,7 %. Tutkimuksessa havaittiin, että komplikaatioilla on tyypillinen esiintymisajankohta ja suurin osa (87 %) niistä ilmaantuu ensimmäisen kolmen vuoden aikana. Kuuden vuoden jälkeen potilailla ei esiintynyt komplikaatioita tai lisätoimenpiteiden tarvetta. Tulosten pe-

rusteella näyttää siltä, että kaikki aortan stenttiproteesilla hoidetut potilaat eivät välttämättä tarvitse nykyisin suositeltua elinikäistä seurantaa.

Tutkimuksen kolmannessa vaiheessa selvitettiin pitkäaikaisseurannan tuloksia 78:lta rinta-aortan aneurysman tai B-tyyppin dissekaation vuoksi stenttiproteesilla vuosina 1998–2013 hoidetulta potilaalta. Heistä 41 %:lla jouduttiin toimenpiteessä peittämään vasen solisvaltimo stenttiproteesilla, mutta näille potilaille ei kehittynyt merkittävästi enempää aivoverenkierron tai selkäytimen verenkierron häiriöitä. Päivystyksenä hoidetuilla potilailla oli merkittävästi enemmän aivoverenkiertohäiriöitä. Pitkäaikaisseurannassa stenttiproteesi osoittautui kestäväksi. Potilaista 24 %:lle täytyi seurannan aikana tehdä lisätoimenpide, joista suurin osa oli mini-invasiivisia suonensisäisiä toimenpiteitä.

Tutkimuksen neljännessä vaiheessa arvioitiin ns. hybriditoimenpiteen pitkäaikaistuloksia kymmenellä vuosina 2005–2013 hoidetulla potilaalla. Sairaakuolleisuus oli 0 %, ja yhdelle potilaista kehittyi alaraajojen halvaus (10 %). Pitkäaikaisseurannassa komplikaatiot olivat vähäisiä ja hoidettavissa suonensisäisillä menetelmillä. Kaksi viimeistä tutkimusta korostaa toimenpiteen jälkeisen seurannan tärkeyttä mahdollisen alaraajojen halvausoireen ehkäisemiseksi.

Yhteenvedona voidaan todeta, että endovaskulaarinen hoito on kehittynyt ja sillä on hyvät lyhyt- ja pitkäaikaisseurannan tulokset.

# LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following articles, which are referred to in the text by their Roman numerals:

- I Väärämäki S, Pimenoff G, Heikkinen M, Suominen V, Saarinen J, Zeitlin R, Salenius J (2007). Ten-year outcomes after endovascular aneurysm repair (EVAR) and magnitude of additional procedures. *Scan J Surg* 96: 221–228.
- II Väärämäki S, Suominen V, Pimenoff G, Saarinen J, Salenius J (2012). Long-term experience of endovascular aneurysm repair with Zenith prosthesis: diminishing graft-related complications over time. *Ann Vasc Surg* 26: 845–851.
- III Väärämäki S, Suominen V, Pimenoff G, Saarinen J, Uurto I, Salenius J (2016). Long-term experience of endovascular repair for thoracic aortic aneurysms and dissections. *Vasc Endovascular Surg* 50: 335-342.
- IV Väärämäki S, Suominen V, Pimenoff G, Saarinen J, Uurto I, Salenius J (2016). Hybrid repair of thoracoabdominal aortic aneurysms is a durable option for high-risk patients in endovascular era. *Vasc Endovascular Surg* (accepted).

# ABBREVIATIONS

AAA	abdominal aortic aneurysm
ASA	The American Society of Anesthesiologists
BEVAR	branched endovascular aortic repair
CAD	coronary artery disease
CDUS	colour duplex ultrasonography
CVE	cerebrovascular event
CT	computed tomography
CTA	computed tomography angiography
EVAR	endovascular aneurysm repair
FEVAR	fenestrated endovascular aortic repair
ICU	intensive care unit
IFU	instructions for use
IMA	inferior mesenteric artery
LCCA	left common carotid artery
LSA	left subclavian artery
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
MOF	multiorgan failure
OR	open repair
PTA	percutaneous transluminal angioplasty
RAAA	ruptured abdominal aortic aneurysm
REVAR	endovascular repair of ruptured abdominal aortic aneurysm
SCI	spinal cord ischaemia
TAA	thoracic aortic aneurysm
TAAA	thoracoabdominal aortic aneurysm
TAUH	Tampere University Hospital
TEVAR	thoracic endovascular aortic repair
US	ultrasonography

# 1 INTRODUCTION

An abdominal aortic aneurysm (AAA) is usually asymptomatic until rupture occurs, and the goal of treating an AAA is to exclude the aneurysm from the circulation and prevent the rupture. Despite the improvements in technique and perioperative care, open AAA repair is still associated with significant mortality of up to 10% (Malas et al. 2010). Minimally invasive endovascular aortic repair (EVAR) was first undertaken by Ukrainian surgeon Nicholas Volodos in 1987, but, it was a later publication by Juan Carlos Parodi in 1991 that was responsible for the widespread introduction of EVAR across the globe (Volodos et al. 1988, Parodi et al. 1991). Since then, a variety of device designs and implantation techniques have been established. The initial hypothesis was that EVAR would substantially reduce patient discomfort as well as decrease morbidity and mortality, especially in high-risk patients, in addition to reducing costs. It also offered treatment to patients with severe comorbidities that are contraindicated for open repair. Since then, numerous reports have established the feasibility and safety of this method, and the short-term results are undeniably better than in open repair (EVAR trial participants 2005a, Blankensteijn et al. 2005, Leurs et al. 2007a, Lederle et al. 2009, Becquemin et al. 2011).

In follow-up, the first-generation stent-grafts were associated with high complication and re-intervention rates, but the development of stent-grafts has improved the durability of EVAR. Second-generation stent-grafts are associated with better aneurysm-related survival, but the complications, especially endoleaks, remain a long-term problem. Due to the number of noted complications, a major drawback of this method has been the number of necessary secondary procedures and the need for life-long surveillance (Greenberg et al. 2008, Conrad et al. 2009, Moll et al. 2001). As a result of additional procedures and annual screening, the expected reduction in costs has not yet been achieved (Epstein et al. 2014).

Following technical development and encouraging short-term results in EVAR, the endovascular technique was extended to the treatment of descending thoracic aortic aneurysms (TAAs), and thoracic endovascular aortic repair (TEVAR) is currently used as the primary treatment method in high-risk patients. Owing to the good clinical success, TEVAR is also increasingly applied to patients with dissections and traumatic aortic ruptures (Eggebrecht et al. 2006, Walsh et al. 2008, Ultee et al. 2016). Due to the good results of EVAR and TEVAR, the hybrid approach of treating thoracoabdominal aortic

aneurysm (TAAA) with an open revascularization of the visceral arteries, followed by an endovascular exclusion of the aneurysm was introduced (Quiñones-Baldrich et al. 1999). Furthermore, total endovascular repair of the aorta has been developed, but the number of reports on the technique is still small.

The aim of this thesis was to evaluate the long-term results of EVAR in first- and second-generation stent-grafts. In addition, the long-term durability of TEVAR and hybrid repair of TAAA was analyzed.



## 2 REVIEW OF THE LITERATURE

### 2.1 Aortic aneurysms

#### 2.1.1 Types of aortic aneurysm

An aneurysm is defined as a permanent localised dilatation of the aorta, involving an at least 50% increase in diameter compared to normal aortic diameter (Johnston et al. 1991). The diameter of the aorta varies with sex, age and body weight, and an infrarenal aortic diameter greater than 30 mm is estimated to be pathologic (McGregor et al. 1975, Bengtsson et al. 1996, Grimshaw et al. 1997). An abdominal aortic aneurysm (AAA) is the most common of aortic aneurysms and it is classified according to the anatomic extent of the aneurysm (Figure 1).

Thoracic aortic aneurysms (TAAs) account for one fourth of all aortic aneurysms, and they are divided as follows: 60% in the ascending aorta, 10% in the aortic arch and 40% in the descending aorta, while 10% are thoracoabdominal aortic aneurysms (TAAAs) (Isselbacher 2005). In 1986, Crawford described the first TAAA classification scheme based on the anatomic extent of the aneurysm (Crawford et al. 1986 (a), Figure 2).

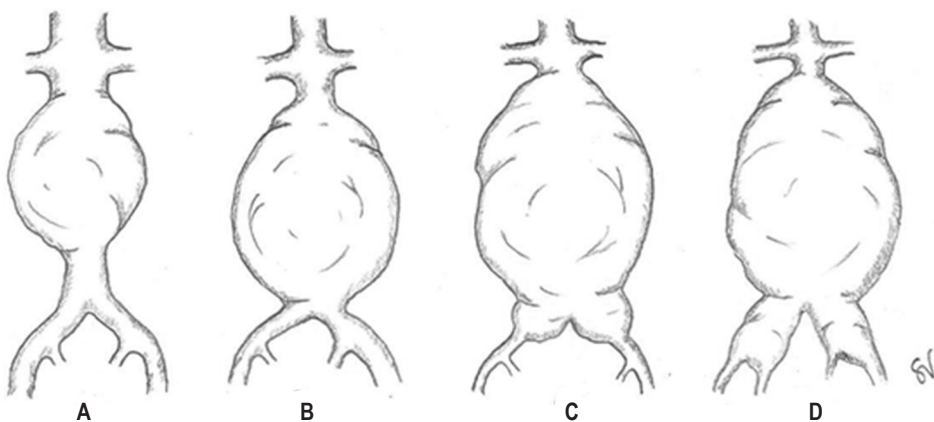


Figure 1. Classification of AAA (Modified from: Droc et al. 2012).

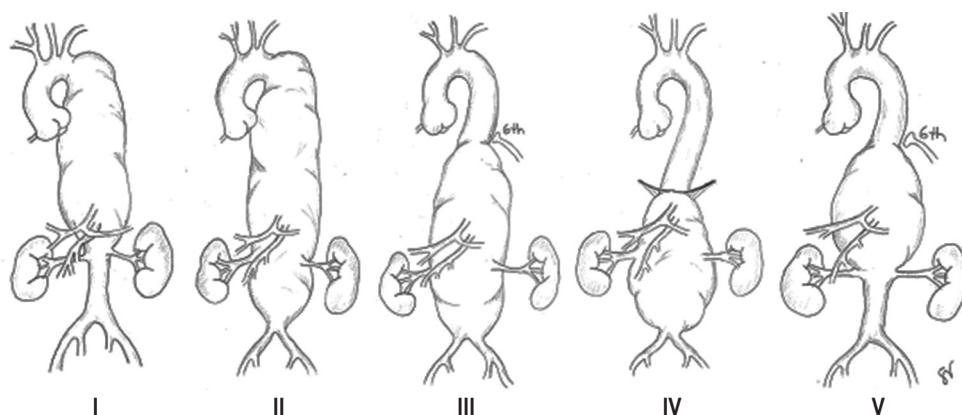


Figure 2. Crawford classification of TAAAs (Modified from: Frederick et al. 2012).

### 2.1.2 Epidemiology

Based on the recent national aneurysm screening programmes, the prevalence of AAA is declining, and the current prevalence is 1.5–1.8% (Norman et al. 2004, Lindholt et al. 2008, Svensjö et al. 2011, Earnshaw et al. 2011). This is probably due to decreased smoking and good medical treatment of hypertension and hypercholesterolemia. An AAA is four times more common in men than in women (Cornuz et al. 2004). The incidence of AAA has increased during recent decades, probably due to the ageing of the population and the increased use of ultrasound (Heikkinen et al. 2002a, Best et al. 2003). In Finland, the incidence of ruptured abdominal aortic aneurysm (RAAA) is approximately 6.1/100,000 (Kantonen et al. 1999). The number of RAAAs has remained the same even though the diagnosis and treatment methods have evolved. Screening and follow-up of identified aneurysms has been demonstrated to be effective in reducing AAA-related mortality (Ashton et al. 2002).

The prevalence of asymptomatic TAAs has been measured to be from 0.16% to 0.34%. The incidence of TAAs is roughly 5.9–10/100,000 per year (Bickerstaff et al. 1982, Clouse 1998). The mean age at the time of diagnosis ranges from 59 to 69 years, with men predominating over women with a ratio of 2:1 to 4:1 (Clouse et al. 1998, Coady et al. 1999).

### 2.1.3 Aetiology, risk factors and pathophysiology

In most aortic aneurysms, the aetiology is non-specific. The main risk factors for the development of an aortic aneurysm are age, smoking, male sex, family history and atherosclerotic diseases (Brown et al. 1999, Lederle et al. 2000, Vardulaki et al. 2000, Singh et al. 2001, Frydman et al. 2003, Brady et al. 2004, Forsdahl et al. 2009). In an AAA, the

presence of concomitant coronary artery disease (CAD) is greater than 70%, but patients with a TAAA have a much lower incidence of CAD, less than 30%, indicating that the respective aetiologies of aortic dilatation differ to a degree (Ferro et al. 2007). Furthermore, a patient with one aortic aneurysm is at an increased risk of developing an aneurysm in another aortic segment (DeBakey et al. 1975, Crawford et al. 1989, Lawrie et al. 1993)

Aneurysm formation is likely to be the result of several factors that involve local haemodynamic elements as well as those intrinsic to the arterial segment itself. The medial layer of the aorta is responsible for elasticity. The normal media consists of multiple proteins, of which collagen and elastin are the most prominent. The elastin content of the ascending aorta is high and diminishes progressively in the descending thoracic and abdominal aorta. Elastic fibre fragmentation and loss with the degeneration of the media result in a weakening of the aortic wall, a loss of elasticity and consequent dilation. The elastic fibres in the aortic wall are arranged as circumferential lamellae. The thoracic aorta media consists of 45 to 65 lamellar units and the abdominal aorta of 28 units, which could be one of the contributing factors in the prevalence of AAA compared to TAA (Wolinsky et al. 1967). Fibrillin is another structural protein in the aortic wall, and a mutation of fibrillin has been demonstrated in patients with Marfan's syndrome (Dietz et al. 1991). Other extracellular matrix proteins, such as laminin, glycosaminoglycans, proteoglycans and fibronectin, may also contribute to aneurysm formation (Xu et al. 2014).

#### 2.1.4 Rupture risk

The size of an aneurysm has been shown to be the most important risk factor for aortic rupture (Szilagyi et al. 1966) (Table 1). The mean growth rate of a small AAA is 2–3 mm per year (Guirguis et al. 1991, Coady et al. 1999). The enlargement is exponential – as the aneurysm expands, the growth rate also increases (Dapunt et al. 1994, Rizzo et al. 1998). Large studies have shown that the surveillance of small aneurysms (<5.5 cm) is safe and early surgery does not save lives (Powell et al. 1998, Lederle et al. 2002, Filardo et al. 2015). Women tend to rupture their AAA in smaller sizes, but have poorer outcomes after AAA repair (Heikkinen et al. 2002b, Walschot et al. 2002, Grooterboer et al. 2010, Egorova et al. 2011, Sweeting et al. 2012, Bown et al. 2014). This might be explained by the fact that the normal aortic diameter is smaller in women than in men and therefore aneurysm rupture occurs in smaller sizes. Also, aneurysm diameter indexed to body size has been proven to be an important determinant of rupture for women (Lo et al. 2014).

Table 1. 12-month AAA rupture risk by diameter. (AAA, abdominal aortic aneurysm) (Modified from: Brewster et al. 2003)

AAA diameter (mm)	Rupture risk (%)
<40	0
40–49	0.5–5
50–59	3–15
60–69	10–20
70–79	20–40
>80	30–50

For TAA, the longitudinal studies have shown that the risk of rupture doubles for every 1 cm of growth over 5 cm (Juvonen et al. 1999). Untreated, nearly 80% will progress to rupture (Birkerstaff et al. 1984, Perko et al. 1995). In the descending thoracic aorta, once the diameter reaches 6 cm, the risk of rupture increases markedly and is approximately 7% per year (Kuzmick et al. 2012) (Figure 3). Patients with a connective tissue disorder such as Marfan's syndrome have an increased risk of TAA rupture even in smaller sizes (Coady et al. 1999).

Patients with a TAAA have an especially high mortality, and the reported 2-year and 5-year survival rates untreated are 24% and 13%, respectively. Of the deaths, 47–74% are due to aneurysm rupture (Crawford et al. 1986b, Cambria et al. 1995, Hansen et al. 2000).

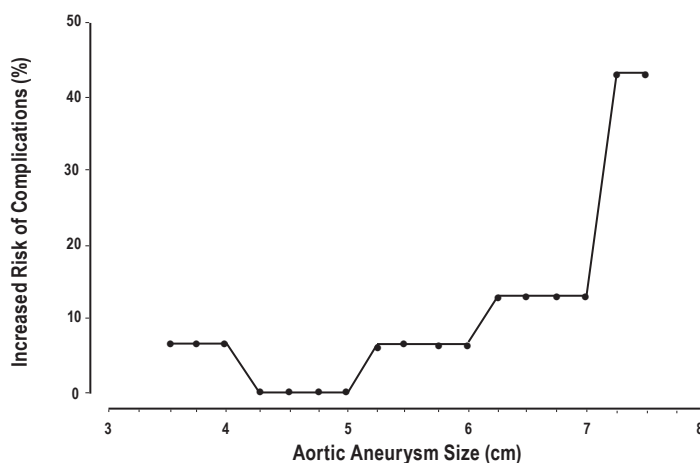


Figure 3. Increase in risk for rupture or dissection as the descending thoracic aorta enlarges to specific dimensions. (Source: Crawford MH: *Current diagnosis and Treatment: Cardiology, 3rd Edition*, <http://www.accessmedicine.com>)

## 2.1.5 Diagnosis and treatment

Most of the AAAs are asymptomatic and diagnosed incidentally when they are detected during a physical examination or when abdominal ultrasonography (US), computed tomography (CT) or magnetic resonance imaging (MRI) is performed for other reasons. Rapidly enlarging aneurysms that are about to rupture are frequently tender. Compression of adjacent structures can also cause pain. Patients may also be aware of an abnormally prominent abdominal pulsation. If an AAA ruptures, it causes sudden, severe abdominal or back pain, hypotension and tachycardia, which is unfortunately often the first onset of symptoms. Approximately half of the patients with a RAAA die before reaching the hospital, and hospital mortality is roughly 40–50%, leading to an overall RAAA mortality of 80–90% (Bengtsson et al. 1993, Kantonen et al. 1999, Reimerink et al. 2013). There is evidence that not only is the prevalence of AAA falling, but the rate of mortality from aneurysm rupture is also decreasing. This is likely due to multiple reasons, especially better medical management of cardiovascular diseases, but EVAR might also play role in this (Anjum et al. 2012, Choke et al. 2012). The rupture of a TAA has a worse prognosis as the overall mortality related to a ruptured TAA is 97%, even though roughly 40% of the patients reach the hospital alive (Johansson et al. 1995).

The cost-effectiveness of screening men for AAA with a single US examination at the age of 65 years has been demonstrated and the screening recommended (Ashton et al. 2002, Chaikof et al. 2009, Moll et al. 2011, Glover et al. 2014). Sweden has adopted a nationwide AAA screening programme targeting 65-year-old men since 2006, and a similar AAA screening programme was set up in England in 2009 and has been offered throughout the UK since the end of 2013. A screening scheme has also been discussed in Finland, but as yet such a programme is not available (THL-raportti 30/2011).

Treatment is recommended when an AAA reaches the diameter of 5.5 cm in men and 5.0 cm in women (Heikkinen et al. 2002b, Brewster et al. 2003, Norman et al. 2007). Today, there are two main techniques of intervention – open repair (OR) and endovascular aneurysm repair (EVAR). OR has been associated with quite high operative mortality rates of 4–10%, although the operative risks have decreased in recent years (Greenhalgh et al. 2004, EVAR Trial participants 2005a, Vascular Society of Great Britain and Ireland, the National Abdominal Aortic Aneurysm Quality Improvement Programme [AAAQIP] 2012). The repair is very durable and is likely to provide lifelong protection against AAA rupture. EVAR was introduced in 1991 by Parodi, and the first endovascular repairs in Finland were performed in Helsinki in November 1996; the first procedure in Tampere was carried out in February 1997. EVAR is less invasive than OR and can be performed through small incisions even under local anaesthesia. It has a lower perioperative mortality risk and shorter recovery time, rarely requiring treatment in an intensive care unit (ICU), and the overall hospital stay remains shorter. However, not all patients have an aortic anatomy that is suited to EVAR (Greenhalgh et al. 2004, Prinssen et al. 2004, Lederle et al. 2009). Also, long-term data on EVAR is still limited.

As the TAA rupture risk increases substantially at 6 cm, it has been set as the threshold for intervention. In the descending aorta, the endovascular treatment has gained popularity since becoming available, because the 30-day mortality and morbidity rates are significantly lower than those of open surgery (Cheng et al. 2010). Despite improvements in operative technique and anaesthetic support, the operative mortality after OR is approximately 10% and that of TEVAR 2.1–7.6% (Stone et al. 2006, Bavaria et al. 2007, Goodney et al. 2011, Hughes et al. 2014). Therefore, TEVAR should always be considered, over surgery, when the anatomy is suitable (Erbel et al. 2014). The advantages of TEVAR in the short term have been proven, but the long-term durability remains unknown. Furthermore, the mortality after open repair in patients under the age of 60 years seems to be low and caution is needed when considering endovascular treatment for young patients (DiLuzzo et al. 2013, Johns et al. 2014).

Historically, the treatment of TAAA has been open surgery; however, modern-day advances in endovascular techniques have led to the emergence of innovative stenting techniques such as the chimney, fenestrated, branched and sandwich techniques for the treatment of TAAA as well as hybrid techniques combining open and endovascular approaches.

## 2.2 Aortic dissection

### 2.2.1 Classification

In an aortic dissection, a tear in the aortic intima causes the separation of the intima and media layers and thereby the creation of a false lumen. The dissection can occur in any part of the aorta and extend proximally or distally to other arteries.

Aortic dissections are commonly classified anatomically by two different classifications: the DeBakey and Stanford systems (Table 2). Approximately 60% of aortic dissections are type I, 10–15% type II and 25–30% type III. The Stanford classification is the most widely used, but recently a more comprehensive aetiological classification has been proposed in addition as the observational studies have demonstrated that the intramural haematoma (IMH) and penetrating aortic ulcer (PAU) may be signs of an evolving dissection (Table 2) (Erbel et al. 2001).

Table 2. Aortic dissection classification. (Modified from Erbel et al. 2001)

<b>DeBakey classification:</b>	
Type I	The dissection originates in the ascending aorta and extends to the descending aorta.
Type II	The dissection originates in and is restricted to the ascending aorta.
Type III	The dissection originates in the descending aorta, and the ascending aorta is intact.
<b>Stanford classification:</b>	
Type A	Dissection of the ascending aorta with or without dissection of the descending aorta.
Type B	The dissection of is restricted to the descending aorta.
<b>New classification:</b>	
Class 1	Classical aortic dissection with an intimal flap between the true and false lumen.
Class 2	Medial disruption with formation of intramural haematoma (IMH).
Class 3	Discrete/subtle dissection without haematoma, eccentric bulge at tear site (discrete dissection).
Class 4	Plaque rupture leading to aortic ulceration, penetrating aortic atherosclerotic ulcer (PAU) with surrounding haematoma, usually subadvential.
Class 5	Iatrogenic and traumatic dissection.

## 2.2.2 Epidemiology

Because of the high mortality rates in acute aortic dissections, the exact frequency is difficult to define. The prevalence ranges from 0.2% to 0.8% based on large series of autopsies (Levinson et al. 1950). The incidence of acute aortic dissection in the general population is estimated to range from 2.6 to 3.5/100,000 person-years. The reported incidence in a Finnish obduction study is 14/1,000,000 persons per year (Mykkanen et al. 1986). In the most recent study, an incidence as high as 6/100,000 person-years was reported, probably due to a more comprehensive inclusion of deaths and developments in vascular imaging (Howard et al. 2013). It is more common in males than females, with a male-to-female ratio of 1.5:1 (Mykkanen et al. 1986, Howard et al. 2013).

## 2.2.3 Aetiology, risk factors and pathophysiology

Hypertension is an important contributor and is found in two thirds of the patients (Mészáros et al. 2000, Golledge et al. 2008, Howard et al. 2013). Based on a recent population-based study, the mean age of onset for acute aortic dissection is 72 years. Female patients tend to be older than their male counterparts (79 vs. 67 years) at the time of presenting (Nienaber et al. 2004, Howard et al. 2013). Patients with congenital connective tissue disorders (e.g. Marfan syndrome, Ehlers-Danlos syndrome, Loeys-Dietz syndrome) are at risk for aortic dissection at an even younger age due to weakening in the aortic wall (Coady et al. 1997). The nature of these diseases mandates aggressive treatment strategies



and close surveillance programmes. Patients with first-degree relatives with a history of thoracic dissection are also at a higher risk of aortic dissection (Biddinger et al. 1997, Albornoz et al. 2006).

The primary event in aortic dissection is a tear in the aortic intima. Blood passes into the aortic media through the tear, separating the intima from the surrounding media and adventitia thereby creating a false lumen. It is debatable whether the initiating event is a primary rupture of the intima with a secondary dissection of the media, or haemorrhage within the media and subsequent rupture of the overlying intima. The most common site of dissection tear is the first few centimetres of the ascending aorta (type A), and the second most common site is just distal to the left subclavian artery (type B).

## 2.2.4 Complication risk

Aortic dissection is classified as acute (<14 days), subacute (15–90 days) and chronic (>90 days) according to the onset of symptoms. An acute ascending aortic dissection (type A) has a mortality rate of 1% per hour initially, 30% in 48 hours, 50% by the third day, and almost 80% by the end of the second week (Coady et al. 1999). The high mortality is related to coronary ischaemia due to the complete or persistent obstruction of coronary flow and cardiac tamponade. Patients with acute descending aortic dissection (type B) have a better prognosis. It can be uncomplicated or complicated, defined as perfusion complication, recurrent pain or hypertension despite full medication, or with signs of rupture. Uncomplicated descending aortic dissection have a 30-day mortality of up to 10% when treated conservatively, and those with a complicated descending aorta dissection require urgent aortic repair (Hagan et al. 2000, Suzuki et al. 2003). Patients treated conservatively in the acute phase require subsequent late elective aortic interventions in 25–30% of the cases for aneurysmatic expansion, an extension of the progressive dissection, or other related complications (Erbel et al. 2001, Suzuki et al. 2003&2012).

A descending aortic dissection can also be chronic and requires careful surveillance in case of creating an aneurysmatic expansion. As the aortic diameter exceeds 60 mm, the risk of rupture is estimated to be 30% per year (Kuzmik et al. 2012).

## 2.2.5 Diagnosis and treatment

The diagnosis of aortic pathology is usually made by means of computed tomography angiography (CTA). A chest X-ray is often the initial imaging method in an acute situation, but it is ineffective in excluding aortic pathology (Hartnell et al. 1993). The availability of CTA is common, and the ability to image the whole aorta and branch vessels quickly at the same time has its advantages. MRI is also an accurate modality, but its availability especially in acute situations is not as common as that of CTA.



Surgical treatment is always indicated if a dissection involves the proximal aorta, as an untreated ascending aortic dissection is associated with high mortality. Open repair of a Stanford type A dissection was introduced in 1966 by DeBakey, and it reduced the mortality dramatically. The in-hospital mortality rate for patients treated with open surgery at an experienced centre is between 15% and 35% (Sabik et al. 2000, Lai et al. 2002, Mehta et al. 2002, Trimarchi et al. 2005). The short-term survival rate after acute type A dissection has ranged from 52% to 94% at 1 year, with the long-term survival rate ranging from 45% to 88% at 5 years and from 30% to 60% at ten years among patients who survived the initial hospitalization (Tsai et al. 2006, Stevens et al. 2009).

Earlier, complicated Stanford type B dissections were traditionally treated with open repair, but even in the most experienced hands, early open surgery is associated with a high mortality rate of 10–50% as well as a high rate of major adverse events such as stroke, paraplegia, heart failure or respiratory insufficiency (Trimarchi et al. 2006, Zeeshan et al. 2010, Szeberin et al. 2015). Patients with an unstable dissection manifesting renal or mesenteric ischaemia have an operative mortality rate as high as 50% and 88%, respectively (Trimarchi et al. 2006, Fattori et al. 2013). Owing to the good clinical success of TEVAR among TAA patients, the technique was embraced to replace open surgery for managing complicated type B dissections without any randomized data and is today recommended as a first line therapy (Erbel et al. 2014). The reported 30-day mortality rates in TEVAR are 5–17% and major complication rates 8–10% (Parker et al. 2008, Swee et al. 2008, Szeto et al. 2008, Zeeshan et al. 2010, Ehrlich et al. 2013, Faure et al. 2015).

In stable, uncomplicated Stanford type B dissections, drug therapy alone is appropriate, as routine operative management has no proven superiority over medical treatment (Tsai et al. 2006, Nienaber et al. 2009). Long-term survival among medically treated patients is 60–83% at 4–5 years and 40–50% at ten years (Bernard et al. 2001, Umaña et al. 2002, Nienaber et al. 2013). There is some evidence, however, suggesting that patients with an acute uncomplicated type B dissection might benefit from early TEVAR. Early endovascular repair does not seem to improve either early survival or the adverse event rates, but a 5-year aortic-related survival benefit of TEVAR compared to medical treatment has been demonstrated in a small randomized cohort (Nienaber et al. 2013). Also, the International Registry of Acute Aortic Dissection (IRAD) showed that patients undergoing TEVAR have a lower death rate (15.5% vs. 29.0%,  $p=0.018$ ) at five years (Fattori et al. 2013). Furthermore, observational evidence shows that depressurisation and shrinkage of the false lumen in the acute phase by a stent-graft is beneficial, with the goal of achieving thrombosis of the false lumen and remodelling the dissected aorta (von Kodolitsch et al. 1998, Evangelista et al. 2012). Therefore, TEVAR has been shown to lower delayed disease progression and the need for later treatment (Nienaber et al. 2013).

Additionally, a number of studies have suggested prognostic factors of early or late adverse events, such as the patency of the false lumen in the follow-up, an initial aortic diameter of  $\geq 40$  mm with a patent false lumen, an initial false lumen of  $\geq 22$  mm in the

proximal descending aorta, a proximal entry tear size of  $\geq 10$  mm, or a spiral configuration of the dissection. It has been proposed that patients fulfilling one or more of these predictors should undergo early intervention, or at least close follow-up (Winnerkvist et al. 2006, Marui et al. 2007, Song et al. 2007, Kitai et al. 2010). Also, the advent of TEVAR has led to renewed interest in the progression of the disease and the degree of aortic remodelling. It has been suggested that a type B dissection represents a subacute phase in the transition from acute to chronic and the current definition is set at 14 days. There is data implying that an intervention in the subacute phase might lower complication risk of TEVAR in patients who are stable enough to wait (Steuer et al. 2013). In the future, TEVAR may become a first-line therapy for uncomplicated type B dissection, but more trials are necessary to create a paradigm shift.

Patients with a connective tissue disorder may benefit from open surgery also in the case of acute uncomplicated distal dissection (Coady et al. 1997). Moreover, TEVAR is not recommended for patients with a connective tissue disorder, because it is associated with a high risk of early and mid-term complications and reinterventions. A retrograde type A dissection after TEVAR in patients with Marfan syndrome has been reported in up to 50% of cases (Dong et al. 2009). Furthermore, Marfan syndrome is the strongest independent predictor of late conversion after TEVAR (Ehrlich et al. 2008).

In surveillance, once the aortic diameter exceeds 60 mm, the risk of false lumen rupture is estimated to be at 30% per annum and treatment is indicated (Davies et al. 2002, Nordon et al. 2009).

