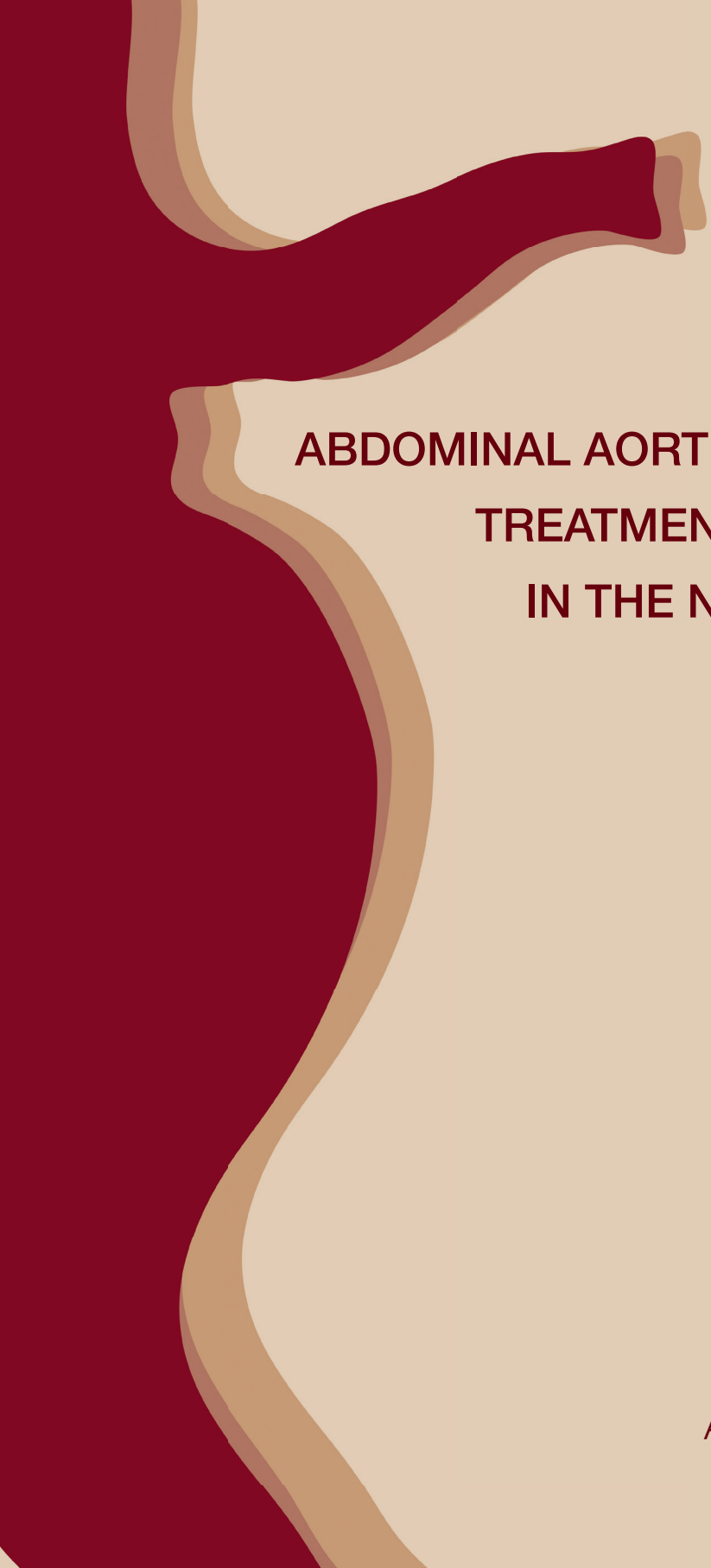

ABDOMINAL AORTIC ANEURYSM TREATMENT OUTCOMES IN THE NETHERLANDS

Anna Judith Alberga

Abdominal Aortic Aneurysm Treatment Outcomes in the Netherlands

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1

GENERAL INTRODUCTION AND THESIS OUTLINE

GENERAL INTRODUCTION

Aortic aneurysms

An aneurysm is a pathological dilation of the segment of a blood vessel that exceeds the normal diameter of at least 1.5 times[1]. The risk of having an aneurysm is rupture which causes life-threatening bleeding needing emergent treatment. Aortic aneurysms could be classified based on their location. The predominant location for aortic aneurysms is the abdominal aorta (abdominal aortic aneurysm = AAA) which is the part of the aorta located below the diaphragm within the abdomen. Most AAAs are at the infrarenal location. Less frequently, aortic aneurysms are located in the chest cavity (thoracic aortic aneurysm = TAA) or in a combination of both (thoracic-abdominal aortic aneurysm (ThAAA). Known risk factors for developing an AAA are male gender, increased age, family history of aneurysmal disease, and cardiovascular disease[2]. In studies examining screening programs, the prevalence of an AAA is between 1 and 2% in 65-year-old men[3,4]. Usually, an aneurysm grows slowly at around 2-3 mm per year[5]. However, larger aneurysms grow faster and are at a higher risk of rupture[6,7]. Rupture rates are higher in women and smokers and are increased in patients with higher blood pressure[6].

Aortic aneurysm treatment

Aortic aneurysm repair is the most effective treatment option for patients with either an intact (non-ruptured) or ruptured aneurysm. In patients with an intact aneurysm, aneurysm repair is performed to prevent rupture. Patients with an intact aneurysm may have an asymptomatic or symptomatic aneurysm. The decision to treat asymptomatic patients is based on the perioperative risks, the risk of rupture (determined by size and morphology), and the patient's estimated life expectancy since aneurysm repair is associated with perioperative risks[8]. The threshold diameter for considering AAA treatment in men is 5.5 cm, while in women, despite higher perioperative mortality[9], a lower threshold of 5.0 cm may be considered due to a higher risk of rupture[8]. Patients presenting with a symptomatic aneurysm (abdominal pain, back pain, or a tender aneurysm) are thought to have a higher rupture risk than patients with an asymptomatic aneurysm. Symptomatic aneurysms should be treated under optimal conditions in a delayed setting since emergency repair is associated with a higher risk of perioperative complications[8]. For patients with a ruptured AAA, aneurysm repair is the only life-saving treatment and can be offered to most patients that reach the hospital. About one-third of all patients presenting with a ruptured aortic aneurysm die before reaching a hospital[10]. Of all patients that reach a hospital, 40% do not undergo surgery due to refusing aneurysm repair or being in such a poor condition that surviving aneurysm repair, including a meaningful quality of life, is very unlikely[10].

Treatment modalities

Two treatment methods are available to accomplish aneurysm repair for intact and ruptured aneurysms: open surgical repair (OSR) and endovascular aortic repair (EVAR). OSR involves the replacement of the diseased aortic segment with a prosthetic graft through a midline or retroperitoneal incision. In contrast, EVAR involves the placement of a stent inside the aorta, delivered via the femoral arteries. Treatment of AAAs is the least complex in infrarenal AAAs. In contrast, treatment is more complex for juxtarenal and suprarenal AAAs due to involvement of the renal arteries and/or superior mesenteric artery. In patients with a juxtarenal AAA, OSR requires suprarenal clamping, while in patients with a suprarenal AAA, it might be needed to position the aortic clamp above all visceral vessels. In patients with a juxtarenal or suprarenal AAA receiving endovascular treatment, the proximal landing zone for stent-grafts needs to be extended by incorporating arteries in the graft with fenestrations Preferences for treatment modality depend on the setting in which the treatment is performed, patients' age, comorbidities, life expectancy, and morphology[8].

Treatment outcomes of intact abdominal aortic aneurysms

Since the introduction of EVAR in 1991[11] EVAR has been increasingly performed to treat intact AAAs. However, both EVAR and OSR appear to have their advantages and disadvantages. Over the years, the performance of EVAR versus OSR has been compared by several RCTs[12–15]. In the pooled results of these studies, patients treated with EVAR had a significant survival benefit for up to 3 years. This effect was lost during mid-term follow-up[16]. Moreover, long-term reinterventions appear to be more frequent following EVAR[16] due to stent-related complications. However, the actual difference in reinterventions might be less as the largest trial included in the pooled results did not report laparotomy-related complications[16] which occur more often following OSR[17]. To prevent stent-related complications, frequent follow-up or surveillance is needed following EVAR, especially in patients treated outside the instructions for use (IFU)[8,16]. Comparable to the RCTs, observational studies examining data from vascular registries or administrative databases identified lower perioperative mortality rates following EVAR[18–20]. The guidelines of the European Society for Vascular Surgery (ESVS)[8] and the Dutch guideline[21] suggest that in most patients with suitable anatomy and reasonable life expectancy (>2-3 years), EVAR should be considered as the preferred treatment option. While in patients with a long life expectancy (>10-15 years) OSR should be considered. No treatment is recommended in patients with limited life expectancy (<2-3 years).

Treatment outcomes of ruptured abdominal aortic aneurysms

In patients with a ruptured AAA, the choice for EVAR is less evident than for patients with an intact AAA. Ruptured AAA treatment outcomes of EVAR and OSR were compared

in several RCTs and observational studies. Interestingly, no statistical difference was found in perioperative mortality between EVAR and OSR in the performed RCTs[22], but this may also be due to the chosen set-up of the study. Observational studies and data from administrative registries showed lower perioperative mortality for EVAR[23]. These opposite results could also be explained by selection bias[23], as in observational studies, stable patients are more likely to undergo EVAR as patients must be stable enough to undergo a computed tomography angiography (CTA) to be considered for EVAR. The most recent guidelines suggest that EVAR is recommended as the first option in patients with ruptured AAA and suitable anatomy[8,21].

Treatment outcomes of complex aortic aneurysms

Complex aortic aneurysms involving the renal arteries and/or superior mesenteric artery were traditionally treated with OSR. However, in recent years endovascular techniques including fenestrated EVAR (FEVAR) and branched EVAR (BEVAR) have been increasingly introduced in several hospitals due to improvement in stent technology and advancement in endovascular experience. No RCTs have been performed to compare OSR with endovascular treatment for complex aortic aneurysms so far, and most observational data comparing FEVAR and OSR are prone to selection bias[24].

Real-world data

Knowledge about treatment outcomes is important for clinicians and patients to make optimal treatment choices. Although RCTs are still the gold standard in comparing clinical interventions[25], the results of RCTs could be misleading when applied in the real world, potentially due to an unrepresentative selection of patients or improved outcomes over time[26]. Moreover, RCTs only include the results of a limited number of hospitals, potentially centers of excellence. Therefore, complementary to RCTs, observational cohort studies consisting of real-world data provide vital information[27], especially to examine outcomes following treatment of elderly patients or to evaluate nationwide outcomes over time. Nowadays, several national and regional vascular registries have been established to reflect on real-world clinical outcomes[28] and drive national improvement programs to optimize outcomes after aneurysm repair[29].

