General introduction
GENERAL INTRODUCTION

The word aneurysm, derived from ancient Greek, is used as a medical term to describe “a permanent localized dilatation of an artery, having at least a 50% increase in diameter compared to the expected normal diameter artery in question”.¹ Most aneurysms occur in the aorta. The aorta is the main artery of the body, originating from the left ventricle of the heart extending down to the abdomen, supplying oxygen-rich blood to all parts of the body. Every section of the aorta can be affected, but most aortic aneurysms occur in the abdominal aorta. These are known as abdominal aortic aneurysms (AAAs). AAAs can be classified as infrarenal or pararenal and may or may not extend into the iliac arteries. Infrarenal AAAs are situated below the renal arteries, whereas pararenal AAAs start just at the level of the renal arteries without involving them (juxtarenal) or extend above at least one renal artery but end below the celiac axis (suprarenal).²³ A thoracic aortic aneurysm (TAA) is an aortic aneurysm that presents primarily in the thorax. It may involve the descending part or the arch with all its essential branch vessels. Aneurysms that coexist in both segments of the aorta (thoracic and abdominal) are termed thoracoabdominal aneurysms (TAAA).

Aortic aneurysms are usually asymptomatic and incidental discoveries during the investigation of backache, hip pain or urinary tract complaints. The prevalence varies with a number of demographic factors, including advancing age, family history, male gender, and tobacco use. In general, the prevalence of AAAs reported in population-screening programs is up to 7-8%.⁴⁻⁶ The prevalence is approximately six times greater in men than women.⁵ AAAs continue to be a leading cause of death. Mortality after rupture is high; approximately 70% of those who reach the hospital and 50% of those who undergo surgery for a ruptured AAA will die.¹⁰⁻¹² The risk of AAA rupture increases with aortic diameter.¹³ It is recommended that patients with infrarenal or juxtarenal AAAs measuring 5.5 cm or larger should undergo elective repair to eliminate the risk of rupture.¹⁴

At present, open surgical repair of AAA is still the gold standard. It is a major operation that requires direct exposure of the aorta usually through a transperitoneal approach. The aorta is cross-clamped, the aneurysm opened and replaced by a tubular or bifurcated graft. This procedure has proven to be an effective and durable solution, yet despite technical improvements in perioperative care, it is associated with perioperative mortality rates of 5%.¹⁵
Endovascular repair

Over the past 20 years, endovascular aortic aneurysm repair (EVAR) has emerged as a less invasive alternative for traditional open repair. Compared to conventional open repair, EVAR has the advantage of a less extensive operative exposure by circumventing transcavitary incision. Moreover, EVAR reduces tissue ischemia due to little interruption of blood flow and the possible use of regional and local anesthetics. EVAR is ideally suited for the higher-risk patient with poor cardiac, pulmonary, or renal performance and for those with prior aortic or other abdominal operations. EVAR typically requires single or bilateral femoral artery cut-downs. Under fluoroscopic guidance, a self-expandable endovascular stent-graft (endograft) is then passed through the aortic lumen to fit tightly above and below the aneurysm. The endograft excludes the aneurysm sac from systemic circulation, thereby decreasing or eliminating the risk of rupture (Fig. 1).

Multicenter randomized trials,\textsuperscript{16-18} have demonstrated early advantages of EVAR over open repair, including reduced perioperative mortality, shorter operative time, decreased transfusion requirements, shortened intensive care unit and hospital stay. On the other hand, EVAR is associated with a higher rate of re-interventions and questions remain regarding the long-term efficacy of EVAR in preventing aneurysm-related death for all patients treated with this technique. However, with future advances in endograft technology, expanded operator experience and improved surveillance techniques, the current trend of expanding the indication for EVAR is likely to continue.

Worldwide there are a number of endografts approved for commercial distribution. All of the grafts in clinical use have recognizable strengths and weaknesses that make them more or less useful in various clinical situations. However, all require sufficient proximal and distal aneurysm “neck” length for secure fixation and aneurysm exclusion. Absent or short proximal and distal aneurysm necks like in pararenal aortic aneurysms prohibit standard EVAR. Open repair of these aneurysms can be a real challenge due to the location of this part of the aorta high in the retroperitoneum and just below the diaphragm. It involves wide aortic exposure and interruption of blood flow to abdominal organs that have little tolerance for ischemia. It is therefore still associated with high mortality and morbidity rates.\textsuperscript{19} These factors contribute to the appeal of a less invasive approach for these complex aneurysms. To overcome these problems fenestrated and branched endografts have been designed.
Figure 1: an aortic endograft is placed within the aneurysm, thereby excluding it from circulation.

**Fenestrated and branched endografts**

Fenestrated and branched endografts allow for aneurysm exclusion while incorporating one or several essential aortic branch vessels into the seal of the graft. The blood flow to the branch vessels is preserved through holes (fenestrations) or by branches incorporated in the fabric of the endograft. Fenestrated endovascular aortic aneurysm repair (F-EVAR) is the simplest form of preserving blood flow to any aortic branch vessel. Fenestration refers to the creation of one or multiple holes within the fabric of an endograft. The primary goal of F-EVAR is to move the sealing and fixation site of an endograft into a non-
dilated segment of the aorta from which essential branch vessels arise, without excluding blood flow to these branch vessels. F-EVAR thereby circumvents the problem of inadequate neck length.

Fenestrations divide into three types: small fenestrations (6–8 mm) that occupy the spaces between stent struts, large fenestrations (8–12 mm) that are usually crossed by stent struts, and scallops that are open at the boundary of the endograft. While there is no fluid tight seal at the fenestration, direct apposition of the endograft with the aortic wall is necessary to assure complete exclusion of the aneurysm from blood flow.

