Re-interventions after endovascular aortic repair: Clinical and experimental studies

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To my beloved roses

Contents

List of publications

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I Roos H, Djerf H, Brisby Jeppsson L, Fröjd V, Axelsson T, Jeppsson A, Falkenberg M. Re-interventions after endovascular aortic repair for infrarenal abdominal aneurysms: A retrospective cohort study. Submitted

II Roos H, Sandström C, Koutouzi G, Jeppsson A, Falkenberg M. Predisposing factors for re-interventions with additional iliac stent grafts after endovascular aortic repair. Submitted

III Roos H, Ghaffari M, Falkenberg M, Chernoray V, Jeppsson A, Nilsson H. Displacement forces in iliac landing zones and stent graft interconnections in endovascular aortic repair: an experimental study. Eur J Vasc Endovasc Surg 2014;47:262-7

IV Roos H, Tokarev M, Chernoray V, Ghaffari M, Falkenberg M, Jeppsson A, Nilsson H. Displacement forces in stent grafts - influence of diameter variation and curvature asymmetry. Submitted

V Falkenberg M, Roos H, Lepore V, Svensson G, Zachrisson K, Henrikson O. Endovascular closure of chronic dissection entries in the aortic arch using the Amplatzer vascular plug II as a sealing button. J Endovasc Ther 2016;23:378-83

Abstract

Background: Endovascular aortic repair (EVAR) has lower morbidity and mortality than open surgery. Late complications and re-interventions are more common, however, and the timing of different re-interventions and their respective underlying causes are not fully understood.

Aims: The overall aim was to describe re-interventions after EVAR and to identify possible underlying causes. Specific aims were as follows:
1. To describe re-interventions after EVAR, including incidence, indications, procedures, and outcome, concentrating especially on non-access-related re-interventions. 2. To determine underlying causes and to identify anatomical factors associated with additional iliac stent grafting. 3. To study flow-induced displacement forces in iliac limb stent grafts and the influence of stent graft angulation, fluid pressure, pulsation frequency, distal diameter of the stent graft, and asymmetric graft curvatures in an experimental aortic model. 4. To describe a new endovascular technique to close small entries that persist in the aortic arch.

Materials and methods: Studies 1 and 2 were retrospective single-centre cohort studies of re-interventions after standard EVAR, focusing especially on non-access-related re-interventions. In Study 1, incidence, indications, procedures, and outcome were analyzed in 405 patients. In Study 2, 24 patients with additional iliac stent grafts after EVAR were studied. Computed tomography examinations were reviewed in detail regarding causes of re-intervention and underlying anatomic factors. These patients were compared with 420 patients treated with bifurcated EVAR during the same time period who did not require additional iliac stent grafts during follow-up, regarding patient characteristics and preoperative anatomic measurements. Studies 3 and 4 involved investigation of flow-induced displacement forces in iliac limb stent grafts in an experimental flow model mimicking physiologic conditions. In Study 3, the forces on a tubular stent graft with symmetric curvature were studied in relation to graft angulation, fluid pressure, and stroke rate. In Study 4 tapered, non-tapered, and bell-bottom grafts were studied at symmetric graft curvature and non-tapered grafts were studied at asymmetric curvature. Study 5 involved a new endovascular techni-

que for closure of persistent small entries in selected patients with aneurysmal dilatation of chronic aortic dissections.

Results: Study 1 showed that embolization of endoleak type II and placement of additional iliac stent grafts were the most common re-interventions after EVAR. These interventions were performed long after the initial intervention. Medium-term outcome in patients with re-intervention was comparable to that in patients without re-intervention. Study 2 showed that a considerable number of additional iliac stent graftings were caused by rupture. Migration at the distal landing site or graft interconnections was the most common cause, followed by disease progression. Study 3 demonstrated that flow-induced displacement forces were of similar magnitude at both ends of a non-tapered iliac stent graft, and the force increased with increasing graft angulation and fluid pressure but not with increasing pulse frequency. There was a high correlation between pulsatile graft movement and displacement forces. Study 4 showed that there were particularly high displacement forces in bell-bottom grafts, and that the forces were dependent on distal graft diameter and shape of the curvature. Study 5 showed that endovascular closure of persistent entries in chronic dissections is feasible, and in selected patients it may be an alternative to open surgery.

Conclusions: Re-interventions are still common after EVAR, but most are percutaneous procedures and outcomes are generally good. Additional iliac stent grafting is one of the more frequent re-interventions, and in most cases it is related to stent graft migration, with a higher risk in patients with large iliac diameters and short attachment zones. Flow-induced displacement forces may have a role in the increased risk of migration. Patients with EVAR landing zones in wide iliac arteries may need improved graft fixation and more vigorous surveillance.

Abbreviations

AAA	Abdominal aortic aneurysm
CT	Computed tomography
EVAR	Endovascular Aortic Repair
IFU	Instructions for use
mmHg	Millimeters of mercury
N	Newton
OAR	Open aortic repair
Swedvasc	The Swedish Vascular Registry

Introduction

The work for this thesis has been done as a collaborative project involving the Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy and the Department of Applied Mechanics, Division of Fluid Dynamics at Chalmers University of Technology. In this work, clinical and experimental studies of re-interventions after endovascular aortic repair were analyzed. The main topic of interest was the frequency of different types of re-interventions after EVAR and their underlying causes. There was an in-depth analysis of additional iliac stent grafting after EVAR. The underlying causes studied were flow-induced displacement forces and patient-specific factors

Aortic anatomy and pathology

The aorta is the body's largest artery, with its origin at the aortic valve in the superior aspect of the heart and descending through the thoracic and abdominal cavities (Fig. 1.) (1). There are three main branches in the aortic arch and five branches in the abdominal cavity before the aorta bifurcates into the iliac arteries at the level of the umbilicus. The three branches in the aortic arch are grouped closely together and are followed by the descending aorta, which only has smaller muscular branches.

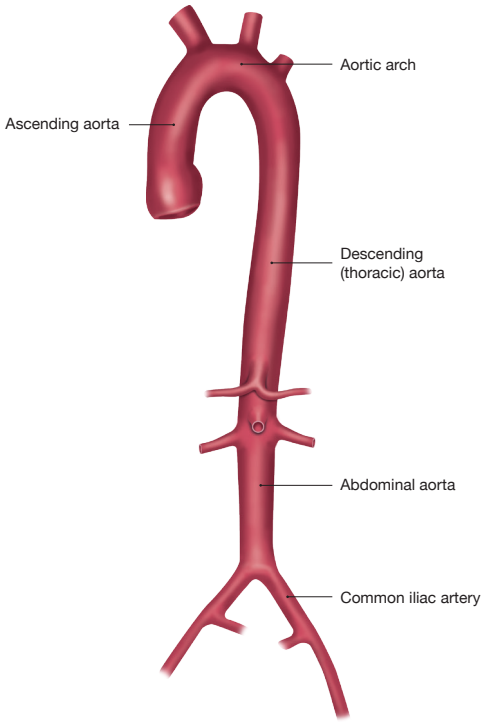


Figure 1. Aortic anatomy

Also in the abdominal cavity, the four most important branches have their origin in a short segment of the aorta. Again, this segment with branches is followed by a part of the vessel with mainly

smaller muscular branches. Only the inferior mesenteric artery originates separately in the infrarenal aorta. The iliac arteries have one bifurcation into external and internal iliac arteries. There is a rich collateral network between the visceral branches, which allows occlusion of the inferior mesenteric artery–and in selected cases, internal iliac arteries (2-4). The most frequent location of aneurysms, below the renal arteries (5, 6), is in the part of the aorta without major branches, which is essential in planning of treatment, as described below.

Aortic pathology can be versatile. The most common diseases are aneurysm formation, dissection, atherosclerotic disease, and vasculitis (6). From here on, we will focus on aneurysm formation (Fig. 2) and dissection (Fig. 3).

Aortic aneurysms

Aneurysm formation is generally defined as an increase in the vessel diameter of over 50% (7-9). The most frequent location of aortic aneurysms is in the part below the origin of the renal arteries, and in clinical practice an abdominal aortic diameter of over 30 mm is generally considered an aneurysm (10, 11). Arterial aneurysms are most commonly caused by a degenerative process in the vessel wall (12-14), although other causes exist–including infection and post-traumatic aneurysms.

Figure 2. Aortic aneurysm.

Abdominal aortic aneurysms (AAAs) usually occur in the part of the aorta below the renal arteries. The natural history of an aortic aneurysm is progressive dilatation, which is why known aneurysms are followed with surveillance (15-17). An increase in vessel diameter is associated with an increased risk of rupture. Studies have shown that the rupture risk is small with diameters of less than 50 mm (18-21), and 55 mm is generally considered to be the

threshold when the risk of rupture reaches a level when an elective operation is justified. The risk of rupture is directly related to the increase in vessel diameter (20, 22), and at a diameter of 70 mm the risk is as high as 30% per year.