Quality improvement initiative in Dutch healthcare

In the Netherlands, quality of care has gained more attention from doctors, politicians, the government, and health insurance companies in the last two decades. Clinicians and hospitals were forced to become more open and transparent about their treatment outcomes and accountable for the care provided. However, there was a lack of valid information on the quality of care. Therefore, some surgeons decided to monitor the results of their performed colorectal surgical procedures, whereafter the results were shared

with all Dutch colleagues to learn from it. This resulted in a decrease in complications following colorectal surgery, and after this success, several other national clinical audits were established[30]. These national clinical audits, also quality registries, were based on the clinical auditing principle, which was first described by Ernest Codman, an American surgeon who lived in the early 20th century[31].

Dutch Surgical Aneurysm Audit

Within this quality improvement movement, the Dutch Surgical Aneurysm Audit (DSAA) was established in 2013 by the Dutch Society for Vascular Surgery. The aim of the DSAA is to evaluate and improve the actual quality of Dutch aneurysm care. For all hospitals and Dutch vascular surgeons, it is mandatory to register all performed aortic surgeries in the DSAA. The DSAA is facilitated by the Dutch Institute for Clinical Auditing (DICA). Currently, DICA facilitates 21 disease-specific quality registries and supports quality registries with processes such as supporting the registration of clinical data by clinicians and data managers, providing feedback to clinicians and hospitals on their clinical outcomes, comparing outcomes of hospitals with the benchmark (national mean) using indicators and funnel plots, and making hospital results transparent (based on indicators)[32]. Each year, the scientific committee of the DSAA consisting of vascular surgeons discusses, together with stakeholders such as health insurers and patient associations, which indicators should be used for comparing hospital results and which results should become transparent. In addition to the transparent indicators, some indicators are used to provide internal feedback to hospitals. Finally, the DSAA is used to perform observational cohort studies that evaluate the nationwide quality of aortic aneurysm care, reflecting outcomes in the real world. However, besides many advantages and possibilities, our mandatory nationwide registry also has its shortcomings as a limited follow-up and its threats as a high registration burden for clinicians.

Therefore, this thesis aims to gain insight into the quality and real-world outcomes of the current practice of aortic aneurysm treatment in the Netherlands. Moreover, this thesis investigates new opportunities to develop the DSAA further.

The main study questions of this thesis are:

- Have the outcomes of AAA care improved in the Netherlands since the introduction of the DSAA?
- What are the outcomes of subgroups treated for abdominal aortic aneurysms in the Netherlands, and is there room for improvement in these outcomes?
- What are the outcomes of the Dutch patients treated for complex aortic aneurysms, and does hospital volume influence these outcomes?
- How can the DSAA be developed further?

THESIS OUTLINE

This thesis consists of three parts.

In the first part of this thesis, abdominal aortic aneurysm treatment outcomes are evaluated.

The DSAA aims to evaluate and improve the quality of Dutch aneurysmal care by providing feedback to hospitals. Auditing and feedback generally lead to small but potentially significant improvements in professional practice[33]. However, it is unknown whether outcomes have improved since the introduction of the DSAA. Therefore, in **Chapter 2**, we evaluate whether the main outcomes of intact AAA repair (mortality, major complications, and textbook outcome) have improved since the establishment of the DSAA.

Several RCTs have compared outcomes of EVAR versus OSR in a predetermined population. In the last decade, the number of patients over 80 years (octogenarians) that qualify for elective AAA repair was increasing[18], probably due to an aging population. However, performed RCTs barely have enrolled patients over 80 years, and current studies, including observational data, have not described detailed outcomes for octogenarians. **Chapter 3** describes the results of octogenarians following intact AAA repair, assesses the influence of comorbidities on these outcomes, and identifies which octogenarians have high and low perioperative risks. Also, ruptured AAA perioperative outcomes for octogenarians based on nationwide data reflecting real-world practice are scarce. **Chapter 4** investigates the outcomes of octogenarians following ruptured AAA repair and assesses which preoperative factors influence perioperative outcomes of octogenarians.

Previous studies have reported that perioperative mortality is higher among women compared to men, despite correction for patient-related risk factors[9]. However, hospital-related factors may influence patient outcomes as well. **Chapter 5** examines the influence of whether hospital-related factors declare the higher mortality of women following intact AAA repair compared to men.

Finally, in order to optimize perioperative outcomes following OSR, those postoperative complications that most affect postoperative outcomes need to be highlighted. In **Chapter 6**, we investigate which complications are most common following OSR and what the influence of these complications is on perioperative outcomes.

In the second part of this thesis, we examine the outcomes of complex aortic aneurysm treatment.

No RCTs have been performed to examine treatment outcomes of complex aortic aneurysms, while observational cohort studies reporting on FEVAR and BEVAR predominantly describe the results from centers of excellence. Moreover, it is unclear whether a volume outcome relationship exists in patients receiving FEVAR or BEVAR. In **Chapter 7**, we describe the nationwide perioperative outcomes of complex EVAR and assess the influence of hospital volume on perioperative mortality. **Chapter 8** assesses the current practice and outcomes of OSR and complex EVAR for juxtarenal AAAs.

In the third part of this thesis, we examine new opportunities for feedback and outcome measurement.

The DSAA includes perioperative outcomes that occur up to 30 days following surgery. However, complications and reinterventions that occur after 30 days are not scarce following EVAR and OSR[17]. A limited registration burden is essential for quality registries. Therefore, adding administrative healthcare data to evaluate mid-term outcomes following AAA repair might be valuable. In **Chapter 9**, we assess the feasibility and the potential benefit of adding administrative healthcare data to the DSAA to evaluate mid-term reinterventions following intact AAA repair.

Currently, funnel plots comparing the outcomes of individual hospitals with the national average outcomes are used to provide feedback to hospitals on their performances over the last 36 months, which makes it challenging to determine whether outcomes improve or deteriorate over shorter periods. In industrial processes, real-time process control systems such as the CUSUM method are widely applied. In **Chapter 10**, it is investigated whether real-time feedback could be provided to hospitals using the CUSUM method, in addition to the currently used funnel plots.

REFERENCES

1 Evans GH, Stansby G, Hamilton G. Suggested standards for reporting on arterial aneurysms. *J Vasc Surg* 1992;**15**(2):452–8. Doi: doi: 10.1016/0741-5214(92)90269-e.

2 Kent KC, Zwolak RM, Egorova NN, Riles TS, Manganaro A, Moskowitz AJ, et al. Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals. *J Vasc Surg* 2010;**52**(3):539–48. Doi: 10.1016/j.jvs.2010.05.090.

3 Jacomelli J, Summers L, Stevenson A, Lees T, Earnshaw JJ. Impact of the first 5 years of a national abdominal aortic aneurysm screening programme. *British Journal of Surgery* 2016;**103**(9):1125–31. Doi: 10.1002/bjs.10173.

4 Svensjö S, Björck M, Gürtelschmid M, Djavani Gidlund K, Hellberg A, Wanhainen A. Low prevalence of abdominal aortic aneurysm among 65-year-old swedish men indicates a change in the epidemiology of the disease. *Circulation* 2011;**124**(10):1118–23. Doi: 10.1161/CIRCULATIONAHA.111.030379.

5 Brady AR, Thompson SG, Fowkes FGR, Greenhalgh RM, Powell JT. Abdominal aortic aneurysm expansion: Risk factors and time intervals for surveillance. *Circulation* 2004;**110**(1):16–21. Doi: 10.1161/01.CIR.0000133279.07468.9F.

6 Thompson SG, Brown LC, Sweeting MJ, Bown MJ, Kim LG, Glover MJ, et al. Systematic review and meta-analysis of the growth and rupture rates of small abdominal aortic aneurysms: implications for surveillance intervals and their cost-effectiveness. *Health Technol Assess* 2013:1–118. Doi: 10.3310/hta17410.

7 Parkinson F, Ferguson S, Lewis P, Williams IM, Twine CP. Rupture rates of untreated large abdominal aortic aneurysms in patients unfit for elective repair. *J Vasc Surg* 2015;**61**(6):1606–12. Doi: 10.1016/j.jvs.2014.10.023.

8 Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(1):8–93. Doi: 10.1016/j.ejvs.2018.09.020.

9 Ulug P, Sweeting MJ, von Allmen RS, Thompson SG, Powell JT, Ulug P, et al. Morphological suitability for endovascular repair, non-intervention rates, and operative mortality in women and men assessed for intact abdominal aortic aneurysm repair: systematic reviews with meta-analysis. *The Lancet* 2017;**389**(10088):2482–91. Doi: 10.1016/S0140-6736(17)30639-6.

10 Reimerink JJ, van der Laan MJ, Koelemay MJ, Balm R, Legemate DA. Systematic review and meta-analysis of population-based mortality from ruptured abdominal aortic aneurysm. *British Journal of Surgery* 2013;**100**(11):1405–13. Doi: 10.1002/bjs.9235.

11 Parodi J, Palmaz J, Barone H, Aires B, Antonio S. Transfemoral Intraluminal Graft Implantation for Abdominal Aortic Aneurysms. n.d.

12 Blankensteijn JD, de Jong SECA, Prinssen M, van der Ham AC, Buth J, van Sterkenburg SMM, et al. Two-Year Outcomes after Conventional or Endovascular Repair of Abdominal Aortic Aneurysms. *New England Journal of Medicine* 2005;**352**(23):2398–405. Doi: 10.1056/nejmoa051255.

13 Greenhalgh R, Brown L, Kwong G, Powell J, Thompson S, EVAR trial participants. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet* 2004;**364**:843–8.

