

# Endovascular repair of aortic disease

Clinical and radiological outcomes

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UNIVERSITY OF GOTHENBURG

Gothenburg 2024

Cover illustration: *EVAR dancing cancan*. 3D computed tomography of a ruptured infrarenal aortic abdominal aneurysm after endovascular aortic aneurysm repair (post-EVAR rupture). There is a component separation in the stent graft's overlap zone in the left limb.

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ISBN 978-91-8069-647-0 (PRINT)  
ISBN 978-91-8069-648-7 (PDF)  
<http://hdl.handle.net/2077/79706>

Printed in Borås, Sweden 2024  
Printed by Stema Specialtryck AB

Keep on looking and keep on reading, please. This is my attempt to leave a footprint on the beach of current research, and future knowledge.

Never smoke and keep on surfing!

*“Doubt thou, the stars are fire;  
Doubt, that the sun doth move;  
Doubt truth to be a liar;  
But never doubt I love.”*

(Shakespeare, W. Hamlet)

*To my beloved ones*



## ABSTRACT

**Background:** Endovascular repair of aortic disease has improved but long-term outcome is questioned. **Aims:** To evaluate radiological and clinical outcome of endovascular aortic repair. Specifically: I. To evaluate if expansion of chronic aortic dissection can be prevented by occluding proximal entries with endovascular plugs. II. To determine underlying causes for additional iliac stent grafting after endovascular aortic repair (EVAR). III. To define precursors for post-EVAR rupture. IV. To investigate frequency and mechanisms for loss of seal in EVAR sealing zones.

**Material and methods:** All studies were retrospective with review of CT images using structured protocols. Study I, 14 consecutive patients with expanding aneurysms after chronic aortic dissection were treated with plug occlusion of proximal entries. Study II, 24 patients with distal stent graft extensions after EVAR were compared to 420 patients who had not required distal extension. Study III, 1805 patients treated with standard EVAR were assessed regarding post-EVAR rupture, 51 ruptures were analyzed. Study IV, 399 consecutive patients were analyzed using pre- and postoperative CTs and in-depth review of patients' charts.

**Results:** Study I, occlusion of proximal entries was achieved in 10/14 patients, and they had no further expansion of the descending aorta. Study II, graft migration at distal sealing zone or interconnections were common causes for additional distal stent grafting and associated with large diameters and short sealing lengths. Study III, post-EVAR ruptures were due to type I and III endoleaks and often caused by vessel dilatation in sealing zones. Precursors of failure were noted in routine follow-up in 31% of patients, compared to 84% in structured CT analysis. Study IV, a large proportion of stent grafts had lost the seal in the sealing zones, and this was associated with post-EVAR rupture. The predominant cause was progressing vessel dilatation. Large diameters and short apposition lengths in the sealing zones predisposed for loss of seal.

**Conclusion:** Occlusion of proximal entries with endovascular plugs may be considered in some patients with chronic aortic dissection. Postoperative surveillance with structured CT analysis detects most precursors of EVAR failure. Sealing zone complications after EVAR are frequent and associated with post-EVAR rupture. Stent graft manufacturers should consider requiring smaller vessel diameters and longer sealing zone lengths in their instructions for use.

**Keywords:** Aorta, aneurysm, dissection, EVAR, rupture, long-term, sealing

ISBN 978-91-8069-647-0 (PRINT)

ISBN 978-91-8069-648-7 (PDF) <http://hdl.handle.net/2077/79706>



# List of papers

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

- I. Sandström C, Roos H, Henrikson O, Fagman E, Johnsson Å, Jeppsson A, Falkenberg M.  
**Endovascular plugs to occlude proximal entries in chronic aortic dissection**  
*Interactive CardioVascular and Thoracic Surgery*. 2022 Aug 3;35(3):ivac201
- II. Roos H, Sandström C, Koutouzi G, Jeppsson A, Falkenberg M.  
**Predisposing Factors for Reinterventions with Additional Iliac Stent Grafts After Endovascular Aortic Repair.**  
*Eur J Vasc Endovasc Surg*. 2017 Jan;53(1):89-9.
- III. Andersson MB\*, Sandström C\*, Stackelberg O, Lundqvist R, Nordanstig J, Jonsson M, Roy J, Andersson M, Hultgren R, Roos H  
**Structured CT analysis can identify the majority of patients at risk of post-EVAR rupture**  
\*first author Editor's choice – *Eur J Vasc Endovasc Surg*. 2022;64(2):166-174
- IV. Sandström C, Andersson MB, Bogdanovic M, Fattahi N, Lundqvist R, Andersson M, Roy J, Hultgren R, Roos H  
**Aortic Endovascular Aneurysm Repair long-term integrity impaired by stent graft sealing zones failure**  
*Submitted manuscript*

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# Abbreviations

3D	Three-dimensional
AAA	Abdominal Aortic Aneurysm
AD	Aortic dissection
CI	Confidence interval
CT	Computed tomography
CTA	Computed tomography angiography
DAP	Dose-Area product
EVAR	Endovascular Aneurysm Repair
IFU	Instructions for use
MR	Magnetic resonance
OAR	Open aortic repair
rAAA	Ruptured Abdominal Aortic Aneurysm
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
Swedvasc	The Swedish Vascular Registry

# Introduction

Minimal invasive procedures in vascular surgery has since the introduction of the “Seldinger technique”<sup>1</sup> 1952, evolved from diagnostic angiograms and angioplasty<sup>2</sup> to complex endovascular interventions of vessels. Stent grafting of the aorta was pioneered by Volodos,<sup>3</sup> and Parodi.<sup>4</sup> Patients too fragile for open surgery can now be treated with endovascular procedures for extensive disease in the acute and elective setting.<sup>5</sup>

It is important to know to what extent a pathology is engaging the aorta in choosing the best treatment option. Pre-operative imaging is crucial,<sup>6</sup> and several imaging modalities are used, often in a combination. There are also challenges in the postoperative evaluation of the procedures. It is necessary to know how to interpret anatomy and pathology, to use this information for selecting interventional techniques and devices, and to be aware of what pathophysiological factors that are crucial for a successful outcome. Quite often there are signs and details, precursors, visible in follow-up imaging that imply possible subsequent complications. This knowledge, essential for tailoring of individual follow-up imaging protocols and for timely decisions on elective reinterventions, is yet not complete.

## Radiological modalities

### *X-ray fluoroscopy and digital subtraction angiography*

Continuous, or pulsed, X-ray exposures resulting in real-time imaging as a movie, fluoroscopy, is used for guidance during endovascular procedures. Radiopaque materials as guidewires and catheters can be manipulated under fluoroscopic guidance. An angiogram can be achieved by administration of a contrast agent in the targeted artery. If the background (pre-contrast image) is subtracted from the angiogram it is called digital subtraction angiography and has excellent diagnostic accuracy.

### *Computed tomography*

As in plain X-ray examinations computed tomography (CT) utilizes radiation in producing images. The CT scanner is formed like a tube. A sliding table moves the patient lying down on it, through the gantry during rotation of the scanner (X-ray source and detectors) and produces thin-sliced trans-axial images that are post-processed in the computer. Dependent on how much of the radiation is absorbed within the examined tissues, the attenuation in the images differs. This attenuation gives a greyscale image where the attenuation is measured in Hounsfield units (HU), named after the Nobel Prize winner of 1979, Sir Godfrey Hounsfield.<sup>7,8</sup> The tissues can be enhanced by administration of a iodine-based contrast agent in the blood. Timing of the scanning procedure to achieve contrast enhancement in the tissue/organ that is desired to image is important. The delay between the administration of the contrast agent to the blood and the CT scan can be individually adjusted to achieve optimal enhancement in the arterial phase, computed tomography angiography (CTA). The scans can be repeated and thereby visualizing the examined body part in more phases of contrast enhancement enabling analysis of normal or pathological patterns.

### *Ultrasound*

Diagnostic ultrasound uses high-frequency soundwaves transmitted through the examined body part that are reflected by tissues resulting in an echo signal enabling high spatial resolution characterization. Simultaneous processing of the echoes results in real-time greyscale images. The direction and velocity of moving tissues, as a bloodstream, can be determined with doppler ultrasound (DUS).<sup>9</sup> The ultrasound technique does not use radiation or iodine contrast but is limited by observer skills and patients' habitus.

### *Magnetic resonance imaging*

Magnetic resonance imaging (MRI) is dependent of a strong magnetic field. The patient is examined in a scanner similar in appearance to the CT scanner, but the principle of imaging is completely different. The technique is based on the measuring of the relaxation of proton spins in hydrogen molecules (present in all water molecules) after excitation of a radiofrequency pulse. This modality offers a wide variety of diagnostics including MR angiography (MRA) but has a lower spatial resolution and is not as fast as either CT or ultrasound.<sup>10</sup>

## The aorta

The aorta is the largest artery in the body connecting the heart with other organs via multiple bifurcations of arteries and supplying the body with oxygenized blood. The cardiac output, the volume of blood that is pumped from the heart per minute, is about five liters in a healthy individual at rest. The aorta is divided into the thoracic and the abdominal aorta by the diaphragm. Further, the thoracic aorta is segmented into the ascending aorta, the arch of the aorta and the descending aorta. The abdominal aorta is segmented into the suprarenal abdominal aorta from the diaphragm to the renal arteries and the infrarenal abdominal aorta below the renal arteries to the aortic bifurcation where it is divided into the left and right common iliac arteries (Figure 1).

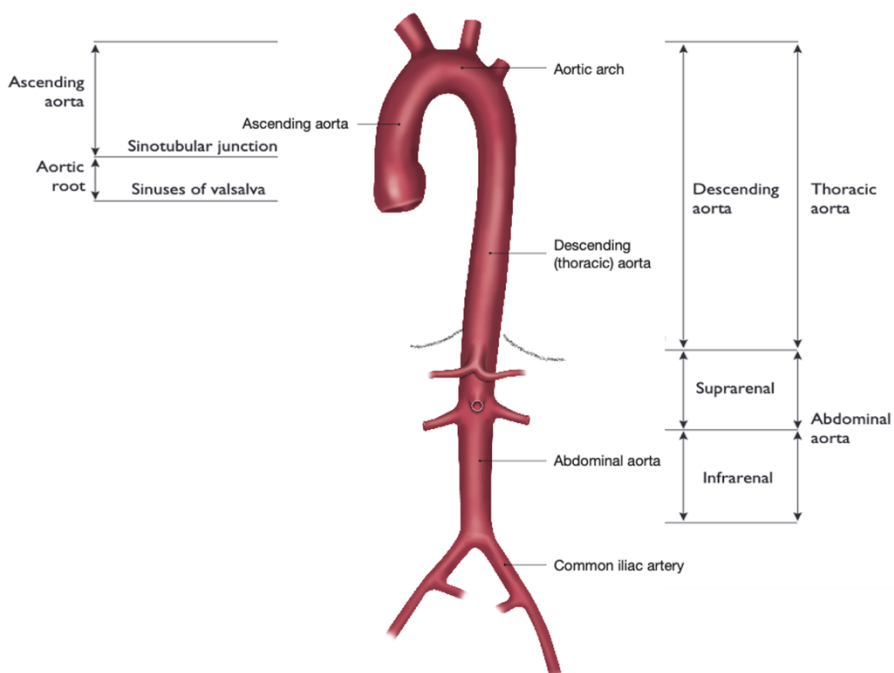
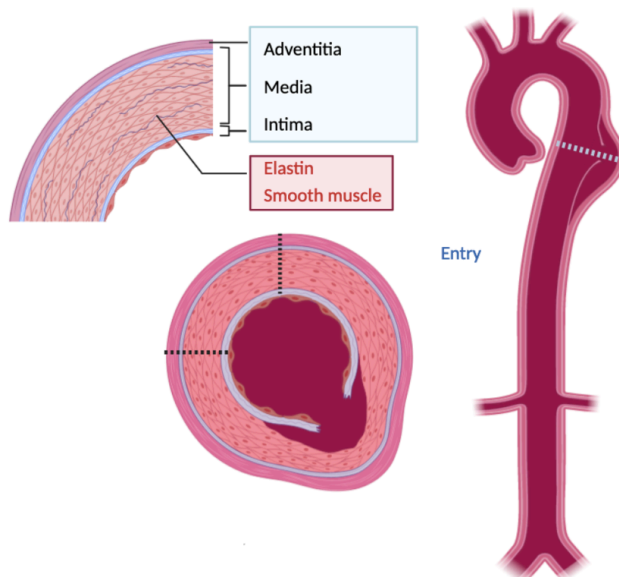


Figure 1. Anatomy of the aorta

The diameter of a healthy adult thoracic aorta is less than 4 cm and tapered to smaller size in the downstream direction. The diameter of a healthy abdominal aorta is less than 3 cm.<sup>11-13</sup> There is a normal expansion of the aorta with aging.

In the aortic root the expansion per decade of life is 0.9 mm in men and 0.7 mm in women, respectively.<sup>14</sup> The expansion of the thoracic aorta has been observed to continue between the second and the fifth decades of life. Thereafter it plateaus with further aging while continuing to elongate.<sup>15</sup> A similar pattern of diameter growth rate of the infrarenal aorta has been shown in a study in the Chinese population.<sup>16</sup> The diameter expansion growth rates of less than 1 cm per decade of healthy aortas peak in persons 50 – 60 years of age and thereafter the growth rate declines.<sup>16</sup> The infrarenal abdominal aorta is classified as aneurysmal if the diameter exceeds the diameter of normal aorta by a factor of 1.5, resulting in a pragmatic and practical threshold of  $\geq 3$  cm.<sup>17</sup>

The aortic wall consists of three layers from the artery lumen in order; the intima, media and adventitia.<sup>11</sup> The intima consists of a strong but thin layer of endothelial cells and connective tissue. The intima is permeable in healthy arteries. The media is composed of  $> 50$  layers of elastic lamellae, including smooth muscular cells, and is the thickest layer, providing strength and distensibility to the aorta. The outer layer, the adventitia is thin and includes connective tissue, but also nerves, lymphoid tissue, and the vasa vasorum, small vessels that provide the adventitia and the outer part of the medial layer with oxygen.<sup>18</sup>



*Figure 2. Arterial wall with an entry to the media and formation of an aortic dissection. Exaggerated wall thickness for illustration.*

## Aortic disease

The aortic diseases studied in this thesis includes aortic dissection and abdominal aortic aneurysm.

The overall global death rate from aortic dissection and aortic aneurysms was 2010 increased to 2.78 per 100 000 inhabitants according to the Global Burden Disease project in comparison to 2.49 per 100 000 twenty years earlier, despite the decrease of the prevalence and incidence rate of abdominal aortic aneurysms during the period.<sup>19,20</sup> The incidence of acute aortic dissection is estimated to 0.5 – 3<sup>11</sup>(or even 6)<sup>21</sup> per 100 000 people and year (person-years), and has not changed over the years suggesting a difference in the risk profile between the two diseases even though sharing the same risk factors for developing the disease.<sup>22</sup>

## Aortic dissection

If there is a tear, an entry, in the inner layer of the aortic wall, the intima, an aortic dissection may develop. An extra channel for the bloodstream, a “false lumen”, can be formed, running parallel to the original “true lumen”.

Hypertension and age are the most important risk factors for aortic dissection. Patients with connective tissue diseases, bicuspid aortic valves and smokers also have an increased risk. Aortic dissections can be classified anatomically with the Stanford classification (Figure 3).<sup>23</sup> A dissection in the ascending aorta is a Stanford type A and constitutes two-thirds of the incidence of acute aortic dissection.<sup>21</sup> This condition carries a high risk of retrograde progression of the dissection with risk of heart tamponade, aortic valve dysfunction and coronary artery occlusion. These patients will normally have immediate open surgery and receive a supra-coronary graft.<sup>24</sup> If the dissection involves the descending thoracic and/or the abdominal aorta only, it is a Stanford type B. Another classification model is to refer the dissection from the origin of tear and how far the dissection has propagated, as in the DeBakey classification.<sup>25</sup> A recently published recommendation has suggested that when the aortic arch is affected but not the ascending aorta, it should be classified as “Stanford non-A–non-B aortic dissection”.<sup>26</sup> Another recommendation states that the dissections should be reported in the Stanford classification with Stanford A if the entry is in the ascending aorta and B if the entry is in the arch or descending aorta but with

further information of aortic segment involved.<sup>27</sup> This classification includes persisting chronic dissections after surgery for dissection in the ascending aorta.