## 2.3 Endovascular aneurysm repair (EVAR)

### 2.3.1 Technique

EVAR is increasingly used today for treating AAA, but it is limited by anatomical requirements, such as aneurysm morphology and size, as well as the elongation and calcification of access vessels. Different stent-grafts have their own instructions for use (IFU), but to perform standard EVAR, the anatomic criteria are a proximal neck length of  $\geq 10$  mm, a neck diameter of  $\leq 32$  mm, a neck angulation of  $\leq 60$  degrees and a diameter of access vessels (iliac artery) of  $\geq 7$  mm. At the beginning of the EVAR era, it was estimated that only 30% of AAA patients would be suitable for EVAR due to anatomic limitations. As a result of increased experience as well as developing techniques and stent-grafts, approximately 68% of the patients are suitable for classical EVAR today (Moll et al. 2011). Planning the EVAR begins with detailed measurements of the aneurysm anatomy and an evaluation of access arteries based on CTA. Proximal 10–20% oversizing of the stent-graft is necessary for optimal sealing. The proximal neck fixation is extremely important for long-term durability after EVAR (Malas et al. 2005).

In the early years, EVAR patients were treated under general anaesthesia; currently, patients usually receive spinal anaesthesia, but the procedure is possible to carry out even under local anaesthesia. Especially high-risk patients benefit from minimally invasive anaesthetic techniques. Also, in a ruptured abdominal aortic aneurysm treated with EVAR (REVAR), lower 30-day mortality has been proven when using only local anaesthesia (Powell et al. 2014). Typically, access is gained through the femoral arteries using percutaneous or open access, but an iliac artery approach is also possible. Fluoroscopic monitoring is applied in the delivery and deployment of the stent-graft. The basics of the technique are presented in Figure 4.

The most common stent-graft is bifurcated, but for patients with a unilateral iliac artery occlusion or significant stenosis, the aorto-uni-iliac devices are used. In REVAR, an aorto-uni-iliac stent-graft is in common use, as it is faster and technically easier to apply if the patient is particularly unstable or the operator less experienced (Powell et al. 2014). The main differences between the stent-grafts are the proximal fixation, deployment mechanism, graft flexibility, graft size and the size of the introducer system.

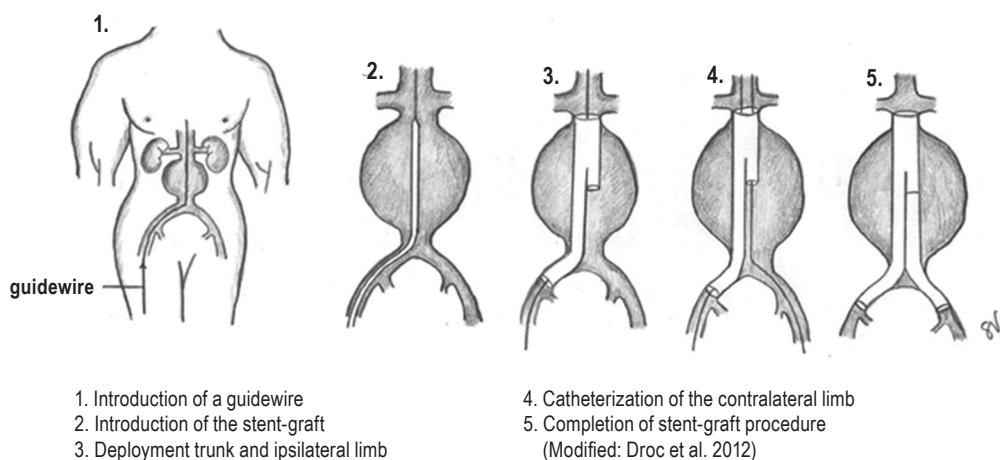


Figure 4. The steps in the introduction of a stent-graft.

### 2.3.2 First-generation stent-graft Vanguard®

Parodi's first devices were tubular aorto-aortic stent-grafts that were attached proximally, but not distally. Retrograde leakage into the aneurysm sac left behind the risk of rupture. Quite soon, bifurcated stent-grafts with distal attachment to the common iliac arteries became preferred. Still, the distal aorta is often calcified, thrombus-lined and wide, making it a poor attachment site, and the first-generation stent-grafts could not tolerate the high forces, and structural failures were common. In addition, the limb grafts were often

undersized and flexible, and, as a result, the distal ends slowly pulled out from the common iliac arteries, causing twisting and finally limb thrombosis or migration in the aneurysm sac, and further endoleak.

The first commercially available bifurcated stent-grafts were the Endovascular Grafting System (EGS) developed by Endovascular Technologies® (EVT, Menlo Park, California) and the Stentor system (Mintec Ltd®, Bahamas). Vanguard® (Boston Scientific, Natick, Mass) was a two-piece derived, improved version of the original Stentor® system and was adopted worldwide in 1997 (Figure 5). Experiences with these first-generation stent-grafts were disappointing in mid-term follow-up, and Vanguard® was withdrawn from the market in November 1999 after several reports of fractures in the polypropylene sutures and nitinol stents (Medical Device Agency Safety Notice, February 1999). The late failures of the Vanguard® started focusing the attention on the issues of durability.

### 2.3.3 Second-generation stent-graft Zenith®

The second-generation stent-graft Zenith (Cook Inc®, Bloomington, Ind) was released on the European market in 1999 and in the US in 2003. The first endovascular repair with a Zenith® stent-graft at TAUH was performed in March 2000. Since then, it has undergone several improvements, especially in regard to the release system. It was the one of the most employed stent-grafts during the study years. The Zenith® is a modular three-piece stent-graft with multiple stainless steel stents and polyester fabric (Figure 6). What is unique is the suprarenal fixation with a barbed stent maximizing the proximal attachment, which allows the treatment of short necks with a lower risk of migration. On the other hand, this allows only small angulation between the suprarenal stent and the proximal end of the graft, and the distortion can result in type I endoleak. In a Zenith® device, the main body is long and both limb grafts can be chosen after the insertion of the main graft. The stent-graft also had a wider range of sizes available than previous devices, supporting accurate sizing. The reported freedom from aneurysm-related mortality for the Zenith®-stent-graft is high (98%) at five years (Greenberg et al. 2008).



Figure 5. The first-generation stent-grafts. From the left: AneuRx (Medtronic Inc®, Santa Rosa, Calif), Gore Excluder (Gore and Associates®, Flagstaff, Ariz), Vanguard (Boston Scientific Corp®, Natick, Mass), Talent (Medtronic Inc®) and Teramed (Teramed Inc®, Maple Grove, Minn) (Modified: Minor et al. 2004)

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Figure 6. The second-generation stent-graft Zenith®. Reprinted with permission from Cook Inc®.

### 2.3.4 Follow-up

Although minimal follow-up is required after open surgical repair of an AAA, lifelong surveillance imaging is preferred for patients undergoing endovascular repair to detect some of the unique complications related to EVAR (Moll et al. 2011). CTA has been the primary imaging modality and the surveillance regimen varies between the institutions. Early device IFU schedules recommended CTA imaging at 1, 6, and 12 months postoperatively and yearly thereafter. In the early years, only native- and arterial-phase CTs were taken, but as knowledge of endoleaks increased, the delayed phase was added in the imaging protocol. Triple-phase imaging gives important information as to when the contrast enters and exits in the aorta. The characteristic finding of an endoleak upon CTA is a collection of contrast outside the stent-graft lumen and inside the aneurysm sac. The delayed images often yield important information about the endoleak: a type II endoleak is typically due to slow

perigraft flow and seen only in the delayed images, whereas a type I endoleak is seen already in early-phase images. Because curvilinear calcifications can appear similar to contrast in some images, a native CT should be performed at first.

The follow-up protocol has changed over the years due to the increased knowledge. A plain abdominal X-ray has been recommended since 2001 as related to problems seen with first-generation stent-graft. The radiation exposure of a single CTA scan is within acceptable levels, but there is concern associated with the risk of carcinogenesis from repeated exposure to ionizing radiation and the risk of contrast-induced nephropathy. Furthermore, surveillance imaging is a significant contributor to the overall costs of EVAR (EVAR trial participants 2005a). For these reasons, there has been a shift towards colour duplex ultrasound (CDUS) imaging for surveillance. Current recommendations include CTA at 1 and 12 months after EVAR. If no complication is detected during the first year after EVAR, CDUS is suggested as an alternative to CTA for annual postoperative surveillance (Moll et al. 2011). Recent guidelines from the European Society for Vascular Surgery state that CDUS is a safe and sensitive surveillance method, but it should not be the only modality for follow-up after EVAR (Moll et al. 2011).

Magnetic resonance angiography (MRA) is another option for postoperative surveillance, and it has been used successfully to detect endoleaks in patients with stent-grafts made from materials such as nitinol which produce little MR artefacts owing to their low magnetic susceptibility. However, most stainless-steel stent-grafts cause large MR artefacts, and detecting potential endoleaks in patients with these devices is very difficult. MRA is better at detecting endoleaks of small size and low flow, but the superior finding compared to CTA does not seem to translate into therapeutic consequences as these “low flow” endoleaks seldom cause an increase in AAA diameter and further lead treatment (Alerci et al. 2009). Newer MR techniques might make a difference in future imaging, but so far their use in surveillance has been minimal.

### 2.3.5 Graft-related complications

An endoleak means persistent blood flow into the aneurysm sac outside the stent-graft, and it is the most frequent complication of EVAR (Figures 7 and 8).

**Type I endoleak** is classified as blood flow from the proximal (1A) or distal (1B) attachment zones of the stent-graft due to inadequate or ineffective sealing. It is associated with postoperative aneurysm expansion and should be treated as soon as detected. Based on EUROSTAR data, it correlates with a higher risk of late conversion and rupture (van Marrewijk et al. 2002). It can be detected immediately after endografting (primary), or it may develop later (secondary). A primary type I endoleak can be related to unsuitable anatomy, the selection of a wrong type of stent-graft or failure in the stent-graft insertion. A secondary type I endoleak can be related to continued dilatation of the aorta. Other stent-graft failures, such as migration, can also lead to a type I endoleak. A possible endovascular



solution includes balloon dilatation or an additional stent-graft and most recently represented EndoAnchors. The risk factors for a type IA endoleak are a short, angulated, wide, calcified, irregular or conical neck (Brown et al. 1999, Albertini et al. 2000, Mohan et al. 2001, van Marrewijk et al. 2004). These are also the most common reasons for patient rejection for EVAR.

**Type II endoleak** is classified as persistent retrograde blood flow into the aneurysm sac from a patent inferior mesenteric artery, lumbar arteries or other collateral vessels. It is typically seen in the delayed phase of CTA, and knowledge of detecting it in CTA has increased over the years. The understanding of the complication as well as the indication for its treatment has changed significantly over the years. According to the EUROSTAR data, a type II endoleak does not increase the risk of rupture (van Marrewijk et al. 2004). However, a type II endoleak has been associated with continued aneurysm dilatation and, based on current knowledge, should be treated if there is any sign of aneurysm expansion (Jones et al. 2007). The treatment options are transarterial embolization using coils, glue or thrombin or direct percutaneous puncture embolization.

**Type III endoleak** is caused by mechanical failure of the stent-graft, usually due to a fracture of the stent-graft, a defect in the graft fabric or junctional separation of the modular components. The causes may be related to defective device material, extreme angulation or improper overlapping of the modular components. A type III endoleak is associated with an increased aneurysm rupture risk and requires further procedures, usually involving the placement of a new stent-graft component across the defect or junctional separation (van Marrewijk et al. 2002).

**Type IV endoleak** occurs when blood leaks across the stent-graft due to its porosity. It is typically diagnosed immediately after the primary procedure as the patient is anticoagulated with heparin perioperatively. These endoleaks are self-limited and resolve when the patient's coagulation returns to baseline values, requiring no secondary procedures (Rosen et al. 2008).

**Endotension** is defined as an increase in intrasac pressure after EVAR without evidence of an endoleak, although there is no definitive test to determine whether endoleakage is present or absent. The reasons for developing endotension are unknown, but it might be related to the graft design, including stent structure and fabric compliance (Dias et al. 2004). It is considered less urgent, but may warrant continued endovascular evaluation. The incidence of endotension is decreasing, and it rarely occurs with the development of new stent-grafts (Haider et al. 2006, Toya et al. 2008). Moreover, the diagnostic measures for detecting a possible endoleak are better today. It has been suggested that endotension is always associated with an endoleak, even if none is detected, and conversion to open repair was earlier therefore suggested (Görich et al. 1999). A conservative approach for asymptomatic patients has also been reported, with good results (Mennander et al. 2005, Toya et al. 2008).

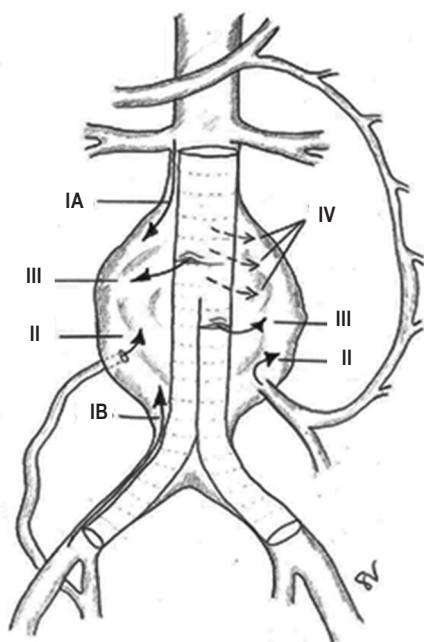


Figure 7. Types of endoleak.

**Row separation** means the separation of graft components. It was a significant problem with first-generation stent-grafts, but occurs rarely with modern stent-grafts (Beebe et al. 2001) (Figure 9).

**Migration** refers to a caudal movement of the stent-graft. Continuous downward displacement forces are exerted on the device by the pulsatile nature of blood flow with cumulative effects over time and can lead to migration and a further type I or III endoleak. The predictors of migration are a low deployment of the stent-graft, below the renal arteries, and a short proximal fixation length (Zarins et al. 2003). Migration has been observed with all previous endovascular aortic devices, but it is unusual with current devices.

**Kinking** means bending of the stent-graft and it usually affects limb grafts. It is considered notable when it causes complications and leads to additional procedures.

**Thrombosis** of the stent-graft can be acute soon after implantation, but late thrombosis is more common. It can be caused by the kinking of the stent-graft or angulated iliac arteries. Limb thrombosis is more common than thrombosis of the entire stent-graft.

### 2.3.6 EUROSTAR Registry and randomized EVAR trials

Comparable short-and midterm results comparing EVAR and OR are based on the EUROSTAR Registry (European Collaborators on Stent Graft Techniques for Abdominal Aortic Aneurysm Repair Registry) (Leurs et al. 2007) and four large randomized trials: the UK EVAR Trial (UK Endovascular versus Open Repair of Abdominal Aortic Aneurysm



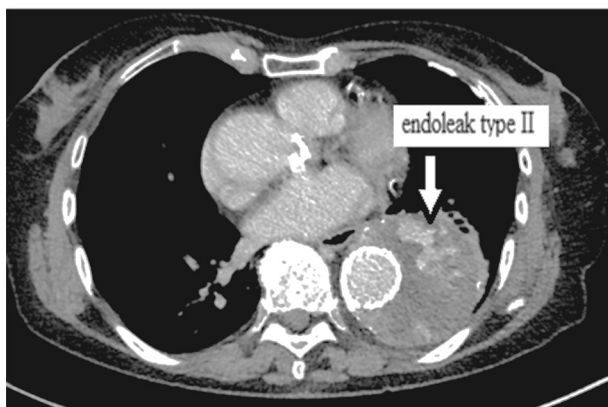


Figure 8. CTA of a patient with type II endoleak.

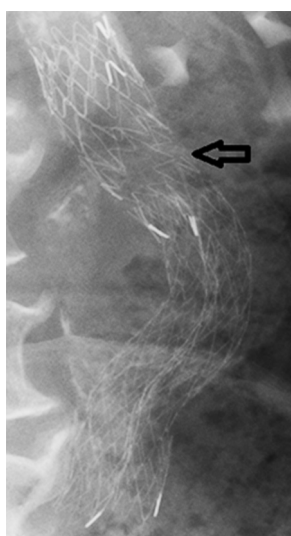


Figure 9. Plain abdominal X-ray of a patient treated with a Vanguard® stent-graft who suffered a row separation of the stent-graft during follow-up.

Trial) (EVAR trial participants 2005a,b), DREAM (Dutch Randomized Endovascular Aneurysm Management) (Blankensteijn et al. 2005), OVER (Open versus Endovascular Repair Veterans Affairs Cooperative Study) (Lederle et al. 2009) and ACE (Aneurysme de l'aorte abdominale: Chirurgie versus Endoprothese) (Becquemin et al. 2011). During the study years, the durability of the stent-grafts had undergone major improvements. In the UK EVAR and DREAM trials, older stent-grafts were used than in the OVER and ACE trials, making the comparison of results difficult, but this only highlights the lessons that have been learned in graft design and technique. Furthermore, the results are affected by improvements in patients' pre-, intra- and postoperative management.

### 2.3.6.1 Short-term results

The reported technical success rate in these randomized trials is over 90%. The 30-day mortality is 0.5–2.3% in EVAR as opposed to the 3–6.2% in OR. The postoperative moderate or severe complication rate is 3.5% in EVAR and 10% in OR. Patients treated by endovascular means have shorter procedure times, ICU stays and overall hospital stays, in addition to less blood loss, and it is clear that EVAR has superior early results in comparison to open repair.

The most common stent-graft-related complication is an endoleak. A primary endoleak is present in as many as 30% of the cases (Becquemin et al. 1999). A type I endoleak is reported in 1.5–10% of the cases and seems to be related, to the device employed (Veith et al. 2002, van Marrewijk et al. 2002, Hinchliffe et al. 2004, Bos et al. 2008). According to EUROSTAR data, the incidence of type I endoleaks decrease as the degree of oversizing increases from 10% to 20% (Mohan et al. 2001). The estimated occurrence of type II endoleaks is 10–25%, but it has been reported to be up to 40% (Silverberg et al. 2006, Jones et al. 2007, Higashiura et al. 2007). Preoperative IMA embolization has been reported to reduce the incidence of type II endoleaks, which has led to routine IMA embolization prior to stent-graft placement if open (Axelrod et al. 2004, Sheehan et al. 2006). However, although preoperative IMA embolization has decreased type II endoleaks, an effect in terms of any significant reduction in AAA diameter has not been shown (Nevala et al. 2010). Furthermore, 60–80% of the primary type II endoleaks seal spontaneously during the first six postoperative months, requiring no further procedures (Steinmetz et al. 2004, Jones et al. 2007, AbuRahma et al. 2011). The timing of CTA is crucial for detecting a type II endoleak as it might be seen only in the delayed phase. Therefore, some of the type II endoleaks may not have been detected in the early studies. A type III endoleak affects approximately 4% of the patients with an older device but seldom occurs with the current stent-grafts (Wilt et al. 2006). Most of the endoleaks are detected in early surveillance (Buth et al. 2000).

### 2.3.6.2 Mid- and long-term results

In mid- and long-term follow-up, migration affects approximately 0–25% of EVAR patients (Peterson et al. 2007, Pitton et al. 2009). The reported migration rates, especially with the Zenith® stent-graft, are low, 0–2.9% (Greenberg et al. 2008, Bos et al. 2008). On the other hand, the reported rates with Vanguard® and other old stent-grafts are high, 6–25% (Sampaio et al. 2005, Van Herzele et al. 2008, Leurs et al. 2007a, Pitton et al. 2009). Row separation is also related to older stent-grafts, and its prevalence has been reported to be up to 21% with Vanguard® (Medical Device Agency Safety Notice, February 1999, U.S. FDA. Warning letter 2001, Jacobs et al. 2003).

Thrombosis of the stent-graft is seen 0.9–3.5% and kinking in 0.5–1.6% of EVAR patients (Verhoeven et al. 2004, EVAR Trial participants 2005a, Brown et al. 2007, Hiramoto et al.

2007). Infection of the stent-graft is a rare complication, affecting 0–0.7% of the patients (Fiorani et al. 2003, Veraldi et al. 2009). Compared to the corresponding rate in OR (0.7–1.3%), it is lower (Hallett et al. 1997, Lovegrove et al. 2008). The EUROSTAR data showed that the annual rupture risk is still 1% after endografting (Harris et al. 2000). Even the most recent meta-analysis shows a 0.9% incidence of rupture after EVAR (Antoniou et al. 2015). It has been suggested, however, that rupture after EVAR may carry a better chance of survival than would otherwise be expected (May et al. 1999, Antoniou et al. 2015).

The high rate of complications and secondary procedures remains the long-term problem with EVAR. With first-generation devices in the EUROSTAR data, the early and late rate of conversion to open repair was 7.1%, while in more recent studies the corresponding rate is 3.7% (Kouvelos et al. 2015). The complication rates are very similar in the studies mentioned earlier. In the EUROSTAR registry, for every 100 person-years, an endoleak manifested in 13 cases, thrombosis in 4.6 cases and migration in 4.3 cases, resulting in a secondary intervention in 11.6 cases (Leurs et al. 2007). In the UK EVAR trial, graft-related complications occurred in 12.6 patients/100 person-years, and the secondary intervention rate was 5.1 patients/100 person-years (EVAR trial participants 2005a). At 8 years of follow-up in the EUROSTAR registry, 48% of the patients were event-free survivors (Leurs et al. 2007). Patients treated with EVAR needed three to four times more re-interventions than those who underwent OR, and the DREAM trial showed that the intervention rate for EVAR was already three times higher at nine months of follow-up (Blankensteijn et al. 2005). The reported secondary intervention rates in prospective studies are 7–20% (Greenberg et al. 2008, Conrad et al. 2009). Most of the secondary interventions are performed using the endovascular technique (Conrad et al. 2009). In addition, a major concern in randomized trials has been the number of late ruptures associated with EVAR that did not occur in the OR groups. A recent systematic review and meta-analysis confirms these concerns on high re-intervention rates and late aneurysm ruptures (Stather et al. 2013).

EVAR was originally developed for patients who were considered to be physically unfit for OR, since it was thought that their life expectancy would be prolonged by eliminating the risk of fatal rupture of an aneurysm. In long-term surveillance, EVAR leads to fewer aneurysm-related deaths than OR, and the advantage is sustained for up to four years, but the difference in overall survival does not persist beyond the first two postoperative years (Blankensteijn et al. 2005, EVAR trial participants 2005). Therefore, only a very limited overall difference is reached in expected survival. This is mainly explained by the fact that these patients have multiple comorbidities and, therefore, life-expectancy is not long in the first place. The reported 2-, 5- and 8-year cumulative survival rates are 90%, 52–72% and 52–63%, respectively, after EVAR (Brewster et al. 2006, Mertens et al. 2011). In the EVAR trial 2, a randomized prospective study comparing endovascular repair to surveillance in patients unfit for open aneurysm repair, EVAR was associated with a significantly lower rate of aneurysm-related mortality than no repair, but showed no significant difference in all-cause mortality after four years (EVAR trial participants 2005b).

Further, the DREAM trial was undertaken to assess the balance of costs and effects in endovascular versus open aneurysm repair (Blankensteijn et al. 2005). The DREAM trial showed that endovascular repair was associated with an additional 4,293 € in immediate costs (18,179 € vs. 13,886 €). The expense of the procedure comes from the stent-grafts, which are clearly more expensive than the conventional prostheses used in OR. Several studies have documented reduced hospital and ICU stays after EVAR in comparison to OR, and these reductions, together with the improvement in patient recovery time, reduce the costs of EVAR. However, this initial cost advantage is offset by the life-long and frequent follow-up as currently recommended (Epstein et al. 2014).

### 2.3.7 REVAR

Endovascular repair of a ruptured abdominal aortic aneurysm (REVAR) has similar 30-day benefits as elective EVAR (Powell et al. 2014). In a meta-analysis of observational studies and registries, REVAR has been associated with a 50% risk reduction in mortality compared to OR, but there is possible bias as patients treated with EVAR are usually selected because of hemodynamic stability and aneurysm morphology (van Beek et al. 2014). To date, there are three published randomized controlled trials comparing REVAR to OR: the Dutch AJAX trial (Reimerink et al. 2013), ECAR (Endovasculaire ou Chirurgie dans les Anévrismes aorto-iliaques Rompus) (Desgranges et al. 2015) and IMPROVE trial (Immediate management of patients with rupture: open versus endovascular repair) (Powell et al. 2014). All these trials have suggested that EVAR does not improve 30-day mortality or reduce severe complications. Still, the IMPROVE trial showed that patients treated under local anaesthesia are three to four times more likely to survive than those who require general anaesthesia, supporting this approach in the emergency setting. However, not all patients are suitable for EVAR under local anaesthesia, especially those who are treated with an aorto-uni-iliac stent-graft. As a remark, in all these randomized trials the most commonly used stent-graft design was an aorto-uni-iliac stent-graft.

## 2.4 Thoracic endovascular aortic repair (TEVAR)

### 2.4.1 Technique

TEVAR has been adopted as the first-line treatment for several aortic pathologies. The most common indications are TAA and type B dissection. The technique in TEVAR is similar to that of EVAR, but it is more complex to implement. The required diameter of the access vessels is larger as the application system and stent-graft are wider. Also, in approximately 40% of the patients, the aortic pathology extends to the aortic arch and coverage of branch vessels by a stent-graft is required in the primary procedure. Accurate placement in the arch

is also made more challenging by the high blood flow and significant movement of the arch with each heartbeat. Furthermore, in type B dissection, the deployment of the stent-graft in the aortic arch increases the risk of retrograde type A dissection (Mani et al. 2012).

The aortic arch is mapped based on different landing zones for the stent-graft (Figure 10). The coverage of the left subclavian artery (LSA) is often necessary to gain adequate sealing due to anatomic and technical reasons. Current guidelines from the Society for Vascular Surgery recommend preoperative LSA revascularization in elective TEVAR, although this remains an area of debate (Matsumura et al. 2010). Some specialists support reactive revascularization only if arm claudication or subclavian steal occurs after routine covering of the origin (Kotelis et al. 2009, Maldonado et al. 2013). Patients have considerable anatomical variations in the vertebro-basilar blood supply. The presence of a left dominant vertebro-basilar system or the existence of a left internal mammary coronary artery bypass graft is a strong indication to consider pre-emptive carotid-subclavian bypass or transposition of the subclavian artery in the elective intervention (Diethrich et al. 2008). If the stent-graft extends to cover the left common carotid artery (LCCA), reconstruction of the LCCA is always required prior to the stent-graft placement to guarantee adequate blood flow to the brain. However, to overcome these anatomic challenges, more complex endovascular techniques, such as parallel grafting of LSA or LCCA have been described, but their use remains limited (Moulakakis et al. 2013).

A minimum of 15 mm of normal aortic wall is needed for adequate sealing of the stent-graft. The aneurysmatic expansion is covered over its total length by a stent-graft. The extent to which the coverage of the descending thoracic aorta is necessary remains a dilemma; the

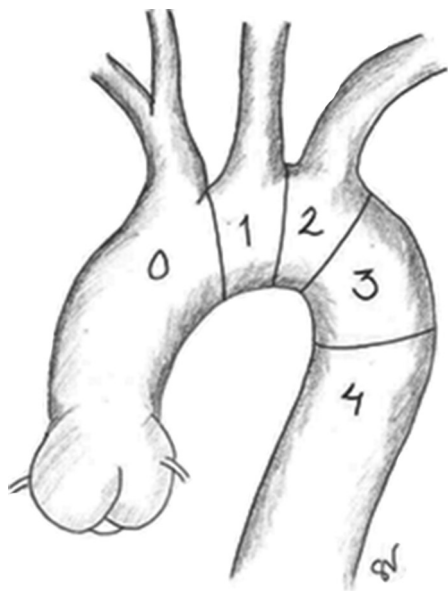


Figure 10. The landing zones for a stent-graft in the aortic arch (Modified from Ishimaru 2004).

need for a durable repair must be balanced against retaining intercostal blood flow. In an acute dissection, covering the primary entry tear is adequate and, as a result, the stent-graft depressurises the false lumen (Nienaber et al. 2013).

## 2.4.2 Complications

The graft-related complications of TEVAR are similar as those seen with EVAR. All types of endoleak are also present in TEVAR, but type I is the most common.

As the procedure closely involves the aortic arch, the three branch vessels are at a high risk of complications. Therefore, reported SCI and CVE rates are higher after TEVAR than EVAR (Berg et al. 2001, Cooper et al. 2009, Rizvi et al. 2010, Maldonado et al. 2013). There is data suggesting that covering the LSA increases the risk of stroke and SCI after TEVAR, but LSA coverage is associated with an increased risk of stroke and SCI, with or without revascularization. Prior studies have also failed to identify whether routine LSA revascularization actually protects patients from stroke or SCI (Peterson et al. 2006, Buth et al. 2007, Riesenman et al. 2007, Kotelis et al. 2009). Also, SCI is related to the extent of the covered aorta, 20.5cm being reported as a critical length (Amabile et al. 2008). The potential mechanisms of ischaemic damage to the cord include coverage of critical extrinsic vertebral, intercostal, lumbar and internal iliac supply to the anterior spinal artery as well as perioperative hypotension and possible embolization during device insertion and deployment (Griep et al. 2007).

## 2.4.3 Follow-up

There is no clear evidence to support a strict follow-up protocol after TEVAR. The post-discharge TEVAR follow-up scheme usually consists of routine CTA at 1, 6 and 12 months, and annually thereafter in the absence of symptoms, but the protocols vary between centres. Also, the originally treated aortic pathology guides the surveillance as it is the most important variable impacting survival and the need for secondary interventions (Scali et al. 2014). If, after TEVAR for TAA, the patient shows a stable course without evidence of an endoleak over 24 months, it may be safe to extend CTA intervals to every 2 years (Erbel et al. 2014). CDUS is used for post-EVAR follow-up, but it cannot be used in TEVAR surveillance as the chest causes artefacts from the ribs and lungs.

## 2.4.4 Short-term results

As the technique is currently used in a variety of conditions, the reported numbers differ somewhat. The reported technical success rates are over 90% (Kotelis et al. 2009,



Wiedemann et al. 2013, Zahn et al. 2013). The 30-day mortality rate after TEVAR is 3.6–7.9% and the reported SCI and CVE rates approximately 1.5–7.5% and 3.0–6.4%, respectively (Patel et al. 2006, Cooper et al. 2009, Rizvi et al. 2010, Goodney et al. 2011, Maldonado et al. 2013, Hughes et al. 2014). In comparative studies, the 30-day mortality, paraplegia, cardiac complications and renal dysfunction rates are lower and the ICU and overall hospital stays shorter in TEVAR than in open surgery (Stone et al. 2006, Cheng et al. 2010, Hughes et al. 2014).

For ruptured TAAs, the reported 30-day mortality rates range between 11.4% and 18.9% after TEVAR (Cambria et al. 2009, Jonker et al. 2010). TAA patients older than 75 years have significantly more postoperative complications than younger ones, and the reported stroke rate is very high, up to 24%, and the rate of pulmonary complications as high as 40%. The age of over 75 years is an independent risk factor of 30-day mortality after TEVAR (Jonker et al. 2010). In an acute complicated type B dissection treated with TEVAR, the IRAD registry (the International Registry of Acute Aortic Dissection) demonstrated an in-hospital mortality of 10.6%. Complications during the hospitalization occurred in 21% of the patients, and the most common complications were acute renal failure and mesenteric ischaemia (both 7.4%) (Fattori et al. 2013).

#### 2.4.5 Mid- and long-term results

Single-centre studies of mixed aorta pathologies (TAAs, dissections, traumatic aortic ruptures) treated with TEVAR demonstrate the overall survival at 1, 5, and 10 years to be 82–86%, 63–79%, and 44%, respectively, with significantly higher survival noted in patients treated in recent years and with newer stent-grafts (Wiedemann et al. 2013, Scali et al. 2014). Meta-analysis has shown a mortality rate of 19.4% at 1 and 27.8% at 3-years (Cheng et al. 2010).

An endoleak is the most common complication and type I endoleak is the most common type. The reported incidence of type I endoleak is 12–17% (Parmer et al. 2006, Cheng et al. 2010, Alsac et al. 2011, Saari et al. 2013, Boufi et al. 2014). A unique feature in TEVAR as compared to EVAR is that type I endoleaks resolve spontaneously in up to 38% of the cases and the reported re-intervention rate for type I endoleaks is as low as 57% (Veith et al. 2002, Parmer et al. 2006, Alsac et al. 2011, Boufi et al. 2014). Type II endoleaks, row separation and migration are relatively uncommon in surveillance (Leurs et al. 2004, Cheng et al. 2010).

