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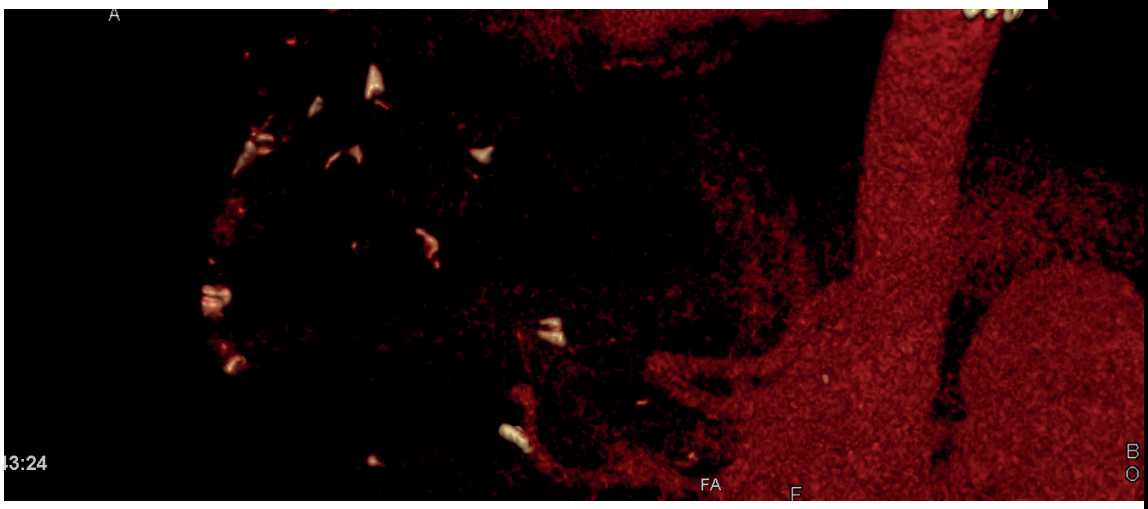
Petri Saari

Endovascular Treatment of Thoracic Aortic Diseases



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PETRI SAARI

Endovascular treatment of thoracic aortic diseases

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ABSTRACT

Thoracic aortic aneurysms and dissections can lead to devastating complications and eventually to premature death. A diseased segment of the aorta has traditionally been replaced with a surgical prosthesis. Open surgery is, unfortunately, associated with relatively high mortality and morbidity. Stent graft treatment was introduced on the side of open surgery 20 years ago, and there have been high hopes that mortality and morbidity could be lowered with this kind of mini-invasive procedure. Experiences have been promising, and patients tend to survive better after stent graft treatment, at least in the short term. However, the long-term durability of the first-generation stent grafts was not sufficient, which led to unnecessary reoperations and even ruptures of the treated segments. Stent design has been improved since, but the survival benefit of the stent graft–treated patients seems to vanish in 5 years. To be successful, stent graft treatment must overcome some limitations: Stent grafts need adequate landing zones in both ends of the graft, and important side branches of the aorta cannot be covered without consequences. The latest in stent graft design is the fenestrated graft, which was developed to overcome these obstacles. These grafts are very expensive, however, and because they have to be tailored individually to each patient, cannot be used in acute situations.

Intraoperative fenestration of the stent graft may be a way to make this treatment more available. Stent graft fabrics are quite difficult to traverse, though, and the dilatation of the fenestration is greatly facilitated when a cutting balloon is used. Nevertheless, the device to be used in the creation of fenestration needs some improvements.

Endovascular treatment of a thoracic aortic aneurysm is relatively safe, at least in the elective setting. However, to reduce the risk of periprocedural and postoperative complications, multidisciplinary and detailed preoperative imaging-based planning is helpful. A rigorous postoperative surveillance program is still compulsory for early detection and prompt treatment of late type I or III endoleak and to reduce the risk of late ruptures.

Marfan syndrome and especially Loeys–Dietz syndrome are debilitating connective tissue disorders, and these patients are very prone to developing vascular complications, particularly of the aorta. The nature of these diseases mandates aggressive treatment strategies and close surveillance programs. Open surgery remains the mainstay of the treatment, but endovascular options should be considered whenever possible to reduce operative complications. Endovascular treatment should be planned so that the landing zones lie within the previously treated aorta.

National Library of Medicine Classification:

Medical Subject Headings: aorta, thoracic aorta, aortic diseases, aortic rupture, aortic dissection, endovascular procedures, stent, Marfan syndrome, Loeys–Dietz syndrome

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TIIVISTELMÄ:

Rinta-aortan aneurysmat ja dissekaatiot ovat vakavia sairauksia, joiden akuuttien komplikaatioiden, kuten esimerkiksi aortan repeämän, seurauksena potilas sairastuu vakavasti ja pahimmillaan tilanne voi jopa johtaa ennenaikaiseen kuolemaan. Sairas aortan segmentti on perinteisesti korvattu avokirurgisessa leikkauksessa proteesilla. Kirurgiseen hoitoon valitettavasti liittyy varsin runsaasti komplikaatioita, minkä vuoksi on etsitty vähemmän potilasta rasittavia hoitomuotoja. Noin 20 vuotta sitten esiteltiin ensimmäisen kerran suonen sisäisesti tehtävä stettigraftihoito avokirurgian rinnalle ja sittemmin hoitomuoto on vallannut alaa varsin nopeassa tahdissa. Ainakin lyhyellä aikavälillä stenttigraftilla hoidetut potilaat selviytyvät paremmin kuin avokirurgisesti hoidetut potilaat, mutta varsinkin alkuvaiheessa stenttigraftien rakenne ei ollut riittävän luja, mikä johti tarpeettomiin uusintaoperaatioihin ja jopa aortan repeämiin. Stenttigraftien rakennetta on sittemmin parannettu, mutta siitä huolimatta ainakin toistaiseksi näyttää, että setenttigraftipotilaiden parempi ennuste kestää vain noin 5 vuotta operaatiosta. Stenttigraftihoito ei myöskään valttämättä sovellu kaikille potilaille, sillä proteesin molempiin päihin tarvitaan riittävän pitkät kiinnittymisalueet ja tärkeitä aortan haaroja ei voi peittää ilman vakavia komplikaatioita. Viimeisimmät kehitysaskeleet näiden ongelmien kiertämiseksi ovat ns. fenestroidut stenttigraftit. Nämä ovat kuitenkin huomattavan kalliita ja koska ne pitää suunnitella ja valmistaa jokaiselle potilaalle yksilöllisti, ne eivät sovellu akuutteihin tilanteisiin.

Stenttigraftin asennuksen yhteydessä tehtävä fenestraatio voisi olla yksi tapa, jolla stenntigraftihoitoa voisi tarjota myös potilaille, joilla kiinnittymisalue jää lähellä sijaitsevan aortan sivuhaaran vuoksi muuten liian lyhyeksi. Stenttigraftien kangasmateriaali on tosin varsin vaikeasti läpäistävissä, joskin leikkaavan pallon avulla muodostettu fenestraatio on mahdollista laajentaa täyteen mittaansa. Fenestraation luomisessa käytetty neulakatetri vaatii kuitenkin vielä jatkokehittelyä.

Rinta-aortan aneurysmien hoito suonensisäisesti on ainakin elektiivisillä potilailla verrattaen turvallista. Operaation liittyvien komplikaatioiden minimoimiseksi edeltävä kuvantaminen on kuitenkin syytä suunnitella ja analysoida huolellisesti. Operaation jälkeinen seuranta on myös syytä toteuttaa säännöllisenä koko potilaan loppuelämän ajan, jotta mahdollisesti myöhemmin kehittyvät tyyppi I tai III lekaasit voitaisiin ajoissa hoitaa ja ehkäistä aneurysman puhkeaminen.

Marfanin syndrooma ja erityisesti Loeys-Dietz syndrooma ovat sidekudossairauksia, jotka johtavat hyvin nuorella iällä verisuonikomplikaatioihin erityisesti aortan alueella. Sairauksien luonne edellyttää varhaista puuttumista näihin verisuoniongelmiin ja potilaita on seurattava säännöllisesti. Avokirurgia on näiden potilaiden kohdalla yleensä pääasiallinen hoitomuoto, mutta suonensisäistä hoitoa kannattaa harkita avokirurgian ohessa vähentämään leikkauskomplikaatioita. Stenttigraftihoidot on näillä potilailla yleensä suunniteltava siten, että suonensisäisen proteesin kiinnittymisalueet tulevat aina aiemmin protetisoidun aortan alueella.

Luokitus:
Yleinen Suomalainen asiasanasto: aneurysma, aortta, aortan dissekoituma, suonensisäinen verisuoniproteesi, aortan repeämä, Marfanin oireyhtymä, Loeys-Dietz oireyhtymä

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Kuopio September 2013

Petri Saari

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List of the original publications

This dissertation is based on the following original publications:

I Saari P, Manninen H. Fenestration of Aortic stent grafts—in vitro tests using various device combinations. *Journal of Vascular and Interventional Radiology 22: 89-94, 2011.*

II Saari P, Lähteenvuo M, Honkonen K, Manninen H. Antegrade *in situ* fenestration of aortic stent graft: *in-vivo* experiments using a pig model. *Acta Radiologica 53: 754-758, 2012.*

III Saari P, Biancari F, Ihlberg L, Jaakkola P, Nevala T, Perälä J, Roth W-D, Manninen H. Early and Mid-term Outcomes After Endovascular Treatment of Degenerative Aneurysms of the Descending Thoracic Aorta: A Finnish Multicenter Study. *Journal of Endovascular Therapy. 20: 257-264, 2013.*

IV Saari P, Jaakkola P, Perälä J, Manninen H. Hybrid treatment of aortic pathology in connective tissue disorders. Submitted.

Contents

Abbreviations

AoD	Aortic dissection
BT	Brachiocephalic trunk
CCA	Common carotid artery
CI	Confidence interval
CoA	Coarctation of aorta
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
CTA	Computed tomographic angiography
DTA	Descending thoracic aorta
ePTFE	Expanded polytetrafluoroethylene
EVAR	Endovascular aortic repair
FEP	Fluorinated ethylene-propylene
FNB	Fibrillin
GCA	Giant cell arteritis
IMH	Intramural hematoma
LDS	Loeys–Dietz syndrome
LSA	Left subclavian artery
MFS	Marfan syndrome
MR	Magnetic resonance
MPR	Multi planar reformat
MRA	Magnetic resonance angiography
NIS	Nationwide Inpatient Sample
OR	Odds ratio
PAU	Penetrating atherosclerotic ulcer
PET	Polyethylene terephthalate
PTA	Percutaneous transluminal angioplasty
PTCA	Percutaneous transluminal coronary angioplasty
TAA	Thoracic aortic aneurysm
TEVAR	Thoracic endovascular aortic repair
TGF	Transforming growth factor
VRT	Volume rendering technique

1 Introduction

Diseases of the thoracic aorta can be divided into two main groups: congenital diseases, such as coarctation, and acquired diseases. The latter group can be further divided into three groups:

1. Aneurysms
2. Dissections, penetrating ulcers, and intramural hematoma (IMH)
3. Traumatic ruptures

Aneurysm formation can eventually lead to further enlargement of the aorta, which finally ruptures, and to the death of the patient, if left untreated. In dissection or IMH, the blood enters between the layers of the aortic wall, which can lead to the rupture of the aorta, pericardial tamponade, or aneurysm formation, which are associated with high mortality. Traumatic rupture of the aorta usually leads to death on location. Some patients, however, survive, and along with the treatment of other injuries, the ruptured aorta should also be repaired to prevent further complications.

From the early 1950s, diseases of the thoracic aorta have been treated by replacing the diseased segment with a prosthesis. Surgery of the thoracic aorta is usually very demanding and associated with high morbidity and mortality. From the early 1990s, the endovascular technique has emerged on the side of surgical repair as less invasive. There have been hopes that an endovascular approach could reduce the rate of complications associated with the operative treatment. However, long-term durability of endovascular treatment is still lacking, and these patients need lifelong surveillance. Some unresolved issues in stent design also persist, such as how to handle the vitally important side branches in the aortic arch.

2 Review of the literature

2.1 DISEASES OF THORACIC AORTA

2.1.1 Etiology and pathophysiology

The wall of the aorta is composed of three layers: intima, media, and adventitia. The intima is a single layer of endothelial cells, lying on the basal lamina. The media consists of elastic fibers and interposed muscular cells, collagen, and ground substance. The elastic fibers give distensibility to the aorta and function in cooperation with the heart, maintaining the aortic pressure during diastole, while collagen gives tensile strength to the aortic wall. The adventitia is, on the other hand, the strength layer of the aorta, maintaining aortic integrity and preventing it from deformation or rupture.

Aneurysm is defined as a permanent localized dilatation of the aorta, involving at least a 50% increase in diameter compared with the normal measure. All three layers of the aorta must be present at the wall of the aneurysm. The incidence of thoracic aortic aneurysm (TAA) is about 10/100 000/y [(1)]. Women and men have a similar incidence, but the age at diagnosis is higher in women than in men (mean age, 75.9 vs. 62.8 years) [(1)].

