EVAR of AAA: Long term outcomes, disease progression and risk stratification

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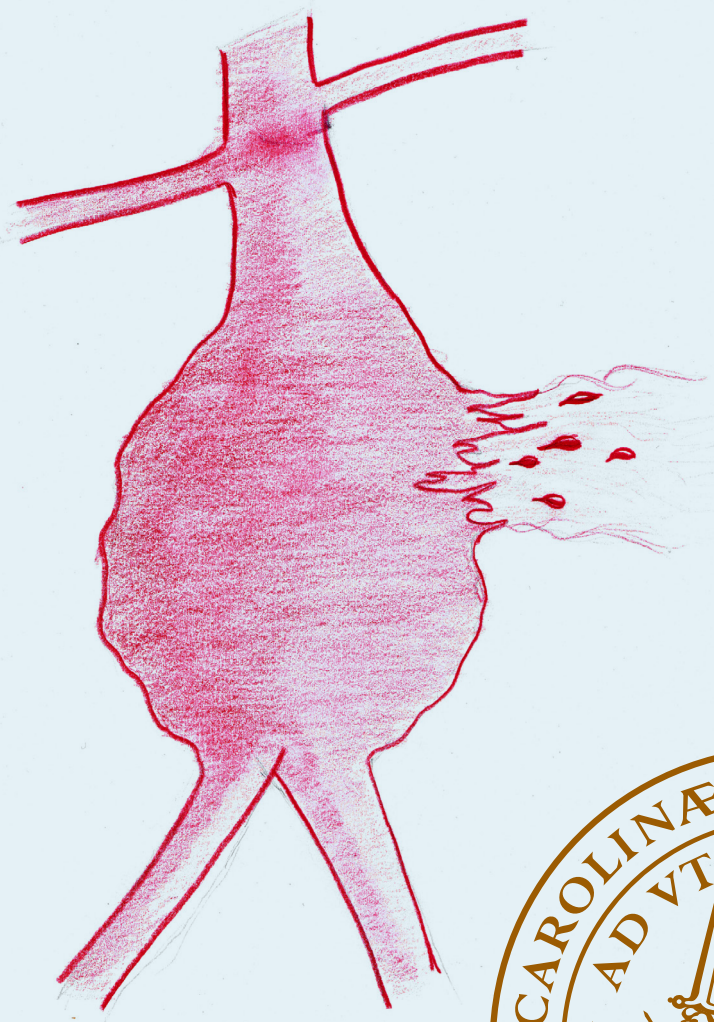
MOHAMMED ABDULRASAK
FACULTY OF MEDICINE | LUND UNIVERSITY



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EVAR of AAA:
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Mohammed Abdulrasak

LUND
UNIVERSITY

DOCTORAL DISSERTATION

By due permission of the Faculty of Medicine, Lund University, Sweden.
To be defended on the 18th March, 2020.

Faculty opponent
Professor Hence Verhagen
Erasmus University Medical Center, Rotterdam, the Netherlands

Organization LUND UNIVERSITY Department of clinical sciences, Malmö Vascular Center, Skåne University Hospital Author: **Mohammed Abdulrasak**	**Document name** DOCTORAL DISSERTATION **Date of issue** 18th March, 2020 Sponsoring organization

Title and subtitle:
EVAR of AAA: Long term outcomes, disease progression and risk stratification

Abstract

Background
Endovasvular aortic repair (EVAR) is the most commonly utilised technique for the treatment of abdominal aortic aneurysms (AAA) in tertiary referral centers. Detailed long-term outcomes of this technique are relatively scarce, especially for patients presenting symptomatically with AAA. Intra-operatively, proximal type Ia endoleak, involving blood circulating into the AAA – due to poor proximal seal of the endograft to the aortic neck region – is a feared complication which is usually promptly treated, given its association with post-operative AAA expansion and rupture. Aneurysmatic disease is usually considered a progressive pathology with potential for progression to areas of the aorta beyond the known aneurysmatic segment. Arterial calcifications are established as a marker for atherosclerosis, yet the association of ilio-femoral calcification with post-operative mortality after EVAR is not known.

Aims
1. Evaluate the long-term results of EVAR of AAA using a single endograft
2. Compare the early and late results of EVAR of symptomatically presenting patients to those treated asymptomatically
3. Study the long-term results of intra-operative treatment of type Ia endoleak using large, balloon-expandable stents
4. Study the progression of aortic disease for patients treated with endovascular means in the post-operative period
5. Assess the novel ilio-femoral calcium score as a potential predictor for overall and cardiac-specific mortality after EVAR

Results
EVAR of AAA yields sustainable results in the long-term, for both symptomatic and asymptomatic patients. There is ≈ x4 elevated early mortality in symptomatic patients as compared to asymptomatic ones. Intra-operative treatment of type Ia endoleaks using large, balloon-expandable stents should be reserved to patients treated acutely with EVAR. Aortic expansion beyond the sealing zone is relatively uncommon, and seems related to the force exerted on the aortic wall by the endograft. Ilio-femoral calcium score may predict long-term overall and cardiac mortality after EVAR, albeit the relation is weak. Therefore, further studies are needed to establish this association.

Key words: abdominal aortic aneurysm, Endovascular aortic repair, ilio-femoral calcium score, type Ia endoleak

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Coverphoto by H.Abdulrasak, representing an artistic illustration of an aneurysm rupture

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وَفَوْقَ كُلِّ ذِى عِلْمٍ عَلِيمٌ

But over every possessor of knowledge is the All-knower

The holy Quran, Yusuf, verse 76

Dedicated to my parents

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Abbreviations

(r)AAA	(ruptured) abdominal aortic aneurysm
(F)EVAR	(Fenestrated) Endovascular aortic repair
IBD	iliac branched device
CTA	computed tomography angiography
CT/TC	Celiac trunk (used interchangeably)
SMA	Superior mesenteric artery
RRA	Right renal artery
LRA	Left renal artery
PTFE	Polytetrafluoroethylene
BESG	balloon expandable stentgraft
SESG	Self expanding stentgraft
EVAS	EndoVascular Aneurysm Sealing
OR	Open repair
AD	aortic neck dilatation
IFU	instructions for use
RCT	randomised controlled trial
KM	Kaplan – Meier (curves)

List of papers

1. **Abdulrasak M**, Sonesson B, Singh B, Resch T, Dias NV. Long-term outcomes of infrarenal endovascular aneurysm repair with a commercially available stent graft. Journal of vascular surgery. 2019. *In press*
2. **Abdulrasak M**, Sonesson B, Vaccarino R, Singh B, Resch T, Dias NV. EVAR for symptomatic AAAs has comparable results to elective repair in the long-term. *Submitted manuscript*
3. **Abdulrasak M**, Resch T, Sonesson B, Holst J, Kristmundsson T, Dias NV. The Long-term Durability of Intra-operatively Placed Palmaz Stents for the Treatment of Type Ia Endoleaks After EVAR of Abdominal Aortic Aneurysm. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2017;53(1):69-76.
4. **Abdulrasak M**, Sonesson B, Resch T, Dias NV. Fate of visceral and supravisceral aortic segment after EVAR and FEVAR. *In manuscript*
5. Vaccarino R*, **Abdulrasak M** *, Resch T, Edsfeldt A, Sonesson B, Dias NV Low Ilio-femoral Calcium Score may predict higher survival after EVAR and FEVAR. *Submitted manuscript*.
   *Equal contribution

Introduction

AAA: diagnosis and repair outcomes

Etymology and short anatomical preface

The word aorta originates from the ancient Greek word *aorté*, meaning "the arteries originating from the heart",[1] while the word aneurysm originates in the Greek words "aneurunein" (widen out) and "aneurusma" (dilatation).[2]

An aortic aneurysm is a dilatation of the aorta involving the three layers comprising the vessel wall (tunica intima; media and adventitia).[3] These are mainly due to degenerative process of the vessel wall, and less commonly due to infectious or inflammatory processes. The most common location for the development of an aortic aneurysm is infrarenally.[4] Aortic aneurysms are defined, size-wise, either as a dilatation ≥ 30 mm or ≥ x1.5 increase in diameter relative to the normal aortic diameter, suprarenally.[5] The prevalence of AAAs in the population is variable, reported to be at around 1.5 – 8 %[6-8] depending on the age of participants and location of the study performed.

Establishing of AAA Diagnosis

Given the generally indolent nature of aneurysmatic disease, clinical diagnosis is challenging. Diagnosing by abdominal palpation has low sensitivity and specificity, especially when performed by inexperienced physicians.[9] Incidental diagnosis through abdominal X-Rays is possible, through e.g rim calcification.[10] However, this is of low specificity as well. The increased use of computed tomography angiography (CTA) has made the establishment of the diagnosis easier, given the ≈ 100% sensitivity,[11,12] especially if done with intravenous contrast administration. This provides good quality imaging especially for operative decision making.[13] However, CT is associated with high doses of radiation,[14] along with risk of renal impairment when contrast administration occurs,[15] make CT unsuitable for population screening. Ultrasound (US) has > 90% sensitivity and specificity for AAA diagnosis[16] and, albeit being dependent on both user experience and patient-related factors (mainly abdominal gaseous distension and adiposity),[17] it is a good method for screening given the speed it can be performed.[18]

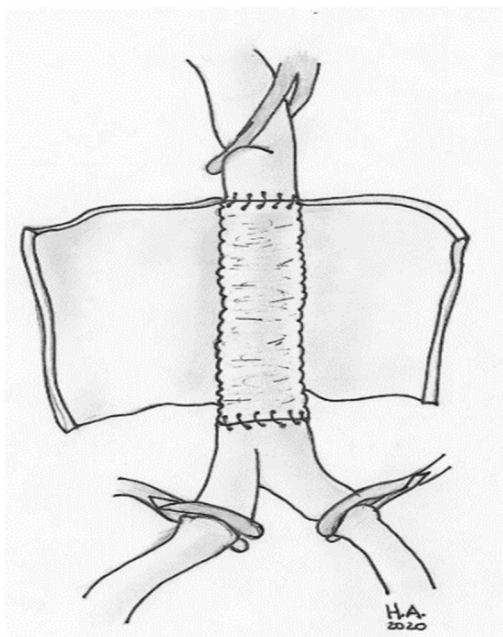
In spite of AAAs being generally silent,[19] there can be dramatic presentations involving abdominal pain, back or flank pain, and groin pains.[20] These symptoms arise due to pressure causing irritation of the abdominal musculature and associated nervous structures. If the AAA ruptures, these symptoms may be accentuated due to blood causing additional irritation, alongside the exsanguination causing hypotension, syncope and death.[21]

Treatment options

Open repair

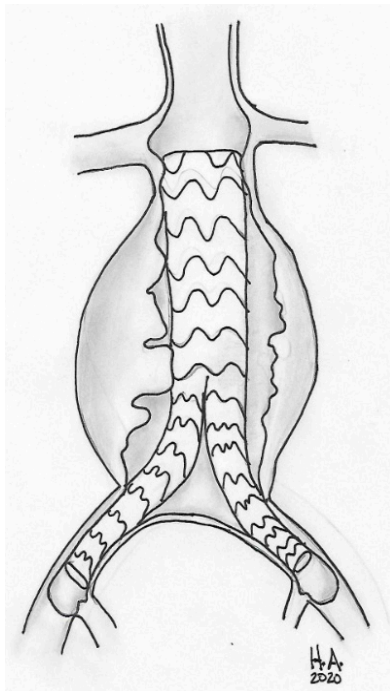
Several "open" methods were used to treat aortic aneurysms. These involved, amongst others, "wire-induced" thrombosing of aneurysmal clot formation,[22] "wrapping" the aneurysm with various materials (cellophane, polyethene plastic)[23] and simple ligation of the aorta after rupture.[24] Endoaneurysmorrhaphy,[25] a technique employed during the the first portion of the 20th century, involving opening the aneurysmal sac and approximating it to a normal lumen size, was also employed. Afterwards, developments towards aneurysmal resection where replacement with native material (e.g autologous femoral vein)[26] and, ultimately, synthetic (polyester or PTFE; Polytetrafluoroethylene)[27,28] sutured inside the aortic sac, where the aortic sac is left in situ surrounding the synthetic "tube".

The current standard of care, when it comes to open repair (OR)[29] of an infrarenal AAA, in short, involves the exposure of the retroperitoneum either through a midline, transverse or retroperitoneal incision. Afterwards clamps are placed proximally infrarenally (or suprarenally in more complex repairs) and distally at the level of the common iliac vessels, the aortic sac is then opened, whereby a synthetic tube graft is sutured proximally close to the lowest renal artery, and distally to the aortic bifurcation. Afterwards the clamps are removed, the aneurysmal sac is sutured around the tube graft, and the abdomen closed (*Figure 1, inset*).