For a TAA, a secondary intervention is performed primarily to treat type I and III endoleaks (Scali et al. 2014). In the EUROSTAR data, most of the secondary procedures were transfemoral (68%) (Leurs et al. 2007b). The re-intervention rate after TEVAR is approximately 12% (Leurs et al. 2007b, Scali et al. 2014). According to EUROSTAR data on degenerative TAAs, the rate of freedom from re-interventions at 1 and 2 years was 86% and 83%, respectively. The data demonstrated a better 2-year cumulative survival rate

in patients with no secondary intervention when compared to patients with a secondary intervention (85% vs. 58%) (Leurs et al. 2007b).

In mid-term follow-up, TAA patients initially treated with TEVAR for rupture have a 4-year aneurysm-related mortality rate of approximately 25%. At 4 years, only 55% of the patients are alive without a re-intervention. Aneurysm-related survival is significantly lower in patients over 75 years of age (Jonker et al. 2010).

For patients treated for type B dissection with TEVAR, the most common indication for re-intervention is a persistent false lumen, dilatation of the aorta and extension of the disease proximally or distally (Scali et al. 2014). Type B dissection treated in the early stage of onset leads more likely to a remodelling of the aorta, and the reported overall outcomes in the mid-term for chronic type B dissection treated with TEVAR are suboptimal. Approximately 50% of the patients do not show a reduction in the maximal descending thoracic aortic diameter, and patients with no aortic remodelling have a lower survival rate at three years than those with a decreasing aortic diameter (54% vs. 89%) (Mani et al. 2012). This raises the question of timing when it comes to both the initial procedure and the re-intervention.

In an acute type B dissection, patients are usually younger than those with a TAA – in the EUROSTAR data the age difference was approximately 10 years – and therefore have fewer risk factors and comorbidities (Leurs et al. 2004). They tolerate the procedure well and, consequently, have a good outcome in terms of short- and mid-term survival. The treatment strategy is clear in an acute complicated type B dissection, but acute uncomplicated cases are more debatable. Medical treatment has been the gold standard for years, but TEVAR offers an intriguing treatment option. As mentioned before, at the early stage of onset, aortic remodelling is more likely to occur (Patterson et al. 2014, van Bogerijen et al. 2014). It is unclear whether this aortic remodelling of the aorta has a positive effect on long-term survival. It is well known, however, that an increasing diameter of the patent false lumen is a significant independent predictor of aortic rupture and aneurysmal degeneration (Juvonen et al. 1999, Sueyoshi et al. 2004).

There are two reported randomized controlled trials comparing medical therapy alone with additional TEVAR for the treatment of an uncomplicated type B dissection. The INSTEAD-XL trial (Nienaber et al. 2013) evaluated the long-term outcomes in patients with an acute or subacute uncomplicated type B dissection. The study demonstrated that all-cause mortality tended to be lower in medically treated patients at two years, but TEVAR turned out to be beneficial at five years after initial randomization in regard to aortic-related causes of death (aorta-specific mortality 6.9% vs. 19.3%,  $p=0.045$ , all-cause mortality 11.1% vs. 19.3%,  $p=0.13$ ). After two years of randomization, medically treated patients had clearly less false lumen shrinkage and true lumen recovery and more often needed procedures related to dissection. Therefore, the early disadvantages of TEVAR are possibly counterbalanced by the prevention of late complications. Yet another notable feature of the study was that the outcomes of medically treated patients were better than in



previous registries, showing significant development in the pharmacological field as well. It also emphasises the patients' commitment to the treatment in a controlled trial. Similar findings of long-term surveillance have been demonstrated from the International Registry of Acute Aortic Dissection (IRAD) that showed that patients undergoing TEVAR had a lower death rate (15.5% v. 29.0%,  $p=0.018$ ) at five years (Fattori et al. 2013). Another randomized trial, the ADSORB trial, included only patients with acute uncomplicated type B dissections and, so far, the one-year results have not demonstrated a benefit for TEVAR over medical therapy alone (Brunkwall et al. 2014).

## 2.5 Hybrid repair of a thoracoabdominal aortic aneurysm

The reported operative mortality in an open repair of a TAAA is up to 20% and increases with age (Chiesa et al. 2004, Rigberg et al. 2006, Coselli et al. 2007, Schepens et al. 2009, Piazza et al. 2012). Following encouraging results with EVAR, a hybrid approach was introduced in 1999 by Quiñones-Baldrich et al. in a patient with a Crawford type IV TAAA. Hybrid repair combines an open surgical bypass with TEVAR. The stent-graft is positioned over major aortic branches such as the renal arteries, the celiac trunk and the superior mesenteric artery. While such a position would normally cause problems related to the distribution of blood flow to the covered branches, the prior placement of bypass grafts to these critical vessels allows the deployment of the stent-graft at a level that would otherwise not be possible. The hybrid approach attempts to exploit the benefits of both techniques. It provides a treatment option for high-risk patients deemed unfit for surgical repair and avoids the need for an extensive thoracoabdominal incision. It avoids the disadvantages of TEVAR – the need for excessive amounts of nephrotoxic contrast medium required to visualise and accurately position totally endovascular devices and the danger of covering vital visceral vessels. Also, in total endovascular repair, even more extensive aortic coverage is often required to achieve adequate landing zones and to allow the branches to open.

However, since the morbidity from the open stage of the procedure remains high, this approach is reserved for high-risk non-surgical candidates. Nevertheless, selected centres have reported it as the preferred option even in low-risk patients because of its superior safety compared to total open repair (Lee et al. 2007).

Overall, the 30-day mortality rates for the hybrid repair range from 0–31% (Resch et al. 2006, Chiesa et al. 2009, Patel et al. 2009). The morbidity ranges from 17–36%, with a paraplegia risk of 0–10% and graft occlusion rate ranging from 0–13% (Black et al. 2006, Patel et al. 2009, Chiesa et al. 2009, Schepens et al. 2009, Ham et al. 2011, Hughes et al. 2012).

The procedure can be performed in one or two stages, i.e. both the surgical and endovascular elements at the same time or in a staged fashion. A two-staged procedure reduces the operative burden of the procedure and has shown a reduction in SCI numbers

(Moulakakis et al. 2011, Canaud et al. 2013). The reduction is probably explained by vascular remodelling stimulated by previous surgery, as patients who have undergone previous thoracic surgery similarly tend to have less paraplegia during TAAA repair. Also, decreased SCI rate has been demonstrated in staged open TAAA repair in swine models, with ligation of the spinal arteries stimulating vascular collateralisation (Coselli et al. 1997, Zoli et al. 2010, Bischoff et al. 2011). However, a two-staged operation carries the risk of interval rupture between the stages if, for any reason, the interval is prolonged (Drinkwater et al. 2009, Lin et al. 2012). Furthermore, a single-staged procedure carries a risk of renal injury of up to 60% due to the lengthening of the procedure and contrast agent exposure immediately after renal revascularization (Lin et al. 2012). In addition, a significant correlation of renal function and SCI injury has been reported (Coselli et al. 2000, Buth et al. 2007). The underlying metabolic mechanism is not known.

Most of the major complications are related to the operation and early stages. The occurrence of type I and II endoleaks after hybrid repair is reported to be similar to TEVAR (Muehling et al. 2010, Johnston et al. 2012). A meta-analysis has shown high graft patency in surveillance (96.5%) (Moulakakis et al. 2012). The longest reported survival rates are 94.8%, 85.8% and 66.6% at 2, 5 and 10 years, respectively (Kuratani et al. 2010)1.

## 2.6 The chimney, sandwich, FEVAR and BEVAR techniques

Anatomically complex aneurysms that involve the aortic arch and the mesenteric vessels, or those that have a short or diseased landing zone, have limited the application of endovascular therapy. More complex totally endovascular techniques have been developed to provide a solution to these problems. In the chimney technique, the additional grafts provide flow into the branch vessels beside the stent-graft (Figure 11A). The snorkel configuration provides antegrade perfusion to the visceral and renal vessels in a downward orientation, while the periscope configuration provides retrograde perfusion to the branch vessels. Access to the visceral arteries is achieved with an axillary or brachial approach, while the aortic main stent-graft is deployed in the standard fashion from the femoral or iliac arteries. In the chimney technique, the components are easily available, but neither the aortic main stent-graft nor the parallel grafts are specially designed for the parallel graft configuration. There are many arguments against the chimney technique, focusing particularly on branch thrombosis and the rate of endoleaks (Patel et al. 2013, Hertault et al. 2015, Lindblad et al. 2015). If there is a high degree of angulation between the side branch and the aorta or the graft is small in diameter, there is a risk of occlusion of the side graft. Also, there is concern about areas between the aortic wall, parallel grafts and the aortic main device that are a potential source of a type I endoleak if the wall contact is inadequate.

Therefore, most recently the sandwich technique has been presented (Figure 11B). It involves the deployment of the parallel grafts between two or three aortic main devices to increase the stability of all components. Both renal parallel grafts are deployed between the

two aortic main devices, but the more proximal parallel grafts are deployed traditionally, between the aortic main body and the aortic wall. This technique has appeared in only a few reports to date (Schwierz et al. 2014).

In fenestrated endovascular aortic repair (FEVAR) and branched endovascular aortic repair (BEVAR), the continuation of blood flow to the renal and visceral arteries is ensured through holes in the graft (Figure 12). These fenestrations and branches are designed to match the diameter of these arteries, and their location needs to be customized to fit the anatomy of the patient. Fenestrations and branches can be used in combination to achieve a repair that is optimally designed to fit specific aortic anatomy. There is no clear evidence favouring the use of fenestrations versus branches in the thoracoabdominal aorta.

All these newer techniques require upper extremity access, and concern has been raised about the increased risk of an iatrogenic stroke. This concern applies particularly to cases where extensive navigation of multiple arterial sheaths and the deployment of a number of branch grafts is required and especially when a bilateral upper extremity access is needed. The procedures are technically demanding, they last longer than traditional TEVAR, and the duration of the procedure has been associated with severe complications (Marzelle et al. 2015).

There are no large multicentre studies on the fenestrated or branched techniques. Results for these total endovascular procedures are available from few pioneer centres, the national UK registry (British Society for Endovascular Therapy and the Global Collaborators on Advanced Stent-Graft Techniques for Aneurysm Repair [GLOBALSTAR] Registry 2012, Lowe et al. 2016) and a number of single-centre reports. The reported technical success rate is 90–100%, and the 30-day mortality rate 1.7–8% (Marzelle et al. 2015, Linsen et al. 2012, Suominen et al. 2013, Bisdas et al. 2015, British Society for Endovascular Therapy and the GLOBALSTAR registry 2012, Semmens et al. 2006, Verhoeven et al. 2010, Michel et al. 2015, Ou et al. 2015). The reported in-hospital mortality rates for patients with an aneurysm extending to the suprarenal aorta are up to 21% and the results correlate strongly with the extent and the level of the aneurysm (Marzelle et al. 2015). Permanent renal impairment is the most common complication (14–22%), and a postoperative need for permanent haemodialysis has been associated with an up to 93% mortality rate (Linsen et al. 2012, Marzelle et al. 2015). The reported SCI rates range from 1.6% to 4.1%, and the mesenteric ischaemia rate is 3.3% (Marzelle et al. 2015, British Society for Endovascular Therapy and the Global Collaborators on Advanced Stent-Graft Techniques for Aneurysm Repair (GLOBALSTAR) Registry 2012, Michel et al. 2015). Furthermore, multiorgan failure (MOF) has been reported to be the most common primary cause of death (26%), highlighting the risks also in the endovascular field (Marzelle et al. 2015). However, the incidence of major complications in open repair is significant in complex cases, and it is clear that there is a need for less-invasive solutions.

However, total endovascular repair requires individually customized stent-grafts for each patient, and the inherent delay in manufacture limits the applicability of multibranched

endovascular repair in emergency cases. A new standard design with the fixed branches configuration has been established, the t-branch device (Cook Medical®, Bloomington, IN, USA), with the unique advantage of direct implantation with no delay for manufacture. It has been evaluated to be suitable for at least for 50% of TAAAs (Bisdas et al. 2013, Gasper et al. 2013). Whether the new standard design with the fixed branches is as equally effective as the traditional custom-made version remains to be seen.

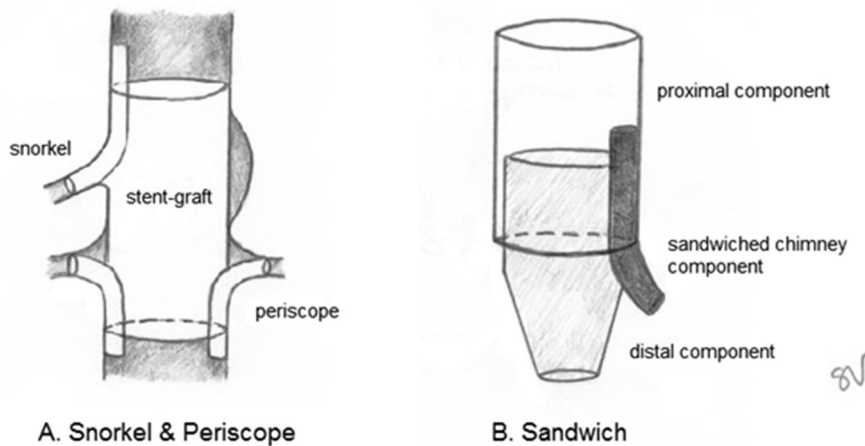


Figure 11. Chimney graft orientations. (Modified from Patel et al. 2013)

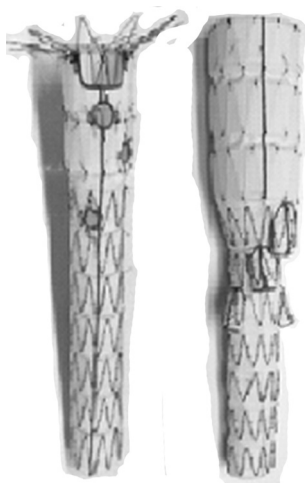


Figure 12. A modern fenestrated (left) and multi-branched (right) endovascular device for a thoracoabdominal aortic aneurysm with its own branch or fenestration for each visceral and renal artery.

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### 3 AIMS OF THE STUDY

The purpose of the present study was:

1. To assess the endovascular technique and experiences with a first-generation stent-graft at the beginning of the EVAR era.
2. To evaluate the long-term results of a second-generation stent-graft as the technique had developed.
3. To assess the success and durability of TEVAR in patients with a TAA or dissection.
4. To evaluate the long-term results of a hybrid procedure in TAAA patients at our institute.

## 4 MATERIALS AND METHODS

### 4.1 Study population

The present study was a retrospective, single-centre study based on a prospective database, which was conducted at Tampere University Hospital (TAUH). The study comprises 418 patients treated with endovascular aortic repair for an AAA, TAA, TAAA or thoracic aortic dissection. The need for ethical approval was waived due to the registry-based nature of the study. The causes of death were obtained from the hospital's patient documents and from Statistics Finland.

#### *Study I*

Study I included 48 AAA patients who underwent elective EVAR with the first-generation stent-graft Vanguard® between February 1997 and November 1999. The patients were followed until February 2007. Long-term assessment was carried out by means of CTA, angiography, CDUS and clinical controls.

#### *Study II*

Study II included 282 AAA patients who were treated electively with EVAR using the second-generation stent-graft Zenith® between March 2000 and March 2010. They were followed until the end of April 2010. The patients' long-term surveillance was assessed by clinical, CTA and CDUS controls.

#### *Study III*

Study III included 78 patients who underwent TEVAR between February 1998 and February 2013. The indication for treatment was a TAA in 51 cases and thoracic aortic dissection in 27 cases. The study included both elective (43 TAAs and 11 dissections) and emergency cases (8 TAAs and 16 dissections). The patients were followed until the end of April 2014. Long-term assessment was undertaken by means of CTA and clinical controls.

### *Study IV*

Study IV included ten TAAA patients treated electively with a hybrid procedure between March 2005 and September 2013. The patients were followed until the end of the April 2016. Long-term surveillance was carried out in the form of clinical and CTA controls.

## 4.2 Methods

The patients' data were reviewed from the hospital's electronic database and paper versions for all cases. Further, preoperative and control CTAs, angiographies and X-rays were reanalyzed with a radiologist. It was verified from the hospital database that all patients treated with the mentioned method were included in the study. If a delay in control was noted during the collection of the study data, the control examination was arranged. The data collection form for EVAR and TEVAR patients is shown in the appendix. In some cases, part of the surveillance was carried out in local central hospitals and the vascular colleagues in charge of the surveillance were contacted to obtain follow-up data. All additional procedures after EVAR were performed at TAUH.

### 4.2.1 Indication for treatment

In Studies I and II, the indication for initial treatment was an aneurysm with a diameter of over 55 mm in men and 50 mm in women. Patients with an increase in AAA diameter of  $\geq 5$  mm over a six-month period were also treated. In Study III, asymptomatic TAAs with a minimum diameter of 60 mm were treated as were patients with an increase in aneurysm diameter of  $\geq 5$  mm over a period of six months. Patients with symptomatic or saccular aneurysms were also included, in addition to two cases of LSA aneurysm with combined dilatation of the corresponding aortic arch. Patients with a chronic dissection were treated in the case of aneurysmatic expansion of 60 mm or more in the aorta. Acute dissections were treated in the case of rupture, perfusion complication, recurrent pain or hypertension despite full medication. In Study IV, for patients with a TAAA, the threshold for treatment was an aneurysm size of 55 mm or more.

### 4.2.2 Operative technique

The procedures were carried out by a vascular surgeon together with an interventional radiologist in a specially designed hybrid suite since May 2001; before that time, they were carried out in an angiography suite. The endovascular procedures were performed under local, spinal or general anaesthesia. The stent-grafts were installed through the common femoral artery utilizing fluoroscopic guidance. In some of the hybrid procedures the stent-

graft was installed through the infrarenal prosthetic graft. Bifurcated grafts were used in most of the EVAR procedures, but an aorto-uni-iliac graft was employed if another iliac artery was occluded or severely stenosed.

In TEVAR, the left subclavian artery was covered if evaluated necessary due to anatomic or technical reasons without preoperative revascularization. Since 2010, all elective patients with planned LSA coverage underwent preoperative CTA in order to evaluate their supra-aortic vascular anatomy and Circulus Willisii. Consequently, if the left vertebral artery was considered dominant and/or there was any doubt concerning the condition of the basilar or communicating arteries, the left subclavian artery was revascularized. Also, since 2011, spinal drains were placed prophylactically in all cases before the procedure for possible spinal fluid drainage. Earlier, it was used in selected cases when the coverage of the aorta was long and in all cases of hybrid repair. Spinal drains were left in place for 48 hours postoperatively, and a spinal fluid pressure of 15 mmHg or over with or without neurological signs induced drainage. The objective mean arterial pressure (MAP) was kept at 90 mmHg or over for the duration of ICU treatment.

#### 4.2.3 Follow-up

At the beginning of the EVAR era, CTA was performed at 2 or 3 days as well as 3, 6 and 12 months after the operation and annually thereafter. Angiography was carried out six months after the treatment and when graft-related complications were suspected. Since 2001, plain abdominal X-rays have been taken annually due the recommendation brought on by Vanguard®-related problems. A routine angiography was abandoned in 2003. Based on the available data and our own experience at that time, the surveillance protocol was modified in 2005 by replacing the annual CTA with CDUS performed by an experienced vascular surgeon. For all patients, a routine CTA was still performed at 24 months after the initial procedure to confirm the reliability of the CDUS examinations and also if a complication was suspected in CDUS. Patients treated with TEVAR had taken CTA annually, but if no complication was observed within 2 to 3 years of follow-up, the CTA was taken every 2 years with a plain X-ray in the years between.

#### 4.2.4 Primary outcome measures

The primary endpoints were technical success during implantation, 30-day mortality, aneurysm-related and all-cause mortality as well as surgical conversion. The technical success of EVAR and TEVAR was defined as successful deployment of the stent-graft, no surgical conversion or intraoperative death, and no signs of type I endoleak at the end of the procedure. In the case of dissections, technical success also included complete coverage



of the primary entry tear. In a hybrid procedure, technical success also entailed successful open visceral bypasses.

#### 4.2.5 Secondary outcome measures

The secondary endpoints were the number of procedure-related complications and secondary procedures. In Study II, possible risk factors for graft-related complications were also assessed. The effect of complications on all-cause survival was analyzed. A complication was defined as any graft-related complication: endoleak, endotension, row separation, migration, kinking or thrombosis of the stent-graft. A primary endoleak was defined as an endoleak that was detected during the primary procedure, within 2 to 3 days after the procedure, or at the one-month control CTA. A secondary endoleak was defined as any endoleak that was detected later than the first month of control. Aneurysm size was measured as the maximum diameter of axial images upon CT. Endotension was defined as an increase in aneurysm size of  $\geq 5$  mm with no signs of endoleak. Kinking was defined as noteworthy when it required secondary interventions.

A secondary procedure was defined as any endovascular or surgical intervention to restore or maintain proper stent-graft function after the initial procedure, and they were also analyzed as an endpoint. Primary conversion was defined as converting to open repair during the initial procedure. Secondary conversion was defined as a conversion to open repair at any time during surveillance.

#### 4.2.6 Statistical methods

Statistical analysis was performed with IBM SPSS Statistics software versions 17.0/22.0 (SPSS, Chicago, IL). The Kaplan-Meier method was used to estimate survival. Logistic regression analysis was applied to evaluate associations between different factors.  $P < 0.05$  was considered to indicate statistical significance.

## 5 RESULTS

### 5.1 Long-term results of EVAR using the first-generation Vanguard® stent-graft (I)

#### 5.1.1 Operative and 30-day results

Patient characteristics are presented in Table 3. The mean diameter of an AAA was 57 mm at the time of treatment (range 40–90 mm). The first twelve (25%) procedures were performed under general anaesthesia and the rest (N=36, 75%) under spinal anaesthesia. The technical implant success rate was 100%, and there were no intraoperative deaths or primary conversions. In addition, no primary type I endoleaks were detected, resulting in complete primary success. The 30-day mortality was 0%.

Table 3. Baseline characteristics of 48 AAA patients treated with a Vanguard® stent-graft.

Characteristics	Value	%
<b>Age (yr.)</b>		
mean	70	92
range	54–85	8
<b>Sex</b>		
male	44	
female	4	
<b>Coexisting conditions (no. of patients)</b>		
hypertension	272	56
coronary heart disease	23	48
hypercholesterolemia	7	15
diabetes	8	17
chronic renal insufficiency	2	4
cigarette smoking	15	31
cerebrovascular disease	8	17
respiratory disease	10	21
previous artery reconstruction or amputation	5	10
no coexisting risk factors	3	6
<b>Size of aneurysm (mm)</b>		
mean	57	
range	40–90	
<b>Length of aneurysm neck (mm)</b>		
mean	27	
range	5–65	

## 5.1.2 Long-term results

### 5.1.2.1 Late survival

The median follow-up time was 91 months (range, 7.6–120 months). None of the patients were lost during follow-up. There were 25 (52%) subsequent deaths during the follow-up, and the main causes of death were coronary artery disease (N=9, 19%) and cancer (N=6, 13%). Two aneurysm-related deaths (4.2%) were encountered at 48 and 62 months, respectively, after the initial procedure. The first aneurysm rupture was caused by type III endoleak and the second by row separation and a further type I endoleak. The overall survival rates at 3, 5 and 9 years were 81%, 69% and 44%, respectively (Figure 13).

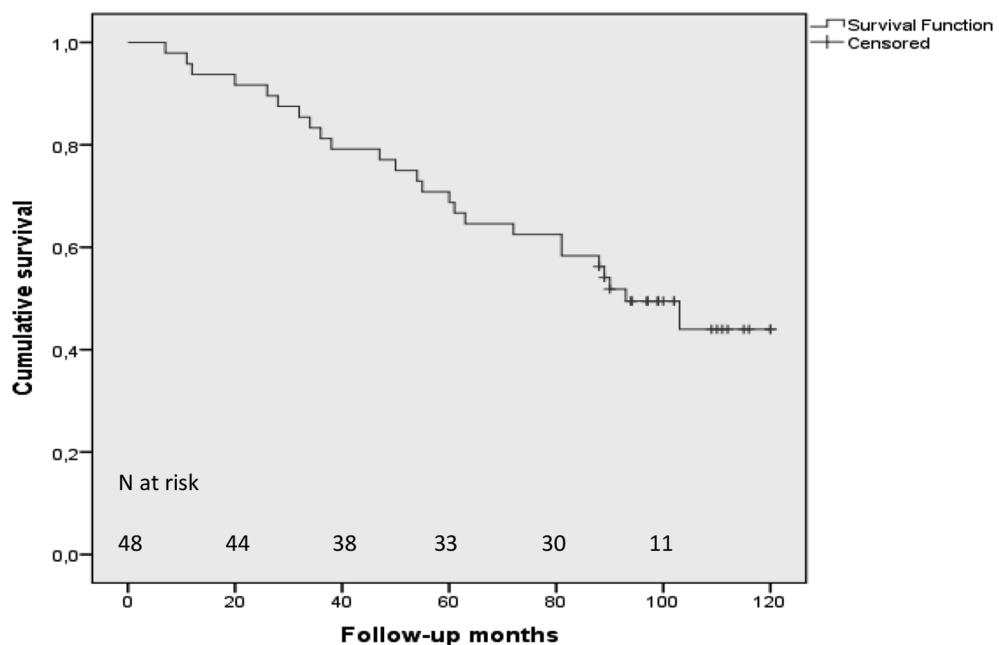


Figure 13. Cumulative survival of patients treated with a Vanguard® stent-graft (Kaplan-Meier survival analysis).

### 5.1.2.2 Complications

Stent-graft-related complications were encountered in 43 patients (90%), and all types of complications were found in the first-generation stent-graft (Table 4). The most common complication was an endoleak (56%), and 25% of the endoleaks were primary (all type II, N=12). Five of these (42%) disappeared spontaneously during the first six months, and

only two were persistent. In follow-up, a type III endoleak was the most common (N=18). Eight of them developed due to a disjunction of the modular parts and ten were related to a fabric tear. Additionally, there were 16 type I endoleaks, four of which were proximal and 12 distal. Furthermore, there were 25 cases of row-separation, and three of them were associated with an endoleak and five with migration. The total number of migrations was 22, and 13 of them were distal and 9 proximal. Seven of the migrations developed an endoleak. One main graft thrombosis was operated on by means of emergency Y-prosthesis reconstruction, and all other thromboses were limb occlusions.

The total number of aneurysm ruptures was three (6%). As mentioned earlier, two patients died of an AAA rupture at 48 and 62 months. Additionally, one case of row separation developed into a type III endoleak and rupture, but it was successfully open-repaired at 53 months after the initial EVAR.

Typical timing was observed for the various complications, as endoleaks were mostly seen in the early stages of follow-up while migration and row separation were later complications. After approximately five years, complications became extremely infrequent.

#### 5.1.2.3 Secondary interventions

A total of 81% (N=39) of the patients required a secondary procedure due to graft-related complications (Table 5). Complications were first treated by endovascular means if possible to avoid open repair. A maximum of eight additional procedures were undertaken for a single patient. There was one severe complication related to an additional procedure (renal insufficiency requiring permanent dialysis). The total number of late conversions was ten (21%). At two-years, the re-intervention-free survival rate was 54%. As with complications, secondary interventions also became rare after five years of follow-up.

Table 4. Graft-related complications in 48 AAA patients treated with a Vanguard® stent-graft

Complication	Number of cases	Number of patients	%
Endoleak	48	27	56
type I	16	13	
type II	14	14	
type III	18	10	
type IV	0	0	
Endotension (>5 mm)	1	1	2
Row separation	25	22	46
Thrombosis	20	15	31
Migration (>5 mm)	22	16	33
Kinking	3	3	6
AAA rupture	3	3	6
<b>Total</b>	<b>122</b>		

Table 5. Secondary procedures in 48 AAA patients treated with a Vanguard®-stent-graft.

Secondary procedure	Number of cases
Re-endografting	4
Limb graft repair	33
Infrarenal cuff	19
Embolization	8
Thrombolysis	6
Femoro-femoral bypass	9
Axillo-femoral bypass	2
Amputation	2
Conversion to open repair	10
for rupture	2
for thrombosis	1
for previous endovascular procedures	7
<b>Total</b>	<b>93</b>

## 5.2 Long-term results of EVAR using the second-generation Zenith® stent-graft (II)

### 5.2.1 Operative details and 30-day results

Patient characteristics are presented in Table 6. The median diameter of the treated AAA was 60 mm (range 40–110 mm). Spinal anaesthesia was used in most cases (96%, N=271). A bifurcated stent-graft was used for 95% (N=268) of the patients and a uni-iliac stent-graft for the rest. The inferior mesenteric artery (IMA) was open in 186 cases, and it was

always attempted to be embolized prior to stent-graft placement. This was successful in 78% of the cases (N=146). All graft implantations were technically successful, and there were no intraoperative deaths or primary conversions. The 30-day mortality was 1.4%, and the causes of death were brainstem infarction (one patient) and cardiac failure (three patients).

Table 6. Baseline characteristics of 282 AAA patients treated with a Zenith® stent-graft.

Characteristics	Value	%
<b>Age (yr.)</b>		
mean	75	
range	49–92	
<b>Sex</b>		
male	249	88
female	33	12
<b>Coexisting conditions (no. of patients)</b>		
hypertension	138	49
coronary heart disease	148	52
hypercholesterolemia	66	23
diabetes	41	15
chronic renal insufficiency	28	10
cigarette smoking	57	20
cerebrovascular disease	46	16
respiratory disease	81	29
previous artery reconstruction or amputation	10	3.5
<b>Size of aneurysm (mm)</b>		
median	60	
range	40–110	
<b>Length of aneurysm neck (mm)</b>		
median	25	
range	5–80	

## 5.2.2 Long-term results

### 5.2.2.1 Late survival

Patients were followed for a median 40 months (1–119 months). None of the patients were lost during follow-up. There were 80 (28%) late deaths, and the most common causes of death were cardiac death (N=22, 8%) and cancer (N=17, 6%). There were two aneurysm-related deaths due to rupture (0.7%). Both of these were derived from a type I endoleak. The first patient declined a further procedure for type I endoleak and died 34 months after diagnosis. The second patient died 24 hours after an unsuccessful proximal cuff placement for a type I endoleak. The cumulative survival of the cohort was 62% at 5 years and 52% at 8 years (Figure 14). No significant difference in survival was detected between those with or without graft-related complications (Figure 15).

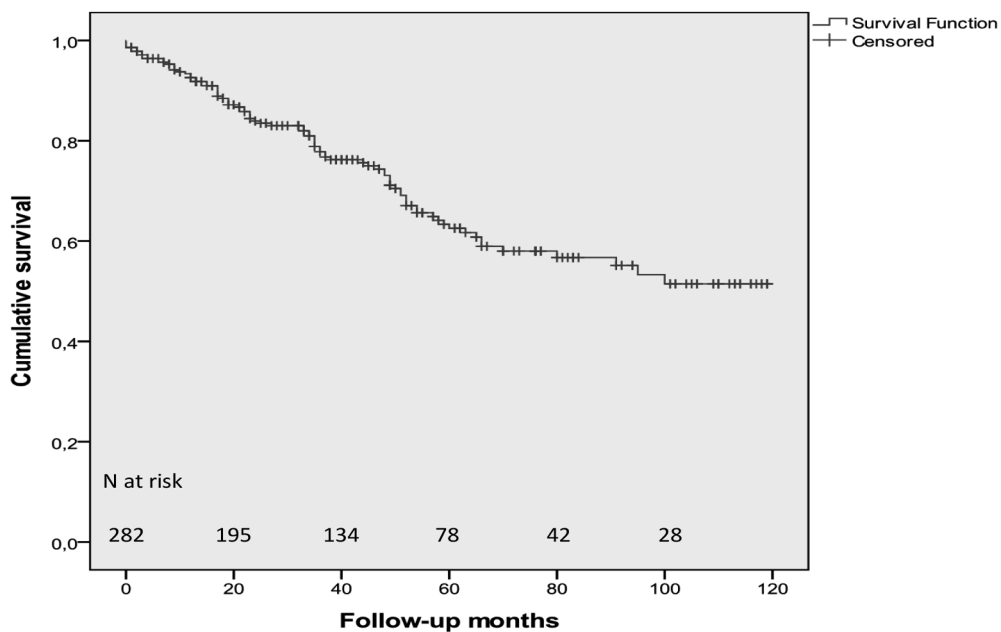


Figure 14. Cumulative survival of patients treated with a Zenith® stent-graft (Kaplan-Meier survival analysis).