Aortic dissection (AoD) is a disruption of the media layer of the aorta with bleeding within and along the aortic wall. It can occur with or without aneurysm being present. Because of the high mortality associated with AoD, the exact incidence is difficult to define. Population-based studies suggest it to be 2–3.5/100 000/y. Mean age at presentation is about 63 years with a slight male predominance (65%) [(2)].

The pathology associated with TAAs and dissections is termed as medial degeneration, which is characterized by disruption and loss of elastic fibers and increased deposition of proteoglycans. There are also areas of smooth muscle cell loss in the medial layer. Atherosclerosis can be present in the thoracic aorta, but these changes are usually superimposed on medial degenerative disease. Some inflammatory cell infiltration has also been found in these diseases [(2)].

Penetrating atherosclerotic ulcer (PAU) and IMH are variants of AoD in which blood enters between the layers of the aortic wall. In contrast to dissection, however, there is no false lumen formation; instead, the blood coagulates and forms a hematoma. Whether the IMH results from rupture of the small vasa vasorum located in the medial layer of the aorta or from a small intimal tear is still controversial. When present, penetrating ulcers often arise in the areas where the atherosclerosis is most predominant.

Marfan syndrome (MFS) is an autosomal dominant connective tissue disorder. It predisposes patients to aortic pathology, especially to aortic aneurysm and eventually to AoD. In 2010, Loeys et al. [(3)] defined the revised set of criteria for the diagnosis of MFS. It is caused by mutation in the FNB1 gene on chromosome 15. The gene encodes fibrillin 1 glycoprotein, which is essential for the formation of elastic fibers found in connective tissue, provides a scaffold for elastin deposition in the extracellular matrix, and serves as a regulator of TGF-β (transforming growth factor beta) signaling [(4)]. In MFS, typical pathological findings in the vessel wall are disorganization and fragmentation of elastin microfibrils. Virtually every patient with the syndrome shows evidence of aortic pathology during their lifetime. Other typical manifestations of the disease are, for example, bone overgrowth, joint laxity, ectopia lentis or lens dislocation, and valvular diseases. It is estimated that about 50% of patients under 40 years of age with AoD have a history of MFS

[2]. Without treatment, the prognosis of the disease is poor. In the early 1970s, mean age at death of these patients was 32±16 years, and the median (50%) cumulative probability of survival was only 48 years [5]. The life expectancy has, however, increased >25% since then, and the mean age at death was 41±18 years in 1993, and the median (50%) cumulative probability of survival was 72 years [5]. This increase is partly explained by overall improvement in life expectancy but also by benefits from modern cardiovascular surgery and maybe by a greater proportion of milder cases because of greater diagnostic capture.

Loeys–Dietz syndrome (LDS) is a rare, autosomal dominant aortic aneurysm syndrome, which includes involvement of many other systems [6,7]. The syndrome results from mutations in TGF receptor I or II genes (TGFBR1 or TGFBR2), and the diagnosis is confirmed by mutational analysis of these genes. Characteristic findings are marked arterial tortuosity or aneurysm formation, hypertelorism, and bifid uvula or cleft palate (Figure 1a and 1b). The vascular disease is very aggressive, and if left untreated, associated with a mean age at death of 26 years [7]. The majority of patients have an aortic root aneurysm leading to AoD.

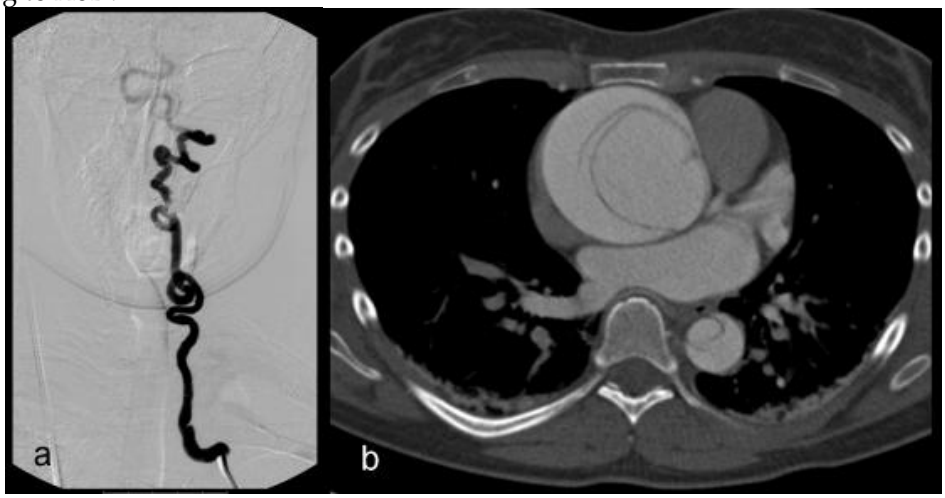

Figure 1. Loeys–Dietz syndrome. (a) Marked tortuosity of the left vertebral artery. (b) Aneurysmal dilatation of the ascending aorta and acute DeBakey type I, Stanford type A dissection.

Ehlers–Danlos syndrome is a rare autosomal dominant disorder characterized by easy bruising, characteristic facial features, and rupture of arteries, uterus, and intestines [2]. Most fatal complications are attributable to arterial dissections or ruptures involving the thoracic or abdominal aorta. Life expectancy is reduced, and mean lifespan is only 48 years [2].

Turner syndrome is defined as complete or partial absence of one sex chromosome, and the most common karyotype is 45,X. These patients have increased cardiovascular mortality, especially AoD [2]. However, the majority of dissections in women with Turner syndrome occur in patients with known risk factors for dissections such as bicuspid aortic valve, coarctation, or systemic hypertension.

Bicuspid aortic valve is found in 1–2% of the population and is the most common congenital abnormality affecting the aorta [2]. It can be inherited as an autosomal dominant condition and is associated with TAA formation. As many as 15% of patients with AoD have bicuspid aortic valves [2].

In adult patients with an **aberrant right subclavian artery**, the aorta is usually pathologic and prone to dilate, dissect, and rupture [2]. In these patients, the right subclavian artery arises as a fourth branch from the aorta and courses behind the esophagus.

Coarctation of the aorta (CoA) is usually treated soon after birth, but these patients can present later in life with multiple problems such as heart failure, intracranial hemorrhage, hypertension aneurysm, or AoD. The incidence of coarctation is 40–50 /100 000 live births [2].

Takayasu arteritis is an idiopathic T-cell–mediated vasculitis involving the aorta and its branches [2]. The incidence is about 2.6/1 000 000 persons. The disease affects women 10 times more often than men, and the age of onset is usually under 40 years. The vascular involvement is characterized by either stenosis or aneurysm formation including aortic aneurysms, most commonly in the descending thoracic aorta (DTA).

Giant cell arteritis (GCA) is a vasculitis involving the aorta and its branches. In contrast to Takayasu arteritis, patients tend to be older, over age 50 years, and the incidence is about 20/100 000 persons. Aortic involvement, namely AoD or aneurysm, has been found in 18% of patients with GCA [2].

Infectious arteritis resulting from bacterial, fungal, viral, spirochetal, or tubercular organisms can also lead to aneurysm formation in the aorta, although it is very rare. Infection of the aorta may arise from direct spread from adjacent structures, e.g., mediastinitis or abscess, septic embolus arising from bacterial endocarditis, or hematogenous dissemination of microbes in the setting of sepsis or intravenous drug abuse [2].

Overall, known risk factors for development of AoD are conditions that result in aortic medial degeneration or that place extreme stress on the aortic wall. Up to 75% of patients have hypertension, which is often uncontrolled [2]. Genetic syndromes and inflammatory conditions increase the risk, as described before.

2.1.2 Clinical presentation

Aneurysms of the thoracic aorta are usually insidious and often asymptomatic until the rupture. They can be diagnosed by chest x-ray or computed tomography (CT) scan obtained for other reasons. Aneurysm can, of course, cause compression symptoms to the adjacent structures. Aortic valve regurgitation may develop because of aortic root dilatation, and embolization of atherosclerotic debris with end-organ symptoms may occur.

Dilatation of the aorta and aneurysm formation eventually lead to rupture of the aorta with massive hemorrhage or pericardial tamponade in the case of ascending aortic aneurysm. With rupture of an aneurysm, almost 100% of patients die, and only half of such patients even reach the hospital [8].

Risk of the rupture grows markedly after the diameter of the aneurysm reaches 6 cm in the ascending aorta and 7 cm in the descending aorta [9]. The lifetime cumulative risk of rupture jumps to about 40% after the diameter reaches this “hinge point”. The yearly risk of rupture, dissection, or death is as high as 14.1% at 6 cm.

Acute aortic syndromes often present in a similar fashion regardless of the underlying pathology (AoD, PAU, IMH, or contained rupture). About 9 out of 10 patients present with severe, instantaneous pain that may, if the patient survives the acute phase, subsequently ease. Location of the pain reflects the site of disruption; dissection of the ascending aorta usually causes chest pain, and dissection in the descending aorta usually triggers back or abdominal pain [2]. However, older patients or patients with MFS or who are on steroids can

present without pain, which needs to be remembered. Other presenting symptoms can be hypotension or shock (~27%), cardiac tamponade (~5%), ischemic nerve or spinal damage (~5%), lower extremity ischemia (~10%), or cerebrovascular accident (~8%) [2].

Perfusion deficits, which usually result from dissection flap occlusion of the ostium of the side branch, have long been recognized as a common clinical manifestation of AoD. Pulse deficits are present in up to one third of patients [2]. Mesenteric and renal ischemia are feared complications in case of dissection of the descending aorta as are cerebrovascular insults when the dissection is in the ascending aorta.

Cardiac complications are not infrequent, especially when the ascending aorta is involved. Over half of patients with ascending AoD develop aortic regurgitation. The dissection flap may occlude the ostium of coronary arteries, and along with the hemodynamic stress associated with AoD, myocardial infarct may occur. Myocardial ischemia is present in up to 19% of patients [2]. Pericardial pathology is also a relatively frequent complication of dissection of the ascending aorta. Pericardial fluid may collect in up to a third of patients, or because of rupture of the dissection directly into the pericardium, a cardiac tamponade can arise because of hemopericardium. Cardiac tamponade is diagnosed in 8–10% of patients [2].

AoD should be classified based on anatomical landmarks because that forms the basis for decisions regarding surgical versus conservative management. The two most commonly used classification systems are the DeBakey and Stanford systems.

The **DeBakey** system categorizes the dissection into one of three groups based on the site of origin and the extent of the dissection:

- Type I: Dissection originates in the ascending aorta and extends to the descending aorta.
- Type II: Dissection originates in and is restricted to the ascending aorta.
- Type III: Dissection originates in the descending aorta, and the ascending aorta is intact.

The **Stanford** classification categorizes the dissection into two groups:

- Type A: Dissection of the ascending aorta occurs with or without dissection of the descending aorta.
- Type B: Dissection is restricted to the descending aorta, and the ascending aorta is intact.

Dissection of the ascending aorta is prone to lead to the cardiac complications already described. These complications can be fatal, and to prevent these devastating consequences, prompt surgical intervention is usually mandated [2].

The natural history of **IMH** is variable, and the hematoma can in some cases entirely resolve (10%) or, in the worst case, eventually rupture. The natural course of the disease is difficult to predict, so surgical or endovascular treatment should usually be considered [2].

Traumatic rupture of the thoracic aorta is usually a result of a motor vehicle accident. Most commonly, the aorta transects below the level of the left subclavian artery (LSA). Patients usually also have other trauma such as head injury, injury to the thoracic and abdominal organs, and multiple fractures. Patients with traumatic rupture of the thoracic aorta usually die where the event occurred because of massive bleeding. It is estimated that only ~10% of these patients ever reach a hospital and that only 2% will ultimately survive [2]. Traumatic rupture should be corrected immediately either surgically or by endovascular means along with the treatment of other injuries.

2.1.3 Diagnostic imaging

The diagnosis of aortic pathology and follow-up of these patients require dedicated imaging. Chest x-ray is usually the initial imaging method, especially in acute situations. The sensitivity and specificity are, however, poor in excluding aortic pathology, so other modalities are needed as well.

To assist in the decision-making process, aortic imaging has certain essential requirements:

1. To reliably show or exclude the aortic pathology and its location
2. To give a reliable and reproducible estimate of aortic diameter at the level of pathology and also at certain points (aortic valve, sinuses of Valsalva, sinotubular junction, ascending aorta, arch, and descending aorta)
3. To show or exclude aortic rupture, mediastinal hematoma, pericardial fluid, and continuing bleeding
4. To show the potential extension of aortic pathology in branch vessels and evidence the possible end-organ injury

CT has many advantages and has proven its usefulness in diagnostic workup of these patients. The availability of CT is common, and the ability to image the whole aorta and branch vessels and the short acquisition time are great advantages. Three-dimensional data are usually readily available, and electrocardiogram-gated techniques give motion-free images of the aortic root as well. The sensitivity can be as high as 100% with a specificity of 98–99% [(2)].

