Treatment of ruptured abdominal aortic aneurysms in the Amsterdam area

Reimerink, J.J.

Publication date
2014

8

CHAPTER 8

SUMMARY AND GENERAL DISCUSSION

SUMMARY AND GENERAL DISCUSSION

This thesis focuses on the treatment and outcome of patients with ruptured aneurysm of the abdominal aorta (rAAA), and in particular on the treatment with endovascular aneurysm repair (EVAR).

For **Chapter 2**, evidence on total mortality of rAAA was systematically reviewed. Studies were included if they included descriptions of both outside and in-hospital mortality from rAAA. The estimated pooled total mortality rate of rAAA in the 24 included population-based studies was 81 percent (95% CI 78 - 83). When arranged chronologically, a meta-regression analysis showed a significant decline in the risk of death (p=0.002) over time. The pooled estimate of total mortality in high-quality studies before 1990 was 86 (95% CI 83 - 89) per cent, compared with 74 (95%CI 72 - 77) percent since 1990. This is probably the result of improvements in diagnostics, logistics, surgical treatment and intensive care over the last decades.
Furthermore, our analysis shows that a large proportion of patients with rAAA do not undergo surgery. Thirty-two percent (32%) of the patients die without presentation to a hospital and another 27% die in the hospital without intervention. Consequently, less than half of all rAAA patients are treated by surgery. An improvement in surgical technique, no matter how significant, will only affect the patients treated by surgery. So next to improving surgical mortality, it is important to try to reduce the number of patients left untreated by improving the diagnostic accuracy outside the hospital, and optimise logistics and conditions before arriving at the hospital.

In **Chapter 3,** the feasibility and possible harm of a protocol for controlled hypotension is described. To optimise conditions during transport by ambulance for patients with a possible rAAA, the protocol was introduced as part of the AJAX study. The protocol prescribes that patients suspected of rAAA (possibly with a different final diagnosis) should be administered intravenous fluids only if systolic blood pressure is below 80mmHg. The majority (71%) of the 295 patients suspected of having rAAA had a systolic blood pressure of over 100mmHg. The protocol was followed in 83% of all patients. Of 295 patients suspected of having rAAA, 28% had rAAA as a final diagnosis. Our analysis showed that it is very unlikely that a protocol for controlled hypotension causes any harm to patients who ultimately did not have rAAA. Furthermore, this study showed that conditions were optimised for patients with rAAA.

After introduction of the minimally invasive EVAR technique in elective aneurysm repair, the hypothesis was that in the acute patient, the advantage would be more significant. Earlier observational studies of EVAR for rAAA suggested a significant reduction in mortality and complications compared to OR.[1,2] However, these observational studies were flawed by selection bias. To create an objective comparison between the two treatments, the Amsterdam Acute Aneurysm Trial was designed.[3]

In **Chapter 4,** the results of our randomised trial comparing EVAR and OR for rAAA are reported. During 2004-2011, a total of 116 patients suitable for both EVAR and OR were included and randomised. The primary endpoint for our study was combined mortality and major complications at 30 days. For the primary endpoint, an absolute risk reduction of 5.4% (95%CI -13% - 23%) was found, which differed significantly from the initially hypothesized 25% difference. On secondary endpoints, patients with EVAR had significantly less acute kidney failure, and less blood products were administered. Secondary endpoints such as hospital and

ICU stay, the number of complications, and re-interventions were in favour of EVAR but did not reach statistical significance, possibly because of the relatively small sample size.
The results from the trial were different than what we initially anticipated. Most importantly, the mortality after OR was surprisingly low, contributing to a smaller risk difference compared with EVAR. The low mortality after OR can be partly explained by improved logistics including pre-operative CT scanning, and centralized care. Furthermore, the number of failures from EVAR was relatively high. Intraoperative conversion from EVAR to OR occurred in 8 of 57 patients randomised for EVAR. An additional 6 patients were surgically treated because of a type I endoleak. If failures can be reduced, results after EVAR could be even better.

In **Chapter 5,** we describe the analysis of all patients with rAAA in the Amsterdam region who presented to any of the participating hospitals. A change in logistics and centralisation of care for rAAA patients was organised in light of the Amsterdam Acute Aneurysm trial. In this chapter the regional cooperation is described and survival is analysed.
Of 453 identified patients with a rAAA in our region, 61 patients (13.5%) were not surgically treated. Of all surgically treated patients, over 90% were treated in one of three vascular centres. Multivariate and propensity adjustment showed that patients had a higher chance of survival in one of the vascular centres. Outcome was corrected for confounders such as age, gender and hemodynamic stability (based on systolic blood pressure and resuscitation). Analysis also showed that referral from a regional hospital to a vascular centre was not correlated with a higher chance of dying, despite possible delay in treatment.
The regional admission survival rate (58.5%, CI 53.9 – 62.9%) observed in our study was higher than a previously published study on Dutch admission survival rate (46%, CI 43 – 49). We concluded that regional cooperation with centralised care was successful, safe and most likely improves survival.