The incidence of AAA increases with age and is higher in males (23, 24). AAAs are uncommon in people below 60 years of age and the male-to-female ratio is 1:4–1:6 (23-25). Other risk factors for the development of AAA are smoking, abdominal adiposity, coronary artery disease, hypertension, and hypercholesterolaemia. A family history of AAA is also an important risk factor for developing AAA, with an up to 6-fold elevated risk for first-degree relatives (26). A combination of the most important risk factors, i.e. family history, smoking, and atherosclerotic disease, can increase the risk by a factor of 32 when all three are present (26)

Aortic dissection

Artery dissection is defined as a dissection of blood along the laminar planes of the aortic media, leading to the formation of a blood-filled channel

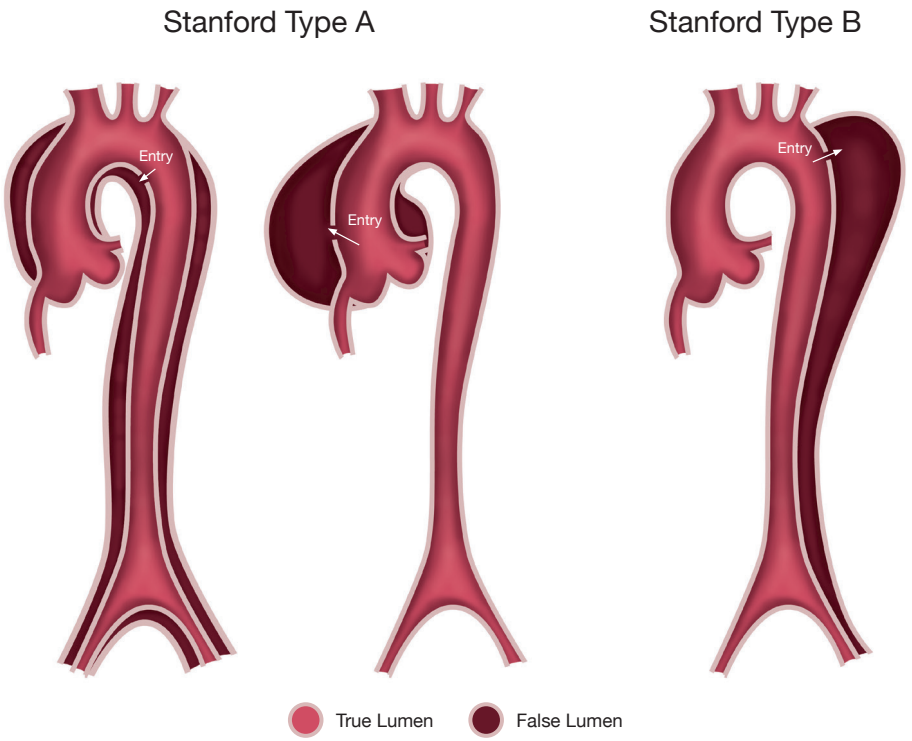


Figure 3. Aortic dissection

within the aortic wall (6, 27, 28). The division of the different layers of the vessel wall forms a false lumen, allowing blood flow between the vessel's intima (inner layer) and adventitia (outer layer). Dissection is caused by arterial hypertension (6, 27), resulting in a tear in the intima, allowing blood to enter and dissect the vessel wall. Aortic dissection can be divided into Stanford type A, which involves the ascending aorta, and Stanford type B, which only involves aorta distal to the subclavian artery (6, 27, 28) (Fig. 3).

Acute complications of aortic dissection type A are cardiac tamponade, aortic valve insufficiency, aortic rupture, and ischaemia due to involvement of the coronary arteries (29). Acute complications of aortic dissection type B are rupture and ischaemia. The complications of aortic dissection type A are more common and have higher mortality (30, 31); operative management is therefore indicated if there are no contraindications. The primary treatment for aortic dissection type B is medical management aimed at reducing the arterial pressure (32).

Invasive treatment of aortic dissection type B is indicated when there are complications such as bleeding, organ ischaemia, or rapid aneurysmal expansion–or if clinical or radiological signs suggest a high risk of complications (32). Late complications of both type A and type B aortic dissection include aneurysm formation with the risk of subsequent rupture, ischaemia due to branch vessel involvement, and progression of dissection. Anti-hypertensive medication is essential in these patients. The aim of operative treatment for aortic dissection is to close the proximal entries, restore flow into the true lumen, and induce false lumen thrombosis. In cases of aneurysm formation involving the aortic arch after aortic dissection of type A, open arch reconstruction in combination with thoracic stent grafts is still the treatment of choice (33, 34), even if endovascular branched grafts have been introduced (35). Stent grafting of the descending aorta is the standard treatment in dissections of type B (36-39).

Treatment of aortic aneurysms

Open aortic repair

Aneurysm treatment has been performed with open surgery since 1817, when the first operation was performed, with ligation of the artery to prevent rupture (40). Twenty-four operations with aortic ligation have been identified before 1940, and the patient survived in only five of these cases. In the years that followed, different techniques to induce thrombosis of the

aneurysm or to induce fibrosis of the aortic wall were used to prevent rupture. The techniques used were (among others) needling, wiring, proximal banding, and cellophane wrapping. The first end-to-end aortic anastomosis was performed in 1944 in Sweden, by Crafoord and Nylin, in a patient with aortic coarctation (40, 41). In 1948, the first aortic resection with homograft replacement was performed; this was also in a patient with coarctation (40). Subsequent developments in technique led to the first successful replacement of the aneurysmal part of the aorta in 1951. This operation was performed by Dubost, and an aortic homograft was used (40).

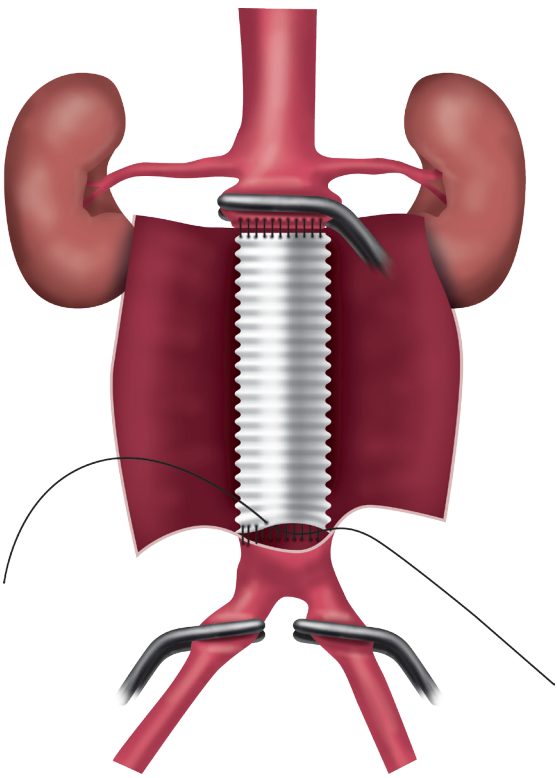


Figure 4. Open aortic repair.

The first procedure on a patient with a ruptured AAA was performed two years later, by Bahnson (42). The introduction of synthetic aortic grafts dates to 1958, with the development of Dacron® (43). The operative technique used in these early procedures was total resection of the aneurysm and an end-to-end anastomosis. In 1966, the first operation was performed where the aneurysm was left in place and wrapped around the graft (40, 44). Further development led to the current technique for open aortic surgery where prosthetic material is most commonly used to replace the aneurysmal part of the vessel. The prosthesis is sutured to the aortic wall proximal and distal to the aneurysm. Open surgery for AAA has developed significantly, but the same general concept is still used–with replacement of the aneurysmal part of the vessel through a laparotomy (Fig 4).

Endovascular aortic repair

Endovascular technique for treatment of an aortic aneurysm was first performed by Volodos in 1987 (45, 46). The principle of endovascular aortic repair (EVAR) is based on relining of the aorta, which is supported from the inside, and the aneurysm is excluded from the circulation (Fig. 5). EVAR is performed with a stent graft, which is a self-expanding metallic mesh covered with a membrane, most commonly Dacron® or Gore Tex®.

There are some important anatomical considerations to take into account when planning and performing EVAR. Since the stent graft is attached to the inner aortic wall, successful aneurysm exclusion depends on

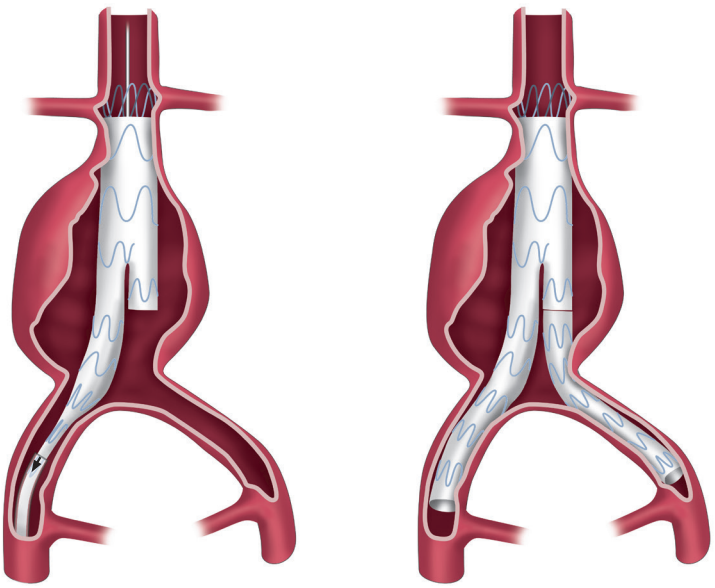


Figure 5.. Endovascular aortic repair (EVAR). Left picture shows stent graft during deployment. Right picture shows fully deployed stent graft.

a fixation of the graft to the aortic wall that ensures that the stent graft does not move from its intended position, and that there is no blood flow between the vessel wall and the stent graft. If the stent graft moves after placement, this is referred to as migration. A leakage into the remaining aneurysm sac is referred to as an endoleak (32, 47). There are five different types of endoleaks. Endoleak type I is a leakage between the stent graft and the vessel wall; type Ia is located at the proximal landing site whereas endoleak type Ib is located distally. Endoleak type II is caused by persistent flow through a vessel with its origin in the stented part of the aneurysm.

Endoleak type III is caused by separation of graft components (type IIIa) or a hole in the graft fabric (type IIIb). An endoleak typ IV is defined as a leakage through the graft fabric due to porosity. Lastly, endoleak type V, also referred to as endotension, is a continued expansion of the aneurysmal sac without visible signs of leakage.

The most feared endoleaks are types I and III, since they are associated with a direct flow into the aneurysm–which is thus perfused and pressurized (48). The stent graft is placed in a part of the vessel that has as normal a diameter as possible, to achieve a proper seal. Each stent graft has predetermined limits of aortic anatomy that define the range of vessel diameters, lengths, and angulations where EVAR can be performed with safety and expected long-term durability. Such instructions for use (IFU) are specified for each type of stent graft. Most EVAR stent grafts require between 10 and 15 mm of normally calibrated aorta above the aneurysm and 10 to 15 mm of normally calibrated iliac arteries below the aneurysm for stent graft fixation.

In the early experience with EVAR, migration at the proximal attachment site was a common cause of endoleak type I, and the stent grafts were therefore equipped with hooks and barbs that anchored the graft to the aortic wall (49-51). Studies have shown that stent grafts without this additional fixation may be displaced from their position if a force of 2−4 N is applied to the graft (52-54). With the additional anchoring of fixating hooks, a force of up to 24 N has been reported to be required to dislodge the graft (52, 55). Shorter fixation length has been shown to correlate with lower proximal dislodgement forces (55). Also, in many other respects the EVAR technique and stent graft design have evolved significantly, with smaller introducers, easier deployment, and conformability with a wider range of anatomic variations being among the most important (56-58). However, distal anchoring and fixation at stent graft interconnections are in most cases still solely dependent on the self-expanding force of the stent graft.