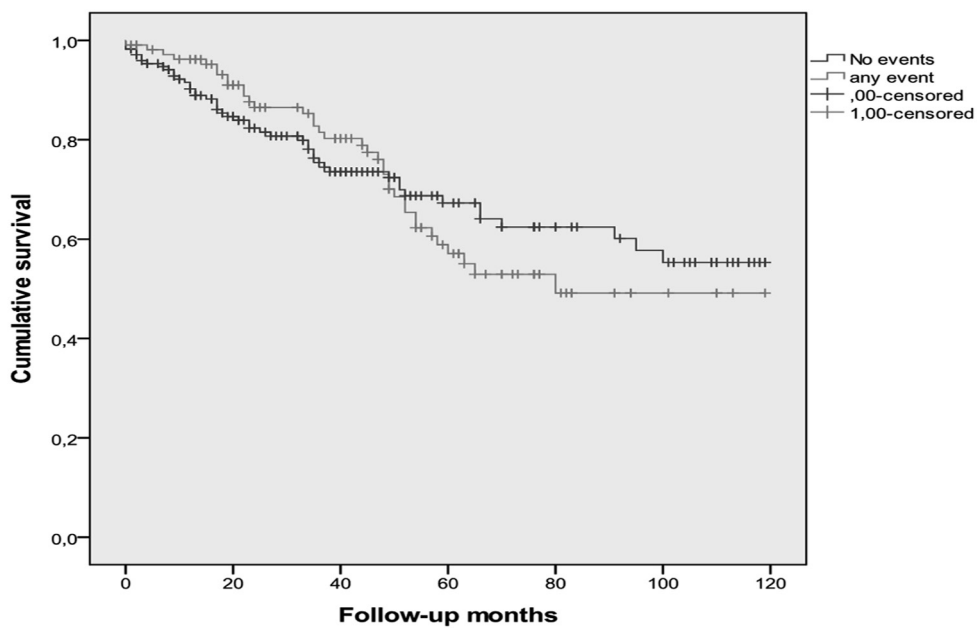


Figure 15. Cumulative survival of patients with and without graft-related complications (Kaplan-Meier survival analysis).

### 5.2.2.2 Complications

A total of 120 other graft-related complications were encountered in a total of 107 patients (38%). The most common complication was an endoleak (33%), especially type II (N=73, 26%). Most of them (78%) were treated conservatively as they sealed spontaneously (N=46) or caused no aneurysm expansion (N=11). Complications accumulated in the first three years of follow-up, and no new complications were discovered after six years of follow-up. Nearly all endoleaks (93%) in particular were seen within the first three years. Migration, row separation and type III endoleak were rare complications with the second-generation Zenith® stent-graft (1.1%, 0% and 0.4%, respectively). Aneurysm-related factors showed no significant association with endoleaks (separately for type I and II endoleaks) or graft-related complications in general. All complications encountered are presented in Table 7 and complication-free survival in Figure 16.

Table 7. Graft-related complications in AAA patients treated with a Zenith® stent-graft.

Complication	Number of cases	%
Endoleak	95	33
type I	21	
type II	73	
type III	1	
type IV	0	
Endotension (>5mm)	11	3.9
Thrombosis	9	3.2
Migration (>5mm)	3	1.1
Kinking	2	0.7
Row separation	0	0
AAA rupture	2	0.7
<b>Total</b>	<b>122</b>	



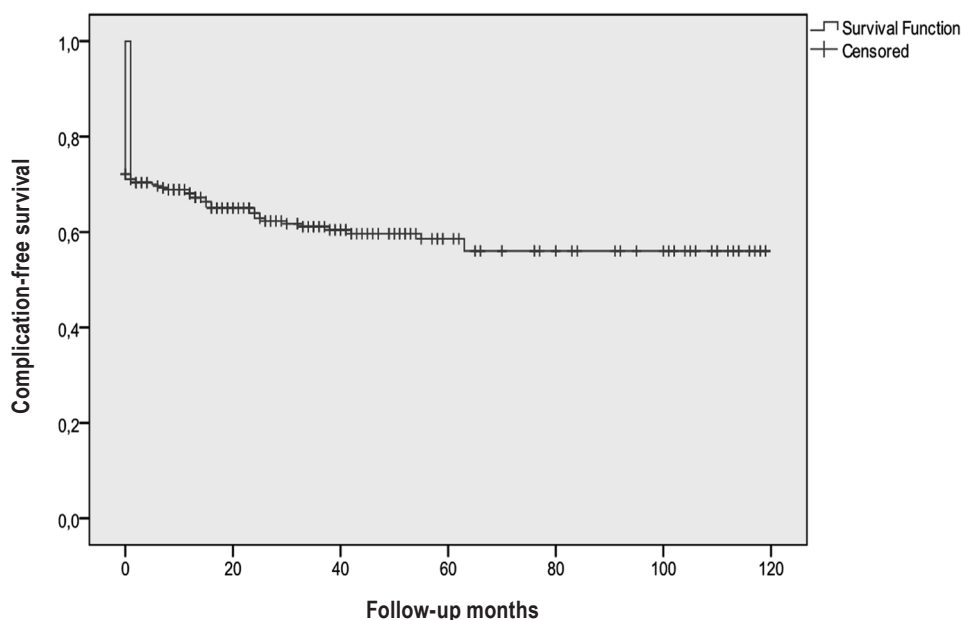


Figure 16. Complication free-survival of patients treated with a Zenith® stent-graft (Kaplan-Meier survival analysis).

### 5.2.2.3 Secondary interventions

In all, 37% of the complications required a secondary procedure, and a total of 59 additional procedures were performed for a total of 38 (13%) patients (Table 8). These included one case of re-endografting due to endotension; other cases of endotension were, as a rule, treated conservatively. There was one late conversion to open repair 28 months from the initial procedure after failed proximal cuff placement to exclude a type IA endoleak. The most often treated complication was an endoleak (type I: 14, type II: 16, type III: 1). Two patients were treated for both type I and II endoleaks and one patient for type I and III endoleaks. Additionally, there were seven cases of limb graft thrombosis, and six of them were treated with femoro-femoral bypass. One case of limb graft thrombosis with only mild claudication and one asymptomatic case of total stent-graft thrombosis did not necessitate any interventions. One limb thrombosis occurred during an additional procedure and was simultaneously treated with femoro-femoral bypass.

The mean time of the first re-intervention was 22 months from the primary procedure. Most of the secondary procedures were performed during the first four years of follow-up, and only four additional procedures were needed after five years. Kaplan-Meier analysis shows a re-intervention-free survival rate of 76% at six years (Figure 17).

Table 8. Re-interventions for Zenith®-graft-related complications.

Secondary procedure	Number of cases
Re-endografting	1
Limb graft repair	5
Infrarenal cuff	7
Embolization*	35
PTA	3
Femoro-femoral bypass	7
Conversion to open repair	1
Total	59

\* includes 3 angiographies with no further interventions

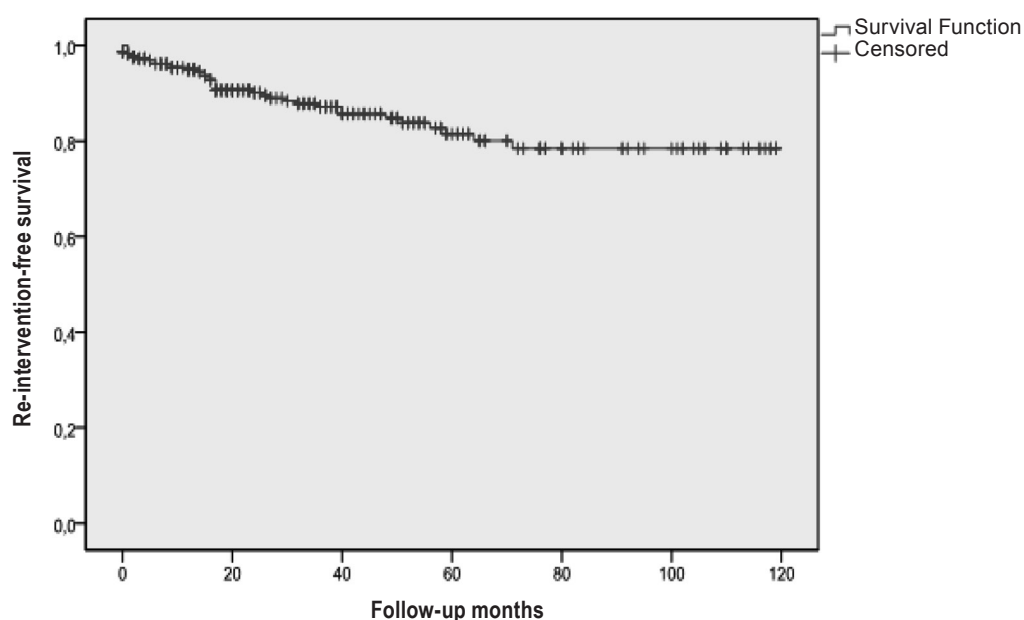


Figure 17. Re-intervention-free survival of patients treated with Zenith® stent-grafts (Kaplan-Meier survival analysis).

## 5.3 Long-term results of TEVAR

### 5.3.1 Operative details and technical success

The first TEVAR was performed in 1998, but the case load started to increase rapidly in 2003 and, consequently, 95 % of the cases were performed since then (Figure 18). A total of 51 (65%) patients were treated for TAA (43 elective and 8 emergency cases) and 27 (35%) for type B dissection (11 elective and 16 emergency cases). Patient characteristics

are presented in Table 9. The median diameter of the thoracic aneurysms was 67 mm at the time of treatment (range, 48–102 mm). Six patients had a saccular aneurysm. Eight cases of TAA were treated in an emergency setting, six due to aneurysm rupture. Of the dissections, 16 were treated in an emergency setting: five due to a perfusion complication, recurrent pain or hypertension despite full medication, and eleven due to signs of rupture. Eleven chronic dissections were treated for aneurysmatic dilatation of a thoracic aorta of  $\geq 60$  mm (Tables 10 and 11). All of the various aortic landing zones were applied in the treatment of the patients (Figure 10, Table 12).

General anaesthesia was used in 36 cases (46%), spinal anaesthesia in 41 cases (53%) and local anaesthesia in one case (1%). Thirty-two patients (41%) required stent-graft deployment in the aortic arch: five in zone 1 and 27 in zone 2 (Table 12). Two patients with an ascending aortic dissection (zone 0) were primarily treated urgently with open repair for type A dissection and secondarily one and five months later, respectively, with a thoracic stent-graft. In first the case, the aortic root and arch were replaced with the frozen elephant trunk technique. In the second case, the ascending thoracic aorta was reconstructed with supra coronary Dacron prostheses up to the brachiocephalic trunk. In zone 1, an extra-anatomic carotico-carotid bypass together with a revascularization of the left subclavian artery (LSA) was performed for two patients, while, in three cases, left common carotid artery (LCCA) revascularization was considered sufficient. Regarding the patients with a proximal stent-graft landing in zone 2 (N=27), the LSA was deliberately covered in 24 cases and, for three patients, LSA revascularization was considered necessary prior to the endovascular procedure. These three patients included one young patient with an LSA aneurysm, one with simultaneous open repair of an AAA and one with previous AAA repair. A total of seven different thoracic stent grafts were used in thoracic aortic repair: Excluder/Gore TAG® (W.L. Gore & Associates Inc, Flagstaff, AZ, USA) (N=45), Zenith® (Cook Medical, Bloomington, IN, USA) (N=24), Valiant/Talent® (Medtronic, Inc., Minneapolis, MN, USA) (N=6), Relay Plus® (Bolton Medical, Sunrise, FL, USA) (N=2), and Vanguard® (Boston Scientific, Natick, MA, USA) (N=1). The mean number of devices per case was 1.4 (range 1–3).

Six patients underwent simultaneous open repair of an AAA, while in one case the AAA was repaired endovascularly. All were elective cases and the AAA was open repaired if the patient was considered fit for open AAA surgery. Thirteen patients had undergone a previous surgical OR for AAA.

The technical success rate was 81%. There were no intraoperative deaths or surgical conversions. All failures were caused by a type I endoleak; if it was minor and occurred at the end of the procedure, it was left without any treatment at this point if spontaneous resolution was expected. The spontaneously resolved endoleaks were still taken into account as a complication.

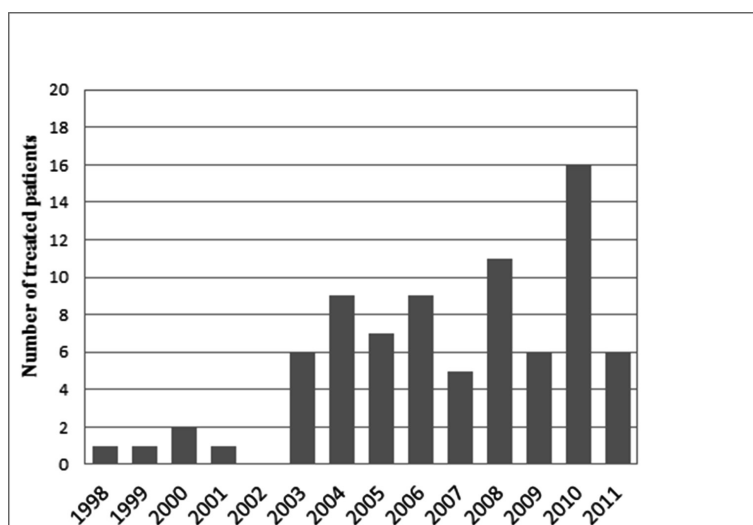


Figure 18. The distribution of TEVAR procedures across the study years at TAUH.

Table 9. Baseline characteristics of 78 patients treated with TEVAR.

Characteristics	Value	%
<b>Age (yr.)</b>		
mean	66	
range	18–88	
<b>Sex</b>		
male	58	74
female	20	26
<b><sup>1</sup>ASA classification</b>		
2	7	9
3	30	38
4	38	49
5	3	4
<b>Coexisting conditions (no. of patients)</b>		
hypertension	46	59
coronary heart disease	18	23
hypercholesterolemia	22	28
diabetes	10	13
chronic renal insufficiency	6	8
cigarette smoking	18	23
cerebrovascular disease	3	4
respiratory disease	19	24
previous artery reconstruction or amputation	21	27

<sup>1</sup> ASA: American Society of Anesthesiologists

Table 10. Indications for primary treatment of thoracic aortic aneurysm.

	TAA elective (N=43)	TAA emergency (N=8)
Size (>6 cm) or rapid growth	36	
LSA aneurysm	2	
Saccular aneurysm	5	1
Acute rupture		6
Symptomatic		1

Table 11. Indications for primary treatment of thoracic dissection.

	Dissection chronic (N=11)	Dissection acute (N=16)
Aneurysmatic dilatation (>6 cm)	11	
Failure of medical therapy		3
Extravasation		11
Malperfusion		1
Symptomatic		1

Table 12. Location of thoracic aortic lesions and stent-graft landing zones in 78 patients.

Lesion zone	Number of patients	%	Stent-graft landing zone	Number of patients	%
0	2	2.6	0	0	0
1	0	0	1	5	6.4
2	8	10	2	27	35
3	39	50	3	26	33
4	29	37	4	20	26

### 5.3.2 30-day outcomes

The overall 30-day mortality was 6.4% (n=5; 3 elective and 2 emergency cases). The causes of death were thoracic aortic aneurysm rupture (N=2), visceral malperfusion (N=1), myocardial infarction (N=1) and chronic obstructive pulmonary disease (N=1). A postoperative stay in the intensive care unit (ICU) was needed for 32 (41%) patients. There was no significant difference in the ICU or overall hospital stay between elective and emergency cases (mean ICU stay 6.8 vs. 7.0 days, range 1–40 days, p=0.972; mean hospital stay 8.6 vs. 10.5 days, range 2–49 days, p=0.347).

Spinal cord ischaemia (SCI) resulted in permanent paraparesis in two patients (2.6%), whereas an additional two patients (2.6%) developed transient symptoms that resolved with

spinal fluid drainage. Two cases of SCI were emergencies and one underwent simultaneously open repair of an AAA. Six patients (7.7%) suffered a postoperative cerebrovascular event (CVE) without permanent effect on the patients' previous physical condition. There was no correlation between SCI and CVE rates and the number of stent-grafts used ( $p=0.751$  and  $p=0.057$ ). Also, there was no statistical difference in SCI and CVE rates between patients treated for a TAA and those treated for dissection (SCI: 2.0% vs. 3.7%,  $p=0.648$ , CVE: 3.9% vs. 14.8%,  $p=0.088$ ). SCI and CVE were more frequent in the emergency setting compared to the elective setting (SCI: 4.2% vs. 1.9%,  $p=0.557$ , CVE: 16.7% vs. 3.7%,  $p=0.048$ ). Furthermore, patients with previous or simultaneous OR of an AAA ( $N=19$ ) did not have significantly higher SCI or CVE rates ( $p=0.399$  and  $p=0.152$ , respectively).

The incidence of CVE was higher among those with LSA coverage, regardless of revascularization, than those without it, although this difference was not statistically significant (12.5% and 4.3%,  $p=0.18$ ). One of the five patients with preoperative LSA revascularization had a postoperative stroke. The incidence of SCI was not higher among those with LSA coverage (with or without revascularization) compared to patients without coverage (3.1% and 2.2%,  $p=0.79$ ). Patients with LSA coverage without revascularization ( $N=27$ ) had a 30-day mortality rate of 7.4% ( $N=2$ ) and patients without LSA coverage 6.5% ( $N=3$ ) ( $p=0.47$ ) (Table 13). The results are presented according to aortic pathology in Table 14.

In all, 17 secondary interventions during 30 days were required in a total of 13 patients, including one open repair of a RAAA, one thigh amputation, 4 additional stent-graft applications, two transthoracic haematoma evacuations, two laparotomies, two embolizations, one embolectomy, one evacuation of a wound haematoma, two cases of surgical haemostasis, and one stenting of a renal artery. One patient required two laparotomies due bowel ischaemia, which later resulted in partial bowel resection. Of these secondary interventions, 85% were performed during the first postoperative week, and 54% of these cases were primary urgent TEVARs.

### 5.3.3 Long-term results

#### 5.3.3.1 Late survival

The mean follow-up for the entire study group was 55 months (range 1–160 months). An additional 24 deaths occurred during the follow-up, the main causes of death being cardiovascular diseases ( $N=6$ , 7.7%) and cancer ( $N=4$ , 5.1%). The overall survival was 85%, 78%, 62% and 57% at 1, 3, 5 and 8 years, respectively (Figure 19).

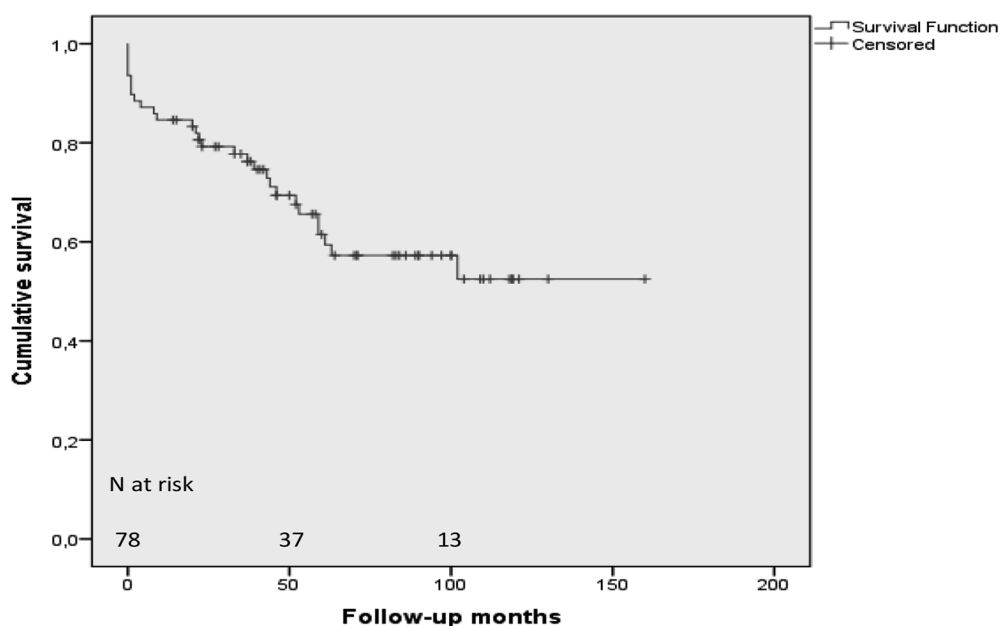


Figure 19. Cumulative survival of TEVAR patients (Kaplan-Meier survival analysis).

Table 13. Approach to the LSA in patients with a stent-graft on landing zones 1 and 2 (primary and secondary procedure) and the number of patients with associated complications. (CVE= cerebrovascular event, SCI=spinal cord ischaemia)

	Total number of patients	30-day mortality N (%)	CVE N (%)	SCI N (%)
<b>Primary procedure</b>				
LSA not covered	46	3 (6.5)	2 (4.3)	1 (2.2)
LSA covered	32	2 (6.3)	4 (12.5)	1 (3.1)
Primary revascularization	5	0	1 (20)	0
No primary revascularization	27	2 (7.4)	3 (11)	1 (3.7)
Secondary revascularization	2	0	0	0
<b>Secondary procedure</b>				
LSA covered	6	0	0	0
No revascularization	3	0	0	0
Revascularization	3	0	0	0

Table 14. Mortality, CVE and SCI rates during 30 days according to aorta pathology.

	Number of patients	Mortality N (%)	CVE N (%)	SCIN (%)
<b>TAA</b>	51	4 (7.8)	2 (3.9)	1 (2.0)
Elective	43	3 (7.0)	2 (4.7)	1 (2.3)
Emergency	8	1 (12.5)	0	0
<b>Dissection</b>	27	1 (3.7)	4 (14.8)	1 (3.7)
Chronic	11	0	0	0
Acute	16	1 (6.3)	4 (25)	1 (6.3)

### 5.3.3.2 Complications

One additional patient died of a TAA rupture six months after the initial procedure caused by a type I endoleak, resulting in a total aortic-rupture-related death rate of 3.8% (N=3). In this case, there were no signs of an endoleak at the one-month postoperative CTA, but at the time of rupture seven months later, it was seen in emergency CTA.

The most common complication was an endoleak (38%). A primary endoleak occurred in 28 (36%) patients (15 type I and 13 type II). Of these, 12 (43%) resolved spontaneously, including five primary type I endoleaks. Seven patients with a type I endoleak required an additional procedure, whereas 2 were carefully followed as the aneurysm size remained stable with no signs of growth. By the end of the study, these 2 patients had been followed for 84 and 55 months, respectively. One patient died during the initial hospitalization due to complications related to the aneurysm rupture he was initially treated for. Only two primary type II endoleaks led to an additional procedure as the aneurysm sac was growing during the surveillance.

Ten secondary endoleaks were detected in a total of nine patients (8 type I and 2 type II). Two secondary type IA endoleaks were caused by graft migration and four by obvious aortic degeneration. Four cases of type I endoleak were treated with an additional device. One case was deemed to be a poor endovascular and OR candidate, and no further procedures were performed. This patients died six months later due to prostatic cancer. In one case, the endoleak was impossible to repair by endovascular means and no further procedures were done. In one case, further procedures were abstained from as the aorta showed shrinkage in follow-up, and by the end of the study, this patient had been followed 60 months. One case of type I endoleak was diagnosed at the time of rupture, as mentioned earlier. None of the patients in careful surveillance died of aneurysm-related causes. Secondary type II endoleaks required no further procedures.

Additionally, there was one case of endotension that was only carefully followed. One case of row separation was detected 11 years after the primary procedure and was treated with an additional device before there was notable endoleak or sac enlargement.



### 5.3.3.3 Secondary interventions

One late elective conversion (1.3%) was necessary in a case of type B dissection due to a progression of a false lumen and dilatation of the aorta. It was performed five years after the initial procedure. Unfortunately, the patient died after OR. Overall, 24% of the patients required an additional procedure in follow-up. Of all additional procedures, 84% were done during the first two years of the surveillance and the mean interval to the first graft-related secondary intervention was 16 months after the initial procedure (range 1 day to 68 months). All procedure-related complications and secondary procedures are presented in Table 15.

Table 15. Number of complications and procedure-related secondary procedures in 78 TEVAR patients.

	TAA		Dissection	
	elective	emergency	chronic	acute
<b>Complication</b>				
<b>Endoleak</b>				
I	16	2	2	3
II	8	1	3	3
migration	3	0	0	0
row separation	1	0	0	0
endotension	1	0	0	0
<b>Graft-related secondary procedures</b>				
<b>Transfemoral intervention</b>				
– embolization	1	0	0	3
– additional stent-graft	10	1	1	3
<b>Extra-anatomic procedure</b>				
– surgical subclavian closure	1	0	1	0
– carotico-subclavian bypass	4	0	0	1
– carotico-carotid bypass	2	0	0	1
<b>Transthoracic surgery</b>				
– conversion to open repair	0	0	0	1

## 5.4 Results of hybrid repair for thoracoabdominal aortic aneurysm

### 5.4.1 Operative details and 30-day outcomes

All patients were high-risk patients, classified as ASA 3–4. The mean aneurysm size at the time of treatment was 72 mm (range 58–84 mm), and Crawford classification types I–IV were presented. The patients' detailed characteristics are presented in Table 16.

Nine patients were treated electively and one urgently due to a symptomatic TAAA. Visceral debranching was performed in a transperitoneal approach. All four visceral vessels were revascularized in eight patients, and one underwent three-vessel and one two-vessel

revascularization. The patient with only two-vessel revascularization had two aneurysms: a Crawford class I TAAA in the descending thoracic aorta and in the abdominal aorta. The suprarenal aorta was stent-grafted and the SMA and celiac trunk bypassed, and the infrarenal aorta was repaired with Y-protheses during the same procedure. One patient had only three-vessel revascularization as right renal artery revascularization turned out technically impossible in the operation. The inflow sites were retrograde, i.e. the native iliac arteries, the distal aorta or infrarenal prosthetic graft. A total of five patients (50%) had simultaneous open repair of an infrarenal aorta (Table 17).

All patients were treated under general anaesthesia. Eight patients underwent the procedure in a single-staged fashion. Following the example of studies reporting a more favourable outcome after a two-staged approach for hybrid TAAA repair, the treatment strategy was amended in 2013 and the remaining two patients were treated accordingly. The intervals between the procedures were 36 and 97 days, respectively, while the planned interval was two weeks. In the first case visceral revascularization resulted in an open abdomen- situation and prolonged the interval between the two stages by over a month. In the second patient, on the other hand, one of the renal grafts thrombosed at 45 days after the first stage. It was successfully thrombolysed and the patient was assigned to permanent clopidogrel-medication.

Two types of stent-graft were used: Zenith® (Cook Inc, Bloomington, IN, USA) (N=9) and Endurant® (Medtronic AVE, Santa Rosa, CA, USA) (N=1). The stent-grafts were landed in zones 3 to 4 and the LSA was not covered in any cases. The visceral grafts utilised were synthetic (polyester or polytetrafluoroethylene) and, in the last two cases, the Gore Hybrid Vascular Graft® (GHVG; W. L. Gore & Associates, Flagstaff, AZ, USA) was employed for renal revascularization.

The primary technical success rate was 100% and the 30-day mortality 0%. There were no primary endoleaks. The patients stayed in the ICU for a median of 3.5 days (range 2–29 days), and the median hospital stay was 11 days (range 8–58 days). One patient had immediate irreversible SCI resulting in paraplegia (10%), and four additional patients suffered from transient lower extremity paresis which resolved with spinal fluid drainage. As a CSF pressure over 15 mmHg induced drainage with or without symptoms, a total of seven patients (70%) had CSF drainage. There were no CSF-drainage-related complications. Three patients required temporary haemodialysis, but none permanent. Patients with an extensive Crawford type II TAAA had clearly more postoperative complications than others as 100% of them developed SCI (transient or permanent) and two out of three required temporary dialysis. Three patients underwent additional explorative laparotomy during the hospitalisation, one of which resulted in partial bowel resection and colostomy after the second operation of a two-staged procedure. In another case, the clinical status and increasing blood lactate level suggested visceral ischaemia, but no further procedures were required. Unfortunately, the patient developed irreversible lower extremity paraplegia after the procedure. In the third case, a decreasing blood haemoglobin level with hypotension

proceeded to laparotomy, but there were no signs of active bleeding at the time of the procedure. A cardiac complication was observed in one case and a pulmonary one in two cases, prolonging the ICU stay to up to 29 days. There were no strokes during hospitalization. Nine out of ten patients returned to live at home after the initial hospitalization.

Table 16. Characteristics of TAAA patients treated with hybrid repair.

Patient no.	1	2	3	4	5	6	7	8	9	10	Mean
<b>Sex</b>	F	M	F	M	F	M	F	M	M	M	<b>66</b>
<b>Age (Yr.)</b>	55	59	64	62	77	64	71	71	81	54	
<b>ASA class<sup>1</sup></b>	3	4	4	3	4	3	3	3	3	3	
<b>Crawford class</b>	I	I	III	III	II	II	II	III	III	IV	
<b>Aneurysm diameter (mm)</b>	80	68	69	60	74	84	76	58	78	72	<b>72</b>
<b>Previous aortic repair</b>	Yes	No	No	No	Yes	No	Yes	No	Yes	No	
<b>Renal insufficiency</b>	No	Yes	No	No	No	No	No	No	No	No	
<b>Hypertension</b>	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	
<b>Coronary heart disease</b>	No	Yes	No	No	No	No	No	No	Yes	No	
<b>Hypercholesterolemia</b>	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	
<b>Diabetes</b>	Yes	No	No	No	No	No	No	Yes	No	Yes	
<b>Cerebrovascular disease</b>	No	Yes	No	No	No	No	No	No	No	No	
<b>Respiratory disease</b>	No	No	No	No	Yes	No	No	No	No	No	
<b>Cigarette smoking</b>	Yes	Yes	No	No	No	Yes	No	No	No	No	

<sup>1</sup>The American Society of Anesthesiologists (ASA) classification.

## 5.4.2 Long-term results

### 5.4.2.1 Late survival

Patients were followed for a median of 55 months (4–133 months), and the overall mortality was 40% during follow-up. There were no aneurysm-related deaths. One patient died of ischaemic colitis, but at the time of the diagnosis all the grafts were patent in CTA. All causes of deaths are listed in Table 18.

### 5.4.2.2 Complications and secondary interventions

As mentioned, one acute renal graft thrombosis was noted 45 days after the initial procedure, and it was thrombolized successfully. This renal artery graft was patent at the end of the follow-up. The calculated bypass graft patency rate was 97%. There were no other late major complications.

Table 17. Characteristics of hybrid procedure and related morbidity. Landing zone of stent-graft by aortic arch map proposed by Ishimaru.

Patient no.	1	2	3	4	5	6	7	8	9	10
Procedure	1-stage	1-stage	1-stage	1-stage	1-stage	1-stage	1-stage	1-stage	2-stage	2-stage
Number of revascularized visceral arteries	3	2	4	4	4	4	4	4	4	4
Landing zone of stent-graft	3	4	4	4	3	3	3	4	4	4
Previous aortic repair	yes	no	no	no	yes	no	yes	no	yes	no
Simultaneous open repair of infrarenal aorta	no	yes	no	yes	no	yes	yes	yes	no	no
Operation time (min)	540	465	440	500	475	515	470	315	450+95	480+85
Max. CSF pressure (mmHg)	>20	<15	<15	22	>20	20	14	25	20	-
CSF drainage	yes	no	no	yes	yes	yes	yes	yes	yes	no
Postop. paresis	transient	no	no	transient	transient	permanent	transient	no	no	no
Preop. Creatinine ( $\mu\text{mol/l}$ )	50	162	39	100	74	101	73	73	118	55
Postop. Creatinine ( $\mu\text{mol/l}$ )	45	132	41	104	141	309	244	338	99	104
Postop. dialysis	temporary	no	no	no	no	temporary	temporary	no	no	no

Table 18. Summary of the follow-up and outcome of TAAA patients treated with a hybrid procedure.