Magnetic resonance (MR) imaging is also very accurate in the diagnosis of aortic disease. However, the availability of MR is usually not as common as for CT, and the acquisition times are considerably longer; thus, in the acute setting, CT is usually the preferable imaging modality. In elective situations and in the follow-up, MR should be used whenever accessible, especially in younger patients, to reduce radiation dose. The other major advantage of MR over CT is the ability to image without contrast media.

Ultrasound is a relatively good and reproducible method in imaging of the heart and aortic root. However, ultrasound is usually highly operator dependent, and the visibility of the other parts of the thoracic aorta is usually limited.

Angiography is not usually considered as a primary diagnostic method in aortic syndromes. However, in the guidance of endovascular procedures and sometimes in preoperative planning, it has an invaluable role.

2.2 TREATMENT OF THORACIC AORTIC PATHOLOGY

2.2.1 Acute aortic syndromes

After the definitive diagnosis of **AoD** or its variants (**IMH, penetrating ulcer**) is made, the first goal of the treatment is to stabilize the patient and limit the propagation of the disease while the decision between conservative and operative management is made. To limit the progression of the false lumen, the aortic wall sheer stress should be reduced. The wall stress is affected by the velocity of ventricular contraction, rate of ventricular contraction, and blood pressure. β-blockers control all three parameters and should be titrated to maintain the heart rate and blood pressure at the lowest tolerable levels. For most patients,

blood pressure between 100 to 120 mmHg and a heart rate <60 bpm are attainable [10]. In patients who cannot tolerate β-blockers, calcium channel blockers such as diltiazem or verapamil should be used. If adequate blood pressure control is not achieved, vasodilators, such as sodium nitroprusside, should be added. If the patient is hypotensive or even normotensive, possible bleeding in the pericardial space, mediastinum, or pleura must be considered.

The patients with dissection of the ascending aorta (**Stanford type A or DeBakey type I or II**) are at a high risk of life-threatening complications. Medical treatment alone is associated with a mortality of 30% by 48 hours [10]. The aim of operative treatment is to prevent the complications associated with the dissection such as cardiac tamponade, aortic rupture, or end-organ ischemia. In 1966, DeBakey [11] introduced a surgical technique to reconstruct the ascending aorta that dramatically reduced the mortality associated with the disease. At present, the implantation of a composite graft, i.e., replacement of the ascending aorta and aortic valve, is usually recommended [10]. Adjunctive methods, such as hypothermic circulatory arrest and selective retrograde perfusion of head vessels, have been used with good outcomes [10]. Operative mortality at experienced centers varies between 15 and 35%, which is considerably lower than the 50% mortality associated with medical therapy [10].

Stanford type B dissections (the disease confined to the descending aorta) are at present treated with medical therapy because routine operative management has no proven superiority over medical treatment [10,12]. In the hospital, the mortality with type B dissections has been reported to be about 10%, and long-term survival with medical therapy is 60–80% at 4–5 years and 40–45% at 10 years [10]. Operative treatment should be considered to prevent or relieve life-threatening complications, such as progression of dissection, aneurysm expansion, aortic rupture, and end-organ ischemia or severe pain.

Modern surgical techniques have been presented elsewhere by Coselli et al. [13]. Surgical repair of the descending aorta is usually done from a left thoracotomy and includes moderate systemic heparinization, mild hypothermia, and sequential aortic clamping. Left heart bypass is often used to reduce the spinal and visceral ischemia time.

Endovascular repair of the aorta was first introduced in the early 1990s [14,15]. The endovascular stent graft consists of a supporting metallic frame and a fabric attached to this frame. The prosthesis is packed in a catheter with an external diameter of 6–10 mm. The catheter is usually introduced from the groin and navigated through the arteries under fluoroscopic control. Once the catheter is in place, the stent graft is released by pulling away the sheet covering it, and the graft expands by itself, attaching to the aortic wall and excluding the pathologic segment away from the bloodstream.

Unfortunately, no published randomized trials have compared the outcomes of endovascular stent grafting with conventional open operation. Current recommendations are based on observational studies and comparisons of cohorts of patients. Endovascular treatment has a potential advantage over open surgery because a thoracotomy incision can be avoided as can extracorporeal circulatory support and clamping of the aorta. Therefore, in-hospital mortality rates seem to be significantly lower after endovascular treatment, and the hospital stay tends to be shorter [16-18]. However, long-term durability is still not proven, and the survival advantage of endovascular treatment seems to vanish after 5 years (endovascular vs. open, 53.4% vs. 53.3%) [17]. The intersection of the survival curves may be partly explained by the re-operations associated with the endovascular treatment and

partly because older patients and patients with severe co-morbidities tend to shift to the endovascular group. There have also been some flaws in the design of the first-generation stent grafts, and there are hopes that the second- and third-generation versions will be more durable.

Endovascular grafting may be well suited especially for patients with severe comorbidities and who thus would be poor surgical candidates. However, although definitive evidence of the superiority of endovascular treatment is lacking, this treatment is continuously gaining popularity over open surgical repair and at present is considered a first-line option in most centers treating these patients. Nevertheless, with younger patients, caution is needed because long-term durability is still unresolved and patients require regular and lifelong surveillance after endovascular treatment, which is quite restrictive for them and markedly increases their cumulative lifetime radiation dose.

Implantation of the endovascular prosthesis requires adequate landing zones in both ends, and the neck above and below the pathologic segment should be at least 10 mm to prevent long-term complications [19]. Important side branches of the aorta cannot be covered without serious consequences, and in certain situations where an adequate landing zone cannot be otherwise achieved, additional procedures such as fenestrated or branched stent grafts, chimney procedures, carotid(–carotid)–subclavian bypasses, or bypass of the visceral arteries have to be considered. These alternatives will be discussed later.

IMH and **PAU** should be treated, according to the present knowledge, following the same principles as with dissections [2]. Pure intimal defects without IMH are usually insidious findings and are treated as saccular aneurysms based on their maximum diameter. When there is IMH present with or without intimal defect, the treatment should be based on the anatomical location of the disease as described previously in the section dealing with dissections.

2.2.2 Thoracic aortic aneurysms

Once the aortic diameter reaches 6 cm, the risk of rupture increases markedly. Ruptured aneurysms have a very poor prognosis, and the aneurysm therefore should be treated before its diameter reaches this hinge point. However, in patients with connective tissue disorders such as LDS and MFS, the risk of complications is considerably increased even at smaller diameters. Thus, the current recommendation states that the aorta should be repaired when the diameter reaches 4.5 cm in LDS patients and 5.0 cm in MFS patients [2]. At present, two options are available for the operative management of aneurysmal disease: open surgical and endovascular treatment. These can also be used in combination.

Open surgery of the thoracic aorta is usually very demanding and requires good surgical expertise. The postoperative mortality can be high, and the experience of the surgeon in treating these patients and the volume of the center have a significant impact on survival [20].

For patients with isolated **aneurysm of the ascending aorta**, open surgical resection and graft replacement are usually the recommended procedure. Patients with aortic valvular disease should be considered also for valve replacement at the same time [2]. Only some anecdotal case reports have been published on the endovascular treatment in the ascending aorta. The present recommendations state that open surgical treatment is the first-line option and that endovascular treatment should be done only in combination with surgical procedures as hybrid operations [2].

Aneurysms of the aortic arch are usually associated with aneurysmal disease of the ascending aorta or the adjacent descending aorta. Indications for treatment are those for the adjacent aortic segment. At present, endovascular treatment has not been officially accepted for treatment of aortic arch aneurysms. Therefore, the aortic arch is usually replaced with a synthetic graft, and the arch vessels are attached to the graft using a patch of aorta or using a graft containing three branches. Also, an "Elephant trunk" procedure has been employed when it is necessary to provide a landing zone for the endovascular graft at the descending aorta. However, experience is accumulating with operative procedures in which arch vessels are translocated or bypassed from the ascending aorta and an endovascular graft is then placed in the aortic arch covering the diseased segment [(2)]. Open surgery requires cardiopulmonary bypass and hypothermia, so these kinds of hybrid procedures are tempting alternatives especially for patients who are otherwise considered to be poor surgical candidates.

At the **descending aorta**, open surgical treatment is usually done from a posterolateral thoracotomy [(13)]. The majority of complications result from the end-organ ischemia during the operation, so sequential aortic clamping, hypothermia, and systemic heparinization are used to maximize organ protection. Left heart bypass can serve to reduce the spinal and visceral ischemia time. Segmental artery reattachment at the level of T8–L1 is also recommended as well as cerebrospinal fluid drainage to prevent neurological complications resulting from spinal ischemia. Endovascular treatment is gaining popularity because the operative and postoperative mortality and morbidity seem to be significantly lower than those of open surgery [(16,17,21-24)]. However, long-term durability is still unproven, and because the mortality after open surgery of patients under age 60 years seems to be relatively low [(25)], caution is needed when considering endovascular treatment for younger patients.

Implanting the endovascular prosthesis has some anatomical requirements to be successful. The access vessels must be of suitable size (>8 mm diameter), and pronounced elongation and calcification of iliac vessels increases the risk of complications. However, these obstacles can be overcome with the use of conduits, i.e., short stubs of synthetic prosthesis implanted directly into the iliac artery or aortic bifurcation. To securely seclude the aneurysm from the bloodstream, the proximal and distal necks, i.e., the zone where the stent graft attaches to the aortic wall, must be at least 15 mm or longer. Continuous blood flow directly from the aorta to the aneurysm, the so-called endoleak (Table 1, Figure 2), results in further aneurysm growth and eventual rupture if left untreated. Important side branches of the aorta, such as the brachiocephalic trunk (BT), carotid arteries, or renal or mesenteric arteries, cannot be covered without serious consequences. Even covering of the LSA can expose the patient to neurologic complications, such as stroke, spinal ischemia, and paraparesis [(26,27)]. Thus, if the length between the aneurysm and an important side branch is less than 15 mm, surgical repair must be considered or some additional procedures be performed to increase the length of the landing zone.

Table 1. Classification of endoleaks

Type	Cause of perigraft flow	Treatment strategy
I	Inadequate seal proximal to distal graft attachment site	Should be repaired when diagnosed.
II	Retrograde aortic branch arterial blood flow into aneurysm sac	May spontaneously thrombose. If aneurysm is expanding, embolic occlusion of branch artery is indicated.
III	Structural failure of endograft	Should be repaired when diagnosed.
IV	Stent graft fabric porosity	Usually is resolved, with reversal of anticoagulation.
V	Expansion of aneurysm without demonstrable endoleak, so-called endotension	Reline the endograft with a second endograft.

Adapted from Hiratzka et al. [(2)].

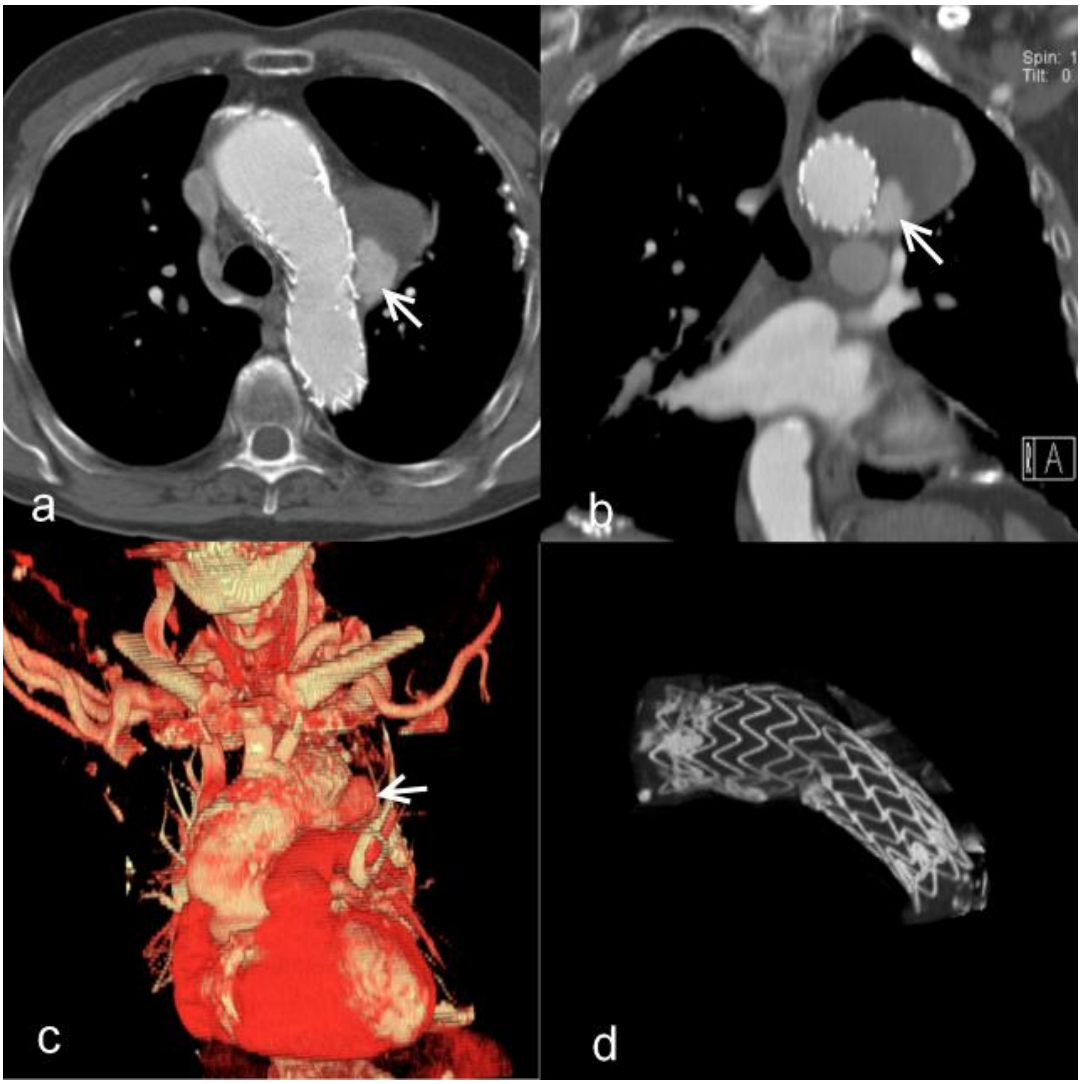

Figure 2. Type III endoleak. (a) Axial image at the aortic arch level. Continuous blood flow through the graft fabric directly into the aneurysm. (b) Coronal and volume rendering technique reconstructions of the same situation. (d) No visible fractures in the metallic skeleton of the stent graft.

