Advances in Abdominal Aortic Aneurysm Care - Towards personalized, centralized and endovascular care

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Chapter 1

Introduction and outline of the thesis
The infrarenal abdominal aorta is the largest abdominal artery and serves to supply blood to the lower part of the human body, specifically the most distal part of the intestines, the pelvic organs and the legs. An abdominal aortic aneurysm (AAA) is an aorta with a diameter exceeding 3 cm. Risk factors for developing an AAA are male gender, advancing age, a family history of AAA and smoking. In the most recent screening study in Swedish men aged 65 years, a prevalence of 2.2% was reported (95% confidence interval (CI) 2 to 2.4%). Although sometimes a patient may have noticed a painless, pulsatile abdominal mass, in general there are no symptoms and the aneurysm is often found incidentally on physical examination or on imaging studies carried out for other reasons.

The natural course of an AAA is that it grows until it ruptures or until the patient dies from another cause. A 3 cm AAA has an estimated mean growth rate of 1.3 mm (95% CI 1 to 1.5 mm) per year and a 5 cm AAA has an estimated mean growth rate of 3.6 mm (95% CI 3.3 to 3.9 mm) per year. The risk of AAA growth is higher in smokers and is lower in diabetics. The precise moment of rupture cannot be predicted. In AAAs less than 5.5 cm in diameter the risk of rupture is less than 1% per year, in AAAs of 5.5-6 cm this is approximately 9% per year, in AAAs of 6-7 cm approximately 10% per year, and in AAAs exceeding 7 cm approximately 32% per year. It is interesting to note that this reported risk of rupture of AAAs exceeding 5.5 cm is based on just a single study comprising a total of 198 patients only, which limits definite conclusions on this matter. Possibly, the risk of rupture is higher in women and in smokers. Moreover, the risk of rupture seems to increase with higher age, blood pressure and pulse pressure. Interestingly, in obese patients the risk of rupture seems to be lower. Nonetheless, these reported risk factors for rupture have to be interpreted with caution since proper multivariable adjustment has never been done.

In patients with an AAA, the ultimate aim is to prevent rupture. So far, the only treatment to prevent rupture is surgical or endovascular intervention. The European Society for Vascular Surgery recommends possible surgical intervention for an asymptomatic AAA exceeding 5.5 cm in diameter in males and 5.2 cm in females. Decision making for elective aortic surgery comprises three treatment options; endovascular aneurysm repair (EVAR), open repair (OR) or conservative/non-operative therapy. EVAR is the minimal-invasive placement of an endograft inside the aneurysm via the arteries of the groin. EVAR was developed in the nineteen-nineties and has since been used with ever-increasing frequency. OR is the traditional intervention and comprises
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laparotomy and exclusion of the aneurysm by either a synthetic tube or a bifurcated graft.

Assessment of anatomical suitability for EVAR is an important part of decision making for surgical intervention. New developments in technical endovascular devices mean that patient suitability for EVAR is constantly changing. OR may be performed in those patients with unsuitable anatomy for EVAR or other specific situations in which OR is preferred. To date, in patients eligible for both interventions, four large randomized controlled trials (RCT) have been conducted. These trials consistently reported a lower short-term death rate after EVAR than after OR, but from two years onwards the survival is comparable again throughout a follow-up of at least eight years. Moreover, there is a higher risk of reintervention and endograft-related complications after EVAR. Therefore, a lower short-term risk of death after EVAR has to be balanced with a lower long-term risk of complications after OR. Nowadays in the Netherlands, approximately 70% of patients are treated with EVAR.10

Another important part of decision making is whether patients unfit for OR benefit from EVAR when compared with no intervention at all. In a large RCT in patients physically unfit for OR who had an AAA exceeding 5.5 cm, 6-year survival was no better after EVAR than after conservative therapy.7

If unnoticed, an AAA can grow until it ruptures or until the patient dies from another cause. A ruptured abdominal aortic aneurysm (RAAA) is defined as bleeding outside the adventitia of an abdominal aorta with a diameter exceeding 3 cm. The incidence of an RAAA is approximately 10 to 14 per 100,000 person-years in a Western population.11, 12 Of all patients with an RAAA, the death rate is estimated to be as high as 74% (95% CI 72 to 77%).13 The only treatment to prevent death in these patients is immediate surgical intervention. A third of all patients with an RAAA do not reach hospital, a third do not have an intervention after reaching hospital and half of the remaining group do not survive the intervention.13 As in elective aortic surgery, the traditional intervention is OR with exclusion of the aneurysm by a synthetic graft. The vast experience with elective EVAR has led to an increasing use of this technique in the emergency setting as well.

This thesis comprises several aspects of elective aortic surgery (Chapters 2 and 3) and of acute ruptured aneurysm care (Chapters 4 to 10).
Towards personalized care

Prediction models are helpful in assessing individual outcomes after an intervention and are able to contribute to tailoring individual patient care. Three phases can be distinguished in studies that evaluate prediction models. The first phase is the development of such a model including internal validation. The second phase is the external validation including updating of the model in other cohorts of patients. These ‘external validation studies’ answer the question of whether the predictions of a model also correspond with the observed outcomes in a group of patients other than the developing cohort. The third phase is to assess the impact and benefit of the prediction model on clinical practice. In patients in whom decision making is most difficult, risk-assessment by a prediction model can be expected to be the most beneficial. Predictions are based on a small number of preoperative variables such as age, sex, previous history and/or aneurysm characteristics. Nowadays, the increasing use of electronic charts in clinical practice may lead to automatic generation of predictions.