Endovascular repair

Endovascular repair (EVAR) was established in the Ukraine by Nicholay Volodos in 1987 through repair of a thoracic aortic aneurysm,[30] with its popularisation through the work of Juan Parodi[31] and his travels to the United States to perform EVAR cases there. The main principle of EVAR (*figure 2, inset*) is to introduce (usually through the common femoral artery in the groin) a stentgraft, made of (usually) synthetic fabric and metallic supporting "skeleton", into the aorta to divert the flow of blood from the inside of the aneurysm wall into a more laminar flow through the introduced endograft, thereby de-pressurizing the aneurysm and potentially causing aneurysm to regress in size, essentially decreasing the risk for AAA rupture.[32] Several designs and materials are used to attain durable aneurysm repair, with grafts that have fenestrations (FEVAR) or branches to accommodate for complex (thoracoabdominal and juxtrarenal) aneurysms[33] involving visceral vessels**.**



Endografts and imaging

A stentgraft requires proximal and distal anchoring. This may be achieved through the action of rigid, balloon-expandable stentgrafts (BESG) fixating the seal, or through the action of self-expandable stentgrafts (SESG).[34] Most of the current-generation endografts are SESGs. Endografts are usually sized larger than the aortic neck, so called "oversizing".[35] This is done to ensure improved graft conformability to the aortic neck. Oversizing is recommended to 10 – 20 % and in some studies < 30 %. Insufficient oversizing yields poor seal with elevated risk for type I endoleak, while excessive oversizing may be associated with aneurysm expansion, albeit aortic neck dilatation was not observed.[36]

Apart from the standard EVAR grafts, the concept of EVAS (EndoVascular Aneurysm Sealing) emerged in later years. Such concept uses polymer filled "endobags" with embedded grafts to allow for blood flow. Mid-term results suggest high rates of type I endoleaks, AAA enlargement and rupture for patients treated using this concept.[37]

Imaging, both pre-operatively for procedural planning and for the sake of follow-up, is an integral part of the EVAR process. High resolution CTA[38] is the most commonly used imaging modality for EVAR planning, given the ease and speed at

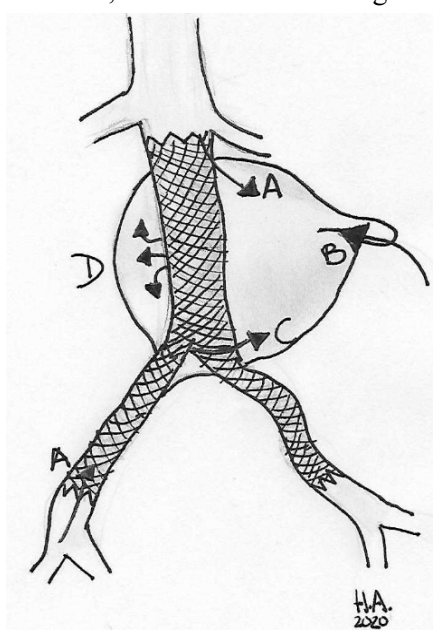
which imaging is acquired. In addition, a high degree of 3D-postprocessing is available through different computer software, thus aiding graft choice and intra-operative graft placement. For the sake of follow-up, US is usually used in standard infrarenal repair, while CTA is the main modality used for complex repairs, to screen for complications such as progressive branch thrombosis.[39]

Open vs EVAR outcomes

Open repair has been compared to EVAR (for AAA-treatment) in 4 trials, EVAR-1 (UK)[40], DREAM (Netherlands)[41], ACE (France)[42] and OVER (USA)[43]. The main results from these trials were the superiority of EVAR versus open repair with regards to early (up to about 3 years) post-operative survival. This survival advantage is however lost after this period. AAA-related mortality in the late (>8 years post-operatively) was higher in the EVAR group (except in the OVER trial, no difference), especially with regards to late aneurysm rupture. The rate of post-operative interventions was also higher in the EVAR group as compared to open repair in these trials, albeit the absolute majority of these interventions are amendable through procedures under local anaesthesia. A problematic aspect with regards to the aforementioned trials is the usage of older-generation endografts, where a higher rate of device-associated failures were present compared to current devices. In addition, higher degree of inexperience was present during the previous trials, given that relative infancy of EVAR at the early stage the trials were initiated.

Long-term Open repair vs EVAR complications

Open repair, as with other open abdominal procedures, is associated with higher peri-operative mortality[44] than EVAR, mainly secondary to the intra-operative "stress" associated with the procedure. Post-operatively, however, open repair is associated, amongst others, with incisional hernias,[45] risk for bowel obstruction due to adherences[46] and (rarely) potential of aorto-enteric fistula[47] formation.



On the other hand, EVAR is associated with some specific complications. One potential problem with EVAR is migration,[48] where the stentgraft may move (usually caudally) due to poor seal proximally. Blood coming into an endovascularly excluded aneurysm, namely "endoleak", is another complication.[49] There are three main types of endoleaks, where types I and III are the most clinically relevant. Type I endoleak (*figure 3*, inset, A) is

associated with poor seal proximally (type Ia) or distally (type Ib) endoleak. Type III (C) endoelaks occur due to separation of graft components (type IIIa) or fabric damage (type IIIb) causing blood to enter the aneurysm sac. Both these endoleaks occur at a high pressure and are associated with aneurysmal expansion and rupture. Type II endoleak (B), due to "back-bleeding" of (often) lumbar or inferior mesenteric arteries, is of lower pressure perfusion and is rarely associated with adverse outcomes. Type IV endoleak (D) occur due to porosity of graft wall material, causing bleeding through the graft material into the aneurysm sac. Endotension (type V endoleak) involves AAA expansion without demonstrable cause.

Limb thrombosis, where stentgraft limbs occlude, is yet another complication,[50,51] which may need urgent intervention (thrombolysis, re-stenting) depending on the presenting symptoms. As with OR, EVAR is also associated with a small risk of post-operative graft infection and the potential for fistula formation.[52]

Type Ia endoleaks

This type of endoleaks occur due to poor proximal sealing of the graft to the aortic wall,[53] causing circulation of the aortic sac and expansion.[54] Risk factors for developing type I endoleaks include short aortic neck,[55] increased tortuosity and thrombus-ridden aortic neck.[56] This may be discovered intra-operatively, or during follow-up.[57]

Intra-operative treatment of the type Ia endoleak may involve, initially, the proximal ballooning (and re-ballooning) of the upmost graft portion to ensure increased seal and conformity of the used stentgraft to the aortic neck.[58] If this does not yield ceasing of the endoleak, use of large bare-metal stents,[60,61] proximal cuffs[62,63] and endoanchors[64,65] may be justified. In select cases, observation of the type Ia endoleak may be justified with early follow-up imaging, with deferral of corrective procedure based on the outcome of the conservative approach.[66]

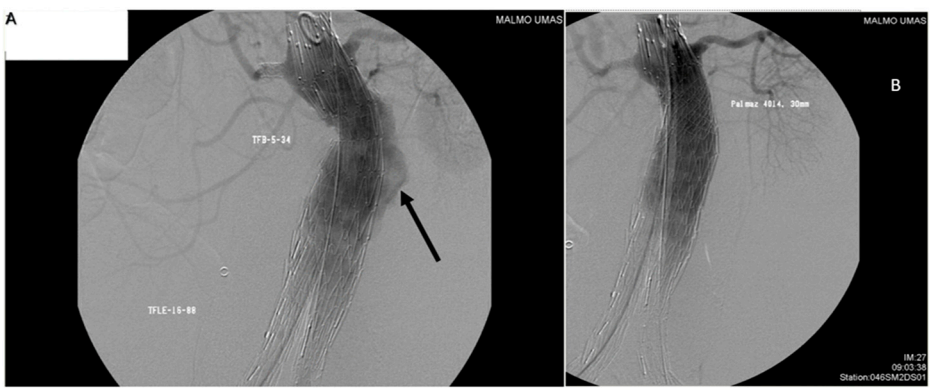


Figure 4 – Intra-operative type Ia endoleak (arrow), treated by insertion of a Palmaz™ stent (Palmaz P4014; Cordis, Miami Lakes, FL, USA)

Late treatment, when the endoleak is found during the follow-up, may involve the aforementioned techniques in combination and/or selectively. In addition, custom-made fenestrated/branched cuffs[67,68] incorporating visceral vessels may be of use to ensure increased seal. Endoanchors, mentioned previously, may also be employed in the late treatment of type Ia endoleak Embolisation of aneurysmal sac with liquid/metallic materials[69] may also be employed, albeit with questionable results and efficacy. Open methods of treatment, such as aortic neck banding,[70] or frank open conversion[71] with the explantation of the stentgraft and insertion of tube/aortobifemoral graft, may be utilized.

Progression of aneurysmatic disease

Given the experimental theories regarding the generation of aortic aneurysms (e.g with regards to increased metalloprotease activity),[72] the presence of a general "degenerative" and "aneurysmatic" tendency within other arterial walls, included of the supra- and infra-aneurysmatic segments, is expected. This partially provides the theoretical basis for strong association of AAAs with other aneurysmatic pathologies.[73-75]

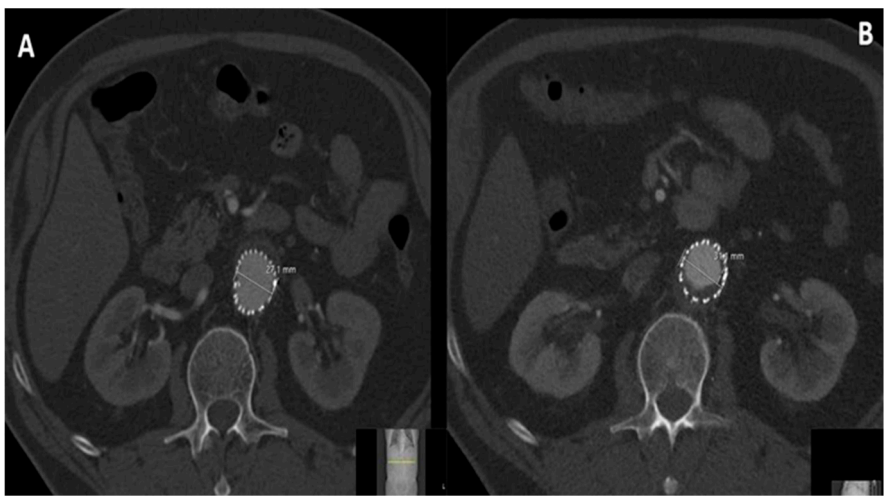


Figure 5 – aortic diameter at first (A) post-operative CTA versus last (B) CTA, measured at 15 mm below lowest renal artery

Aortic neck dilatation (AD) has been reported after both OR and EVAR. In OR, expansion at a rate of ≈ 0.2 – 0.6 mm/year has been reported, in up to a third of treated patients.[76,77] This however carried little clinical relevance.[78] In contrast, AD seems to be more prevalent among patients treated with EVAR, where rates of 1 –

2 mm/year of expansion have been reported in certain studies,[79] with higher expansion rates occurring after EVAR for rAAAs.[80] This translates to around 20 – 45 %[81-83] of all treated patients having some expansion of the neck region. The expansion was more common with regards to patients receiving EVAR with SESG, and not present in patients with BESG.[84,85] The aforementioned expansion has been partially attributed to stentgraft oversizing. Such AD in EVAR patients – commonly studied at renal vessels and infrarenally yet rarely at visceral segment – has been associated with poor post-operative outcomes, with special regards to graft migration, endoleaks formation and post-operative re-interventions.[86,87] Some studies have also suggested an association of AAA sac expansion with increased, concomitant aortic neck dilatation, albeit this finding is not universal.

The reporting standards[88] have proposed some guidelines with regards to standardisation of aortic neck measurements, with the cornerstones being that any diameter changes should be compared to the first post-operative control, and should be presented in an actuarial (life-table) analyses, with time to event and percentage of subjects were event occurred is clearly presented, very few studies abide by these requirements. Both absolute (most often > 2 – 3 mm expansion) and percentage expansions (usually > 20 % diameter) have been utilised. A large proportion of studies that have been performed in this regard have compared the dilatation to the pre-operative measurements. Yet another drawback with the available studies assessing AD post-EVAR is the irregular usage of "measurement markers", whereby some studies used absolute anatomical landmarks (e.g the lowest renal artery), some have utilised aspects of the graft (e.g gold-markers symbolising start of graft; first visible part of graft strut) as a set-point for measurements.

Risk stratification

"Operative" risk stratification

Patients undergoing AAA repair are usually high-risk individuals,[89] given the presence of a multitude of co-morbid conditions relating to (amongst other factors) cigarette smoking, a well-known risk factor for the development of AAAs. This entails elevated operative risk.[90]

A frequently used risk stratification system for the peri-operative risk of surgery is the American society of anaesthesia (ASA) classification.[91] This, however, is a general system that does not pertain to the potential differences posed in different surgical disciplines given its broad applications.[92] The Goldman index,[93] predicting cardiac-related mortality in non-cardiac surgery, is a more specific system, yet it does not consider the type surgical intervention performed.