Open aortic repair or EVAR

EVAR and open aortic repair (OAR) have been compared in three large randomized controlled trials (RCTs) (28-30). These showed an early survival benefit for patients treated with EVAR, but a higher incidence of late complications and re-interventions. In the UK Endovascular Aneurysm Repair trial 1 (EVAR1) (59), early mortality in the EVAR group was 1.8%, as op-

posed to 4.3% in the OAR group (p = 0.02). Corresponding figures from the Dutch Randomized Endovascular Aneurysm Repair study (DREAM) (60) were 1.2% and 4.6% (p = 0.10), and from the Open Versus Endovascular Repair study (OVER) (61) they were 0.5% and 3.0% (p=0.004). The lower early mortality for the EVAR patients was not sustained during long-term follow-up in the RCTs. The difference in total mortality between the two groups disappeared after 1−3 years of follow-up.

Furthermore, late complications and re-interventions have been shown to be more frequent after EVAR than after OAR. Re-intervention rates in the EVAR1 trial were 6.9% per 100 patient years after EVAR and 2.4% per 100 patient years after OAR (p < 0.0001) (59). The DREAM trial found a re-intervention-free survival rate at 6 years of 70.4% after EVAR and 81.9% after OAR (p = 0.03)(60). The most frequent re-interventions after OAR were re-explorations after surgery and correction of incisional hernias whereas for EVAR, treatment of endoleaks and graft thrombosis predominated (59, 61). The occurrence of late ruptures after EVAR with a higher frequency of re-interventions has been put forward as one of the major disadvantages of endovascular technique in the treatment of AAA (62).

EVAR re-interventions

Despite the evolution of modern EVAR stent grafts, re-intervention rates are considerable and ruptures after EVAR still occur at a rate of approximately 1% (63-65) (3-year follow-up). The most common causes of these ruptures are endoleaks of types I and III (63). Re-intervention rates are still reported to be in the 12−19% range (3- to 7-year follow-up) (65-67).

One of the most commonly reported re-interventions after EVAR is implantation of additional iliac stent grafts (65, 68-70), but the underlying causes are not fully understood. Waasdorp et al. have shown a higher re-intervention rate in patients in whom sideways stent graft movement could be detected on follow-up imaging (71), indicating that stent graft migration might play a role. Furthermore, patients with wide iliac arteries have been shown to have higher re-intervention rates (72, 73).

Flow-induced displacement forces

Flow-induced forces in a tubular structure are induced by the internal pressure acting normal to the tube wall (Fig. 6A) and shear stress (Fig. 6B) acting tangentially (74). Furthermore, if the tubular structure–in our case

a stent graft–is angulated, there is also a reaction force that comes from redirection of flow, as shown in Fig. 6C (74). Reaction forces increase with increased angulation (74). In grafts or tubes with changes in diameter, a reaction force comes from acceleration/deceleration of flow. The sum of the forces acting on the graft is transferred to the ends of the stent graft and, in

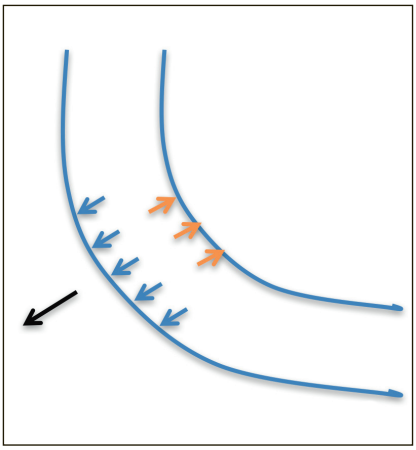


Figure 6 A. Pressure forces
Fluid pressure acts normal to (perpendicular) the graft surface. Blue arrows show pressure forces on graft outer curvature, yellow arrows forces on inner curvature. The area on outer curvature is larger compared to inner curvature, pressure is therefore acting on a larger area in the direction towards the outer curvature. Black arrow show resultant force acting on the graft .
Also material properties influence the transfer of force. Since the graft is stretched in the outer curvature it allows for a larger transfer of force to the graft ends compared to the inner curvature, which is compressed and wrinkled.

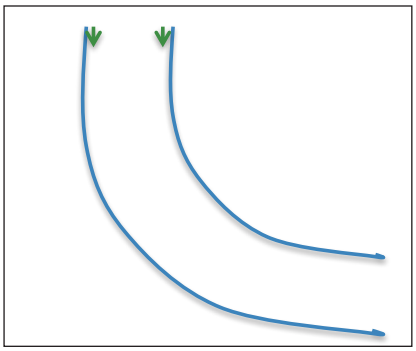


Figure 6 B. Shear stress
Shear is the force that arises due to friction between the fluid and the graft surface.

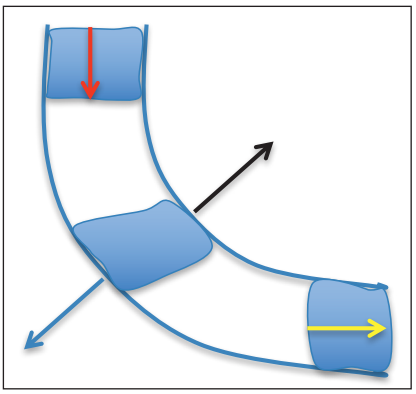


Figure 6 C. Change in momentum
Direction of momentum (mass x velocity) when a fluid lump enters the graft is shown with red arrow, momentum when exiting the graft is shown in yellow.
To achieve a change in momentum a force must act on the lump in the direction that the momentum changes (black arrow). This force is counteracted by a force acting on the inner surface of the graft (blue arrow)
Forces from change of momentum are added to pressure forces when there is flow through the graft.

a flexible graft, may also cause movement of the graft (75). Computational studies have given estimates of the forces in abdominal and thoracic aortic stent grafts (76-79). These studies have also shown that the contribution of shear stress is small in angulated grafts (1–3%), where the main contributors are the influence of pressure forces and redirection of flow due to the geometry of the graft (79). In computational studies, the magnitude of flow-induced forces in stent grafts has been shown to increase with fluid pressure and graft angulation (80).

Experimental studies have investigated factors that influence fixating forces (49, 52) and displacement forces under steady flow (81). In general, computational and experimental studies are complementary; both are based on the need to simplify and study separate factors that potentially influence graft migration and fixating forces. The real-life factors influencing stent graft migration are multifactorial and to a large extent vary between individuals (82). Furthermore, factors that influence migration may also have a role in fixating the graft, as exemplified by the pressure force. Perfusion pressure influences the forces inducing migration, but it also contributes to fixation of an oversized graft by increasing the outward pressure of the graft on the vessel wall.

Study objectives

The EVAR technique is well established, and an increasing number of AAAs are being treated by endovascular means (83). As an example, the proportion of AAAs treated with EVAR increased from 25% in 2003 to 59% in 2013, as reported in the Swedish National Registry for Vascular Surgery (Swedvasc) (83, 84). Long-term EVAR results are well described, but re-interventions and late ruptures are still a concern–along with the need for life-long surveillance. One of the challenges in EVAR development is to identify the possible factors associated with re-interventions. If the use of endovascular technique is to increase further, particularly in the younger patient groups, a dedicated effort to increase long-term durability is essential.

To enable further development of EVAR, a deeper knowledge of the different types of re-interventions and their possible causes is needed. Several authors have reported a decrease in re-interventions after EVAR in recent years, and have promoted less vigorous surveillance (85-89). The-

re have, however, been very few publications on the broader spectrum of re-interventions after EVAR, which would give detailed insight in the possible causes of late EVAR failures in particular. In **Study 1**, we gave a detailed description of re-interventions after EVAR, concentrating especially on the frequency and timing of different types of non-access-related re-interventions.

Additional iliac stent grafting is one of the more frequent re-interventions that occur late after primary repair. Furthermore, endoleaks of types Ib and III have been reported to be associated with a high proportion of late ruptures after EVAR (63). The underlying causes are, however, not well described. There have been publications categorizing all re-interventions with additional iliac stent grafts as caused by progression of disease, i.e. successive aneurysm formation in the iliac landing zones (65). There are, however, other possible causes behind the need for additional iliac stent grafting, including migration and inadequate landing zones after primary repair. In **Study 2**, we therefore concentrated on identifying underlying anatomical causes behind additional iliac stent grafting.

Stent graft migration is poorly understood, and a deeper knowledge of the forces affecting stent grafts under physiological flow conditions may be essential for our understanding of the causes of EVAR re-interventions. Computational studies have indicated that flow-induced displacement forces may influence stent graft migration. Furthermore, patients with sideways graft movement detectable on computed tomography (CT) follow-up imaging have been shown to have a higher risk of re-intervention after EVAR (71). A deeper knowledge of the forces that affect iliac limb stent grafts could potentially give an indication of possible causes of iliac stent graft migration and, if so, facilitate further development of EVAR stent grafts and planning of procedures.

To investigate the forces affecting iliac limb stent grafts under physiological conditions, we studied flow-induced displacement forces in relation to stent graft angulation and fluid pressure (**Study 3**). Computational studies have previously shown that the changes in graft diameter in aorto -uni-iliac grafts influences displacement forces (78). With the introduction of bell-bottom grafts for the use of ectatic iliac arteries as EVAR landing zones, there are theoretical reasons to believe that flow-induced forces may

be influenced by changes in stent graft diameter also in iliac limb stent grafts. We therefore performed studies of displacement forces in relation to stent graft distal diameter and asymmetric graft curvature in **Study 4**. A better understanding of the displacement forces under physiological pulsatile conditions, the relation to fluid pressure, graft angulation, and graft diameter, and their distribution between the proximal end and the distal end of the graft would aid in improvement of graft development and procedural planning.

Minimally invasive endovascular techniques have been developed as a treatment option in cases in which only major cardiovascular surgery was an alternative. With the morbidity and mortality associated with the open or endovascular options in cases of dissection involving the aortic arch, less invasive options are needed. To possibly induce false lumen thrombosis and prevent further aneurysm growth in patients with chronic dissection and aortic expansion, early experience with a new technique for closure of entry tears was evaluated in **Study 5**.

Aims

The overall aim was to assess re-interventions after EVAR and to identify possible underlying causes.