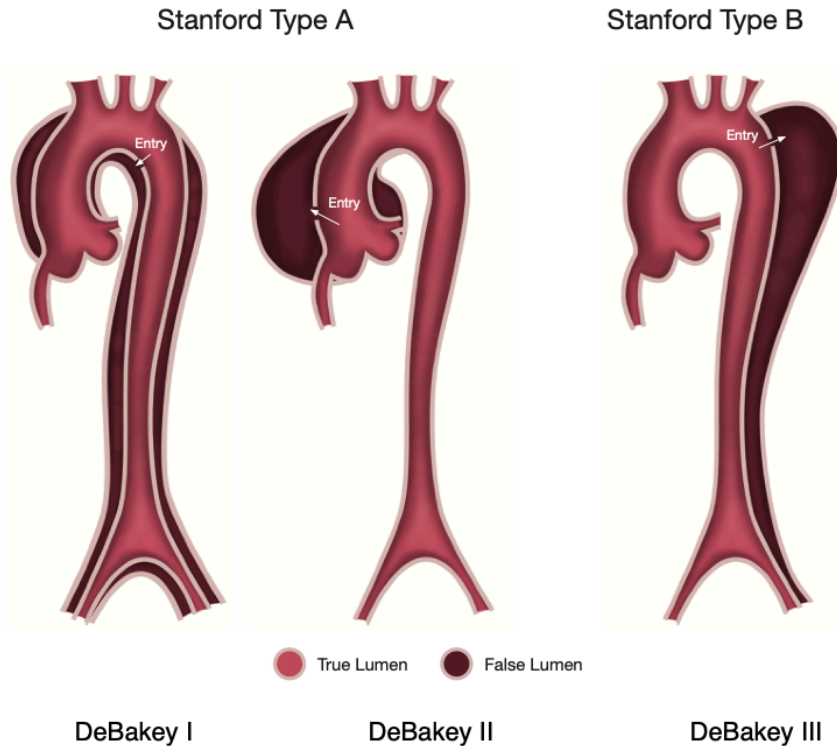


Figure 3. Stanford and DeBakey classifications of aortic dissection

### Treatment in a Stanford type B aortic dissection

Aortic dissections are also classified according to time from onset. The acute phase is defined as from onset of symptoms to 14 days. The sub-acute phase lasts from 15 until 90 days. Thereafter the dissection is defined as chronic. All patients are treated with best medical therapy with intention to control pain, heart rate and blood pressure.<sup>11</sup> In the chronic phase the dissection membrane turns less elastic, and an aneurysmal degeneration of the aorta often develops over time.<sup>28</sup> The outer wall is weakened already at onset of dissection and in combination with the law of La Place, that the wall stress increases with larger diameter, the thinner wall is at high risk of aneurysm development, and therefore vigilant follow-up is necessary.<sup>28,29</sup>

If the dissection leads to an acute aortic rupture or occludes visceral branches and causes organ malperfusion, either open aortic repair (OAR) or thoracic endovascular aortic repair (TEVAR) may be considered. According to guidelines<sup>24,26</sup> TEVAR is the treatment of choice in complicated type B dissection when the anatomy is suitable for stent graft placement. TEVAR with a stent graft designed for the dissection indication, requires sealing zones of enough length, at least 2.5 cm according to current recommendations,<sup>24</sup> in a healthy aortic segment. If there is no indication for acute invasive intervention of the aortic dissection the patient gets the medical treatment only, with the primary aim to reduce blood pressure.<sup>26</sup>

## Surgical treatment of aortic dissection

Generally, in the elective setting, aneurysm development of the dissected thoracic aorta with a diameter of 5.5 – 6 cm or above, is considered an indication for treatment and performed to prevent rupture.<sup>11,26</sup> The aim is to close the inflow to the false lumen and thereby redirect the flow into the original (true) lumen and thereby reducing the flow in the dissected aortic wall (false lumen). This redirection of flow is performed to enable a normalization of the aorta with an increase of the true lumen cross section area and simultaneous decrease of the false lumen area. The aim of this remodeling is to decrease the total aortic diameter and the risk of subsequent rupture.

### *FET and TEVAR*

If the entry is in the arch, the standard treatment is a hybrid-open surgery with the frozen elephant trunk-technique (FET); an open surgery replacement of the arch combined with a stent graft in the proximal descending aorta, resembling an elephant's trunk.<sup>30,31</sup> If the entry is in the descending aorta, the recommended treatment is TEVAR, covering the proximal entry tear (Figure 4).

### *Vascular plugs*

The Amplatzer™ Muscular VSD Occluders and Amplatzer™ Septal Occluders are designed to close septal defects, holes in the wall between the heart's chambers, with two discs connected by a waist that is positioned in the wall defect. The two discs appose to the surrounding vessel wall, thereby patching the hole. The septal occluders are covered with a polyester material and clot formation is not desirable. Eventually the surface is covered by endothelium. These devices are considered safe and effective in the use on the indication septal defects.<sup>32</sup> The Amplatzer vascular plugs are designed to be an

embolization product.<sup>33</sup> They consist of a nitinol mesh in different designs and sizes to match the vessel that is supposed to be closed. The Amplatzer™ Vascular Plug II is of a three-disc design with narrow waists between the discs. The discs are constrained in a delivery sheath when introduced into the vessel. When the device is placed in the desired position, the sheath is withdrawn allowing the device to reassume its original shape with flat discs if there is enough space, since it is made of a memory metal alloy. When used as an embolization agent the device is oversized to securely anchor the device in the vessel.<sup>34</sup> The mesh induces thrombus formation and clotting aggregation. This results in occlusion of the vessel which is followed by tissue in growth in the uncovered plugs.<sup>24,35</sup> The feasibility to occlude the proximal entry with an endovascular plug, as a sealing button, has previously been shown by our group.<sup>36</sup> Data on how targeted entry closure with plugs effects clinical events and aortic remodeling over time are scarce.

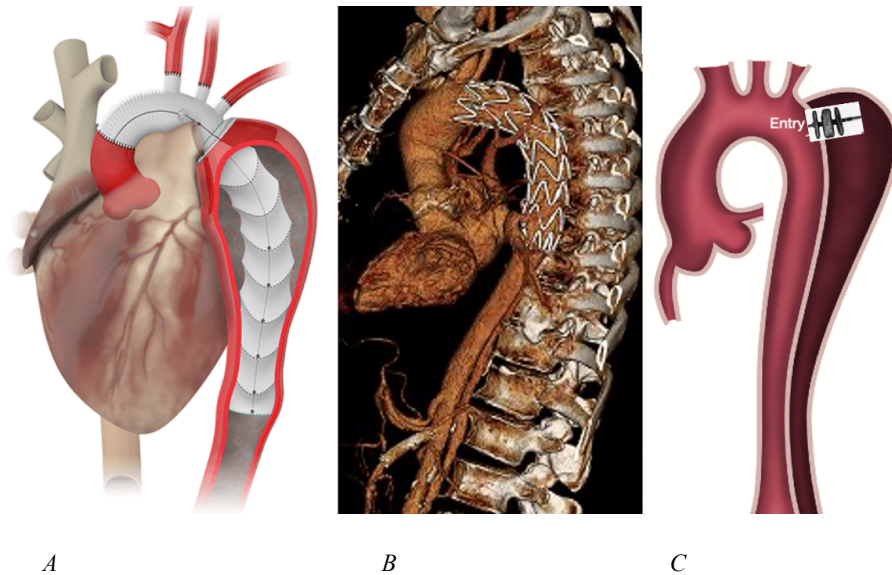


Figure 4. A) FET (a Thoraflex hybrid graft, by courtesy of Terumo Aortic). It can be extended downstream with a stent graft inserted in a later endovascular procedure. B) CTA 3D image of a TEVAR with a dissection stent graft (without hooks in the proximal sealing zone). C) An image of the concept of a vascular plug in the proximal entry of the ascending aorta.

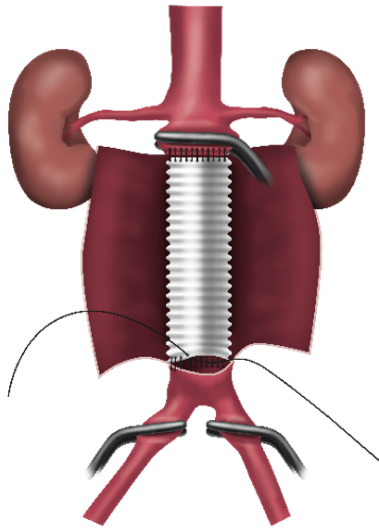
## Abdominal Aortic Aneurysm

The most widespread definition of an abdominal aortic aneurysm (AAA) is an abdominal aortic diameter of 3.0 cm or more.<sup>17</sup> The aging process of the aortic wall is characterized by fractures of the elastic laminae resulting not only in dilatation but also in stiffening.<sup>37</sup> In the abdominal aorta the expansion rate is higher with large aneurysms, 3.6 mm/year in 5 cm aneurysms compared to 1.3mm/year in 3 cm aneurysms.<sup>38</sup> Active smoking increases the risk of expansion.<sup>39</sup> Risk factors for aneurysmal development are age, male sex (4 – 6:1 compared to female), smoking and genetics but hypertension and increased levels of lipoprotein are also, to a somewhat lower extent, considered as risk factors.<sup>22,38</sup> Diabetes has a lowering effect on the risk of aneurysmal growth.<sup>38</sup> In Sweden the prevalence of AAA in 65 year old men were 1.5%.<sup>40</sup> It is considered safe to not surgically treat AAA when the largest diameter is still less than 5.5 cm in men and 5.0 cm in women.<sup>39</sup> Accordingly, the European and American vascular societies guidelines recommend surveillance of infrarenal aneurysm  $\leq 5.5$  cm for men, and  $\leq 5.0$  cm for women.<sup>17,41,42</sup> There are no exact and validated data on the risk of rupture depending on the aortic diameter but studies indicate a 3.5% – 4.1% yearly risk of rupture for aneurysms with a diameter of 5.5 – 7 cm and 6.3% for aneurysms  $> 7$  cm.<sup>43</sup> The risk of rupture relative to size is higher amongst women, active smokers and individuals with hypertension.<sup>38</sup>

As described above the indication for operation is often set to a diameter of  $> 5.5$  cm, or earlier at rapid growth, symptoms from the aneurysm or rupture of the aorta. There has been a paradigm shift in treatment technique over the last two decades from open aortic repair (OAR) to endovascular aneurysm repair (EVAR), even in the acute setting of ruptured aortic aneurysm (rAAA). The 30-day mortality is significantly lower in favor of EVAR compared to OAR<sup>44-46</sup> but a meta-analysis has reported that the survival benefit for EVAR is lost at 3 years.<sup>47</sup> The meta-analysis was based on long-term follow-up of several well-known randomized trials: EVAR-1,<sup>44</sup> DREAM,<sup>46</sup> OVER,<sup>48</sup> and ACE.<sup>49</sup> In the follow-up trial of EVAR-1<sup>50</sup> a clearly increased aneurysm-related mortality in the EVAR group after 8 years was shown. This was mainly attributable to secondary aneurysm sac rupture, post-EVAR rupture. However, increased cancer mortality was also observed in the EVAR group. Aneurysm reintervention rates in the EVAR group were 41 per 1000 person-years, with reinterventions occurring throughout follow-up.

## Open aortic repair

In open surgery of the abdominal aorta a laparotomy in general anesthesia is necessary to access the aorta in its course in the retroperitoneal space. The aneurysmal sac is replaced with a synthetic graft, with sutures as close beneath the origins of the renal arteries as possible and below the sac above the aortic bifurcation with a straight graft if possible, while clamping the aorta for proximal control and the iliac arteries for distal control (Figure 5).<sup>51</sup> A bifurcated graft is used when the bifurcation is affected.

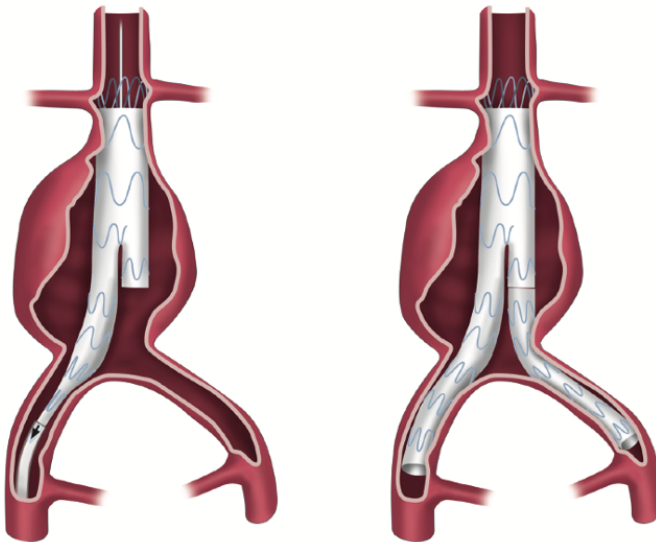


*Figure 5. Open aortic repair.*

## Endovascular aneurysm repair

Endovascular aneurysm repair (EVAR) can be performed in local anesthesia in the groins where the femoral arteries are suitable sites for vascular access using the Seldinger technique.<sup>1,52</sup> Introducer sheaths placed in the femoral arteries allow for insertion of the EVAR components.<sup>53</sup> The stent graft placement is performed under fluoroscopy guidance and by intermittent aortic contrast injections to visualize the important landmarks. The components of the EVAR are constrained in narrow introducer sheaths when introduced into the aorta and the iliac arteries. When each component is in its desired position the introducer sheaths are retracted allowing the stent graft to regain its original

shape and size. The stent material is made of a metal that in body temperature regains the original shape and size. Each stent graft component's ordinal size is chosen to fit the artery with an oversizing according to the instructions for use provided by each stent graft's manufacturer. The stent graft components are interconnected with overlapping zones and attaches to the artery wall in the sealing zones at the edges of the stent grafts (Figure 6).



*Figure 6. The EVAR procedure with deployment of the stent graft inserted from the right groin of the patient (left image). The main component has a proximal tube sized to match the diameter of the infrarenal aortic neck plus an extra 10 – 20 % in a so-called oversizing. In the same manner, the stent graft limbs are matched to the iliac arteries. Insertion of the contralateral limb is performed from the other groin (in the right image performed from the left groin) and the components are attached to one another with an overlap in the interconnection of the components.*

### *EVAR seal*

The stent grafts must have apposition to the artery wall at the proximal and distal sealing zones and between the interconnecting components to exclude the aneurysmal sac from the circulation. The principle of EVAR is based on a redirection of flow into the stent graft and thereby excluding the aneurysm from the circulation. This result in a reduction of the pressure in the aneurysmal sac and thereby the reducing risk of rupture. In a standard infrarenal EVAR the proximal sealing zone is in the abdominal aorta beneath the lowest renal artery,

the aortic neck, and the distal sealing zones are in the common iliac arteries above the bifurcations of the internal iliac arteries. In literature the sealing zones can also be called landing zones or attachment zones. It has been proposed to call the actual length of postoperative seal for the real achieved sealing zone.<sup>54</sup> In the latest guidelines of management of abdominal aortic aneurysms,<sup>42</sup> the concepts sealing zones and seal is used in the text but not defined as a standard.

## Endoleaks

An endoleak is a flow of blood in the aneurysmal sac outside the stent graft. Endoleaks are classified according to the location of sac flow origin.<sup>55-57</sup>

Type I endoleak: A peri-graft flow in the aneurysmal sac occurring from the sealing zone sites at:

- Type IA: the proximal end of the stent graft
- Type IB: the distal end of the stent graft
- Type IC: the internal iliac artery if the sealing zone is in the external artery

Type II endoleak: Peri-graft flow occurring from retrograde flow in aortic branches originating from the excluded aneurysm:

- Type IIA: inferior mesenteric artery
- Type IIB: lumbar arteries

Type III endoleak: Peri-graft flow occurring from stent graft defect or overlap zones:

- Type IIIA: leak from overlaps or component separation
- Type IIIB: fabric holes

Type IV endoleak: Peri-graft flow occurring from stent graft fabric porosity.