2.2.3 Hybrid operations

If coverage of the LSA is anticipated, the patency of the contralateral subclavian artery must be confirmed, and verification that vertebral arteries communicate in the basilar artery must be done before implantation of the stent graft. However, as stated before, these patients may be at increased risk of postoperative neurologic complications. Revascularization is most commonly done with a bypass operation from the left carotid artery. When the left carotid artery must also be covered, a carotid–carotid–subclavian bypass is a feasible alternative. Additionally, when treating aortic arch aneurysms and the innominate brachiocephalic artery has to be covered, all of the arch vessels can be bypassed from the ascending aorta before stent graft implantation (Figure 3).

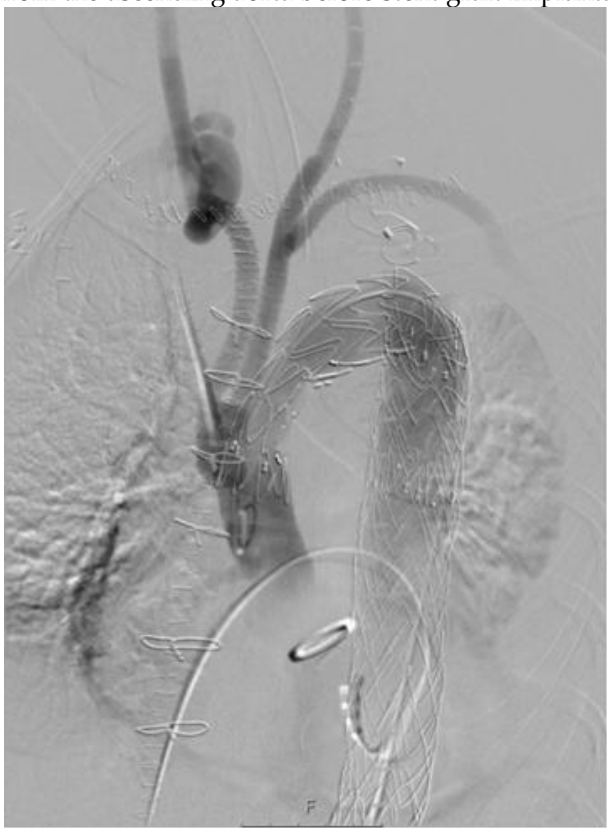

Figure 3. Stent grafting of the aortic arch after de-branching of the supra-aortic vessels with a Y-prosthesis and left carotid–left subclavian bypass.

Hybrid techniques have been used with noteworthy results [28], as the reported primary success rate has been 69–100% with an overall mean perioperative mortality of 9% and perioperative morbidity (strokes excluded) of 14%. In published reports, the overall mean stroke rate has been 7% and the spinal cord ischemia rate 0.5%. There are, unfortunately, no randomized controlled studies comparing these two treatment options, so the results are based on small patient series. Regardless, these figures are at the same level with the open surgical treatment, but direct comparison is very difficult because of the heterogeneity of the patient populations. An endovascular option has been considered as good for patients who are at high surgical risk, which distorts the analysis.

Another option to handle aortic arch vessels is to use either **fenestrated** [29] or **branched** [30-33] stent grafts. Fenestrated stent grafts are customized prostheses tailored individually for

each patient. Fenestrations, i.e., holes in the fabric, are placed according to the pre-procedural imaging so that after implantation of the main prosthesis, the stent grafts are placed in the side braches securing adequate blood flow in the branches and excluding the aneurysm away from the bloodstream.

In branched grafts, there is a side branch or branches implanted in the main prosthesis, and these can be stent grafted after the deployment of the main body. This approach allows more secure sealing of the side branch stent grafts and reduces the risk of endoleak. These methods have also been used with success but are still evolving, and published series are small. Definitive analysis of the safety and feasibility of fenestrated or branched endografts is still lacking. These kinds of endografts are expensive, and because they are custom made for each patient, cannot be used in acute situations.

The so-called **chimney procedure** may be a way to reduce expenses and make endovascular stent grafting of the aortic arch available for acute situations and possible without extra-anatomical surgical revascularization of the vessels [34,35]. In this technique, covered stents are deployed parallel to the main aortic stent graft, protruding somewhat proximally, like a chimney, to preserve flow to vital side branches covered by the aortic stent graft. Use of a chimney graft makes it possible to employ standard off-the-shelf stent grafts to instantly treat lesions with inadequate fixation zones, providing an alternative to fenestrated stent grafts in urgent cases and in aneurysms with challenging neck morphology. So far, only small case series have been published on this technique. It may be a feasible alternative, but it remains somewhat experimental.

Intraoperative fenestration has also been tested and used successfully as an alternative for hybrid operations or prefabricated fenestrated grafts [36-39]. As with the chimney operation, individually designed stent grafts are not needed with this technique. The fenestration is created after the stent graft is implanted by puncturing the fabric with a needle or burning a hole with a laser or radiofrequency probe. The hole is then sequentially dilated with percutaneous transluminal angioplasty (PTA) balloons until it reaches adequate size, and it is then stent grafted. Because the dilatation results in tearing the fabric material, some concerns remain about the durability of this approach.

2.2.4 Follow-up

Patients treated with endovascular prostheses need lifelong surveillance to prevent late complications[40]. Long term durability of first generation stent grafts was actually a disappointment and although the materials and design of the stent graft have improved over the years, there is still risk of graft material break down, which leads to type III endoleak. As the stent graft itself is attached to the aortic only by its radial force, there is also a potential for development of type I endoleak, if the native aorta continues to dilate.

The surveillance regimen varies between the institutions, but usually the protocol involves imaging either immediately or one month after operation, at 3-6 months and 1 year after the procedure. Surveillance is then done on an annual basis. Standard chest X-ray imaging and CT-angiography are recommended imaging modalities [40].

Direct costs are somehow difficult to estimate and direct estimations of long term cost benefits of endovascular treatment of thoracic aorta compared to the open surgery, haven't been done. The initial costs of the endovascular treatment seem to be lower [41]. However, from the studies comparing endovascular treatment of abdominal aorta between the open surgery, the cost benefit of the endovascular treatment seems to diminish in two years [42-44]. This is due to the need for regular surveillance and reoperations.

The radiation exposure of a single follow up CT is at acceptable levels, when compared to increased mortality and morbidity associated with the aneurysmal disease itself and also when compared to the mortality and morbidity associated with open surgical treatment [45]. Nevertheless, repeated CT-scans over the years may significantly increase the risk of cancer and one has to bear this in mind especially when treating younger patients. The precise risk is somehow difficult to estimate, but it has been estimated that in a patient with life expectancy over 15 years, the surveillance program leads to a lifetime risk increase in radiation-induced leukaemia and solid-tumor cancer >2.7% [45].

3 Aims of the study

The aim of this study was to evaluate the present state of endovascular treatment of thoracic aortic diseases and develop it further to reduce expenses and make it more available.

The more specific aims were as follows:

1. To evaluate how different fabrics of stent grafts respond to dilatation after fenestration
2. To test and develop a method for intraoperative fenestration of a stent graft in an animal model
3. To evaluate the treatment outcome of degenerative TAAs in consecutive Finnish patients
4. To evaluate the utility of hybrid endovascular and open surgical treatment of aortic pathology in connective tissue disorders

4 Materials and methods

4.1 IN VITRO TESTS

Commercially available stent grafts from three manufacturers were tested: Zenith (William Cook, Baereskov, Denmark); Gore TAG (W.L. Gore, Flagstaff, AZ, USA); and Valiant, Talent, and Endurant (Medtronic Inc., Minneapolis, MN, USA). For the first test, a small hole was created with a 22-gauge needle, and the hole was sequentially dilated with 2.5-mm and 4-mm coronary PTA balloons (Maverick; Boston Scientific, Natick, MA, USA) and 7-mm and 10-mm peripheral PTA balloons (Opta Pro Cordis, Miami Lakes, FL, USA). Stent grafts were manipulated by hand, and balloons were placed manually through the hole created with a needle. With each balloon, the pressure was gradually increased until the balloon was fully open with no waist caused by the prosthesis.

The prospective goal was to create a fenestration with a diameter of 10 mm. Fenestrations were assessed visually by two observers and recorded on x-ray images. For the second test, a hole created in the fabric with the needle was dilated with a 5-mm cutting balloon (Boston Scientific). Results were recorded as before. Residual diameter stenosis caused by the fabric was measured from x-ray images of the balloon. A 6-mm/38-mm Advanta V12 (Atrium Medical; Hudson, NH, USA) stent graft was placed through the fenestration and dilated. The joint between the main prosthesis and the side branch stent graft was assessed visually for evidence of possible gaps. Finally, an additional fenestration was created in the Talent prosthesis, puncturing the hole as close as possible to the stent strut.

4.2 IN VIVO PIG MODEL

Three domestic pigs, weighing 50–60 kg each, were anesthetized. Both femoral arteries were punctured and an 8F sheath introduced. Both renal arteries were catheterized under fluoroscopic control (GE Innova IQ 3100 Excellence, GE Healthcare, Waukesha, WI, USA) from the left groin, and 5 mm/20 mm PTCA (percutaneous transluminal coronary angioplasty) balloon catheters (Maverick, Boston Scientific, Natrick, MA, USA) were advanced into both renal arteries. A 16-mm iliac extension stent graft (Endurant, Medtronic, Minneapolis, MN, USA) was deployed in the abdominal aorta covering the renal arteries in the first pig, and a Talent (Medtronic) stent graft in the second and the third pigs. Thereafter, a Channel steerable sheath (CR Bard, Murray Hill, NJ, USA) was advanced into the aorta from the right groin. This device with an 8F or 9F inner diameter is intended to access the left atrium for purposes of diagnosing and treating left-sided atrial arrhythmias. The device has a flexible tip that can be bent at a 0–180° angle, and the sheath remains in the precise position once set. The steerable sheath is necessary to point the needle in an exact manner towards the renal artery ostium and to give support to the re-entry catheter during needle penetration of the resilient stent graft fabric. Balloons in the renal arteries were inflated and served as markers when the stent graft was punctured with an Outback re-entry catheter under the guidance of fluoroscopy (Cordis, Miami Lakes, FL, USA). The Outback catheter is a 6F system that uses orthogonally oriented radiopaque markers, and the main indication of the device is to aid the re-entry of the dissecting wire

into the true lumen distal to an occlusion in the peripheral arteries. In the experiment, the 22-gauge re-entry needle was directed towards the arterial orifice.

Once the deflation of the balloon in the renal artery indicated successful puncture, a 0.014-inch guide wire was advanced through the fabric into the renal artery. The Outback device was changed to a PTCA balloon and the fenestration sequentially dilated to 5 mm. A 6-mm balloon expandable renal stent (Racer, Medtronic) or a 6-mm covered stent (Jostent, Abbot Vascular Instruments, Rangendingen, Germany) was placed in the fenestration to keep it patent. After the procedure was completed, the pigs were euthanized and autopsied.

4.3 DEGENERATIVE ANEURYSMS

4.3.1 Patient population

From June 1998 to March 2010, 158 consecutive patients with diseases of the DTA underwent endovascular stent graft placement either alone or in combination with surgical treatment in three Finnish university hospitals. Of these, 69 patients (58 men; mean age 71.7 years, range 54–90) had an aneurysm of the descending aorta and were included in this retrospective analysis (Helsinki University Hospital, n=19; Kuopio University Hospital, n=37; and Oulu University Hospital, n=13). Medical records, radiological imaging studies, and national death records were collected and analyzed on an intention-to-treat basis. Table 2 gives the baseline characteristics of the study sample.