The specific aims were:

• To describe re-interventions after EVAR, including incidence, indications, procedures, and outcome, concentrating especially on non-access-related re-interventions (**Study 1**);

• To determine underlying causes and to identify anatomical factors associated with additional stent grafting (**Study 2**);

• To study the flow-induced displacement forces in iliac limb stent grafts and the influence of stent graft angulation, fluid pressure, and pulsation frequency in an experimental aortic model (**Study 3**);

• To investigate how flow-induced displacement forces and stent graft movement depend on the distal diameter of iliac limb stent grafts and asymmetric graft curvatures in an experimental aortic model (**Study 4**);

• To describe a new endovascular technique to close small entries that persist in the aortic arch (**Study 5**).

MATERIAL AND METHODS

Patient characteristics

Studies 1 and 2 were approved by the Research Ethics Committee in Gothenburg (number 508-14), which waived individual patient consent. Study and patient characteristics are summarized in Table 1.

	Study 1	Study 2
No. of patients	405	444
Age	74.8 (7.3)	75.0 (7.4)
Male gender	338 (83.5%)	376 (84.7%)
Study period	Jan 2005 to Dec 2013	Jan 2005 to Dec 2015
Length of follow-up (months)	29 (0–108)	24(0–127)
AAA status at primary repair		
Non-ruptures	337 (83%)	365 (82%)
Ruptures	68 (17%)	79 (18%)
Re-interventions studied	113	31
Patients included in both studies	370	370

Table 1. Study and patient characteristics in **Studies 1 and 2**. Data are mean (standard deviation), number (%), or median (range). AAA, abdominal aortic aneurysm.

Study design

Study 1

All patients operated with EVAR for infrarenal AAA (n = 405) at Sahlgrenska University Hospital during the period 2005–2013 were included in a retrospective study. The patients were identified in the Swedvasc registry (90) and additional data were collected from the institutional database and patient records. Review of data was done regarding primary repair, patient characteristics, complications, re-interventions, and survival.

All re-interventions were identified and divided into access-related re-interventions such as suture of access bleeds, distal thrombembolectomy, patch angioplasty, or thrombendarterectomy of the common femoral artery. All remaining re-interventions related to the primary EVAR were considered to be non-access-related. Parameters studied were the timing of re-intervention in relation to primary EVAR, the number and types of re-intervention, clinical outcome, and indication for re-intervention. Early mortality was defined as in-hospital or within 30 days, and aneurysm rupture as retroperitoneal haematoma and/or extravasation of contrast on preoperative CT. Patient follow-up included postoperative CT at one month, one year, and on an annual basis thereafter.

Study 2

All patients with primary bifurcated EVAR for infrarenal abdominal aneurysms treated at Sahlgrenska University Hospital in the period 2005–2015 (n = 439) were included in the study. In addition two patients treated before the study period and three patients with primary EVAR in other hospitals that all required re-interventions with additional iliac stent grafts were included. Patients were identified in the Swedvasc registry and additional data were collected from the institutional database and patient records. An in-depth analysis was performed in all patients with re-interventions with additional iliac stent grafting.

The analysis was performed in three steps. Firstly, baseline demographics were compared between patients with and without re-interventions. Secondly, limbs with and without re-interventions in the entire study population were compared regarding preoperative anatomical variables from EVAR planning protocols. Thirdly, treated and untreated limbs in the

group requiring re-interventions were compared, with detailed review of each patient's CT follow-up at one month and the last CT scan before re-intervention.

Parameters studied were vessel lengths, vessel diameter, attachment length, graft angulation, and migration. Iliac artery attachment zones were compared with each stent graft's IFU and an attachment zone shorter than that stipulated in the IFU was considered inadequate. Migration was defined as an increase in the distance from the internal iliac artery orifice to the distal edge of the stent graft along the central lumen line and a corresponding decrease in the distance from the aortic bifurcation to the end of the stent graft of > 5 mm during follow-up. In cases with a landing zone in the external iliac artery, a decrease in the distance to the internal iliac artery of > 5 mm was regarded as migration. Progression of iliac artery disease was defined as an increase in vessel diameter of more than the diameter of the stent graft, leading to loss of attachment.

Statistics, Studies 1 and 2

No formal sample size calculations were done due to the exploratory design of the studies. Data are presented as mean and standard deviation (for data with normal distribution) or median and interquartile range (for data that were not normally distributed). Follow-up time is presented as median and range. Normality of data was checked with the Kolmogorov-Smirnov test. Categorical data are presented with numbers and percentage, and they were compared between groups with Fisher's exact test. Cox regression was used to identify independent predictors for non-access-related re-interventions. Kaplan-Meier curves were used to analyze cumulative long-term survival, followed by log-rank test for group comparisons. Any p-value < 0.05 was considered to be statistically significant. All statistical calculations were performed with SPSS 22 (IBM Corp., Armonk, NY, USA).

Studies 3 and 4

An experimental model with pulsatile flow mimicking aortic in vivo pressure curves (91) was constructed. Iliac limb stent grafts were inserted in the flow model and fixated to strain gauge load cells (Fig. 7). To simulate aortic flow, perfusion of water at room temperature was established with a computer-triggered roller pump connected to a closed circuit in which silicone tubing was used. Pinch valves in combination with water-filled containers

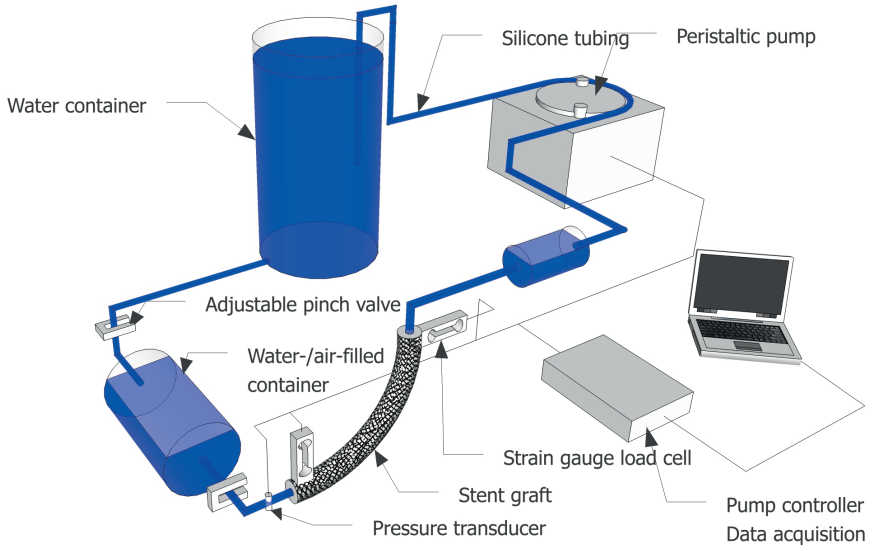


Figure 7. Aortic flow model.

were used to achieve peripheral resistance. The ends of the stent graft were firmly fixed to connectors attached to the load cells, and flow-induced forces at each end of the graft could be measured. Measurements of sideways graft movement were performed on film sequences with high-resolution imaging. Forces and graft movement were studied at different fluid pressures, different stent graft angulations, and different pump frequencies.

The experiments in **Study 3** were performed with an even and symmetric graft curvature and a non-tapered graft with a diameter of 16 mm at both ends (Fig. 8).

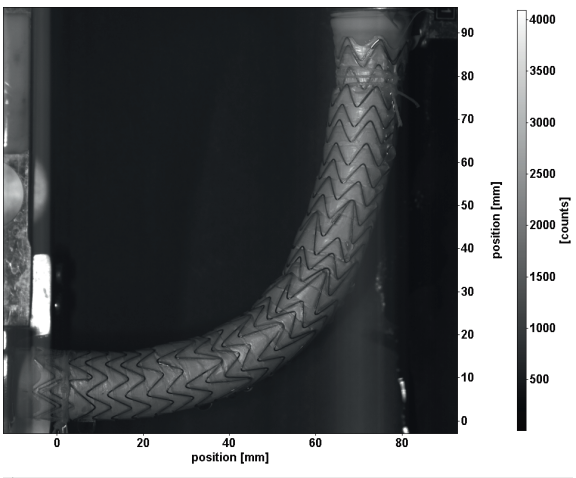


Figure 8. Non-tapered graft with symmetric curvature.

The experiments in **Study 4** were performed with a tapered graft (Fig. 9A), a non-tapered graft (Fig. 8), and a bell-bottom graft (Fig. 9B)–with symmetric curvature in the tapered graft and with asymmetric curvature in the non-tapered graft (Fig. 10).

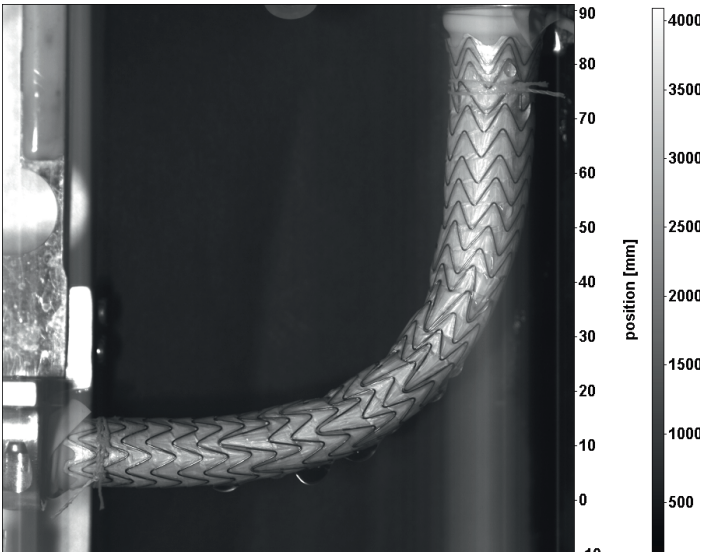


Figure 9A. Tapered graft with symmetric curvature.