Type V endoleak: No peri-graft flow is detectable. The phenomenon of sac growth was considered to occur because of endotension or of yet unknown reason.

## Re-interventions of endoleaks

Type I and III increase the pressure in the aneurysmal sac and should be treated without delay according to guidelines.<sup>17,41</sup> It is unclear if the presence of type II is associated with post-EVAR rupture.<sup>58</sup> In case of a shrinking or stable aneurysmal sac they are left untreated. If the aneurysmal sac expands > 1 cm they are recommended to be treated.<sup>17,41,56</sup>

*Type IA re-interventions:*

Proximal extension with a cuff can be performed if there is a sufficient segment free of aneurysm between the lowest renal artery and the existing stent graft edge. In other cases, when the infrarenal segment is insufficient for seal with a standard tubular cuff, proximal seal of type IA endoleak can be achieved with a fenestrated cuff. This is a complex procedure with separate bridging stent grafts into the renal and superior mesenteric artery, sometimes also the coeliac trunc.<sup>42,57</sup>

*Type IB re-interventions:*

Distal extension is in most cases a relatively simple procedure with an additional extending stent graft overlapping the existing distal component. If there is not enough common iliac artery length between the existing stent graft edge and the origin of the internal iliac artery, it is possible to extend the stent graft in the external artery usually with a tapered stent graft because of the reduction in the diameter. In these cases, the internal artery is occluded to prevent retrograde flow into the aneurysm sac. This can be performed with an Amplatzer Plug or similar devices.<sup>59</sup> If the circulation to the internal iliac artery is to be preserved an iliac branched device can be used. This reduces the risk for gluteal claudication and organ ischemia.<sup>60</sup>

*Type II re-interventions:*

The retrograde flow in the patent artery originating from the aneurysm is embolized via collateral arteries with embolization materials as coils, vascular plugs, or Onyx®, filling the endoleak cavern when feasible.<sup>57</sup>

*Type III re-interventions:*

Endoleak type III is most often treated with re-lining using a size matched stent graft placed inside the existing stent graft creating a reinforced overlap zone or covering a tear in the graft fabric.<sup>61</sup>

*Type IV re-interventions:*

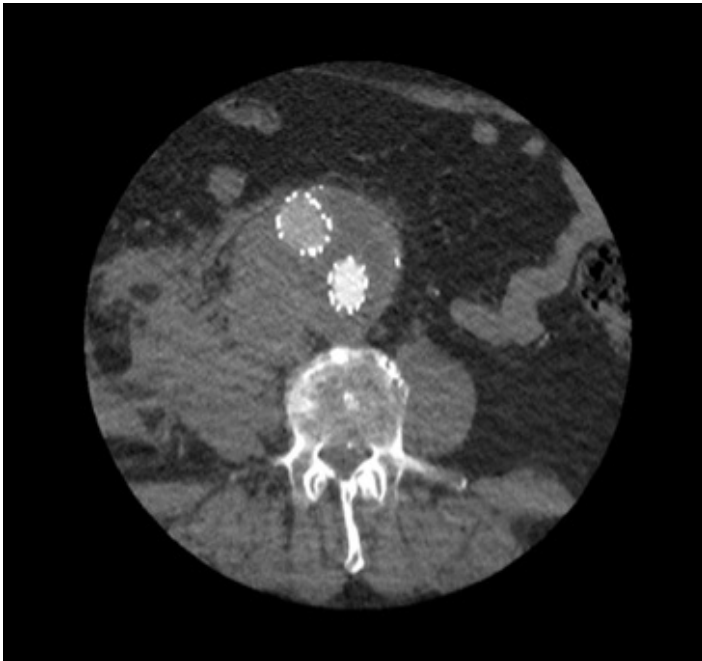
Endoleak type IV is usually not treated since the porous graft material is sealed by the blood clotting system in a few days.<sup>62</sup>

*Type V re-interventions:*

Since the causes of aneurysm sac expansion in type V has been unclear and it is unclear if type V endoleaks really exist, treatment options has been open surgery, graft re-lining or extensions in search of solutions.<sup>62</sup>

## Post-EVAR ruptures

Post-EVAR ruptures has a cumulative incidence of 0.9 – 3.1 % within five years after the index EVAR<sup>63,64</sup> and has been reported as 2.0 – 7.0/1000 person-years of follow up.<sup>48,65</sup> In a recent Swedish multicenter study, the cumulative incidence of post-EVAR rupture was reported to be 1.3% over a mean follow-up time of 3.9 years.<sup>66</sup> The incidence rate was 3.4/1000 person-years. Independent risk factors were rAAA at index surgery and age. In a Swedish two-center study<sup>67</sup> sixteen patients with post-EVAR rupture were included. The median time from index EVAR to rupture was 3.8 years. The 30-day mortality for the rupture subgroup was 7/16 (44%), and for those who underwent reintervention 3/12 (25%). Eleven patients had had imaging follow-up within 12 months before the rupture. No precursors of failures were reported in clinical imaging surveillance reports in seven of these eleven patients (64%).<sup>67</sup>



*Figure 7. Post-EVAR rupture. Contrast enhanced blood is in the stent graft limbs in the CTA image. To the left in the image (patient right) there is blood in the retroperitoneal space.*

## Imaging

### Pre-operative imaging

Current guidelines recommend pre-operative imaging of the aorta with CTA with not more than 1 mm slice thickness. Assessment of angulation, diameter, and length of the aortic neck, if there are wall calcifications or thrombosis, diameters of aortic bifurcation, iliac arteries and accessing arteries is done and analyzed for the eligibility for OAR or EVAR. A hostile neck,<sup>68</sup> an anatomy including sharp angulation of the aorta in the length axis, wall calcifications and thrombus, short and/or conic neck may disqualify the patient for standard EVAR. Planning of the procedures is preferably performed in workstations with software enabling 3D reconstructions.<sup>42</sup> Measuring the diameter orthogonal to the aortic length axis is proposed to be standard in pre-operative evaluation.<sup>12,17</sup> In CT this can be achieved by multiplanar reconstruction (MPR) or by central lumen line (CLL) reconstruction in workstations with dedicated software. The intra-observer variability is considered to be acceptable in both techniques,<sup>69</sup> 80% within 5 mm difference.<sup>70</sup> CLL measurements has been shown to have better inter-observer congruency than measurements in MPR also when less experienced radiologists have performed the measurements,<sup>69</sup> but this has been in semi-automated settings which can differ between manufacturers.<sup>69</sup>

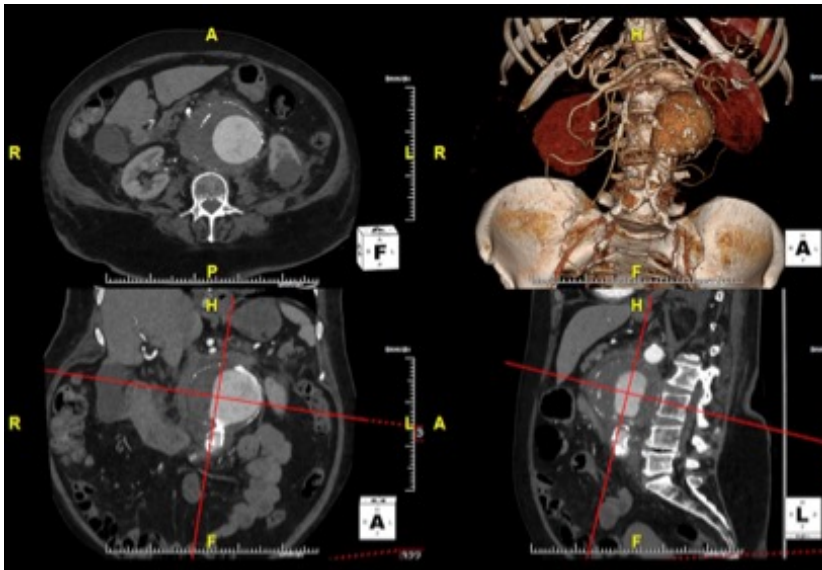


Figure 8. Pre-operative measurement of the AAA in MPR.

## Post-EVAR surveillance

The reason to follow up patients after EVAR is to prevent aneurysm rupture and aneurysm related death. Surveillance is generally focused on detection of sac growth, blood flow into the aneurysmal sac (endoleak), device migration or general aneurysmal progression.<sup>42</sup> Other detectable complications might be related to operative technique, as bleedings either from the sites where the devices were introduced in the vessels, most often in the femoral artery, or from arteries in the abdomen. Complications such as an occlusion of the stent graft by thrombosis or kinking of the stent graft components can occur both early and late after the implantation of the stent graft. Complications after EVAR do not decline over time.<sup>71,72</sup>

According to the guidelines of the care of patients with abdominal aortic aneurysms, a triple-phase CTA within 30 days from the standard EVAR procedure is recommended.<sup>41,73,74</sup> In the update of the European guidelines 2024<sup>42</sup> the imaging recommendations are less vigorous for established stent grafts, with only an unspecified CTA within a month. From the CT findings of the proximal and distal seals, endoleaks and aortic morphology, a stratification of the patients into three groups according to the assumed risk of need of a re-intervention is suggested: the low risk, the high-risk and the EVAR failure group.<sup>42</sup>

In the European guidelines 2019,<sup>17</sup> less computed tomography in favor for ultrasound was suggested and has been adopted for surveillance at many centers worldwide.<sup>41,75,76</sup> There are concerns about the less vigorous surveillance.<sup>77,78</sup>

Measuring the diameter orthogonal to the aortic length axis is proposed to be standard in pre-operative evaluation.<sup>12,17</sup> A widely accepted standard of how to perform the analysis and report of the postoperative aorta in EVAR follow-up imaging does not exist, even though the current recommendation in guidelines is to measure the aneurysm diameter orthogonal to the length axis.<sup>17</sup>

## Radiological modalities in aortic imaging

The arterial phase is often the most important phase in imaging of the aorta. A triple-phase CT consists of a scan without contrast enhancement, one in the arterial phase and one in a late phase.

CTA has occasionally been replaced by computed tomography without contrast, in fear of contrast induced nephropathy (CIN) especially in patients with renal failure. In recent studies an association between contrast medium and CIN has not been confirmed.<sup>79,80</sup> According to current international guidelines caution is mainly needed when glomerular filtration rate (GFR) is  $< 30$ .<sup>81,82</sup> Endoleaks cannot be detected in CT without contrast, therefore CTA with  $\leq 1$ mm slice thickness has been recommended in the postoperative EVAR surveillance.<sup>17</sup>

Ultrasound has common availability, is non-invasive and therefore well suited for screening of aortic aneurysmal expansion. Aortic diameter measured with ultrasound should be measured in the anteroposterior plane preferable by the same observer in follow-up.<sup>83</sup> Ultrasound cannot detect endoleaks but is reliable in measuring the aortic diameter. Body fat and gas in the bowel can limit the ultrasound waves to penetrate down to and reflect the aorta and iliac arteries in the retroperitoneal space. Doppler ultrasound (DUS) can with the doppler technique detect blood flow in addition to measuring the diameter of the aneurysm but cannot detect stent graft migration or evaluate sealing zones attachment. DUS is somewhat less sensitive than contrast enhanced ultrasound (CEUS) in detecting endoleaks.<sup>84,85</sup> CEUS is almost as sensitive as CTA in finding endoleaks,  $> 90\%$ , and have a slightly lower specificity according to a review from 2017.<sup>85</sup>

Magnetic resonance angiography (MRA) is better than CT in detecting low-flow type II endoleaks but has a lower spatial resolution and can be affected by metal artefacts, making visualization of the sealing zone difficult. MRA is suggested as an alternative to CT in young patients or in case of contraindication for iodine contrast, which is used in CTA.<sup>73</sup>

## Radiation in imaging and endovascular repair

The CT workup, the endovascular procedure, the follow-up CTs and endovascular re-interventions all contribute to the patient accumulated radiation dose. It is not easy to evaluate the negative side effects from the radiation. The long-term adverse effect of radiation is the risk of cancer. There is an overall baseline lifetime cancer risk is approximately 40%.<sup>86</sup> The attributed risk in 15 years for a man receiving an EVAR at 55 or 75 years of age has been estimated to be 0.65% and 0.37%, respectively. The main contributor to the cumulative radiation dose was follow-up CTs, with an estimated dose of 8mSv for each examination.<sup>87</sup> The background radiation dose is of a mean of 2.4 mSv yearly.<sup>88</sup>

### Radiation dose in CT

At Sahlgrenska University Hospital the current patient radiation effective dose (ED) in aortic CTA is about 7 mSv in patients of 60 – 90 kg weight and 14 mSv in patients 95 – 125 kg. The arterial phase in aortic CTA has been reported to give a median radiation dose to the patient of 12.6 mSv with a large range (1.3 – 27.3).<sup>89</sup> The corresponding dose for a triple-phase CT was 24.5 (3 – 60.3) mSv.

### Radiation dose in the EVAR procedure

In a meta-analysis the radiation dose of the EVAR procedure for patients of average weight was a median of 13.4 mSv compared to obese patients with a median of 45.7 mSv.<sup>89</sup> In interventional procedures it is easy to measure the radiation to the patient as the dose-area product (DAP), the absorbed dose of radiation, and can be used for estimating the stochastic risk to the patient. To achieve an estimated effective dose, the DAP value is combined with a tissue dependent coefficient, the dose conversion coefficient, and is for abdominal interventions reported as an estimate of 0.26 and somewhat lower in the thoracic procedures.<sup>90</sup>

According to a study comparing patient radiation doses for a standard EVAR performed in a hybrid operating room to EVAR performed in a conventional operating room using mobile C-arm imaging, the DAP was a median of  $154 \text{ Gy cm}^2$  ( $\pm 102.9$ ) vs  $61.5 \text{ Gy cm}^2$  ( $\pm 42.4$ ).<sup>91</sup> The same technique of the imaging during the procedures was used and the difference in dose could therefore not be explained by the potential use of cone beam CT. Other studies report similar results.<sup>92,93</sup> Intraoperative contrast enhanced cone beam computed tomography (ceCBCT) has quite recently been introduced as a diagnostic tool with postprocessed 3D imaging resembling CT imaging and may have higher accuracy in finding EVAR complications than plain angiograms and enabling immediate intraoperative revision.<sup>94-96</sup> The reported mean radiation doses (DAP) were  $71 \text{ Gy cm}^2$  in one of the studies,<sup>95</sup> and  $53 \text{ Gy cm}^2$  in another study, corresponding to 15 mSv in effective dose.<sup>96</sup>

It is possible to lower the radiation doses in the hybrid operating rooms by three-dimensional guidance.<sup>97</sup> Fusion with preprocessed images from the preceding CTA with markers at strategical anatomical landmarks, is then used as a road map overlay on the two-dimensional fluoroscopy screen and may facilitate the procedure, in particular for more complex cases. This technique has been shown to be accurate, but still in need to be adjusted by intraoperative angiograms.<sup>98</sup> Measures to reduce the intraoperative radiation dose during EVAR are to use x-ray radiation dose reductive software as well as common knowledge of collimation to confine the field of view, limiting the gantry angulation and keeping as low frame rate as possible.<sup>99</sup> Also, operator skills can reduce fluoroscopy time and may be achieved by a structured procedure work flow and simulator training.<sup>100</sup>

# Aims

## General aim

The overall aim was to evaluate radiological and clinical outcomes of endovascular aortic interventions.

## Specific aims

- I. To evaluate if aneurysmal expansion of chronic aortic dissection can be prevented by occluding the proximal entry with an endovascular plug.
- II. To determine underlying causes and identify anatomical factors associated with additional iliac stent grafting after EVAR.
- III. To define mechanisms and precursors for post-EVAR rupture with a structured CT protocol.
- IV. To investigate the frequency and mechanisms for loss of seal in EVAR sealing zones.

