Treatment of ruptured abdominal aortic aneurysms in the Amsterdam area

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1

CHAPTER 1

GENERAL INTRODUCTION AND OUTLINE OF THE THESIS

GENERAL INTRODUCTION

Aortic Dilatation

An aneurysm is a localised, permanent dilation of an artery up to 1.5 times the normal diameter. Given that the normal diameter of the abdominal aorta is approximately 2.0 cm, an abdominal aortic aneurysm (AAA) is present when the diameter exceeds 3.0 cm, but may vary according to age, sex and body size. Not all abdominal aneurysms need surgery; it has been shown that operative repair offers no benefit in relation to rupture risk when the aneurysm diameter is less than 5.5 cm.[1,2] The prevalence of aneurysms of the abdominal aorta in the population is correlated with risk factors such as increased age, male gender, smoking and positive family history of AAA.[3-5] An AAA is mostly asymptomatic; most patients are unaware that they have an AAA.

Rupture

The main risk for patients with an AAA is rupture, and the risk increases with a larger aneurysm diameter.[1,6] Also, high blood pressure, smoking and fast diameter growth are associated with increased risk of rupture.[1,2,5,6] A ruptured AAA (rAAA) results in massive haemorrhage in the retroperitoneal space or abdominal cavity. The intra-abdominal blood loss results in hemodynamic instability and eventually decreased perfusion to major organ systems. Without intervention, a ruptured aneurysm of the abdominal aorta invariably leads to death.

It is difficult to diagnose an rAAA based on clinical symptoms only; many patients will die of massive intra abdominal haemorrhage, before reaching a hospital.[7-9] A precise determination of the incidence of rAAA is difficult, as some deaths from rAAA are wrongfully attributed to a different cause. Therefore, most studies focus on the in-hospital mortality of rAAA patients. However, in order to get a good estimate of the actual total mortality rate from rAAA, community mortality or out-hospital deaths have to be considered as well.

Logistics and transport

Centralisation and transport to a dedicated treatment centre has been reported to have a beneficial effect on mortality. The higher caseload in high-volume centres has a positive effect on surgical mortality [10-12]. Although centralisation of care may result in longer travelling distances, this possible negative effect seems to be outweighed by the benefits of treatment in an expert center.[13]

During transport of the patient and during assessment in the emergency room, permissive hypotension or controlled hypotension should be implemented. Accepting lower systolic blood pressures has been reported to increase survival rates for patients with traumatic haemorrhargic shock.[14,15] Increasing systolic blood pressure by excessive saline infusion can lead to 'popping' of a previously formed blood clot and thus further haemmorhage. Also, the restriction in saline infusion during controlled hypotension reduces dilution of clotting factors. There is sufficient evidence to suggest that these principals of trauma care have beneficial effects in patients with rAAA as well.[16-19]

Treatment

For patients with rAAA, two treatment options exist: the conventional open repair (OR) and newer, minimally invasive endovascular repair (EVAR). Withholding surgical treatment, of course, is an option in patients who are moribund due to severe co-morbidity.

Open repair (OR)
In open repair, the patient is being operated on under general anaesthesia. Following a midline laparotomy, the retroperitoneal space is opened and the aortic bleeding is controlled by clamping of the aorta. Next, a vascular graft, either tube or bifurcated, is inserted. Circulation is restored and the abdomen closed.

Endovascular Repair (EVAR)
Through small groin incisions, access to the common femoral arteries is created. After placement of guide-wires, the endovascular graft is inserted into the aneurysm. The endograft is designed to be fixated and to seal both proximally and distally from the aneurysm, thereby excluding the aneurysm in order to prevent rupture. This procedure can be performed under local anaesthesia.

In rAAA repair, open conventional surgery has been the gold standard since 1954.[20] Over the last decades, no improvement in mortality of open rAAA repair has been observed, despite improvements in both prehospital and post-surgical care.[21] The mean age of surgically treated patients did increase.[21] Based on data from elective repair of AAA[22], the hypothesis arose that, in patients with a ruptured abdominal aortic aneurysm, the use of a minimally invasive technique such as endovascular repair might reduce surgical mortality as compared to open surgery.

Patient selection
Not all patients with rAAA are suitable to be treated by EVAR.[23] Both the proximal segment just below the renal arteries, as well as the distal iliac segment, must be suitable to accommodate an endograft. Moreover, other anatomical factors such as angulation, femoral access and wall calcifications are important for EVAR suitability. After possible ultrasound examination, anatomic suitability for EVAR is assessed with ct-angiography (CTA). However, some rAAA patients are too haemodynamically unstable to undergo CTA, and these patients will consequently be treated with open repair.