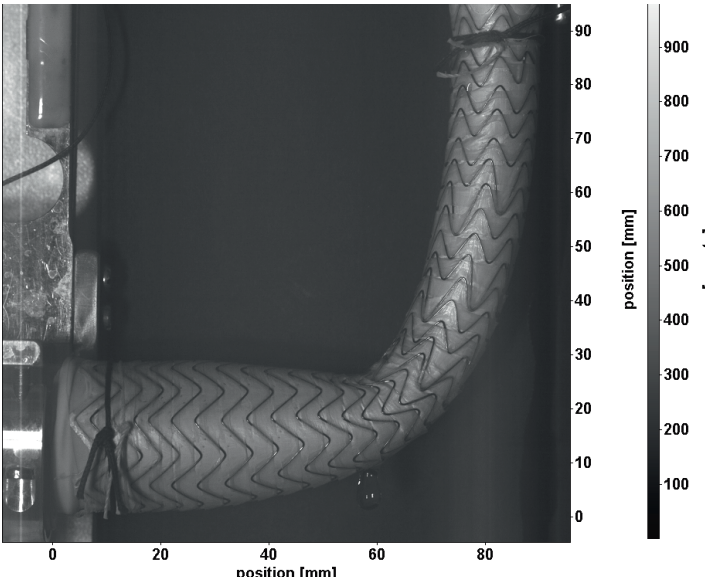


Figure 9B. Bell-bottom graft with symmetric curvature.

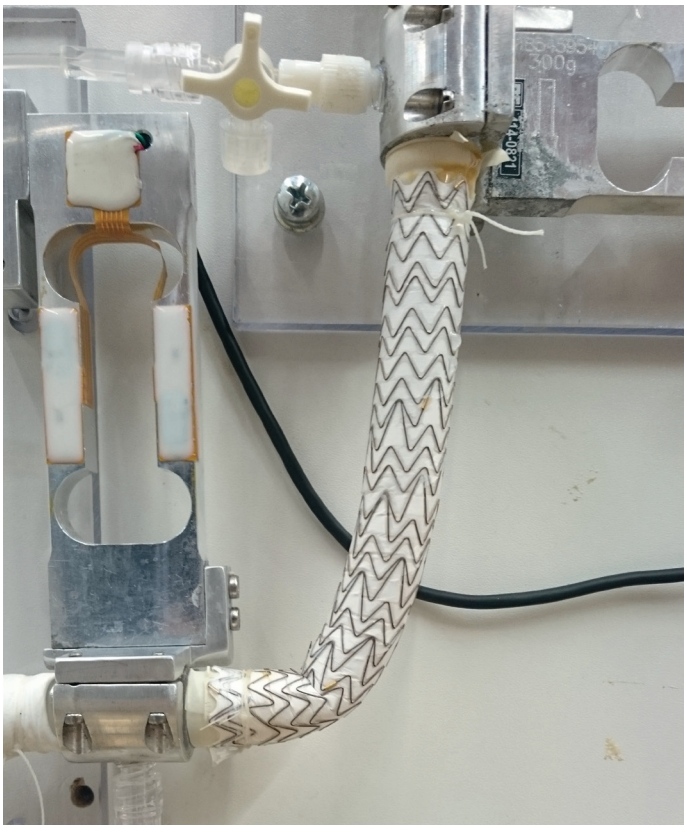


Figure 10. Non-tapered graft with asymmetric curvature

Study 5

After introducing a new technique for occlusion of small dissection entries in the aortic arch, four patients were closely followed regarding false lumen flow, development of aneurysm, and clinical follow-up. Data were collected from the institutional database and patient records. In-depth analysis was done for each of the patients by analyzing follow-up CT scans and re-interventions.

Results

Study 1

General

In total, early mortality was 2.5%. It was 0.6% in the non-rupture group and 12% in the group with aortic rupture. One hundred and thirteen re-interventions were performed in 89 of the 405 patients (22%) during the follow-up period. Access-related re-interventions accounted for one quarter, while the remaining re-interventions were non-access-related. There were 28 access-related re-interventions in 27 patients (7%) and 85 non-access-related re-interventions in 65 patients (16%). Three patients underwent both types of re-interventions.

Non-access-related re-interventions

Median time from primary EVAR to first non-access-related re-intervention was 14 months (range 0–91). The overall incidence was 7 per 100 patient years. The incidence was highest during the first year after primary intervention (12 per 100 patient years). Fifty-one (60%) of the non-access-related re-interventions were performed due to findings at follow-up and the remaining 34 (40%) were performed due to symptoms.

Of the non-access-related re-interventions, 69 of 85 (81%) were performed with endovascular technique, 15 of 85 (18%) were performed with open surgery, and one (1%) was performed with hybrid technique. Embolization of endoleaks (n = 21) and additional iliac stent grafting (n = 19) were the most common re-interventions. These re-interventions were performed significantly later after primary repair compared to thrombolysis and bare metal stent (p = 0.05). A tendency in the same direction was observed in comparison with proximal extension. A summary of the most frequent groups of re-interventions, time after primary repair, and detection is given in Table 2.

In multivariate analysis, aneurysm rupture at primary repair (hazard ratio (HR) = 2.23, 95% confidence interval (CI)1.13−4.40; p = 0.020) and male gender (HR = 2.97, 1.07−8.20; p = 0.036) were associated with non-access-related re-interventions.

	No. of re-intervention procedures	No. of patients	No. of days after primary EVAR*	Detected by follow-up	Detected by symptoms
Embolization	21	17	1029 (578–1357)*	20	1
Additional iliac stent graft	19	17	821 (539–1414)*	15	4
Proximal extension	12	12	239 (68–1163)*	6	6
Thrombolysis	8	7	41 (18–90)*	0	8
Iliac bare metal stent	6	6	27 (8–242)*	3	3
Relining	5	5	0; 40; 44; 415; 2151 **	4	1

Table 2. Number of re-intervention procedures performed for the most frequent groups of re-interventions. Number of patients, days after primary repair and number of re-interventions performed due to findings on follow up imaging or due to symptoms.
Key: * Days after primary EVAR presented as median and interquartile range
**Presented as days after primary EVAR for each procedure.

Study 2

During the study period, 24 patients underwent 31 re-interventions with additional iliac stent grafting. Five of the procedures were performed due to aneurysm rupture. Median time to re-intervention from primary EVAR was 46 months (range 2–92). All patients in the re-intervention group were males (p = 0.03). Median aneurysm growth in the patients with re-intervention was –0.1 mm (–7 to 7).

Computed tomography follow-up

Comparison between treated and untreated limbs in the entire cohort showed significantly larger artery diameters at stent graft landing zones in limbs with re-intervention: 18 mm (25th to 75th percentile 17–20) vs. 15 mm (13–17) in limbs without re-intervention (p = 0.001) (Fig. 11). All patients with additional iliac grafting had iliac artery lengths that would have allowed iliac artery attachment zones well above the lengths suggested in the IFU, but a considerable proportion of the patients had iliac stent graft attachment zones that did not reach the lengths stipulated in the IFU (Fig. 12). In the patient group with additional iliac grafting, artery diameter at landing zones was not significantly different, but significantly shorter iliac artery attachment zones were observed in limbs with re-interventions: 23 mm (25th to 75th percentile 11–34) vs. 34 mm (25–44) (p = 0.01).

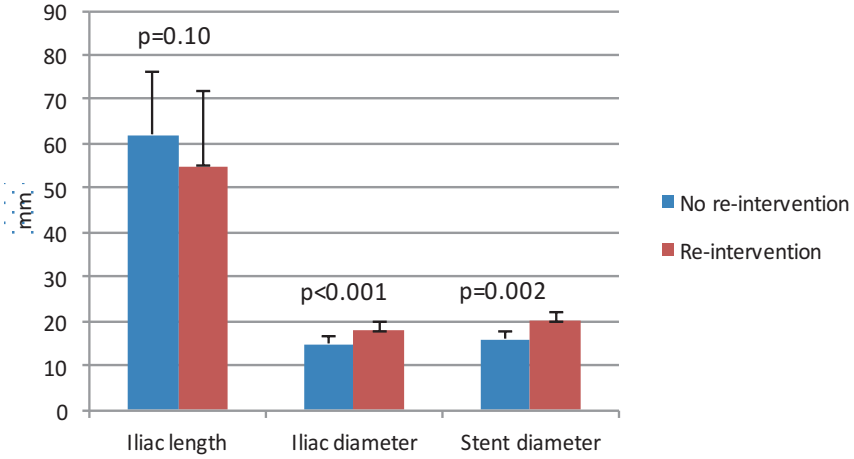


Figure 11. CT measurements of diameters and lenghts of common iliac arteries and diameters of stent graft in limbs with and without re-interventions with additional iliac stent grafts.

Causes of additional iliac stent grafting

Sixteen of the 31 additional iliac stent graft re-interventions (51%) were placed due to migration (Fig. 12). Distal graft extension was performed in ten limbs due to migration at the distal landing site, and six bridging grafts were placed due to migration at stent graft interconnections.

Landing zones were within the IFU in 11 out of 16 of the limbs with migration. Progression of disease, i.e. landing zone dilatation, was the cause of nine re-interventions (29%). Attachment zones were within the IFU in 7 of 9 of these limbs. Three limbs (10%) were treated with extension solely due to attachment zones being shorter than the IFU at the first fol-

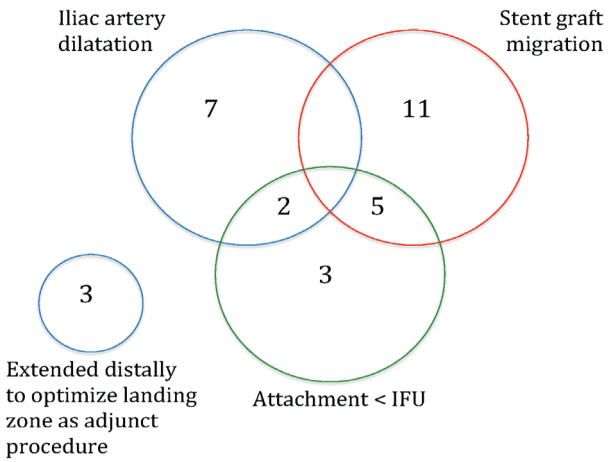


Figure 12. Reason for re-intervention with additional iliac stent graft after EVAR.

low-up CT. Furthermore, three other limbs (10%) were extended distally as adjunct procedures, to optimize landing zones in patients who underwent re-interventions for other causes.