## Patients and Methods

	Study I	Study II	Study III	Study IV
No. of patients	14	444	1805	399
Age, years mean/median	60 (43–78)	74.9 ±7.4	75.2 ±7.5	74.2 ±6.8
Male sex	57%	84.7%	85.6%	89.2%
Max diameter aneurysm mm	66 (38–80)	64 (IQR 58– 74.5)	63.6 ±12.8	63.9 ±13.1
rAAA at index repair	0%	18%	14%	9.5%
Study period for index AR	Oct 2007 to Feb 2016	Jan 2005 to Dec 2015	Jan 2008 to Dec 2018	Jan 2010 to Dec 2012
Length of clinical follow- up (all patients) years	7.3 (0.5–10.3)	1,96 (IQR 0.83–3.76)	5.2 ±3.2	7.62 (IQR 4.19–8.88)
No. of patients (cases) CT follow-up	10	24 (31)	48 (51)	399
Length of CT follow-up, years	7.6 (2–10.3)	6,11 (IQR 3.85–7.49)	4.1 (IQR 2.7– 6.9)	5.1 ±2.5

*Table 1. Study and patient characteristics. rAAA: ruptured AAA at index aortic repair. Index AR: The aortic repair of the study follow-up. Means are presented with standard deviation, medians with range or interquartile range: IQR*

## Patients

### Study I

All patients treated with a vascular plug for chronic aortic dissection with aneurysm expansion at the Sahlgrenska University hospital 2007 – 2016 were studied for long-term aneurysmal development. Of the total 14 patients that were included, six had residual Stanford type A dissections and at least one entry in the aortic arch. The other eight patients had Stanford type B dissections with proximal entries in the descending aorta.

## Study II

During the period 2005 – 2015 primary EVAR was conducted in 439 consecutive patients at the Sahlgrenska University hospital and patients were included in this study of distal re-interventions after EVAR. In addition, two patients with primary EVAR before that period and another three patients with primary EVAR performed at another hospital but treated with iliac extension at Sahlgrenska during the timeframe in question, were included for CT analysis.

## Study III

In the Swedish National Vascular register (Swedvasc) 1805 consecutive patients were registered with standard EVAR treatment for AAA at five centers 2008 – 2018, including both University and regional hospitals. Meticulous review of all patients' medical charts and radiological reports found 45 post-EVAR ruptures in 43 patients. These were analyzed for clinical outcome and included in the structured CT analysis of post-EVAR rupture mechanisms and signs of impending complication. Another 5 patients with 6 post-EVAR ruptures treated at Sahlgrenska, but outside the Swedvasc cohort, were also included in the CT analysis of mechanisms.

## Study IV

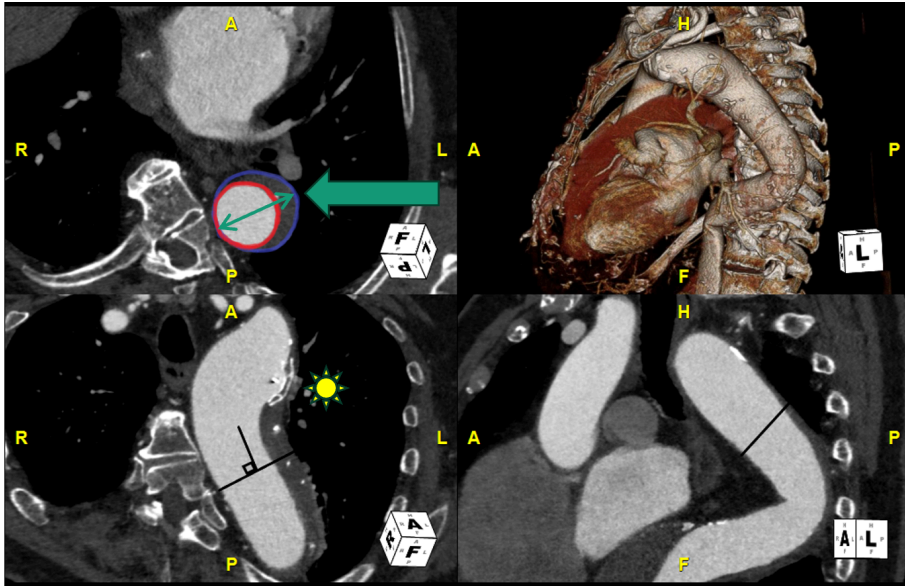
From the previous study of 1805 consecutive patients at five hospitals during 2008 – 2018, a subset of a total of 399 consecutive treated patients from the period 2010 – 2012 was studied. The cohort was selected matching the inclusion criteria of standard infrarenal bifurcated EVAR and imaging follow-up including at least pre-operative, postoperative 1-month CT and 1-year CT.

## Imaging protocols

In all papers I – IV the CT studies performed were according to local protocols at the time they were carried out. The performed CT scans were on single slice spiral or 16 – 64 sliced multidetector scanners and original slice thickness  $\leq 1.25$  mm but in the long-term archive saved slice thickness differed from 0.5 to 5 mm due to server capacity and local economic decisions. The thinnest slices available were transferred to a workstation for reconstruction and

analysis. In papers I – III Aquarius (TeraRecon) and in paper IV the updated version Intuition (TeraRecon) were used at Sahlgrenska University hospital and at Jönköping regional hospital. In paper IV workstations Syngo.Via (Siemens) and 3mensio were used at the Institute of Karolinska and the South General hospital of Stockholm.

Multiplanar reconstruction as earlier described in paper I enables measurements of the diameter perpendicular to the aortic axis. It is more reliable than semi-automatic center lumen line, especially in complex anatomy of the aortic lumen in tortuous and spiraling dissections.



*Figure 9. CTA of the thoracic aorta with focus on the descending aorta. In MPR the diameter is measured perpendicular to the length axis of the aorta (black lines). The green arrow points at the maximal diameter of the total lumen. The true lumen is demarcated in red (the intima), and the false lumen is between the intima and the outer border (the adventitia) outlined in blue. The sun marks a septal occluder. In the upper right image is a 3D CT reconstruction of the thorax.*

Center lumen line has an acceptable intra- and inter observer validity<sup>70</sup> and enables measurement of length along the aortic center line and simultaneous visualization of the aortic cross-section and vessel boundaries. This technique met the requirements of study II – IV (Figure 10).

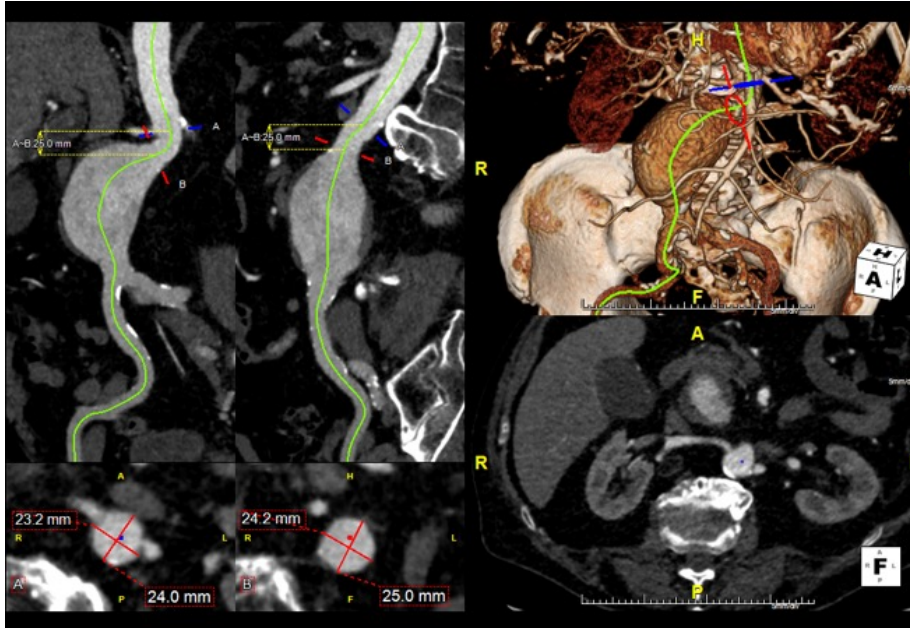


Figure 10. Measurements of diameters (red lines) in the aortic neck, along the CLL.

In study I, technical success of the procedure in closing the proximal entries with endovascular plugs was determined by postoperative CTA evaluation in the arterial phase. The diameters and areas of the total lumen, the true lumen, and the false lumen of the aorta were assessed in MPR at anatomical landmarks in the ascending aorta and the aortic arch, distal to the left subclavian artery and thereafter every 5 cm measured along the length axis of the aorta.

In study II a protocol for measurements of the iliac stent grafts both along the CLL and in MPR were developed by two of the paper's authors, CS and HR. The length between the stent graft edge and the bifurcation of the internal artery was validated by comparing the CLL results with concordant measurements in MPR. All measurements were performed by one vascular imaging specialist (CS) and analyzed in consensus (CS, HR). In study III, two vascular imaging specialists (CS, HR) measured and analyzed the CTs according to the structured protocol designed for this study. In study IV the protocol was further developed, EVAR Foresee (EVAR4c) and an electronic case report file (eCRF), a database where the data was entered consecutively during review of the CT scans, was designed. Another vascular surgeon (MBA) was trained by CS and HR in structured post-EVAR analysis, and in study IV accordingly three vascular imaging specialists (CS, HR, MBA)

performed the CT analysis with EVAR4c. Maximal aneurysm diameter was measured in MPR in all studies.

Results of measurements were in paper I – III kept in key protected local databases excel files. Measurement data in study IV was kept in the eCRF (MediCase) and provided data in excel files exports. Clinical data were kept in excel files in local databases. All data were pseudonymized.

## Definitions

Attachment in the sealing zone was defined as a continuous circumferential apposition of the stent graft to the arterial wall. In study IV this was called seal instead of attachment.

Total loss of seal was defined as the absence of apposition of the stent graft to the vessel wall in the entire affected sealing zone.

Definition of partial loss of seal was when the length of seal fell short of the requirements in the IFUs.

Dilatation as the cause for loss of seal was when there was a loss of seal of the stent graft and the diameter of the artery in the sealing zone exceeded the stent graft diameter.

The maximal diameter was the largest measurement from the center of the arterial wall or stent graft strut to the opposite corresponding measurement point.

Migration was a change in position of the graft edge  $> 5$  mm compared to a predefined anatomic landmark, such as a vessel bifurcation or another graft edge. 5 mm was chosen as cut-off instead of as in guidelines<sup>17</sup> 10 mm because the sealing zone lengths in current recommendations are only 10 mm.

Aneurysmal sac change was defined as  $> 5$  mm difference in maximal diameter perpendicular to the aortic length axis.

EVAR failure is defined in the guidelines<sup>42</sup> as a post-EVAR occurrence of a direct endoleak (type I or III), an obvious degradation of the seal with impending endoleak, or an aneurysm sac growth  $> 10$  mm.

## Clinical outcomes and image analyses

### Study I

Clinical and radiological findings in patients' charts and radiological reports were collected. A review of all the patients' imaging was performed according to the preset protocol. Results after treatment with endovascular plugs and septal occluders were compared with literature reports for standard treatment.

### Study II

Patients that had iliac re-interventions were compared to those who did not regarding demographic data and preoperative CT measurements. In patients with iliac re-interventions, reviews of postoperative CTs were performed for analysis of underlying mechanisms of EVAR limb failure.

### Study III

Assessment of whether the patient's anatomy was within the instructions for use (IFU) of the stent graft was done in the pre-operative CT. Whether the EVAR placement was correct according to the IFU was established in the analysis of the first postoperative CT. The mechanism of rupture was determined in the last CT. With knowledge of the rupture mechanism, the CTs preceding the ruptures were reviewed with the structured protocol for CT analysis for signs, precursors, of the impending complication. Comments in the clinical follow-up of any detected complication after EVAR or radiological finding of stent graft failure were recorded.

### Study IV

Review of CTs for signs of impending complication, endoleaks and aneurysmal sac size were performed with the CT EVAR4c analysis until the end of study 2020. Frequencies of loss of seal and underlying mechanisms as dilatation in the sealing zone, migration, component separation or primary incorrect placement of the stent graft were analyzed. Detection rate in clinical routine follow-up was assessed. Clinical parameters such as complications, re-interventions, post-EVAR ruptures and deaths were registered. An extend follow-up regarding post-EVAR ruptures was performed in 2023.

## Statistical analysis

Study I only included 14 patients and therefore a more descriptive style of presenting categorial data with numbers and percentage was chosen. Continuous data were presented as median and range and calculated in Excel (Microsoft). Differences in diameters and area ratio over time were also calculated in Excel. Reversed Kaplan-Meier estimate median CT follow-up time was calculated in SPSS (IBM).

In study II-IV continuous data was presented as means and standard deviations if the data was of normal distribution. When the distribution of data was skewed, numbers were presented as median with range or quartiles. Categorical data was presented as numbers and percentage.

Differences between groups were calculated in SPSS. To determine if there was a statistically significant association between categorial variables and proportions of outcome the Pearson's Chi-square paired test was used. Continuous data means were compared with student t-test. Comparison of mean differences between three groups were performed by one-way ANOVA with correction for multiplicity with Bonferroni post-hoc. Any p-value of  $< 0.05$  was considered statistically significant. Compared variables between groups were presented with 95% confidence intervals. Survival analysis with Kaplan-Meier was performed in SPSS for frequencies of freedom of post-EVAR rupture and absence of loss of seal (intact EVAR).

## Ethical considerations

Ethical approval was acquired for all studies. All studies were retrospective, and the Regional Ethics Review Boards waived the need for informed patient consent.

## Results

### Study I

Fourteen consecutive patients with chronic aortic dissection were treated by occluding the proximal entries with vascular plugs or a septal occluders. The type and size of the endovascular device chosen was based on pre-operative assessment of the diameter of each entry. Small entries were treated with vascular plugs and large entries with septal occluders. In six patients with Stanford type A dissection the proximal entries were located in the suture line of a previously inserted tube graft in the ascending aorta (n=3), in the arch of the aorta (n=2) or at the origin of the left subclavian artery (n=1). In eight patients with Stanford type B dissections entries were located in the descending aorta. In two patients two entries were treated. In four patients another entry was treated at a very early re-intervention, with closure of an entry that was found in the first post-operative CT.

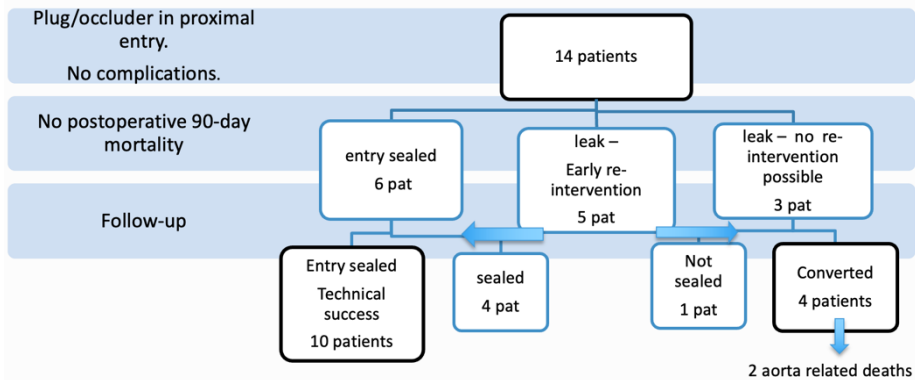


Figure 11. Flow chart after the treatment with vascular plugs or septal occluders in proximal entries in thoracic aortic dissection.

There was no 90-day mortality, post-operative symptoms of spinal cord ischemia, stroke, major bleeding, or renal failure. Technical success with primary seal, including the adjacent procedures, was achieved in ten patients and these were included in the long-term follow-up of aneurysm development. In four patients, primary seal of the dissection entries was not achieved, and the treatment strategy was converted to either FET (n=1), combination FET/TEVAR (n=2) or TEVAR (n=1). Two of the converted patients subsequently died of aneurysmal rupture, one after TEVAR and one after FET/TEVAR. The other patient with FET/TEVAR had a continuing

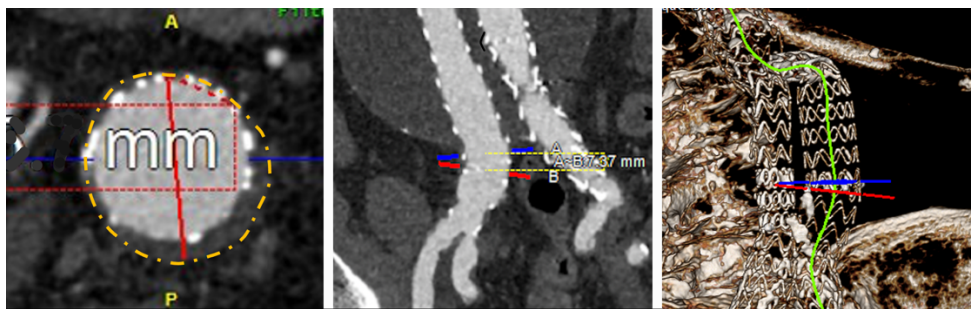
aneurysmal expansion in the abdominal aorta and was converted to open thoracoabdominal aortic repair, illustrating the complexity of treatment of chronic aortic dissection with aneurysmal expansion.