14 Becquemin JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, et al. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients. *J Vasc Surg* 2011;**53**(5). Doi: 10.1016/j.jvs.2010.10.124.
15 Lederle FA, Freischlag JA, Kyriakides TC, Matsumura JS, Padberg FT, Kohler TR, et al. Long-Term Comparison of Endovascular and Open Repair of Abdominal Aortic Aneurysm. *New England Journal of Medicine* 2012;**367**(21):1988–97. Doi: 10.1056/nejmoa1207481.
16 Powell JT, Sweeting MJ, Ulug P, Blankensteijn JD, Lederle FA, Becquemin JP, et al. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. *British Journal of Surgery* 2017;**104**(3):166–78. Doi: 10.1002/bjs.10430.
17 Schermerhorn ML, Buck DB, O'Malley AJ, Curran T, McCallum JC, Darling J, et al. Long-Term Outcomes of Abdominal Aortic Aneurysm in the Medicare Population. *New England Journal of Medicine* 2015;**373**(4):328–38. Doi: 10.1056/nejmoa1405778.
18 Budtz-Lilly J, Venermo M, Debus S, Behrendt CA, Altreuther M, Beiles B, et al. Editor's Choice – Assessment of International Outcomes of Intact Abdominal Aortic Aneurysm Repair over 9 Years. *European Journal of Vascular and Endovascular Surgery* 2017;**54**(1):13–20. Doi: 10.1016/j.ejvs.2017.03.003.
19 Schermerhorn ML, O'Malley AJ, Jhaveri A, Cotterill P, Pomposelli F, Landon BE. Endovascular vs. open repair of abdominal aortic aneurysms in the medicare population. *New England Journal of Medicine* 2008;**358**(5):464–74. Doi: 10.1056/NEJMoa0707348.
20 Dansey KD, de Guerre LEVM, Swerdlow NJ, Li C, Lu J, Patel PB, et al. A comparison of administrative data and quality improvement registries for abdominal aortic aneurysm repair. *J Vasc Surg* 2021;**73**(3):874–88. Doi: 10.1016/j.jvs.2020.06.105.
21 NVVH. Aneurysma van de abdominale aorta (AAA). https://richtlijnendatabase.nl/richtlijn/aneurysma_van_de_abdominale_aorta_aaa/startpagina_-_aaa.html. 05/24/2022.
22 Sweeting MJ, Balm R, Desgranges P, Ulug P, Powell JT. Individual-patient meta-analysis of three randomized trials comparing endovascular versus open repair for ruptured abdominal aortic aneurysm. *British Journal of Surgery* 2015;**102**(10):1229–39. Doi: 10.1002/bjs.9852.
23 van Beek SC, Conijn AP, Koelemay MJ, Balm R. Editor's choice - Endovascular aneurysm repair versus open repair for patients with a ruptured abdominal aortic aneurysm: A systematic review and meta-analysis of short-term survival. *European Journal of Vascular and Endovascular Surgery* 2014:593–602. Doi: 10.1016/j.ejvs.2014.03.003.
24 Jones AD, Waduud MA, Walker P, Stocken D, Bailey MA, Scott DJA. Meta-analysis of fenestrated endovascular aneurysm repair versus open surgical repair of juxtarenal abdominal aortic aneurysms over the last 10 years. *BJS Open* 2019;**3**(5):572–84. Doi: 10.1002/bjs5.50178.
25 Jones DS, Podolsky SH. The history and fate of the gold standard. *The Lancet* 2015:1502–3. Doi: 10.1016/S0140-6736(15)60742-5.
26 Paraskevas KI, de Borst GJ, Veith FJ. Why randomized controlled trials do not always reflect reality. *J Vasc Surg* 2019:607-614.e3. Doi: 10.1016/j.jvs.2019.01.052.
27 Barnish M, Turner S. The value of pragmatic and observational studies in health care and public health. *Pragmat Obs Res* 2017;**Volume 8**:49–55. Doi: 10.2147/por.s137701.
28 Sutzko DC, Mani K, Behrendt CA, Wanhainen A, Beck AW. Big data in vascular surgery: registries, international collaboration and future directions. *J Intern Med* 2020:51–61. Doi: 10.1111/joim.13077.
29 Waton S, Johal A, Birmpili P, Li Q, Cromwell D, O'Neill R, et al. Updated version with case ascertainment information NATIONAL VASCULAR REGISTRY 2021 Annual Report. 2021.

30 Eddes EH, van Leeuwen A, Tollenaar R, Wouters M. Beter dokteren. Prometheus Amsterdam; 2020.
31 Donabedian A. The End Results of Health Care : Ernest Codman ' s Contribution to Quality Assessment and Beyond. *Milbank Q* 1989;**67**(2):233–56.
32 Beck N, van Bommel AC, Eddes EH, van Leersum NJ, Tollenaar RA, Wouters MW. The Dutch Institute for Clinical Auditing: Achieving Codman's Dream on a Nationwide Basis. *Ann Surg* 2020;**271**(4):627–31. Doi: 10.1097/SLA.0000000000003665.
33 Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, et al. Audit and feedback: Effects on professional practice and healthcare outcomes. *Cochrane Database of Systematic Reviews* 2012;**2012**(6). Doi: 10.1002/14651858.CD000259.pub3.

PART 1

ABDOMINAL AORTIC ANEURYSM TREATMENT OUTCOMES

CHAPTER

2

TREATMENT OUTCOME TRENDS FOR NON-RUPTURED ABDOMINAL AORTIC ANEURYSMS: A NATIONWIDE PROSPECTIVE COHORT STUDY

Anna J. Alberga, Eleonora G. Karthaus, Janneke A. Wilschut, Jorg L. de Bruin, George P. Akkersdijk, Robert H. Geelkerken, Jaap F. Hamming, Jan. J. Wever, Hence J.M. Verhagen, in collaboration with the Dutch Society of Vascular Surgery, the Steering Committee of the Dutch Surgical Aneurysm Audit and the Dutch Institute for Clinical Auditing

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ABSTRACT

Objective

The Dutch Surgical Aneurysm Audit (DSAA) initiative was established in 2013 to monitor and improve nationwide outcomes of aortic aneurysm surgery. The objective of this study was to examine whether outcome sof surgery for intact abdominal aortic aneurysms (iAAA) have improved over time.

Methods

Patients who underwent primary repair of an iAAA by standard endovascular (EVAR) or open surgical repair (OSR) between 2014 and 2019 were selected from the DSAA for inclusion. The primary outcome was peri-operative mortality trend per year, stratified by OSR and EVAR. Secondary outcomes were trends per year in major complications, textbook outcome (TbO), and characteristics of treated patients. The trends per year were evaluated and reported in odds ratios per year.

Results

In this study, 11 624 patients (74.8%) underwent EVAR and 3 908 patients (25.2%) underwent OSR. For EVAR, after adjustment for confounding factors, there was no improvement in peri-operative mortality (aOR [adjusted odds ratio] 1.06, 95% CI 0.94-1.20), while major complications decreased (2014: 10.1%, 2019: 7.0%; aOR 0.91, 95% CI 0.88-0.95) and the TbO rate increased (2014: 68.1%, 2019: 80.9%; aOR 1.13, 95%CI 1.10-1.16). For OSR, the peri-operative mortality decreased (2014: 6.1%, 2019: 4.6%; aOR 0.89, 95% CI 0.82-0.98), as well as major complications (2014: 28.6%, 2019: 23.3%; aOR 0.95, 95% CI 0.91-0.99). Furthermore, the proportion of TbO increased (2014: 49.1%, 2019: 58.3%; aOR 1.05, 95% CI 1.01-1.10). In both the EVAR and OSR group, the proportion of patients with cardiac comorbidity increased.

Conclusion

Since the establishment of this nationwide quality improvement initiative (DSAA), all outcomes of iAAA repair following EVAR and OSR have improved, except for peri-operative mortality following EVAR which remained unchanged.

INTRODUCTION

As a result of endovascular aneurysm repair (EVAR), the management of intact abdominal aortic aneurysms (iAAA) has changed dramatically in the last decades resulting in improved peri-operative outcomes. Since the first EVAR was performed in the 1990s, many patients with suitable anatomy have received EVAR rather than open surgical repair (OSR) because of the lower peri-operative risks of EVAR[1], with a subsequent decrease in the number of patients treated by OSR[2–5]. Furthermore, frail patients can receive EVAR rather than conservative treatment[6]. These changes in treatment strategy probably have resulted in fewer OSRs per hospital, which may have negatively influenced the outcomes of OSR[7].

Previous studies have reported trends in the management and outcomes of iAAA repair. A study of an international cohort of vascular registries that described trends in the management and outcomes of iAAA repair from 2005 up to 2013 reported an overall decrease of peri-operative mortality from 3.0% to 2.4% while the peri-operative mortality after OSR increased from 3.9% to 4.4%[8]. Although this international study reported numerous patient outcomes, many of the registries included patients on a voluntary basis[9]. Furthermore, Swedvasc, the Swedish national vascular registry, reported a decrease in 30 day mortality rates following OSR (3.1% in 2006-2011, 2.5% in 2012-2016)[1]. To date however, no studies have examined the most recent trends in the management and outcomes of iAAA repair, reflecting real world nationwide data.

The Dutch Surgical Aneurysm Audit (DSAA) is a mandatory quality registry for all aortic aneurysm repairs performed by vascular surgeons in The Netherlands, established in 2013, to monitor and improve the outcomes of the treatment of abdominal aortic aneurysms (AAAs). In the DSAA, all hospitals that perform AAA repair have insight into their results, using quality indicators, with other hospitals presented anonymously with a 95% confidence interval around the national average for comparison. In this way, internal feedback on the performance of hospitals is provided[10,11]. Although audit and feedback generally lead to small but potentially important improvements in professional practice[12], it is not known yet whether the outcomes of iAAA repair have improved in The Netherlands since the establishment of the DSAA. The aim of this study was to evaluate whether national outcomes of iAAA repair have improved since the establishment of the DSAA. Furthermore, changes in patient selection, hospital volumes, and preferred operative technique since 2014 were investigated.

METHODS

This was a retrospective nationwide study of patients who underwent repair of an iAAA in The Netherlands. The study followed the STROBE statement[13].

Datasource

The dataset was retrieved from the DSAA, a prospective registered compulsory quality registry for all aortic aneurysm repairs performed by vascular surgeons in The Netherlands. The DSAA was established in 2013 and started by registering all Dutch patients undergoing infrarenal and juxtarenal AAA repair without previous aortic surgery. Since 2016, complex endovascular aneurysm repair, thoracic aortic aneurysm repair, and revision surgery have been registered. Data verification took place over 2015 through a random sample of hospitals showing a case ascertainment of 98.4% and no discrepancies in deaths or re-interventions[14,15]. Data verification will be repeated in the near future.

Participants

All consecutive participants that were registered in the DSAA and underwent primary iAAA repair using either standard EVAR or OSR, between January 2014 and December 2019 were included. Patients with missing data on variables date of birth, date of surgery, sex, and survival status at the time of discharge or 30 days post-operatively, as well as patients aged <18 or >110 years were excluded. No ethical approval or informed consent was required for this study according to Dutch law. No distinction exists between private and public healthcare in The Netherlands.

Definitions

Intact AAA repairs included both electively treated aneurysms and aneurysms that caused symptoms. Aneurysm treatments were categorised by intention to treat; attempts at endovascular treatment for aneurysms that were converted from EVAR to OSR during surgery were categorised as EVAR. The variables "pulmonary comorbidity" and "cardiac comorbidity" were dichotomised per patient into categories "present" or "absent". From 2014 to 2018, the variables regarding pulmonary and cardiac comorbidities were based on parameters from the V-POSSUM[16], while from 2019, "pulmonary comorbidity" and "cardiac comorbidity" were based on ICD-10 codes (**Table S1**). During the study period, some hospitals have been merged. When hospitals have been merged during the study, the hospitals were classified as one hospital in the years before the merger.