Table 2. Baseline characteristics of patients who underwent stent grafting of the descending aorta in three Finnish university hospitals from 1998 to 2010

Demographics	
Age, y	71.7 (54–90)
<60	3 (4%)
60–79	56 (81%)
>80	10 (15%)
Male	58 (84%)
Risk factors	
Hypertension	54 (78%)
Coronary artery disease	34 (49%)
Renal failure	19 (28%)
Cerebrovascular disease	15 (22%)
Diabetes	14 (20%)
Congestive heart failure	4 (6%)
COPD	16 (23%)
American Society of Anesthesiology Classification	
3	34 (49%)
4	30 (43%)
5	2 (3%)
TAA classification (Crawford) [46]	
Type I	49 (71%)
Type II	4 (6%)
Type III	5 (7%)
Type IV	0 (0%)
Type V	10 (14%)
Missing information	1 (1%)
Proximal landing zone (Ishimaru) [47]	
0: Proximal to the BT	2 (3%)
1: BT to left CCA	1 (1%)
2: Left CCA to LSA	9 (13%)
3: LSA to T4 level	19 (28%)
4: Distal to T4 level	36 (52%)

BT, brachiocephalic trunk; CCA, common carotid artery; COPD, chronic obstructive pulmonary disease; TAA, thoracic aortic aneurysm

Fifteen (21.7%) patients presented with acute symptoms, either aneurysm rupture or uncontrollable pain, that were considered aneurysm-related. Fifty-four patients were treated on an elective basis, which was indicated if the DTA diameter was ≥6.0 cm or displayed a growth rate ≥1 cm/y. Patient selection, evaluation, and procedures were done in close cooperation with interventional radiologists and cardiovascular surgeons. At the beginning of the study period, endovascular treatment was considered as an option for high-risk surgical patients, but later on, the trend shifted more toward endovascular treatment. If there were factors hampering the endovascular treatment (e.g., short proximal or distal neck, difficult access), hybrid procedures were considered as second-line options.

4.3.2 Preoperative imaging

Computed tomographic angiography (CTA) with multiplanar reformatting of the entire aorta was performed in all patients to evaluate the location, diameter, and length of the aneurysm; the diameter of the landing zones; and the suitability of the access routes. Stent graft diameters were also calculated from the CTA images and were oversized by 10% to 15% according to the manufacturers' instructions.

4.3.3 Operations

Four different stent grafts were used: TAG (W. L. Gore & Associates, Inc., Flagstaff, AZ, USA), Talent and Valiant (Medtronic Vascular, Santa Rosa, CA, USA), and Zenith (Cook Inc., Bloomington, IN, USA).

If coverage of the LSA was required to achieve an adequate proximal neck (≥1.5 cm; n=14), cerebral imaging determined the status of the intracranial circulation. Coverage of the LSA was required when the left vertebral artery was dominant (n=9); revascularization was done by carotid–subclavian bypass (n=8) or transposition (n=1). The LSA was covered without additional surgery in 5 patients (3 elective and 2 acute). If the left common carotid artery was to be covered by the stent graft (n=6), a carotid–carotid–subclavian bypass was performed. Revascularization of the supra-aortic vessels was usually performed 2 to 3 days before stent grafting.

Stent grafts were deployed under fluoroscopic guidance using standard techniques and general, spinal, or epidural anesthesia. During the last 2 to 3 years, if the proximal landing zone was at the level of the aortic arch, rapid pacing was used to aid the deployment of the stent graft at the precise position. To prevent spinal cord ischemia during or after the operation, spinal drainage was employed in cases with a lengthy covered segment of the aorta, especially if the patient had an abdominal aortic stent graft or a Y-prosthesis. When a type I or III endoleak was detected during the procedure, additional stent grafting or coil embolization was performed as necessary.

4.3.4 Definitions

All data are presented in accordance with current reporting standards [48]. Aneurysms were classified according to the Crawford classification [46] and proximal landing zones according to the Ishimaru classification [47].

Technical success was defined as achieving access to the arterial system and deployment of the graft with secure fixation, absence of type I or III endoleak on postoperative imaging, and a patent endoluminal graft. Primary technical success was reported on an intention-to-treat basis. A major complication was defined as an event requiring major therapy, unplanned increase in the level of care, prolonged hospitalization, or leading to permanent adverse sequelae or death.

4.3.5 Follow-up

Patient follow-up included clinical examination, standard chest radiography, and CTA or magnetic resonance angiography (MRA) in selected cases at 2 to 4 days after operation, at 3 and 12 months postoperatively, and annually thereafter. If a type I or III endoleak was found on the immediate postoperative CTA, another CTA was scheduled for 2 weeks to 1 month after the primary operation to ensure that the endoleak had resolved. If this did not happen, additional procedures were performed as necessary.

4.3.6 Statistical methods

Logistic regression was employed to identify predictors of 30-day mortality. The results are presented as odds ratios (ORs) with 95% confidence intervals (CIs). The Kaplan–Meier method was used to estimate survival. $P<0.05$ was considered to indicate statistical significance. Statistical analysis was performed with IBM SPSS Statistics software (version 19; IBM Corporation, Somers, NY, USA).

4.4 MARFAN AND LOEYS–DIETZ SYNDROMES

In three tertiary care centers, 158 consecutive patients were treated for thoracic aortic pathologies during 1998–2010 with endovascular stent grafts. In this patient population, 1 patient had LDS and 2 patients had MFS. The patient baseline characteristics are presented in Table 3.

Table 3. Baseline characteristics of patients with connective tissue disorder

Pt.	Age	Gender	Diagnosis	Symptoms and findings
1	39	Female	LDS	Dilatation of aortic root, aortic dissection, hypertelorism, bifid uvula, marked tortuosity of carotid and vertebral arteries, mutation in TGF-β receptor 1 gene
2	25	Female	Marfan	Aortic root dilatation, ectopia lentis
4	22	Male	Marfan	Aortic dissection, FNB1 mutation, mitral valve prolapse, pectus excavatum, scoliosis

4.5 APPROVAL OF ETHICS COMMITTEE AND THE NATIONAL ANIMAL EXPERIMENT BOARD

Project approvals were obtained from the ethics committee of Kuopio University Hospital (September 2009) and from the National Animal Experiment Board (March 2010).

5 Results

5.1 PATTERNS OF FABRIC DISRUPTION AFTER BALLOON DILATATION OF THE FENESTRATION

5.1.1 Fenestration with a standard balloon

Results from the radiologic and visual assessments after standard balloon dilation are summarized in Figure 4. Creation of a fenestration was easiest with the Talent and Valiant grafts. There was no residual stenosis at the balloon profile after dilation with a 4-mm diameter balloon up to 26 atm (Talent) and 24 atm (Valiant). The fenestration widened with low pressure during dilation with 7-mm and 10-mm balloons. Gore TAG and Endurant grafts resisted 2.5-mm and 4-mm balloon dilation. The waist of the balloon disappeared after dilation with a 7-mm balloon up to 12 atm, and there was no difficulty widening the fenestration up to 10 mm. The fabric of the Zenith stent graft was most resilient and resisted, to some degree, all dilation attempts; a residual diameter stenosis of 29% remained even after dilation with the largest 10-mm balloon.

Visually, the hole created in the Gore TAG endoprosthesis was very clean-cut. The hole was slightly oval, and the edges were smooth with no indication of fraying. In Talent and Valiant prostheses, the tears were oriented transversally, but the edges were round and showed only slight fraying. The hole in the Zenith graft was round, and there was moderate fraying on the edges; the tear in the Endurant graft was oriented longitudinally, and there was heavy fraying on the edges.

5.1.2 Fenestration with a cutting balloon

Technically, traversing the fabrics was more challenging with the cutting balloon compared with standard coronary balloons. The visual appearance of various fabrics after dilatation with a cutting balloon is presented in Figure 5. Talent, Valiant, and Endurant fabrics responded favorably to dilation with the cutting balloon, and the balloon was fully open at 6 atm. Gore TAG and Zenith stents needed dilation up to 10 atm, however, before the waist of the balloon disappeared. Dilation with the cutting balloon resulted in fringed edges in all stent grafts except Gore TAG, in which the hole was oval, and the edges were relatively smooth.

5.1.3 Side branch stent graft

On visual inspection, good apposition of the side branch stent graft to the main prosthesis was achieved in all fabrics if the hole was not close to metallic stent struts. If the fenestration was located in close proximity to a stent strut, the metallic structure could obstruct the hole so that the side branch stent graft could not be fully opened; tight sealing of the fenestration was not accomplished.

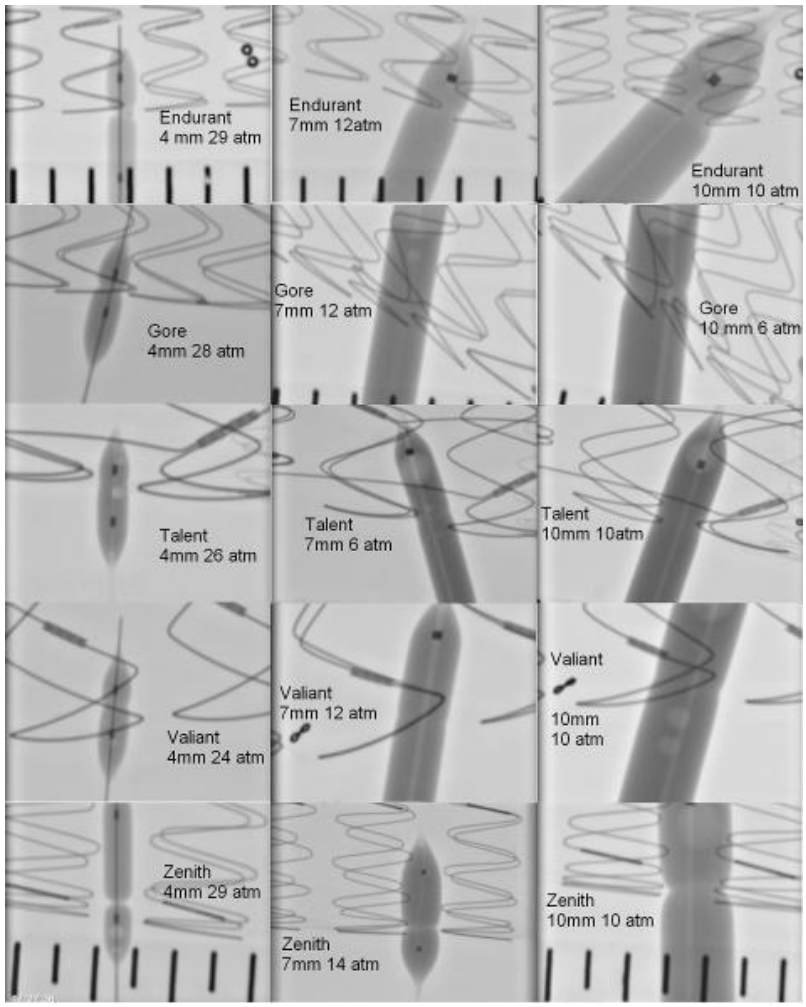

Figure 4. Residual stenosis and visual appearance of various fabrics after sequential dilation with a standard PTA balloon.

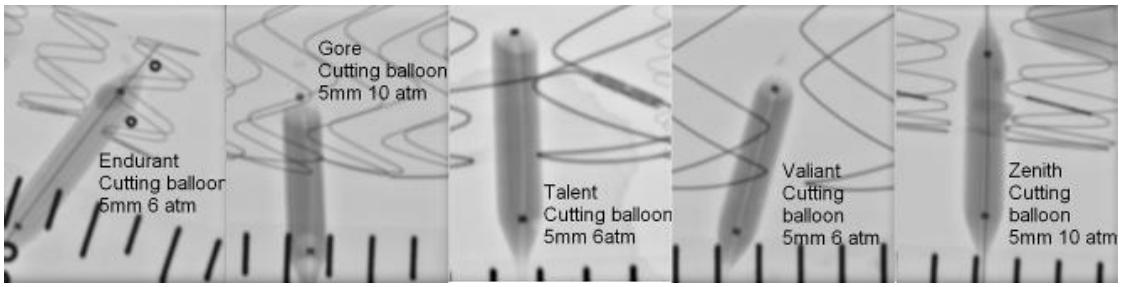

Figure 5. Visual appearance of various fabrics after dilation with a cutting balloon.

5.2 IN VIVO FENESTRATION OF AORTIC STENT GRAFTS

In all three cases, the steerable sheath gave enough support that it was easy to maneuver to point towards the ostium of the renal arteries.

In the first pig, successful needle puncture and the introduction of a 0.014-inch guide wire through an Endurant stent graft were achieved in both renal arteries. Unfortunately, the available guide wire (ATW, Cordis) did not give enough support for the 3-mm PTCA balloon (Maverick, Boston Scientific), and we could not advance the balloon through the fenestration. In the second pig, using a Talent stent graft and a heavy-duty guide wire (Mailman, Boston Scientific), a low-profile 1.5-mm PTCA balloon (Maverick, Boston Scientific) was advanced into the fenestration, which was then sequentially dilated to 5 mm. A 6-mm/18-mm (Racer, Medtronic) renal stent was delivered into the right renal artery and a 6-mm/28-mm (Jostent, Abbot Vascular Instruments) balloon-expandable stent graft was delivered into the left kidney. During the experiment with the third pig, the needle of the Outback device fractured, and the procedure had to be discontinued. In the case of completed intervention, the ischemia time was 24 min and 55 min for the right and left kidneys, respectively. The left kidney showed clear signs of ischemic injury when autopsied (Figure 6). No hematoma was found around the aorta in any of the three pigs, indicating that there was no retroperitoneal bleeding, despite several punctures through the stent graft with the Outback needle.