One of the first "aneurysm-surgery specific" indices was the Hardman index (HI).[94] This consisted of 5 variables (age (> 76 years), creatinine (> 190 umol/L), loss of consciousness after arrival, Hb (< 90 g/L), and ECG changes consistent with myocardial ischemia, and was constructed to stratify patients presenting with rAAA to those where surgery could provide a benefit, versus those where operative mortality is too abhorrent to undertake a surgical approach. Other scores with similar goal to the HI include the Vancouver Score (VS),[95] Glasgow Aneurysm score (GAS)[96] and the Edinburgh ruptured aneurysm score (ERAS).[97] These scores have been shown to somewhat underestimate operative mortality, suggesting questionable clinical use.[98,99]

Cardiac risk factors, such as the presence of pre-operative congestive heart failure have constituted major predictors for post-operative mortality and major adverse cardiac events (MACE) in both vascular and non-vascular surgical procedures.[100,101] This is partially highlighted by the aforementioned risk scores which all have cardiac risk factors included in their calculations, along with the presence of major cardiovascular comorbidities in the patients treated for AAAs.

"Imaging-based" stratification

With regards to patients treated with EVAR, being within the instructions for use (IFU) for a stentgraft is one of the first "imaging" considerations with regards to predicting potential operative outcomes. Being within the IFU, generally speaking, entails long aortic neck, presence of parallel aortic walls, along with absence of extensive thrombus. The specific measurements are manufacturer specific (table 1).

Table 1 – Anatomical criteria for some types of stentgrafts commonly used in infrarenal EVAR (Retrieved from the respective company)

Anatomical criterion	Excluder	Zenith	Talent	Endurant II
CFA diameter (mm)	≥ 8	≥ 8	≥ 8	≥ 8
CIA length (mm)	≥ 10	≥ 10	≥ 15	≥ 15
CIA Diameter (mm)	8 – 18.5	7.5 – 20	8 – 22	8 – 25
Neck length (mm)	≥ 15	≥ 15	≥ 10	≥ 10
Neck diameter (mm)	19 – 29	18 – 28	13 – 32	19 – 32
Neck angle (º)	≤ 60	≤ 60	≤ 60	≤ 60

Conflicting reports exist with regards to IFU as a predictor of EVAR outcomes, however there is a tendency towards worse long-term outcomes[102] with regards to higher rates of type Ia endoleaks and re-interventions,[103-105] in patients treated outside the IFU. However, overall survival remains unaffected[106] compared to patients with favourable anatomy, according to available evidence.

Another "imaging consideration" with regards to outcomes is the size of aneurysm to be treated. Smaller aneurysm are associated with lower peri-operative and long-term mortality in contrary to large aneurysms. On the other hand, large aneurysms are associated with higher reinterventions and mortality.[107-109]

Vascular calcification and Calcium (agatston) score

Coronary calcification implies the presence of atherosclerotic process[110] in these vessels. Such calcifications may be found post-mortem during an autopsy,[111] or through imaging studies[112]. This has long been associated with ischemic heart disease, given the fact that vascular calcification implies intimal disease with subsequent risk for vascular plaque formation and rupture.[113,114]

A formalised assessment of calcifications present in the coronary vasculature was presented by Agatston[115], whereby a score of the available calcification in the coronary vessels, derived through non-contrast CT acquisition, was proposed. This is calculated through assignment of a "factor number" to any lesion ≥ 130 Housefield units (HU) (130–199 HU = 1; 200–299 HU = factor 2; 300–399 HU = 3; and ≥ 400 HU = 4). These factor numbers are then multiplied by the area of the lesion specified in mm^3, whereby a sum value for each coronary artery and then, finally, the patient, is calculated in Agatston units (AU). This coronary artery calcium (CAC) score is a predictor of both coronary events[116-118] in populations with cardiovascular risk, and overall mortality in both high and low-risk populations.[119-121] CAC is currently the number one screening method for coronary artery disease in low to medium risk populations, given the high sensitivity and specificity it provides along with the ease of acquisition of the images and the virtually absent influence of patient factors (e.g poor exercise tolerance, obesity) on the results obtained.[122]

The applications of the arterial calcifications have also found place outside the field of cardiology, both as estimation of calcification burden on plain radiographs[123-125] and usage of non-contrast CT to assess for presence of vascular calcification in aortic and iliac vasculature.[126-128] In the aforementioned vascular beds, elevated calcification was associated with increased mortality. There has been studies associating iliac calcifications with mortality and renal function outcomes in patients undergoing renal transplantation, given the operative anastomoses of graft renal artery to the hosts´ iliac circulation.[128]

Thesis objectives

EVAR treatment of AAAs is well established, and increasingly popular in Western Europe, for both elective and ruptured cases.[129,130] The outcomes are well reported, with several advantageous key points with regards to EVAR, such as relatively low operative mortality. However, the post-operative re-intervention rate is higher for EVAR, therefore it is necessary to have detailed outcomes. Previous reports, such as those earlier cited in the comparative RCTs, have been during a time at which the EVAR technique was still in its relative infancy, therefore there was a potential for relative inexperience amongst those operators which may have affected the EVAR outcomes negatively. Another potential bias with regards to the aforementioned trials is the fact that the first generation stentgrafts used in those trials are now obsolete, with many improvements likely yielding better outcomes in the newer generation of stentgrafts. Yet another difference is the usage of EVAR technique in increasingly younger patients, therefore making the need for more improved treatment longevity a necessity. Therefore, **project 1** was used to give a thorough account of relevant outcomes, all of which in patients treated for asymptomatic, non-ruptured infrarenal AAAs with a single stentgraft at our vascular referral centre.

A subgroup of patients undergoing EVAR for AAA which has been somewhat understudied are the patients presenting symptomatically yet without radiographic or clinical signs of aneurysmal rupture. These patients are usually treated semi-urgently within 24 hours of presentation, therefore often not well examined with regards to underlying pre-operative co-morbidities, along with the possible for undermined pre-operative stentgraft planning and thus a hypothetically less befitting endovascular repair anatomically, with the potential post-operative complications (e.g type Ia endoleak and overall increased re-interventions rate) and – in the worst case, aneurysm rupture – related to those treated outside of anatomical restrictions for EVAR. This made **project 2** a springboard for having an elaborative description of the same outcomes reported in project 1, yet with infrarenal AAA patients presenting symptomatically; along with a direct comparison to the "reference group" of asymptomatic cases that project 1 entailed. All the patients in this project were treated in our center, with the same stentgraft system, therefore potentially reducing selection bias.

Type Ia endoleaks are a major cause of EVAR failure and post-operative rupture. These are generally treated aggressively whether they are discovered intra-operatively or during post-operative follow-up. One of the most common methods

for treatment is usage of balloon expandable stents to increase proximal seal of the stentgraft to the aortic neck. Therefore, **project 3** was intended to study the effect of intra-operative placement of Palmaz^{TM} stents for patients treated for infrarenal AAAs, who had an intra-operative type Ia endoleak discovered during angiography. This was for both treatment specific outcomes (e.g type Ia endoleak recurrence) and for general outcomes of treatment success (e.g clinical success).

Aneurysmatic disease is generally described as a progressive disease, therefore the increased likelihood of developing other aneurysms in patient with index aortic aneurysm. Therefore, **project 4** was aimed to study the fate of treated and non-treated segments of the aorta in patients treated for abdominal aneurysms, using both EVAR and FEVAR.

Several methods for operative risk stratification have been formulated. Arterial calcification has been hypothesised to be a means of estimating cardiovascular related mortality as mentioned earlier. Therefore **project 5** was utilised to explore potential association of ilio-femoral calcification with overall and cardiac-specific mortality, using a standardised method (Agatston method), in patients undergoing EVAR and FEVAR with available pre-operative CT.

Aims of the thesis

The general aim of this thesis was to assess the long-term outcomes of EVAR for infrarenal AAA, specifically with regards to intra-operative outcomes, clinical success and survival. Further aims include the assessment of risk stratification after EVAR using the novel ilio-femoral calcium score, and assessment of aneurysmatic disease progression.

The specific aims of the thesis were:

- **Project 1** – To assess the long-term outcomes of elective infrarenal EVAR with regards to long-term survival, re-intervention rates, clinical success, causes for post-operative failure and aneurysm-related mortality, amongst other outcomes
- **Project 2** – To establish the outcomes of infrarenal EVAR in patients presenting symptomatically but without signs of rupture, and compare them to the reference group of asymptomatically treated patients presented in project 1
- **Project 3** – To evaluate the outcomes with regards to intra-operatively detected and treated type Ia endoleak, using a commonly used method of placement of large, balloon – expandable stents (Palmaz^{TM} stent) in patients undergoing infrarenal EVAR, irrespective of their initial presentation (asymptomatic, symptomatic or ruptured), along with an overview of anatomical changes of the aortic neck during follow-up
- **Project 4** – To scrutinize the progression of aneurysmatic disease after infrarenal EVAR and FEVAR during the post-operative follow-up period, with regards to the sealing zone, visceral and supra-visceral aortic segments
- **Project 5**– To investigate the usage of novel marker of ilio-femoral calcification for patients who have underwent infrarenal EVAR and FEVAR, and assess its potential as a marker for assessing post-operative survival in general and, more specifically, cardiac mortality

Materials and methods

General methods applicable to all projects

All the projects within this thesis were ethically approved by the regional ethics committee (Nr 2014/732). Given the retrospective nature of the projects in this thesis, patient consent was waivered.

All the patients included in the aforementioned projects were treated with endovascular means at the index procedure for AAA, at the vascular center in Skåne University hospital, Malmö. The general period for inclusion was within the years 1998 – 2012. The patients were retrospectively included and identified through local patient database, with the subsequent review of available patient files mainly through the local electronic charting system along with, in few cases, usage of paper charts for patients treated in the early part of the study. Available pre- and post-operative imaging was assessed through the local PACS (picture archiving and communication system) software. Intra-operative angiographies and available reports, both for the pre-, intra- and post-operative imaging, were reviewed. Radiology reports were reviewed especially when available imaging was not available due to the archiving of the non-digital imaging. In our center, a shift towards digital imaging occurred around year 2004, making availability of imaging somewhat inconsistent for parts of the thesis.

For all the projects included in the thesis, non-normal distribution was assumed and therefore non-parametric tests were used for the purpose of statistical analyses.

Specific methods for projects

Projects 1, 2 and 3

All patients operated for infrarenal EVAR for AAAs using the Cook-Zenith^{TM} stentgraft system (other grafts as well for project 3), during the years 1998 – 2012, were consecutively included in the study. Project 1 included patients treated for asymptomatic AAA, while project 2 included both patients presenting asymptomatically and symptomatically (but without aneurysm rupture).

Where available, pre-operative CTAs were analysed to assess for pre-treatment aneurysm diameter and neck length (both in mm). The majority of CTAs were at reconstructions with 0.75 – 5 mm apart. Neck length was estimated using the difference between the table position at the start of the aneurysm and the level at which the lowest renal artery is at. Other anatomical aspects, such as aortic neck shape and angulation, were not assessed given the inability to perform three-dimensional (3D) reconstructions for patients with non-digital CTA imaging.

Having neck length ≥ 15 mm was considered being within the IFU. Aneurysmal diameter was estimated by measuring the diameter perpendicular to the long axis to avoid potential overestimations. CTAs were also assessed for signs of rupture for the purpose of exclusion. Pre-operative patient characteristics were collected through chart review, mainly with regards to co-morbidities.

Immediate outcomes, as per the reporting standards, with regards to technical success and 30-day mortality were collected and analysed. The causes for 30-day mortality were registered. Intra-operative adjunctive procedure were registered and reported according to their cause (for project 1). The following causes were used for the sake of intra-operative adjuncts´ classification:

- *Proximal seal – related*: generally due to proximal (type Ia) endoleak and poor intra-operative seal
- *Distal related*: due to either distal endoleaks (type Ib/III) and/or distal limb issues or access – related procedure. This included both open and endovascular adjuncts.
- *Renal – artery related*: Due to concomitant renal stenosis and/or intra-operative renal complications during EVAR requiring treatment
- *Type II Endoleak*: usually embolization of back-bleeding vessels (e.g lumbar arteries or inferior mesenteric artery)

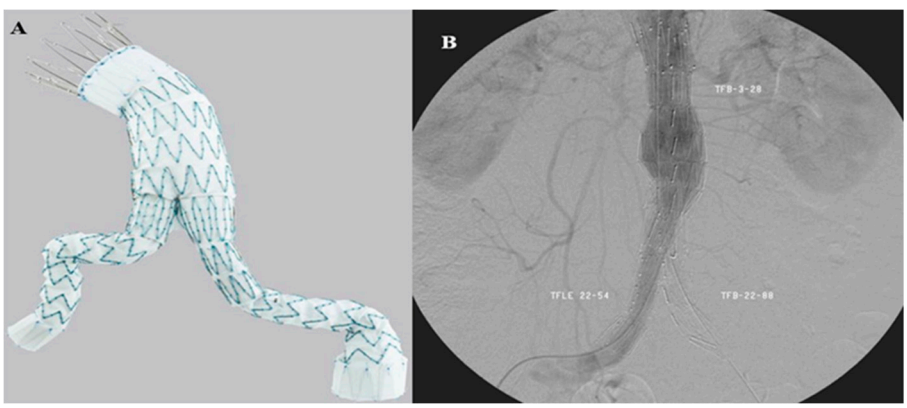


Figure 6 – Zenith Flex system (A, courtesy of Cook), and completion angiography (B) in a patient with successful implantation

Post-operative outcomes were also recorded, from both available charts and imaging. All imaging available in the post-operative period, whether within follow-up programme for EVAR (Ultrasound and/or CTAs) and outside of it, were analysed for AAA-related outcomes. This was done to ensure long follow-up. Serial AAA diameters were measured, with clinically significant expansion entailing ≥ 5 mm diameter increase. In addition, available imaging was assessed for the presence of endoleaks, mainly types I/III, and stentgraft migration; the latter of which considered significant when > 10 mm migration occurred, measured from lowest renal artery to first visible portion of the top-stent on the CTA.