In **Chapter 6**, we assess the potential of semi-automatic software to determine EVAR suitability. Not all patients with rAAA can be treated with EVAR because of unsuitable anatomy.[4] Suitability is determined with the help of CTA. Aortic diameters, lengths and angles are usually measured on axial planes. Adequate patient selection is very important, as endoleaks and graft dislocation should be avoided. In previous research, differences between observers (inter-observer variability) were described when assessing anatomy for EVAR suitability.[5] With the help of a semi-automated generation of a central lumen line, vessel diameters and lengths can be measured. The software (3mensio Vascular, Bilthoven Netherlands) has been used in elective patients with AAA[6] but never in rAAA. We hypothesised the software could help the observer in the assessment of EVAR suitability.
Six observers assessed 50 patients with rAAA by using the software. In the majority of assessments a semi-automatic assessment was possible (median 76%, range 64-78%). Failures were mainly the result of inadequate contrast load, probably as a result of low cardiac output. The group agreement on suitability was moderate (kappa value of 0.55, CI 0.48-0.62), and the agreement between individual observers differed (kappa values between 0.40 and 0.72). The median time for assessment was 7.5 minutes (interquartile range 5.5-10.6).
By introducing a semi-automatic method to assess suitability, we hoped to minimise the influence of the clinician on the final interpretation. Although some observers liked the way of measuring with the software, most experienced observers preferred measuring on axial and transverse planes.

In **Chapter 7,** the role of aneurysm anatomy as a confounding factor on outcome after open repair was investigated. Patients with anatomy considered unsuitable for EVAR usually have shorter infrarenal necks. This hostile anatomy could be difficult to treat with open repair as compared to a more friendly anatomy, resulting in differences in mortality. Because of our randomised cohort, we have a unique group of patients with EVAR friendly anatomy who have been treated by open repair. These patients were compared with patients with hostile anatomy for mortality and complications.
Of 279 included patients, 71 had friendly anatomy and 201 had hostile anatomy. Suprarenal cross-clamping was considered necessary in 43% of patients with hostile anatomy versus 27% of patients with friendly anatomy (p=0.02). The 30-day or in-hospital mortality was 38% (CI 28-50) in patients with friendly anatomy versus 30% (CI 24-37) in patients with hostile anatomy (p=0.23). No significant difference was observed in combined mortality and severe complication rate, secondary endpoints and long-term survival.
Contrary to what one would expect, anatomy did not influence mortality after open surgery. Probably other factors such as hemodynamic stability play a much more important role in the survival rate.

Limitations and Future Perspective

The Amsterdam Acute Aneurysm study was designed as a regional study in a defined area of 1025 km^2 with 1.38 million inhabitants and thus a population density of 1375/km. All hospitals and ambulance services cooperated in the centralised logistics in order to treat patients in vascular centres and data collection. Employees of the ambulance services and in the emergency rooms, vascular surgeons, radiologists and other treating staff all reported data, and a truly unique prospective cohort of rAAA patients was created. From an epidemiological point of view, this provides for a population-based cohort in which selection bias is limited. However, generalising and comparing results directly to other regions may not be appropriate due to differences in infrastructure, the size of the region and population-based confounding factors. Also, because of the ongoing randomised trial, efforts to achieve a lower mortality and improve cooperation might have been higher compared to a normal situation.

With a randomised study design in groups suited for both treatments, we minimised the bias typically seen in observational studies, yielding comparable results after EVAR and OR. 116 patients of all rAAA were eventually included. Because of this relatively small sample size, some outcome measures may not have been significant due to a type II error. Newer data from the IMPROVE trial in the UK[7,8], in which an EVAR strategy is compared to an all-OR strategy, yields results comparable to the Acute Aneurysm Trial, but in a larger sample size (35 versus 37% regional 30-day mortality, odds ratio 0.92 (95%CI 0.66 to 1.28; P=0.62)).
Although of relative importance in relation to the endpoint of mortality, EVAR is likely to offer advantages for secondary endpoints, such as complications per patients, ICU stay and time to discharge. In addition, a minimally invasive procedure with a smaller scar and quick recovery are important factors in the eyes of the patient. From the hospital management and healthcare perspective, a comparison of costs between the two treatment options is also important and should be studied further.[8,9]
Our study did not show a significant benefit of EVAR compared with open surgery regarding mortality and major complications. However, one might expect that with improving technology, more aneurysms can be successfully treated by EVAR and might reduce mortality. Using hybrid theatres with sophisticated angiography and possible CTA already in place are elements that are within reach, and will help to improve the success of interventions.