Visual inspection of the stent grafts showed no damage to the graft material despite several punctures.

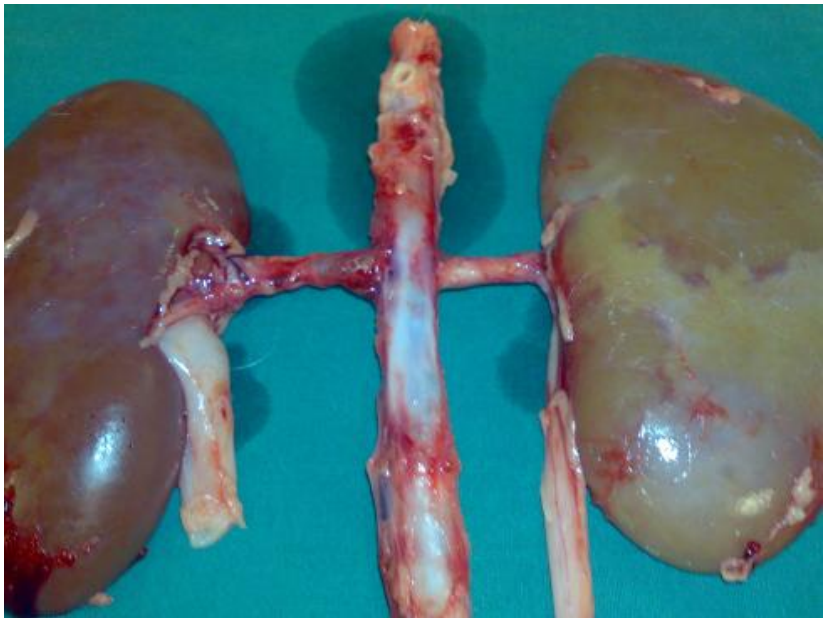

Figure 6. The left kidney was pale and appeared nonviable, indicating a definitive ischemic injury. No signs of hematoma or bleeding were seen around the aorta.

5.3 ENDOVASCULAR TREATMENT OF DEGENERATIVE ANEURYSMS OF THE DESCENDING AORTA

5.3.1 Primary success

Technical success was achieved in 44 (81.5%) of the 54 elective patients; there were nine type I endoleaks, which were graded as mild and assumed to resolve without any further procedures. One patient died of pulmonary embolism at the beginning of the operation before stent grafting.

Among the 15 patients undergoing urgent repair, technical success was achieved in 11 (73.3%); there was one type I endoleak and three access failures due to narrow iliac arteries. In 1 patient, a new attempt with a conduit was planned, but unfortunately this patient died of aneurysm rupture beforehand. Two remaining patients were deemed to be poor surgical candidates, and no additional attempts were planned.

Two TAA patients who also had aneurysms of the ascending aorta were treated with an elephant trunk in the first stage and then the stent graft repair of the descending aorta.

Spinal drainage was used in 12 (17.4%) patients; in 1 (1.4%), spinal drainage was employed as a rescue therapy after the operation due to paraparesis. The use of elective spinal drainage was associated with >200 mm coverage of the aorta (72% vs. 22%, P=0.04).

5.3.2 Complications

Major complications occurred within 30 days after the procedure in 10 (18.5%) patients who underwent elective repair (Table 4). Paraparesis occurred postoperatively in 3 patients (3/69, 4.3%); 2 were permanently paralyzed. Paraparesis was not associated either with the extent of aortic repair or with the covering of the LSA, with or without revascularization of the arch vessels.

Stroke occurred in 3 (4.3%) patients, all of whom had aortic arch vessel reconstructions (1 carotid–carotid–subclavian bypass and 2 carotid–subclavian bypasses). One of these patients had a cerebellar infarction, and two had infarctions of the right middle cerebral artery territory. All patients with postoperative stroke had a heavily atheromatous ascending aorta. No neurological complications occurred among the 3 elective patients who had the LSA covered without revascularization.

On elective patient suffered an iliac artery rupture, and 3 had myocardial infarctions (including one paralysis patient).

In the 15 acute patients, major complications occurred in 7 (47%) patients, and all were fatal. In addition to 4 aneurysm ruptures (described below), there were individual cases of fatal renal dysfunction, pneumonia, and an ischemic brain insult.

Table 4. Complications

	n
Paraplegia	3
Stroke	3
Myocardial infarction	3
Access artery rupture	1
Pulmonary embolism	1
Renal dysfunction	1
Pneumonia	1
Hypoxia-induced brain damage/pyelonephritis	1
Elective/acute	10/7
Mortality	9/69 (13.0%)
Elective	2/54 (4.3%)
Pulmonary embolism	1
Multiorgan failure	1
Acute	7/15 (46.7%)
Aneurysm rupture	4
Unrelated to aorta	3

5.3.3 Thirty-day mortality

The 30-day mortality was 13.0% (9/69), with a striking difference between the urgent group (46.7%, 7/15) and the elective group (3.7%, 2/54; P<0.01). As noted above, 1 patient died during an elective procedure because of a pulmonary embolism. Another elective patient died 2 days after the procedure from multiple organ failure consequent to iliac artery rupture.

Among the acute patients, 4 experienced aneurysm rupture during the immediate postoperative period (27% aortic-specific mortality). Two of them died at 4 and 13 days, respectively, after the primary operation despite apparently good primary results. The other two were patients with access failure. One of these patients was in critical condition, and no other treatment attempts were planned; the patient died 11 days later due to aortic rupture. The other patient had a new attempt planned but died of aortic rupture 4 days after the initial attempt. The 3 further deaths were unrelated to their aortic pathologies.

Perioperative blood loss (OR 3.2, 95% CI 1.3 to 7.5, P=0.009) and patient age >75 years (OR 6.0, 95% CI 1.1 to 31.7, P=0.03) were independent predictors of 30-day mortality. There were no statistically significant differences in death rates among the three centers.

5.3.4 Early endoleaks

Ten (19%) patients had type I endoleaks at their first control CTA immediately after the operation. In 5 patients, the endoleaks resolved spontaneously without any further intervention. Among the 5 persistent endoleaks, 2 patients had coil embolization. In the first patient, the proximal end of the stent graft was embolized. The endoleak had disappeared on the 3-month CT, but it later reappeared, along with an increase in the diameter of the aneurysm. The endoleak was successfully embolized by placing coils between the stent graft and aortic wall 3.5 years after the primary operation.

In the second embolotherapy patient, there was insufficient sealing of the distal end of the stent graft due to a short distal neck, and the aneurysm continued to grow. After an ineffective attempt at embolization, additional stent grafting at the distal end and a bypass operation of the visceral arteries was performed 2.5 years after the primary operation.

Two further type I endoleak patients underwent additional stent graft placement at the proximal landing site; in one, a carotid–subclavian bypass was necessary due to a short

proximal neck. The 5th patient with a persistent type I endoleak was lost to follow-up; he presented with aneurysm rupture because of a significant increase in the aortic diameter from the baseline 35 months after the primary procedure. He underwent a successful re-do stent graft repair.

5.3.5 Late endoleaks

Two patients who had no signs of endoleak previously developed late type I endoleaks at 12 and 52 months after the primary operation, respectively. Both were successfully treated, one with additional stent grafting at the distal end and the other by coil embolization. The presence of late type I endoleaks detected during follow-up was not associated with survival.

One patient developed a type III endoleak 37 months after the primary operation. At that stage, the patient was in poor general health and was considered inoperable; he died 91 months after the primary operation due to head trauma.

5.3.6 Long-term follow-up

Mean follow-up was 34.8±29 months (range 0.1–121). In that time, two graft migrations were noted (one Zenith and one Valiant stent graft). The only structural defect occurred in a TAG stent graft with type III endoleak. Altogether, eight re-interventions were performed on 7 (10%) patients during follow-up, as noted above. An additional 4 patients died, 1 from retrograde dissection of the ascending aorta 3 months after the operation, possibly because of the oversizing of the stent graft by 30%. In this particular patient, the aneurysm in the descending aorta was intact and was actually shrinking. Three of four (6%) late aneurysm ruptures (all elective repairs) were fatal. One patient had no signs of endoleak or aneurysm growth until she was lost to follow-up 2 years after the primary operation; unfortunately, the aneurysm ruptured 10 years after the index operation, which led to her death. The 2 (3%) other fatalities were due to acquired infections in their aneurysms, which led to rupture at 27 and 32 months, respectively, after the primary operation.

Overall survival was 72.5% at 1 year and 53.2% at 3 years (Figure 7). At the same intervals, the rates for freedom from aneurysm-related deaths were 88% and 83%, respectively. The rates for freedom from type I or III endoleaks were 84% and 81%, respectively, and 93% and 90% for freedom from any re-intervention, respectively.

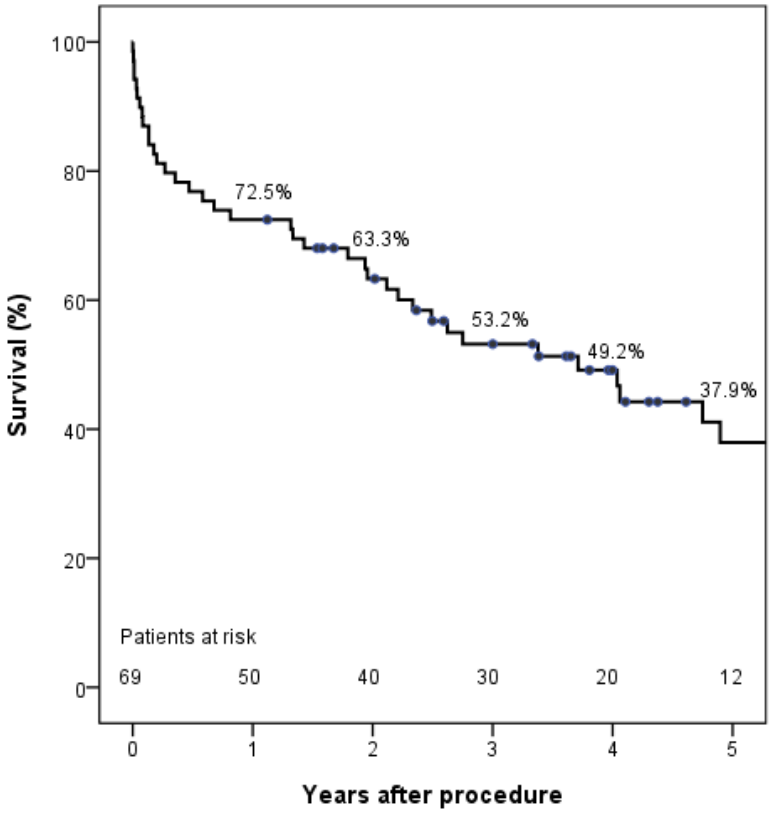

Figure 7. Kaplan–Meier survival curve of all patients.

5.4 HYBRID TREATMENT OF AORTIC PATHOLOGY IN CONNECTIVE TISSUE DISORDERS

5.4.1 Loeys–Dietz syndrome

Patient 1 was a previously healthy woman, and an acute Stanford type A, DeBakey type I dissection of the whole aorta was the first sign of her disease. At the same time, dilatation of the aortic root was noted (Figure 8a and b). The ascending aorta and aortic valve were replaced with a composite graft. The patient had a pericardial effusion postoperatively, which resolved spontaneously.

After the first insult, rapid progression in the dilatation of the remaining aorta and also the subclavian artery (Figure 8c and 8d) necessitated further interventions until her whole aorta was replaced with surgically implanted prostheses and endovascular stent grafts. Ten weeks after the first insult, the supra-aortic vessels were bypassed with a Y-prosthesis originating from the previously implanted composite graft, and the legs were implanted onto the BT and left carotid artery. An additional carotid–subclavian bypass was performed in the same procedure. The left vertebral artery originating from the aortic arch was closed by coil embolization, and the proximal LSA was closed using an Amplatzer plug. The aortic arch and the entire DTA were sequentially stent grafted (Figure 9a and 9b). The patient made a full recovery without any major complications.

The first suspicion of LDS arose 2.5 months after the first operation, but the final results of genetic testing became available only 11 months after the primary insult. They confirmed the LDS diagnosis.

The right subclavian artery was also dilating rapidly, and as its diameter had reached 25 mm, it was resected and replaced with a surgical prosthesis 12 months after the primary insult. The right vertebral artery, which originated from the aneurysm, was transplanted to the right carotid artery.