Study 3

Flow-induced displacement forces

Displacement forces in the experimental model were similar at both ends of the graft and increased significantly with increasing graft angulation and

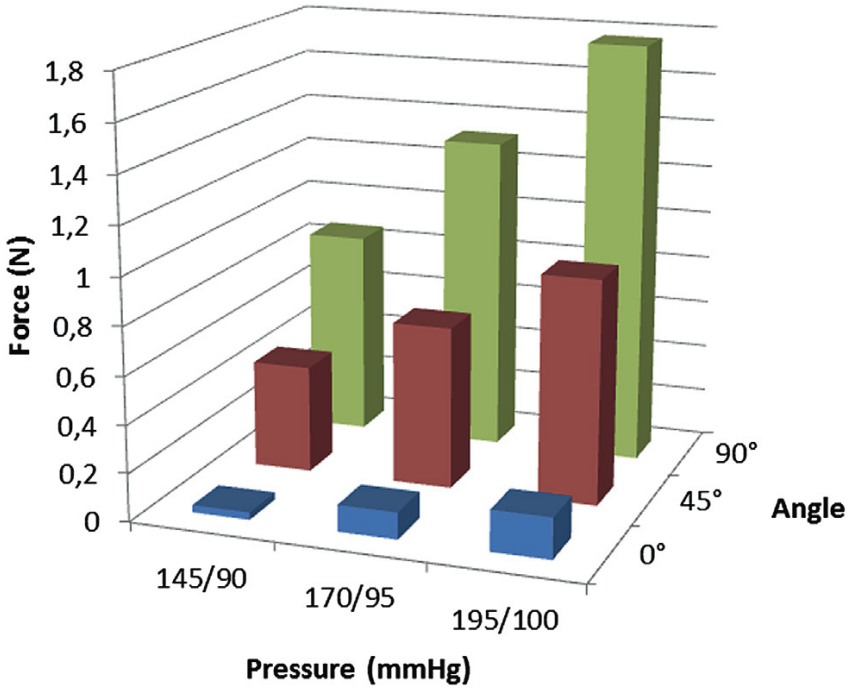


Figure 13. Peak force at the distal strain gauge cell at different perfusion pressures and stent graft angles.

fluid pressure (Fig. 13), but not with increasing stroke rate.

A significant correlation was observed between forces at the proximal end and the distal end of the graft, at all pressures and angulations ($r = 0.98$; $p = 0.001$). Peak forces at both the proximal end (1.71 N) and the distal end (1.77 N) were observed at a perfusion pressure of 195/100 mmHg and 90° angulation. The directions of measured forces defined as positive are shown in fig 14.

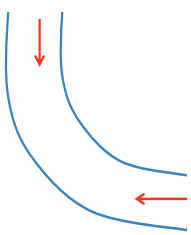


Figure 14. Directions of measured forces defined as positive

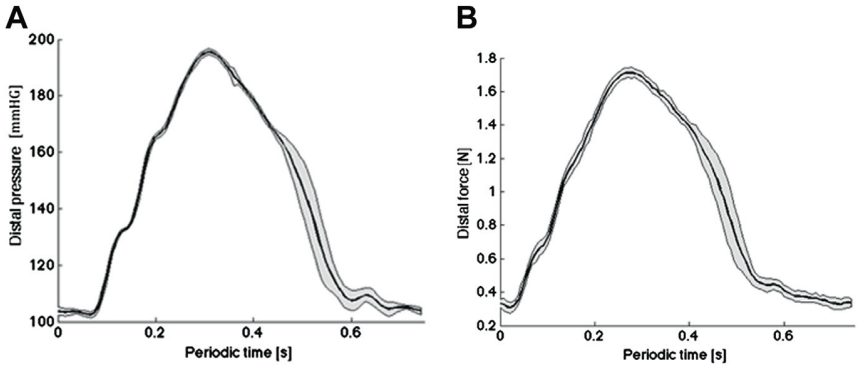


Figure 15. Perfusion pressure waveform (panel A) and flow-induced force (B). Both curves at 195/100 mmHg and 90° angulation. Mean and range is shown for 10 repeat measurements.

The displacement force and perfusion pressure curves had similar shapes and temporal behaviour (Fig. 15).

Stent graft movement

The movement of the graft increased with elevated forces and was greatest at 195/100 mmHg and 90° angulation. There was a highly significant correlation between graft movement and displacement forces ($r = 0.98$; $p = 0.001$). The direction of stent graft movement is shown in Fig. 16.

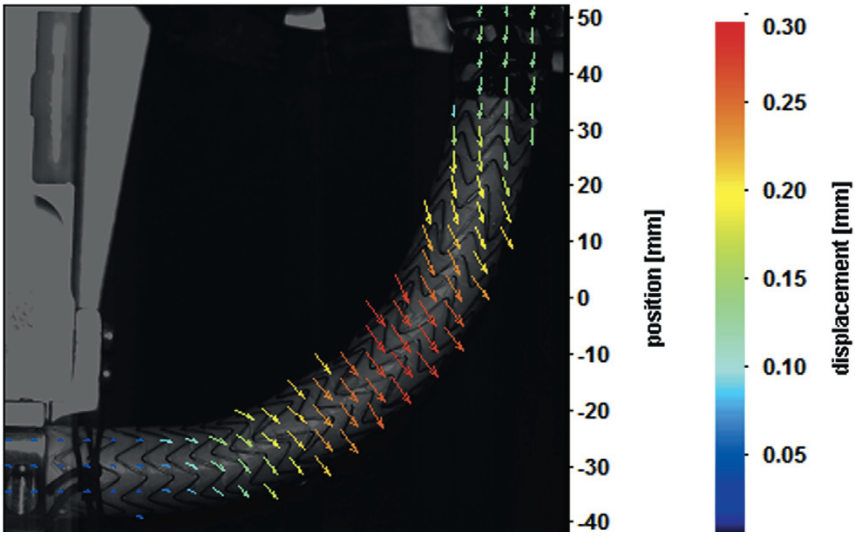


Figure 16. Sideways movement of the stent graft at 195/100 mmHg perfusion pressure and 90° angulation.

Study 4

Displacement forces were higher at both ends of the graft in the tapered graft than in the non-tapered graft at all angulations and pressures. The difference varied between 0.3 N and 0.9 N. Peak forces reached 2.4 ± 0.01 N.

Displacement forces were considerably higher at the distal end in the bell-bottom graft at all angulations and pressures. Peak forces reached 6.9 ± 0.05 N at the distal end as compared to 2.3 ± 0.06 N at the proximal end, at 90° angulation and a pressure of 195/100 mmHg (Fig. 17).

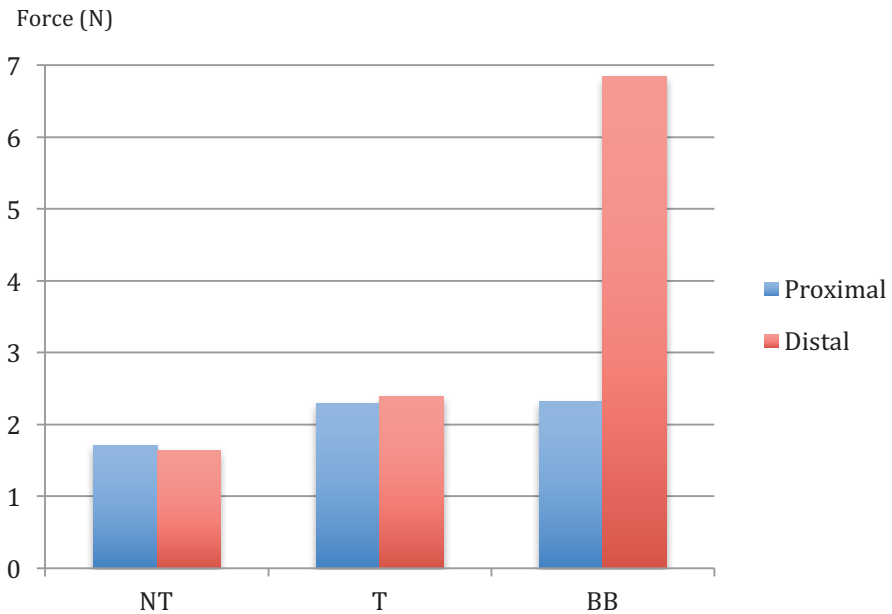


Figure 17. Peak forces at the proximal and distal end of a stent graft in relation to its distal diameter. Non-tapered (NT), tapered (T), and bell-bottom (BB) grafts. Values at 195/100 mmHg and 90° angulation.

Asymmetric stent graft curvature

The distribution of force between the proximal end and the distal end of the graft was altered if the bend of the graft was moved closer to one of the ends. The force at the end closest to the bend showed an increase of up to 0.2 N, whereas the end further away from the bend showed a corresponding decrease of up to 0.34 N.

Study 5

Four cases of closure of small entries in the aortic arch in patients with chronic dissection and secondary aneurysm expansion showed that the technique is feasible and that it may–in selected cases–be an alternative to open surgery. In three of the four patients, a false lumen obliteration and a decrease in aortic diameter was found. One patient required open reconstruction.

Discussion

This thesis focuses on different aspects of re-interventions after EVAR. Re-interventions, late complications, and the need for long-term follow-up are the main disadvantages of EVAR compared to open technique. Of the late complications, ruptures are the most important, due to their high mortality. Ruptures occur in up to 1% of all EVARs (63, 64, 92). The relatively low frequency and the multifactorial background to these complications may reduce the general awareness of the problem. Furthermore, the low frequency makes studies difficult.

The introduction of increased proximal fixation resulting in a decrease in migration at the proximal landing site (49-51), and the awareness that endoleaks of type II do not always need treatment (93-96) are two factors that contribute to a reduced frequency of EVAR re-interventions today compared to the early years of EVAR (51, 67). Since the introduction of increased proximal fixation, stent graft development has focused on easier deployment, conformability with a wider range of anatomic variations and smaller introducer sizes (56-58) rather than improved durability.

Our detailed study of frequencies of different types of re-interventions and their occurrence in time after primary repair in **Study 1** showed re-intervention rates similar to those in other reports (65-67). Survival in patients with re-interventions showed a trend of better survival compared to patients without, which contrasts with a recent multi-centre analysis showing higher aneurysm-related mortality in patients with re-interventions (97). The findings in the review are based on aneurysm-related mortality, not all-cause as in our series, which may have contributed to the difference.