Patient no.	Complication	Secondary graft-related interventions	Interval between primary and secondary procedure (months)	Follow-up time (months)	Outcome
1	Endoleak I due to stent-graft migration	Endovascular stent-graft placement	10	26	died (ICH)
2				133	Alive
3				44	died (pulmonal cancer)
4				91	Alive
5	Endoleak II, Endoleak III	Embolization attempt twice, endovascular stent-graft placement	16, 17 49	78	Alive
6				4	died (ischaemic colitis)
7				33	died (complications related to oesophagus perforation)
8				61	Alive
9	Endoleak II	Coil embolization	26	36	Alive
10	Renal graft thrombosis	Thrombolysis	1	35	Alive
<b>Median</b>			<b>17</b>	<b>55</b>	

Two cases of type II endoleak were noted in follow-up at 14 and 25 months after the initial procedure. In the first case, embolization was attempted twice, but as the aneurysm showed shrinkage, further procedures were abstained from. The second patient was successfully treated by means of coil embolization. There was one type I endoleak due to stent-graft migration at 10 months, and it was successfully treated with an additional stent-graft. One case of type III endoleak was also successfully treated with an additional stent-graft at 49 months (Table 18). In long-term surveillance, 90% of the aneurysms showed a decrease in diameter of a mean of 23 mm (range 7–45 mm).

## 6 DISCUSSION

### 6.1 General aspects

Since the advent of EVAR, it has been increasingly used to treat AAAs, and it has currently replaced open repair for the majority of patients. EVAR was originally developed to offer a less-invasive treatment for patients with multiple co-morbidities. The short-term results were promising, and the technique fulfilled the expectations placed on it: less surgical trauma, less blood loss, a shorter ICU stay, lower mortality and faster recovery. There was great enthusiasm for this new method of treatment, and soon all AAA patients were seen as candidates for endovascular repair, if anatomically suitable. There are early reports where most of the patients were classified even in ASA 1–2 (Becquemin et al. 1999). In follow-up, after reports of cumulating adverse events, more attention was paid to patient selection: EVAR was no longer offered to patients with low operative risk and long life-expectancy. This also led to the fast development of new, more durable stent-grafts, i.e. second-generation stent-grafts. They were expected to overcome the problems after the disappointing results with first-generation stent-grafts.

As the endovascular technology reached the threshold for the treatment of more complex infrarenal aortic aneurysms, its application was quickly extended to the thoracic aorta. The aortic arch is a specific challenge for endovascular repair, which mainly arises from high blood flow, the involvement of the supra-aortic branches and the tight inner curve. The endovascular technique was further deployed in a variety of thoracic aortic pathologies, not only aneurysms, and at present TEVAR is recommended as a first-line therapy in emergency settings (Erbel et al. 2014). Hybrid repair, a combination of open and endovascular techniques, was introduced as a less-invasive method for treating complex TAAAs.

### 6.2 Long-term results of EVAR using the first-generation Vanguard® stent-graft

In the present study, the primary technical success rate was excellent, with no primary conversions and a 30-day mortality of 0%. The problems, however, were detected in surveillance as 90% of the patients experienced a graft-related complication. The most

alarming graft complications, type III endoleak and row separation, which imply corruption of the stent-graft, were observed in 21% and 46% of the patients, respectively. The main target, the exclusion of the aneurysm from the circulation also, failed as 56% of the patients developed an endoleak and 33% of the grafts migrated during surveillance. The stent-graft was withdrawn from the market because of these problems, but all complications led to a major follow-up protocol and multiple secondary procedures during the follow-up that lasted years after the primary procedure. There is always a risk when a new technology is applied into practice, but experiences with the first-generation stent-grafts have caused some insecurity even though the devices and the technique have evolved. Life-long surveillance is still recommended for all EVAR patients (Moll et al. 2011). An endoleak has remained the long-term problem of EVAR, even though the graft-related complications observed earlier, such as row separation and migration, are mainly related to older stent-grafts.

The total number of complications detected in the present study was high, but the follow-up was well-planned in advance and there was complete compliance with the surveillance protocol. This might have resulted in a high number of detected problems as well as early treatment thereof. Many available reports lack a systematic follow-up, and a number of patients are lost to follow-up (Antoniou et al. 2015). In the current study, the re-intervention-free survival at two years was already as low as 54% in contrast to the French Vanguard trial with a two-year re-intervention-free survival of 67% (Becquemin et al. 1999). Interestingly, complications and re-interventions also became rare after five years in the current study, but this could be explained by previous additional procedures with a new device providing durability for the primary stent-graft. Shrinkage of the aneurysm sac over the years may also have affected this phenomenon. Despite high rate of complications, AAA ruptures were sparse.

Even though the complications of EVAR appeared soon, there was scant data on how they should be treated. A conversion to open repair has been classified as a clinical failure of EVAR. The perioperative mortality rate among patients with a conversion is reported to be as high as 22%–24% in the EUROSTAR registry and, in the most recent systematic review, 29% among emergency cases and 3.2% in elective cases (Harris et al. 2000, Kouvelos et al. 2015). From the perspective of the complication and re-intervention rate in the current study (90% and 81%, respectively), the number of conversions to open repair was low. This was partly because the patients were considered poor candidates for open repair preoperatively, but mainly because we preferred the endovascular approach for detected complications and the threshold for elective conversion was high. This approach led to multiple repeated endovascular procedures and, eventually, ten late conversions (21%). Seven of these conversions were elective and there were no deaths among these patients. In addition, multiple endovascular secondary procedures led to only one severe complication (kidney failure requiring permanent dialysis) and no deaths. Our results show a higher rate of secondary procedures in mid-term follow-up than what is reported in another Finnish study (Aho et al. 2002). This is mostly explained by a different approach to complications



as the endovascular technique was used repeatedly to avoid open conversion (Aho et al. 2005). Our problems with first-generation stent-grafts trained us to understand the significance of different types of complications and the approach that should be adopted to manage them. Furthermore, the most important lesson from our findings is that a new technology can always cause unpredictable problems which can magnify the workload and incur substantial costs over several years after the initial procedure.

The initial expected operative and short-term superiority over OR was achieved with this first-generation stent-graft. Also, despite the number of re-interventions, the survival rate was acceptable, 69% and 44% at five and nine years, respectively, and comparable with other reported survival rate with Vanguard® (six year survival 57%) (van Herzele et al. 2008).

### 6.3 Long-term results of EVAR using the second-generation Zenith® stent-graft

The reported results regarding second-generation stent-grafts are strongly affected by experiences with first-generation stent-grafts similar to our study. Patients treated with a Zenith® stent-graft had more co-morbidities and the follow-up protocols changed even during the study period with increasing experience and updated knowledge. In the surveillance protocol, CDUS replaced most of the CTA controls. The approach to a type II endoleak became less aggressive, and, at later phase in this study, they were treated if the size of aneurysm increased. An open IMA was also always embolized if open prior to stent-graft placement in the primary procedure to reduce the risk of a type II endoleak. Furthermore, the expertise of the team as well as imaging methods have improved during the study years, possibly impacting on the results. The Zenith® stent-graft also changed and improved over the time without the name of the system being changed, and these differences in the types of the same stent-graft have not been considered in any study, but obviously there have been improvements in the stent-graft system.

In the present study, the 30-day mortality rate was 1.4%. Considering these patients' co-morbidities, the rate is low. It is also in accordance with another Zenith®-study and reported randomized trials (EVAR trial participants 2005a, Blankensteijn et al. 2005, Bos et al. 2008, Lederle et al. 2009). The complication rate was 38%, and the most common complication was an endoleak (33%), especially of type II (26%). As mentioned, 78% of the type II endoleaks either sealed spontaneously or showed no aneurysm expansion and, therefore, required no further procedures. Other complications were uncommon as previously reported with Zenith® stent-grafts (Greenberg et al. 2008). A review article from the same study period showed a re-intervention-free rate of 72% at 7 years (Nordon et al. 2010). Our study demonstrates somewhat better results, with a rate of 76% at 7 years. Open repair of an AAA is associated with secondary-procedure-freedom rates of 94–98% at five

years and 88–94% at ten years (Biancari et al. 2002, Conrad et al. 2007). Even though these rates are lower in EVAR, the need for secondary interventions in this high-risk population is reasonable and usually safe. It is likely that, with the current understanding and management of complications, these re-intervention rates would today be even lower, approaching the numbers of open repair. Either way, the prosthesis turned out to be durable and the aneurysm-related mortality was only 0.7%.

The unique feature in this study was that nearly all (87%) complications appeared within the first three years of surveillance and, after five years, they became practically non-existent (Greenberg et al. 2008, Nordon et al. 2010). Nearly all endoleaks (93%) appeared within a period of three years. Even though IMA was successfully embolized in 78% of the cases, a type II endoleak was still the most common complication. Furthermore, its treatment became more liberal as the study proceeded, and most of the additional procedures were still due to persistent type II endoleak, comprising up to two thirds of all re-interventions in our series. Perioperative IMA embolization and treatment has recently polarised the specialists' opinions (Biancari et al. 2015). Also, most of the additional procedures were performed within the first four years and none after six years. This finding suggests that life-long surveillance might not be necessary for all patients, and surveillance could be limited to five years in patients with no complications in early follow-up. Moreover, it has been shown that surveillance scans alone lead to an additional procedure in 1.4–9% of the cases, and over 90% of the patients receive no benefit from control examinations (Lederle et al. 2009, Dias et al. 2009). Another notable detail is that complications had no negative effect on overall survival in the current series. Furthermore, US-based surveillance has shown no negative effects on aneurysm-related survival, and US is suggested for long-term follow-up for patients with no early endoleaks (Greenberg et al. 2008, Bargellini et al. 2009, Sternbergh et al. 2008). We have adopted a similar long-term surveillance scheme.

The data for the Zenith® study was collected at a time when different new stent-grafts were being adopted in a short time span. The enthusiasm towards a new technology led to a liberal use of stent-grafts in various anatomical configurations, and the instructions for use (IFU) for a particular device were not necessarily followed, making it difficult to assess whether adherence to the device's IFU affected the rate of complications. This makes the interpretation and comparison of the results troublesome. It has also been suggested that registries tend to overestimate the better outcome of the newly introduced treatment and that randomized trials therefore yield the only viable information. Still, findings from non-randomized long-term studies on EVAR have implied that the early advantages of endovascular treatment vs. open repair may not persist over time (Lederle et al. 2012, Schermerhorn et al. 2015).

The first randomized trial comparing open and endovascular treatment was the UK EVAR Trial 1. It showed a 3% reduction in aneurysm-related mortality even though there was no difference in all-cause mortality. EVAR was also more expensive and led to a greater number of complications in follow-up. Further, the EVAR Trial 2 compared EVAR and

conservatively treated patients and it also showed significantly lower aneurysm-related mortality in the EVAR group ( $p=0.02$ ), although, the study further discovered that EVAR does not lower the all-cause mortality when compared to conservative treatment (EVAR trial participants 2005b, 2010). This is probably explained by the fact that EVAR was originally developed for patients who were evaluated unfit for OR and life-expectancy among these patients was therefore not long in the first place. The survival rate at five years was 48% in the UK EVAR trials, which is in line with our rate (52%), but our rate is somewhat lower than in other Zenith® studies (Bos et al. 2008, Greenberg et al. 2008, EVAR trial participants 2010). It might be explained by the higher mean age and higher prevalence of coronary heart disease in the current study.

The DREAM trial was a randomized trial comparing EVAR and open repair in patients who were considered suitable for both types of treatment. EVAR demonstrated a 3.4% reduction in perioperative mortality, but, after two years, the perioperative survival advantage was not sustained. Also, there was a trend toward reduced aneurysm-related death in the EVAR group (2.1% EVAR vs. 5.7% OR,  $p=0.05$ ), but this difference was not statistically significant. In long-term surveillance of up to six years, the cumulative survival rates were similar: 69.9% for open repair and 68.9% for EVAR. The rate of secondary interventions was significantly higher for EVAR. The cumulative rates of freedom from secondary interventions were 81.9% for OR and 70.4% for EVAR (Blankensteijn et al. 2005).

The ACE trial consisted of low- and moderate-risk patients and produced similar findings – there was no difference in the cumulative survival rates between open repair and EVAR. However, EVAR was associated with more re-interventions and a trend towards higher aneurysm-related mortality (Becquemin et al. 2011).

The good short-term results also seem to transfer to the long-term as the stent-grafts, imaging, knowledge of possible complications and reinterventions, as well as the surgeons' expertise have increased. Still, the overall benefits of EVAR will not be seen until the upcoming years.

## 6.4 Long-term results of TEVAR in TAAs and type B dissections

There are no randomized controlled studies comparing TEVAR with open surgery among TAA patients. Based on multiple series, TEVAR has proven to be an excellent alternative to open surgery in anatomically suitable candidates. In the current study, the 30-day mortality was low for both elective (5.6%) and emergency cases (8.3%). Especially emergency patients did well also compared to other studies, despite the fact that 71% of them were treated due to an aortic rupture (Saari et al. 2013, Jonker et al. 2010).

Despite the excellent short-term results of TEVAR, there is less data of long-term results compared to EVAR. In contrast to AAA, patients with an open-repaired TAA surprisingly have similar or even higher rates of secondary procedures compared to patients

who undergo endovascular repair, and this difference is predominately related to wound complications. There are also continuously new problems related to open surgical TAA repair months and years after the original surgery (Stone et al. 2006). The significant perioperative advantages of TEVAR have been proven to persist for more than five years after the operation (Makaroun et al. 2008). In the current study, only one aneurysm rupture occurred in long-term surveillance (1.3%). The number of secondary procedures in surveillance was also acceptable as only 22% of the patients required an additional procedure after the hospitalization. The overall survival rate was high considering these patients' comorbidities (85%, 78%, 62%, and 57% at 1, 3, 5 and 8 years, respectively). A recent meta-analysis shows similar three-year survival (74%) for TAAs treated with TEVAR (Biancari et al. 2016). Reported survival rates with mixed aorta pathologies (TAA, dissection, PAU) are also similar (5- and 10-years rates, 63-79% and 44%, respectively) (Wiedemann et al. 2013, Scali et al. 2014). Patients treated for TAA are usually older than those with a dissection or traumatic aortic rupture and they are also mainly treated in an elective setting making comparison difficult.

Another feature of TEVAR is that, in contrast to endoleaks seen after EVAR, the endoleaks after TEVAR are predominately of type I, as was also seen in our study (Makaroun et al. 2008). Therefore, the overall rate of endoleaks is also lower in TEVAR than in EVAR, but the rate of type I endoleaks is a reminder to be reasonable in patient selection, aware of careful follow-up and aggressive in treatment when appropriate. Our study showed a high incidence of type I endoleaks, but no predictive factors for its development were found. In most of the cases with a primary type I endoleak, there were some kind of issues with the release of the stent-graft or minor migration from the planned proximal landing zone. These findings confirm that the aortic arch is technically the most challenging area for endografting. The development of more flexible stent-grafts may help prevent some cases of type IA endoleak. Also, the current valid techniques, such as rapid pacing, was not used in TAAH at the time of the study. The high incidence may also be explained by the fact that, at the beginning of the study, the first CTA was conducted already 2 or 3 days after the procedure and, if a minor type I endoleak was discovered, it was, as a rule, left without treatment at this point. To support this idea, only three endoleaks were discovered after the revision in the follow-up protocol that was made in 2010. However, it has been observed that a type I endoleak after TEVAR does not necessarily have the same significance as after EVAR (Parmer et al. 2006, Alsac et al. 2011, Boufi et al. 2014). This was also true in our study as a third of the primary type I endoleaks sealed spontaneously and, overall, only 57% of the type I endoleaks were treated.

Like with EVAR, we also found that in TEVAR, graft-related problems and additional procedures accumulated in the early phases of the surveillance as 84% of the additional procedures were performed during the first two years of the follow-up. This indicates that, after uncomplicated early surveillance, the follow-up CTA controls could be infrequent.

Achieving proximal and distal landing zones of sufficient length is essential for the successful exclusion of a thoracic aorta lesion. The proximal landing zone is often limited by the origins of supra-aortic vessels, and many aorta pathologies are close to or involve the left subclavian artery (LSA), requiring coverage of its origin by a stent-graft. Although associations between LSA coverage and perioperative adverse neurologic events have been identified in multiple studies, it is not clear that routine revascularization would result in a reduction in perioperative stroke and SCI complications (Kotelis et al. 2009, Buth et al. 2007, Cooper et al. 2009, Riesenman et al. 2007). Also, in the current study, one in five patients with preoperative revascularization of the LSA had a postoperative stroke.

The incidence of permanent neurological events in the current study was similar (CVE 7.7% and permanent paraparesis 2.6%) to other reports (Buth et al. 2007, Cooper et al. 2009). All patients who developed spinal cord symptoms received cerebrospinal fluid drainage shortly after onset and were monitored in the ICU. An additional two (2.6%) patients had transient symptoms that resolved with spinal drainage, and the premeditated protocol probably saved them from a permanent neurological defect. In the current study, the treated pathology, previous or simultaneous AAA repair, LSA coverage or number of stent-grafts used did not correlate with SCI and CVE rates, but emergency treated patients had significantly more CVEs ( $p=0.048$ ). This is probably explained by technical difficulties and possible hypotension related to the emergency setting in addition to a lack of preoperative brain CTA. Since 2010, all elective patients with planned LSA coverage underwent preoperative CTA in order to evaluate the supra-aortic vascular anatomy and *Circulus Willisii*. Consequently, if the left vertebral artery was considered dominant and/or there was any doubt concerning the condition of the basilar or communicating arteries, the LSA was revascularized. This seems to be the current approach in many institutions, although reconstruction of the LSA is still recommended prior the stent-graft placement (Matsumura et al. 2010, Ameli-Renani et al. 2015). After adopting this new protocol, there have been no postoperative CVE complications and no need for late bypass procedures due to symptoms, and we plan to continue with this approach.

Since the first case report by Dake on TEVAR in elective aortic dissections, the technique has undergone a dramatic expansion and has become accepted as the first-line treatment in acute type B dissections as well (Dake et al. 1999, Erbel et al. 2014). Single-centre studies and a meta-analysis have reported early mortality rates of 10–25% and two- and three-year survival rates of 60–73% in acute type B dissection after TEVAR (Eggebrech et al. 2006, Parsa et al. 2010, Verhoye et al. 2008, Criado et al. 2005). Our study comprised only 16 cases of acute complicated type B dissections, and among these, the 30-day mortality rate was only 6.3%. In comparison to the results of open repair in the acute phase with mortality rates of 10–50%, there is no doubt about TEVAR's benefits.

The treatment of a type B dissection currently focuses on care in the acute phase of an uncomplicated type B dissection – whether it should be actively treated by endovascular means or only medically. Traditionally, stable patients are managed with medical treatment,

with an annual survival of over 80%, but as many as 25–30% of these patients require later interventions (Erbel et al. 2001, Suzuki et al. 2003, 2012). In an acute dissection, the stent-graft depressurises the false lumen, causing the thrombosis of the false lumen and remodelling of the dissected aorta, likely reducing need for later procedures. It is still unclear whether this positive remodelling further causes a reduction in long-term mortality sufficient to balance the early perioperative risks related to TEVAR.

The INSTEAD trial was the first randomized trial comparing TEVAR and medical therapy in the management of acute and subacute uncomplicated type B dissections (Nienaber et al. 2009). The pre-emptive TEVAR was associated with an excess early mortality, but the procedure turned beneficial at five years. It showed lower all-cause mortality (11.1% vs. 19.3%,  $p=0.13$ ), aorta-specific mortality (6.9% vs. 19.3%,  $p=0.04$ ) and aortic progression (27.0% vs. 46.1%,  $p=0.04$ ) compared to medical therapy. However, the study sample size was too small to make strict guidelines, and the overall benefits remain to be demonstrated. Also, the International Registry of Acute Aortic Dissection (IRAD) showed that patients undergoing TEVAR have a lower death rate (15.5% v. 29.0%,  $p=0.018$ ) at five years (Fattori et al. 2013). Another of the latest randomized trials, the ADSORB-trial, focused on patients with acute uncomplicated type B dissection and showed better aortic remodeling at one year, but there was no statistical difference in overall mortality as there was only one death in the TEVAR group (Brunkwall et al. 2014). In both randomized trials, the patient sample was small, and larger randomized trials with longer follow-up are required. In the future, TEVAR may emerge as the first-line therapy for uncomplicated type B dissections. The attempt to heal and remodel the dissected aorta may replace the current complication-specific strategy. However, the timing of therapy still remains undefined. It has been suggested that the dissecting membrane is fragile in the acute phase and an intervention in the subacute phase would be safer because of the stabilization of the intimal flap (Steuer et al. 2013).

Our study consisted only of complicated acute type B dissections and the uncomplicated ones were treated only medically during the study years.

## 6.5 Results of hybrid repair

Various surgical techniques have been adopted for treating TAAA, but the perioperative complications remain substantial. Open repair of a TAAA carries a reported 5–10% overall risk of paraplegia and 5–20% 30-day mortality risk even in the most successful series from high-volume centres (Coselli et al. 2007, Schepens et al. 2009, Rigberg et al. 2006). Most of the reported series of hybrid repair are single-institution studies with varying early and mid-term results, but the data indicates that the hybrid approach is a reasonable option for high-risk patients. Our study shows similar acceptable results expressed by the primary technical success (100%), SCI (10%) and renal failure requiring permanent dialysis (0%), but the 30-day mortality rate (0%) in our series was exceptionally low (van de Mortel et al.



2008, Biasi et al. 2009, Donas et al. 2009, Moulakakis et al. 2012). Again, an additional four patients suffered from transient lower extremity paresis which resolved with spinal fluid drainage. Furthermore, overall, 70% of the patients underwent CSF drainage as the CSF pressure exceeded 15 mmHg.

However, no long-term data exist to ascertain the durability of this method. An important determinant for the late success is bypass graft patency. In our study, only one of the 37 grafts was occluded, and it was also successfully opened with thrombolysis. The reported bypass graft patency rates (89–100%) are similar to ours (97%) (Farber et al. 2009, Donas et al. 2009, Quiñones-Baldrich et al. 2009, Moulakakis et al. 2012).

One of the unanswered questions relating to the hybrid procedure is also whether to operate as a single procedure or a two-stage procedure. One view is that, after an extensive intra-abdominal dissection, the patient should not immediately undergo stent-grafting due to an increased risk of perioperative complications associated with contrast agent use and prolongation of the procedure. However, single-stage surgery minimises access site-related complications because the stent-graft can be transferred directly into the aorta or iliac vessels. In contrast, in a two-stage procedure, there is a risk of interval rupture (Drinkwater et al. 2009). Furthermore, staged procedures have been shown to reduce the risk of SCI in open surgical and hybrid repair, and it is possibly explained by the vascular remodelling stimulation after the first intervention. Also, clinical studies of open and endovascular repair have documented a significant correlation of renal function and SCI injury, implying further higher risks of SCI in a one-stage procedure (Buth et al. 2007, Coselli et al. 2000). The underlying metabolic mechanism is not exactly known. The existing evidence comprises mostly of single-centre reports with small sample sizes, and current data is insufficient to support uniform recommendations, although there is the impression that a staged procedure is safer despite lacking statistical proof. Due to these reports, the last two patients in the current series were treated in two stages. The planned interval was two weeks, but it was prolonged due to treatment-related reasons. Fortunately, there was no rupture during the interval, and the second procedure was carried out successfully in both cases. Moreover, neither of these cases developed postoperative SCI or renal injury.

Further research is required to consolidate the outcomes of this treatment and define its role in the management of TAAA, but the fast evolution of the total endovascular technique may surpass this method in the near future before larger studies become available. Patient selection and careful preoperative planning are crucial to the success of both approaches.

## 6.6 Future prospects

It is becoming evident that the technological development of aortic stent-grafts has now enabled the treatment of the vast majority of aortic pathologies. Some areas, such as infrarenal EVAR and descending TEVAR, are more mature than others with regard to long-term outcomes, but data on even more complex treatments is accumulating and we

are beginning to have more specific treatment options. Furthermore, the understanding of the natural history of aortic diseases is increasing, affecting their treatment. Especially, the treatment and its timing of uncomplicated type B dissection, is less than clear-cut at the moment. In addition, the potential risks related to the contrast agent and radiation that are necessary for the successful practice of endovascular repair are currently more studied than in the beginning of the endovascular era. With more challenging aortic repairs, the use of radiation and contrast tend to increase. As the radiation effect is cumulative, the significance to the operators and staff is generally greater than to the patient. To overcome these disadvantages, further development not only in endovascular repair but in the imaging options is required. Still, endovascular repair can probably never completely replace open surgical repair. The problems encountered with endovascular repair may, in some cases, be amendable only with open repair.

## 6.7 Limitations of the present study

The retrospective nature is a limitation of the study, although the data was collected from a prospective database. The number of patients was small in Study I, but it was limited due to device-related reasons. In Study III, two major patient groups were mixed, dissections and thoracic aortic aneurysms, but the aim was to evaluate the technique's durability and not the prognosis of the disease. Study IV included only ten patients and it is impossible to draw any larger conclusions based on such a small patient group. However, the results draw a picture of the possibilities of combining open and endovascular procedures and support the use of a hybrid technique also in these rare entities.



## 7 SUMMARY AND CONCLUSIONS

1. The first-generation stent-graft Vanguard® was associated with a high number of complications, but most of them were successfully treated with the endovascular technique. The problems encountered with this stent-graft yielded valuable information about complications and their treatment options. As a drawback, the problems revealed a possible need for a life-long surveillance of EVAR patients.
2. The second-generation stent-graft Zenith® was associated with a lower number of complications, but especially endoleaks remained the long-term problem of EVAR, resulting in repeated re-interventions after the primary procedure. The results were partly affected by experiences with first-generation stent-grafts in regard to patient selection, surveillance protocol, imaging modalities and expertise. Complications and secondary procedures accumulated in the early stages of follow-up. After five years complications became practically non-existent and, after five years, follow-up may not be needed for all patients.
3. TEVAR is a viable treatment modality for patients with a TAA or type B dissection. The short-term results are good, and they also persist in the long term. Most of the complications appear soon after the primary procedure. An emergency setting significantly increases the risk for CVE. LSA coverage does not seem to significantly increase the risk of SCI or CVE.
4. Hybrid repair of a TAAA seems to be an advisable treatment modality for high-risk patients and a low number of complications in both the short and the long term were found in the current study.

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**AAA ENDOGRAFT- seurantalomake**

Potilasnumero:

Nimi:

Henkilötunnus:

Ikä:

Sukupuoli:

FV-riskipisteet:

Riskitekijät:

Tulopäivä:

Toimenpidepäivä:

Kotiutus:

Kuolinpäivä:

Kuolinsyy:

AAA:

Tyyppi:

Halkaisija:

Kaulaosuus: 1) pituus:

2) halkaisija:

3) laatu:

1= ei riskitekijöitä

2= diabetes

3= hyperkolesterolemia

4= hypertonia

5= CHD

6= neurologinen

7= pulmonaalinen

8= renaalinen

9= aik. rekonstruktio tai amputaatio

10= tupakointi 5 vuoden sisällä

IMA:

**TOIMENPIDE:**

Anestesia:

Toimenpideaika:

Läpivalaisuaika:

Varjoainemäärä:

IMA/ IIA embolisatio:

Konversio (1=kyllä, 2=ei):

**PROTEESI:**

Nimi:

Koodit:

Lahkeet:

proksimaalisen pään halkaisija:

lahkeen halkaisija:

**KOMPLIKAATIOT:****1. endoleak**

tyyppi:

ajankohta:

**2. tromboosi**

ajankohta:

**3. kinking**

tyyppi:

ajankohta:

**4. dissekoituma****5. migraatio**

ajankohta:

**6. row separation**

ajankohta:

**7. endotensio**

ajankohta:

**SEURANTA:**

aneurysman koon muutos:

aneurysma koko:

1. 2-3vrk

2. 1kk

3. 3kk

4. 6kk

5. 12kk

6. 24kk

7. 36kk

8. 48kk

9. 60kk

10. 72kk

**Lisätoimenpiteet:**

**TAA ENDOGRAFT-seurantalomake**

Potilasnumero:

Nimi:

Henkilötunnus:

Ikä:

Sukupuoli:

Riskitekijät:

Riskipisteet:

Tulopäivä: Toimenpidepäivä: Kotiutus:

Päivystystoimenpide:

Indikaatio: Halkaisija:

Kuolinpäivä: Kuolinsyy:

1= ei riskitekijöitä

2= diabetes

3= hyperkolesterolemia

4= hypertonia

5= CHD

6= neurologinen

7= pulmonaalinen

8= renaalinen

9= aik. rekonstruktio tai amputaatio

10= tupakointi 5 vuoden sisällä

1= degeneratiivinen aneurysma (a.stabiili, b. rupturoitunut)

2= dissektio

3= pseudoaneurysma

**ANATOMIA JA TOIMENPIDETIEDOT:**

Lokaloisaatio: 1=laskeva torakaaliaortta, 2=aortan kaari (a.itsenäinen, b osana laskevan aortan aneurysmaa), 3=torakoabdominaalinen

Stenttityyppi:

Käytettyjen stenttien lkm:

Aortan kaaren suurten suonien peittäminen:

Subclavia l. sin.

Carotis l. sin.

Truncus brachiocephalicus

Liitännäistoimenpiteet:

Endovaskulaarinen

Kirurginen

\* eksta-anatominen ohitus

\* hybridi

**MORTALITEETTI JA KOMPLIKAATIOT:**Intraoperatiiviset komplikaatiot: kyllä/ei

a) stenttigrafit ei saa vietyä paikalleen

b) stenttigrafit ei avaudu

c) graftin laukaisu vääriin paikkaan

d) grafti obstruo aortan

e) aortan seinämän vaurio

f) vuoto

g) exitus

Postoperatiiviset komplikaatiot: kyllä/ei

a) neurologiset

\* paraplegia/pareesi

\* stroke

b) sydänperäiset:

\* AMI

\* vajaatoiminta

c) respiratoriset

d) dialyysi

e) aortan ruptuura

f) exitus

Lisätoimenpiteet (30vrk):

**SEURANTA:**

aneurysman koon muutos:

aneurysma koko:

1. 2-3vrk

2.

3.

Endoleak:

Tyyppi:

Ajankohta:

Aorttaruptuura:

**Muu komplikaatio:****Lisätoimenpiteet:**



## ORIGINAL PUBLICATIONS



## TEN-YEAR OUTCOMES AFTER ENDOVASCULAR ANEURYSM REPAIR (EVAR) AND MAGNITUDE OF ADDITIONAL PROCEDURES

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### ABSTRACT

**Background and Aims:** With any new technology complications are possible, and problems with first-generation aortic stentgrafts have been extensively reported. The long-term outcome of this patient population and the magnitude of additional secondary procedures are, however, less well covered.

**Materials and Methods:** Between February 1997 and November 1999, 48 patients (44 men and 4 women; mean age 70 years; range 54–85) with AAA (average 57mm, range 40–90mm) were treated with a Vanguard® endoprosthesis. Stentgrafts were sized by CT and angiography-based measurements. Results were continuously assessed using contrast-enhanced CT before discharge, 1, 3, 6 and 12 months after the procedure and thereafter annually. Since 2001 plain abdominal X-rays have been performed annually.

**Results:** The technical implant success rate was 100%. Median follow-up was 91 months (range 7.6–120 months). None of the patients was lost during this period. Hospital mortality was 0%. There were 25 subsequent deaths (52%), the most common cause being coronary artery disease. There were ten late conversions to open surgical repair, including three emergency operations: two due to rupture and one to thrombosis. EVAR-related complications were encountered in 43 patients (90%): 12 primary endoleaks (all type II), 36 late endoleaks (16 type I, 2 type II and 18 type III), 22 migrations, 25 row separations, 20 thromboses, one endotension and 3 ruptures of the AAA. Secondary procedures were required in 39 patients (81%): 1 re-endografting by aortoiliac bifurcated graft and 3 with a uni-iliac graft; 33 limb graft repairs were performed and 19 infrarenal cuffs were placed. There were 4 late embolizations and 4 attempts, and 6 thrombolyses, four of which were successful. Further, 9 femoro-femoral crossover by-pass and 2 axillo-femoral by-pass operations and 2 amputations were carried out during the follow-up. Only one patient was alive without complications.