The median follow-up from index treatment to death or to end of the study was 7.6 years in the CT follow-up group. In all these patients in whom occlusion of flow to the false lumen had been achieved, a stable or reduced diameter of the thoracic aortic aneurysm was seen with a favorable change in the true/false lumen ratio in most of the patients. Below the diaphragm, in the abdominal aorta, the aortic diameters generally progressed in a manner similar to untreated dissected abdominal aortas. In one patient the diameter of the abdominal aorta exceeded the threshold for treatment of abdominal aneurysms, and that patient eventually had an open thoracoabdominal aortic repair.

## Study II

After a median of 46 months (range 2 – 92) from the index EVAR, 24 patients, all male, treated with bifurcated EVAR had 31 re-interventions with additional iliac stent grafting in 30 limbs. Post-EVAR rupture was the indication for five (21%) of the patients. Three were preceded by an aneurysmal sac growth, one had an unchanged diameter of the aneurysmal sac, and one had a shrinking aneurysmal sac before rupture.

The iliac arteries were pre-operatively significantly wider in the patients that had re-interventions compared to those that did not require any re-intervention, median diameter 18 vs 15 mm ( $p < 0.001$ ). In patients who had a re-intervention in at least one limb, the stent graft attachment length at the first postoperative CT was significant shorter in limbs that later had a stent graft extension compared to limbs that did not, median 23 vs 33 mm ( $p < 0.01$ ). In these patients there was no difference in pre-operative iliac diameters between the limbs. Review of the last CTs to determine the underlying mechanisms to the need of re-interventions showed stent graft migration in 16/31 of the cases of re-interventions. Ten were in the distal sealing zone and 6 were in interconnections. Dilatation was the cause in 9/31 limbs. Sealing length not within IFU requirements was found to be the only cause in three patients and in combination with migration and dilatation in five and two patients, respectively. Another three re-interventions were performed prophylactically in adjunction to other endovascular procedures.



A

B

C

Figure 12. A) Vessel dilatation, the yellow dotted line outlines the arterial wall. The lumen of the stent graft is light grey because of contrast enhancement of the blood. B) Short sealing zone in the right common iliac artery caused by migration. The blue line is placed at the upper limitation of the sealing zone. The red line marks the distal edge of the stent graft. C) Component separation in the interconnection between stent graft components.

### Study III

In the cohort of 1805 patients 43 patients had 45 post-EVAR ruptures. The cumulative incidence was 2.5% during follow-up of 5.2 years and the incidence rate 4.5/1000 person-years. The median time from index EVAR to rupture was 4.1 years, only including the first time of post-EVAR rupture per patient.

All the 51 cases of post-EVAR rupture in 48 patients were included in CT review to determine mechanisms and precursors for post-EVAR rupture. In two patients there was no CT performed at the event of rupture, but autopsy verified diagnosis and previous CTs showed endoleaks.

#### *Mechanisms for post-EVAR rupture*

The cause for rupture was a type IA endoleak in 39% of the cases. Type IB endoleak in either of the limbs was present in another 39%. One patient had both type IA and IB endoleaks and was reported in both groups. In 22% of the cases the cause for rupture was either a type IIIA or a type IIIB endoleak. Type II endoleak was not the mechanism for rupture in any of the patients. In one patient the cause of rupture was deemed as due to graft infection.

In the proximal sealing zone, the precursors were vessel dilatation in 16/20 patients, migration in 3/20 and in one patient the aneurysm sac progression was because of infection. In the distal sealing zones the precursors were dilatation in 8/20 limbs, migration in 8/20 and primary inadequate stent grafting seal in the other four. In the interconnections between the main body–limb or between limb–limb, stent graft component separation occurred in nine cases. Two patients had stent graft fabric tears.

In total, 43/51 (84%) of the post-EVAR ruptures were preceded by precursors recorded by the structured CT analysis. Three patients had only the 1-month postoperative CT and thereafter no CT until the post-EVAR rupture. In the patient with rupture caused by infection no preceding precursor was seen.

Only 31% of the precursors (in 16 patients) had been mentioned in routine radiology or vascular surgeons' notes. These 16 patients either had the post-EVAR rupture in waiting for re-intervention (n=6), after doctors' or patients' decision not to treat (n=8) or had of an unclear reason not been treated (n=2).

## Study IV

The 399 included patients could be categorized into three groups, according to the attachment in the sealing zones at the last CT: 1) total loss of seal group, 2) partial loss of seal group and 3) preserved seal group (intact). There were statistically significant differences in sealing lengths and artery diameters in the sealing zones between the loss of seal and preserved seal groups in the first post-operative CT. A high frequency of loss of seal was noted during the mean follow-up time of 5 years. All the post-EVAR ruptures that eventually occurred were from the loss of seal groups. Dilatation in the proximal sealing zone was the most common mechanism of failure. Wider diameters and shorter sealing lengths were all associated with post-EVAR failure. A structured CT analysis could detect most of the causes of loss of seal before post-EVAR rupture.

## Discussion

This thesis covers different aspects of endovascular treatment of aortic aneurysms. The most fatal complication, aneurysm rupture, is lethal if not treated. A large population study<sup>22</sup> showed that the acute mortality in patients with thoracic or abdominal aneurysm rupture, was 41% and 34%, respectively, before reaching the hospital or during the first hours of hospital care. The corresponding figure for acute aortic dissection was 39%.<sup>22</sup> The surgical treatment options are open surgery, hybrid, or endovascular aortic repair.

The focus of this thesis was mainly on long-term follow-up of endovascular treatment of aortic disease. In paper I, a new alternative endovascular treatment of chronic aortic dissection with aneurysm expansion is investigated and in paper II-IV, an established endovascular stent graft method to treat infrarenal abdominal aortic aneurysm is studied.

There are similarities in the follow-up routines of aneurysmal disease in the thoracic and abdominal aorta. Potential aneurysmal progression does not only occur in the treated segment but often the patient has an aneurysmal disease engaging other segments of the aorta.

The current knowledge in the area of diagnostics in chronic aortic dissection has been analyzed and summarized in an American Heart Association scientific statement in an attempt to give recommendations in imaging protocols and measurement technique.<sup>101</sup> The recommendation to measure the dissected aneurysmatic aorta using the MPR manually at anatomic landmarks instead of with the semiautomated centerline measurement tools was explained by difficulties to get reliable centerlines due to heterogeneity in the concentration of contrast agent in the false lumen and the often existing tortuosity of the aorta. In study I the choice to perform the measurements of the aortic diameters perpendicular to the aortic axis in MPR were on the same grounds. By repeating the measurements, and also measuring the total length of the aorta with small margins of error, the method was assessed as robust. This thesis does not advocate for which of the methods, MPR or CLL, is best in analyzing the complex anatomy of the dissected thoracic aorta. Both methods are more accurate in measuring the aneurysm diameter than the non-reconstructed CT axial view. As pointed out in the guidelines, it is important to describe how and where measurements have been performed in the absence

of a single accepted and endorsed method.<sup>11</sup> CLL measurements of the thoracic aorta have been shown to be as accurate and faster achievable compared to MPR,<sup>69</sup> and might be considered in CT follow-up after thoracic aortic repair.

## Open or endovascular repair of chronic aortic dissection with aneurysm expansion

Treatment of chronic aortic dissection is challenging. Many patients are assessed too fragile to endure open surgery.<sup>11</sup> Open thoracoabdominal aortic surgery with total replacement of the arch has at high-volume centers reported postoperative mortality < 6% and long-term survival close to population mean.<sup>102</sup> The current American guidelines emphasize that high-volume centers, defined as centers performing surgery in at least 7 proximal aortic (ascending aorta and/or arch) dissections yearly,<sup>103</sup> have better outcomes than centers with low-volume.<sup>11</sup>

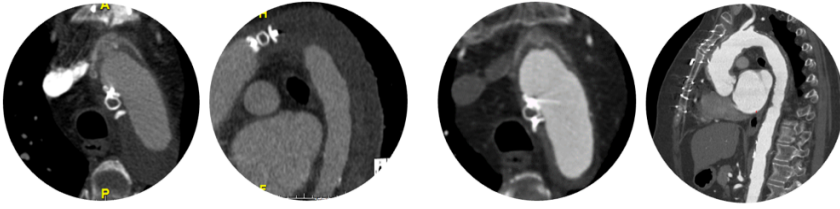
In descending thoracic aortic aneurysm as indication for treatment, the short-term outcomes have been in favor for TEVAR compared to open repair, but concordant to abdominal aneurysm, open aortic repair has a slightly lower mortality rate after 5 years and more evidently after 10 years (52% vs 33%) and lower rates of re-interventions (4% vs 21%).<sup>104</sup> In chronic dissection type B, TEVAR is the treatment of choice if the dissection does not involve the arch,<sup>11</sup> but some patients have unfavorable anatomy for stent graft repair.<sup>101,105</sup> Hybrid operations combining open surgery with endovascular stent graft extension like the frozen elephant trunk technique is considered less invasive compared to the thoracoabdominal aortic surgical repair but is still not tolerable for all patients. Several endovascular techniques involving the arch and the branches to the head and upper extremities are evolving, but the risk of complications and long-term outcome is yet to study.<sup>101</sup>

## Endovascular aortic repair with vascular plugs and septal occluders

Study I supports the hypothesis that a targeted mechanical closure of the proximal entry of chronic aortic dissection, without the mechanical reinforcement of the true lumen provided by a stent graft, is sufficient to promote positive remodeling and prevent further aortic dilatation, at least in a downstream segment until the next significant entry tear appears, similar to remodeling results after TEVAR.<sup>106</sup> That potential aneurysmal progression does not only occur in the treated segment was shown in study I in patients with a primary successful closure of primary entries and favorable remodeling in the downstream thoracic segment but no effect on the aneurysmal progression of the abdominal aorta. The progress of the aneurysmal growth in patients with chronic aortic dissection engaging also the abdominal aorta is similar to what is seen in patients treated with TEVAR.<sup>106</sup> There is more often a continuing expansion of the abdominal aorta if the large abdominal arteries are engaged by the dissection.<sup>107</sup>

Since there were no peri-operative complications this could be a base for further studies of this concept, potentially allowing minimally invasive treatment of more patients with aneurysmatic expansion due to chronic aortic dissection. Another study of 10 patients has been published with short-term outcomes with similar findings.<sup>108</sup> Assumably the remodeling of the thoracic and abdominal segment has a similar long-term pattern as after TEVAR, with a higher rate of re-interventions compared to open surgery. Theoretically occlusion of entries with vascular plugs or occluders could have a better sustainability since it follows the aortic wall in the natural history of continuous degeneration and expansion with age. Therefore, it could have a lower risk of being outgrown compared to the TEVAR stent graft that has a fixed nominal diameter at the sealing zones. Lifelong surveillance as is recommended in the TEVAR surveillance<sup>11</sup> should be mandatory also after endovascular occlusion of entries with vascular plugs and occluders.

The cohort in study I is the largest single center cohort of its kind reported, and a further follow-up of outcomes would be of interest for the decision basis needed in treatment of the variety of complications the dissected aorta often gives rise to. Multidisciplinary teams in treatment of dissected aorta is to be recommended.<sup>109</sup>



*Figure 13. Axial and sagittal images from the first and last postoperative CTAs in a patient after occlusion of a proximal entry in the arch of aorta with a vascular plug. Remodeling of the aorta has occurred. Contrast enhancement is seen in the true lumen in the arterial phase. Contrast enhancement elevates the attenuation in the image and makes it “whiter”. In the two images to the left, the timing of contrast agent administration was not as good as in the later CT and the enhancement of the blood in the aorta was therefore not as concentrated.*

## Timing of treatment in aortic dissection

There is a discussion on the timing of treatment for aortic dissection. In acute Stanford type B aortic dissection with signs of retrograde dissection to the heart or organ ischemia caused by decreased blood perfusion, open or endovascular repair has to be conducted promptly since the mortality otherwise is very high.<sup>26</sup> The membrane, the detached intimal layer of the aorta, is still elastic and moldable in the acute and subacute phase, enabling treatment remodeling of the dissected aorta with shrinkage of the false lumen if the flow can be redirected.<sup>110,111</sup> Some advocate for an early treatment with TEVAR in uncomplicated Stanford type B aortic dissections in the acute phase (2 – 14 days after onset). This is because of a more favorable aortic remodeling, a better long-term outcome with lower rates of re-interventions and disease related mortality,<sup>112</sup> and safer than compared to best medical treatment only.<sup>113</sup> Other studies considered the subacute phase to be the safer,<sup>114</sup> and with similar effects on remodeling of the aortic lumen.<sup>111</sup>

It is unknown if the intimal tears in the acute or subacute phase can endure the interventional procedure of passing through the entry and the placement of an occluding device. Such maneuvers in the acute and subacute phase may even enlarge the entry and worsen the outcome. There are now a few case reports that claim early closure may be safe,<sup>115,116</sup> but the literature is scarce and negative case reports are generally rarely published. At Sahlgrenska, first in

reporting a small case study of treatment with entry occluding devices in dissection,<sup>36</sup> the decision therefore was to only treat patients with aortic dissection older than 90 days. A rigid membrane might limit the vascular plugs or septal occluders ability to conform and results might have been affected by a learning curve in sizing of the occluding plug and assessing the anatomical prerequisites to achieve primary technical success. The planning of and performance of the procedures were conducted by highly experienced endovascular radiologists and vascular surgeons and in the introduction of the method to occlude the entries, an interventional cardiologist, specialized in endovascular closure of cardiac septal defects, was involved in the first procedures.

## Follow-up after EVAR treatment

In clinical praxis and assigned by current European guidelines<sup>42</sup>, the established signs of EVAR failure are detection of aneurysm sac growth and type I and III endoleaks.<sup>72</sup> Surveillance after EVAR has been questioned and at many vascular centers changed their primary follow-up method from CTA to ultrasound since surveillance has not been shown to be effective in preventing aneurysm related mortality. The EVAR surveillance paradox<sup>76</sup> is that there is no difference in survival if the patients are compliant to the follow-up regime or not. The post-EVAR rupture rate has been unchanged over the last two decades,<sup>66,72,117-119</sup> and the technique appears to fail in excluding the aneurysmal sac in all patients. An aim of this thesis has been to find out why.

Current practice in Sweden was shown in study III to be insufficient in finding the signs of impending complications. This finding is in line with the pattern referred to as the EVAR surveillance paradox.<sup>76</sup> The findings that a large proportion of precursors to EVAR failure are not noticed in routine follow-up, offers a possible explanation to the EVAR surveillance paradox. If follow-up focuses on indirect signs instead of direct signs of EVAR failure it will be ineffective. In our studies the patient compliance with the follow-up visits and examinations was high. Patient compliance is less than 50% in many other countries and this is considered to be a major concern.<sup>77,78</sup>

## Imaging

The European and American vascular guidelines<sup>41,42</sup> do not guide in how to analyze post-EVAR imaging. It is proposed to look for new endoleaks, migration of the stent graft or sac growth,<sup>74</sup> but analysis of sealing zones is not explicitly mentioned. Many vascular surgeons propagate for less vigilant imaging follow-up or reducing CT scans in favor for ultrasound.<sup>42</sup> Ultrasound, if performed by a specialist with knowledge of EVAR, with doppler and even better with contrast enhanced ultrasound, performs at the same level as CTA in finding endoleaks. As shown in studies II – IV, endoleaks are not apparent as precursors in most patients with post-EVAR ruptures and thus not reliable enough to prevent post-EVAR complications. Three-dimensional contrast enhanced ultrasound (3D CEUS) has been suggested to be more sensitive to detect endoleaks compared to CTA.<sup>120,121</sup> 3D ultrasound techniques have been proven to give accurate assumptions of aneurysm sac development compared to CT.<sup>121,122</sup> The detection rate of endoleaks with 3D CEUS and the ability to determine the type of endoleak is, even though somewhat higher compared to CTA, still not shown to be 100%. The true rate of endoleaks is not known since there is no current technique that can give the true answer of their occurrence.