Our finding that additional iliac stent grafting was one of the more frequent re-interventions confirms previous reports (65, 68, 69). A particularly noteworthy finding was the late occurrence of additional iliac stent grafts after EVAR in our study, with a median time to re-intervention of 27 months after primary repair. It has recently been shown that endoleaks of types I and III are the main reasons for ruptures after EVAR (63). The relatively high frequency and late occurrence of additional iliac stent grafting indicates that distal landing site problems may have a more important role in late EVAR failures than previously recognized. Several publications on

iliac landing zones have mainly focused on the influence of iliac landing zones on proximal fixation, not on the integrity at the distal landing site itself (98, 99). Our results show that re-interventions with proximal extension are performed early after primary repair: 7 out of 12 were performed during the first year after EVAR, whereas 14 of 19 procedures with additional iliac grafting were performed more than two years after EVAR. These findings indicate that reasons for failure at the proximal and distal landing sites should be regarded as separate entities.

Until now, the issue of stent graft migration has mainly focused on migration at the proximal landing site. In our analysis in **Study 2**, we found that migration at the distal landing site or at stent graft interconnections was the most common cause of additional iliac stent grafting. The factors affecting stent graft integrity were iliac artery diameter and stent graft attachment lengths. Comparison of maximal iliac artery angulation in patients with re-intervention in **Study 2** did not show any difference between the limbs with and without re-intervention. However, the angulation was considerable in all patients with re-intervention, which reduces the chance of identifying differences. A larger iliac artery diameter has previously been shown to be associated with an increased re-intervention rate (100).

A recent publication has shown that migration at the distal landing site, also in short-term and non-dilated iliac arteries, is correlated to shorter attachment lengths (101). The findings in **Study 2** suggest that wide iliac arteries and short attachment lengths in combination increase the risk of migration at the distal iliac landing site. Also, the elevated displacement forces in bell-bottom grafts in **Study 4** indicate that the risk of migration related re-interventions is higher in patients with wide iliac arteries used as landing sites. In clinical follow-up, wide iliac arteries have also been shown to have a greater risk of progressive dilatation after EVAR (102), further increasing the risk of loss of attachment in these patients. This is also supported by the previously published findings that the rates of re-interventions and distal type I endoleaks are higher in patients with wide iliac arteries. One example of significant stent graft migration and sideways graft movement leading to distal endoleak of type I is shown in Fig. 18.

Since the median time to additional iliac stent grafting was as long as 46 months, follow-up programs, in particular in patients with wide iliac arteries treated with bell-bottom grafts, should be designed accordingly. A

more vigorous surveillance may be needed for patients with bell-bottom grafts also in the long term. It is noteworthy that AAA diameter did not increase in this group of patients, and ultrasound may therefore not be sufficient to predict the need for re-intervention. Another aspect requiring special attention concerns the specifications for iliac artery attachment lengths given in the IFU for a particular stent graft. The most commonly used stent grafts in our series have 10- to 15-mm landing zones as restrictions for treatment. These lengths may be sufficient in many conditions but may, according to our findings, be associated with late EVAR failures if there are wide iliac landing zones. Furthermore, our study on preoperative measurements in **Study 2** shows that most of the patients have iliac artery lengths that would allow iliac artery attachment zones well above the lengths suggested in the IFUs. It is thus reasonable to believe that a better iliac attachment would prevent some of these late EVAR failures. One possibility for prevention of migration at the iliac landing zone and at stent graft interconnections is to increase the fixation also at the distal landing end of the graft and at interconnection. Another option, which is readily available with the stent grafts that are on the market, is to change IFU specifications to longer landing zones, at least in cases where wide iliac arteries are used

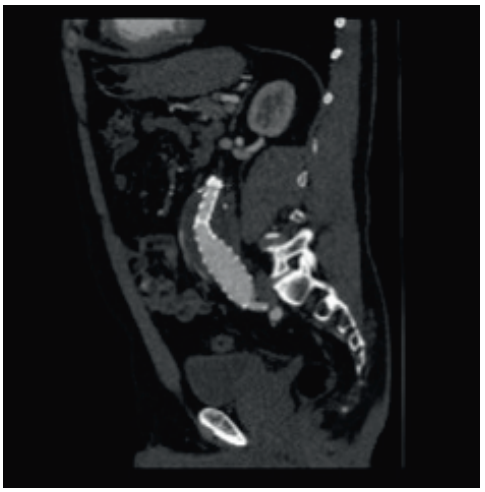


Figure 18A. Postoperative computed tomography scan showing a stent graft in the correct position.

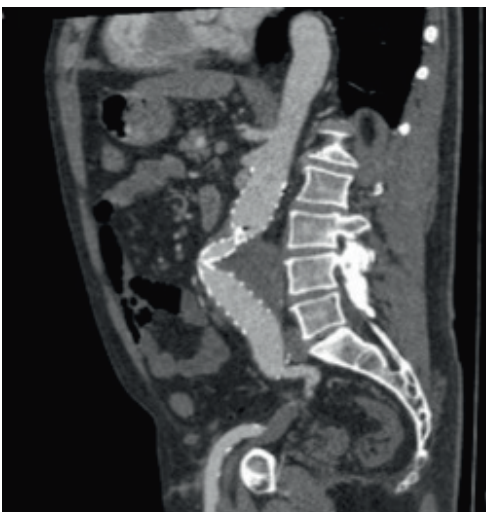


Figure 18B. Computed tomography scan before re-intervention, showing migration of the iliac limb at the distal landing site with loss of attachment and severe kinking of the graft.

as landing zones. Supported by the close association between short iliac landing zones and graft migration, this suggests that the entire landing zone that is available should be used. It is noteworthy that grafts are currently available where the attachment at the graft interconnection has been improved with additional fixation (103).

In the majority of EVAR stent grafts, distal stent graft attachment still depends on the fixating force of the self-expanding stent graft alone. As mentioned above, 10–32% of EVAR re-interventions are caused by inadequate iliac artery attachment, making additional iliac grafting mandatory. In line with these findings, in **Study 3** we could show that flow-induced displacement forces in stent grafts were of similar magnitude at both ends of the graft and that they were highly associated with graft angulation and perfusion pressure. In angulated stent grafts, the forces measured were close to the forces required to pull out a stent graft without additional anchoring. The role of flow-induced displacement forces in iliac limb stent grafts may well have been underestimated as a cause of EVAR re-interventions. In studies by Wassdorp et al. (71), sideways graft movement on follow-up CT was found to be associated with an increased risk of re-interventions, graft migration, and type I and type III endoleaks. This finding supports the idea that graft movement over time is an important factor in the integrity of a stent graft. In **Study 3**, we found a highly significant correlation between displacement forces and pulsatile graft movement. It is possible–but not proven–that pulsatile graft movement over time may contribute to sideways movement of a stent graft on follow-up CT, and therefore also to stent graft migration.

The factors influencing stent graft integrity are multifactorial, and patient anatomy varies significantly. As shown in **Studies 2, 3, and 4**, patient-specific anatomical factors including iliac angulation, landing zone diameter, and perfusion pressure are factors associated with stent graft migration. There are also several factors that influence stent graft fixation–such as thrombus in the aneurysm sac, vessel calcification, and shape of the landing zones (cone shape vs. reverse cone shape). Since several of these factors are difficult to influence and predict, it would most likely be preferable to maximize stent graft fixation in all patients, which would increase the safety margins in EVAR treatment and–in some patients–possibly prevent graft migration.

One consideration that may require special attention is the gender difference in selection and outcome among EVAR patients. Women are under-represented in studies of vascular disease (104), and have been shown to have a higher ratio of acute to elective repairs, higher mortality at rupture, and a lower frequency of treatment at rupture (105). In **Studies 1 and 2**, we observed lower rates of re-intervention in women–which may be a result of insufficient statistical power but could also indicate that the awareness of treatment and follow-up strategies in women with AAA should be improved.

Treatment of aortic dissection, particularly if it involves the aortic arch, can in many cases be quite demanding, both for the surgeon and for the patient. Open aortic surgery for the aortic arch is also associated with considerable co-morbidity, which makes minimally invasive solutions preferable. In **Study 5**, we described our initial experiences of endovascular closure of small entries in chronic aortic dissection. Although the results are promising, larger numbers of patients and longer follow-up will be needed for proper evaluation of the technique.

Limitations

The studies in the thesis had some important limitations. The main limitation regarding **Studies 1 and 2** was the retrospective design, with the risk of selection bias and unregistered confounders. Furthermore, these single-centre series may have had insufficient power to detect rare events, resulting in type II errors. The experimental set-up in **Studies 3 and 4** was aimed at isolating the forces at each end of the graft, to enable studies of the factors potentially influencing migration. It should be noted that other factors, including counteracting forces, were not studied.

Conclusions

• Additional iliac stent grafts and embolization of endoleaks are the most common re-interventions after EVAR (**Study 1**);

• Re-interventions with additional iliac stent grafts are performed late after EVAR, and are often caused by endoleak type I (**Studies 1 and 2**);

• Wide iliac arteries used as landing zones for EVAR stent grafts are associated with an increased risk of re-interventions with additional iliac stent grafts (**Study 2**);

• Stent graft migration was the most common cause behind the need for treatment with additional iliac stent grafts (**Study 2**);

• In an experimental model, flow-induced displacement forces in iliac limb stent grafts are significant and of similar magnitude at both ends of the graft, and they are highly dependent on angulation and fluid pressure (**Study 3**);

• Stent graft pulsatile movement showed a strong correlation to flow-induced displacement forces in an experimental model (**Study 3**);

• The flow-induced displacement forces were markedly greater at the distal end of bell-bottom grafts compared to straight and tapered grafts in an experimental model (**Study 4**);

• Endovascular closure of small dissection entries that persist in the aortic arch with an Amplatzer Vascular Plug II is feasible and may be an alternative to open surgical arch reconstruction in selected patients **(Study 5)**.

