Endovascular approaches to complex aortic aneurysms

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CHAPTER 10

SUMMARY AND FUTURE PERSPECTIVES
The advocated treatment of abdominal aortic aneurysms (AAAs) has shifted from an open surgical repair towards a total endovascular approach. After introduction of endovascular aneurysm repair (EVAR) for infrarenal AAAs, endografts for juxtarenal AAAs, suprarenal AAAs and thoraco-abdominal aortic aneurysms (TAAAs) have been developed to enable a more cranial deployment of an endograft in a healthier part of the aorta while maintaining visceral artery vascularization. This thesis focused on the clinical outcome of these devices, designed for infrarenal and complex aneurysms, and the considerations of these endografts in relation to patients’ anatomy.

Since their introduction, endografts for EVAR have been further developed and newly designed endografts have been added meanwhile. Despite the fact that long-term follow-up results of infrarenal endografts were not available yet, alterations were already made to these endografts throughout the whole time period. In Chapter 2 an overview of currently available endografts for infrarenal AAA repair and their mid- to long-term follow up results is shown. Main variations between the endografts were the way of proximal fixation (infrarenal or suprarenal), the use of either Z- or circular stents and the fabric of the endograft. In comparison to first generation devices, currently available endografts are more flexible, have improvements for a more controlled deployment, and are delivered in smaller sheaths. The Zenith SP Flex® (Cook Medical), Incraft® (Cordis corp), Excluder® (Gore), Endurant™ (Medtronic) and the Anaconda™ (Terumo aortic) have similar results for peri-operative outcome and early reintervention rate. Although studies with these newer generation devices show good results, there is still a 10-20% reintervention rate during a mean of three year follow-up, and as a consequence close follow-up remains necessary. Important factors influencing outcome seem to be the anatomical suitability, the adherence to the instructions for use, and the experience with a certain endograft by the treating clinician. The constant change in designs and lack of large long-term follow-up studies still demand careful conclusions on long-term outcome of these endografts for EVAR.

Once the AAA extents towards or beyond the visceral arteries or there is an unfavorable infrarenal neck, infrarenal sealing of EVAR might not be sufficient. To this context, the use of fenestrated EVAR (FEVAR) allows a more cranial deployment of the endograft while maintaining vascularization to the visceral arteries. In Chapter 3 an overview is given of
fenestrated endografts with special emphasis on clinical outcome. Most experience had been gained with the custom-made Zenith® Fenestrated AAA Endovascular Graft (Cook Medical, Bloomington, IN, USA). The custom-made Fenestrated Anaconda™ System (Terumo Aortic, Inchinnan, Scotland, UK) was designed a few years later, and in contrast to the fenestrated Cook device, the fenestrated Anaconda device has an unsupported proximal part enabling wider options for placement of fenestrations. The off-the-shelf Endologix Ventana™ fenestrated graft (Endologix, Inc. Irvine, CA, USA) was applicable in cases with a specific location of the superior mesenteric artery and the renal arteries preventing waiting time for customization, and therefore could be used in emergency cases also. Early results however were, unsatisfactory, urging the manufacturer to withdraw the device from the market. Only recently the custom-made E-xtra Design Engineering endograft (JOTEC GmbH, Hechingen, Germany) was introduced. Consequently, there was very little literature available on results with this newly introduced device. The available data varied between the four endografts, but procedural results including procedure time, used contrast volume and technical success were very similar. The 30-day post-operative mortality varied between 0 to 9% independent of the used endograft. Longer term follow-up series with FEVAR are mainly available with the fenestrated Cook device. Only a few series, containing small sample sizes, with variable follow-up periods are available with the other three devices making them unfeasible for statistical comparison.