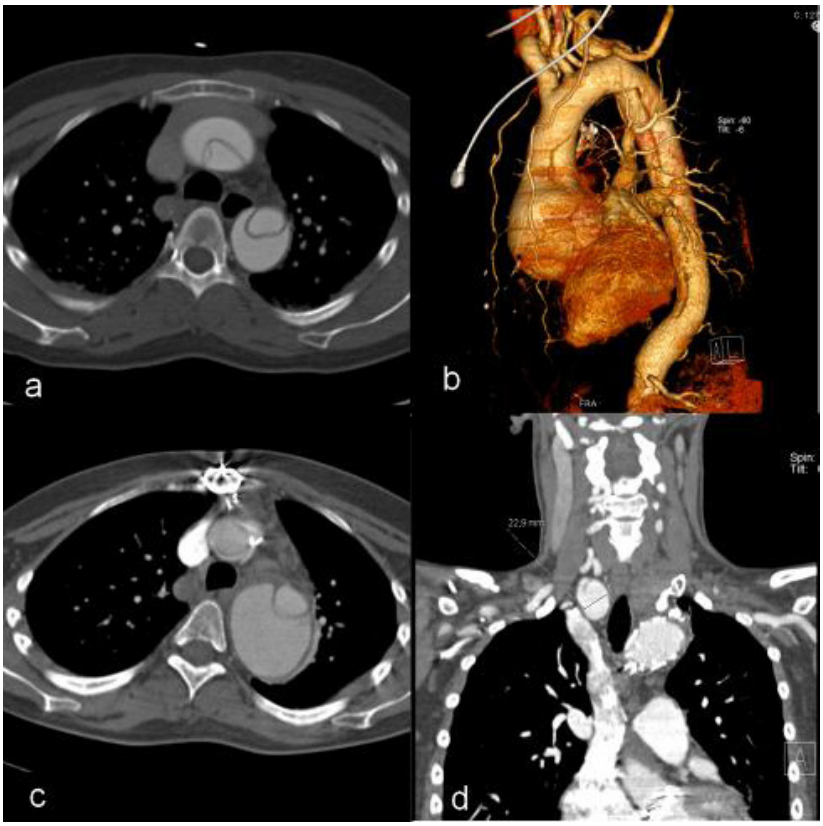

Figure 8. Dissection of the whole aorta in patient 1 (a). Volume rendering technique reconstruction of the CT of the thoracic aorta in patient 1 showing marked dilatation of the aortic root (b). Axial CT image approximately at the same level as that in 1a but acquired 2 months after the first insult. Image shows rapid dilatation of the aortic arch and descending aorta in patient 1 (c). Aneurysm of the right subclavian artery in patient 1 (12 months after the primary operation) (d).

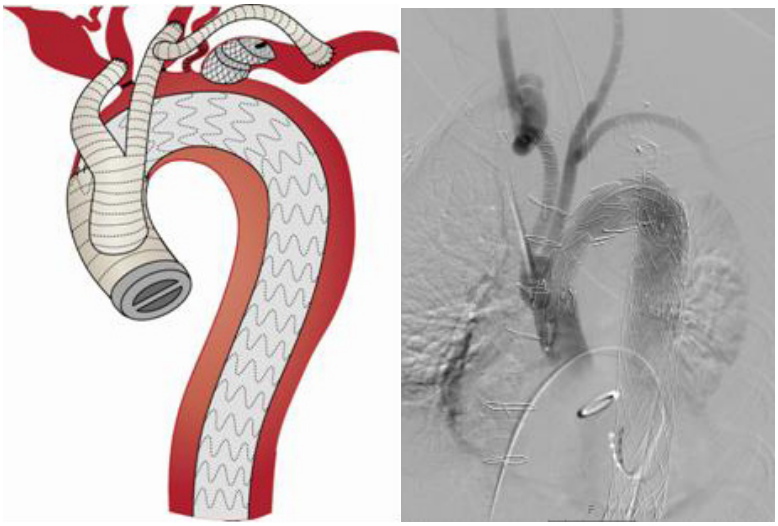

Figure 9. Vascular reconstructions of the aortic arch of patient 1 (a). Angiography of patient 1 after the stent grafting of the aortic arch (b).

The thoraco-abdominal aorta, however, continued to dilate, and after it had reached a diameter of 54 mm, a new operation was scheduled for 14 months after the primary insult. In this procedure, a Y-prosthesis was first implanted into the abdominal aorta, and the legs were implanted upon the common iliac arteries. The superior mesenteric artery, coeliac trunk and both renal arteries were bypassed with separate prostheses from the main body of the Y-prosthesis. The operation was then completed by introducing an endovascular stent graft between the previously implanted thoracic endoprosthesis and newly implanted bifurcated graft (Figure 10). The operation was complicated by a retroperitoneal hematoma, but this later resolved spontaneously. Three months later, CTA demonstrated a pseudoaneurysm in the anastomosis between the left leg of the Y-prosthesis and the common iliac artery. It was treated by extension of the stent graft and coil embolization of the left internal iliac artery. The patient has been able to return to a normal life, and the total follow-up was 3 years and 2 months without any additional vascular complication.

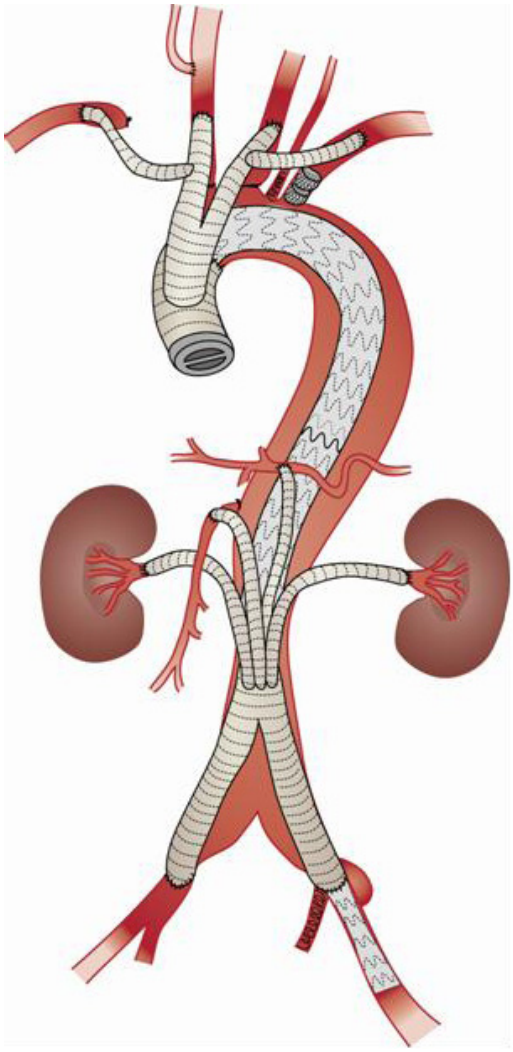

Figure 10: Vascular reconstructions after the last operation of patient 1.

5.4.1 Marfan syndrome

Patient 2 was a 25-year-old woman with previously diagnosed MFS. She had a Stanford type A, DeBakey type I dissection of the whole aorta, which was treated with a composite graft at the first stage. Rapid dilatation of the distal aortic arch necessitated an urgent open reconstruction of the arch and proximal part of the descending aorta 1 week after the primary procedure. After this operation, the patient had a chylous leak into the thoracic cavity, which resolved with drainage.

Eventually, 4 years later, progressive dilatation of the thoraco-abdominal aorta led to replacement of the whole aorta and re-implantation of the visceral arteries into the aortic prosthesis. At the first stage, stent grafts were implanted from the femoral artery so that the proximal end took up a position inside the previously implanted prosthesis in the aortic arch. The distal end of the stent grafts reached the level of the celiac trunk. At the second stage, the thoraco-abdominal aorta was replaced with a combination of tubular and bifurcated prostheses.

The proximal end of the prosthesis was sutured directly to the endograft with a tapered aortic wall and circumferential felt reinforcement (Figure 11). Postoperatively, the patient had a hematoma in the left thoracic cavity, which was evacuated surgically. The patient made a full recovery and has returned to an active, independent lifestyle. The duration of the follow-up to date is 7 years, 9 months.

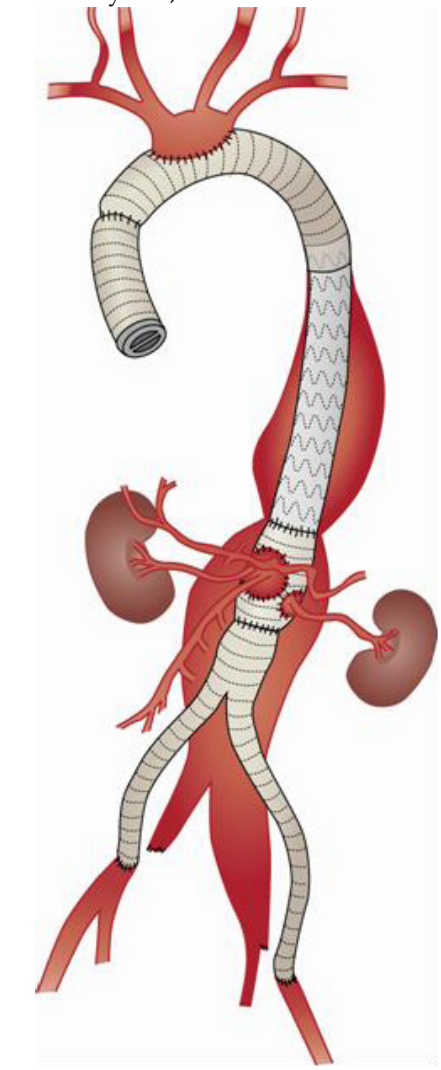

Figure 11. Vascular reconstructions of patient 2.

Patient 3 was a 22-year-old man with previously diagnosed MFS. He had an emergency operation for a Stanford type A, DeBakey type I AoD with a composite graft implanted. First years after the initial insult went uneventfully, but 14 years after the primary insult the aortic arch and descending aorta were dilated up to 60 mm and required a further operation. The supra-aortic vessels were bypassed from the previously implanted surgical prosthesis with a Y-prosthesis, and both the arch and the descending aorta were then stent grafted from the composite graft. At the follow-up, a type I endoleak emerged, and it was treated with an additional stent graft procedure at the proximal end of the previously implanted stent graft at

11 months after the first stent graft operation. At present, 17 years after the primary insult, the patient has returned to an independent daily life, and the aneurysm is shrinking (most recent diameter, 45 mm).

6 Discussion

6.1 ROLE OF INTRAOPERATIVE FENESTRATION OF AORTIC STENT GRAFTS

An intraoperative percutaneous technique for fenestration of stent grafts would overcome problems associated with customized stent grafts. This technique may increase the availability of endovascular aortic repair to more patients because of its potential to decrease costs and waiting times. It would also offer a bailout option if important side branches are inadvertently occluded.

In the experimental **in vitro study**, a hole created with a needle could be enlarged up to 10 mm with sequential standard coronary and peripheral PTA balloon dilation in all grafts except one. The fabric of the Zenith graft was very resilient, and some residual stenosis remained after all dilations using various balloon sizes and even at very high pressure. Other fabrics responded more favorably, although they also needed quite high pressures (~20 atm).

The cutting balloon proved to be very useful for facilitating a fully open fenestration in all five grafts while using a dilation pressure of 10 atm or less. The cutting balloon also seemed to be valuable for reducing unnecessary steps during fenestration and reducing the warm ischemia time of the end organ.

Long-term effects from fabric tearing are worrisome. A potential hazard is that the tear would eventually enlarge and lead to an endoleak. The hole in the Gore TAG graft was round with smooth edges, which theoretically could be more resistant to wear and tear. In other fabrics, dilation with the standard PTA balloon and cutting balloon resulted in fringed edges. The fabrics of Endurant, Talent, Valiant, and Zenith consist of thin fibers of polyester woven together. As the fenestration is punctured and enlarged, the fibers break, leading to fraying of the edges of the fenestration. The fabric of Gore TAG is a multi-film layer of expanded polytetrafluoroethylene, which seems to respond to dilation mainly by stretching.

The experiment also showed that the hole should not be created close to the metallic struts of the stent graft. The hole cannot be reliably sealed if a stent strut overlaps the fenestration, which increases the risk of endoleak. Good apposition of the side branch stent graft to the main prosthesis was registered in visual assessment when the fenestration was not obscured by the metallic network. More conclusive evidence for excluding the leakage between the fenestration and side branch stent graft would be obtained, however, only from a pressurized flow model with circulating blood.

In situ fenestration with a re-entry catheter and steerable sheath seems technically feasible, though some refinements have to be made. The warm ischemia time was too long in our experiments, and definite renal infarction was found at autopsy. Because the animals were euthanized immediately after the procedure, possible renal failure could not be monitored. Results from clinical human studies indicate that kidney damage occurs when warm ischemia is longer than 30 min and that the damage is only partially reversible [49]. In a test conducted by Riga et al. [50] in which the investigators performed antegrade fenestration into the renal arteries of a pig model with the help of a robot arm (the Sensei system), the total operation time was 45 min, which is also too long for warm ischemia of the kidneys. Tse et al. [51] tested both the Pioneer catheter and Brockenbrough needle in the same setting in a canine model. The Brockenbrough needle performed better, but the ischemia time reached 60 min. Notably, these

experiments were conducted with healthy, young animals, in which the anatomy is very straightforward. In real-life patients, the anatomy is usually more challenging, leading to catheterization difficulties.