The main reason for exclusion from the randomised trial was unsuitable anatomy for EVAR. The assessment of suitability is an observer-dependent process, in which experience is likely to influence the percentage of patients deemed suitable. Other studies report higher rates for suitability compared to our region, and the inclusion possibly could have been higher if less strict anatomical criteria were used. As EVAR technology progresses and with increasing experience, more challenging anatomy can be treated by EVAR. However, it should be noted that this might increase the number of patients with type 1 endoleak. Such a complication can lead to conversion to open repair — and, as our study shows, is a source of severe complications and death.[10]
An aorto-uni-iliac graft was used throughout the trial period, mainly to achieve rapid haemodynamic control and because of the simple technique. A meta-analysis shows no difference in outcome between bifurcated and aorto-uni-iliac graft when corrected for hemodynamic stability [11]. Nowadays, probably as a result of the worldwide increase in experience, the bifurcated graft is more widely used.
Standardization in assessment of suitability with (semi)automatic software may improve results and comparisons between different cohorts of patients. With a (semi)automatic approach, opinions on suitability of different observers are better aligned. The potential of using improved software and its impact on patient outcome needs further study.

The data from the regional cohort study, including the patients of the Acute Aneurysm trial, showed an overall improved regional survival rate after open repair. This is likely the result of well-organised care in a cooperative, well-structured and geographically dense region. Logistics and protocols were optimised as part of the randomised trial.
A large proportion of rAAA will always remain untreated and even undiagnosed, the goal is to keep this number as low as possible. Reducing mortality from rAAA is achieved by optimising conditions in several important phases — before, during and after surgery. The conditions include accurate initial diagnosis outside the hospital to controlled hypotension during transport, direct computed tomography, a low non-operative rate, proper selection for EVAR, experienced anesthesiological care, an experienced surgical team and well-experienced intensive care after surgery. Many factors in the process from diagnosis to discharge contribute to the survival rate of rAAA patients. The route to lower mortality from rAAA should be well organised and well structured.

REFERENCE LIST

(1) Lachat ML, Pfammatter T, Witzke HJ, Bettex D, Künzli A, Wolfensberger U, et al. Endovascular Repair with Bifurcated Stent-Grafts under Local Anaesthesia to Improve Outcome of Ruptured Aortoiliac Aneurysms. European Journal of Vascular and Endovascular Surgery. 2002;23(6):528-36.

(2) Peppelenbosch N, Yilmaz N, van Marrewijk C, Buth J, Cuypers P, Duijm L, et al. Emergency treatment of acute symptomatic or ruptured abdominal aortic aneurysm. Outcome of a prospective intent-to-treat by EVAR protocol. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2003;26(3):303-10.

(3) Amsterdam Acute Aneurysm Trial: Background, Design, and Methods. Vascular. 2006;14(3):130-

(4) Hoornweg LL, Wisselink W, Vahl A, Balm R, Amsterdam Acute Aneurysm Trial C. The Amsterdam Acute Aneurysm Trial: suitability and application rate for endovascular repair of ruptured abdominal aortic aneurysms. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2007;33(6):679-83.

(5) Hoornweg LL, Wisselink W, Vahl AC, Reekers JA, van Delden OM, Legemate DA, et al. Interobserver and intraobserver variability of interpretation of CT-angiography in patients with a suspected abdominal aortic aneurysm rupture. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2008;35(3):295-300.

(6) Ghatwary TM, Patterson BO, Karthikesalingam A, Hinchliffe RJ, Loftus IM, Morgan R, et al. A systematic review of protocols for the three-dimensional morphologic assessment of abdominal aortic aneurysms using computed tomographic angiography. Cardiovascular and interventional radiology. 2013;36(1):14-24.

(7) Powell JT, Sweeting MJ, Thompson MM, Ashleigh R, Bell R, Gomes M, et al. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. Bmj. 2014;348:f7661.

(8) Investigators IT. An endovascular strategy for suspected ruptured abdominal aortic aneurysm brings earlier home discharge but not early survival or cost benefits. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2014;47(4):333-4.

(9) Kapma MR, Dijksman LM, Reimerink JJ, de Groof AJ, Zeebregts CJ, Wisselink W, et al. Cost-effectiveness and cost-utility of endovascular versus open repair of ruptured abdominal aortic aneurysm in the Amsterdam Acute Aneurysm Trial. The British journal of surgery. 2014;101(3):208-15.

(10) Richards T, Goode SD, Hinchliffe R, Altaf N, Macsweeney S, Braithwaite B. The importance of anatomical suitability and fitness for the outcome of endovascular repair of ruptured abdominal aortic aneurysm. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2009;38(3):285-90.

(11) Karkos CD, Sutton AJ, Bown MJ, Sayers RD. A meta-analysis and metaregression analysis of factors influencing mortality after endovascular repair of ruptured abdominal aortic aneurysms European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2011;42(6):775-86.

(12) Schlosser FJ, Vaartjes I, van der Heijden GJ, Moll FL,Verhagen HJ, Muhs BE et al. Mortality after hospital admission for ruptured abdominal aortic aneurysm. Ann Vasc Surg 2010; 24: 1125–1132.