**Conclusions:** The impact of long-term follow-up of patients treated with the new technology was emphasized in this patient population. A careful surveillance protocol and active endovascular treatment of complications can yield acceptable results and low AAA

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**rupture and aneurysm mortality rates, also with the first-generation endovascular graft. A new technology, however, may involve unpredictable problems which can magnify the workload and incur high costs over several years after the initial procedure.**

**Key words:** Abdominal aortic aneurysm; endovascular repair; long-term outcome; complications; migration; endoleak; secondary interventions

## INTRODUCTION

During the last decade endovascular aneurysm repair (EVAR) has gained wide acceptance in the treatment of abdominal aortic aneurysm (AAA). The less invasive endoluminal exclusion which can be achieved without a major abdominal operation has many advantages. Endovascular repair offers less prolonged surgery, superior hemodynamic stability, less blood loss, fewer severe complications and shorter hospital stay (1–6). However, while early postoperative morbidity and mortality rates are low in EVAR, problems have been encountered with graft durability. According to the available literature, endovascular devices are associated with a relatively high rate of complications during mid-term follow-up, culminating in a frequent need for secondary procedures, including open surgical repair (3, 7–11). Long-term results are, however, as yet obscure and advantages must be assessed against the risk of further procedures, increased costs and outcome in the long term.

The most frequent mechanism of failure after EVAR is the occurrence of an endoleak. Other well-known graft-related complications include row separation, migration and thrombosis. There is common consensus as to which complications require treatment, but there are scant of data regarding how they should be treated. For example, type I and III endoleaks and migration involve a significantly greater risk of rupture and require treatment, whereas type II endoleak and endotension divide opinions (9, 12–18).

The Vanguard® endoluminal aortic graft was a derived, improved version of the Stentor® system. It was taken into worldwide use in 1997, but was withdrawn from the market in November 1999 after several reports of fractures of polypropylene sutures and nitinol stents. After the release of warnings of this alarming complication numerous cases of row separation in patients treated with the Vanguard®-endoprosthesis were found.

The purpose of this prospective follow-up study was to assess the magnitude of additional procedures and the overall outcome of patients treated with a first-generation EVAR device, Vanguard®, over a ten-year period.

## MATERIAL AND METHODS

From February 1997 to November 1999 48 patients, 44 men and 4 women, with a mean age of 70 years (range 54 to 85), were treated for a non-ruptured AAA with a Vanguard® endoprosthesis in Tampere University Hospital. Patients were continuously followed up to February 2007.

The indication for the initial procedure was an AAA diameter over 55 mm in men and 50 mm in women. Patients with an increase in AAA diameter of more than 5 mm over a period of 6 months were likewise treated. According to the endovascular protocol and surveillance program, plain radiographs, spiral CT and angiography were performed before surgery to identify patients suitable for EVAR. Criteria for the infrarenal neck were a minimum length of 10 mm and less than 60 degrees angulation. Criteria for iliac arteries were an angulation of less than 90 degrees. Procedures were undertaken by the same vascular surgeon and interventional radiologist in the angiography suite. General anesthesia was used in the first 12 cases and spinal anesthesia in the last 36. Follow-up CT scans were obtained postoperatively on the 2nd or 3rd day, 1, 3, 6 and 12 months and annually thereafter. CT scans were contrast-enhanced 5-mm-thick sections through the endograft. Angiography was done six months after the treatment and also when graft-related complications were suspected. Since 2001 plain abdominal X-rays have also been taken annually.

At the beginning of the follow-up the maximum diameter of the aneurysm was measured from the axial sections in the first postoperative CT scan two or three days postoperatively. The mean diameter of the AAA was 57 mm at the time of treatment (range 40 to 90 mm). Length of neck was defined as the distance between the most caudal renal artery and the upper aneurysm sac border in the preoperative CT scan. The average length of the neck was 27 mm (range 5 to 65 mm). Of all aneurysms 60% (n=29) were type B, 33% (n=16) type C, 4% (n=2) type A and there was only one patient with type D.

Primary outcomes were technical success during implantation, 30-day mortality, aneurysm rupture, aneurysm-related and all-cause mortality and surgical conversion. Secondary endpoints were endoleak, row separation, migration, thrombosis and secondary procedures. The descriptive analysis of this study was performed using Microsoft Excel-program®.

## RESULTS

### PRIMARY OUTCOME MEASURES

The technical implant success rate was 100%. The median follow-up was 91 months (range, 7.6–120 months), during which time none of the patients was lost.

### Mortality

Thirty-day mortality was 0%. Subsequent deaths (n=25, 52%) were caused by coronary artery disease (n=9, 19%), cancer (n=6, 13%), respiratory disease (n=2, 4%), intracerebral hemorrhage (n=2, 4%), AAA rupture (n=2, 4%) and other (n=4, 8%). All-cause mortality and survival are presented in Fig. 1.

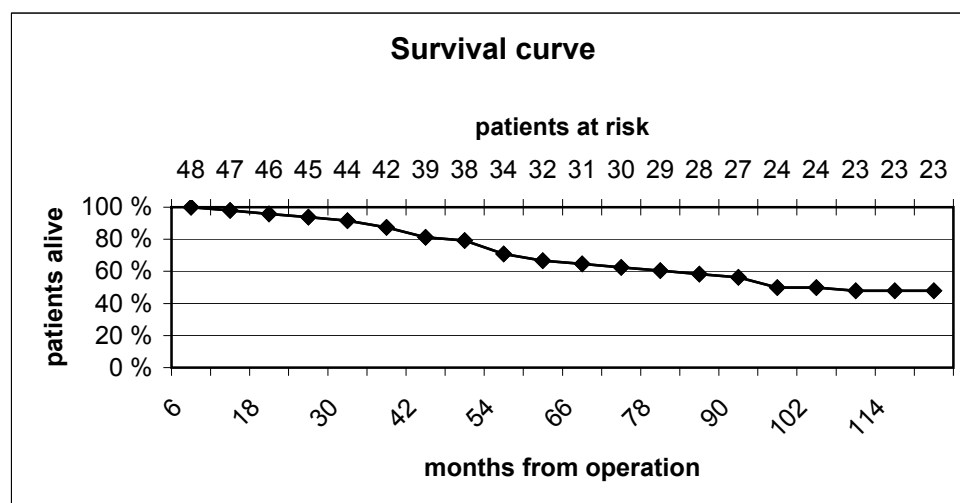


Fig. 1. Survival curve of patients with AAA treated with Vanguard endoprosthesis.

### AAA-related death and rupture

There were three AAA ruptures and two resulted in death. The first occurred after 48 months due to the development of a type III endoleak. The patient in question died in the emergency room. The second patient developed a rupture at 53 months due to migration and endoleak type III. He was successfully treated by emergency open repair. At 62 months the development of row separation and a type I endoleak caused an AAA rupture in a third patient. He was immediately transferred to the operation theatre for open repair, but died during the operation.

### Surgical conversion

None of the patients with AAA was converted primarily to open surgical aneurysm repair. Ten late conversions were required, three as emergencies (two AAA ruptures and one graft thrombosis) and seven electively after previous endovascular repairs (Table 2).

### SECONDARY OUTCOME MEASURES

Technique-related complications were encountered in 43 (90%) patients (Fig. 4). The most common graft-related complication was endoleak.

### Endoleak

Twenty-seven patients (56%) developed endoleaks, a total of 48 endoleaks being encountered (Table 1). Twelve (25%) were primary and all type II. Five of these disappeared spontaneously during the first six months and only 2 proved persistent. The total number of type II endoleaks was 14. There were 16 type I endoleaks, four proximal and 12 distal. Eighteen type III endoleaks were noted. Eight of the type III endoleaks developed due to disjunction of modular parts and ten were related to fabric tear. One patient developed endotension without any endoleak (Fig. 2).

TABLE 1

Number of complications in AAA patients treated with Vanguard endograft.

Complication	Number of patients (%)	Number of cases
Endoleak	27 (56)	48
– type I	13	16
– type II	14	14
– type III	10	18
– type IV	0	0
Endotension	1 (2)	1
Row separation	22 (46)	25
Thrombosis	15 (31)	20
Migration	16 (33)	22
Kinking	3 (6)	3
AAA rupture	3 (6)	3

TABLE 2

Secondary procedures in patients with endograft-related complication.

Secondary procedure	Number of cases
Re-endografting	4
Limb graft repair	33
Infrarenal cuff	19
Embolizations	8
Thrombolysis	6
Femoro-femoral by-pass	9
Axillo-femoral by-pass	2
Amputation	2
Conversion to open repair	10
– rupture	2
– thrombosis	1
– several endovascular procedures	7
Total	93

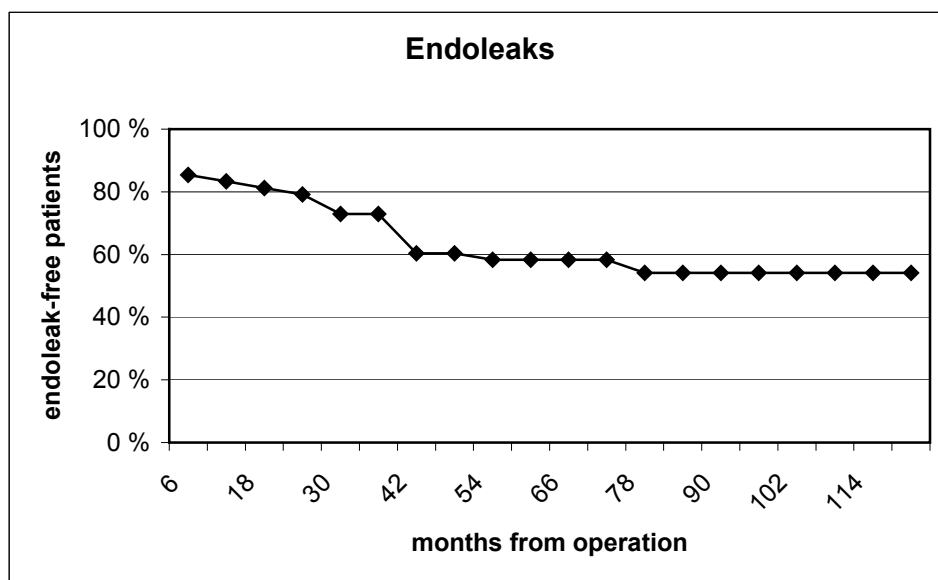


Fig. 2. Number of endoleak-free patients during follow-up. Excluded from the graph are five additional cases of type II endoleaks which were noticed in the first CT control, but closed spontaneously in the first six months of follow-up.

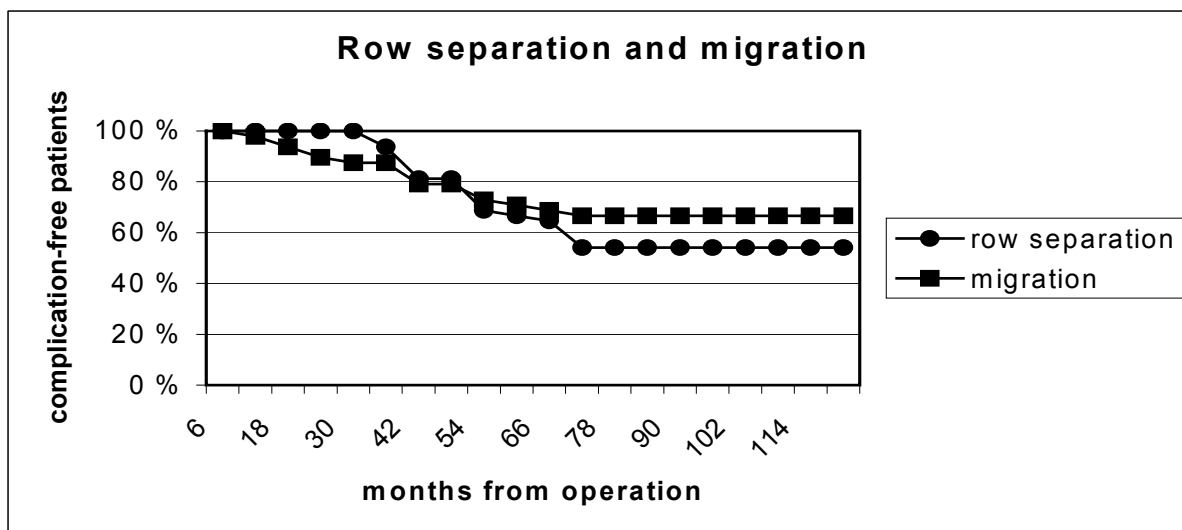


Fig. 3. Number of row-separation- and migration-free patients during follow-up. There were no row-separation cases during the first two years, as plain abdominal X-rays were performed only after 2001.

#### Row separation and migration

Row separation was observed in 22 patients (46%) with a total of 25 cases (Table 1, Fig. 3). Row separation was associated with endoleak in three cases and with migration in five. Overall 22 migrations of the endograft were noted in 16 patients, 13 distal and 9 proximal, respectively (Table 1, Fig. 3). Seven of the migrations developed an endoleak.

#### Thrombosis

There were 20 endograft thromboses in 15 patients (31%) (Table 1). One main graft thrombosis was operated by emergency Y-prosthesis reconstruction. All others were limb thromboses.

#### Secondary procedures

Altogether 93 additional procedures were required in 39 patients (81%), including ten late conversions (Table 2, Fig. 5). In all possible cases endovascular repair was applied to avoid open surgery. There were no deaths related to these secondary endovascular procedures. One procedure-related complication led to renal insufficiency and permanent dialysis. The number of additional procedures varied, but most patients underwent one (Fig. 6).

#### DISCUSSION

Endovascular abdominal aortic aneurysm repair has gained acceptance as a minimally invasive alternative

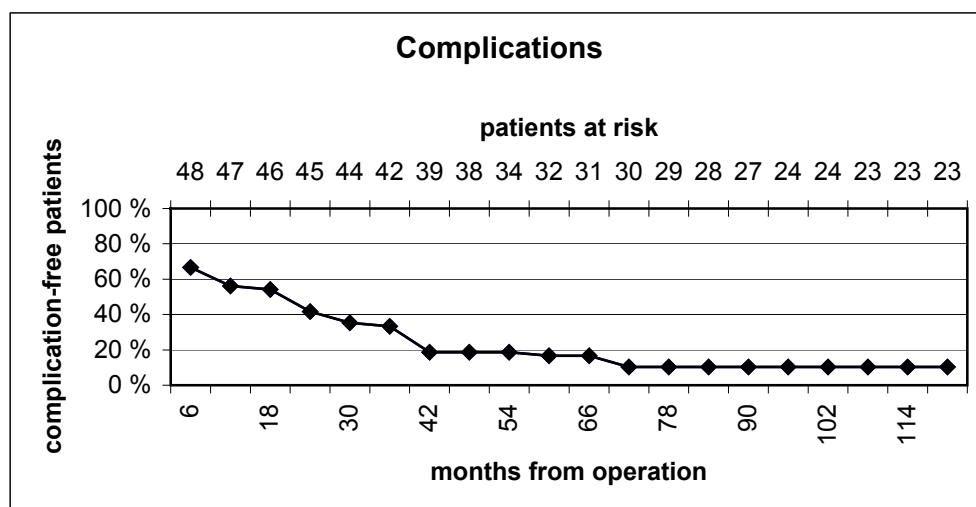


Fig. 4. Proportion of complication-free patients during follow-up.

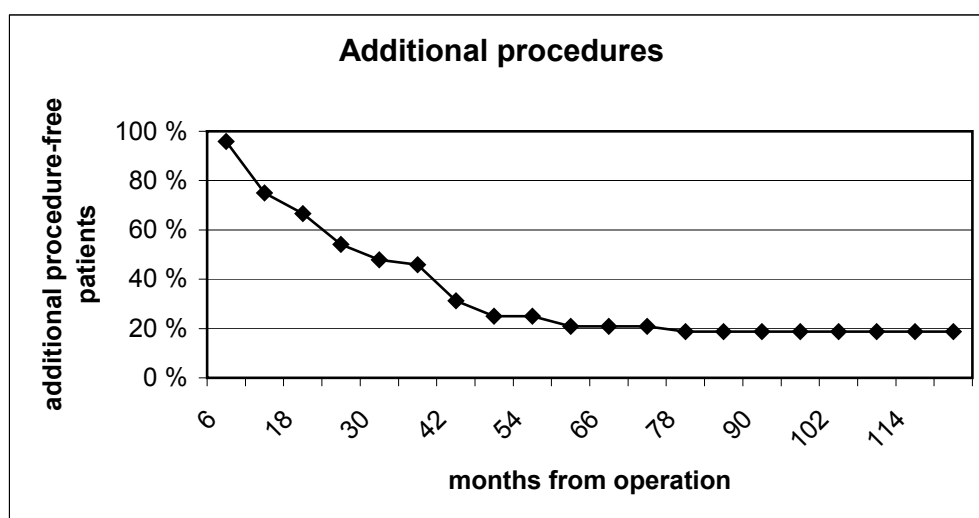


Fig. 5. Re-intervention-free patients during follow-up.

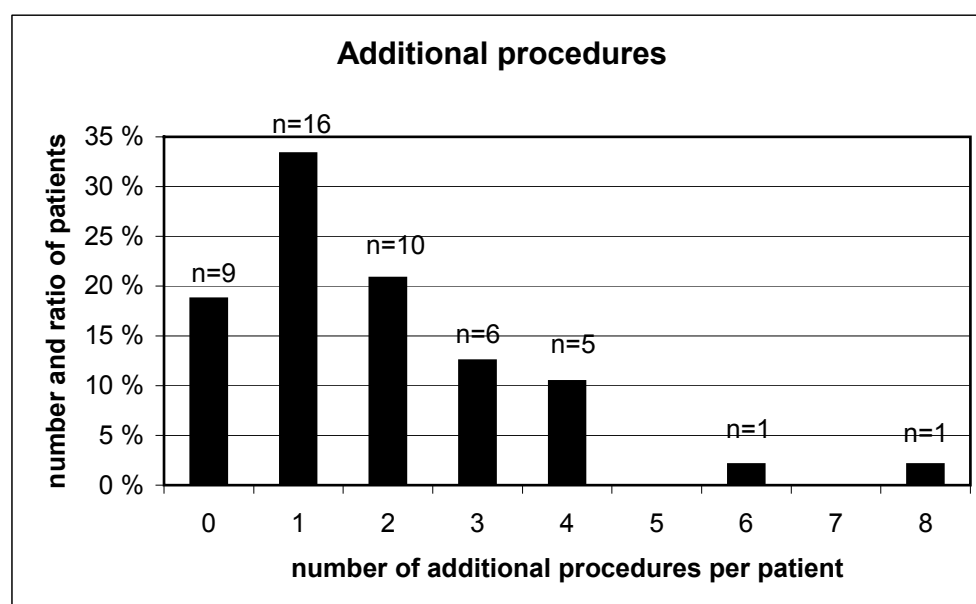


Fig. 6. Number of additional procedures per patient. The figure also includes all repair attempts.



to open surgery in selected patients. Like open aneurysm repair, endovascular repair has one primary objective in treatment: to prevent the death of the patient from rupture of the aneurysm. A further purpose of EVAR is protection against aneurysm-related death without the discomfort and risks associated with a major open surgical procedure.

EVAR has many benefits compared to open repair. It involves fewer severe complications and causes significantly less discomfort with less pain and shorter hospital stay (1, 3–6). Technical success has ranged between 72% to 100% and has risen as the technique has improved over the years (5, 6, 12, 19). Current operative mortality rates for patients undergoing elective open repair are reported to be from 4.1 to 5.6% and with EVAR from 0 to 2.7% (1, 3, 8, 20–22). In the available literature the 30-day mortality rate is 3.7 to 10.5% in open repair and 0 to 3.2% in EVAR (1, 5, 7, 8, 12, 19, 23, 24).

In EVAR 1 (6), a randomized prospective study comparing endovascular repair to open surgery for AAA, the 30-day mortality was significantly lower in the EVAR group. Also in the current study the short-term results have proved excellent and well comparable with those previously reported. Technical success was 100% and there were no primary conversions. This may be due to the fact that the same interventional radiologist and vascular surgeon performed the operations and the technique had been practiced before the study in other experienced institutions. Further, there were no operation-related deaths and the 30-day mortality was 0%.

Compared to open surgical procedures where graft durability is generally 20–30 years, with the endovascular technique there have already been problems in short- and mid-term follow-up. A variety of issues may underlie the poor durability of endovascular devices. Some of these may relate to attachment of the graft, progressive changes in the morphology of the aortic neck, changes in aneurysm diameter, and the device material. In EVAR 1, the proportions of patients with some complication after 4 years of follow-up were 41% in the EVAR group and only 9% in open repair (6). The most common complication and reason for readmission after EVAR has been endoleak (10, 19). In our study the most common complication was likewise endoleak. Row separation, the alarming complication which led to the withdrawal of this first-generation endoprosthesis from the market, was observed in 46% of the patients. In long-term follow-up complication-free survival was as low as 10%. We also noted that new complications appear as the time of follow-up increases and some of them seem to emerge at a typical time-point. During the first two years after EVAR, only few migrations and no row separations could be seen. After 3 years, however, the incidence of these complications started to increase, leading to endoleak, kinking and an increasing need for secondary procedures. Interestingly, after approximately five years complications and additional procedures are exceptional. This phenomenon might be attributable to aneurysm shrinkage or additional procedures with new devices which give durability for the primary endograft and reduce the risk of complications.

The need for secondary procedures after EVAR with the first-generation endograft has been high. In the French Vanguard trial (7) the 2-year survival rate free of reintervention was 67%. In our material, only 54% of the patients had needed no secondary procedure within two years and by the end of the follow-up at least one additional procedure was required in 81% of patients. Our mid-term results show a higher rate of secondary interventions than reported in previous Finnish studies (25, 26). At the end of the follow-up there was only one patient alive without any complications related to endoprosthesis. This low number is a sign of the high incidence of complications and may also be attributed to the careful, regular follow-up and early detection and treatment of complications. Type II endoleaks, which are nowadays only followed unless the aneurysm sac size increases, were treated actively. Also, all row separations were treated with re-intervention despite the absence of endoleak. Open conversion was the last option and all complications were treated with an endovascular procedure before that if possible.

In this population conversion to open repair is associated with a significant risk of serious complications. In the EUROSTAR registry the perioperative mortality rate among patients with conversion was as high as 22 to 24.4% (12, 19). We applied open repair in only one case during the first three years and the total number of open conversions was ten, three of them emergency operations due to rupture or massive graft thrombosis. None of the electively converted patients died during the first month after open repair. This is consistent with results from another Finnish center (26). Endovascular repair was possible in most cases and there was only one severe complication related to additional endovascular repair, and no deaths.

EVAR has as yet brought no diminishing of the risk of AAA rupture. In the EUROSTAR data, the annual risk of AAA rupture was 1% after endografting (12). A recent randomized study shows that aneurysm-related deaths occur less frequently in patients treated with EVAR compared to open repair (6). It has been suggested that rupture after endovascular repair might carry a better survival rate than would otherwise be expected (27). In the current series, there were three aneurysm ruptures during a median follow-up of 7.6 years, the annual risk of rupture being 0.8%. Despite the fact that the rate of stent-related complications was high, AAA ruptures were sparse. The 100% rate of compliance with the surveillance protocol and active treatment of complications might have had an impact on this result.

Some authors have suggested that endovascular repair may provide an initial survival advantage over conventional surgery, but that this superiority may not persist longer than the first year after repair (28). EVAR-1 confirmed that despite the magnitude of complications, mid-term results show a 3% aneurysm-related survival benefit for EVAR compared to open repair (6). Nonetheless, there was no difference in all-cause mortality and HRQL. EVAR was also more expensive by reason of the great number of complications and reinterventions. The question of



how those unsuitable for open repair should be treated still remains. EVAR 2, a randomized prospective study comparing endovascular repair to surveillance in patients unfit for open aneurysm repair, shows no significant difference in all-cause survival over four years among patients treated with EVAR compared to those undergoing no intervention (29). In EVAR 2, the aneurysm rupture rate was surprisingly low in patients in the surveillance group. The DREAM study (28) showed advantages for EVAR over open repair in the perioperative period and no difference in aneurysm-related mortality, severe complications or cumulative survival. Furthermore, the mid-term study by Buth and associates suggests that patients unfit for open surgery would benefit from EVAR (30).

Most of the studies reported are based on the results in the AAA patient registry and follow-up has seldom been prospectively planned. Many complications may not have been detected owing to the lack of a systematic follow-up program and some may have been repaired in another hospital without notification to the primary hospital. Also the magnitude of all necessary procedures and the long-term outcome of this patient population go unmentioned in most reports. In our study, none of the patients was lost to follow-up and thus all complications and secondary procedures were included. We also demonstrated that it is possible to use endovascular repair instead of open surgical repair in most endoprostheses-related complications in this high-risk patient population.

It is important to note that the stentgraft used in this study was the first-generation device, which is no longer in use. The current stentgrafts have been developed with a knowledge of the problems encountered with the early devices and the main emphasis has been on avoiding migration and solving the problems with the material. The mid-term results with these second- and third-generation grafts seem to be significantly better. The most important lesson of the current findings is that a new technology can always lead to unpredictable problems which can magnify the workload and incur substantial costs during several years after the initial procedure.

In conclusion, EVAR is a treatment modality under evolution for selected patients with infrarenal AAA. A careful surveillance protocol and active endovascular treatment of complications can lead to acceptable results and low AAA rupture and aneurysm mortality rates, also with the first-generation endovascular graft. Long-term follow up with the new-generation stent grafts will show in due time which therapy is preferable for patients who are suitable candidates for either procedure.

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# Long-Term Experience of Endovascular Aneurysm Repair With Zenith Prosthesis: Diminishing Graft-Related Complications Over Time

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**Background:** Only limited data on the long-term results after endovascular aneurysm repair exist to date.

**Materials:** Data on 282 patients with an abdominal aortic aneurysm treated with a Zenith endoprosthesis between March 2000 and March 2010 were retrospectively analyzed from a prospective database. Operative, total, and aneurysm-related mortality was assessed, as were graft-related complications and reinterventions.

**Results:** All procedures were performed successfully without primary conversions. Median follow-up was 40 months (range: 1–119 months). Thirty-day mortality was 1.4%, and aneurysm-related mortality was 0.7%. Cumulative survival was 62% at 5 years and 52% at 8 years. Graft-related complications occurred in 107 (38%) patients. The most common finding was a type II endoleak ( $n = 73$ ) that sealed mainly spontaneously ( $n = 46$ , 63%). Most endoleaks, and complications in general (87%), appeared during the first 3 years of follow-up, and no events occurred after 6 years. Altogether, 59 additional procedures, mainly embolizations ( $n = 35$ ), in 38 patients (24%) were required owing to graft-related complications. Of all the reinterventions, 82% were performed during the first 4 years, and no new complications were treated after 6 years.

**Conclusion:** Complications and reinterventions related to endovascular aneurysm repair become practically nonexistent after 5 to 6 years. This finding suggests that a lifelong follow-up may not always be needed after treatment with a Zenith endoprosthesis.

## INTRODUCTION

Endovascular abdominal aortic aneurysm repair (EVAR) has been disseminated rapidly as an alternative to open surgical repair of an abdominal aortic aneurysm (AAA). The technique has evolved

significantly in recent years, and currently available devices have undergone multiple technical improvements. Even so, the method is still associated with considerable complications and, therefore, a need for prolonged surveillance with periodical imaging, which has raised a question regarding the overall benefits of EVAR.<sup>1–4</sup> The assessment of long-term results may provide useful information about the natural history of endoleaks and other complications. Furthermore, these results may eventually help us to define which patient groups may not require lifelong surveillance. Unfortunately, only limited long-term data are available as yet.

An endoleak, that is, persisting flow to the aneurysm sac, produces a major surveillance problem after EVAR and can affect even up to one-third of

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the patients.<sup>5</sup> Type I and type III endoleaks are associated with a risk of aneurysm rupture and should therefore be treated on diagnosis, but on the other hand, the management of type II endoleaks without evidence of sac enlargement is still under debate.<sup>6</sup> Other possible graft-related complications that may require additional interventions include graft kinking and migration, thrombosis, and endotension. Therefore, the reintervention rate is perhaps more accurate in characterizing the overall success of endovascular treatment for AAA.

The aim of the present study was to describe our single-center long-term results of AAA patients treated with a Zenith endograft (Cook Medical, Brisbane, Australia).

## MATERIAL AND METHODS

### Patients

Between March 2000 and March 2010, 282 patients were electively treated for AAA with a Zenith endoprosthesis in our academic institution. There were 249 men and 33 women with a mean age of 75 years (range: 49–92 years). The following baseline characteristics were identified from case records and the hospital vascular registry: age, sex, diabetes mellitus, hyperlipidemia, hypertension, smoking within 5 years, coronary heart disease, cerebrovascular disease, respiratory disease, chronic renal failure, and previous arterial reconstructions and amputations. Patient characteristics are summarized in Table I.

### Indications for EVAR

The indication for the initial procedure was an infrarenal AAA with a diameter of  $\geq 55$  mm in men and  $\geq 50$  mm in women. Patients with an increase in AAA diameter of  $> 5$  mm over a period of 6 months and those with a symptomatic aneurysm were also treated. The median maximal diameter of the aneurysms was 60 mm at the time of treatment (range: 40–110 mm), and length of aneurysm neck was 25 mm (range: 5–80 mm). According to our endovascular protocol, spiral computed tomography (CT) and angiography were performed before surgery to identify candidates for EVAR. The initial postoperative CT was used as the baseline in measuring the possible sac enlargement during the follow-up.

### Technique

All procedures were performed by a vascular surgeon together with an interventional radiologist in a hybrid suite. Spinal anesthesia was used in 96% ( $n = 271$ ) of

the cases. A uni-iliac endoprosthesis was used only for 14 (5.0%) patients, whereas the rest were treated with a bifurcated graft. An attempt to embolize an open inferior mesenteric artery (IMA) was always made before the stent-graft placement ( $n = 186$ ). There were 146 (78%) successful embolizations. Unilateral inferior iliac artery embolization was performed in 31 patients and bilateral in two cases.

### Follow-Up

Our initial follow-up included contrast-enhanced CT at postoperative days 2 or 3, at 1 and 12 months, and annually thereafter. Angiography was done when graft-related complications were suspected. Based on available data and our own experience at the time, the surveillance protocol was modified by replacing the annual CT scan with ultrasonography (US) in 2005.<sup>7,8</sup> Thereafter, all US examinations were performed by experienced vascular surgeons. However, CT scans were performed for all patients at 24 months after the initial procedure to confirm the reliability of the US examinations. For obese individuals and for patients with a suspected complication at US, a CT scan was also performed. Plain abdominal radiographs were taken annually from the year 2001 onward. Patients were continuously followed up until April 30, 2010.

### Outcome Measures

The primary outcome criteria were technical success, in-hospital mortality, late all-cause mortality, and aneurysm-related mortality. Deaths were ascertained by record linkage between the study and the National Causes-of-Death Register on the basis of the personal identification code unique to every resident. Moreover, patients were evaluated for graft-related complications and reinterventions, as defined in Tables III and IV. Reintervention was defined as any endovascular or surgical intervention to restore or maintain proper endograft function after the initial EVAR procedure. Possible risk factors (length of aneurysm neck, neck calcification/atherosclerosis grade, stent oversizing, and patent IMA) for graft-related complications were also assessed.

### Statistical Analysis

SPSS 17.0 for Windows was used for statistical analysis (SPSS, Chicago, IL). Kaplan–Meier survival analysis was used to examine overall survival, complication-free survival, and reintervention-free survival. Logistic regression analysis was applied to evaluate the independent associations between



**Table I.** Baseline characteristics of 282 AAA patients

Characteristics	Value	%
Age (yr)		
Mean	75	
Range	49–92	
Sex		
Male	249	88
Female	33	12
Coexisting conditions (number of patients)		
Hypertension	138	49
Coronary heart disease	148	52
Hypercholesterolemia	66	23
Diabetes	41	15
Chronic renal insufficiency	28	10
Cigarette smoking	57	20
Cerebrovascular disease	46	16
Respiratory disease	81	29
Previous artery reconstruction or amputation	10	3.5
Size of aneurysm		
Median	60 mm	
Range	40–110 mm	
Length of aneurysm neck		
Median	25 mm	
Range	5–80 mm	

AAA, abdominal aortic aneurysm.

complications and aneurysm-related factors. *P* value of <0.05 was considered statistically significant.