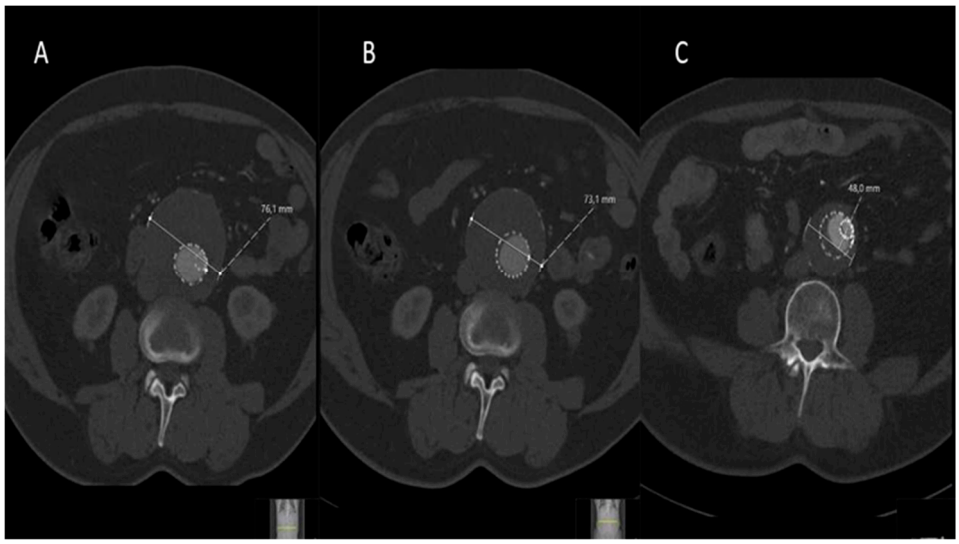


Figure 7– aortic diameter at AAA at 1-month (A), 1-year (B) and last (8 years post-operatively, C) CTA

Post-operatively, clinical success was assessed, as detailed in the reporting standards. Briefly, this entails the absence of post-operative AAA expansion, type I/III endoleak, stentgraft dysfunction and migration. When follow-up was mainly done through ultrasound, absence of significant AAA expansion was used as a marker of clinical success. Clinical success was presented as primary success in the case of no re-interventions were required; primary assisted success in cases where an endovascular re-intervention was needed to achieve success status (e.g post-operative type II endoleak embolization or distal limb re-lining through re-stenting); secondary clinical success was achieved in the cases requiring open re-interventions (e.g sacotomy for post-operative AAA-infection with intact stentgraft left in place). In the cases where the re-interventions were a failure, clinical failure would ensue. In addition, patients who were considered unfit for a re-intervention, or where the magnitude of "clinical failure" (As per the reporting standards) was considered "de facto" clinically irrelevant to justify a re-intervention, clinical failure was registered. The aforementioned decisions were left at the discretion of attending physician.

Open conversions for any reason involving the explantation of parts or the entire stentgraft was considered a clinical failure. Late (or persistent) clinical failure were the main outcome measure when assessing clinical failure.

In the cases where post-operative re-interventions were used, causes for this were recorded, along with type of re-intervention required. In the cases where post-operative AAA-related mortality occurred, the cause of this was recorded. The Swedish mortality registry, along with available patient files, were used to derive the cause of death for included patients.

Life-table analyses were used to assess for the following outcomes: freedom from type I/III endoleaks, freedom from re-interventions, clinical success, overall mortality and freedom from late-AAA-related mortality. The tables were formulated in Kaplan – Meier (KM) format for visual illustration, where rate ± standard error (in %) were presented. A subsection of *project 1 and 2* was allocated to compare outcomes based on being of favourable versus those of unfavourable anatomy. In the cases where survival outcomes required comparison, this was done through the log-rank test. Comparative analyses were used extensively in *project 2* to compare primarily both short- and long-term differences between symptomatic and asymptomatic patients. Statistical analyses were performed in IBM SPSS package (SPSS Inc., Chicago, IL, USA; ver.23 for *project 1*, ver.25 for *project 2* and ver.22 for *project 3*).

Apart from the aforementioned aspects with regards to clinical success and endoleak freedom (specifically type Ia endoleak freedom), *project 3* also entailed the analyses of anatomical changes of the aortic neck in the post-operative period. Specifically, measurements (in mm) of the aorta at the celiac trunk (CT), superior mesenteric artery (SMA), lowest renal artery and 9 mm below that were performed on the available pre-operative, 1st- and last post-operative CTA. Diameter increase ≥ 4 mm at each level of comparison was considered significant. AAA diameter increase > 5 mm was considered significant. In addition, measurements of the stentgraft diameter and the Palmaz stent diameter, along with migration, were assessed, respectively. Comparison of relevant outcomes between the elective and acute (ruptured and symptomatic) cases was undertaken, both for entire patient cohort ("crude" rates), and only including those surviving > 90 days post-operatively, i.e "relative rates".

Project 4

All patients undergoing EVAR or FEVAR for AAA between years 2004 – 2007 were included. This was done to ensure adequately long CTA follow-up, especially for patients treated with EVAR. Only patients with overall clinical success, and without post-operative re-interventions, with high quality imaging (≤ 3 mm) were included in the study. Patients with short post-operative follow-up (< 24 months post-operatively) were excluded.

Follow-up was structured differently for patients undergoing standard infrarenal EVAR versus those undergoing complex EVAR, i.e FEVAR or EVAR with IBD (iliac branched devices). Put simply, infrarenal EVAR follow-up constituted of yearly CTA up to year 2010, where follow-up was instead re-structured to ultrasound scans at specific intervals. Complex repairs had a CTA at 1 months post-operatively, and yearly thereafter.

CTAs were exported to a 3D-workstation (iNtuition, TeraRecon, San Mateo, CA, USA), whereby a centreline with orthogonal reconstructions was created to avoid overestimation of aortic diameter in tortuous portions of the aorta, thereafter the maximum diameter was measured. Measurements of the aortic diameter (mm) were made at the following anatomical levels of the aorta: 5 cm over CT, at CT, at SMA, at right renal artery (RRA), left renal artery (LRA), then 5-, 10-, and 15-mm below the lowest renal artery. The aforementioned measurements were made on the pre-operative CTA along with every CTA done post-operatively done for the sake of follow-up.

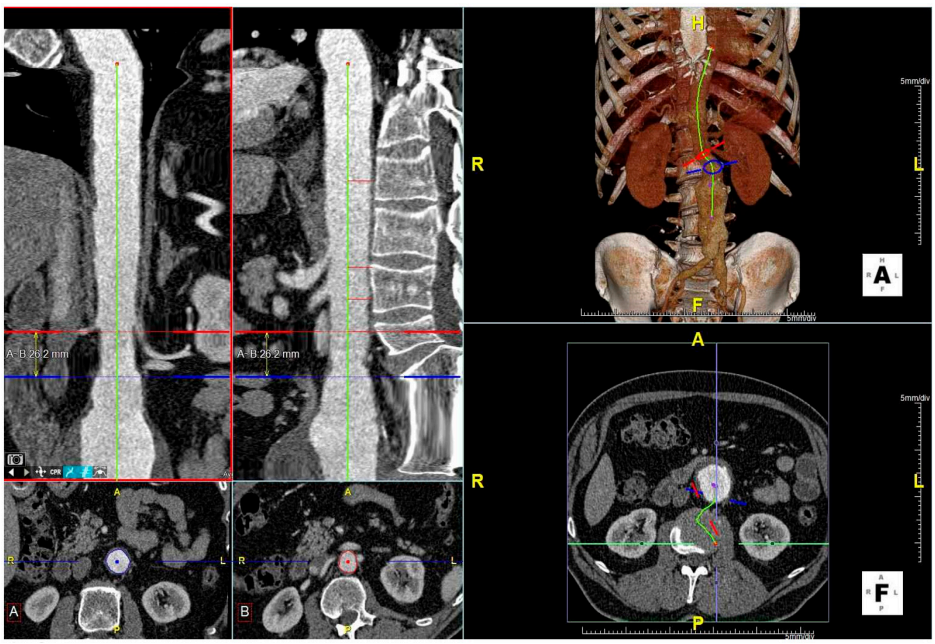


Figure 8 – programme interface for centreline generation with the "outstretched" aortic view

The pre-operative CTA was used to assess the aortic neck through measurement of aortic neck length, being the distance between lowest renal artery and aneurysm start, specifically where aortic diameter > 32 mm. Aortic neck conicity was determined by increase > 2 mm in aortic neck diameter for 10 mm of aortic neck length. Being within the IFU (for patients undergoing infrarenal EVAR) was assessed on the basis of the following:

1. Absence of aortic neck conicity
2. Neck length ≥ 15 mm
3. Neck diameter ≤ 32 mm

The presence of neck thrombus, calcification or severe angulation was not assessed.

Oversizing of the proximal portion of the stentgraft was performed in relation to the diameter of the native aorta at the level of the lowest renal artery such that:

$$oversizing\ in\ \% = \frac{nominal\ SG\ diameter - diameter\ at\ lowest\ renal\ artery}{diameter\ at\ lowest\ renal\ artery}\ x\ 100$$

Two groups with regards to oversizing were therefore created, one with ≤ 30 % and the other with > 30 % oversizing, respectively. This was done based on earlier studies[35] demonstrating that > 30 % oversizing is associated with increased graft migration and AAA expansion.

Anatomical comparisons were divided into "early" and "late" changes. Changes such that dilatation between pre-operative CTA (reference for "early" changes) and 1-year follow-up CTA was deemed "early", while "late" changes entailed expansion as compared to the 1-year follow up CTA (reference for "late" changes). An increase in diameter of ≥ 4 mm compared to the reference was considered as significant expansion in the actuarial analyses.

Life-table analyses (with KM-Curves) were used to assess for late expansion. Comparisons of population characteristics were done using non-parametric methods, whereby Fisher´s exact test was used for categorical variables (e.g early expansion), while Kurskal-Wallis was used for the continuous variables. SPSS ver.25 was used for the analyses.

Project 5

All patients treated for AAA using EVAR and FEVAR techniques during the years 2004 – 2012 with pre-operative non-contrast CT imaging series available, and surviving beyond the first 30-postoperative days, were retrospectively included. Patients were excluded in the cases of absent non-contrast imaging and/or exclusively contrast-enhanced pre-operative CTAs being present, earlier ilio-femoral stenting or the presence of hip arthroplasty. The two latter causes of exclusion were mainly performed due to potential of artefacts making calcium score measurements difficult to perform without errors.

Available charts were reviewed to assess for the presence of pre-operative co-morbidities e.g pre-operative ischemic heart disease, chronic obstructive pulmonary disease (COPD) and peripheral arterial disease (PAD), along with smoking status.

The patients´ pre-operative medications were assessed with regards to the usage of anti-platelet agents (e.g ASA or ADP-receptor blockers), statins, beta-blockers, Angiotensin converting enzyme inhibitors (ACE-I), other blood pressure medications and anticoagulants (warfarin or New Oral Anticoagulants, NOAC). Mortality was acquired through both available patient files and the Swedish mortality register. Cardiac mortality, due to coronary ischemic event, was especially assessed for and collected.

Pre-operative CT scans of thickness 3 – 5 mm between the slices were included. These were performed with 16 – 64 detector row spiral CT-scanners, with tube settings 80 – 120 kVP/20 mAs. Anatomical landmarks of jugulum sterni / diaphragm to the femoral minor trochanter were used to be the limits of image acquirement, to ensure the inclusion of the arterial segments up to and including the bifurcation of the common femoral artery.

Images were imported to a dedicated post-processing software (iNtuition, TeraRecon, San Mateo, CA, USA). This was done to calculate the Agatston calcium score, whereby the software identifies structures > 130 HU and gives them a yellow colour. Manual marking of arterial calcifications present in the common iliac artery, external iliac artery and common femoral artery bilaterally was performed on each slice. The software thereby added the calcium score of each segment and a final calcium score in AU was obtained.