When essential branch vessels originate from the aneurysm itself standard fenestrated grafts are not sufficient. To accommodate these aneurysms branched endografts are required. In a branched repair covered-stents bridge the gap between the lumen of the main-graft and the branch artery, therefore ensuring blood flow to the target vessel while excluding the aneurysm from circulation. Branched endografts are categorized as modular or unibody, depending on whether they are assembled in situ from several components or inserted whole. Modular branched endografts have one or more directional branches, or cuffs, surrounding the fenestrations. These branches are not long enough to reach the target vessels without the addition of overlapping extensions in the form of covered stents. The zone of contact between the cuff and the covered stent contribute to stability, regardless of whether the covered stents are self-expanding or balloon-expandable. Branches can be of different length, on the inside or outside of the main graft and placed transversely or longitudinally. The direction of the branches depends on the orientation of the target vessel; longitudinal branches can be placed caudally or cranially. If cranially orientated covered stent insertion is performed through the femoral arteries, cannulation of caudally oriented branches requires additional proximal access, usually through the brachial artery. Branches can be coupled with preloaded wires and catheters, allowing sheats to be directly advanced into the target vessel. Unibody branched endograft are pre-assembled outside the patient. There are no extensions; the branches are permanently attached to the trunk. The length, diameter, position, and orientation cannot be adjusted in situ, and must replicate the native anatomy exactly. During deployment the endograft is maintained in a compressed state while the branches are manipulated into position by either pushing or pulling them into the target vessel, depending on the availability of downstream branch vessel access. The advantage of such a device would be the elimination of modular joints, further limiting the risks of component separation.
Aim of this thesis

The aim of this thesis was to develop and investigate alternative strategies to widen the indication for EVAR. Furthermore, techniques to prevent or treat EVAR associated complications were studied.

The chapters 2 and 3 describe the feasibility of a branched endograft-system in an animal and human cadaver experimental model. This endograft-system is developed for the treatment of short or no-neck aortic aneurysms and contains a main endograft and two separate branch grafts for the renal arteries. After creation of fenestrations into the proximal part of the main endograft, it is mounted on a modified delivery system. This system is equipped with a partial deployment feature to allow optimal maneuverability and ensuring longitudinal and rotational maneuverability for proper alignment of the fenestrations with the vessel ostia. The
separate branch grafts are composed of a balloon-expandable stent. The stent is covered with an extended tube of expanded polytetrafluoroethylene (ePTFE) over which is molded a silicone flange. The silicone flanges are designed to easily slide into the fenestration and the target vessel, lock into place, and create a fluid-tight seal with the main endograft.

Chapter 4 investigates the feasibility of a novel approach for endograft delivery. Delivery of endografts to the thoracic aorta routinely utilizes the femoral arteries for access. However, the long distance between the access point and the target site makes it difficult to maneuver and deploy an endograft in its correct position. The usually large-caliber sheaths that are necessary for fenestrated and branched endograft delivery complicate things even more, especially in patients with tortuous, calcified, or stenotic iliac arteries. In an animal model a direct videoscopic approach to the descending thoracic aorta for endograft delivery is tested.

A new technique often comes with new complications. Also EVAR has complications not seen with open repair. These include endoleaks, endograft migration, structural failure and endograft distortion. The most frequent is the occurrence of an endoleak, i.e., persistent blood flow outside the endograft and within the aneurysm sac. Under these circumstances, the sac may continue to expand and the aneurysm can still rupture.

In Chapter 5 we assess the problem of endograft migration. When proximal fixation of endografts fails, a sealing failure at the attachment site of the graft to the vessel wall may occur (type I endoleak). Fenestrated and branched techniques allow for endograft deployment further into non-aneurismal aorta, which may improve proximal fixation. We describe an in vitro study that investigates proximal fixation of a fenestrated and the earlier described branched endograft-system, in comparison with an infrarenal endograft with suprarenal bare stent fixation and a conventional hand-sewn anastomosis. Human aortas were obtained at autopsy and transected 20 mm below the renal arteries to mimic an infrarenal aneurysm neck. In random order, the infrarenal, fenestrated and branched endografts were deployed in the aorta similar to clinical practice. Proximal fixation was tested using a hydraulic material-testing machine. Longitudinal traction was applied to the distal end of each endograft until migration occurred. Subsequently a hand-sewn infrarenal anastomosis was tested in a similar manner.

Chapter 6 presents the results of a retrospective review of patients that underwent endoscopic type II endoleak repair (EER) following EVAR. In type II endoleaks,
retrograde flow through aortic branch vessels continues to fill the aneurysm sac. Vessels that are usually involved are the lumbar arteries, inferior mesenteric artery or internal iliac artery. Patients underwent endoscopic ligation or clipping of feeding branch vessels. Procedures were performed by an experienced vascular surgeon and an experienced endoscopic surgeon. All patients underwent computed tomography-angiography (CTA) on the first post-operative day. Standard follow-up with CTA, magnetic resonance angiography (MRA) and/or duplex ultrasound imaging was carried out at 6 and 12 months and then yearly thereafter.

Finally, Chapter 7 describes a systematic review of the current literature to analyze the immediate and follow-up results of fenestrated endovascular aneurysm repair in patients with juxtarenal and Crawford type IV thoracoabdominal aortic aneurysms. A meta-analysis was performed for technical success (successfully completed procedure with endograft patency, preservation of target vessels and no evidence of type I or III endoleak at post-procedural imaging), 30-day mortality, all-cause mortality, branch vessel patency, renal impairment, and secondary interventions.

References