Outcomes

The primary outcome was the peri-operative mortality trend per year (30 day mortality and in hospital mortality). Secondary outcomes were trends per year in the outcomes major

complications and textbook outcome (TbO), and trends per year in patient characteristics, hospital volume, and applied surgical technique (OSR or EVAR). As described before[17,18], major complications were defined as either intra-operative complications or peri-operative complications within 30 days that caused a prolonged stay (length of hospital stay above the 75th percentile of living patients registered in the DSAA, stratified by OSR, EVAR, elective, or symptomatic [thresholds: EVAR, elective >3 days; EVAR, symptomatic >7 days; OSR, elective >12 days; OSR, symptomatic >14 days]), intra-operative complications or peri-operative complications that caused a re-intervention or death. The specific complications included in the categories of peri-operative complications that were included in the DSAA are shown in **Table S3.** TbO is a desirable composite outcome measure that provides information on the overall quality of care that can be used for internal quality improvement[19–22], and could be valuable in shared decision making processes. As described by Karthaus et al.[21], TbO is achieved in the elective setting if no intra-operative or post-operative surgical complications, no re-interventions, no prolonged stay (≤4 days for EVAR, ≤10 days for OSR), no re-admissions and no peri-operative mortality occur within 30 days.

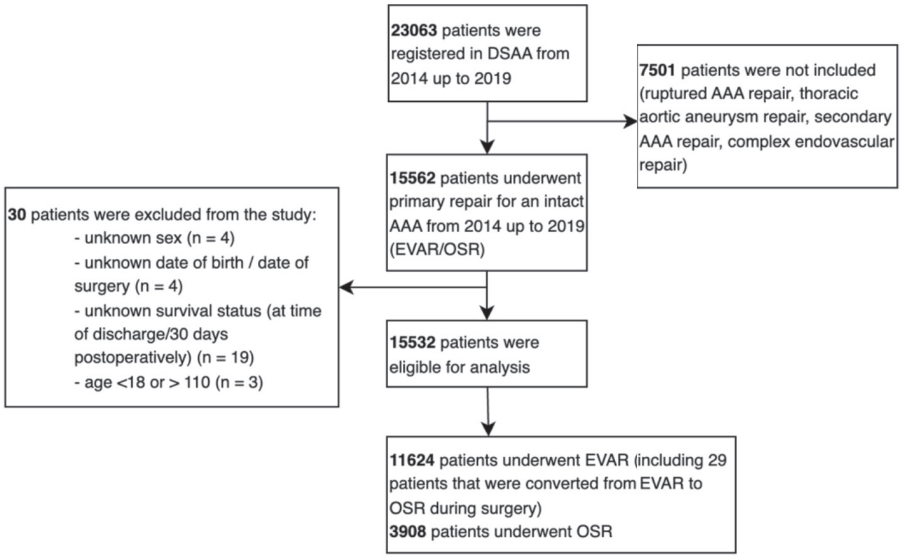
Statistical methods

Firstly, descriptive statistics of outcomes per year were shown for both EVAR and OSR patients together, as well as separately. To examine the linear time trends per year for outcomes, univariable as well as multivariable logistic regression analyses, using known confounders "sex", "age", "pulmonary comorbidity", "cardiac comorbidity", "haemoglobin", "creatinine", "urgency", "aneurysm diameter", and "aneurysm location" were performed. For these multivariable analyses, the missing values of categorical variables were included in the models as separate categories. Missing values of continuous variables were not included in the multivariable analyses as these were <5%. Because of the low missing value rate, it was decided not to impute these using multiple imputation. Secondly, linear time trends per year of patient characteristics were examined from 2014 to 2019 using univariable logistic and linear regression analyses for dichotomous variables and continuous variables, respectively. Trends per year regarding hospitals that treated fewer than 30 patients per year and number of hospitals were examined using univariable linear regression analyses. Additionally, the trends regarding hospital volume were shown using boxplots. For linear regression analyses, the beta coefficients, including 95% confidence intervals, were reported. For logistic regression analyses, the odds ratios, the exponent of the beta coefficient, including 95% confidence intervals, were reported. All analyses were performed using R version 4.0.1.

RESULTS

A total of 23063 patients (2587 - 4176 patients per year) were registered in the DSAA between January 2014 and December 2019. Of these, 15562 patients treated in 61 hospitals underwent EVAR or OSR for a primary iAAA, of whom 15532 (99.8%) were eligible (2445 - 2753 patients per year) and 30 (0.2%) were excluded (**Figure 1**). The 7501 patients who were not included in this study underwent ruptured AAA repair, thoracic aortic aneurysm repair, secondary AAA repair, or complex endovascular repair.

Figure 1: Flow diagram of patients included in the study



Time trends in perioperative outcomes

All patients

Table 1 shows that the peri-operative mortality of all patients included in this study remained stable (aOR0.95; 95% CI 0.89-1.02). In 2019, the crude peri-operative mortality of all patients was 2.2%. The crude percentage of major complications decreased after correction for con-founders, from 14.7% in 2014 up to 11.8% in 2019. Details of the peri-operative complications that are defined as a major complication are shown in **Table 2.**

Table 1: Univariable and multivariable logistic regression analyses to examine the trend in outcomes per year of all 15532 patients who underwent endovascular (EVAR) or open surgical (OSR) repair for intact abdominal aortic aneurysm in The Netherlands

	2014 (n = 2753)	**2015 (n = 2709)**	**2016 (n = 2655)**	**2017 (n = 2481)**	**2018 (n = 2489)**	**2019 (n = 2445)**	
Peri-operative mortality α	62 (2.3)	61 (2.3)	52 (2.0)	50 (2.0)	42 (1.7)	55 (2.2)	
Univariable							0.98 (0.91 – 1.04)
Multivariable*							0.95 (0.89 – 1.02)
Major complications β	405 (14.7)	350 (12.9)	332 (12.5)	318 (12.8)	296 (11.9)	288 (11.8)	
Univariable							0.95 (0.93 – 0.98)
Multivariable*							0.93 (0.90 – 0.96)

Data are presented as n (%), unless stated otherwise. Missing values of dichotomous variables were added as separate categories to the multivariable models (number of missing values for variable cardiac comorbidity: 400 patients [2.6%], number of missing values for the variable, pulmonary comorbidity: 275 patients [1.8%]). Multivariable analysis: type of surgery, sex, age, pulmonary history, cardiac history, creatinine (per 10mmol/L), haemoglobin, diameter of the aneurysm (per 10 mm), urgency, location of aneurysm (abdominal or aorto-iliac).*

α Peri-operative mortality: 30 day mortality and in hospital mortality.

β Major complication: post-operative death or an intra-operative or post-operative complication leading to a re-intervention or prolonged hospital stay. Prolonged hospital stay: EVAR, elective repair: >3 days, EVAR, repair for a symptomatic AAA: >7 days, OSR, elective repair: >12 days, OSR, repair for a symptomatic AAA: >14 days.

Table 2: Details of the peri-operative complications that are defined as a major complication, stratified per category of peri-operative complications of 15532 patients who underwent endovascular (EVAR) or open surgical (OSR) repair for intact abdominal aortic aneurysm

	All patients (n = 15532)	**EVAR (n = 11624)**	**OSR (n = 3908)**
Patients with major complications	1989	1030	959
Abdominal	448 (22.5)	117 (11.4)	331 (34.5)
Neurological	191 (9.6)	82 (8 .0)	109 (11.4)
Pulmonary	491 (24.2)	163 (15.8)	328 (34.2)
Cardiac	340 (17.1)	125 (12.1)	215 (22.4)
Reconstruction	110 (5.5)	74 (7.2)	36 (3.8)
Re-bleeding	176 (8.8)	95 (9.2)	81 (8.4)
Renal	257 (12.9)	64 (6.2)	193 (20.1)
Wound	153 (7.7)	65 (6.3)	88 (9.2)
Arterial occlusion	310 (15.6)	170 (16.5)	140 (14.6)
Infection	252 (12.7)	112 (10.9)	140 (14.6)
Other	491 (24.7)	279 (27.1)	212 (22.1)

Data are presented as n (%). Patients can suffer from more than one complication. Specific complications included in the categories of peri-operative complications are detailed in Table S3.

Open surgical repair and endovascular aneurysm repair patients

In **Table 3**, time trends in peri-operative outcomes per year of EVAR patients and OSR patients are shown. In EVAR patients, no linear mortality time trend was found (1.0% in 2014; 1.3% in 2019). Major complications decreased from 10.1% in 2014 to 7.0% in 2019. TbO increased from 68.1% in 2014 to 80.9% in 2019. For OSR patients, mortality decreased from 6.1% in 2014 to 4.6% in2019. The percentage of major complications decreased after adjustment for confounders, from 28.6% in 2014 to 23.3% in 2019. The TbO rate increased from 49.1% in 2014 to 58.3% in 2019.

Table 3: Univariable and multivariable logistic regression analyses to examine the trend in outcomes per year, stratified for endovascular (EVAR) and open surgical (OSR) aneurysm repair of intact abdominal aortic aneurysm in a total of 15532 patients

	2014	2015	2016	2017	2018	2019	OR per year (95% CI) (ref: 2014)
EVAR patients - n	2070	2124	2003	1860	1833	1734	
Peri-operative mortality[α]	20 (1.0)	18 (0.8)	15 (0.7)	21 (1.1)	16 (0.9)	22 (1.3)	
Univariable							1.06 (0.95 – 1.18)
Multivariable*							1.06 (0.94 – 1.20)
Major complications[β]	210 (10.1)	202 (9.5)	181 (9.0)	171 (7.2)	144 (7.9)	122 (7.0)	
Univariable							0.93 (0.89 – 0.97)
Multivariable*							0.91 (0.88 – 0.95)
Textbook Outcome (elective)[π]	1326/1948 (68.1)	1498/1962 (76.4)	1380/1813 (76.1)	1330/1689 (78.7)	1333/1682 (79.3)	1291/1596 (80.9)	
Univariable							1.13 (1.10 – 1.16)
Multivariable*							1.13 (1.10 – 1.16)
OSR patients - n	683	585	652	621	656	711	
Peri-operative mortality[α]	42 (6.1)	43 (7.4)	37 (5.7)	29 (4.7)	26 (4.0)	33 (4.6)	
Univariable							0.90 (0.83 – 0.98)
Multivariable*							0.89 (0.82 – 0.98)
Major complications[β]	195 (28.6)	148 (25.3)	151 (23.2)	147 (23.7)	152 (23.2)	166 (23.3)	
Univariable							0.95 (0.91 – 0.99)
Multivariable*							0.95 (0.91 – 0.99)
Textbook Outcome (elective)[π]	287/585 (49.1)	291/499 (58.3)	318/550 (57.8)	291/532 (54.7)	337/593 (56.8)	361/619 (58.3)	

Table 3: *Continued.*

	2014	2015	2016	2017	2018	2019	OR per year (95% CI) (ref: 2014)
Univariable							1.05 (1.01 – 1.09)
Multivariable*							1.05 (1.01 – 1.10)

Data are presented as n (%), unless stated otherwise. OR = odds ratio. CI = confidence interval. Missing values of dichotomous variables were added as separate categories to the multivariable models (EVAR patients: number of missing values for variable cardiac comorbidity: 308 patients [2.6%], variable pulmonary comorbidity: 185 patients [1.6%], OSR patients: variable cardiac comorbidity: 92 patients [2.4%], variable pulmonary comorbidity: 90 patients [2.3%]).