The life expectancy in the Western world is increasing and the number of cases with an AAA at older age will most likely increase. Chapter 4 focuses on the clinical outcome of octogenarians treated for complex AAAs with FEVAR and comparing those with non-octogenarians. No statical difference was seen between non-octogenarians and octogenarians with an estimated survival of 42% in the octogenarian group at five years. Eyeballing the survival curves, it seems the octogenarians have a lower survival. Except renal function and age, no difference was seen for other comorbidities between groups and the difference between groups might simply be related to shorter survival at older age. However, survival is not the only relevant outcome measure. Endograft specific variables such as reintervention rate, target vessel patency and number of endoleaks during follow-up might be more suitable, and no differences were seen between the two groups. Older age is considered more challenging because of more angulation in aortic anatomy, but the current results and previously published results suggest no influence
of age to endograft related outcome.5,6 Age itself should not be a reason to withhold treatment with FEVAR, but a few questions still remain. FEVAR is an expensive treatment compared to open surgical treatment, and a balance in cost-effectiveness, gained life years and gained quality adjusted life years has yet to be settled.7

The commercially available fenestrated endografts from Cook Medical and Terumo Aortic are both custom-made. To perfectly fit the endograft to the patient’s anatomy, dedicated software with 3D-reconstructions of computed tomography angiography (CTA) is used. The use of a central lumen line in the aorta and target vessels enables accurate determination of the locations of proximal and distal landing zones and fenestrations. Deployment of the endograft with stents in the fenestrations into the target vessels might, however, influences native anatomy and thereby may lead to endograft related complications.8 Specifically in FEVAR, the placement of a stent in a visceral artery could influence the tortuosity of the artery and give rise to complications such as stenosis, occlusion, kinking or fracture of the placed stent. In Chapter 5 the tortuosity index (TI) to measure the tortuosity of visceral arteries was introduced and successfully tested for reproducibility. As discussed in Chapter 3, there are some differences in used material and design for the Zenith® Fenestrated and the Fenestrated Anaconda™ endografts. The Zenith® Fenestrated endograft consists of self-expandable stainless steel Z-stents, while the Fenestrated Anaconda™ contains circular nitinol stents and has, in contrast to the Zenith® Fenestrated endograft, an unsupported area for the fenestrations. Chapter 5 focused on the differences between these two endografts and the influence of the specific endograft on native anatomy. Both fenestrated endografts clearly influenced the anatomy of the aorta and the stented visceral arteries, but the Zenith® Fenestrated endograft seemed to influence native anatomy more than the Fenestrated Anaconda™ endograft. In the Zenith® Fenestrated endograft the angle of both visceral arteries moved more perpendicular. It was postulated that the Z-stents were more rigid, therefore the docking of the stents in the fenestrations affect native anatomy more than the unsupported part in the Fenestrated Anaconda™. On the other hand, the diameter of the aorta at the level of the SMA in the Zenith® Fenestrated endograft was reduced to the diameter of the endograft, while no such decrease in aortic diameter was seen with the Fenestrated Anaconda™ endograft. Possibly the blood pressure pushed the unsupported part against the aortic wall, while the endograft was designed to be straight. Although this was not shown in this study, this might influence the
conformability of the endograft. Furthermore, the clock position of both the renal arteries moved more anteriorly in the Zenith™ Fenestrated endograft. After releasing the Zenith® Fenestrated endograft from the sheath, diameter reducing ties are still present so the location of the endograft can be changed slightly. These diameter reducing ties are located on the back of the endograft, and releasing of these ties was usually done after stenting of the fenestration. After releasing the diameter reducing ties the clock position of the stented fenestration changes, consequently pushing clock position slightly anteriorly. No large changes in tortuosity indices for target vessels were seen, but this variable might be beneficial in the prediction of target vessel related complications. Additional studies should be done to find the cut-off value for TI change mandating more aggressive intervention or closer follow-up. In this chapter, the changes in native anatomy were small and it is still unclear in what extent this influenced clinical outcome. The measurements in this chapter were done in static images, but might behave very differently during cardiac cycle. Therefore, it was suggested to study anatomic changes with dynamic CTAs to find the true anatomic conformability of FEVAR.