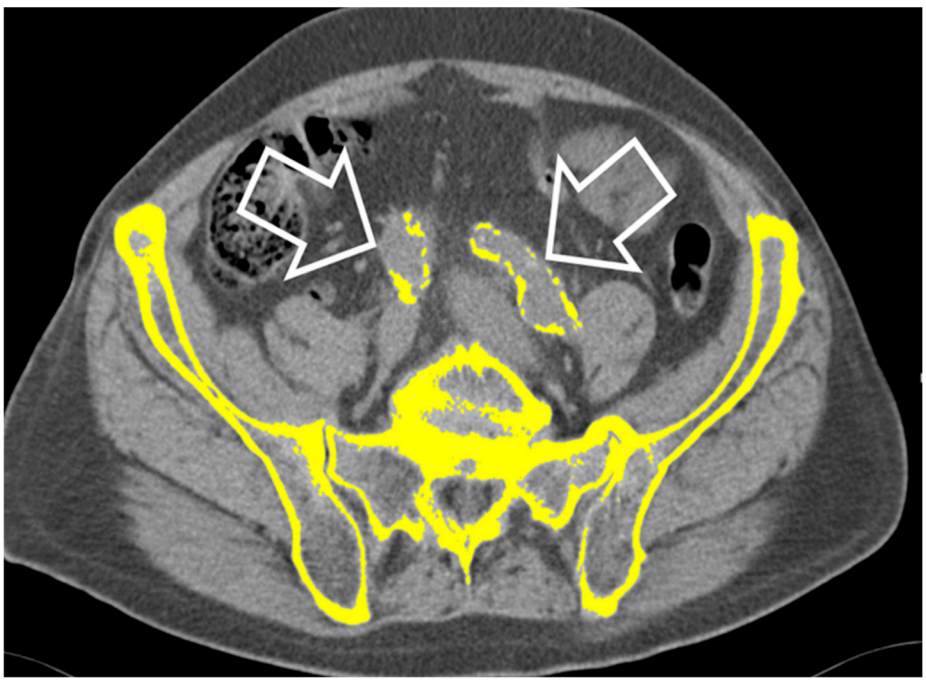


Figure 9 – yellow colour indicating presence of calcium with attenuation > 130 HU, with arrows showing calcifications in the common iliac arteries bilaterally.

Patients were stratified according to being within the lowest quartile of ilio-femoral calcium score (Q1), versus those with calcium score in the second through fourth quartiles (Q2-4), with results of both pre-operative characteristics, overall survival and cardiac mortality being compared in this fashion. Life-table analyses (with KM-curves) were constructed for both overall and cardiac mortality based on the aforementioned stratification. In addition, univariate logistic regression was used to assess if the calcium score would retain significance for prediction of both overall mortality and cardiac mortality, when placed in a regression model involving other pre-operative patient characteristics. Cox (multivariate) regression analyses was planned if the calcium score retained significance in the univariate model. SPSS ver.23 was used for the aforementioned analyses.

Results

Project 1 and 2

General population characteristics

Some 1250 patients treated for an aneurysm were identified at our center through local registries, during the period 1998 – 2012, of which 680 (54.4 %) were treated for an infrarenal, non-ruptured AAA treated with the Cook-Zenith stentgraft system. The majority (543 (79.9 %)) were asymptomatic while 137 (20.1 %) were symptomatic (of which abdominal pain (109 (76.2 %))) at presentation. Both populations were comparable, except in regards to higher creatinine ($p = 0.001$) and presence of COPD ($p = 0.049$) in asymptomatic versus symptomatic cases (table 2). Pre-operative AAA diameter was somewhat smaller in asymptomatic cases versus symptomatic AAAs ($p = 0.082$).

Table 2 – General patient characteristics for asymptomatic and symptomatic cases

Group / Characteristics	Asymptomatic (N= 543)	Symptomatic (N= 137)	p-value
Gender (Male)	476 (87.7 %)	119 (86.9 %)	0.774
Age at operation (Years)	69 (74 – 79)	69 (74 – 79)	0.923
AAA diameter (mm)	58 (53 – 66)	61 (52 – 73)	0.082
Hypertension	453 (83.4 %)	111 (81.0 %)	0.526
Hyperlipidemia	150 (27.6 %)	30 (21.9 %)	0.194
Diabetes	86 (15.8 %)	22 (16.1 %)	1.000
Active smokers	203 (37.4 %)	56 (40.9 %)	0.460
COPD	174 (32.0 %)	32 (23.4 %)	0.049
Cardiac disease	275 (50.6 %)	67 (48.9 %)	0.774
Creatinine (µmol/L)	97 (83 – 121)	90 (77 – 107)	0.001

Intra-operatively, asymptomatic patients (N = 282; 51.9 % of asymptomatic) received one or more of a multitude of potential adjuncts. The main indication for an intra-operative adjunctive procedures (178 adjuncts) was due to ilio-femoral causes, e.g extra stent placement in the limb for improved configuration. Proximal seal-related adjuncts (97 adjuncts) were also indicated, and were more common

(used in 48/199 vs 49/344 patients; p = 0.001) in the initial part of the experience. The remaining intra-operative adjuncts are detailed in table 3

Table 3 – intra-operative adjuncts used in asymptomatic patients

Reason for Intraoperative adjunct	Frequency and percentage (N, %)
Proximal seal-related	97 (26.6)
Distal related procedures	178 (48.9)
Endovascular	131 (36.0)
Open	47 (12.9)
Renal artery related	67 (18.4)
Type II Endoleak	22 (6.0)

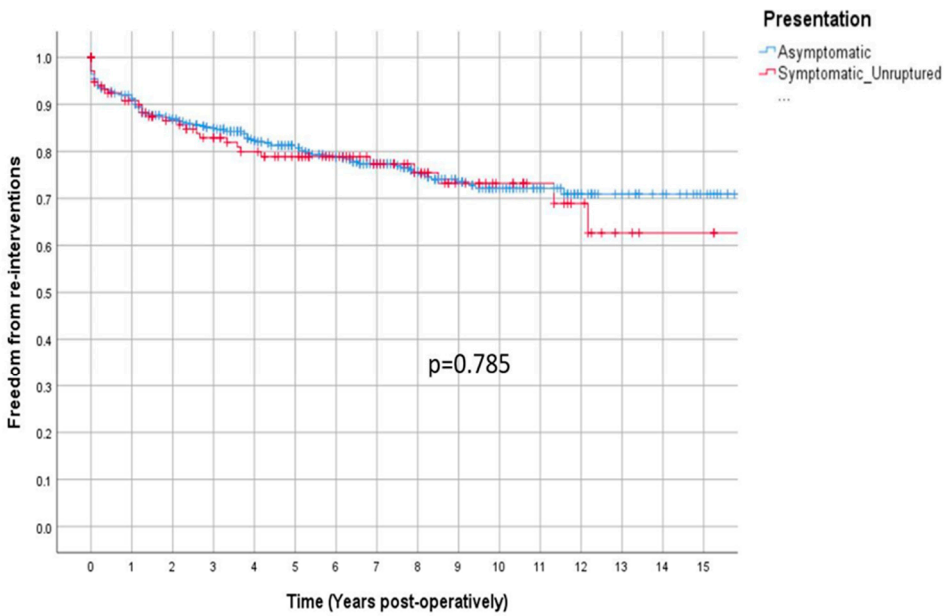
Technical failure occurred in 21 (3.9 %) asymptomatic versus 7 (5.1 %) symptomatic patients (p = 0.477). the most common cause for this was the presence of uncorrected type Ia endoleak (N = 13 in asymptomatic and N = 6 in symptomatic group). In the symptomatic group, the majority (N = 99; 72.3 %) had symptom resolution post-operatively, 2 (1.5 %) had continued pain and for 36 (26.3 %) patients the information was not discernible from available charts. Thirty-day mortality occurred less commonly (p = 0.002) in asymptomatic (N = 8; 1.5 %) versus symptomatic (N = 9; 6.6 %).

Post-operative re-interventions and endoleak freedom

For both groups, the most common post-operative re-intervention was due to distal causes, specifically related to iliac stenosis/occlusion or femoral access. There were no differences (p > 0.05; table 4) between asymptomatic and symptomatic cases with regards to re-interventions. In the asymptomatic group, with regards to early re-interventions, 15 (8.2 %) were due to distal causes, 5 (2.7 %) renal-artery related and 2 (1.1 %) related to bowel-ischemia. While within the symptomatic group, all (4 (8.9 %)) of the early re-interventions were due to distal causes. At 10-years post-operatively, freedom from re-interventions (figure 10) was 72 ± 3 % and 73 ± 5 % (p = 0.785) for asymptomatic and symptomatic patients, respectively.

Table 4 – post-operative re-interventions in both asymptomatic and symptomatic cases

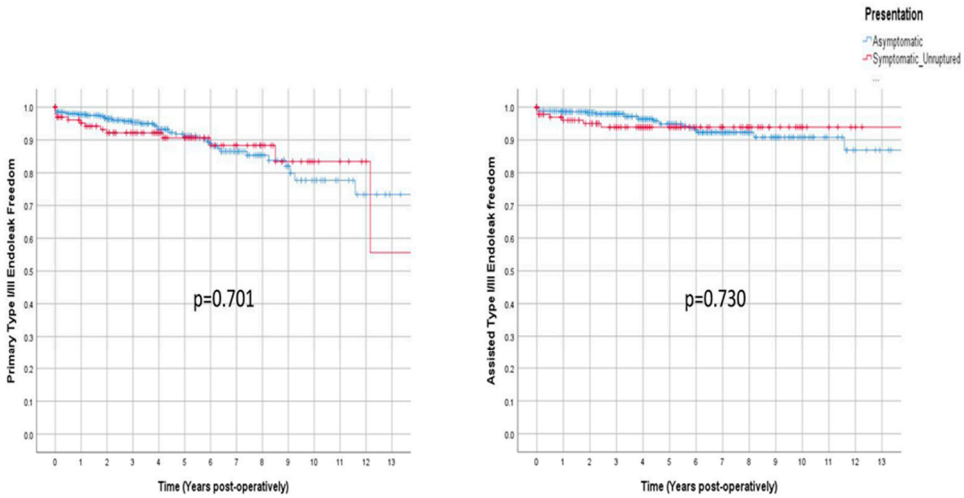
Group / Reason for re-intervention	Asymptomatic	Symptomatic	p-value
Total number- re-interventions	182	45	0.663
Early (within 30-days) (%)	22 (12.1 %)	4 (8.9 %)	0.661
Late (%)	160 (87.9 %)	41 (91.1 %)	0.808
Proximal Re-interventions			
Type I (a) endoleak related (%)	13 (7.1 %)	3 (6.7 %)	0.588
Proximal-related (%)	13 (7.1 %)	3 (6.7 %)	0.888
Type II endoleak related (%)	30 (16.5 %)	9 (20.0 %)	0.947
Distal-related (%)	97 (53.3 %)	23 (51.1 %)	0.291
Infection-related (%)	15 (8.2 %)	5 (11.1 %)	0.340
Bowel-ischemia related (%)	2 (1.1 %)	0 (0 %)	0.477
Renal-artery related (%)	12 (6.6 %)	2 (4.4 %)	0.866



Year	1	5	10	15
Asymptomatic	477 (92 ± 1 %)	298 (81 ± 2 %)	89 (72 ± 3 %)	19 (71 ± 3 %)
Symptomatic_Unruptured	110 (91 ± 3 %)	71 (79 ± 4 %)	23 (73 ± 5 %)	4 (61 ± 9 %)

Figure 10 - Freedom from reinterventions for asymptomatic (blue) and symptomatic (red) patients respectively

Endoleak (type I/III) Freedom (figure 11) was similar between asymptomatic and symptomatic patients for both events of primary (p = 0.701) and assisted (p = 0.730) endoleak freedom. At 10-years post-operatively, the primary type I/III endoleak freedom was 78 ± 4 % for asymptomatic patients and 83 ± 6 % for symptomatic patients; while for assisted type I/III endoleak freedom, the rates were 91 ± 2 % and 94 ± 2 %, respectively.



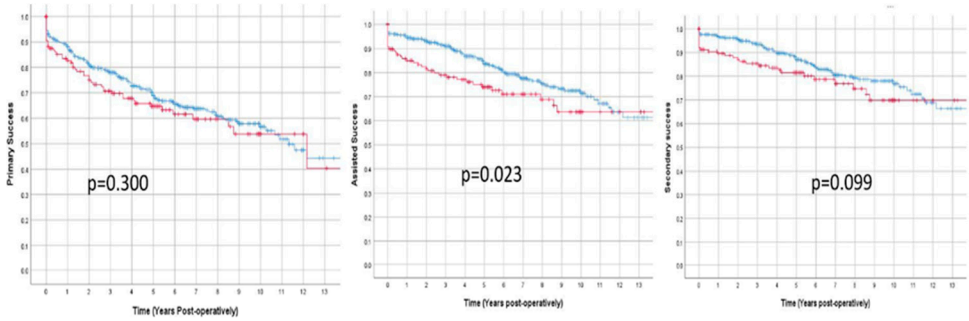
Year	1	5	10	13
Asymptomatic	414 (98 ± 1 %)	176 (92 ± 2 %)	29 (78 ± 4 %)	11 (73 ± 6 %)
Symptomatic_Unruptured	103 (96 ± 2 %)	55 (90 ± 3 %)	9 (83 ± 6 %)	2 (59 ± 21 %)

Year	1	5	10	13
Asymptomatic	418 (99 ± 1 %)	182 (95 ± 1 %)	34 (91 ± 2 %)	14 (87 ± 5 %)
Symptomatic_Unruptured	105 (97 ± 2 %)	57 (94 ± 2 %)	10 (94 ± 2 %)	2 (94± 2 %)

Figure 11 – Primary and assisted Type I/III endoleak freedoms for asymptomatic (blue) and symptomatic (red) patients respectively

Clinical success, overall and Late AAA-related mortality

Primary, assisted and secondary clinical success rates (figure 12) were higher for asymptomatic versus symptomatic (p = 0.300, 0.023 and 0.099, respectively) patients. At 10-years, asymptomatic versus symptomatic success rates were 58 ± 3 % versus 54 ± 6 % (primary); 72 ± 3 % versus 64 ± 6 % (assisted) and 78 ± 2 % versus 70 ± 5 % (secondary), respectively.