** Multivariable analysis: sex, age, pulmonary history, cardiac history, creatinine (per 10 mmol/L), haemoglobin, aneurysm diameter (per 10mm), urgency, location of aneurysm.*

α Peri-operative mortality: 30 day mortality and in hospital mortality.

β Major complication: post-operative death or an intra-operative or post-operative complication leading to a re-intervention or prolonged hospital stay. Prolonged hospital stay: EVAR, elective repair:>3 days, EVAR, repair for a symptomatic AAA:>7 days, OSR, elective repair:>12 days, OSR, repair for a symptomatic AAA:>14 days.

π Textbook outcome: desirable composite outcome measure that could be achieved in the elective setting if no intra-operative or post-operative surgical complications, no re-interventions, no prolonged stay (<4 days for EVAR, <10 days for OSR), no re-admissions and no peri-operative mortality occurred within 30 days.

Time trends in patient characteristics

All patients

Patient characteristic time trends of all patients, EVAR patients, and OSR patients are shown in **Table 4** and **Table S2**. In the group that describes all EVAR and OSR patients, the proportion of patients with cardiac comorbidity increased from 2014 to 2019.

Open surgical repair patients and endovascular aneurysm repair patients

Table 4 and **Table S2** show that the mean age of EVAR patients increased from 2014, whereas it did not in OSR patients. Moreover, both in EVAR patients and OSR patients, the proportion of patients with cardiac comorbidity increased (EVAR: 50.6% in 2014 to 77.4% in 2019; OSR: 47.0% in 2014 to 75.9% in 2019), while the proportion of patients with pulmonary comorbidity remained stable (EVAR: 22.4% in 2014 and 24.8% in2019; OSR: 22.4% in 2014 and 26.0% in 2019), and the mean aneurysm diameter decreased since 2014 (EVAR: 60.4 mm in 2014 to 59.0 mm in 2019; OSR: 63.8 mm in 2014 to 61.6 mm in 2019). The proportion of patients treated for an AAA below the ESVS guideline diameter threshold of 55 mm for men, 50 mm for women[23] was stable (EVAR: 16.0% in 2014 and 13.5% in 2019, OR 1.00, 95% CI 0.99-1.00; OSR: 13.2% in 2014 and 12.1% in2019, OR 1.00, 95% CI 0.99-1.00). In EVAR patients, aneurysms were increasingly treated in symptomatic set-tings (5.9% in 2014 to 8.0% in 2019), while in OSR patients, the reverse applied (14.3% in 2014 to 12.9% in 2019). In both EVAR and OSR patients, the mortality of patients treated in elective settings was lower compared with patients treated in symptomatic settings (EVAR: 0.7% vs. 4.1%, p<.001, OSR: 4.9% vs. 8.7%, p<.001). Additional analysis regarding the proximal clamp location was per-formed in OSR patients. OSR did not seem to be more complex over the years, as the proximal clamp location (suprarenal vs. infrarenal, only registered from 2016) did not change over time (suprarenal clamp 30.9% in 2016,31.4% in 2019; OR 1.02, 95% CI 0.95 - 1.10; not shown in **Table 4**).

Table 4: *Patient characteristics in 2019 and trends in patient characteristics since 2014: stratified by all patients (EVAR and OSR), EVAR patients, and OSR patients*

	Intact AAA – all patients			Intact AAA - EVAR			Intact AAA - OSR		
	2019 (n = 2445)	**Unadjusted OR / β coefficient per year (95% CI) (ref: 2014)**	**P**	**2019 (n = 1734)**	**Unadjusted OR / β coefficient per year (95% CI) (ref: 2014)**	**P**	**2019 (n = 711)**	**Unadjusted OR / β coefficient per year (95% CI) (ref: 2014)**	**P**
Women	385 (15.7)	1.02 (0.99 - 1.04)	.24	245 (14.1)	1.01 (0.98 – 1.05)	.37	140 (19.7)	1.00 (0.96 – 1.05)	.90
Age - Y*	73.57 ± 7.69	0.08 (0.01 – 0.15)	.021	74.89 ± 7.41	0.19 (0.11 – 0.27)	<.001	70.35 ± 7.42	-0.08 (-0.22 – 0.06)	.26
Cardiac comorbidity	1882 (77.0)	1.22 (1.20 – 1.24)	<.001	1342 (77.4)	1.22 (1.19 – 1.25)	<.001	540 (75.9)	1.22 (1.17 – 1.27)	<.001
Pulmonary comorbidity	615 (25.2)	1.02 (0.995 – 1.04)	.13	430 (24.8)	1.02 (0.99 – 1.04)	.18	185 (26.0)	1.02 (0.98 – 1.06)	.41
Hemoglobin-mmol/L*	8.57 ± 1.05	-0.01 (-0.02 – -0.001)	.029	8.58 ± 1.03	-0.02 (-0.03 – -0.004)	.008	8.57 ± 1.10	0.003 (-0.02 – 0.02)	.75
Creatinine, -µmol/L*	89 [75.00-107.00]	-0.25 (-0.64 – 0.13)	.20	90 [76 – 108]	-0.27 (-0.73 – 0.19)	.25	87 [73 – 105]	-0.10 (-0.79 – 0.59)	.76
Symptomatic AAA	230 (9.4)	1.02 (0.99 – 1.05)	.26	138 (8.0)	1.05 (1.01 – 1.09)	.014	92 (12.9)	0.95 (0.90 – 0.996)	.037
Aneurysm diameter - mm*	59.76 ± 12.47	-0.29 (-0.40 – -0.18)	<.001	59.01 ± 11.69	-0.30 (-0.42 – -0.18)	<.001	61.59 ± 14.03	-0.40 (-0.66 – -0.15)	.002

Table 4: *Continued.*

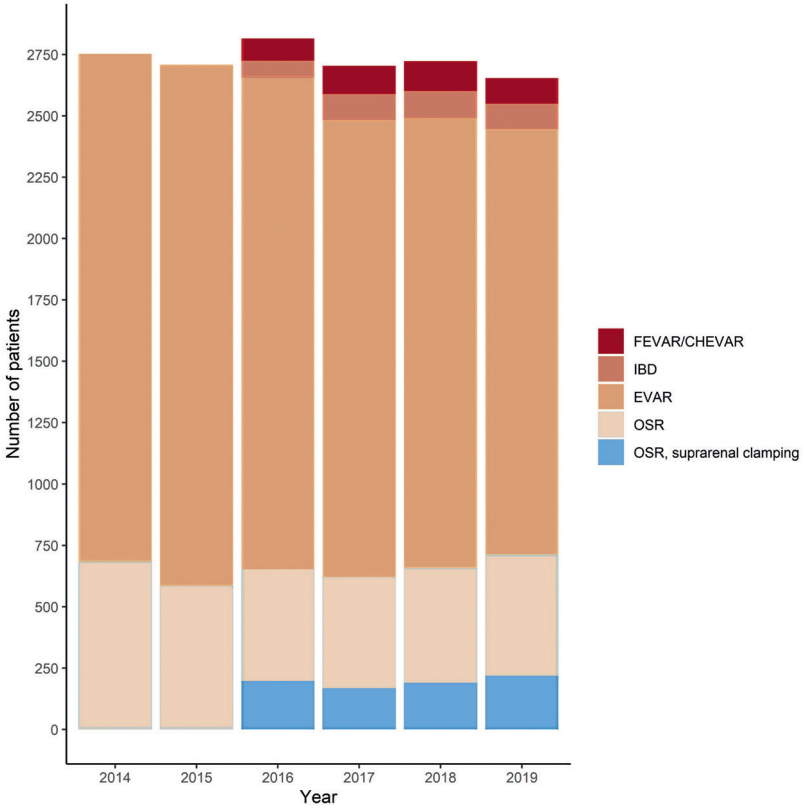
	Intact AAA – all patients			Intact AAA - EVAR			Intact AAA - OSR		
	2019 (n = 2445)	**Unadjusted OR / β coefficient per year (95% CI) (ref: 2014)**	**P**	**2019 (n = 1734)**	**Unadjusted OR / β coefficient per year (95% CI) (ref: 2014)**	**P**	**2019 (n = 711)**	**Unadjusted OR / β coefficient per year (95% CI) (ref: 2014)**	**P**
Aorto-iliac location	189 (7.7)	1.12 (1.08 – 1.16)	<.001	126 (7.3)	1.10 (1.06 – 1.15)	<.001	63 (8.9)	1.15 (1.07 – 1.23)	<.001

Data are presented as n (%) or mean standard deviation or median (interquartile range) unless stated otherwise. OR = odds ratio; CI = confidence interval. Missing values of < 5% per variable are not shown (cardiac comorbidity: 400 patients [2.6% of all patients], pulmonary comorbidity: 275 patients [1.8% of all patients], haemoglobin: 394 patients [2.5% of all patients], creatinine: 387 patients [2.5% of all patients], aneurysm diameter: 108 [0.7% of all patients]).
** For continuous variables, the beta coefficients per year are reported; for other variables, the odds ratios (OR) per year are reported.*

Time trends in the application of surgical techniques

Table 3 and **Figure 2** show the number of patients that received standard EVAR and OSR. Complex EVAR (fenestrated EVAR, chimney EVAR, and iliac branched devices [IBD]), which was registered in the DSAA from 2016, was shown to provide a complete overview of trends in the application of surgical techniques. In 2014 and 2015, the numbers of patients that underwent OSR were 683 (24.8%) and 585 (21.6%) per year, respectively. From 2016, the percentage of patients that underwent OSR increased from 23.2% in 2016 to 26.8% in 2019 (OR 1.07, 95% CI 1.03 – 1.11, ref: 2016). Moreover, the percentage of patients that underwent standard EVAR decreased compared with the percentage of patients that underwent OSR and complex EVAR (standard EVAR: 71.1% in 2016, 65.3% in 2019, OR 0.91, 95% CI 0.88 – 0.95).

Figure 2: The number of patients that received endovascular (EVAR) or open surgical (OSR) aneurysm repair for intact abdominal aortic aneurysm, or complex EVAR (fenestrated EVAR[FEVAR] / chimney EVAR [ChEVAR] / iliac branched device [IBD]) per year. Complex EVAR was not included in the study and is shown only to provide a complete overview. Complex EVAR was registered in the Dutch Surgical Aneurysm Audit (DSAA) since 2016.