The clinical applicability of the Fenestrated Anaconda™ endograft is shown in Chapter 6. Results with this endograft showed a procedural type Ia endoleak of 8.6%, which mostly disappeared without reintervention during further follow-up leading to 0.3% type Ia endoleak at one year. These type Ia endoleaks enable persisting blood pressure into the aneurysmal sac, and therefore the risk of rupture theoretically remains. However, the clinical consequences remain unknown, but seem limited because of the high patient and reintervention-free survival, at least in the current study.

Chapter 7 focuses on mid-term results with the Fenestrated Anaconda™ endograft including cases globally and specifically focused on procedural and post-operative endoleaks. In the 335 cases from 11 centers worldwide the applicability of the Fenestrated Anaconda™ for the treatment of complex AAA was shown. Technical success, mid-term survival and reintervention rates were comparable to the results with the Zenith® Fenestrated endograft, as previously reported in literature. In all these cases a procedural type Ia endoleak was seen in 6.9%, but also mostly spontaneously disappeared and no type Ia endoleak related aneurysm rupture was observed. It was hypothesized that sealing of the proximal endoleak takes some time because the proximal nitinol rings of the endograft fully expand over time. Probably more
anatomical variables, such as oversizing, proximal landing zone diameter and angle, need to be taken into account to predict a persisting, and clinical relevant, endoleak. Another issue noted in this chapter was the decline of renal function over time. Renal function naturally declines when age increases, but high administration of contrast agents and placement of stents in target vessels, could increase the risk of renal function deterioration.\textsuperscript{12,13} This chapter underlined that clinicians should pay special attention to patients with an already borderline renal function in FEVAR.

Patients treated for an AAA remain in close follow-up. Among other risks, the risk after open surgical repair is the development of a proximal para-anastomotic AAA. After EVAR possible risks are the development of neck dilation, AAA growth, endoleaks, endograft migration, and device failure. An open surgical repair in failed EVAR has a 30 day mortality risk of 3\% and in para-anastomotic aneurysm a 14\% 30 day post-operative mortality risk has been described.\textsuperscript{14,15} In these cases, but also in cases with a primary AAA or TAAA with a narrow or otherwise healthy distal aorta and not treated before, a fenestrated aortic cuff can be used.\textsuperscript{16} In Chapter 8 the global mid-term clinical outcomes of the Fenestrated Anaconda\textsuperscript{™} aortic cuff are discussed. In this chapter, 29 cases of the 57 globally treated cases were analyzed. The preoperative patient characteristics possibly made clinicians decide to withhold open surgical repair and choose FEVAR. Furthermore, these cases were probably technically more challenging, reflected by more fenestrations and cranial approaches compared to regular FEVAR. The patient characteristics and complexity of anatomy probably resulted in rather high mortality and reintervention rates within the early post-operative period. Once through this early post-operative period survival up to two years remains relatively stable and no aneurysm related deaths were seen, but the necessity for reinterventions remained an issue. A reintervention free survival of 79\% at two years was seen after primary FEVAR with the Fenestrated Anaconda\textsuperscript{™} endograft, but after redo surgery with these fenestrated aortic cuffs the reintervention free survival was 67\%. Problems like failure of the primary endograft or an endoleak between the primary endograft and the fenestrated cuff were seen, therefore a complete relining of the endograft might be a more suitable option. The choice of a fenestrated aortic cuff was a tailor-made option and possibly only for those cases where no other option is available. Especially in these cases close follow-up will remain necessary.
The aneurysm of the aorta can extend more cranially, consequently the visceral arteries branch from the aneurysmal sac. In these suprarenal AAAs or TAAAs a branched, or combined branched and fenestrated EVAR (B/F-EVAR) was developed and has branches attached to the endograft, to bridge the distance from the endograft to the origin of the visceral artery. Chapter 9 focuses on the long-term results of these endografts with special attention to geometrical changes in the bridging stents. The geometrical changes were more outspoken in branches than in fenestrations, probably related to the longer distance from endograft to the origin of target vessels. Furthermore, it was postulated that migrating endografts strain the stents and will be seen more in branched compared to fenestrated endografts. The aortic wall is adjacent to the endograft in fenestrations allowing less movement. Branches with a bridging stent to the visceral artery are more complex constructions and are more vulnerable to an adverse event. Therefore, overall stent patency was lower in branches than in fenestrations. Meticulous measurement of endograft migration, the angle and length of bridging stents, and comparing these with previous measurements can predict the risk of disconnection, stenosis or occlusion and should be part of the routine during follow-up imaging. In this chapter a substantial number of deaths were seen during long-term follow-up and treatment of TAAAs remains challenging. The study included fragile patients, but aneurysm related deaths were not seen until 4-6 years of follow-up and suggest the benefit of endovascular treatment of patients with a TAAA. Larger multicenter studies, preferably with a prospectively held database, should be done to show the true benefit of B/F-EVAR.