In elective aortic treatment, it is a challenge in clinical practice to determine which of the treatments will benefit the patient most: OR, EVAR, or conservative therapy. A lower risk of short-term death after EVAR has to be balanced with a lower risk of long-term complications after OR. Prediction models can support clinical decision making for elective aortic surgery. For example, OR may be preferable in a young and relatively healthy patient in order to prevent the intensive yearly follow-up which is required after EVAR. Even so, if a model were to accurately predict a low risk of short-term death after OR and a high risk of reintervention and complications after EVAR, it would support the choice for OR. On the other hand, in the elderly patient with severe comorbidity conservative therapy could be chosen, even where aortic anatomy is friendly. Lastly, if in an elderly patient with severe comorbidity a model is able to accurately predict a low risk of short-term death, reintervention and complications after EVAR, an endovascular graft would be the most reasonable treatment option. In Chapter 2, the external validation of the EVAR Risk Assessment (ERA) model predicting survival, reintervention and endograft-related complications after EVAR is described. In Chapter 3 the external validation of the Medicare, the BAR and the VGNW models predicting the short-term death rate after both EVAR and OR is discussed.

In Chapters 4 to 10, care for patients with an RAAA is discussed. In patients with an RAAA, the decision to initiate or withhold surgical intervention is
based on a fast evaluation of the patient’s clinical condition, the surgeon’s past experience and the wishes of the patient. A prediction model is a more objective way to evaluate the chances of successful intervention and might be helpful in these moments of vital choices. In Chapter 4 the external validation of models predicting the short-term death rate after surgical intervention for an RAAA is described.

Chapter 5 is somewhat different regarding personalized care as no prediction models are discussed but the association between acute kidney injury (AKI), as defined by the RIFLE criteria, and death. AKI is a serious complication of RAAA repair. Recently, new multidisciplinary diagnostic criteria (the RIFLE criteria) for AKI were introduced by nephrologists and intensive care specialists. The RIFLE criteria do not estimate a precise risk of dying or of other complications, but can be used to identify high-risk patients. AKI is associated with an increased risk of short-term death and with a poorer long-term survival. So far, only two smaller retrospective studies have applied the RIFLE criteria to patients with an RAAA.

Towards centralized care
The Amsterdam Acute Aneurysm (AJAX) trial, a large RCT comparing EVAR and OR for patients with an RAAA, was conducted in the Amsterdam ambulance region between 2004 and 2011. During the inclusion period of the AJAX trial, all hospitals in the Amsterdam ambulance region agreed to centralize care in three vascular centers; the Academic Medical Center, the VU University Medical Center and the Onze Lieve Vrouwe Gasthuis Hospital. All patients suspected of having an RAAA by ambulance staff, a general practitioner or a surgeon in a referring hospital were to be transported to the vascular center on call. A cohort of all 539 consecutive RAAA patients in the ten hospitals of the Amsterdam ambulance region was assembled. In Chapter 6, the effect of this unique cooperative effort on regional survival is discussed.

An important aspect of the regional cooperation was the transport of patients with an RAAA from a regional hospital to the vascular center on call. The safety of delaying therapy for these patients is controversial because time is limited. In Chapter 7, the duration of in-hospital survival in patients with an RAAA who did not undergo surgical intervention is described.
Towards endovascular care
As mentioned before, vast experience with elective EVAR has led to the increasing use of this technique in an emergency setting. Despite this, high-quality evidence considering the comparison between EVAR and OR for RAAAs is still limited. Moreover, close monitoring of outcomes after EVAR is needed to identify the pitfalls of this relatively new technique. In Chapters 8 to 10 several aspects of outcomes after EVAR versus OR are discussed.

Although many observational studies have reported a lower death rate after EVAR than after OR, two large RCTs were completed just recently.\textsuperscript{16, 17} Chapter 8 offers a systematic review in which all published studies comparing the short-term death rate of EVAR and OR are discussed.

As in Chapter 8, the majority of studies comparing EVAR and OR in RAAA focus on short-term outcomes. In elective aortic surgery, the midterm risk of reintervention is higher after EVAR than after OR. In Chapter 9 the midterm reintervention and survival rates after EVAR and OR in patients with an RAAA in the Amsterdam ambulance region are described. These outcomes may provide new insights into what would be the best intervention in patients with an RAAA, and offer guidance on post-intervention surveillance strategies.

In Chapter 10 the effect of aortoiliac anatomy on outcomes after open repair is discussed. Specifically, we compared the outcomes between patients with aortoiliac anatomy suitable for EVAR (‘friendly anatomy’) and patients with aortoiliac anatomy unsuitable for EVAR (‘hostile anatomy’). Previous studies have shown that outcomes are worse in patients with hostile anatomy. Because patients are selected by aortoiliac anatomy for either intervention, this might be an important confounder in studies comparing EVAR and OR.
Reference List