## RESULTS

### Technical Success and In-Hospital Mortality

All grafts were successfully implanted, and all patients survived the initial procedure. No surgical conversions occurred during the perioperative period. Four patients died during their hospitalization, resulting in a 30-day mortality of 1.4%. The in-hospital causes of death were brain stem infarction (one patient) and cardiac failure (three patients).

### Follow-Up

The 278 patients who survived the initial treatment and hospitalization were followed for a median of 40 months (range: 1–119 months). None of the patients were lost to follow-up.

### Late and Aneurysm-Related Mortality

During the follow-up, 80 (28%) deaths occurred between 2 and 101 months (median: 36 months).

**Table II.** Causes of death during the follow-up (*n* = 84) (including 30-d deaths)

Cause of death	Number of patients
Cardiac death	26
Cancer	17
Cerebral infarction	6
Chronic pulmonary disease	3
AAA rupture	2
Other	30

**Table III.** Graft-related complications (*n* = 122) in AAA patients treated with a Zenith endograft

Complication	Number of cases	%
Endoleak	95	33
Type I	21	
Type II	73	
Type III	1	
Type IV	0	
Endotension (>5 mm)	11	3.9
Thrombosis	9	3.2
Migration (>5 mm)	3	1.1
Kinking	2	0.7
AAA rupture	2	0.7
Total	122	

The causes of death are listed in Table II. The two main causes of death were cardiovascular diseases (*n* = 22, 28%) and cancer (*n* = 17, 21%). Two (0.7%) patients died owing to aneurysm rupture. The first patient declined a further procedure for type I endoleak and died 34 months after the complication was diagnosed. The second patient died of rupture within 24 hours after unsuccessful proximal cuff placement that did not resolve type I endoleak. As Figure 1 demonstrates, the cumulative survival of the cohort was 62% at 5 years and 52% at 8 years. No significant difference in survival was observed between those with or without graft-related complications (Fig. 2).

### Graft-Related Complications and Reinterventions

A total of 120 other aortic graft-related complications in 107 patients (38%) were encountered during the follow-up. The most common graft-related complication was type II endoleak (*n* = 73, 26%). Most of these (*n* = 57, 78%) either sealed spontaneously (*n* = 46, 63 %) or caused no aneurysm expansion (*n* = 11) and were therefore treated conservatively. Additionally, there were 21 type I endoleaks and one type III endoleak. As

**Table IV.** Reinterventions for Zenith endograft-related complications in 38 patients

Secondary procedure	Number of cases
Re-endografting	1
Limb repair	5
Infrarenal cuff	7
Embolization <sup>a</sup>	35
PTA	3
Femorofemoral bypass	7
Conversion to open repair	1
Total	59

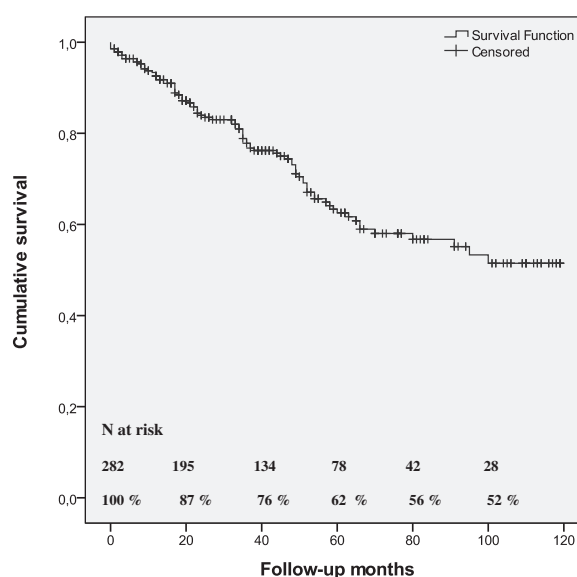
PTA, percutaneous transluminal angioplasty.

<sup>a</sup>Includes three angiographies with no further interventions.

aforementioned, two patients with type I endoleak died. Most (93%) endoleaks and other graft-related complications occurred during the first 3 years of follow-up, and no new complications were revealed after 6 years of surveillance (Fig. 3). All graft-related complications are presented in Table III.

Of the 120 complications, 44 required treatment. Subsequently, 59 additional procedures in 38 patients (24%) were performed during the follow-up (Table IV). The mean time to first reintervention was 22 months. Most (80%) of the additional procedures were performed during the first 4 years of follow-up, whereas only four secondary procedures were needed after 5 years. As Figure 4 illustrates, the reintervention-free survival leveled out to 76% after 6 years of surveillance. More than one additional procedure was required for 15 patients (5%).

As expected, an endoleak was the most often treated complication, requiring additional procedures in 28 patients (type I endoleak: 14; type II endoleak: 16; and type III endoleak: 1). Type I and III endoleaks, as potentially dangerous complications, were treated actively. However, five type I endoleaks seen in the early CT scan performed 2 to 3 days postoperatively sealed spontaneously by the 1-month follow-up, thus requiring no additional interventions. In another patient with type I endoleak, the aneurysm sac showed shrinkage and leakage decreased. For this patient, a close follow-up was considered sufficient. For type II endoleaks, further procedures were opted for only if the aneurysm sac showed expansion over time. Two patients were treated both for type I and II endoleaks and one patient for type I and III endoleaks. Repeated unsuccessful embolizations were performed in nine patients with no further complications. One proximal cuff placement failed to exclude type I endoleak, and the patient was treated successfully with surgical conversion at 28-month follow-up. There

**Fig. 1.** Cumulative survival of patients treated with a Zenith endograft ( $N = 282$ ; Kaplan–Meier survival analysis).

was one limb graft thrombosis during an additional procedure, and it was treated with femorofemoral bypass in the same operation.

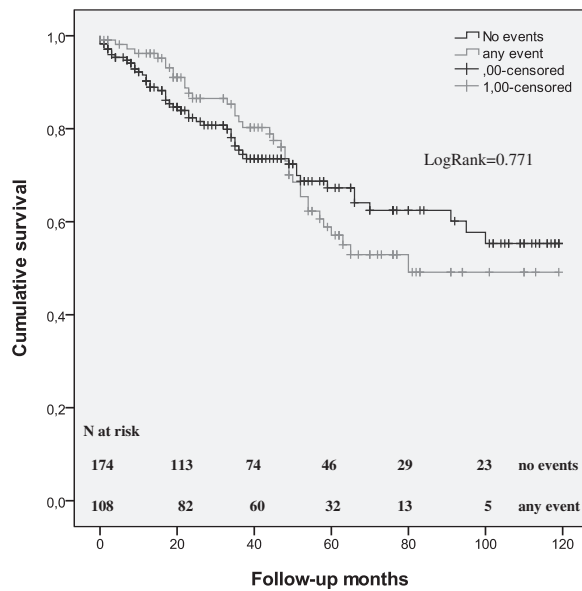
Three patients suffered from graft migration, and two of them were successfully treated with a new proximal graft. Seven graft limb thromboses were treated with a femorofemoral bypass. One patient had only mild claudication not necessitating any interventions. Another patient with a total graft thrombosis was asymptomatic and required no additional procedures. Patients with an endotension ( $n = 11$ ) were carefully followed and, as a rule, treated conservatively. One patient, however, required re-endografting. He died at 61 months after the initial procedure from pneumonia after a thigh amputation.

### Risk Factors for Graft-Related Complications

Regression analysis showed no significant association between aneurysm-related factors and endoleaks (separately for type I and II endoleaks) or graft-related complications in general.

## DISCUSSION

Our results are in concordance with previous multicenter midterm reports demonstrating a significant complication and reintervention rate after endovascular AAA repair.<sup>5,9–11</sup> Owing to the longer follow-up, we were able to show that significant



**Fig. 2.** Cumulative survival of patients with and without graft-related complications (Kaplan–Meier survival analysis).

complications most probably occur during the first 2 to 3 years after treatment with a Zenith endograft, and that reinterventions become unlikely after 6 years of follow-up. These findings suggest that surveillance exceeding to 6 years may not be required after EVAR for this particular endoprosthesis.

Three randomized trials comparing the advantages and disadvantages of endovascular and open repair for AAA have reported low operative mortality (0.5–2.3%) for endovascular repair.<sup>3,4,12</sup> Available registry data show a similar trend.<sup>13</sup> Our findings are in line with these earlier results as well as with two recent clinical studies reported with a Zenith endograft.<sup>11,14</sup> In our series, aneurysm-related mortality was somewhat lower, but all-cause mortality at 5 years was higher (37%) when compared with the aforementioned studies. Two characteristics of our cohort, higher age (mean: 75 years) and prevalence of coronary heart disease (52%), may explain the difference in all-cause mortality. On the other hand, the present data on 8-year survival were similar to what was reported in the EVAR Trial (52% vs. 48%).<sup>4</sup>

Although EVAR is associated with faster recovery and low operative mortality as compared with open surgery, the technique has its drawbacks owing to graft-related complications such as endoleak and migration. These complications may require reinterventions or at least regular long-term follow-up, thus increasing the total costs of the treatment modality.<sup>4</sup> The advantage of EVAR may also be

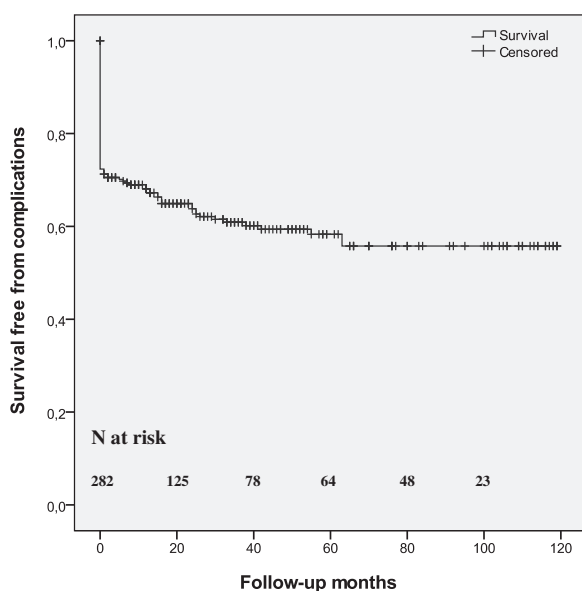
lost over time owing to increased aneurysm-related mortality, as proposed in the EVAR Trial.<sup>4</sup> A recent clinical report, however, has demonstrated high freedom of aneurysm-related mortality (98%) at 5 years for the Zenith endograft.<sup>11</sup>

Our study showed low aneurysm-related mortality (0.7%) despite the number of complications. Persisting postprocedural aneurysm sac perfusion may be associated with a sac enlargement, causing aneurysm rupture with an annual rupture rate of up to 1%.<sup>15</sup> We tried to minimize the risk of type II endoleak and consequent sac enlargement by embolizing the IMA whenever possible. This practice was obtained from our earlier experience with first-generation endografts.<sup>16</sup> Current literature also supports this approach.<sup>17</sup> Despite all our attempts, persistent type II endoleaks required the most additional procedures, comprising up to two-thirds of all reinterventions in our series. This finding is similar to earlier reports.<sup>10,18,19</sup> Whether type II endoleak definitely causes aneurysm sac enlargement and rupture is disputable, and the question has polarized specialists' opinion.<sup>6,20–23</sup>

Migration and kinking are relatively rare complications with current devices, as has been demonstrated in the present and in a previous study.<sup>11</sup> Endotension as a phenomenon is still not completely understood. We have mainly treated endotension conservatively,<sup>24</sup> and, as described, only one patient in the present series required reintervention. Current literature seems to support this approach.<sup>24,25</sup>

The event-free survival after an endovascular AAA procedure varies between studies, but is approximately 70% to 80% at 5 years.<sup>4,11</sup> In our series, the figure was 62% at 5 years. In most studies, the majority of complications seem to occur in the beginning of the follow-up, and the incidence levels out as the follow-up continues.<sup>4,11,18</sup> Again, this is supported by our results. Interestingly, and perhaps surprisingly, complications became practically nonexistent after 5 years. This is in contrast to what was reported in the EVAR Trial.<sup>4</sup> Another notable detail is that complications do not have negative effect on all-cause survival.

Reintervention rate is perhaps a more accurate indicator of successful endovascular AAA treatment. A recent review article showed that 72% of EVAR patients remain reintervention free at 7 years.<sup>18</sup> Our study demonstrates somewhat better results, with a rate of 76% at 7 years. The LIFELINE registry reported that 85% of the reinterventions were performed during the first postoperative month, whereas in our study, only 7% of secondary interventions were performed within 30 days after

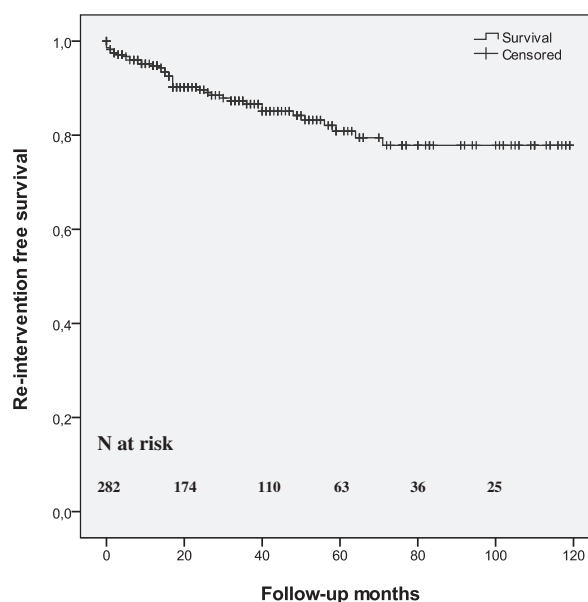


**Fig. 3.** Complication-free survival of 282 patients treated with a Zenith endograft (Kaplan–Meier survival analysis).

deployment.<sup>26</sup> This is probably explained by the fact that the LIFELINE registry contains older grafts or, more likely, that the registry highlights the current more conservative approach of treating early complications, especially with regard to type II endoleaks.

To date, all patients, even those who do not require subsequent reinterventions, have been controlled periodically after EVAR. This has led to an extensive follow-up protocol. As discussed earlier, most complications, including AAA rupture, and reinterventions occur within the first 2 to 3 years postoperatively. Furthermore, our study showed that complications and reinterventions become unlikely after 6 years of follow-up. This underlines the need for follow-up in the first years after treatment but raises a question of the necessity of systematic follow-up after 5 or 6 years, at least when it comes to Zenith endoprotheses. Moreover, it has been shown that surveillance scans alone initiate the secondary intervention in 1.4% to 9% of cases and that >90% of the patients receive no benefits from these control examinations.<sup>12,27</sup>

The follow-up protocol after EVAR should be optimized and individualized to minimize the overall costs related to the treatment and to reduce the frequency of CT scanning in particular. US-based surveillance has shown no negative effects on aneurysm-related survival, which was also noted in our series.<sup>11,28</sup> Therefore, aortic US is suggested for long-term follow-up for patients with no early endoleaks.<sup>29</sup> On the other hand,



**Fig. 4.** Freedom from reinterventions (Kaplan–Meier survival analysis).

the current results suggest that the majority of patients can be discharged from follow-up after 5 to 6 years, especially if they have had no early complications. This has been proposed earlier by Nordon et al. in their meta-analysis of >17,000 EVAR patients.<sup>18</sup>

The present study is affected by several limitations. First, our attitude regarding the treatment of complications became more conservative toward the end of the decade. Second, our follow-up protocol changed during the study from CT-based to US-based surveillance. This may have led to some complications being omitted. Another drawback is the length of the follow-up, with only 26 patients alive after being followed for 8 years or more. The strengths of the current study, on the other hand, include the systematic EVAR registry, the availability of all CT scans and plain abdominal radiographs for review, and, finally, the fact that the number of surgeons and radiologists involved in EVAR procedures is restricted to minimum at our institution.

## CONCLUSIONS

Graft-related complications and secondary procedures after EVAR occur mainly during the first couple of years after the initial treatment. According to our results, these complications and reinterventions become practically nonexistent after 5 to 6 years. This finding suggests that systematic follow-



up may not be beneficial for all patients treated with a Zenith endoprosthesis after this period.

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# Long-term experience of endovascular repair for thoracic aortic aneurysms and dissections

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## ABSTRACT

**Purpose:** To report the long-term results of thoracic endovascular aortic repair (TEVAR) in both elective and emergency cases of thoracic aortic aneurysm (TAA) and type B dissection.

**Material and methods:** A prospective single-center study of 78 TEVAR patients treated between February 1998 and February 2013. Stent-graft implantation was performed in 51 patients (65%) for TAA (43 elective and 8 emergency cases) and in 27 patients (35%) for type B dissection (11 elective and 16 emergency cases). Short- and long-term results were evaluated, and a subgroup of patients with left subclavian artery (LSA) coverage was also analyzed.

**Results:** The patients were followed for a mean of 55 months (1–160 months). The technical success rate was 81% and 30-day mortality 6.4% (n=5). The stroke rate was 7.7% (n=6), and permanent paraparesis 2.6% (n=2). In follow-up, there were 28 (36%) primary (15 type I and 13 type II) and ten secondary endoleaks (8 type I and 2 type II). Multivariate analysis showed no significant predictive factors for developing a type I endoleak. Secondary interventions were required in 24% of the patients. There was one late thoracic aortic rupture and one late conversion (1.3%). Patients with LSA coverage had a higher incidence of stroke (12.5% vs. 4.3%, p=0.18) and paraparesis (3.1% vs. 2.2%, p=0.79) compared to those without LSA coverage, although this difference was not statistically significant. Stroke rates were significantly higher in patients treated in an emergency setting (p=0.048).

**Conclusion:** TEVAR is a relatively safe and effective therapy for different aortic pathologies with good long-term success. The risk of stroke and paraparesis is notable whether the LSA is covered or not, and strokes clearly accumulate in the emergency setting. A type I endoleak is the most common complication, but there are no predictive factors for its development.

## INTRODUCTION

Although the surgical approach is the preferred treatment modality for pathology of the ascending aorta and the proximal arch region, thoracic endovascular aortic repair (TEVAR) is increasingly used for the treatment of the distal arch and descending aorta. The most common indication for the intervention is degenerative thoracic aortic aneurysm (TAA). Owing to the good clinical success of TEVAR among patients with TAA, the technique is used increasingly for patients with dissections and traumatic aortic ruptures, with good short-term results [1-4].

The application of TEVAR for the treatment of varied aortic pathologies and indications is ever expanding, the liberal use of stent grafts in various anatomical configurations does not necessarily adhere to the instructions for use (IFU) for a particular graft, making interpretation of real-world experience with TEVAR difficult [5]. Furthermore, there are a number of technical details and considerations that remain unresolved. Notably, the need for left subclavian artery (LSA) revascularization if covered during the procedure remains controversial [1, 2, 6-8].

Recent short-term results of TEVAR compare favorably with the results of open repair (OR) [9-12]. The 30-day mortality rate is 3.6–7.6% for TEVAR and approximately 10% for OR [9, 10, 12, 13]. Furthermore, the respective paraparesis and stroke rates are 1.5–7.5% and 3.0–6.4% for TEVAR and 3.4–8.6% and 2.7–7.5% for OR [2, 4, 6-10, 13, 14]. In addition, any aortic endovascular procedure carries a certain risk of secondary interventions [15-17]. The reported secondary intervention rate of TEVAR is approximately 12% [17, 18]. While interpreting TEVAR results as a whole, the number of complications and the need for secondary procedures is an important indicator of long-term success after TEVAR.

The purpose of this study was to characterize the long-term experience with TEVAR in an academic institution. Both elective and urgent procedures for TAA and type B dissection were included and analyzed.

## MATERIALS AND METHODS

### *Patients*

A prospectively collected database of 92 TEVARs between February 1998 and February 2013 at our academic institution was evaluated retrospectively. Patients with a thoracic aneurysm or type B dissection were included in the study, while those with a thoracoabdominal aortic aneurysm (TAAA) requiring a hybrid or branched endovascular procedure were excluded. A

total of 78 patients were treated for these two indications during the period, 24 (30.8%) of whom were operated on in an emergency setting. The study cohort included 58 men and 20 women with a mean age of 66 years (range 18–88 years). The caseload began to increase rapidly in 2003, and, consequently, 95% of the procedures were performed since then. The preoperative cardiovascular risk factors of the current cohort are presented in Table 1.

#### *Pre-operative evaluation and follow-up*

According to our endovascular protocol, spiral CT was performed on TEVAR candidates before elective surgery. Since 2010 all elective patients with planned LSA coverage underwent preoperative computed tomography angiography (CTA) in order to evaluate brain perfusion. If the left vertebral artery was considered dominant and/or there was any doubt concerning the condition of the basilar or communicating arteries, the LSA was revascularized. Furthermore, other absolute indications for pre-emptive LSA revascularization were the existence of a left internal mammary coronary artery bypass graft or a dialysis access in the left upper extremity. The relative indications were prior abdominal aortic repair, occluded iliac arteries, and total coverage of the descending thoracic aorta by an endograft. Postoperatively, patients had CTA scans at 2 or 3 days, 1 month, 12 months, and annually thereafter. The CTA scans were performed in three phases (the native, arterial, and delayed phase). Beginning in 2010, the immediate postoperative CTA scan was omitted and the first control CTA was scheduled at one month, provided that the initial procedure had been successful. For young patients (age <21 years, n=2), only a plain X-ray was taken annually after the second CTA scan. If no complication was observed within two to three years of follow-up, the CTA was taken every two years with a plain X-ray in the years between. Patients were followed until the end of April 2014.

#### *Indications for TEVAR*

A total of 51 (65.4%) patients were treated for thoracic aortic aneurysm (TAA) and 27 for type B dissection. Of the 54 electively treated patients, 43 had a TAA and 11 a chronic dissection. The indication for the initial procedure was an aneurysm with a diameter of  $\geq 60$  mm and a symptomatic or saccular aneurysm. In two cases, the indication for treatment was LSA aneurysm with a combined dilatation of the corresponding aortic arch. Patients with a chronic dissection were treated in the case of an aneurysmatic expansion of the aorta (60mm or more). Only complicated acute dissections were treated: end-organ malperfusion, recurrent pain or hypertension despite full medication, or signs of rupture. In total, 24 patients were treated in an emergency setting, 17 due to aortic rupture (Table 2 and 3).

### *Aneurysms and type B dissections*

The median diameter of the thoracic aneurysms was 67 mm at the time of treatment (range 48–102 mm). Six patients had a saccular aneurysm while one presented with symptomatic TAA. The patients treated had a variety of aortic landing zones needed to achieve proximal seal (Table 4) [19]. Two patients with a zone 0 lesion had an ascending thoracic aortic dissection and were treated urgently with open repair. The descending aorta was stented with an endograft secondarily, in the first patient one month later at zone 2 and in the second five months later at zone 4.

### *Procedure*

All procedures were performed in a hybrid suite by a vascular surgeon together with an interventional radiologist. General anesthesia was used in 36 (46%), spinal anesthesia in 41 (53%), and local anesthesia in one case (1%). Thirty-two patients required stent graft deployment in the aortic arch: five in zone 1 and 27 in zone 2 (Table 4). In zone 1, an extra-anatomic carotid-carotid bypass combined with a revascularization of the left subclavian artery (LSA) was performed for two patients while in three cases the left common carotid artery (LCCA) revascularization was considered sufficient. For patients requiring coverage of zone 2 (n=27), the LSA was deliberately covered and not revascularized in 24 cases, and for three patients, LSA revascularization was considered necessary prior to the endovascular procedure. All bypasses were elective.

Six patients underwent simultaneous open repair of an abdominal aortic aneurysm (AAA), while in one patient, the AAA was repaired endovascularly. These were all elective cases, and the patients were treated with open repair if considered fit for open AAA surgery. Thirteen patients had undergone a previous surgical open repair for AAA.

A total of 7 different thoracic stent grafts were used in thoracic aortic repair: Excluder/Gore TAG (W. L. Gore, Flagstaff, Arizona) (n=45), Zenith (William Cook Europe, ApS, Bjaeverskov, Denmark) (n=24), Valiant/Talent (World Medical Manufacturing, Sunrise, Florida) (Medtronic Vascular, Santa Rosa, California) (n=6), Relay Plus (Bolton Medical, Barcelona, Spain) (n=2), and Vanguard (Boston Scientific, Natick, Massachusetts) (n=1). The mean number of endografts per case was 1.4 (1-3).

### *Outcome measures*

The primary outcome criteria were technical success, 30-day mortality, as well as late all-cause and procedure-related mortality. Deaths were ascertained by means of record linkage between the study and the National Causes-of-Death Register on the basis of the personal

identification code unique to every resident in Finland. Kaplan-Meier survival analysis was employed to examine overall survival. Secondly, patients were evaluated for graft-related complications and re-interventions. Technical success was defined as successful deployment of a stent graft without an endoleak of type I or III at the end of the procedure and no intraoperative death. In the case of dissections, technical success also included complete coverage of the primary entry tear. A graft-related secondary intervention was defined as any endovascular or surgical procedure to restore or maintain proper endograft function after the initial TEVAR procedure.

## RESULTS

### *Technical success and 30-day mortality*

Technical success was obtained in 81% of the patients. All failures were caused by a type I endoleak. There were no intraoperative deaths or surgical conversions in 30 days. The overall 30-day mortality was 6.4% (n=5; 3 elective and 2 emergency cases). The causes of death were thoracic aortic aneurysm rupture (n=2), visceral malperfusion (n=1), myocardial infarction (n=1), and chronic obstructive pulmonary disease (n=1). The first of the thoracic ruptures was diagnosed preoperatively, and the patient had an emergency operation.

### *Hospital morbidity*

Postoperative treatment in the intensive care unit (ICU) was needed for 32 patients. Urgently treated patients more often required monitoring in the ICU (elective 24% vs. emergency 79%,  $p<0.001$ ). There was no significant difference in the ICU or overall hospital stay between elective and emergency cases (mean ICU stay 6.8 vs. 7.0 days, range 1–40 days,  $p=0.972$ ; mean hospital stay 8.6 vs. 10.5 days, range 2–49 days,  $p=0.347$ ).

Spinal cord ischemia (SCI) resulted in permanent paraparesis in two patients (2.6%), whereas an additional two (2.6%) developed transient symptoms that resolved with spinal drainage. Two of these cases were emergencies (dissections), and one underwent simultaneous open repair of an AAA (elective TAA). Six patients (7.7%) had a postoperative cerebrovascular event (CVE) with no permanent effect on the patients' previous physical condition (four acute dissections and two elective TAAs) (Table 5). There was no correlation between SCI and CVE rates and the number of stent grafts used ( $p=0.751$  and  $p=0.057$  respectively). Furthermore, there was no statistical difference in SCI or CVE rates between patients treated for TAA and those treated for a dissection

(SCI: 2.0% vs. 3.7%,  $p=0.648$ , CVE: 3.9% vs. 14.8%,  $p=0.088$ ). SCI and CVE were more frequent in the emergency setting compared to elective setting (SCI: 4.2 vs. 1.9% ,  $p=0.557$ , CVE: 16.7% vs. 3.7%  $p=0.048$ ). Also, patients with previous or simultaneous open repair of AAA did not have significantly higher SCI or CVE rates ( $p=0.399$  and  $p=0.152$ , respectively).

In all, 17 secondary interventions during 30 days were required in 13 patients (seven TAAs and six dissections), including one open repair of a ruptured abdominal aortic aneurysm, one above-knee amputation, four additional stent graft insertions, two transthoracic hematoma evacuations, two laparotomies, two embolizations, one embolectomy, one evacuation of a wound hematoma, two cases of surgical hemostasis, and one stenting of a renal artery. Of these cases, 54% ( $n=7$ ) were primary urgent repairs (one TAA rupture and six acute dissections). Eighty-five percent of the secondary procedures were performed during the first postoperative week.

#### *Late and procedure-related mortality*

The mean follow-up for the entire study group was 55 months (range 1–160 months). None of the patients were lost during the study. An additional 24 deaths occurred during follow-up. The two main causes of death were cardiovascular diseases ( $n=6$ ) and cancer ( $n=5$ ). One patient died due to a TAA rupture eight months after the initial procedure caused by a type I endoleak. There were no signs of an endoleak at the one-month postoperative CTA, but at the time of rupture seven months later, it was seen in an emergency CTA. Endovascular repair was not possible, and open repair was abstained from because of the patient's co-morbidities. The overall mortality due to aortic rupture was 3.8% ( $n=3$ ). The overall survival rate was 85%, 78%, and 61% at 1, 3, and 5 years, respectively (Figure 1).

#### *Graft-related complications and re-interventions*

An endoleak was the most common graft-related complication, with a prevalence of 38%. A primary endoleak occurring at the time of surgery was noted in 28 (36%) patients (15 type I and 13 type II). Of these endoleaks, 12 (43%) resolved spontaneously, including five primary type I endoleaks. Seven patients with a type I endoleak required an additional procedure while two were carefully followed as the aneurysm size remained stable with no signs of growth. By the end of the study, these two patients had been followed for 84 and 55 months, respectively. One patient died during the initial hospitalization due to complications related to the aneurysm rupture he was initially treated for. Of the 15 cases of primary type I endoleak, 13 were treated initially for TAA (11 elective, 2 emergencies) and two for dissection (1 elective and 1 emergency). Only two primary

type II endoleaks required an additional procedure as the aneurysm sac was growing during surveillance.

A total of 10 secondary, delayed, endoleaks were detected (8 type I and 2 type II). The secondary type I endoleaks appeared at 1, 8, 28, 32, 38, 39, 52 and 64 months after the initial procedure. Four patients were treated with placement of an extension device. One case was deemed to be a poor endovascular candidate, and no further procedures were performed. This patient died six months later due to prostate cancer. In one case, the endoleak was impossible to repair by endovascular means and no further procedures were done. The patient died traumatically 14 months after diagnosis. As mentioned, one secondary type I endoleak was diagnosed at the time of rupture and no further procedures were done. In one case further procedures were abstained as aorta showed shrinkage in surveillance and by the end of the study patients had been followed 60 months. Of the eight cases of secondary type I endoleak, five were TAAs (all elective) and three dissections (1 chronic and 2 acute). Two secondary type I endoleaks were caused by graft migration and four by obvious aortic degeneration over time. None of the secondary type II endoleaks required further procedures as they showed no signs of aneurysm sac enlargement. Multivariate analysis including sex, aneurysm size, pathology treated, number of stent-grafts used, zone of pathology, landing zone of stent-graft, or emergency setting in the initial procedure showed no predictive factors for developing a type I endoleak.

Additional late graft-related complications included one case of endotension with no detectable signs of an endoleak, which was carefully followed as the aneurysm sac was slowly growing. This patient died of alcoholic pancreatitis two years after the endotension was detected. One case of stent fracture was observed eleven years after the primary procedure and was treated with an additional endograft before there was notable endoleak or sac enlargement. One late conversion (1.3%) five years after the initial procedure was necessary for a type B dissection due to continued retrograde flow in a false lumen and dilatation of the aorta. Unfortunately, this patient died after open repair. All graft-related complications and secondary procedures are reported in Table 6. Two embolizations and four additional endografting procedures were performed during 30 days and the rest at a later time during surveillance. Of all additional procedures, 84% were performed during the first two years of the surveillance and the mean interval to first graft-related secondary intervention was 16 months after the initial procedure (range, 1 day- 68 months).