Time trends in total volume, number of hospitals and hospital volume

Total volume per year and number of hospitals

Table 5 shows the total number of patients per year, including patients that received complex EVAR from 2016. From 2016, the total number of patients per year appears to decline, from 2814 patients in 2016 to 2 647 patients in 2019. Five hospitals stopped performing AAA surgery (from 61 to 56 hospitals), and another six hospitals merged into three hospitals during the study period (not shown in **Table 4**).

Hospital volume

The number of patients treated per hospital (hospital volume) did not change statistically over the years (β coefficient 0.59, 95% CI -0.75-1.94). As shown in **Figure 3A**, in 2014, the median hospital volume was 40 (IQR 26, 58), while in 2019, the median hospital volume was 42 (IQR 34, 56.5). The number of hospitals that treated fewer than 30 patients per year decreased from 20 in 2014, to 10 in 2019 (**Table 5**). **Figure 3B** shows the median hospital volume and IQR, including complex EVAR stratified by OSR and EVAR. The median hospital volume per year of OSR was stable, around 11 patients per hospital per year.

Figure 3: Boxplot summarising the number of patients per hospital in The Netherlands treated for intact abdominal aortic aneurysm (A), stratified for endovascular (EVAR) or open surgical (OSR) aneurysm repair (B). From 2016, the numbers also include patients who received complex EVAR (fenestrated or chimney EVAR or iliac branched device).

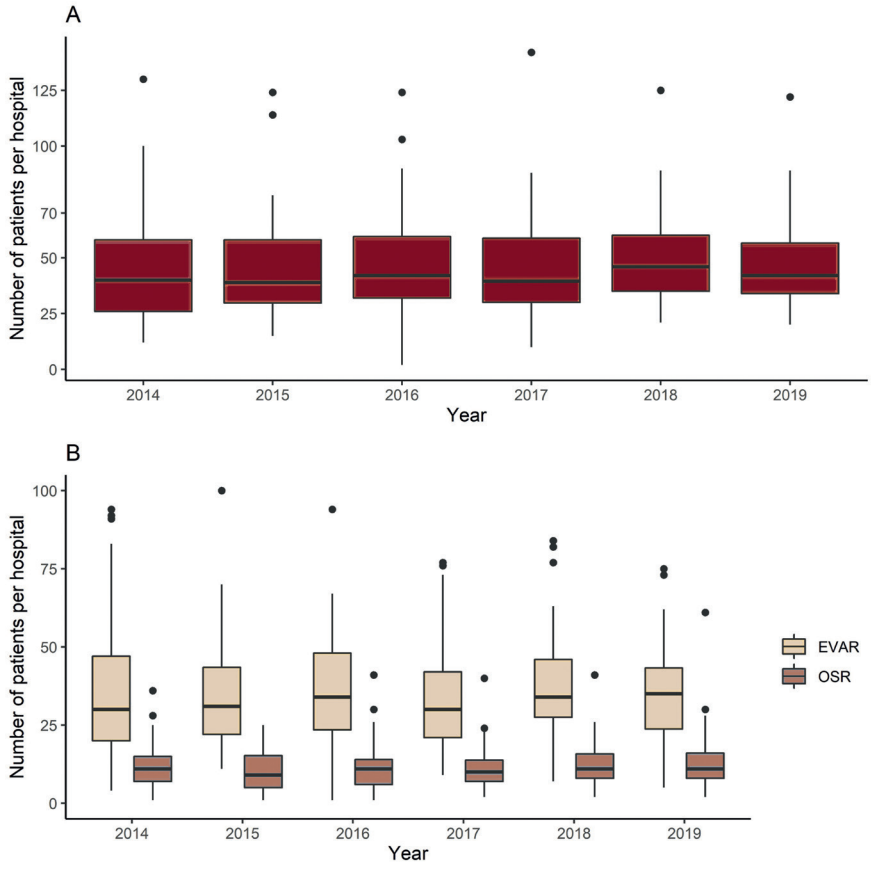


Table 5: Univariable regression analyses to examine the trend in the number of hospitals that treat patients with abdominal aortic aneurysm and the trends in the number of hospitals that treat fewer than 30 patients per year in The Netherlands

	2014	2015	2016	2017	2018	2019	β coefficient per year (95% CI) (ref: 2014)
Total number of patients including complex EVAR	2753	2709	2815	2704	2723	2654	
Numbers of hospitals	61	60	59	58	56	56	

Table 5: *Continued.*

	2014	2015	2016	2017	2018	2019	β coefficient per year (95% CI) (ref: 2014)
Univariable							-1.09 (-1.36 - -0.81)
Number of hospitals that treated <30 patients / year	20	15	12	13	9	10	
Univariable							- 1.91 (-3.19 - -0.64)

Data are presented as n. CI = confidence interval.

DISCUSSION

The present study aimed to evaluate whether iAAA repair outcomes have improved since the establishment of the DSAA, a mandatory registry of all AAAs operated on in The Netherlands. The study demonstrated that several important iAAA repair outcomes in The Netherlands improved from 2014 up to 2019, while patient characteristics showed that patients with similar or more comorbidities underwent surgery. The number of patients per hospital remained stable; however, the number of hospitals that treated fewer than 30 patients decreased, which is a sign of regionalisation of vascular services.

The present study shows that during the study period, patients who received EVAR became slightly older, and more patients had cardiac comorbidities. In contrast to OSR, the peri-operative mortality rate following EVAR did not decrease and remained between 0.7% and 1.3%, consistent with rates described in contemporary literature[8]. Although mortality did not change, the major complications after EVAR declined, and the TbO rate increased remarkably. The decrease in major complications and the increase in TbO suggest that the peri-operative care quality for patients that underwent EVAR has increased. The exact cause of this improvement is hard to determine and is probably multi-factorial, including better patient selection, increased experience, and further regionalisation of services. It is likely that the audit itself also plays an important role, as described previously[12].

Furthermore, this study shows that all examined patient outcomes following OSR for iAAA repair improved overtime, while more patients had cardiac comorbidities but were of similar age during the study period. An important finding from this study is that the peri-operative mortality following OSR improved, from 6.1% in 2014 to 4.7% in 2019, in line with rates described in international registries[8]. However, some of these registries might

be biased by voluntary data contributions[24], while the DSAA is a compulsory registry. Additionally, the percentage of major complications following OSR declined, and the percentage of TbO increased. Altogether, this suggests that the out-comes of patients who received OSR have improved. As for after EVAR, the exact cause of this is likely to be multifactorial, for example a result of stricter case selection.

Several studies have suggested that lower hospital volume is associated with increased mortality[725]. The present study described the trends in hospital volume and the number of hospitals that performed iAAA repair. For OSR, the median hospital volume of 11 per year raises some concern[26], and should be investigated in the near future. Although the hospital volume of all iAAA repairs per year and the median hospital volume of OSR patients did not increase, the number of hospitals that treated patients decreased, and the number of hospitals that treated fewer than 30 patients per year decreased. This regionalisation of aneurysm care is probably a result of the European Society for Vascular Surgery (ESVS) guideline[23] which suggests that a minimum of 30 AAA repairs should be performed per hospital per year or could be related to the clinical auditing process of the DSAA[27]. The DSAA monitors and provides feedback about the number and outcomes of patients that underwent elective AAA repair per hospital, as well as the total number of aortic aneurysm repairs per hospital.

Finally, this study examined the proportion of OSR vs. EVAR per year, including the total number of patients. It was noted that the total number of patients per year has declined since 2016. Interestingly, the proportion of patients with an AAA diameter below the guideline threshold remained stable, while the mean diameter of iAAAs decreased; however, this decrease was small (0.3 mm per year). The National Vascular Registry reported a decrease in the number of elective infrarenal AAA repairs in the UK, and it was stated that this could indicate a more conservative approach in the management of sicker patients[28]. Further-more, including patients that were treated by complex endovascular means for AAA, the applied surgical technique slightly changed with an increase of OSR and decrease of standard EVAR. The increase in OSR might be a result of the recent discussion regarding preferred treatment for specific patients[23,29–31] or published findings indicating inferior long term survival and more secondary interventions after EVAR[32,33]. A decrease in the number of standard EVAR was also reported in the UK in 2018[34]. In 2019, the percentage of patients that received standard EVAR in the present study was 65.3% of all patients, which was similar to the overall proportion of EVAR in international registries from2010 to 2013 but far lower compared with the USA (79%), as reported by Vascunet[35].

To the present authors' knowledge, this is the first study reporting treatment trends for iAAAs based on data from a compulsory national quality registry for all aortic aneurysm

repairs and therefore represents real world data. One important limitation of this study is that the DSAA was initially designed for quality measurement and not for scientific purposes, which may result in some missing variables. The possible influence of these missing variables was considered in the present study and attempts were made to deal accurately with the missing values. Another limitation is that the DSAA does not contain anatomical morphological details, and only patients who underwent aneurysm repair were included in the DSAA. Therefore, selection and con-founding bias cannot be excluded. Finally, the DSAA does not include information on surgeon volumes, and therefore, it was not possible to describe surgeon volume, in contrast to other countries[36,37].

In conclusion, since the establishment of this nationwide quality improvement initiative (DSAA), all iAAA repair out-comes following standard EVAR and OSR have improved except for peri-operative mortality following standard EVAR which remained unchanged, although the proportion of patients with cardiac comorbidity increased over time in this group. The number of major complications after both OSR and EVAR decreased, and the proportion of TbO increased. The peri-operative survival after OSR increased, despite a higher proportion of patients with cardiac co-morbidity. This nationwide audit provides real world data on aneurysm care and can be seen as an important tool for further quality improvement initiatives.

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Conflicts of interest

JJW: Consultant for Cordis/Cardinal Health, former consultant for Baxter. HV: Consultant for Medtronic, WL Gore, Terumo, Endologix, and Arsenal AAA. Speakers bureau: Abbott

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REFERENCES

1 Bergqvist D, Mani K, Troëng T, Wanhainen A. Treatment of aortic aneurysms registered in Swedvasc: Development reflected in a national vascular registry with an almost 100% coverage. *Gefasschirurgie* 2018;**23**(5):340–5. Doi: 10.1007/s00772-018-0414-8.

2 Akkersdijk GJM, Prinssen M, Blankensteijn JD. The impact of endovascular treatment on in-hospital mortality following non-ruptured AAA repair over a decade: A population based study of 16,446 patients. *European Journal of Vascular and Endovascular Surgery* 2004. Doi: 10.1016/j.ejvs.2004.01.003.

3 Suckow BD, Goodney PP, Columbo JA, Kang R, Stone DH, Sedrakyan A, et al. National trends in open surgical, endovascular, and branched-fenestrated endovascular aortic aneurysm repair in Medicare patients. *J Vasc Surg* 2018;**67**(6):1690-1697.e1. Doi: 10.1016/j.jvs.2017.09.046.