Future perspectives

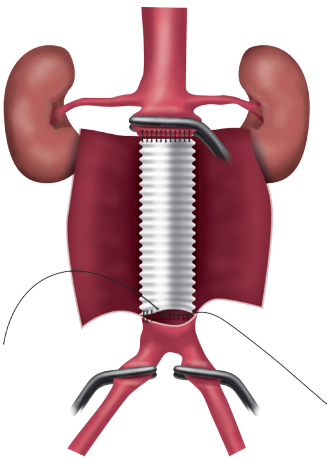
The relatively high crude re-intervention rates after endovascular repair has been one of the most debated topics in vascular surgery since the introduction of EVAR. Despite the technical improvements, re-intervention rates have still been found to be considerable and surveillance is still necessary. Detailed studies on the specific reasons for re-intervention would possibly help to concentrate future EVAR development on further improvement of durability. Efforts to find the underlying causes and to define the events that lead to late EVAR failure could possibly lead to improvements in graft design. The example of additional iliac stent grafting in this thesis is most likely only one possible topic that will need special attention if the durability of EVAR is to be improved.
Improved graft fixation would be one step towards the desired goal of the durability of EVAR being equivalent or superior to that of open surgery, so that surveillance would no longer be necessary. Ways of preventing flow in the remaining aneurysm sac could also be steps in the right direction.

Improved durability of EVAR would also facilitate the ongoing development of a wider treatment range. Endovascular treatment of aortic arch pathology is emerging as an alternative to open surgery. Further development will most likely make this treatment option available to an increasing number of patients. Patient selection and ongoing graft development are important factors in making this development prosper. The dynamic forces in the aortic arch in combination with varying vessel diameters during pulsations are important factors to consider. In view of the history of breaking struts in heart valves, the problem of durability must to be solved before widespread use of arch stent grafts is introduced. Once this has been achieved, endovascular treatment would in many cases lead to lower morbidity and mortality for this group of patients.

Sammanfattning på svenska

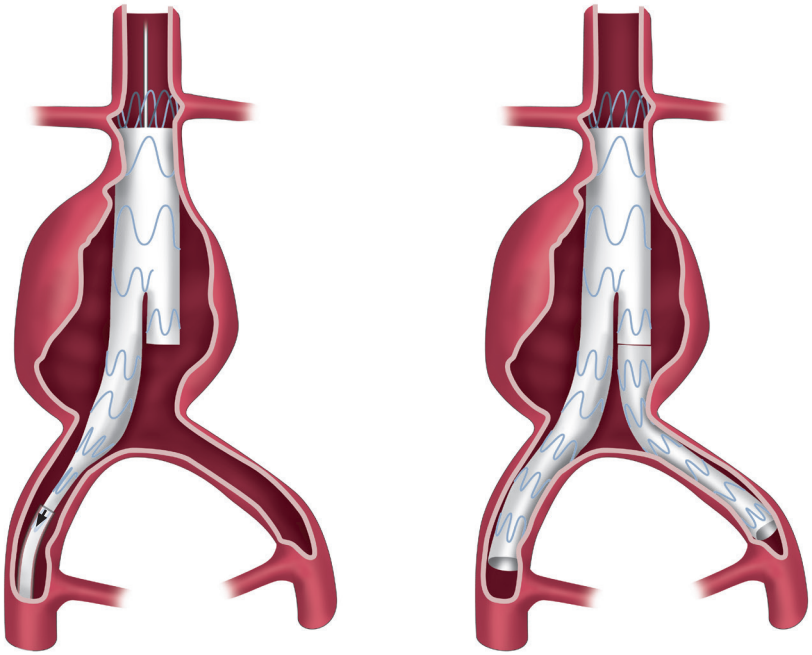
Avhandlingen är ett samarbetsprojekt mellan Sahlgrenska Akademin och Chalmers tekniska högskola. Den behandlar kliniska och experimentella studier av kompletterande ingrepp efter endovaskulär (kateterledd) behandling av bråck på kroppspulsådern. Pulsåderbråck innebär en vidgning av blodkärlet till över 50 % av dess normala diameter, vilket när det gäller kroppspulsådern innebär en vidd över 30 mm. Vid en diameter över 55 mm är risken för att blodkärlet spricker så stor att man brukar rekommendera en förbyggande operation.

Kroppspulsåderbråck kan behandlas med öppen operation där en del av blodkärlet byts ut mot konstgjort material (Figur 1) eller genom förstärkning av blodkärlet inifrån, EndoVascular Aortic Repair (EVAR) (Figur 2). Man för då in en kärlprotes, ett så kallat stentgraft via ljumskartärerna. De stentgraft som används vid EVAR behandling består av ett självvidgande metallnät som är täckt av ett membran av Gore tex eller polyester. Stentgraftet förs in i på avsedd plats i kroppen förpackat i en smal hylsa. När ytterhylsan sedan förs bakåt vidgar sig stentgraftet och förankras i normalvida delar av blodkärlet (Figur 2). Bilden visar att graftet är uppbyggt av olika komponenter som väljs utifrån patientens anatomi varefter delarna sammankopplas inne i patienten. EVAR behandling har jämfört med öppen operation lägre risker i samband med ingreppet men har en ökad risk för att det över tid ska krävas kompletterande ingrepp, så kallade re-interventioner. Det finns också en ökad frekvens av allvarliga sena komplikationer efter EVAR, där den allvarligaste är om kroppspulsådern spricker trots att man har genomgått en operation. De bakomliggande orsakerna till dessa sena komplikationer är inte kända. Den högre förekomsten av kompletterande ingrepp är också anledningen till att patienter behandlade med EVAR kräver uppföljning, vilken oftast innebär datortomografiundersökningar med regelbundna mellanrum. Sedan EVAR infördes under sent 1980-tal har betydande förbättringar av



Figur 1. Öppen operation

tekniken skett, bland annat genom att man har satt krokar på stentgraftets övre del för att förbättra förankringen mot blodkärlet. Stentgrafternas sammankopplingar och nedre förankringar baseras dock fortfarande på att stentgraftets självvidgande kraft fäster graftet mot kärlväggen.



Figur 2. Endovaskulär behandling av kroppspulsåderbråck. Den vänstra bilden visar när stentgraftet läggs på plats. Den högra bilden visar det färdiga behandlingsresultatet.

Denna avhandlings övergripande mål har varit att värdera de kompletterande ingrepp (re-interventioner) som förekommer efter EVAR och att identifiera möjliga bakomliggande faktorer. De specifika målen har varit:

1. Att beskriva re-interventioner efter EVAR utifrån förekomst, typ av ingrepp och resultat.
2. Att beskriva bakomliggande orsaker och anatomiska faktorer relaterade till re-interventioner med förlängningsben i stentgraftets sammankopplingar och nedre infästningar.
3. Att studera de flödesorsakade krafter som påverkar stentgraftet och hur dessa påverkas av stentgraftets angulering (vinkling), tryck, pulsfrekvens, nedre stentgraftsdiameter och asymmetrisk stentgraftskurvatur.

Material och metod

Studie 1 och 2 är en tillbakablickande genomgång av de patienter som är behandlade på Sahlgrenska Universitetssjukhuset under perioden 2005-2015. I studie 1 har en genomgång av frekvens, typ och resultat av de reinterventioner som gjorts bland 405 patienter. I studie 2 har 24 patienter, som har genomgått re-interventioner med kompletterande stentgraft i syfte att förbättra den nedre infästningen eller graftets sammankopplingar (förnyade bäckenkärls stentgrafter) studerats i detalj, genom en genomgång av uppföljande datortomografi-undersökningar. Dessa patienter har också jämförts avseende patienternas bakgrundsdata (ålder, tidigare sjukdomar, kön) och anatomi, med en grupp på 420 patienter utan denna typ av re-interventioner.

I studie 3 och 4 har flödesorsakade krafter i stentgrafter studerats i en mekanisk aortamodell där fysiologiska förhållanden efterliknats. Krafter i stentgraftets båda ändar och stentgraftets rörelse har studerats (Figur 7-10, sid 30-32). I studie 3 har effekten av angulering (hur mycket stentgraftet böjs), tryck och pulsfrekvens studerats i ett stentgraft med samma diameter i båda ändarna. I studie 4 har studierna utförts i stentgraft med avsmalnande-, ökande- respektive oförändrad diameter, samt i asymmetrisk kurvering av stentgraftet. Studie 5 beskriver en ny minimalinvasiv teknik för behandling av förbindelser mellan äkta och falska kärlpipan hos patienter med spaltning av kroppspulsådern.

Resultat

Studie 1 visar att embolisering av endoläckage (man stänger små blodkärl som löper in till det kvarvarande kroppspulsåderbråcket) och kompletterande bäckenkärls stentgrafter var de vanligaste re-interventionerna och att dessa utfördes påtagligt sent efter primäringreppet (Tabell 2, sid 34). I studie 2 visades att en betydande andel av de re-interventioner med kompletterande bäcken stentgrafter var föranledda av ruptur (att kroppspulsådern spruckit). Migration, det vill säga att stentgraftet flyttat på sig över tid, var den vanligaste bakomliggande orsaken följt av fortsatt vidgning av bäckenkärlen (Figur 12, sid 35), vilka båda medförde att stentgraftets nedre infästning blev otillräcklig.

Vida bäckenkärl och korta infästningszoner var viktiga faktorer som ökade risken för att en patient skulle behöva ingrepp med kompletterande bäcken stentgraft. Studie 3 visade att de flödesorsakade krafter som påver-

kar ett stentgraft med oförändrad diameter fördelar sig lika mellan dess övre och nedre infästning. Krafterna ökar med ökat tryck och angulering men inte med pulsfrekvens (Figur 13-15, sid 36-37). Ökade flödesorsakade krafter innebar större rörelse av stentgraftet vid varje pulsslag (Figur 16, sid 37). Studie 4 visar att de flödesorsakade krafterna i stentgrafter var tydligt relaterade till stengraftets diameter och kurvaturens form (Figur 17, sid 38). Krafterna var påtagligt höga i nedre delen i graft med ökande diameter. Studie 5 visar att man hos utvalda patienter med kronisk spaltning av kroppspulsådern kan använda minimalinvasiv teknik för att stänga de förbindelser mellan äkta och falska kärlpipan som medför risk att kärlet vidgar sig ytterligare. För att värdera effekten av denna teknik krävs ytterligare studier.

Slutsatser

Kompletterande ingrepp efter EVAR är fortfarande vanliga, men de flesta kan göras med minimalinvasiv teknik och prognosen är i regel god. Förlängning av stentgraftet i dess sammankopplingar och nedre infästningar är bland de vanligare och är ofta orsakade av att stentgraftet flyttar sig över tid. Dessa kompletterande ingrepp är vanligare bland patienter när stentgraften har en kort infästning och när de förankras i vida bäckenkärl. Flödesorsakade krafter kan vara en orsak till att stentgrafter flyttar sig över tid och därmed tappar sin förankring mot kärlväggen.

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