It is important to realise that different factors influence mortality after rAAA surgery. One of the most important known confounders is haemodynamic stability. Other factors such as age, gender and co-morbidity also have been reported to affect surgical mortality.[24-26]
Early studies on EVAR typically compared haemodynamically stable patients who were treated with EVAR to all patients treated with open repair. The latter group also included the very unstable patients. This selection bias obviously yielded results very favourable for EVAR. Mortality as low as 9.5%[27] after EVAR versus a 32-80% mortality after open repair was reported.[21,27,28] One randomised controlled trial was published and only included 32 patients.[29]

Amsterdam Acute Aneurysm Trial
To adequately compare two treatment options — endovascular repair and open repair — a randomised controlled trial (RCT) was needed. To properly interpret the results of the RCT, outcomes of all patients excluded from the RCT are needed as well. The 'Acute Amsterdam Aneurysm, or AJAX Trial' was designed accordingly.

In the AJAX trial, the entire larger Amsterdam region cooperated to optimise inclusion and patient care. A weekly aneurysm service rotation schedule was implemented in which three experienced EVAR centres and all seven regional hospitals co-operated. All patients suspected of a rAAA, or diagnosed with rAAA, were directed to one of three centres.

Only patient with severe hemodynamic instability, making transport absolutely impossible, were not referred. In the centre on call for that week, a multidisciplinary EVAR team was available and intensive care capacity was reserved for possible rAAA patients.
Alongside the randomised comparison of EVAR and open repair, a prospective cohort of all patients with rAAA in the Amsterdam area was created. This cohort of over 500 patients allowed for analysis and correction of certain confounding factors on survival, and for assessment of the effectiveness of the centralisation. The data were registered during the inclusion for the AJAX trial and the patient cohort was used for the majority of studies in this thesis.

AIM OF THIS THESIS

- To systematically review the available literature on population-based total mortality of rAAA
- To assess the feasibility of a controlled hypotension protocol for patients suspected of rAAA
- To compare EVAR and open repair for patients with rAAA in a regional, multicentre, randomised, controlled trial
- To assess the effect of regional cooperation on outcomes of rAAA patients, especially after correcting for hemodynamic instability
- To assess feasibility of semi-automatic software to determine suitability for EVAR in patients with rAAA
- To assess the influence of anatomic suitability for EVAR on mortality of rAAA patients treated with open repair.

OUTLINE OF THE THESIS

For **Chapter 2,** a systematic review of population-based studies on total mortality of rAAA was performed. Only studies reporting on patients in the community and in-hospital were included. Results are presented in chronological order and meta-analysis and meta-regression analysis were performed. Furthermore, the distribution and chronologic changes of fatalities outside the hospital, patients who did not undergo intervention, and surgically treated patients are reported.

In **Chapter 3,** a retrospective analysis of the prospectively kept cohort of patients suspected of rAAA in the Amsterdam region is presented. A protocol for controlled hypotension was implemented for all patients suspected of rAAA during ambulance transport. This study focuses on the feasibility of the controlled hypotension protocol during transport and the possible harm for patients who have a final diagnosis other than rAAA.

In **Chapter 4,** the primary results of the Amsterdam Acute Aneurysm Trial are presented. In a total of 10 hospitals, the Amsterdam ambulance services and all general practitioners participated in the trial, which included patients from 2004 to 2011. The Amsterdam Acute Aneurysm trial, or AJAX trial, is the first completed randomised study in history to compare EVAR and open repair for rAAA. The aim of the study is to investigate the benefits of the newer, minimally invasive EVAR, compared to conventional open repair. Chapter 4 focuses on the primary outcome of this study, the 30-day mortality rate and major complications of the randomised patients.

In **Chapter 5**, data is presented from the entire population-based cohort of rAAA. Along with the patients included in the randomised trial, all patients with rAAA in the Amsterdam region during the trial were registered. In chapter 5 the intervention rates and surgical mortality of hospitals and rAAA in the Amsterdam region are presented, the effects of the regional cooperation is analysed and survival-related data corrected for hemodynamic stability is presented.

In **Chapter 6,** the fitness of purpose of semi-automatic software for assessing EVAR-suitability of patients with rAAA is described. The software could help the observer in performing measurements to assess suitability. However, most software is designed for assessment of patients with non-ruptured AAA, scheduled for elective treatment. Alongside investigating the technical possibilities of visualising and measuring AAA with the software, the inter-observer agreement was studied.

Finally in **Chapter 7**, the influence of anatomical suitability for EVAR on the outcome of open repair is assessed. The anatomy of patients treated with open repair who are considered suitable for EVAR differs from patients treated with open repair who are considered unsuitable for EVAR. This anatomic difference might be a confounding factor on the outcome after open surgery, and may further contribute to the reported differences between EVAR and open repair in observational research.

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