Year	1	5	10	13
Asymptomatic	455 (89 ± 1 %)	225 (70 ± 2 %)	49 (58 ± 3 %)	12 (45 ± 5 %)
Symptomatic_Unruptured	103 (83 ± 3 %)	56 (64 ± 4 %)	10 (54 ± 6 %)	3 (43 ± 11 %)

Year	1	5	10	13
Asymptomatic	487 (95 ± 1 %)	274 (85 ± 2 %)	68 (72 ± 3 %)	23 (62 ± 5 %)
Symptomatic_Unruptured	105 (85 ± 3 %)	65 (74 ± 4 %)	14 (64 ± 6 %)	4 (64 ± 6 %)

Year	1	5	10	13
Asymptomatic	496 (97 ± 1 %)	283 (88 ± 2 %)	70 (78 ± 2 %)	24 (67 ± 5 %)
Symptomatic_Unruptured	111 (90 ± 3 %)	73 (81 ± 4 %)	17 (70 ± 5 %)	4 (70 ± 5 %)

Figure 12 – Primary, assisted and secondary clinical success for asymptomatic (blue) and symptomatic (red) patients respectively

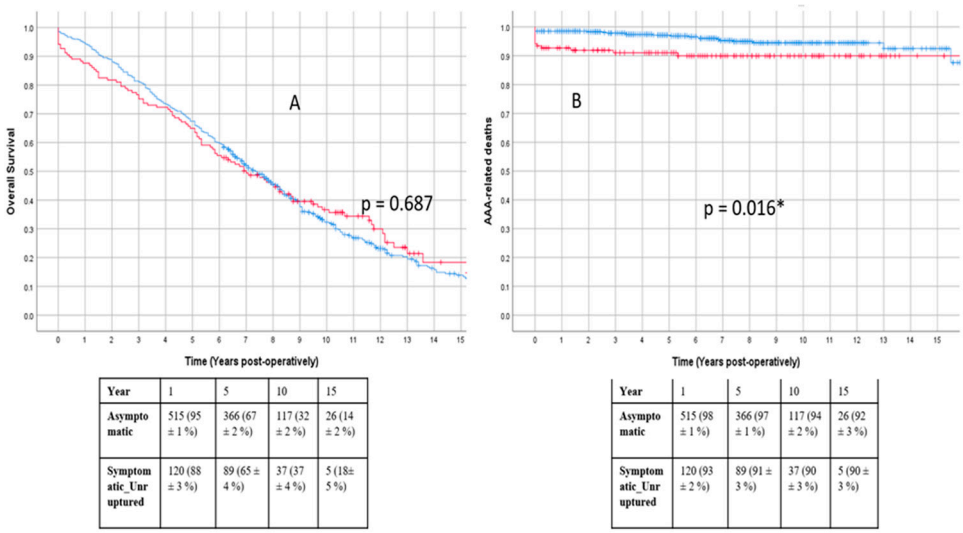
Persistent clinical failures were managed as per table 5. The main causes for non-intervention were presence of clinical unfitness (50.6 % in asymptomatic versus 38.1 % in symptomatic). A proportion of patients (26.0 % asymptomatic versus 19.0 % symptomatic) had findings which were consistent with clinical failure yet deemed clinically insignificant by the treating attending surgeon. No AAA-related mortality occurred in this subgroup of patients.

Table 5 – Management and cause of persistent clinical failures in both asymptomatic and symptomatic group

Group / Cause for persistent failure	Asymptomatic (N = 77)	Symptomatic (N = 21)
Clinical unfitness	39 (50.6 %)	8 (38.1 %)
Conservative due to clinically insignificant failure	20 (26.0 %)	4 (19.0 %)
Open conversion	5 (6.5 %)	4 (19.0 %)
Failure discovered incidentally during study review	4 (5.2 %)	3 (14.3 %)
Other causes	4 (5.2 %) *	2 (9.5 %) **

*For ***asymptomatic*** patients, other causes included planned reintervention yet patient died of non-AAA cause (3 patients, 3.9 %); planned for reintervention with patient alive (1 patient, 1.3 %).**For ***symptomatic*** patients, other causes included patient refusing intervention (1 patients, 4.8 %); planned reintervention yet patient died of AAA-related cause (rupture during the waiting period) (1 patients, 4.8 %).

Overall survival was, at 10-years post-operatively, 32 ± 2 % and 37 ± 4 % for the asymptomatic and symptomatic patients (p = 0.687), respectively. Freedom from AAA-related death was 94 ± 2 % and 90 ± 3 % for asymptomatic and symptomatic patients, respectively (p = 0.016). When 30-day mortality was excluded from the aforementioned analysis, no difference (p = 0.918) was present with regards to freedom late AAA-related deaths (figure 13).



Year	1	5	10	15
Asymptomatic	515 (95 ± 1 %)	366 (67 ± 2 %)	117 (32 ± 2 %)	26 (14 ± 2 %)
Symptomatic_Unruptured	120 (88 ± 3 %)	89 (65 ± 4 %)	37 (37 ± 4 %)	5 (18± 5 %)

Year	1	5	10	15
Asymptomatic	515 (98 ± 1 %)	366 (97 ± 1 %)	117 (94 ± 2 %)	26 (92 ± 3 %)
Symptomatic_Unruptured	120 (93 ± 2 %)	89 (91 ± 3 %)	37 (90 ± 3 %)	5 (90 ± 3 %)

Figure 13 – overall mortality (A), and freedom from AAA-related deaths (B) for asymptomatic (blue) and symptomatic (red) patients, respectively.
*When 30-day mortality is excluded, p = 0.918

Outcomes based on aortic neck-length

Of 680 patients, 554 (81.5 %) had pre-operative imaging where neck-length estimation could take place, of which 438 (85.6 %) were asymptomatic and 116 (84.7 %) had symptomatic presentation. Some 375 (85.6 %) asymptomatic and 93 (80.2 %) symptomatic patients had aneurysm necks > 15 mm (p = 0.152). Adequate necks yielded higher proportion of primary, assisted and secondary clinical success along with higher proportions of type I/III endoleak freedom (p < 0.0001). In addition, longer necks conferred higher overall survival (p = 0.009) and higher freedom from late AAA-related mortality (p = 0.009).

Project 3

General characteristics and intra-operative proximal seal

During the inclusion period (1998 – 2012), 125 patients were treated with intra-operative Palmaz stent placement for a type Ia endoleak during EVAR for infrarenal AAA and therefore included. The majority (N = 83; 66 %) were asymptomatic at presentation, while the remainder presented acutely, either as non-ruptured yet symptomatic (N = 20; 16 %) or ruptured AAAs (N = 22; 18 %). Cook-Zenith stentgrafts were used in 123 (98.4 %) patients.

Intra-operatively, 101 (80.8 %) patients had a successful intra-operative proximal seal, while 24 (19.2 %) had failed proximal seal in spite of Palmaz stent placement. of patients with successful intra-operative seal, 81/101 (80.2 %) had persistent seal, while of those with failed intra-operative seal, 15/24 (62.5 %) had spontaneous seal on follow-up CTA (Figure 14).

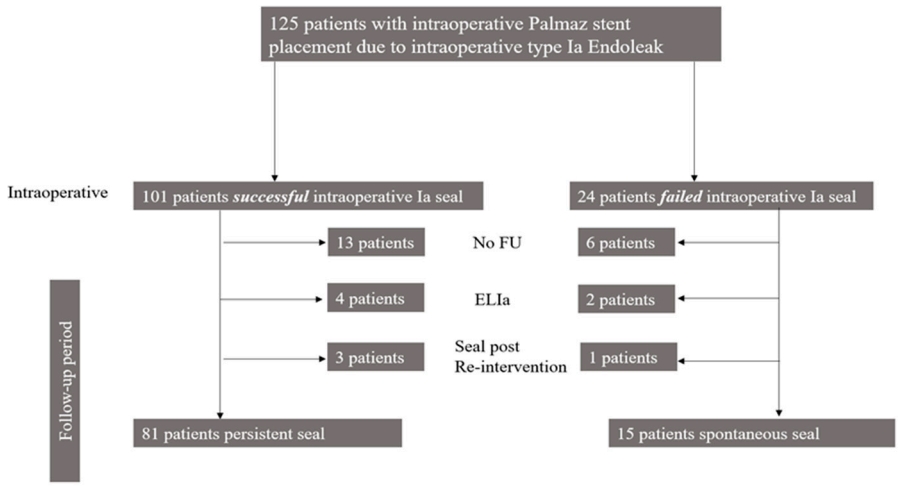


Figure 14 - Occurrence of type Ia endoleak in the cohort. Of the 24 patient with intra-operative persistent endoleak there was a spontaneous seal in the majority (15 patients, of which one had spontaneous seal after the first CTA), six patients had no follow-up available, of which there were three patients with 30-day mortality. One patient had a successful re-intervention. The remaining 2 underwent re-interventions that were not successful (1 type Ia Endoleak embolization and 1 PTA of the Palmaz stent), In summary, of the 18 patients with available follow-up there were persistent endoleaks in 2 patients (in spite of re-interventions), sealing post successful re-intervention in one patient and recurring endoleak in no patients. Moreover, AAA expanded in 2 of these 18 patients. The reasons for "No FU" for the patients with successful intra-operative seal were 6 patients who had 30 day-mortality and 7 patients with no imaging.

Outcomes of Type Ia endoleak

Post-operatively, for all patients treated, at 10-years, primary type Ia endoleak freedom was 74 ± 8 %, increasing for assisted type Ia freedom up to 80 ± 7 %. When the end-point was divided between elective and acute cases, elective patients (with regards to "crude" rates) had slightly higher primary ($p = 0.066$) and assisted ($p = 0.145$) type Ia endoleak freedom, albeit not statistically significant. In addition, when "relative" rates were considered, elective patients had yet again higher primary ($p = 0.025$) and assisted ($p = 0.063$) type Ia endoleak freedom, when compared to the acute patients.

Anatomical overview at the aortic neck and AAA

There was a significant change ($p < 0.05$) of diameter at all levels of comparisons (except for AAA sac when comparing pre-operative CTA to 1st post-operative CTA. The largest increase in diameter was present at the level of lowest renal artery and 9 mm below the lowest renal, specifically when comparing pre-operative CTA to last post-operative CTA, where 65 % of the patients with available imaging had significant expansion at lowest renal level and 68 % of them at 9 mm below lowest renal. With regards to treated AAA, 16/91 (18 %) with at least 2 post-operative CTAs had significant AAA expansion, of which 5/16 (31 %) suffered expansion due to a post-operative type Ia endoleak (table 6).

Table 6 – aortic diameter changes (Δ) at levels of Celiac Trunk (CT), Superior mesenteric artery (SMA), lowest renal (renal), 9 mm below lowest renal (9 mm) and AAA (aneurysm)

Level of measurement in aorta	Preop diam (mm)	Comparison Preop – 1st postop (n = 96)		Comparison Preop – last postop (n = 80)		Comparison 1st postop – last postop (n = 91)	
		Δ median (mm)	N (%) patients	Δ median (mm)	N (%) patients	Δ median (mm)	N (%) patients
CT	25 (23-28)	0 (-1 - +1)	4/96 (4%)	+1 (0 - +3)	17/80 (21%)	+1 (0 - +2)	15/91 (16%)
SMA	25 (22-27)	+1 (0 - +2)	4/96 (4%)	+1 (0 - +3)	15/80 (19%)	+1 (0 - +2)	12/91 (13%)
Renal	24 (22-27)	+2 (0 - +3)	23/96 (24%)	+5 (+2 - +7)	52/80 (65%)	+2 (+1 - +5)	34/91 (37%)
9 mm	25 (23-30)	+2 (0 - +4)	32/96 (33%)	+5 (+3 - +8)	54/80 (68 %)	+3 (+1 - +5)	30/91 (33%)
AAA	63 (55-75)	0 (-3 - +2)	9/96 (9%)	-8 (-17 – 0)	14/80 (18%)	-5 (-14 - +1)	16/91 (18%)

Project 4

General characteristics

Given the strict inclusion criteria, 81 patients were included, of which 64 patients (79 %) were treated with infrarenal EVAR and 17 (21 %) were treated using FEVAR devices (all Cook-Zenith devices). Of the patients treated with EVAR, 42 (52 %) were within the IFU. Shorter follow-up duration ($p < 0.001$) was present in the groups treated with infrarenal EVAR (median ≈ 48 months) versus those treated with FEVAR (median ≈ 84 months). The majority (13/17) of FEVAR patients had exclusively renal fenestrations. Oversizing > 30 % was more common ($p = 0.01$) in patients outside IFU receiving infrarenal EVAR.