Furthermore, as shown in study III and IV, there was a delay in the possibility to detect the endoleaks compared to detecting signs of diminishing lengths of seal in the sealing zones. Study III and IV show that signs of impending EVAR failure are possible to detect on CT before secondary signs as endoleaks and aneurysmal growth occur. However, if it would be possible to determine the apposition of the stent graft to the vessel wall with ultrasound, or in the overlap zone to the other stent graft, this would be a potential alternative to CT. It is well known that the iliac arteries are often difficult to visualize properly with ultrasound in obese patients. If there is gas in the bowel overlying the arteries, sometimes the whole abdominal aorta is affected by similar difficulties.

CTA is also affected by a large body volume with need of more radiation to maintain the signal to noise ratio.<sup>123</sup> There are concerns about radiation doses and long-term risks. The increased risk of cancer from post-EVAR CT

radiation during follow-up in the population over 75 years is low compared to the risk factor age itself. The risk of missing a post-EVAR complication possible to foresee with CT seems to be higher. Nevertheless, it is desirable to examine only those patients that are at risk for complications and for whom a re-intervention would be plausible. A large meta-analysis has showed that the increased risk of medical radiation accelerates at a cumulative dose of > 55 mSv.<sup>124</sup> Reducing the radiation dose in the follow-up is possible by using modern software for dose modulation and image post-processing in the CT machines. Iterative reconstructions have been used during the last 10 – 15 years.<sup>125</sup> New technologies utilizing artificial intelligence, noise-reducing deep learning image reconstructions, have evolved during the past five years.<sup>126</sup> The current generation of fast and powerful CT machines with dual energy features can also reduce the required amount of iodinated contrast agent with preserved diagnostic quality of the images.<sup>127</sup>

The studies in the thesis show that a focus on the EVAR sealing zones is superior in EVAR surveillance compared to detection of endoleaks. To evaluate sealing zones in a single CT arterial phase may be sufficient and the iteration of series to detect endoleaks on a venous phase may be omitted, thus significantly reducing radiation exposure. Analysis of the sealing zones is possible even with non-enhanced CT but not complications as endoleaks, organ perfusion defects or thrombosis. With current semi-automatic technique creating a center lumen line guided by contrast concentration, reviewing the imaging is faster when contrast enhancement in the arterial phase is present. Intraoperative ceCBCT might replace the first postoperative CT if proven to be equal to CTA in accuracy of detecting signs of EVAR failure.

## Thresholds

We showed in paper II that the diameter of the iliac artery in the distal sealing zone matters, with increased need of distal extensions in iliac arteries with larger diameters. These findings were in line with other contemporary studies included in a review article<sup>128</sup> that current guidelines<sup>42</sup> refer to. However, our findings suggest that the cut off diameter for a low risk of re-intervention could be set at a smaller diameter than the diameter of < 20 mm referred to as a low-risk feature in guidelines. The findings in study IV are concordant and implies

that recommendations in the guidelines<sup>42</sup> should be considered to be altered in the stratification of patients to the group of low-risk and to the group in need of more intense surveillance.

In the current European vascular EVAR guidelines, the risk stratification is suggested to divide patients into three groups according to risk for re-interventions to preserve the EVAR integrity: low risk, high risk and EVAR failure group.<sup>42</sup> For low risk stratification the proximal and distal diameters are of < 30 mm and < 20 mm, respectively. Corresponding proximal and distal sealing lengths of > 10 mm are suggested as cut off values measured at the first postoperative CT.<sup>42</sup> The suggested surveillance of these patients is CT imaging every five years only to assure EVAR integrity and to assess any aneurysmal progression in the aorta.<sup>42</sup> Outcomes of study IV indicate that many of the aneurysms excluded by EVAR are still intact after five years but also that a large proportion of the EVAR components are hanging loose or are on the verge of losing apposition to the arterial wall in the sealing zones. The mean diameters of the sealing zones in the groups of patients with loss of seal were statistically significant well below the low risk stratification cut off values stated in the 2024 European guidelines.<sup>42</sup> This is concordant to previous studies that also have shown the importance of analyzing the proximal sealing zone diameters and lengths.<sup>68,129</sup>

### *Reflections*

The ability to foresee complications while they are still possible to treat safely and electively, could both prevent unnecessary suffering and potentially to a lower cost compared to an aneurysmal rupture. The aspect of cost has not been studied in this thesis. There are also concerns raised that there will be more interventions for preventing complications if more signs of impending failure are reported. Notably though in this matter is that preventing rupture is the indication to treat abdominal aneurysms primarily. Considerate decision weighing patients' expectations and co-morbidity still must be done. If re-interventions are based on thorough examination of the existing anatomic prerequisites, considering the mechanisms behind impending EVAR failure, unnecessary re-interventions might be avoided.

Based on the findings and discussion in this thesis, CTA is still the first choice in postoperative surveillance after aortic repair. Recommendations for the postoperative imaging analysis should be stated in the guidelines for management of aortic disease. In my opinion it is easier and faster to analyze the apposition of the stent graft to the vessel wall along the center lumen line

compared to multiple measurements in the multiplanar reconstruction views throughout the aorta. In complex aortic anatomy a combination of the techniques may be necessary. Aging affects the sealing zones both in thoracic and abdominal aortic aneurysm repair. Sealing zone failure has been shown to occur often within 5 years of follow-up even when recommendations in the guidelines and stent graft IFU has been fulfilled. Current recommended sealing zone threshold for risk stratification in the surveillance program after EVAR seems not to be sufficient for low-risk classification.

## Limitations

All the studies are retrospective with the inherited risk of selection bias and not registered confounders. In study I the cohort was selected because of poor suitability for standard treatment and there was no control group. In study II data on pre-operative measurements were collected from a protocol in clinical use, but only the group treated with extensions was postoperatively reviewed with structured analysis. In study III only the patients with a post-EVAR rupture were reviewed with the structured CT analysis and the prevalence of the precursors in the remaining population was unknown. The imaging was performed on different scanners, and often without contrast enhancement and seldom with a late phase. The follow-up programs differed somewhat between sites. Some patients were lost to follow-up. Another main limitation is that the review of the CTs were performed by a few persons, and they were not blinded to radiological reports or clinical results. Study I – II might not have power enough to detect event rates reflecting an unselected larger population. Analysis regarding differences according to sex was underpowered since the number of persons female at birth were low, and the cut off for artery diameter values might be overestimated for women which should be taken in consideration when assessing post-EVAR imaging in women.

## Conclusions

An endovascular plug to occlude the proximal entries in patients with expanding chronic aortic dissection Stanford type B or residual Stanford type A might be considered in patients not eligible for treatment with stent grafts or open surgery.

Re-interventions with distal extensions occur more often in patients with wider iliac arteries and shorter stent graft sealing zones.

The mechanism behind the loss of attachment between the stent graft and vessel wall is most often dilatation of the vessel in the sealing zone and it is more common in patients with large artery diameters.

The risk of post-EVAR rupture does not decline with time.

Loss of seal is underdiagnosed in routine follow-up and diagnostic accuracy could be improved by the use of a protocol for structured CT analysis in the review of postoperative CTs.

Recommendations in current guidelines and instructions for use considering stent graft sealing length should be considered to be increased.

## Future perspectives

Chronic aortic dissection is considered as a complex disease to treat and there could still be a need of a minimally invasive, low risk option as the endovascular plug might offer in selected cases. Further prospective studies for feasibility and safety would be of interest at a specialized, high volume, thoracic vascular center to evaluate the technique as a compliment to hybrid surgery or stent graft techniques.

Further analysis of the EVAR database with aspects of post-EVAR failure predictive factors is ongoing. The results might give new insights to the stratification of patients to low – high risk groups in post-EVAR surveillance. A prospective collection of measurement data and rates of complications in a multi-center population using CT analysis along the center lumen line with a standardized protocol with, or similar to, the EVAR4c protocol would be of value.

Implementing structured CT analysis in post-EVAR surveillance in routine follow-up has been done at Ryhov hospital. The study results should be enough evidence and incentive also for other centers that perform EVAR, to use the same workstations and software in the postoperative follow-up as already used in the pre-operative work-up.

There is a current diagnostic development in photon counting detector CT (PCCT) technology. The PCCT provides an increased spatial resolution combined with full spectral information in all scans. The increased spatial resolution (currently down to 0.2 mm slice thickness) might be a field to explore focusing on the sealing zone. The PCCT can discriminate between multiple different contrast mediums simultaneously by material decomposition. This gives the potential to replace multiphase CT scans with a single CT acquisition thus reducing the radiation dose. The timing and visualization of vessel lumens, wall defects, thrombosis and endoleaks needs to be analyzed and validated in future studies. To investigate which patients and what indications would have the most to gain using this new and not yet widely spread technique compared to standard imaging is another field of interest.

## Sammanfattning på svenska

Endovaskulära metoder att behandla stora kroppspulsådern (aorta), har under de senaste decennierna utvecklats och blivit vanliga. Endovaskulär teknik innebär att man via kärl kan reparera olika sjukdomstillstånd med kateterledd behandling under röntgenomlysning.

Denna avhandling omfattar långtidsuppföljning och analys av datortomografibilder (DT) av två endovaskulärt behandlade sjukdomstillstånd i aortan: aortadissektion och aortaaneurysm (kroppspulsåderbräck).

Aortadissektion uppstår då en skada på aortans innersta vägglager skapat en falsk kanal parallellt med aortans äkta pipa. Denna falska kanal kan utvecklas i riktning mot hjärtat eller nedströms och blockera blodflödet till kroppens organ och därmed vara livshotande. På sikt föreligger det dessutom stor risk att den försvagade väggen i området för aortadissektionen vidgas till ett aneurysm vilket kan brista (aortaruptur). Förebyggande behandling kan göras med öppen operation eller med stentgraft. I vissa fall passar dock inte någon av de behandlingsmetoderna. På Sahlgrenska sjukhuset har en minimalinvasiv metod vidareutvecklats. Med små pluggar bestående av metallnät har hålet till den falska pipan tätats med endovaskulär teknik.

En frisk aorta vidgas långsamt med åldern. En försvagad aorta vidgas snabbare och när vidden av bukaortan  $> 3$  cm räknas det som aneurysm och är i buken vanligast nedom njurartärernas avgångar (infrarenalt bukaortaaneurysm). Rökning, ålder och manligt kön är starka riskfaktorer för aneurysmtillväxt. Med ökad vidd ökar risken för att aneurysmet skall spricka. Förebyggande behandling görs då aneurysmet  $> 5,5$  cm med öppen operation eller med endovaskulär aortareparation (EVAR). Det vidgade partiet av aorta överbryggas med ett rörformat graft (öppen operation) eller stent graft (EVAR) och därmed förhindras blodet att cirkulera aneurysmet. Syftet med behandlingen är att minska risken att aneurysmet spricker. Aorta ruptur efter EVAR (post-EVAR-ruptur) förekommer trots efterföljande uppföljning och detta är ett problem vars orsak varit oklar.

Avhandlingens övergripande mål var att utvärdera både kliniska och radiologiska utfall av endovaskulär behandling med plugg i aortadissektion och EVAR i infrarenalt bukaortaaneurysm. Mer specifika mål var att med hjälp av DT:

- utvärdera om behandling med en endovaskulär plugg kan förhindra vidare aneurysmtillväxt vid aortadissektion.
- klargöra bakomliggande orsaker till tilläggsbehandlingar och post-EVAR-ruptur
- definiera visuella tecken till förebyggande komplikation.
- undersöka förekomst av och orsaker bakom förlust av tätning i infästningszonerna av EVAR.

I **studie I** hade 14 patienter behandlats med en endovaskulär plugg. Ingen fick någon allvarlig komplikation i samband med ingreppen men hos fyra patienter lyckades inte tätningen av dissektionshålet och man återgick till annan behandlingsplan. Tätningen av dissektionshålen var framgångsrik hos tio patienter och under 7 års uppföljningstid sågs minskande eller stabiliserad diameter av bröstaorta. I bukaortan sågs inte samma gynnsamma effekt utan fortsatte att vidgas liksom vid övriga behandlingsmodeller av bröstaorta.

EVAR kompletteras ofta med tilläggsbehandlingar. Detta studerades i **studie II** där 24 patienter som fått EVAR-förlängande behandlingar jämfördes med 420 EVAR-patienter utan sådan tilläggsbehandling. Stor vidd och korta infästningssträckor i det mottagande bäckenkärlet var predisponerande för tilläggsbehandling.

I Sverige registreras EVAR-ingrepp i mycket hög utsträckning. I **studie III** gjordes en grundlig journalgenomgång av 1805 patienter behandlade med EVAR under åren 2008–2016 på fem sjukhus och från detta underlag visades en 5-årig 2,5% kumulativ incidens av post-EVAR-ruptur. 51 rupturer utvärderades radiologiskt med fynd av att stentgraftet inte tätade i alla infästningszonerna och att aneurysmet därmed blivit trycksatt och brustit. Läckage vid den övre infästningen av stentgraftet sågs i 39% av fallen, i de nedre infästningarna i ytterligare 39% av fallen samt mellan stentgraftskomponenter i 22% av fallen. Bakomliggande orsak till att stentgraftet hade lossnat var oftast fortsatt kärilvidgning i infästningszonerna. Aortan hade därmed växt ur sin stentgraft. Förstadier till ruptur kunde med strukturerad DT-granskning ses i 84% av fallen jämfört med att enbart 31% av dessa hade påvisats i den kliniska rutingranskningen.

I **studie IV** gjordes en liknande djupanalys av 399 patienters DT-bilder och analysen visade att förekomsten av minskande eller avsaknad av kvarvarande tätning i infästningszonerna var mycket vanligt efter 5 år med tydlig koppling till risk för ruptur. Gemensamt för studie II – IV var att vida kärl och korta EVAR infästningszoner försämrade behandlingens långtidsresultat.

**Slutsats studie I:** Det är möjligt att behandla aortadissektionshål endovaskulärt och långtidsresultaten talar för att det vara ett relevant alternativ för de fall där kirurgiska behandlingar inte kan utföras.

**Slutsatser studie II-IV:** Granskning av DT med ett strukturerat protokoll förbättrar diagnostik och bör användas i uppföljning efter EVAR. Vida kärl och kort bevarad infästning är vanliga tecken till förebyggande aortaruptur efter EVAR. Komplikationer efter EVAR är vanligt och bör kunna förebyggas om allmänna rekommendationer justeras avseende infästningszoner både inför behandling och i uppföljningen efter EVAR. Frekvensen av post-EVAR-ruptur och död skulle då troligen minska.

## Acknowledgements

I wish sincerely to express my gratitude to all who have made writing this thesis possible and all who have showed interest in its contents.

Especially I would like to thank:

**Håkan Roos**, MD, PhD, for welcoming me to the vascular surgery community, promoting cooperation and introducing me to EVAR research. Your generosity is limitless. Your endless energy, inventiveness, extraordinary practical skills, kindness, devotion, openness – all taken together a joy being with.

Professor **Mårten Falkenberg**, my supervisor, for all support, encouragement, and friendship. I admire your courage and ability to think and act independently, thriving for excellence for us all, still willing to listen. I highly respect you not only as a colleague but as a human being.

My co-supervisors, **Erika Fagman**, MD, PhD, for enthusiastic cheering and interesting conversations. You are a role model, both in research and clinical practice, and your statements are always to count on. Professor **Christian Rylander**, for sharing your curiousness and borderless knowledge from many perspectives. **Manne Andersson**, MD, PhD, for meticulous criticism with wit. You bring color and fun to work!

**Mattias Andersson**, MD, PhD-student, my fellow co-author, for sharing both hard work and personal thoughts, encouraging me and generously sharing your knowledge in life. You are admirable in the effort you put in to everybody and everything around you. We will continue working together and I hope for a lifelong friendship!

**Robert Lundqvist**, MSc for sharing your love for statistics, making it somewhat comprehensive and very inspiring.

My co-authors, for making improvements to the projects, manuscripts and contributing to gathering data. A special thanks to **Rebecka Hultgren**, **Åse Johnsson** and **Anders Jeppsson** for sharing your great minds. **Olof Henrikson**, for your ingenuity and humbleness (Mäster Olof) and for providing your technical skills and having kept track of the performed “plug”-procedures.