The technical failure of the Outback device that we encountered in one of our experiments is worrisome and could lead to unnecessary delays, prolonging the already long ischemia time. Notably, that Outback device is not indicated for traversing graft fabrics.

The fabric of the Endurant stent graft was also very resilient and made it difficult to advance the relatively low-profile 3-mm PTCA balloon through the hole created with the needle. In vitro testing has also indicated that enlarging the hole in the Endurant graft requires high pressure, up to 24–26 atm. The cutting balloon facilitates more effective dilatation of the fabric than the conventional balloon, but traversing the prosthesis with this large-profile device necessitates previous dilatation with a low-profile PTCA balloon.

In the first pig, our guide wire was too slack and did not give enough support for the initial balloon to traverse the fabric. Unfortunately, we did not have stiffer guide wires available in the stock of our animal laboratory. Based on this experience, we were better equipped for the second experiment, and with a stiffer guide wire in combination with a very low-profile balloon, we were able to dilate the fenestration and stent it.

We used both bare metal stents and stent grafts in our experiments. In pre-fabricated fenestrated stent grafts, bare metal stents were used at the beginning to secure the fenestrations. We sought to achieve better sealing of the fenestration, which is usually necessary when fenestration is done to produce an adequate proximal neck for the aortic stent graft. Stent graft systems are often quite stiff, and their crossing profile is considerably higher than that of bare metal stents. Therefore, it may not be possible to place a stent graft in the fenestration in some situations, for example when renal arteries are accidentally covered by an aortic stent graft. In those cases, the distance between the fenestration and the aneurysm is usually sufficient, and there should be no risk for type III endoleak even if bare stents are used.

Based on our experiments, the different fabrics respond differently to puncture and balloon dilatation, and it would be worthwhile to test different kinds of stent grafts under in vivo conditions.

6.2 TREATMENT AND FOLLOW-UP OF ANEURYSMS OF THE DESCENDING AORTA

The experience of three Finnish university hospitals in the use of thoracic endovascular aortic repair (TEVAR) in the DTA encompassed a 13-year period during which stent graft technology and principles of treatment significantly changed. Furthermore, it also included the learning curve in each center, so this study provides a ''real-life'' scenario of an evolving endovascular therapy.

Thirty-day postoperative mortality after urgent endovascular repair was significant (47%) but similar to previous reports. In the case series reported by Geisbüsch et al. [52], for example, the in-hospital mortality was 48% among 23 patients. Analyses of larger populations have shown somewhat lower in-hospital mortality: 28.4% for 299 Medicare patients [21] and 23.4% among 364 patients from the US Nationwide Inpatient Sample (NIS) [22]. In a recent meta-analysis, pooled 30-day mortality was 19% [53].

Our results are biased by the small sample size in the urgent patient group. Furthermore, unlike many other studies, we analyzed our data by the intention-to-treat approach, including those patients for whom the treatment was attempted but a stent graft was never deployed. Of note, we encountered two early ruptures among patients with apparently successful interventions primarily. Initial follow-up CTA had not been performed on either of these patients, which suggests that intraprocedural digital subtraction imaging is not absolutely reliable, especially in acute patients. This observation emphasizes the importance of early CTA verification that any rupture is securely excluded. Two postoperative ruptures were encountered among patients with access failure, which demonstrates one of the many clinical challenges in decision-making that needs to be considered when dealing with acute thoracic aortic syndromes.

Elective repair was performed with low immediate postoperative mortality (3.7%), which is similar to that of previous studies [21]. In the 2732-patient study by Goodney et al. [21], the in-hospital/30-day mortality was 6.1% whereas it was 2.3% in the US NIS database [22]. Stroke rate in our series was 4.3%, which is somewhat higher than in previous studies [22]. All strokes occurred in patients with prior supra-aortic vessel debranching. These strokes were probably due to plaque embolization from the ascending aorta and not connected to the surgical procedure done beforehand.

During the study period, some emerging reports indicated that routine preoperative LSA revascularization may be beneficial, with reduced risks of stroke, paraplegia, and arm ischemia, leading to the recommendation that the LSA should be routinely revascularized, especially in elective patients [54]. This observation was also reflected in our routines, and after 2007, all patients who were to have their LSA covered had preliminary revascularization. This issue remains controversial, however [55].

Although the volume of degenerative TAAs during the 13-year period was relatively low in our study (only 5.8 patients/y on average and a mean 2 patients/y/center), the outcome is still comparable to other registry data. This finding probably indicates that the overall volume of thoracic aortic interventions (158 patients, 13.2/y) is nevertheless sufficient to efficiently perform these procedures with acceptable complication rates.

Access failure or difficulty in access resulted in three treatment failures. In 2 patients, the implantation of the prosthesis could not be completed because of narrow iliac arteries, while in one case, an iliac artery ruptured during deployment. This, together with the fact that atheromatous plaques in the ascending aorta lead to an increased risk of plaque embolization, emphasizes the importance of optimal preoperative evaluation of the status of the aorta and its branches at preoperative CTA.

Material weakness, the potential for stent graft migration, and type I or III endoleaks during follow-up make regular monitoring by CTA or MRA mandatory. Two of four late ruptures were likely related to inadequate follow-up. Stent graft treatment has an inherent risk of type I or III endoleak development and the potential for late aneurysm rupture [56,57], both of which were seen in this study. Type I or III endoleaks were successfully treated with additional stent grafting or embolization without any conversion to open repair, as others have observed [56,58]. Clearly, lifelong serial imaging is mandatory for every TEVAR patient.

When comparing these results with open surgery, one has to bear in mind that endovascular treatment is still an evolving technique and that new refinements to the technique are

developed continuously. The importance of an adequate landing zone has become evident, and a length of proximal and distal neck of >15 mm has been widely accepted. Debranching of the aortic arch vessels greatly facilitates the endovascular treatment and permits much better results because an adequate landing zone is easier to achieve, for example when the LSA can be covered without fear of neurological complications. Introduction of rapid pacing during deployment of the stent graft makes precise positioning of the prosthesis much easier and more accurate [59]. Deployment systems of the stent grafts have also evolved considerably during the last decade, and deployment of the stent graft has become faster, easier, and more accurate. Conformability of the stent graft in the aortic arch has also improved markedly and is a significant factor in the long-term prognosis because it reduces the risk of stent collapse in the inner curve of the aortic arch. Lower-profile deployment systems facilitate treatment and make it easier and more available for a larger patient population [59]. Therefore, it is highly probable that the results with the endovascular technique have significantly improved since its introduction, and they continue to improve further.

6.3 TREATMENT OF AORTIC PATHOLOGY IN CONNECTIVE TISSUE DISORDERS

6.3.1 Marfan syndrome

MFS causes aortic root dilatation and aneurysm formation, which eventually lead to AoD. Without treatment, the prognosis of the disease is poor. In the early 1970s, the mean life expectancy for these patients was 32±16 years, and the median (50%) cumulative probability of survival was only 48 years [5]. The life expectancy has since, however, increased by more than 25% and was 41±18 years in 1993 with a median (50%) cumulative probability of survival of 72 years [5]. This increase may be partly explained by the overall improvement in life expectancy but may also be due to the benefits of modern cardiovascular surgery. Also, perhaps a greater proportion of milder cases are now being identified thanks to increased recognition and diagnosis since the advent of molecular medicine.

6.3.2 Loeys–Dietz syndrome

LDS was first described in 2005 [6]. It is a rare, autosomal dominant disorder characterized by hypertelorism, bifid uvula of the cleft palate, arterial tortuosity, aneurysmal disease, and AoD at a young age. The disease is caused by heterozygous mutations in genes encoding the TGF-β type 1 or 2 receptors. LDS syndrome has some overlap in clinical presentation with MFS, although LDS patients do not have significant long bone overgrowth or eye lens dislocation. Aneurysm development is, however, typically more aggressive than that seen in MFS, and dissection or rupture tends to occur at younger ages and at smaller aortic diameters. Life expectancy is reported to be as low as 26.0 years (range 0.5 to 47.0) [7]. There seem to be some clinical differences between the two types of TGF-β receptor mutations, and those carrying mutations in the TGF-β type 1 receptor may be more likely to die at a younger age [60].

The diagnosis is based on the typical clinical characteristics, family history, and molecular genetic testing for mutations in the TGF-β type 1 or type 2 receptor genes.

6.3.3 Treatment

Patients with MFS and especially LDS are prone to developing vascular complications such as AoD and rupture. β-blocker therapy and AT1 antagonists may be of benefit to these patients [61], but their role remains under investigation [62]. Replacement of the aortic root either with or without aortic valve replacement has been adopted as a standard therapy for the lesions in the ascending aorta, which has increased the life expectancy of MFS patients markedly. However, because of the progressive nature of these diseases, aortic dilatation tends to continue, which may lead to aneurysm formation, dissection, and eventually rupture in other sections of the aorta. Lifelong surveillance is essential, and these patients tend to require additional operations [63]. Preventive surgical reconstruction remains controversial, however [61].

Surgery on the DTA is challenging and requires good surgical expertise. Still, there is a significant risk of complications such as stroke, paraplegia or paraparesis, postoperative hematomas, and even death [64]. Higher complication rates have been reported by low-volume centers with fewer than 4 cases/year, where in-hospital postoperative mortality can be as high as 27%, compared to the 15% recorded in some high-volume centers [20].

Endovascular treatment is a tempting alternative for surgical treatment because patients tend to survive longer and have fewer complications at least in the short term [16,24]. However, in connective tissue disorders such as MFS and LDS, the aortic wall is very prone to further dissection and aortic dilatation. The current recommendation is that endovascular treatment should be reserved as a bailout procedure or as a procedure following prior aortic repair, where both landing zones lie within previously sited prosthetic grafts [65].

The present study clearly demonstrates the progressive nature of these diseases and especially LDS. This progression necessitates aggressive treatment and vigorous follow-up. Unfortunately, the diagnosis is not always clear when the patient becomes symptomatic, as happened with patient 1. The correct diagnosis was suspected only 2.5 months after the first incident, and the final results of genetic testing were received 11 months after the dissection of the ascending aorta. Luckily, this delay did not lead to any further complications, and corrective surgery for the entire aorta and supra-aortic vessels could be performed. Despite corrective surgery, these connective tissue disorders may still lead to new complications, as was the case for all of our patients. Therefore, patients need to be monitored for the rest of their lives with CTA or MRA. The patient cases also demonstrate that if the landing zone of the endograft lies within native, untreated aorta, these patients are prone to developing complications such as further dilatation of the aorta. As the aorta continues to dilate at the level of the landing zone, it eventually leads to type I endoleak and further dilatation and possibly to the rupture of the treated aneurysm.

On the other hand, our experiences demonstrate that complications of the connective tissue disorders can be treated effectively utilizing surgical and endovascular techniques in combination. Patient 2 has survived almost 8 years after the first insult and after the last operation, there have been no signs of further vascular complications and she has even delivered a healthy baby. Patient 3 is living active life and there haven't also been any signs of further complications and the aneurysm is shrinking. The patient has survived up to 17 years, which is quite remarkable, considering the devastating nature of the disease and the natural course, if left untreated.

7 Conclusions

I and II: Intraoperative fenestration of stent grafts can be done, but the surgeon must be familiar with the fact that stent graft materials respond differently to dilatation. Use of high pressure balloons is mandatory, and a cutting balloon aids considerably in the dilatation. The technique can also be used in vivo, but a steerable sheet and Outback device resulted in a too-long ischemia time for the kidneys, and we cannot recommend this technique for elective situations. However, in acute situations and as a bailout procedure, it can be useful.

III: Endovascular treatment of TAA is relatively safe, at least in the elective setting. However, to reduce the risk of periprocedural and postoperative complications, multidisciplinary and detailed preoperative imaging-based planning is helpful. A rigorous postoperative surveillance program is compulsory for early detection and prompt treatment of late type I or III endoleak and to reduce the risk of late ruptures.

IV: Marfan syndrome and especially Loeys–Dietz syndrome are debilitating connective tissue disorders, and such patients are very prone to developing vascular complications, particularly of the aorta. The nature of these diseases mandates aggressive treatment strategies and close surveillance programs. Open surgery remains the mainstay of the treatment, but endovascular options should be considered whenever possible to reduce operative complications. Endovascular treatment should be planned so that the landing zones lie within the previously treated aorta.

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Endovascular Treatment of Thoracic Aortic Diseases

Open surgery of thoracic aorta is associated with relatively high mortality and morbidity. Stent graft treatment was introduced on the side of open surgery to reduce mortality and morbidity associated with the treatment. Stent graft treatment has, however, some limitations, but intra-operative fenestration may be a way to make this treatment more available. This study also confirmed that endovascular treatment of a thoracic aortic aneurysm is relatively safe, but a rigorous postoperative surveillance program is still compulsory. In connective tissue disorders open surgery is still the mainstay of the treatment, but endovascular option should be considered to reduce operative complications.

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