Early post-operative anatomical changes

A higher proportion of expansion ≥ 4 mm was present in the visceral segment in patients undergoing FEVAR and "non-IFU" EVAR ($p = 0.210$ and 0.061 at TC and SMA, respectively), when compared to infrarenal EVAR within IFU. This was also true at the level of renal arteries ($p = 0.029$ and 0.068 at RRA and LRA, respectively). However, infrarenally, ≥ 4 mm expansion was present in all three comparison, albeit more common in patients undergoing EVAR within the IFU versus those undergoing EVAR outside IFU and FEVAR ($p = 1.000$, 0.406 and 0.026 at 5-, 10-, and 15-mm below lowest renal). Table 7 illustrates proportion of expansion in the early and late phase for each treatment group.

Oversizing > 30 % did not seem to have an effect on expansion ($p > 0.05$) at all levels of measurements except 15-mm below lowest renal ($p = 0.049$), where patients with such oversizing had a tendency towards higher rate of expansion early in the follow-up.

Table 7 – proportion of patients having ≥ 4 mm expansion in the early (up to 1-year follow-up), and late (from 1-year standard CTA), stratified by treatment group

Level	Expansion proportion (Infrarenal EVAR with **favourable** anatomy, N=42)		Expansion proportion (Infrarenal EVAR with **unfavourable** anatomy, N=22)		Expansion proportion (FEVAR, N=17)	
	Early	Late	Early	Late	Early	Late
5 cm over TC	0/42	2/42	0/22	0/22	0/17	2/17
TC	0/42	4/42	0/22	0/22	1/17	3/17
SMA	0/42	2/42	1/22	1/22	2/17	4/17
RRA	2/42	3/42	2/22	4/22	5/17	8/17
LRA	3/42	7/42	4/22	2/22	5/17	6/17
5 mm below lowest renal	13/42	7/42	6/22	3/22	5/17	5/17
10 mm below lowest renal	15/42	9/42	6/22	5/22	3/17	6/17
15 mm below lowest renal	18/42	11/42	4/22	2/22	2/17	3/17

Long-term post-operative anatomical changes

At the long-term, comparing 1-year post-operative CTA to consecutive post-operative CTAs, expansion ≥ 4 mm was as common in all groups ($p > 0.05$), albeit a tendency towards higher expansion rates was present 15-mm below lowest renal ($p = 0.076$), for patients undergoing infrarenal EVAR within IFU (figure 15). Table 8 illustrates the rates of freedom from expansion for the different treatment groups.

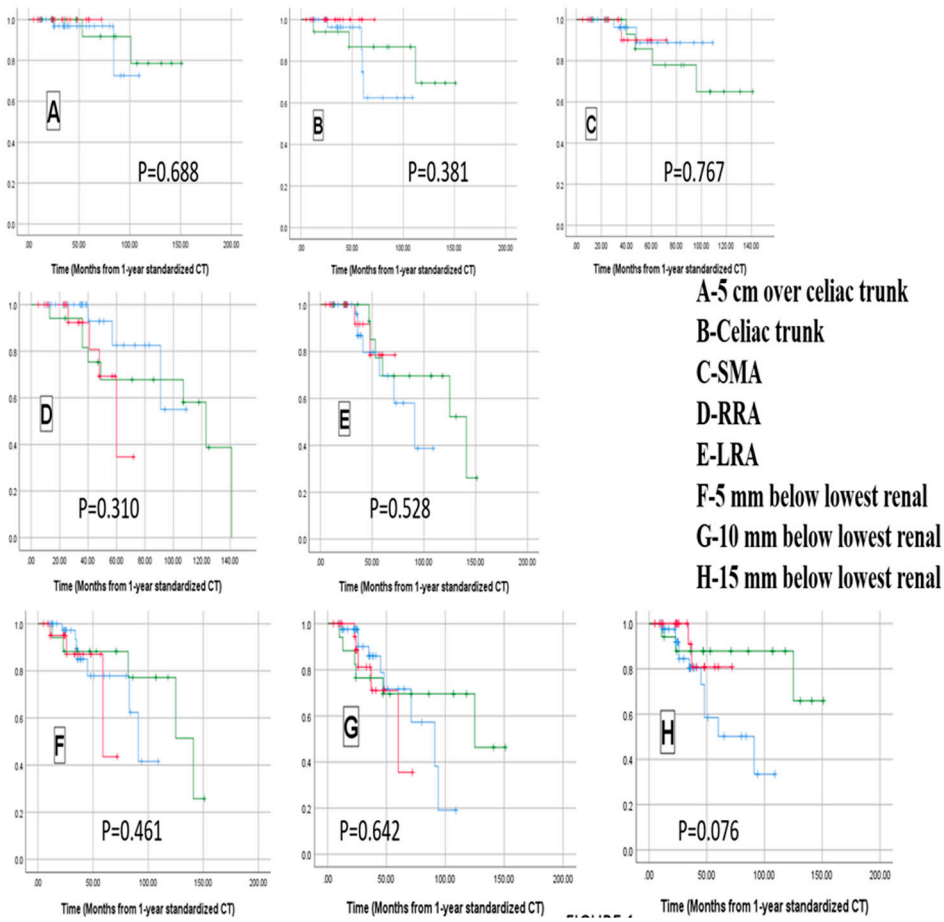


Figure 15 – Kaplan – Meier curves for expansion to ≥ 4 mm in diameter. Blue line illustrates patients within IFU (favorable neck) undergoing infrarenal EVAR, red line for patients outside IFU (unfavorable neck) undergoing infrarenal EVAR and green line for patients undergoing FEVAR

Table 8 – Estimates of freedom from expansion (≥ 4 mm) 3 years after 1-year CTA ie approximately 4 years follow-up. FEVAR have also 5-year estimates considering the longer follow-up. Early expansion has been disregarded to analyze isolated late disease progression. Values are estimates in % ± *standard error.

Level	Infrarenal EVAR with **favourable** anatomy (% ± SE*)	Infrarenal EVAR with **unfavourable** anatomy (% ± SE*)	FEVAR (3 years, (% ± SE*))	FEVAR (5 years, (% ± SE*))
5 cm over TC	96 ± 4	100 ± 0	100 ± 0	92 ± 8
TC	96 ± 4	100 ± 0	94 ± 6	87 ± 9
SMA	96 ± 4	100 ± 0	100 ± 0	86 ± 9
RRA	100 ± 0	92 ± 7	94 ± 6	67 ± 12
LRA	96 ± 4	93 ± 7	100 ± 0	77 ± 12
5 mm below lowest renal	90 ± 5	87 ± 9	88 ± 8	88 ± 8
10 mm below lowest renal	86 ± 7	80 ± 10	76 ± 10	69 ± 12
15 mm below lowest renal	81 ± 7	93 ± 7	88 ± 8	88 ± 8

No differences ($p > 0.05$) were present in (late) expansion rates between patients who had oversizing > 30 % versus those who had ≤ 30 % oversizing, at all levels of comparison.

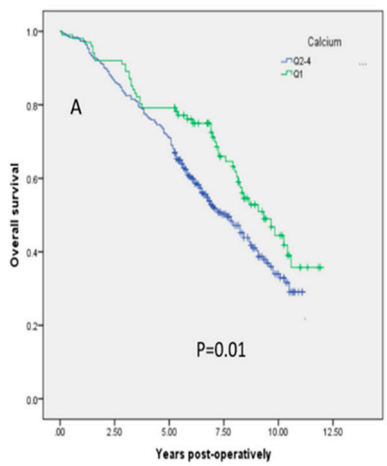
Project 5

General characteristics

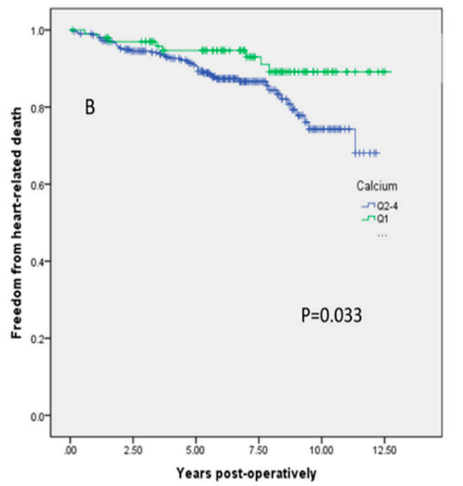
Some 404 patients were included, treated for both infrarenal EVAR and FEVAR, while 247 (37.9 %) were excluded. Most common cause of exclusion was the absence of non-contrast CT images (129 patients; 52.2 % of excluded). No difference in survival (p = 0.33) was found between included and excluded patients. No differences between EVAR (N= 310) and FEVAR (N= 94) were present, except that EVAR patients were older (p = 0.018), had less COPD (p = 0.03) and less ACE-I prescribed (p < 0.001). For the entire cohort, calcium score was 8384 (IQR 3830 – 14179). No differences in calcium score (p = 0.367) was present between EVAR and FEVAR patients.

Survival – overall and freedom from cardiac mortality

Ten-year overall survival was 44 ± 6 % for patients in Q1 (first quartile of calcium score) versus Q2-4 (remaining quartiles 2 through 4) was 34 ± 4 % (p = 0.01), respectively. At ten years post-operatively, freedom from cardiac-related events, for Q1 versus Q2-4, was 89 ± 4 % and 74 ± 6 % (p = 0.033), respectively (figure 16).



Year	0	1	3	5	10	13
Nrs at risk-Low calcium	101	99	92	77	17	3
Nr at risk-High calcium	303	295	252	203	25	3



Year	0	1	3	5	10	13
Nrs at risk-Low calcium	101	97	87	75	15	3
Nr at risk-High calcium	303	290	245	192	23	2

Figure 16 – overall survival (A), and freedom from cardiac-related deaths (B) for Q1 (Green) and Q2-Q4 (Blue) patients, respectively.

Regression analyses

Ilio-femoral calcium score (in thousands) was put in a univariate logistic regression with pre-operative patient characteristics. This did not retain significance for the event of overall mortality (table 9; OR 1.016 (0.988 – 1.045)) nor for freedom from cardiac-related deaths (table 10; OR 1.024 (0.986 – 1.063)). Due to the aforementioned lack of significance, Multivariate regression analyses was not undertaken.

Table 9 - Odds ratio (OR) based on univariate logistic regression, along with confidence intervals (CI) for all-cause mortality

Characteristic	OR	CI 95%	P-value
Male gender	0.670	0.348 – 1.289	0.230
Age At operation (years)	**1.116**	**1.076 – 1.158**	**<0.001**
Hypertension	0.590	0.288 – 1.210	0.150
Smoking	0.694	0.287 – 1.676	0.417
Cardiac disease	1.240	0.780 – 1.970	0.363
Hyperlipidaemia	0.872	0.541 – 1.405	0.573
Diabetes	1.344	0.753 – 2.400	0.317
PAD	0.762	0.475 – 1.224	0.261
COPD	**2.353**	**1.439 – 3.847**	**0.001**
Pre-Operative AAA diameter (mm)	0.990	0.970 – 1.011	0.348
Calcium score (in thousands)	1.016	0.988 – 1.045	0.268
Creatinemia > 105 µmol/L	**2.056**	**1.280 – 3.303**	**0.003**

Table 10 - Odds ratio (OR) based on univariate logistic regression, along with confidence intervals (CI) for freedom from cardiac-related deaths

Characteristic	OR	CI 95%	P-value
Male gender	0.862	0.312 – 2.382	0.862
Age At operation (years)	1.040	0.987 – 1.095	0.140
Hypertension	0.663	0.239 – 1.836	0.429
Smoking	0.353	0.121 – 1.029	0.056
Cardiac disease	**2.376**	**1.174 – 4.812**	**0.016**
Hyperlipidaemia	0.760	0.373 – 1.545	0.448
Diabetes	1.404	0.634 – 3.107	0.403
PAD	1.174	0.593 – 2.326	0.646
COPD	0.853	0.431 – 1.691	0.649
Pre-Operative AAA diameter (mm)	1.004	0.975 – 1.035	0.780
Calcium score (in thousands)	1.024	0.986 – 1.063	0.222
Creatinemia > 105 µmol/L	**5.878**	**2.888 – 11.961**	**<0.001**

Discussion

Long-term EVAR outcomes

Long-term outcomes of standard, infrarenal EVAR were presented in projects 1 and 2 in detail, with focus on type Ia endoleak outcomes in project 3. Operative (30-day) mortality was similar to previous reports with regards to elective repair[131-135], being under 2 %. However, and albeit symptomatic AAAs comprise higher peri-operative mortality rates than elective cases,[136] statistical significance was not achieved in most previous studies,[137-138] while project 2 demonstrated an almost quadrupled early mortality in the symptomatic cohort as compared to asymptomatic cases. This difference may be due to presence of the age difference where patients included in project 2 were, when comparing median age, 3 – 5 years younger than previously cited studies. In spite of this, the asymptomatic and symptomatic patients having 30-day mortality had similar range of age at operation – Range 65 – 87 versus 68 – 85 years, respectively – and therefore it is actually possible that other factors, other than age, may contribute to this early mortality difference. Yet another potential cause for this early mortality difference is the short time available to medically optimise the patients presenting symptomatically. This, in effect, may cause symptomatic patients becoming poorer surgical candidates, yielding in effect higher early mortality. More cautious pre-, peri- and post-operative monitoring of these patients is therefore necessary.