4 Bergqvist D, Mani K, Troëng T, Wanhainen A. Treatment of aortic aneurysms registered in Swedvasc: Development reflected in a national vascular registry with an almost 100% coverage. *Gefasschirurgie* 2018;**23**(5):340–5. Doi: 10.1007/s00772-018-0414-8.

5 Lilja F, Mani K, Wanhainen A. Editor's Choice – Trend-break in Abdominal Aortic Aneurysm Repair With Decreasing Surgical Workload. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(6):811–9. Doi: 10.1016/j.ejvs.2017.02.031.

6 Greenhalgh RM. Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): Randomised controlled trial. *Lancet* 2005;**365**(9478):2187–92. Doi: 10.1016/S0140-6736(05)66628-7.

7 Scali ST, Beck AW, Sedrakyan A, Mao J, Venermo M, Faizer R, et al. Hospital Volume Association With Abdominal Aortic Aneurysm Repair Mortality: Analysis of the International Consortium of Vascular Registries. *Circulation* 2019;**140**(15):1285–7. Doi: 10.1161/CIRCULATIONAHA.119.042504.

8 Budtz-Lilly J, Venermo M, Debus S, Behrendt CA, Altreuther M, Beiles B, et al. Editor's Choice – Assessment of International Outcomes of Intact Abdominal Aortic Aneurysm Repair over 9 Years. *European Journal of Vascular and Endovascular Surgery* 2017;**54**(1):13–20. Doi: 10.1016/j.ejvs.2017.03.003.

9 Björck M, Gibbons CP, Jensen LP, Laustsen J, Lees T, Moreno-Carriles R, et al. Vascular Registries Join to Create a Common International Dataset on AAA Surgery. *European Journal of Vascular and Endovascular Surgery* 2007;**34**(3):257–9. Doi: 10.1016/j.ejvs.2007.05.014.

10 Lijftogt N, Vahl AC, Wilschut ED, Elsman BHP, Amodio S, van Zwet EW, et al. Adjusted Hospital Outcomes of Abdominal Aortic Aneurysm Surgery Reported in the Dutch Surgical Aneurysm Audit. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(4):520–32. Doi: 10.1016/j.ejvs.2016.12.037.

11 Beck N, van Bommel AC, Eddes EH, van Leersum NJ, Tollenaar RA, Wouters MW. The Dutch Institute for Clinical Auditing: Achieving Codman's Dream on a Nationwide Basis. *Ann Surg* 2020;**271**(4):627–31. Doi: 10.1097/SLA.0000000000003665.

12 Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, et al. Audit and feedback: Effects on professional practice and healthcare outcomes. *Cochrane Database of Systematic Reviews* 2012;**2012**(6). Doi: 10.1002/14651858.CD000259.pub3.

13 STROBE Statement- checklist of items that should be included in reports of observational studies. https://www.strobe-statement.org/fileadmin/Strobe/uploads/checklists/STROBE_checklist_v4_combined.pdf. 08/11/2020.

14 Dutch Institute for Clinical Auditing. Eindrapport dataverificatie DSAA. https://dica.nl/media/660/Eindrapport_dataverificatie_DSAA_2016.pdf. 05/11/2020.

15 van der Werf LR, Voeten SC, van Loe CMM, Karthaus EG, Wouters MWJM, Prins HA. Data verification of nationwide clinical quality registries. *BJS Open* 2019;**3**(6):857–64. Doi: 10.1002/bjs5.50209.
16 Grant SW, Grayson AD, Mitchell DC, McCollum CN. Evaluation of five risk prediction models for elective abdominal aortic aneurysm repair using the UK National Vascular Database. *British Journal of Surgery* 2012;**99**(5):673–9. Doi: 10.1002/bjs.8731.
17 Lijftogt N, Karthaus EG, Vahl A, van Zwet EW, van der Willik EM, Tollenaar RAEM, et al. Failure to Rescue – a Closer Look at Mortality Rates Has No Added Value for Hospital Comparisons but Is Useful for Team Quality Assessment in Abdominal Aortic Aneurysm Surgery in The Netherlands. *European Journal of Vascular and Endovascular Surgery* 2018;**56**(5):652–61. Doi: 10.1016/j.ejvs.2018.06.062.
18 von Meijenfeldt GCI, Alberga AJ, Balm R, Vahl AC, Verhagen HJM, Blankensteijn JD, et al. Results from a nationwide prospective registry on open surgical or endovascular repair of juxtarenal abdominal aortic aneurysms. *J Vasc Surg* 2021. Doi: 10.1016/j.jvs.2021.06.031.
19 Tsilimigras DI, Mehta R, Merath K, Bagante F, Paredes AZ, Farooq A, et al. Hospital variation in Textbook Outcomes following curative-intent resection of hepatocellular carcinoma: an international multi-institutional analysis. *Hpb* 2020;**22**(9):1305–13. Doi: 10.1016/j.hpb.2019.12.005.
20 Kuhrij LS, Karthaus EG, Vahl AC, Willems MCM, Elshof JW, de Borst GJ, et al. A Composite Measure for Quality of Care in Patients with Symptomatic Carotid Stenosis Using Textbook Outcome. *European Journal of Vascular and Endovascular Surgery* 2020;**60**(4):502–8. Doi: 10.1016/j.ejvs.2020.06.012.
21 Karthaus EG, Lijftogt N, Busweiler LAD, Elsman BHP, Wouters MWJM, Vahl AC, et al. Textbook Outcome: A Composite Measure for Quality of Elective Aneurysm Surgery. *Ann Surg* 2017;**266**(5):898–904. Doi: 10.1097/SLA.0000000000002388.
22 ten Berge MG, Beck N, Steup WH, Verhagen AFTM, van Brakel TJ, Schreurs WH, et al. Textbook outcome as a composite outcome measure in non-small-cell lung cancer surgery. *Eur J Cardiothorac Surg* 2021;**59**(1):92–9. Doi: 10.1093/ejcts/ezaa265.
23 Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(1):8–93. Doi: 10.1016/j.ejvs.2018.09.020.
24 Mitchell D, Venermo M, Mani K, Bjorck M, Troeng T, Debus S, et al. Quality improvement in vascular surgery: The role of comparative audit and vascunet. *European Journal of Vascular and Endovascular Surgery* 2015;**49**(1):1–3. Doi: 10.1016/j.ejvs.2014.08.026.
25 Phillips P, Poku E, Essat M, Woods HB, Goka EA, Kaltenthaler EC, et al. Procedure Volume and the Association with Short-term Mortality Following Abdominal Aortic Aneurysm Repair in European Populations: A Systematic Review. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(1):77–88. Doi: 10.1016/j.ejvs.2016.10.007.
26 Scali ST, Beck A, Sedrakyan A, Mao J, Behrendt CA, Boyle JR, et al. Optimal Threshold for the Volume–Outcome Relationship After Open AAA Repair in the Endovascular Era: Analysis of the International Consortium of Vascular Registries. *European Journal of Vascular and Endovascular Surgery* 2021;(xxxx). Doi: 10.1016/j.ejvs.2021.02.018.
27 Lijftogt N, Vahl AC, Wilschut ED, Elsman BHP, Amodio S, van Zwet EW, et al. Adjusted Hospital Outcomes of Abdominal Aortic Aneurysm Surgery Reported in the Dutch Surgical Aneurysm Audit. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(4):520–32. Doi: 10.1016/j.ejvs.2016.12.037.
28 Waton S, Johal A, Cromwell D, Boyle J MF. National Vascular Registry: 2019 Annual Report. *Londen: The Royal Colege of Surgeons of England* 2019;(November).

29 Powell JT, Wanhainen A. Analysis of the Differences Between the European Society for Vascular Surgery 2019 and National Institute for Health and Care Excellence 2020 Guidelines for Abdominal Aortic Aneurysm. *European Journal of Vascular and Endovascular Surgery* 2020;(xxxx). Doi: 10.1016/j.ejvs.2020.04.038.
30 Oliveira NFG, Ultee K, van Rijn MJ, Pinto JP, Raa S Ten, Bastos Gonçalves F, et al. Anatomic predictors for late mortality after standard endovascular aneurysm repair. *J Vasc Surg* 2019;**69**(5):1444–51. Doi: 10.1016/j.jvs.2018.07.082.
31 Oliveira NFG, Bastos Gonçalves FM, Van Rijn MJ, de Ruiter Q, Hoeks S, de Vries JPPM, et al. Standard endovascular aneurysm repair in patients with wide infrarenal aneurysm necks is associated with increased risk of adverse events. *J Vasc Surg* 2017;**65**(6):1608–16. Doi: 10.1016/j.jvs.2016.09.052.
32 Patel R, Sweeting MJ, Powell JT, Greenhalgh RM. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. *The Lancet* 2016;**388**(10058):2366–74. Doi: 10.1016/S0140-6736(16)31135-7.
33 De Bruin, Jorg L.; Baas, Annette F.; Buth, Jaap; Prinssen, Monique; Verhoeven, Eric L.G.; Cuypers, Philippe W.M.; van Sambeek, Marc R.H.M.; Balm, Ron; Grobbee, Diederick E.; Blankensteijn JD. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *New England Journal of Medicine* 2010;**362**:1881–9. Doi: 10.1056/NEJMoa0909499.
34 Waton S, Johal A, Cromwell D, Boyle J MF. National Vascular Registry: 2019 Annual Report. *Londen: The Royal Colege of Surgeons of England* 2019;(November).
35 Beck AW, Sedrakyan A, Mao J, Venermo M, Faizer R, Debus S, et al. Variations in Abdominal Aortic Aneurysm Care: A Report from the International Consortium of Vascular Registries. *Circulation* 2016;**134**(24):1948–58. Doi: 10.1161/CIRCULATIONAHA.116.024870.
36 Sawang M, Paravastu SCV, Liu Z, Thomas SD, Beiles CB, Mwipatayi BP, et al. The Relationship Between Operative Volume and Peri-operative Mortality After Non-elective Aortic Aneurysm Repair in Australia. *European Journal of Vascular and Endovascular Surgery* 2020;**60**(4):519–30. Doi: 10.1016/j.ejvs.2020.04.029.
37 Gray WK, Day J, Horrocks M. Editor's Choice – Volume–Outcome Relationships in Elective Abdominal Aortic Aneurysm Surgery: Analysis of the UK Hospital Episodes Statistics Database for the Getting It Right First Time (GIRFT) Programme. *European Journal of Vascular and Endovascular Surgery* 2020;**60**(4):509–17. Doi: 10.1016/j.ejvs.2020.07.069.