#### *LSA coverage*

LSA coverage was necessary for 32 patients (41%) due to anatomic or technical reasons during the primary procedure (landing zones 1–2, Table 4). Only five of these patients



(15.6%) underwent pre- or perioperative LSA revascularization. Patients with LSA coverage without revascularization (n=27) had a thirty-day mortality rate of 7.4% (n=2). This is similar to that seen in patients without LSA coverage (n=3, 6.5%, p=0.47) (Table 6). Furthermore, the overall mortality for the LSA-covered group was 30% as opposed to the 41% among their counterparts with no coverage (p=0.476). The incidence of CVE was higher among those patients with LSA coverage, regardless of revascularization, than among those whose LSA was not covered, although this difference was not statistically significant (12.5% and 4.3%, p=0.18). One of the five patients with perioperative LSA revascularization suffered a postoperative stroke. Similarly, while SCI was higher in patients with LSA coverage when compared to those without coverage, this was not statistically significant (n= 1, 3.1% and N=1, 2.2%, p=0.79). During follow-up, four patients (14.8%) without LSA revascularization presented with mild ischemic symptoms of the left hand. Two of them required late carotid-subclavian bypass, leading to the resolution of their symptoms. Additionally, six late LSA coverages were required to treat type 1A endoleak with a proximal extension cuff, and they were uncomplicated (Table 7).

## **DISCUSSION**

According to our results, TEVAR shows good short- and long-term results. The operative mortality was 0% and all stent grafts were successfully deployed, but 15 primary type I endoleaks remained unresolved at the end of the procedure, reducing the primary technical success rate to 81%. The 30-day mortality was low for both elective (5.6%) and emergency cases (8.3%). The overall secondary intervention rate was 24% and consisted mainly of endovascular procedures. The overall survival was 85%, 78%, and 61% at 1, 3, and 5 years, respectively.

A postoperative CVE occurred in 7.7% of the patients and permanent paraparesis in 2.6%. These findings are consistent with earlier reports [3, 6, 21]. The neurological complication rate was higher in patients with LSA coverage, but there was no statistical difference when they were compared to the patients without the coverage. Furthermore, SCI and CVE rates did not correlate with the pathology treated or number of stent grafts used, but CVE rates were significantly higher in patients treated in an emergency setting. This is probably explained by technical difficulties and possible hypotension related to an emergency operation as well as the lack of a preoperative brain CTA.

The contemporary literature on TEVAR reports comparable short- and long-term results in regard to complications and secondary procedures [17, 20, 22]. Although the most

commonly reported complication following TEVAR is a type I endoleak (incidence 12-17%), our study showed even higher incidence of type I endoleak (primary 19%, secondary 10%). Certainly type I endoleaks cannot be dismissed and should be considered a treatment failure. Fortunately, most type I endoleaks detected on follow-up imaging can successfully be treated by endovascular techniques. Moreover, some type I endoleaks may eventually seal without any intervention [23, 24, 25]. Boufi and colleagues report on 84 patients undergoing TEVAR and describe an type I endoleak in eight patients (9.5%), of which two resolved spontaneously. In our series 5 of 15 primary type I endoleaks also resolved spontaneously. The high rate of primary type I endoleaks in the current may be explained by the fact that early in our experience the first CTA follow-up was conducted two or three days after the procedure. If a minor type I endoleak was encountered, it was, as a rule, left with no treatment at this point. The fact that only three primary type I endoleaks were discovered after the changes in the follow-up imaging protocol were made in 2010 supports the idea. Furthermore, primary procedures were performed in a hybrid operating room using high-resolution, fixed C-arm increasing quality of imaging. As mentioned, one third of the primary type I endoleaks disappeared by the time of the one-month CTA scan. Notably, in nine out of fifteen cases of primary type I endoleak, there were some kind of problems with the release of the stent-graft or minor migration from the planned proximal landing zone in the aortic arch.

Furthermore, patients with a type I endoleak in our series underwent TEVAR for zone 1-3 pathology where the coverage or near coverage of the great vessels is required. The finding is consistent with the notion that the aortic arch is technically the most challenging area for TEVAR. Multivariate analysis showed no predictive factors for developing a type I endoleak. Previously Pamer et al. have found larger aneurysm size, the length of aorta treated by stent-grafts, an increasing number of stents used and male sex predictive for type I endoleak [26].

The number of late complications and re-interventions seem to be relatively low in thoracic endovascular procedures [17, 18]. This is also true for our study as only 13% of the patients had secondary, delayed, endoleaks and only one third of them required additional procedures. Furthermore, both modular component separation and endotension were rare complications, and only one late conversion was considered necessary. Moreover, graft-related problems and additional procedures tended to occur in the early stages of the follow-up as 84% of the procedures were performed during the first two years of the surveillance. The phenomenon is similar to what we found in our EVAR patients and highlights the importance of close surveillance especially in the early follow-up period [14]. Overall, the aneurysm-related death rate was low in our series with only one patient dying of rupture during long-term follow-up.

Coverage of the LSA is often necessary during TEVAR to achieve a proximal seal. The proportion of patients requiring the coverage has been reported to be as high as 40% [1, 21]. This was also true for our patient cohort. There is data suggesting that LSA coverage increases the risk of stroke after TEVAR and, consequently, Society of Vascular Surgery guidelines recommend reconstruction of the LSA prior to or during the endovascular procedure in elective cases [27]. However, this subject remains controversial. Indeed, other studies have failed to identify whether routine LSA revascularization actually protects patients from having a stroke [1, 3, 6, 8]. We changed our strategy in regard to LSA coverage in 2010 when we began to routinely evaluate brain perfusion prior to the elective TEVAR procedure. If the left vertebral artery is considered dominant and/or there is any doubt concerning the condition of the basilar or communicating arteries, we will revascularize the left subclavian artery. Others have adopted a similar strategy of preoperative imaging to help guide the decision-making regarding LSA revascularization [28]. Since adopting this new screening protocol, we have not encountered any post-operative CVEs, nor has there been any need for late bypass procedures.

There are several limitations to our study. First, although this represents prospectively collected data, ours is a retrospective study. Another limitation is the fact that our experience consists of diverse aortic pathologies, aneurysms and dissections. As we were concentrating on reporting the long-term results of the endovascular method itself, we believe combining the groups was appropriate. Finally, our study is limited by the relatively low number of patients treated over a 15-year period making statistical analysis difficult. At our institution, all aortic endovascular procedures (currently approximately 100 procedures annually) are performed by two vascular surgeons together with two interventional radiologists. We therefore believe that our experience is broad in regard to TEVAR procedures and that our results are representative of real world experience.

## CONCLUSION

TEVAR is becoming the preferred treatment modality for diverse aortic pathologies in patients with suitable anatomy and seems to deliver good short- and long-term results even in an emergency setting. CVE and SCI rates are low, although incidence of CVE appears to be increased in for TEVAR in emergent setting. Over-stenting of the LSA does not significantly increase the risk of SCI or CVE, and preoperative evaluation of brain perfusion may help guide decision-making regarding the need for prior LSA revascularization. Type I endoleak is the most common complication after TEVAR and can usually be treated with endovascular techniques. Some type 1

endoleaks can resolve spontaneously but require close surveillance. The current study showed no significant predictive factors for developing a type I endoleak and the need for secondary procedures is low.

**Conflict of interest.** The authors have no conflicts of interest to report.

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**Table 1.** Characteristics of 78 patients treated with thoracic endovascular repair.

Characteristics	Value	%
<b>Age (yr)</b>		
mean	66	
range	18–88	
<b>Sex</b>		
male	58	74
female	20	26
<b>ASA classification</b>		
2	7	9
3	30	38
4	38	48
5	3	6
<b>Coexisting conditions (no. of patients)</b>		
hypertension	46	59
hypercholesterolemia	22	28
previous artery reconstruction or amputation	21	27
respiratory disease	19	24
cigarette smoking	18	23
coronary heart disease	18	23
diabetes	10	13
chronic renal insufficiency	6	8
cerebrovascular disease	3	4

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**ASA: American Society of Anesthesiologists**

**Table 2.** Indications for primary treatment of thoracic aortic aneurysm.

	<i>TAA elective</i> ( <i>N=43</i> )	<i>TAA emergency</i> ( <i>N=8</i> )
Size (>6cm) or rapid growth	36	
LSA aneurysm	2	
Saccular aneurysm	5	1
Acute perforation		6
Symptomatic		1

**Table 3.** Indications for primary treatment of thoracic dissection.

	<i>Dissection chronic</i> ( <i>N=11</i> )	<i>Dissection acute</i> ( <i>N=16</i> )
Aneurysmatic dilatation (>6cm)	11	
Failure of medical therapy		3
Extravasation		11
Malperfusion		1
Symptomatic		1



**Table 4.** The location of the thoracic aorta lesion and endograft landing zone in 78 patients (aortic arch map proposed by Ishimaru [20]). Two patients with an ascending aorta dissection (zone 0) were primarily treated with open repair and secondarily with a thoracic endograft.

<b>Lesion zone</b>	Number of patients	%	<b>Endograft landing zone</b>	Number of patients	%
<b>0</b>	2	2.6	<b>0</b>	0	0
<b>1</b>	0	0	<b>1</b>	5	6.4
<b>2</b>	8	10	<b>2</b>	27	35
<b>3</b>	39	50	<b>3</b>	26	33
<b>4</b>	29	37	<b>4</b>	20	26

**Table 5.** Mortality, CVE, and SCI rates during 30 days according to aorta pathology.

	<b>Number of patients</b>	<b>Mortality N(%)</b>	<b>CVE N(%)</b>	<b>SCI N(%)</b>
<b>TAA</b>	51	4 (7.8)	2 (3.9)	1 (2.0)
<i>Elective</i>	43	3 (7.0)	2 (4.7)	1 (2.3)
<i>Emergency</i>	8	1 (12.5)	0	0
<b>Dissection</b>	27	1 (3.7)	4 (14.8)	1 (3.7)
<i>Chronic</i>	11	0	0	0
<i>Acute</i>	16	1 (6.3)	4 (25)	1 (6.3)

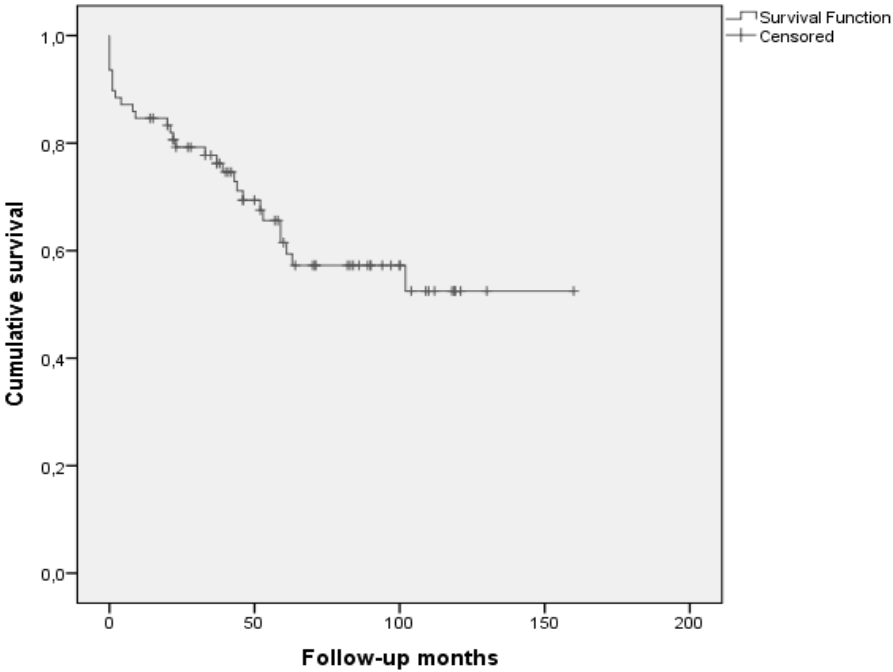
**Table 6.** Complications and adjunctive procedures in 78 TEVAR patients. Four patients had primary and secondary type I endoleak.

	<b>TAA</b>		<b>Dissection</b>	
	<i>elective</i>	<i>emergency</i>	<i>chronic</i>	<i>acute</i>
<b><i>Complications</i></b>				
<b>Endoleak</b>				
I	16	2	2	3
II	8	1	3	3
Migration	3	0	0	0
Stent fracture	1	0	0	0
Endotension	1	0	0	0
<b><i>Graft-related secondary procedures</i></b>				
<b>1. Transfemoral intervention</b>				
- embolization	1	0	0	3
- additional endograft	10	1	1	3
<b>2. Extra-anatomic procedure</b>				
- surgical subclavian closure	1	0	1	0
- carotid-subclavian bypass	4	0	0	1
- carotid-carotid bypass	2	0	0	1
<b>3. Transthoracic surgery</b>				
- conversion to open repair	0	0	0	1

**Table 7.** LSA coverage in patients undergoing TEVAR with landing zones 1–2 (primary and secondary procedure) : number of patients with associated complications. (CVE= cerebrovascular event, SCI=spinal cord ischemia). Of 27 patients who did not undergo primary LSA revascularization, four presented with left arm ischemia in the postoperative period two of whom required subsequent secondary, LSA revascularization.

<b>Primary procedure</b>	<b>Total number of patients</b>	<b>30-day mortality N (%)</b>	<b>CVE N (%)</b>	<b>SCI N (%)</b>	<b>Symptoms</b>
<b>LSA not covered</b>	<b>46</b>	3 (6.5)	2 (4.3)	1 (2.2)	
<b>LSA covered</b>	<b>32</b>	2 (6.3)	4 (12.5)	1 (3.1)	2
- Primary revascularization	<b>5</b>	0	1 (20)	0	0
- No primary revascularization	<b>27</b>	2 (7.4)	3 (11)	1 (3.7)	2
- Secondary revascularization	<b>2</b>	0	0	0	2
<b>Secondary procedure to treat type 1A endoleak</b>					
<b>LSA covered</b>	<b>6</b>	0	0	0	0
- No revascularization	<b>3</b>	0	0	0	0
- Revascularization	<b>3</b>	0	0	0	0

**Figure 1.** Cumulative survival 78 TEVAR patients (Kaplan-Meier survival analysis).



# **Hybrid repair of thoracoabdominal aortic aneurysms is a durable option for high-risk patients in the endovascular era**

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## **ABSTRACT**

**OBJECTIVE:** To report our long-term experience in using the hybrid technique in complex thoracoabdominal aneurysms (TAAAs).

**METHODS:** Between March 2005 and September 2013, ten TAAA patients underwent hybrid procedures with open renovisceral revascularization and thoracoabdominal aortic endografting. Patients were analyzed retrospectively.

**RESULTS:** Six men and four women with a mean age of 66 years (range 54–81 years) were treated electively during the study period. All four visceral vessels were revascularized in eight patients, while one patient underwent three-vessel revascularization and another two-vessel revascularization. The primary technical success rate was 100%. Eight of the procedures were single-staged, and the two most recent cases were performed in two stages. Perioperative and 30-day mortality was 0%. The mean follow-up was 55 months (4–133 months). None of the patients died due to aortic complications. Major complications included paraplegia (10%, N=1) and bowel ischemia (N=1). Postoperative cerebrospinal fluid (CSF) pressure and mean arterial pressure (MAP) measurement were systematically monitored and corrected. CSF drainage solved another four cases of paraparesis. Three patients required postoperative dialysis, but none of them permanently. Postoperative spinal cord ischemia (SCI) and renal complications accumulated in extensive TAAA cases. One renal graft was occluded 45 days after the initial procedure but was successfully treated with thrombolysis. One type I and one type III endoleak were noted and successfully treated with an additional stent graft. Two cases of type II endoleak were detected—one with a growing aneurysm sac was treated successfully, and another showed no growth and further procedures were abandoned after two embolization attempts. In long-term follow-up, 90% of the aneurysms showed shrinkage, by a mean of 23 mm (range 7–45mm).

**CONCLUSION:** The results of hybrid repair on high-risk patients with complex TAAAs are encouraging, and this approach is a valuable alternative when branched and fenestrated endovascular techniques are not considered an option.

## INTRODUCTION

A thoracoabdominal aortic aneurysm (TAAA) carries a significant risk of rupture, and less than 40% of patients with large untreated TAAA survive beyond 3 years [1, 2]. Although open surgical repair of TAAA has evolved significantly, as have anesthesiology and intensive care treatment, the overall 30-day mortality remains high, ranging from 5.0% to 19.0% [3-7]. After encouraging results from endovascular repair of abdominal aortic aneurysms (EVAR), a hybrid approach to TAAA repair with an open revascularization of the visceral arteries followed by an endovascular exclusion of the aneurysm was introduced to improve the outcome and to extend the indications to include high-risk patients [8,9].

Hybrid endovascular repair has the advantage of avoiding thoracotomy and suprarenal clamping, thus reducing both overall operative time and visceral ischemia. Although the renal ischemia time is reduced, the contrast agent required in the endovascular part of the procedure increases the risk of renal injury to up to 60% [10]. Also, extensive aortic repair with a hybrid procedure entails a risk of SCI up to 30%, but systematic postoperative CSF pressure and MAP monitoring has proven to diminish the risk of spinal cord ischemia (SCI) [11]. The staged strategy, i.e. the surgical and endovascular parts in separate procedures, has been suggested to reduce these complications, but the issue remains under debate [12]. As major complications still occur, some authors continue to question the ultimate benefits of this approach [12-15]. Furthermore, new, completely endovascular modalities for the management of TAAA have been introduced recently. These include fenestrated or branched endografts and the chimney technique. These newer techniques, however, are also associated with considerable morbidity and mortality [16,17].

The purpose of this study was to provide a concise overview of a single center's long-term experience with the hybrid approach to TAAA repair.

## MATERIALS AND METHODS

This study comprises ten consecutive patients undergoing a hybrid repair for a TAAA by means of an open renovisceral aortic revascularization together with an endovascular exclusion of the aneurysm in our academic hospital. The patients' data were collected prospectively from the local vascular registry between March 2005 and September 2013 and then analyzed retrospectively. The patients included six men and four women, with a mean age of 66 years (range 54–81 years). All patients were defined as high-risk patients according to the classification of the American

Society of Anesthesiologists (ASA, class 3 or 4) [18]. Hypertension was the most common risk factor (90%), followed by hyperlipidemia (60%). Four patients (40%) had a history of open aortic repair. The patient characteristics are presented in Table 1.

The indication for the treatment was a maximum aneurysm size of 5.5 cm or over. The preoperative anatomy of the aneurysms was classified according to Crawford as follows: 2 (20%), type I; 3 (30%), type II; 4 (40%), type III; and 1 (10%), type IV. Nine patients were treated electively and one urgently due to a symptomatic TAAA. Eight patients underwent the procedure in a single-staged fashion. Following the example of studies reporting a more favorable outcome after a two-staged approach for hybrid TAAA repair, we changed our treatment strategy in 2013, and the remaining two patients were treated accordingly. All procedures were performed under general anesthesia. CSF drains were placed prophylactically before the procedure (before the endovascular part in a two-staged procedure) for possible CSF drainage. In the last case, CSF pressure measurement was abstained from because of an antiplatelet medication (clopidogrel) that was evaluated to be not safe to pause. Spinal drains were left in place for 48 hours postoperatively, and a CSF pressure of 15 mmHg or over with or without neurological signs induced drainage. The objective mean arterial pressure (MAP) was kept at 90 mmHg or over for the duration of ICU treatment.

All procedures were performed by two vascular surgeons together with an interventional radiologist. The median diameter of the aneurysms was 72 mm at the time of treatment (range 58–84 mm). All four visceral vessels were revascularized in eight patients. One patient underwent three-vessel revascularization as the revascularization of the right renal artery turned out to be technically impossible. One patient with a Crawford class I TAAA received only two-vessel revascularization (the superior mesenteric artery [SMA] and the celiac trunk) since the aneurysmatic expansion only extended below the SMA and the renal segment was healthy. The patient also had a separate infrarenal abdominal aortic aneurysm (AAA) that was simultaneously repaired in an open procedure. A total of five patients (50%) underwent simultaneous open repair of the infrarenal aorta. Visceral debranching was performed with a transperitoneal approach. The inflow sites were retrograde, i.e. the native iliac arteries, the distal aorta, or an infrarenal prosthetic graft. The grafts utilized were synthetic vascular grafts (polyester or polytetrafluoroethylene (PTFE)). In the two most recent cases, Hybrid Vascular Grafts® (W.L.GORE) were used. The thoracic endografts were the Zenith® (Cook) (N=9) and Endurant® (Medtronic) (N=1). The stent grafts were landed in zones 3 or 4, and, in none of the cases, the left subclavian artery (LSA) was



covered (Table 2). Patients were followed at 1, 6, and 12 month after the procedure and then annually at the outpatient clinic. Aortic CT scans were performed at every follow-up visit. The six-month follow-up was omitted starting in 2010 if there was no complication at the primary procedure or at the one-month CT control examination. The patients were followed until the end of April 2016.

The end points were defined as primary technical success, 30-day mortality, all-cause mortality, irreversible paraplegia caused by spinal cord ischemia (SCI), permanent renal function impairment, and stent-graft- and visceral-graft-related complications. Primary technical success was defined as completed visceral reconstruction and successful stent graft deployment without a type I endoleak.

## RESULTS

Primary technical success was achieved in all cases, and there were no deaths during the first 30 days. The patients stayed at the ICU for a median of 3.5 days (range 2–29 days), and the median hospital stay was 11 days (range 8–58 days).

The mean follow-up was 55 months (range 4–133 months). No patients were lost during follow-up. There were four late deaths between four and 33 months, none of which were aneurysm- or device-related. One patient died of ischemic colitis, but all grafts were patent in a CT scan at the time of the diagnosis. The causes of death are listed in Table 3.

Irreversible SCI occurred in one patient (10%). An additional four patients suffered from transient lower extremity paresis which resolved with CSF drainage. As a CSF pressure of over 15 mmHg induced drainage with or without symptoms, a total of seven patients (70%) underwent CSF drainage. There were no CSF-drainage-related complications. Three patients required temporary dialysis after the initial procedure, and none required permanent dialysis. Three patients underwent an additional laparotomy during the hospitalization. Bowel ischemia occurred in one case, resulting in a partial bowel resection and colostomy after the endovascular part of the two-staged procedure. Another two patients underwent an explorative laparotomy at the second day. In the first of these, the clinical status and an increasing blood lactate level suggested visceral ischemia, but no further procedures were required. Unfortunately, the patient developed irreversible lower extremity paraplegia after the procedure. In another case, a decreasing blood hemoglobin level with hypotension proceeded to laparotomy, but there were no signs of active bleeding at the

time of the procedure. A cardiac complication was noted in one patient and a pulmonary complication in two, prolonging the ICU stay substantially, to up to 29 days. There were no strokes during hospitalization. Patients with an extensive Crawford type II TAAA had clearly more postoperative complications than others as 100% of them developed SCI (transient or permanent) and two out of three required temporary dialysis. Neither of the two patients treated with a two-staged approach developed SCI or renal insufficiency. Nine out of the ten patients in our cohort continued to live at home after the initial hospitalization.

The interval between the procedures for the two patients who were treated in a two-staged fashion was 36 and 97 days, respectively, while the planned interval had been two weeks. In the first case, visceral revascularization resulted in an open abdomen situation and prolonged the interval between the two stages by over a month. In the second patient, on the other hand, one of the renal grafts thrombosed at 45 days after the first stage/operation. It was successfully thrombolized and the patient assigned to permanent clopidogrel medication, and the renal artery graft was patent at the end of the follow-up. There were no other visceral graft complications, resulting in a graft-patency rate of 97%.

Two cases of type II endoleak were noted in follow-up, at 14 and 25 months, respectively, after the initial procedure. In the first case, embolization was attempted twice, but as the aneurysm showed shrinkage, further procedures were abstained. The second patient was treated successfully by means of coil embolization. There was one type I endoleak due to stent graft migration at 10 months, and it was successfully treated with an additional stent graft (Table 3). In long-term surveillance, 90% of the aneurysms showed a decrease in diameter of a mean of 23 mm (range 7–45 mm).

## DISCUSSION

We have performed ten hybrid repairs for TAAAs during the study period with a primary technical success rate of 100% and zero perioperative and overall aneurysm-related mortality. These findings reiterate the results of previous cohorts [19-21]. Unlike most of the published papers, Kuratani et al. reported the outcome of a relatively large cohort of 86 patients with an only 2% aneurysm-related death rate during long-term (89 months) follow-up [20]. Furthermore, according to a recent meta-analysis, the graft-patency rate is high (96.5%), thus

supporting the good long-term durability of hybrid treatment, and our data demonstrates similar figures (97%) [22].

Spinal cord ischemia remains a major concern after endovascular and open repair of TAAAs, despite the use of simultaneous protective measures such as CSF drainage. In the current study, 70% of the patients underwent CSF drainage as the CSF pressure exceeded 15 mmHg. This method probably saved four patients from permanent paraparesis. Especially extensive coverage or open repair of the descending thoracic aorta is a known risk factor for paraplegia [11,23]. In our cohort, most of the cases of SCI occurred in patients with extensive Crawford type II TAAA. Staged procedures have been shown to reduce this risk of SCI in surgical patients, and it is possibly explained by the vascular remodeling stimulation after the first intervention [24]. Recent studies on hybrid repair of TAAAs demonstrate the same benefits of the staged approach [12,13]. Consequently, we revised our treatment policy in 2013 and continue to treat all our TAAA patients in a two-staged fashion. The numbers in our cohort are too small to draw any conclusions about the impact of this change in treatment strategy on the patients' overall outcome, but neither of the patients treated after the policy was revised developed SCI. However, whatever strategy is used, one cannot overemphasize the importance of close postoperative monitoring of MAP and spinal fluid pressure in the ICU. Especially, patients with a previous aortic repair showed a high incidence of SCI (75%).

Postoperative renal insufficiency is another major complication after TAAA repair, and the need for hemodialysis has been shown to increase the risk of early death after open procedures [25]. The single-staged procedure carries a risk of renal injury of up to 60% due to the length of the procedure and the use of contrast agent right after renal revascularization [10]. Three out of eight patients (38%) in our cohort required temporary postoperative hemodialysis after a single-staged procedure. None of them had preoperative renal insufficiency. In the last two patients, who were treated with a two-staged procedure, we used the new Hybrid Vascular Graft® (Gore) in renal revascularization. There is data suggesting a shortening of renal ischemia and total operative time in open and hybrid repair of TAAA with this graft [26-28]. Neither of the two patients treated with a two-staged procedure in the current cohort required postoperative dialysis.

Despite the seemingly favorable effects of the staged approach, this strategy also has its drawbacks. According to Lin et al., 19% of their patients did not return for the second procedure either because they suffered from anxiety after the first procedure or their aneurysm ruptured during

the interval [10]. Although our planned two-week interval in the last two cases was delayed to up to 97 days, the patients were eventually treated successfully, encouraging us to continue with the two-staged strategy.

Even though endovascular treatment reduces the overall operative risks, high-risk patients who are considered unfit for open repair are also likely to suffer significant complications after hybrid TAAA procedures. The overall 1-year mortality after elective open TAAA repair in the general population is approximately 30%, and the mortality increases with age [29]. At the same time, patients with untreated TAAs have an equally high mortality rate (approximately over 60% in three years), mostly due to aneurysm rupture [1,2]. This indicates that an active treatment strategy should be considered. The reported morbidity and mortality rates in hybrid repair vary in different studies, but by far the longest reported follow-up of 86 patients demonstrated survival rates of 94.8%, 85.8%, and 66.6% at 2, 5, and 10 years, respectively [20]. However, after elective open repair of a TAAA, one third of the patients do not achieve functional benefit—i.e. they are not living at home and ambulatory [30]. This aspect has not been studied in patients treated with a hybrid approach, but it certainly highlights the importance of patient selection for both open and hybrid repair. In current study nine out of the ten patients returned living at home after the procedure.

Total endovascular repair has been introduced for patients unfit for open repair. Fenestrated and branched endovascular modalities have shown lower operative mortality rates than open repair, but major SCI rates remain as high as 30% despite various protective strategies [31]. There is an association between the extent of the aortic disease and the occurrence of SCI [23,31]. Furthermore, in total endovascular repair, even more extensive aortic coverage is often required to achieve adequate proximal and distal landing zones and to allow the branches to open. Experience, standardized protocols, and an early diagnosis of SCI, however, result in a better functional outcome after total endovascular repair [23]. Compared to total endovascular repair, the hybrid technique, combined with a standardized protocol, might even lower the degree of aortic coverage and the risk of SCI.

Our cohort is small, but the results are encouraging, with low rates of SCI, stroke, renal injury, and, most importantly of all, aneurysm-related mortality. When open repair or branched stent grafting is not an option, the hybrid repair offers a valid alternative.

**Table 1.** Characteristics of TAAA patients treated with hybrid repair. <sup>1</sup>The American Society of Anesthesiologists (ASA) classification.

<b>Patient no.</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>	<b>Mean</b>
<b>Sex</b>	F	M	F	M	F	M	F	M	M	M	<b>66</b>
<b>Age (Yr)</b>	55	59	64	62	77	64	71	71	81	54	
<b>ASA class<sup>1</sup></b>	3	4	4	3	4	3	3	3	3	3	
<b>Crawford class</b>	I	I	III	III	II	II	II	III	III	IV	
<b>Aneurysm diameter (mm)</b>	80	68	69	60	74	84	76	58	78	72	<b>72</b>
<b>Previous aortic repair</b>	Yes	No	No	No	Yes	No	Yes	No	Yes	No	
<b>Renal insufficiency</b>	No	Yes	No	No	No	No	No	No	No	No	
<b>Hypertension</b>	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	
<b>Coronary heart disease</b>	No	Yes	No	No	No	No	No	No	Yes	No	
<b>Hypercholesterolemia</b>	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	
<b>Diabetes</b>	Yes	No	No	No	No	No	No	Yes	No	Yes	
<b>Cerebrovascular disease</b>	No	Yes	No	No	No	No	No	No	No	No	
<b>Respiratory disease</b>	No	No	No	No	Yes	No	No	No	No	No	
<b>Cigarette smoking</b>	Yes	Yes	No	No	No	Yes	No	No	No	No	

**Table 2.** Characteristics of the hybrid procedure and related morbidity. Landing zone of stent graft by aortic arch map proposed by Ishimaru [32].

<b>Patient no.</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
<b>Procedure</b>	1-stage	1-stage	1-stage	1-stage	1-stage	1-stage	1-stage	1-stage	2-stage	2-stage
<b>Number of revascularized visceral arteries</b>	3	2	4	4	4	4	4	4	4	4
<b>Landing zone of stent- graft</b>	3	4	4	4	3	3	3	4	4	4
<b>Previous aortic repair</b>	yes	no	no	no	yes	no	yes	no	yes	no
<b>Simultaneous open repair of the infrarenal aorta</b>	no	yes	no	yes	no	yes	yes	yes	no	no
<b>Operation time (min)</b>	540	465	440	500	475	515	470	315	450+95	480+85
<b>Max. CSF pressure (mmHg)</b>	>20	<15	<15	22	>20	20	14	25	20	-
<b>CSF drainage</b>	yes	no	no	yes	yes	yes	yes	yes	yes	no
<b>Postop. paresis</b>	transient	no	no	transient	transient	permanent	transient	no	no	no
<b>Preop. Creatinine (umol/l)</b>	50	162	39	100	74	101	73	73	118	55
<b>Postop.Creatinine (umol/l)</b>	45	132	41	104	141	309	244	338	99	104
<b>Postop. dialysis</b>	temporary	no	no	no	no	temporary	temporary	no	no	no

**Table 3.** Summary of the follow-up and outcome of ten thoracoabdominal aneurysm patients treated with a hybrid procedure.

<b>Patient no.</b>	<b>Complication</b>	<b>Secondary graft-related interventions</b>	<b>Interval between primary and secondary procedure (months)</b>	<b>Follow-up time (months)</b>	<b>Outcome</b>
<b>1</b>	Endoleak I due to stent-graft migration	Endovascular stent-graft placement	10	26	died (ICH)
<b>2</b>				133	Alive
<b>3</b>				44	died (pulmonal cancer)
<b>4</b>				91	Alive
<b>5</b>	Endoleak II, Endoleak III	Embolization attempt twice, endovascular stent-graft placement	16, 17 49	78	Alive
<b>6</b>				4	died (ischemic colitis)
<b>7</b>				33	died (complications related to esophagus perforation)
<b>8</b>				61	Alive
<b>9</b>	Endoleak II	Coil embolization	26	36	Alive
<b>10</b>	Renal graft thrombosis	Thrombolysis	1	35	Alive

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