Given the objective of trying to find as standardised a measure as possible for procedural success, pre-defined technical and clinical success were used as defined per the reporting standards by Chaikof *et al*. However, these binary outcomes, essentially a composite of different outcomes, may be somewhat an over-simplification in real life. For example, should an intra-operatively uncorrected, minimal type Ia endoleak, generally considered a "malignant" feature, deem an EVAR procedure a technical failure if it has spontaneously thrombosed at first post-operative CTA? In addition, should a type II endoleak causing 6 mm expansion be considered a clinical failure? Clinical decision making, with regards mainly to the potential role of conservative yet watchful approach in certain patients, was present in our cohort. About 22 % of all persistent clinical failures (both asymptomatic and symptomatic) were deemed to be having findings that did not justify intervention but instead follow-up, with no aneurysm-related mortality in that subgroup, which may suggest a role for both radiological (as per current guidelines) and pragmatic

clinical decision[139] making in the "synthesis" of the overall clinical success outcome. The newest European guidelines[140] suggest post-operative AAA expansion ≥ 10 mm be deemed significant growth with potential gain from re-intervention, which adds further justification to the premise of delaying intervention and potential consideration of some failure cases to be considered as continued success. To add more, the potential for customised follow-up programmes, which take into account (amongst other factors) pre-operative patient anatomy and type of repair performed, may be further explored. This is mainly due to current follow-up programmes are established based on general guidelines.

The bulk of re-interventions were due to distal causes, mainly due to placement of stents for e.g limb stenosis or occlusion, with a few cases of persistent distal failures. This fact suggest the good success achieved with distal re-interventions given the few persistent failures with regards with this specific failure mode. Furthermore, freedom from re-intervention at 72 % 10-years post-operatively suggest, in part, good durability for the initial repair given the highly acceptable ≈ 80 % secondary success rate (higher if broader success definition used) , along with heightened degree of unfitness in the treated population, given that 40 – 50 % of persistent failures were deemed unfit for further treatment. This is on par with previous series[141].

Long-term survival was, in this patient cohort, similar for asymptomatic and symptomatic cases alike. Previous studies[136-138] have suggested a difference in long-term mortality between the two groups, with symptomatic patients exhibiting lower survival. However, these studies usually compared a bulk of patients undergoing both EVAR and open repair, making them not entirely comparable to the setting presented in this thesis. AAA-related mortality was relatively low, when disregarding the early mortality. This suggests that EVAR has reached its ultimate goal in the majority of patients treated.

In this cohort, patients (both symptomatic and asymptomatic) who had unfavourable anatomy had lower rates of success and endoleak-freedom with higher overall and AAA-specific mortality, for both asymptomatic and symptomatic cases. This is in line with other previous publications where treatment outside IFU was associated with graft failure and increased endoleak rates.[57] However, a few studies suggest extremes of no impact of IFU adherence on outcome[142], while other suggest, along with aforementioned differences, increased mortality[143] as well. In this cohort, a single graft (and therefore single IFU) was considered, unlike aforementioned studies. This should, realistically, yield more uniform results, with lessened risk of selection bias.

Intra-operatively, a fairly large proportion of patients (≈ 25 %) required adjuncts to aid proximal seal. This may be due to the treatment of a fairly large (≈ 15 – 20 % as per available images) proportion of patients outside IFU. In addition, given the long time span of the study, potential underestimation of the proportion of patients treated "Off-IFU" may exist. This is related to poor pre-operative imaging (especially in the early portion of the study), along with the unavailability of FEVAR during the

same early period (pre-2004), causing patients to be treated with suboptimal mode of repair. Good intra-operative seal was achieved for Palmaz stents, the most commonly used proximal adjunct in the cohort.

Type Ia endoleaks were an uncommon cause of re-intervention, suggesting good primary seal. However, type Ia endoleak were the cause of persistent failure in ≈ 20 % of failed cases. In spite of this, and especially for patients with favourable anatomy, good seal was ensured post-operatively given the high endoleak freedom rates. To add more, assisted freedom for patients with unfavourable anatomy was similar to the primary freedom, suggesting re-interventions utilised were not achieving their intended purpose in that cohort of patients. Furthermore, patients treated electively with Palmaz stents had similar type Ia outcomes to those treated acutely, illustrating the need of performing as proper repair as possible from the index procedure, by treating patients outside IFU with e.g FEVAR to ensure improved seal. Therefore, usage of "off-IFU" EVAR for cases should be reserved to urgent cases is more appropriate. If any subsequent intra-operative type Ia endoleak is then present, it may be treated using Palmaz stents or other methods, e.g intra-operative endoanchors, which are currently employed on a larger scale with promising results.[64,65,144]

Disease progression

During EVAR (and FEVAR) follow-up, supra-visceral and visceral aortic exhibited little significant dilatation, both for short- and long-term analyses. This may be attributed to the fact that graft material is not having apposition to those segments, for both EVAR and FEVAR cases, given that the majority of FEVAR patients essentially had renal fenestrations, thus having no visceral and supra-visceral "graft to aortic wall" apposition. The aforementioned data gives credence to the notion of outward radial pressure exerted on the aortic wall by the graft being the cause of neck dilatation post-EVAR,[145,146] given the bulk of the expansion occurring at the level of renal arteries and below that.

Late expansion seems to occur more frequently at the 15-mm below lowest renal level (albeit lower rate for FEVAR/EVAR with unfavourable anatomy). This latter fact may suggest that expansion start closest to the AAA and then proceeds proximally, which may be due to disease activity closest to the degenerative AAA-wall along making the aorta at that location more susceptible to radial pressure exerted on aorta by the graft with subsequent expansion. In spite of this, patients treated with FEVAR/EVAR with unfavourable anatomy had lower rate of expansion at the same level, which may suggest that the expansive effect of (self-expanding) graft apposition to the aortic wall should be considered as cause of expansion.

Risk stratification

Low ilio-femoral calcium score was associated with higher survival and freedom from cardiac events in survival analyses. However, this association was ameliorated when other pre-operative patient characteristics were included in the model, suggesting dependence of calcium score on other factors to achieve the aforementioned result. Other studies have suggested the presence of association of either aneurysm calcium score[147] or a simplified, X-Ray based calcium score[123] in the aorto-iliac segment with survival.

Ilio-femoral calcium score may, however, not be a marker of coronary disease by itself, yet may reflect its presence. Previous studies[148] suggests the strong association of ilio-femoral calcium with coronary calcium, albeit the absence of coronary calcium does not exclude ilio-femoral calcification. This, in effect, suggests the presence of iliac calcification prior to coronary calcification.

Limitations

The main limitation of this thesis compilation is the (retrospective) inclusion of patients treated exclusively at a single-center and therefore elevated risk of selection bias. However, this was necessary to access data that could be internally verified, and ensure the potential for analysing specific outcomes that are not obtainable through registries e.g re-intervention causes and modes of failure.

Yet another methodological limitation with regards to this thesis project was the usage of one set point as reference (lowest renal artery) for estimating percentage oversizing. This is especially true for the cases treated with FEVAR, given that the fenestrated endografts usually have variable diameters due to graft tapering and, therefore, variable apposition to the aortic wall. A potentially more suitable method for estimation of oversizing in this population is to do so at every measurement level (e.g % oversizing at SMA, RRA et cetera).

The usage of Agatston method for estimation of the ilio-femoral calcium score has its limitations as well. The method was initially validated for use on ECG-gated 3 mm Non-contrast CT slices, while the images used for ilio-femoral calcium estimation in project 4 were in both 3- and 5-mm slices. Three-mm slices give consistently larger scores[149] when compared to 5-mm slices in the aorta, therefore there is a risk of underestimating calcium score in our population.

Conclusions

- Long-term outcomes with EVAR of AAA are sustainable, especially if the implanted device is placed in aorta with adequate anatomy (**project 1**).
- Results of EVAR for asymptomatic and symptomatic AAAs are similar with regards to long-term outcomes. However, elevated early mortality is found for symptomatic patients, suggesting the need for more intensive monitoring of treated patients (**project 2**).
- Intra-operative treatment of type Ia endoleak with Palmaz stents yields good intra- and post-operative results. However, this should be restricted to patients presenting acutely (**project 3**).
- Aortic expansion beyond the sealing zone is relatively uncommon, and seems related to the force exerted on the aortic wall by the endograft **(project 4)**
- Ilio-femoral calcium score may predict long-term overall and cardiac mortality after EVAR. However, further studies are needed to establish this relation (**project 5**).

Future perspectives

The potential for customised, patient-specific follow-up schemes post-EVAR have not been extensively studied. This is necessary given the increased application of EVAR for AAA treatment for both extremes of patients: those young and fit enough to undergo either EVAR or open surgery and those with elevated risk and age.

Given the elevated rate of pre-existing cardiac disease in patients undergoing EVAR, the potential for studying the relation between ilio-femoral and coronary calcium score in this population is immense, especially given the already established and accepted usage of coronary calcium score in the predicting of coronary disease. Another potential for ilio-femoral calcium score to be studied is if it can predict potential for (percutaneous) access-related complications during EVAR, and if a potential cut-off which would predict occurring of access-closure complications.

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Populärvetenskaplig sammanfattning

Bukaortaaneurysm (AAA) är vidgning av stora kroppspulsådern (aorta) i buken som förekommer oftast under njurpulsåderna i (oftast) äldre, rökande män. Denna vidgningen orsakar kärlväggs svaghet och kan därefter orsaka bristning, vilket kan leda till död. Sjukdomen är dock, till sin natur, oftast tyst och ger sällan symtom. Därför har det, i Sverige, skapats undersökningsprogram (screening) för att, med hjälp av ultraljud, hitta sjukdomen i högrisk gruppen äldre män, innan AAA spricker och behandla denna i skyddande syfte när den når cirka 5.5 cm. Behandlingen utgjordes tidigare av öppen teknik, men denna har ersatts till större utsträckning av s.k endovaskulär aorta reparation (EVAR). Denna senare teknik innebär införandet av ett kärlprotes via ljumsken och därefter utfällning (lite som en paraply) av protesen på insidan av AAA vilket leder bort blod från den svaga kärlväggen och igenom kärlprotesens insida. Denna kärlprotesen fäster oftast i en område nedom njurpulsåderna, s.k halsen. Vissa komplikationer kan ske vid behandling av AAA med EVAR, bland annat blodtillförsel från den övre änden där kärlprotesen fäster (dvs halsen), s.k typ Ia endoläckage, som kan orsaka AAA vidgning och bristning i senare skede, trots kärlprotesens befintlighet.

Långtidsresultaten av denna tekniken är studerade dock oftast inte i detalj, främst i avseende av behandlingens succé. Dessutom så är dessa resultaten oftast redovisade för patienter som behandlats elektivt alternativ för en brustet AAA, och mer sällsynt redovisas dessa resultat för patienterna som hade symtom (exempelvis buksmärtor) utan kärlbristning. Typ Ia endoläckage, en fruktad komplikation till ingreppet, kan behandlas med införandet av icke-täckta metallnät som håller kärlprotesen an mot kärlväggen och ger den bättre fästning. Aneurysmsjukdom kan sprida sig till andra delar av kroppspulsådern, och inte bara befinna sig i bukpulsådern. Kärlförkalkningar i olika kärl i kroppen, speciellt koronarkärlen (kärl som försörjer hjärtat) har visat samband med förekomsten av hjärtinfarkt.

Således var målen med avhandlingen följande:

- Undersöka långtidsresultaten av EVAR ingrepp i elektivt skede
- Undersöka resultaten av EVAR hos patienter som presenterar med symtomgivande AAA och jämföra de till elektivt behandlade patienter
- Undersöka resultaten av behandling av typ Ia endoläckage som upptäckts under EVAR ingrepp med icke-täckta metallnät

- Undersöka om kärlvidgningen bortom bukpulsådern förekommer efter EVAR ingrepp
- Undersöka om kärlförkalkningar i bäckenkärlen kan förutspå dödlighet efter EVAR

Sammanfattningsvis så visar EVAR goda resultat med behandlingssuccé uppemot 80 % tio år efter ingreppet. Dödligheten pga. ingreppet är dock högre i patienter som presenterar med symtom jämfört med de som behandlas elektivt. Icke-täckta metallnät fungerar som behandling mot typ Ia endoläckage som upptäcks under ingreppet, dock är detta oftast bättre begränsad till patienter som presenterar akut med AAA (exempelvis de med kärlbristning alternativ symtom). Kärlvidgning bortom bukpulsådern förekommer men är hyfsad ovanligt, och brukar ske kring halsregionen och kring områden där kärlprotesen har direkt kontakt mot kärlväggen. Låg andel av kärlförkalkningar i bäckenkärlen kan förutspå lägre dödlighet efter EVAR, dock är skillnaden i dödlighet mellan de med låg och högre andel kärlförkalkningar minimal.

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