All vascular surgeons and interventional radiologists, for registering EVAR procedures in Swedvasc and contributing with invaluable input.

The Seldinger society, for showing interest in my research and granting me with the “Seldingerstipendiet”.

**Karin Zachrisson**, MD, PhD, Head of the Department of the Abdominal Radiology and also an interventional radiologist colleague, for your diplomacy and kindness keeping a welcoming atmosphere at work and supporting my research.

**John Brandberg**, MD, PhD, Head of the Department of Radiology, for encouraging and appreciating good research and for still being a part of the gang, having the ability to think standing on your head and never banging a dance.

All my dear present and past colleagues, for sharing your lives, experiences, laughter, and great knowledge and working so hard. Many of us have worked at the department for decades together and that means a lot! I’ve learned so much from you all. Especially I would like to thank **Kjell Geterud**, my great mentor, for friendship and I will always do nephrostomies “the Kjell way” and keep on teaching it. **Henrik Leonhardt**, for encouraging me way back then as a resident, your clinical tutorial skills are remarkable, a role model to revere. **Magnus Palmér**, for sharing your enthusiasm and knowledge of CT techniques and future developments. All my interventional radiologist friends, for all the fun and interesting work we do together and for the work load you have been keeping up with during my work with the thesis (and otherwise too).

All my friends in the Angio suite, for all your support during the years, sharing both ups and downs. Your never-ending kindness, energy, and accommodating to do the best for the patients is impressive and your technical skills are world class! A special thanks to **Roya Razzazian** and **Marie Broström** for your extraordinary efforts.

All great friends out there in the real world, for joy and laughter, for sorrows and tears, and for making memories for life, living life attentively.

All sweet Roosies, **Karin, Anders, Theodor, Wilmer** and **Isak**, for being warm-hearted and full of life, ready for action and appreciating togetherness.

My dear family, my parents **Tord** and **Madeleine** and my sisters **Christina**, **Ulrika**, and **Catharina**, for giving me a bright childhood that will follow me always, and we will always stick together. My parents, Mamma och Pappa, for your never-ending love and support, always with others best in mind and welcoming everyone. Your devotion for life and each other is inspiring. I'm so proud of you!

My beloved children, **Erik**, **Tuva** and **Alicia**, my beams of sunshine, for just being wonderful. For all your kindness, love, and help. I'm so happy to be a part of your lives. You are everything to me. Love always.

My beloved **Håkan**, for your joy, your endurance, your patience, your heart, your brain. Always a helping hand and a word of comfort when in need. Thank you for letting me in into your life and sharing your exciting world with me. I'm grateful for you, with eternal love.

This thesis was supported by the Västra Götaland region and the Västra Götaland ALF grants (ALF-GBG-77190 to MF who generously supported my work).

## References

1. Seldinger SI. Catheter replacement of the needle in percutaneous arteriography; a new technique. *Acta radiol* 1953;39(5):368-76.
2. Dotter CT. Transluminally-placed Coilspring Endarterial Tube Grafts: Long-term Patency in Canine Popliteal Artery. *Investigative Radiology* 1969;4(5):329-332.
3. Volodos NL. The 30th Anniversary of the First Clinical Application of Endovascular Stent-grafting. *European Journal of Vascular and Endovascular Surgery* 2015;49(5):495-497.
4. Parodi JC, Palmaz JC, Barone HD. Transfemoral Intraluminal Graft Implantation for Abdominal Aortic Aneurysms. *Annals of Vascular Surgery* 1991;5(6):491-499.
5. Hinchliffe RJ, Yusuf SW, Macierewicz JA, MacSweeney STR, Wenham PW, Hopkinson BR. Endovascular Repair of Ruptured Abdominal Aortic Aneurysm – a Challenge to Open Repair? Results of a Single Centre Experience in 20 Patients. *European Journal of Vascular and Endovascular Surgery* 2001;22(6):528-534.
6. Hu DK, Pisimisis GT, Sheth RA. Repair of abdominal aortic aneurysms: preoperative imaging and evaluation. *Cardiovasc Diagn Ther* 2018;8(Suppl 1):S157-s167.
7. DenOtter TD, Schubert J. Hounsfield Unit. *StatPearls*. Treasure Island © 2024, StatPearls Publishing LLC.; 2024.
8. Hounsfield GN. Nobel lecture, 8 December 1979. Computed medical imaging. *J Radiol* 1980;61(6-7):459-68.
9. Morgan M CR, Bell D, et al. Ultrasound (introduction). *Radiopaedia.org*, update 19 Jul 2023.
10. Di Cesare E, Splendiani A, Barile A, et al. CT and MR imaging of the thoracic aorta. *Open Med (Wars)* 2016;11(1):143-151.
11. Isselbacher EM, Preventza O, Black JH, et al. 2022 ACC/AHA Guideline for the Diagnosis and Management of Aortic Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation* 2022;146(24):e334-e482.
12. Erbel R, Aboyans V, Boileau C, et al. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). *Eur Heart J* 2014;35(41):2873-926.
13. Erbel R, Eggebrecht H. Aortic dimensions and the risk of dissection. *Heart* 2006;92(1):137-42.
14. Vrizz O, Driussi C, Bettio M, Ferrara F, D'Andrea A, Bossone E. Aortic root dimensions and stiffness in healthy subjects. *Am J Cardiol* 2013;112(8):1224-9.

15. Endicott KM, Tolaymat B, Farhat-Sabet A, et al. Healthy Thoracic Aorta Diameter Growth Slows by Age 60 Years With Persistent Age-Dependent Centerline Elongation Throughout Life. *J Vasc Surg* 2020;72(1):e90-e91.
16. Wang X, Zhao W-j, Shen Y, Zhang R-l. Normal Diameter and Growth Rate of Infrarenal Aorta and Common Iliac Artery in Chinese Population Measured by Contrast-Enhanced Computed Tomography. *Annals of Vascular Surgery* 2020;62:238-247.
17. Wanhainen A, Verzini F, Van Herzele I, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2019;57(1):8-93.
18. Milutinović A, Šuput D, Zorc-Pleskovič R. Pathogenesis of atherosclerosis in the tunica intima, media, and adventitia of coronary arteries: An updated review. *Biomolecules and Biomedicine* 2020;20(1):21-30.
19. Sampson UK, Norman PE, Fowkes FG, et al. Global and regional burden of aortic dissection and aneurysms: mortality trends in 21 world regions, 1990 to 2010. *Glob Heart* 2014;9(1):171-180.e10.
20. Sampson UK, Norman PE, Fowkes FG, et al. Estimation of global and regional incidence and prevalence of abdominal aortic aneurysms 1990 to 2010. *Glob Heart* 2014;9(1):159-70.
21. Howard DP, Banerjee A, Fairhead JF, Perkins J, Silver LE, Rothwell PM. Population-based study of incidence and outcome of acute aortic dissection and premorbid risk factor control: 10-year results from the Oxford Vascular Study. *Circulation* 2013;127(20):2031-7.
22. Landenhed M, Engström G, Gottsäter A, et al. Risk profiles for aortic dissection and ruptured or surgically treated aneurysms: a prospective cohort study. *J Am Heart Assoc* 2015;4(1):e001513.
23. Daily PO, Trueblood HW, Stinson EB, Wuerflein RD, Shumway NE. Management of acute aortic dissections. *Ann Thorac Surg* 1970;10(3):237-47.
24. Czerny M, Schmidli J, Adler S, et al. Editor's Choice - Current Options and Recommendations for the Treatment of Thoracic Aortic Pathologies Involving the Aortic Arch: An Expert Consensus Document of the European Association for Cardio-Thoracic Surgery (EACTS) & the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2019;57(2):165-198.
25. De Bakey ME, Cooley DA, Creech O, Jr. Surgical considerations of dissecting aneurysm of the aorta. *Ann Surg* 1955;142(4):586-610; discussion, 611-2.
26. Czerny M, Pacini D, Aboyans V, et al. Current options and recommendations for the use of thoracic endovascular aortic repair in acute and chronic thoracic aortic disease: an expert consensus document of the European Society for Cardiology (ESC) Working Group of Cardiovascular Surgery, the ESC Working Group on Aorta and Peripheral Vascular Diseases, the European Association of Percutaneous Cardiovascular Interventions (EAPCI) of the ESC and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur J Cardiothorac Surg* 2021;59(1):65-73.

27. Lombardi JV, Hughes GC, Appoo JJ, et al. Society for Vascular Surgery (SVS) and Society of Thoracic Surgeons (STS) reporting standards for type B aortic dissections. *J Vasc Surg* 2020;71(3):723-747.
28. Isselbacher EM. Thoracic and Abdominal Aortic Aneurysms. *Circulation* 2005;111(6):816-828.
29. Vorp DA. Biomechanics of abdominal aortic aneurysm. *Journal of Biomechanics* 2007;40(9):1887-1902.
30. Xydias S, Mihos CG, Williams RF, et al. Hybrid repair of aortic arch aneurysms: a comprehensive review. *J Thorac Dis* 2017;9(Suppl 7):S629-s634.
31. Moula AI, Romeo JLR, Parise G, et al. The evolution of arch surgery: Frozen elephant trunk or conventional elephant trunk? *Frontiers in Cardiovascular Medicine* 2022;9 (Systematic Review)
32. Turner DR, Owada CY, Sang CJ, Jr., Khan M, Lim DS. Closure of Secundum Atrial Septal Defects With the AMPLATZER Septal Occluder: A Prospective, Multicenter, Post-Approval Study. *Circ Cardiovasc Interv* 2017;10(8):e004212.
33. Ramakrishnan S. Vascular plugs – A key companion to Interventionists – ‘Just Plug it’. *Indian Heart Journal* 2015;67(4):399-405.
34. Tresley J, Bhatia S, Kably I, Poozhikunnath Mohan P, Salsamendi J, Narayanan G. Amplatzer vascular plug as an embolic agent in different vascular pathologies: A pictorial essay. *Indian J Radiol Imaging* 2016;26(2):254-61.
35. Malaisrie SC, Mehta CK. Updates on Indications for TEVAR in Type B Aortic Dissection. *Innovations* 2020;15(6):495-501.
36. 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. *Journal of Endovascular Therapy* 2016;23(2):378-383.
37. O'Rourke MF. Arterial aging: pathophysiological principles. *Vascular medicine* 2007;12(4):329-341.
38. Sweeting MJ, Thompson SG, Brown LC, Powell JT, collaborators obotR. Meta-analysis of individual patient data to examine factors affecting growth and rupture of small abdominal aortic aneurysms. *British Journal of Surgery* 2012;99(5):655-665.
39. Brady AR, Thompson SG, Fowkes FGR, Greenhalgh RM, Powell JT. Abdominal Aortic Aneurysm Expansion. *Circulation* 2004;110(1):16-21.
40. Wanhainen A, Hultgren R, Linné A, et al. Outcome of the Swedish Nationwide Abdominal Aortic Aneurysm Screening Program. *Circulation* 2016;134(16):1141-1148.
41. Chaikof EL, Dalman RL, Eskandari MK, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg* 2018;67(1):2-77.
42. Wanhainen A, Van Herzele I, Bastos Goncalves F, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2024 Clinical Practice Guidelines on the Management of Abdominal Aorto-Iliac Artery Aneurysms.

- European Journal of Vascular and Endovascular Surgery 2024;67(2):192-331.
43. Parkinson F, Ferguson S, Lewis P, Williams IM, Twine CP. Rupture rates of untreated large abdominal aortic aneurysms in patients unfit for elective repair. *J Vasc Surg* 2015;61(6):1606-1612.
  44. EVAR-1. Endovascular versus Open Repair of Abdominal Aortic Aneurysm. *New England Journal of Medicine* 2010;362(20):1863-1871.
  45. Lederle FA, Freischlag JA, Kyriakides TC, et al. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. *Jama* 2009;302(14):1535-42.
  46. Prinssen M, Verhoeven EL, Buth J, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2004;351(16):1607-18.
  47. Powell JT, Sweeting MJ, Ulug P, et al. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. *Br J Surg* 2017;104(3):166-178.
  48. Lederle FA, Freischlag JA, Kyriakides TC, et al. Long-term comparison of endovascular and open repair of abdominal aortic aneurysm. *N Engl J Med* 2012;367(21):1988-97.
  49. Becquemini J-P. The ACE trial: A randomized comparison of open versus endovascular repair in good risk patients with abdominal aortic aneurysm. *J Vasc Surg* 2009;50(1):222-224.
  50. Patel R, Powell JT, Sweeting MJ, Epstein DM, Barrett JK, Greenhalgh RM. The UK EndoVascular Aneurysm Repair (EVAR) randomised controlled trials: long-term follow-up and cost-effectiveness analysis. *Health Technol Assess* 2018;22(5):1-132.
  51. Avishay DM RJ. Abdominal Aortic Repair. (<https://www.ncbi.nlm.nih.gov/books/NBK554573/>). Accessed March 5 2024.
  52. Walker TG, Kalva SP, Yedduka K, et al. Clinical practice guidelines for endovascular abdominal aortic aneurysm repair: written by the Standards of Practice Committee for the Society of Interventional Radiology and endorsed by the Cardiovascular and Interventional Radiological Society of Europe and the Canadian Interventional Radiology Association. *Journal of Vascular and Interventional Radiology* 2010;21(11):1632-1655.
  53. Phade SV, Garcia-Toca M, Kibbe MR. Techniques in endovascular aneurysm repair. *Int J Vasc Med* 2011;2011:964250.
  54. de Vries J-PPM, Zuidema R, Bicknell CD, et al. European Expert Opinion on Infrarenal Sealing Zone Definition and Management in Endovascular Aortic Repair Patients: A Delphi Consensus. *Journal of Endovascular Therapy* 2023;30(3):449-460.
  55. Figueroa C, Zarins C. Computational Analysis of Displacement Forces Acting on Endografts Used to Treat Aortic Aneurysms. 1970:221-246.
  56. Chun JY, de Haan M, Maleux G, Osman A, Cannavale A, Morgan R. CIRSE Standards of Practice on Management of Endoleaks Following Endovascular Aneurysm Repair. *Cardiovasc Intervent Radiol* 2024;47(2):161-176.