In conclusion, over the recent decades great steps have been made towards a total endovascular abdominal aortic aneurysm repair and even extending into the thoracic aorta. Endovascular treatment modalities have increased in complexity and many more challenges remain to perfectly customize the treatment to the patients' anatomy. Although endovascular treatments are done on a large scale, endograft design keeps on changing making true long-term outcome of current available devices still unavailable. Only few designs for fenestrated endovascular aneurysm repair are available with variable applicability and experience. These endografts take time to customize to the patients anatomy and in urgent cases there is only limited availability of an off-the-shelf endograft. Nevertheless, a shift can be seen towards endovascular treatment. With more experience, especially in very complex cases, results will most likely improve for endovascular repair. On the other hand, open surgical repair will lose field. Consequently less experience with open surgical repair is gained by newly trained surgeons, more
Summary and future perspectives

Specifically the skills necessary in unsuitable cases or in failing endovascular repair.

**Future perspectives**

Chapters 5 and 9 show us the influence of endografts to native patient anatomy and the geometrical changes of the endograft over time. These studies are the first steps in gathering knowledge of endograft influence on native anatomy. Moreover, to improve an even better understanding of the anatomic changes after FEVAR, iliac artery tortuosity should be taken into account in further studies.

Larger studies, including multiple endografts and multiple validated anatomic measurements, will allow better understanding of anatomic changes after (infrarenal, fenestrated and branched) EVAR.

There was no clear explanation why decline in renal function shown in Chapters 4 and 7 occurred after FEVAR. Pre-operative renal function and contrast use might, besides obvious reasons like renal stent stenosis or occlusion, elicit decline in renal function. Future studies including multiple possible parameters affecting renal function must be done to be able to protect renal function in patients treated for an abdominal aneurysm.

The aorta is subject to respiration and the cardiac cycle, therefore an endovascular device is repeatedly strained. To gain greater insight of these dynamic changes over time, ECG-gated CTA can be done, allowing 4-dimensional imaging of the endograft and patient anatomy.

Before long-term follow-up results are available, they can be obsolete because constant changes are made to designs of endografts. These endograft alterations can make interpretation of results with (infrarenal, fenestrated and branched) EVAR challenging. As was discussed in Chapters 2 and 3, in a few currently available endografts there are long-term results available. To gain knowledge about the durability of the available endografts long-term follow-up studies need to be conducted, preferably in prospectively held databases.

Reinterventions, because of endograft related complications, remain a problem in (infrarenal, fenestrated and branched) EVAR. Multicenter studies including clinical outcome and patient anatomic characteristics, will allow us to enlarge the study cohorts and to correlate certain anatomic features to long-term complications.

Ultimately, a prediction model allows clinicians to make a tailor-made treatment to patient's anatomy and preferences.
References