57. Orgera G, Tipaldi MA, Laurino F, et al. Techniques and future perspectives for the prevention and treatment of endoleaks after endovascular repair of abdominal aortic aneurysms. *Insights Imaging* 2019;10(1):91.
58. Lal BK, Zhou W, Li Z, et al. Predictors and outcomes of endoleaks in the Veterans Affairs Open Versus Endovascular Repair (OVER) Trial of Abdominal Aortic Aneurysms. *J Vasc Surg* 2015;62(6):1394-1404.
59. Warein E, Feugier P, Chaufour X, et al. Amplatzer Plug to Occlude the Internal Iliac Artery During Endovascular Aortic Aneurysm Repair: A Large Multicenter Study. *Eur J Vasc Endovasc Surg* 2016;51(5):641-6.
60. Kouvelos GN, Katsargyris A, Antoniou GA, Oikonomou K, Verhoeven ELG. Outcome after Interruption or Preservation of Internal Iliac Artery Flow During Endovascular Repair of Abdominal Aorto-iliac Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2016;52(5):621-634.
61. Maleux G, Poorteman L, Laenen A, et al. Incidence, etiology, and management of type III endoleak after endovascular aortic repair. *J Vasc Surg* 2017;66(4):1056-1064.
62. Chen J, Stavropoulos SW. Management of Endoleaks. *Semin Intervent Radiol* 2015;32(3):259-64.
63. Antoniou GA, Georgiadis GS, Antoniou SA, et al. Late Rupture of Abdominal Aortic Aneurysm After Previous Endovascular Repair: A Systematic Review and Meta-analysis. *Journal of Endovascular Therapy* 2015;22(5):734-744.
64. Rajendran S, May J. Late rupture of abdominal aortic aneurysm after endovascular repair. *J Vasc Surg* 2017;65(1):52-57.
65. Wyss TR, Brown LC, Powell JT, Greenhalgh RM. Rate and predictability of graft rupture after endovascular and open abdominal aortic aneurysm repair: data from the EVAR Trials. *Ann Surg* 2010;252(5):805-12.
66. Andersson M, Talvitie M, Benson L, Roy J, Roos H, Hultgren R. A population-based study of post-endovascular aortic repair rupture during 15 years. *J Vasc Surg* 2021;74(3):701-710.e3.
67. Baderkhan H, Wanhainen A, Haller O, Björck M, Mani K. Editor's Choice - Detection of Late Complications After Endovascular Abdominal Aortic Aneurysm Repair and Implications for Follow up Based on Retrospective Assessment of a Two Centre Cohort. *Eur J Vasc Endovasc Surg* 2020;60(2):171-179.
68. Jordan WD, Jr., Ouriel K, Mehta M, et al. Outcome-based anatomic criteria for defining the hostile aortic neck. *J Vasc Surg* 2015;61(6):1383-1390.
69. Müller-Eschner M, Rengier F, Partovi S, et al. Accuracy and variability of semiautomatic centerline analysis versus manual aortic measurement techniques for TEVAR. *Eur J Vasc Endovasc Surg* 2013;45(3):241-7.
70. Mora C, Marcus C, Barbe C, Ecartot F, Long A. Measurement of Maximum Diameter of Native Abdominal Aortic Aneurysm by Angio-CT: Reproducibility is Better with the Semi-automated Method. *European Journal of Vascular and Endovascular Surgery* 2014;47(2):139-150.
71. Väärämäki S, Salenius J-P, Pimenoff G, Uurto I, Suominen V. Systematic Long-term Follow Up After Endovascular Abdominal Aortic Aneurysm

- Repair With the Zenith Stent Graft. *European Journal of Vascular and Endovascular Surgery* 2019;58(2):182-188.
72. Grootes I, Barrett JK, Ulug P, et al. Predicting risk of rupture and rupture-preventing reinterventions following endovascular abdominal aortic aneurysm repair. *Br J Surg* 2018;105(10):1294-1304.
73. Smith T, Quencer KB. Best Practice Guidelines: Imaging Surveillance After Endovascular Aneurysm Repair. *American Journal of Roentgenology* 2020;214(5):1165-1174.
74. Rokosh RS, Wu WW, Schermerhorn M, Chaikof EL. Society for Vascular Surgery implementation of clinical practice guidelines for patients with an abdominal aortic aneurysm: Postoperative surveillance after abdominal aortic aneurysm repair. *J Vasc Surg* 2021;74(5):1438-1439.
75. Geraedts ACM, Mulay S, Vahl AC, et al. Editor's Choice - Post-operative Surveillance and Long Term Outcome after Endovascular Aortic Aneurysm Repair in Patients with an Initial Post-operative Computed Tomography Angiogram Without Abnormalities: the Multicentre Retrospective ODYSSEUS Study. *European Journal of Vascular and Endovascular Surgery* 2022;63(3):390-399.
76. Antoniou GA, Kontopodis N, Rogers SK, et al. Editor's Choice - Meta-Analysis of Compliance with Endovascular Aneurysm Repair Surveillance: The EVAR Surveillance Paradox. *European Journal of Vascular and Endovascular Surgery* 2023;65(2):244-254.
77. Zettervall SL, Schanzer A. ESVS 2024 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms: A North American Perspective. *European Journal of Vascular and Endovascular Surgery* 2024;67(2):187-189.
78. FDA advisory Panel Recommendations on Lifelong Surveillance and Long-Term Postmarket Data Collection for Patients with AAA Endovascular Aortic Repair - Letter to Health Care Providers. In: Administration FaD, ed.2022.
79. McDonald JS, McDonald RJ, Carter RE, Katzberg RW, Kallmes DF, Williamson EE. Risk of intravenous contrast material-mediated acute kidney injury: a propensity score-matched study stratified by baseline-estimated glomerular filtration rate. *Radiology* 2014;271(1):65-73.
80. Hemmett J, Er L, Chiu HH, Cheung C, Djurdjev O, Levin A. Time to revisit the problem of CIN? The low incidence of acute kidney injury with and without contrast in hospitalized patients: an observational cohort study. *Can J Kidney Health Dis* 2015;2:38.
81. European Society of urogenital radiology. ESUR guidelines on contrast agents. (<https://www.esur.org/esur-guidelines-on-contrast-agents/>). Access date Feb 5, 2024.
82. American college of radiology Committee on Drugs and Contrast Media. ACR Manual on Contrast Media. ([https://www.acr.org/-/media/ACR/files/clinical-resources/contrast\\_media.pdf](https://www.acr.org/-/media/ACR/files/clinical-resources/contrast_media.pdf)). Access date Feb 5, 2024.
83. Matthews EO, Pinchbeck J, Elmore K, Jones RE, Moxon JV, Golledge J. The reproducibility of measuring maximum abdominal aortic aneurysm diameter from ultrasound images. *The Ultrasound Journal* 2021;13(1):13.

84. Bredahl KK, Taudorf M, Lönn L, Vogt KC, Sillesen H, Eiberg JP. Contrast Enhanced Ultrasound can Replace Computed Tomography Angiography for Surveillance After Endovascular Aortic Aneurysm Repair. *European Journal of Vascular and Endovascular Surgery* 2016;52(6):729-734.
85. Abraha I, Luchetta M, Florio R, et al. Ultrasonography for endoleak detection after endoluminal abdominal aortic aneurysm repair. *Cochrane Database of Systematic Reviews* 2017;6.
86. Council NR. *Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase 2*. Washington, DC: The National Academies Press, 2006.
87. Nyheim T, Staxrud LE, Jørgensen JJ, Jensen K, Olerud HM, Sandbæk G. Radiation exposure in patients treated with endovascular aneurysm repair: what is the risk of cancer, and can we justify treating younger patients? *Acta Radiologica* 2017;58(3):323-330.
88. IAEA. *Radiation in Everyday Life*. (<https://www.iaea.org/Publications/Factsheets/English/radlife>). Access date March 5, 2024
89. Kalender G, Lisy M, Stock UA, Endisch A, Kornberger A. Identification of Factors Influencing Cumulative Long-Term Radiation Exposure in Patients Undergoing EVAR. *Int J Vasc Med* 2017;2017:9763075.
90. IAEA. *Radiation doses in interventional procedures*. (<https://www.iaea.org/resources/rpop/health-professionals/interventional-procedures/radiation-doses-in-interventional-fluoroscopy>). Access date March 5, 2024
91. Martínez LI, Esteban C, Riera C, Altés P, Llagostera S. Endovascular Infrarenal Aortic Aneurysm Repair Performed in a Hybrid Operating Room Versus Conventional Operating Room Using a C-Arm. *Annals of Vascular Surgery* 2020;69:366-372.
92. Rial R, Vañó E, Del Río-Solá ML, et al. National Diagnostic Reference Levels for Endovascular Aneurysm Repair and Optimisation Strategies. *European Journal of Vascular and Endovascular Surgery* 2020;60(6):837-842.
93. de Ruiter QM, Reitsma JB, Moll FL, van Herwaarden JA. Meta-analysis of Cumulative Radiation Duration and Dose During EVAR Using Mobile, Fixed, or Fixed/3D Fusion C-Arms. *J Endovasc Ther* 2016;23(6):944-956.
94. Lerisson E, Patterson BO, Hertault A, et al. Intraoperative cone beam computed tomography to improve outcomes after infrarenal endovascular aortic repair. *J Vasc Surg* 2022;75(3):1021-1029.
95. Törnqvist P, Dias N, Sonesson B, Kristmundsson T, Resch T. Intra-operative Cone Beam Computed Tomography can Help Avoid Reinterventions and Reduce CT Follow up after Infrarenal EVAR. *European Journal of Vascular and Endovascular Surgery* 2015;49(4):390-395.
96. Tenorio ER, Oderich GS, Sandri GA, et al. Prospective nonrandomized study to evaluate cone beam computed tomography for technical assessment of standard and complex endovascular aortic repair. *J Vasc Surg* 2020;71(6):1982-1993.

97. Goudekettig SR, Heinen SGH, Ünlü Ç, et al. Pros and Cons of 3D Image Fusion in Endovascular Aortic Repair: A Systematic Review and Meta-analysis. *Journal of Endovascular Therapy* 2017;24(4):595-603.
98. Koutouzi G, Sandström C, Roos H, Henrikson O, Leonhardt H, Falkenberg M. Orthogonal Rings, Fiducial Markers, and Overlay Accuracy When Image Fusion is Used for EVAR Guidance. *European Journal of Vascular and Endovascular Surgery* 2016;52(5):604-611.
99. Hertault A, Maurel B, Midulla M, et al. Editor's Choice – Minimizing Radiation Exposure During Endovascular Procedures: Basic Knowledge, Literature Review, and Reporting Standards. *European Journal of Vascular and Endovascular Surgery* 2015;50(1):21-36.
100. Modarai B, Haulon S, Ainsbury E, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on Radiation Safety. *European Journal of Vascular and Endovascular Surgery* 2023;65(2):171-222.
101. Fleischmann D, Afifi RO, Casanegra AI, et al. Imaging and Surveillance of Chronic Aortic Dissection: A Scientific Statement From the American Heart Association. *Circulation: Cardiovascular Imaging* 2022;15(3).
102. Alfonsi J, Murana G, Smeenk HG, et al. Open surgical repair of post-dissection thoraco-abdominal aortic aneurysms: early and late outcomes of a single-centre study involving over 200 patients. *Eur J Cardiothorac Surg* 2018;54(2):382-388.
103. Goldstone AB, Chiu P, Baiocchi M, et al. Interfacility Transfer of Medicare Beneficiaries With Acute Type A Aortic Dissection and Regionalization of Care in the United States. *Circulation* 2019;140(15):1239-1250.
104. Tong MZ, Eagleton MJ, Roselli EE, et al. Outcomes of Open Versus Endovascular Repair of Descending Thoracic and Thoracoabdominal Aortic Aneurysms. *The Annals of Thoracic Surgery* 2022;113(4):1144-1152.
105. Kreibich M, Siepe M, Berger T, et al. The Frozen Elephant Trunk Technique for the Treatment of Type B and Type Non-A Non-B Aortic Dissection. *Eur J Vasc Endovasc Surg* 2021;61(1):107-113.
106. Hellgren T, Kuzniar M, Wanhainen A, Steuer J, Mani K. Clinical and Morphologic Outcomes of Endovascular Repair for Subacute and Chronic Type B Aortic Dissection. *Ann Vasc Surg* 2020;72:390-390.
107. Qin Y-L, Deng G, Li T-X, Jing R-W, Teng G-J. Risk factors of incomplete thrombosis in the false lumen after endovascular treatment of extensive acute type B aortic dissection. *J Vasc Surg* 2012;56(5):1232-1238.
108. Yuan X, Mitsis A, Mozalbat D, Nienaber CA. Novel Endovascular Management of Proximal Type A (DeBakey II) Aortic Dissection With a Patent Foramen Ovale Occluder. *J Endovasc Ther* 2017;24(6):809-813.
109. Yates MT, Lopez-Marco A, Lee M, et al. Decision making of a specialist Aortovascular multidisciplinary team meeting. *AME SurgicalJournal* 2021;2
110. Dohle DS, Laverne T, Bavaria J, et al. Aortic remodelling after thoracic endovascular aortic repair in acute and chronic type B aortic dissections. *Eur J Cardiothorac Surg* 2020;58(4):730-737.
111. The\_Virtue\_Registry\_Investigators. Mid-term Outcomes and Aortic Remodelling After Thoracic Endovascular Repair for Acute, Subacute, and

- Chronic Aortic Dissection: The VIRTUE Registry. *European Journal of Vascular and Endovascular Surgery* 2014;48(4):363-371.
112. Saricilar EC, Patel K, Gatmaitan R, Puttaswamy V. Editor's Choice – Optimal Timing of Thoracic Endovascular Aortic Repair for Uncomplicated Type B Aortic Dissection: A Systematic Review and Meta-Analysis. *European Journal of Vascular and Endovascular Surgery* 2023;65(6):851-860.
  113. Brunkwall J, Kasprzak P, Verhoeven E, et al. Endovascular Repair of Acute Uncomplicated Aortic Type B Dissection Promotes Aortic Remodelling: 1 Year Results of the ADSORB Trial. *European Journal of Vascular and Endovascular Surgery* 2014;48(3):285-291.
  114. Nienaber CA, Rousseau H, Eggebrecht H, et al. Randomized Comparison of Strategies for Type B Aortic Dissection. *Circulation* 2009;120(25):2519-2528.
  115. Hata Y, Iida O, Asai M, et al. Endovascular entry closure using Amplatzer vascular plug for the aortic dissection in sub-acute phase. *J Cardiol Cases* 2018;17(4):111-115.
  116. Chang G, Wang H, Chen W, Yao C, Li Z, Wang S. Endovascular repair of a type B aortic dissection with a ventricular septal defect occluder. *J Vasc Surg* 2010;51(6):1507-9.
  117. Li B, Khan S, Salata K, et al. A systematic review and meta-analysis of the long-term outcomes of endovascular versus open repair of abdominal aortic aneurysm. *J Vasc Surg* 2019;70(3):954-969.
  118. Moulakakis KG LA, Georgiadis GS, Kakkos S, et al. Multicentre Greek Study Assessing the Outcome of Late Rupture After Endovascular Abdominal Aortic Aneurysm Repair. *Eur J Vasc Endovasc Surg* 2023 Dec;26:((23)01043-2.
  119. Yei K, Mathlouthi A, Naazie I, Elsayed N, Clary B, Malas M. Long-term Outcomes Associated With Open vs Endovascular Abdominal Aortic Aneurysm Repair in a Medicare-Matched Database. *JAMA Network Open* 2022;5(5):e2212081-e2212081.
  120. Abbas A, Hansrani V, Sedgwick N, Ghosh J, McCollum CN. 3D contrast enhanced ultrasound for detecting endoleak following endovascular aneurysm repair (EVAR). *Eur J Vasc Endovasc Surg* 2014;47(5):487-92.
  121. Lowe C, Abbas A, Rogers S, Smith L, Ghosh J, McCollum C. Three-dimensional contrast-enhanced ultrasound improves endoleak detection and classification after endovascular aneurysm repair. *J Vasc Surg* 2017;65(5):1453-1459.
  122. Ghulam Q, Bredahl K, Eiberg J, et al. Three-dimensional ultrasound is a reliable alternative in endovascular aortic repair surveillance. *J Vasc Surg* 2021;74(3):979-987.
  123. Fursevich DM, LiMarzi GM, O'Dell MC, Hernandez MA, Sensakovic WF. Bariatric CT Imaging: Challenges and Solutions. *RadioGraphics* 2016;36(4):1076-1086.
  124. Cao C-F, Ma K-L, Shan H, et al. CT Scans and Cancer Risks: A Systematic Review and Dose-response Meta-analysis. *BMC Cancer* 2022;22(1):1238.
  125. Vardhanabhuti V, Loader RJ, Mitchell GR, Riordan RD, Roobottom CA. Image Quality Assessment of Standard- and Low-Dose Chest CT Using

- Filtered Back Projection, Adaptive Statistical Iterative Reconstruction, and Novel Model-Based Iterative Reconstruction Algorithms. *American Journal of Roentgenology* 2013;200(3):545-552.
126. Koetzier LR, Mastrodicasa D, Szczykutowicz TP, et al. Deep Learning Image Reconstruction for CT: Technical Principles and Clinical Prospects. *Radiology* 2023;306(3):e221257.
127. An H, Xie R, Ge Y, Wang T. Progress of CT aortic angiography combined with coronary artery in the evaluation of acute aortic syndrome. *Front Cardiovasc Med* 2022;9:1036982.
128. Schuurmann RCL, De Rooy PM, Bastos Gonçalves F, Vos CG, De Vries J-PPM. A systematic review of standardized methods for assessment of endograft sealing on computed tomography angiography post-endovascular aortic repair, and its influence on endograft-associated complications. *Expert Review of Medical Devices* 2019;16(8):683-695.
129. Zuidema R, Geraedts ACM, van Veldhuizen WA, et al. Diminishing Endograft Apposition during Follow-Up Is an Important Indicator of Late Type 1a Endoleak after Endovascular Aneurysm Repair. *Journal of Clinical Medicine* 2023;12(12):3969.