SUPPLEMENTAL MATERIALS

Table S1

Pulmonary comorbidity	Variables
2014-2018	Dyspnea during exercise, invalidating dyspnea, dyspnea at rest, consolidation, fibrosis
2019	Chronic pulmonary diseases, COPD, CARA, emphysema, chronic bronchitis, fibrosis

Cardiac comorbidity	Variables
2014-2018	Medication for hypertension, angina pectoris, diuretics, or digoxin, peripheral edema, coumarins, borderline cardiomyopathy, elevated central venous pressure, cardiomegaly
2019	Hypertension, angina pectoris, myocardial infarction, PTCA, CABG, valvular heart disease, heart valve replacement, atrial fibrillation, heart rhythm disorders, heart failure, congestive heart failure, cardiomyopathy

Table S2: Patient characteristics per year (2014-2019), and trends in patient characteristics since 2014: stratified by all patients (EVAR and OSR), EVAR patients, and OSR patients

Intact aneurysms – all patients								
	2014	**2015**	**2016**	**2017**	**2018**	**2019**	**OR / β coefficient per year (95%-CI) (unadjusted, ref: 2014)**	**P-value**
Number of patients	2753	2709	2655	2481	2489	2445		
Sex: female	388 (14.1)	393 (14.5)	432 (16.3)	410 (16.5)	345 (13.9)	385 (15.7)	1.02 (0.99 – 1.04)	.242
Age, years*	73.2 ± 7.69	73.1 ± 7.70	72.9 ± 7.92	73.3 ± 7.69	73.5 ± 7.70	73.57 ± 7.69	0.08 (0.01 – 0.15)	.021
Cardiac comorbidity: Present	1369 (49.7)	1416 (52.3)	1365 (51.4)	1454 (58.6)	1725 (69.3)	1882 (77.0)	1.22 (1.20 – 1.24)	<.001
Pulmonary comorbidity: Present	616 (22.4)	671 (24.8)	725 (27.3)	609 (24.5)	657 (26.4)	615 (25.2)	1.02 (0.995 – 1.04)	.131
Hemoglobin, mmol/L*	8.62 ± 1.01	8.68 ± 1.01	8.64 ± 1.04	8.61 ± 1.04	8.64 ± 1.02	8.57 ± 1.05	-0.01 (-0.02 – -0.001)	.029
Creatinine, mmol/L*	89.0 [77.0 – 108]	90.0 [76.0 –106]	89.0 [76.0 –106]	91.0 [76.0 –108]	89.0 [77.0 –107]	89 [75.0 – 107]	-0.25 (-0.64 – 0.13)	.200
Urgency: symptomatic	220 (8.0)	248 (9.2)	292 (11.0)	260 (10.5)	214 (8.6)	230 (9.4)	1.02 (0.99 – 1.05)	.262
Aneurysm diameter, mm*	61.3 ± 12.2	60.3 ± 11.7	60.3 ± 11.9	60.0 ± 12.1	59.5 ± 12.3	59.8 ± 12.5	-0.29 (-0.40 – -0.18)	<.001

Location: aortoiliac	93 (3.4)	197 (7.3)	173 (6.5)	164 (6.6)	193 (7.8)	189 (7.7)	1.12 (1.08 – 1.16)	<.001

Intact aneurysms - EVAR								
	2014	**2015**	**2016**	**2017**	**2018**	**2019**	**OR / β coefficient per year (95%-CI) (unadjusted, ref: 2014)**	**P-value**
Number of patients	2070	2124	2003	1860	1833	1734		
Sex: female	269 (13.0)	284 (13.4)	277 (13.8)	274 (14.7)	240 (13.1)	245 (14.1)	1.01 (0.98 – 1.05)	.367
Age, years*	74.0 ± 7.63	73.8 ± 7.57	73.7 ± 7.86	74.3 ± 7.35	74.4 ± 7.54	74.89 ± 7.41	0.19 (0.11 – 0.27)	<.001
Cardiac comorbidity: Present	1048 (50.6)	1100 (51.8)	1008 (50.3)	1090 (58.6)	1273 (69.4)	1342 (77.4)	1.22 (1.19 – 1.25)	<.001
Pulmonary comorbidity: Present	463 (22.4)	556 (26.2)	564 (28.2)	454 (24.4)	502 (27.4)	430 (24.8)	1.02 (0.99 – 1.04)	.181
Hemoglobin, mmol/L*	8.64 ± 1.02	8.68 ± 1.01	8.66 ± 1.04	8.66 ± 1.04	8.61 ± 1.04	8.58 ± 1.03	-0.02 (-0.03 – -0.004)	.008
Creatinine, mmol/L*	89.0 [78.0-108]	90.0 [76.0-107]	89.0 [76.0-106]	91.0 [77.0-108]	89.0 [77.0-107]	90 [76.0 – 108]	-0.27 (-0.73 – 0.19)	.249
Urgency: symptomatic	122 (5.9)	162 (7.6)	190 (9.5)	171 (9.2)	151 (8.2)	138 (8.0)	1.05 (1.01 – 1.09)	.014

Aneurysm diameter, mm*	60.4 ± 11.0	59.5 ± 11.0	59.8 ± 11.0	59.1 ± 11.1	58.7 ± 11.6	59.0 ± 11.7	-0.30 (-0.42 – - 0.18)	<.001
Location: aortoiliac	64 (3.1)	164 (7.7)	116 (5.8)	119 (6.4)	133 (7.3)	126 (7.3)	1.10 (1.06 – 1.15)	<.001

Intact aneurysms – OSR								
	2014	**2015**	**2016**	**2017**	**2018**	**2019**	**OR / Beta coefficient per year (95%-CI) (unadjusted, ref: 2014)**	**P-value**
Number of patients	683	585	652	521	656	711		
Sex: female	119 (17.4)	109 (18.6)	155 (23.8)	136 (21.9)	105 (16.0)	140 (19.7)	1.00 (0.96 – 1.05)	.898
Age, years*	70.8 ± 7.39	70.7 ± 7.64	70.7 ± 7.68	70.3 ± 7.94	70.7 ± 7.46	70.35 ± 7.42	-0.08 (-0.22 – 0.06)	.261
Cardiac comorbidity: Present	321 (47.0)	316 (54.0)	357 (54.8)	364 (58.6)	452 (68.9)	540 (75.9)	1.22 (1.17 – 1.27)	<.001
Pulmonary comorbidity: Present	153 (22.4)	115 (19.7)	161 (24.7)	155 (25.0)	155 (23.6)	185 (26.0)	1.02 (0.98 – 1.06)	.410
Hemoglobin, mmol/L*	8.56 ± 0.98	8.67 ± 1.01	8.61 ± 1.02	8.47 ± 1.04	8.74 ± 0.951	8.57 ± 1.10	0.003 (-0.02 – 0.02)	.749
Creatinine, mmol/L*	87.0 [74.0-108]	88.0 [75.0-104]	87.5 [74.0-106]	90.0 [74.0-107]	90.0 [76.8-106]	87.0 [73.0-105]	-0.10 (-0.79 – 0.59)	.776

Urgency: symptomatic	98 (14.3)	86 (14.7)	102 (15.6)	89 (14.3)	63 (9.6)	92 (12.9)	0.95 (0.90 – 0.996)	.037
Aneurysm diameter, mm*	63.8 (15.2)	63.2 (13.5)	61.9 (14.3)	62.7 (14.5)	61.9 (13.7)	61.59 ± 14.03	-0.40 (-0.66 – -0.15)	.002
Location: aortoiliac	29 (4.2)	33 (5.6)	57 (8.7)	45 (7.2)	60 (9.1)	63 (8.9)	1.15 (1.07 – 1.23)	<.001

Table S3: Specific complications included in the categories of perioperative complications

Categories of perioperative complications	Specific complications
Abdominal	Abdominal abscess, abdominal sepsis, ileus, spleen injury, bowel ischemia, bowel injury, stoma placement, other abdominal complications
Arterial occlusion	(major) amputation, renal artery arterial occlusion, other arterial occlusion (including trash foot)
Prosthesis-/reconstruction related	Prosthesis infection, Prosthesis migration, other prosthesis-/reconstruction related complications
Wound	Deep wound infection, fascia dehiscence, other wound complications
Cardiac	Myocardial infarction, cardiac decompensation (failure), cardiac rhythm disturbances, other cardiac complications
Pulmonary	Pneumonia, pulmonary embolism, pneumothorax, other pulmonary complications
Neurological	Cerebrovascular accident, paraplegia, delirium, other neurological complications
Renal	Renal insufficiency (without hemodialysis or requiring hemodialysis)
Rebleeding	Rebleeding
Infection	Infections other than pulmonary and surgical
Other	Other postoperative complications

CHAPTER

3

OUTCOMES IN OCTOGENARIANS AND THE EFFECT OF COMORBIDITIES AFTER INTACT ABDOMINAL AORTIC ANEURYSM REPAIR IN THE NETHERLANDS: A NATIONWIDE COHORT STUDY

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ABSTRACT

Objectives

Age is an independent risk factor for mortality after both elective open surgical repair (OSR) and endovascular aneurysm repair (EVAR). As a result of an ageing population, and the less invasive nature of EVAR, the number of patients over 80 years (octogenarians) being treated is increasing. The mortality and morbidity following aneurysm surgery are increased for octogenarians. However, the mortality for octogenarians who have either low or high peri-operative risks remains unclear. The aim of this study was to provide peri-operative outcomes of octogenarians vs. non-octogenarians after OSR and EVAR for intact aneurysms, including separate subanalyses for elective and urgent intact repair, based on a nationwide cohort. Furthermore, the influence of comorbidities on peri-operative mortality was examined.

Methods

All patients registered in the Dutch Surgical Aneurysm Audit (DSAA) undergoing intact AAA repair between 2013 and 2018 were included. Patient characteristics and peri-operative outcomes (peri-operative mortality, and major complications) of octogenarians vs. non-octogenarians for both OSR and EVAR were compared using descriptive statistics. Multivariable logistic regression analyses were used to examine whether age and the presence of cardiac, pulmonary, or renal comorbidities were associated with mortality.

Results

This study included 12054 EVAR patients (3015 octogenarians), and 3815 OSR patients (425 octogenarians). Octogenarians in both the EVAR and OSR treatment groups were more often female and had more comorbidities. In both treatment groups, octogenarians had significantly higher mortality rates following intact repair as well as higher major complications rates. Mortality rates of octogenarians were 1.9% after EVAR and 11.8% after OSR. Age ≥ 80 and the presence of cardiac, pulmonary, and renal comorbidities were associated with mortality after EVAR and OSR.

Conclusions

Because of the high peri-operative mortality rates of octogenarians, awareness of the presence of comorbidities is essential in the decision making process before offering aneurysm repair to this cohort, especially when OSR is considered.

INTRODUCTION

In the last decade, endovascular aneurysm repair (EVAR) has become the preferred treatment for many patients with an intact abdominal aortic aneurysm (AAA)[1], because of its lower perioperative risks. Age is a known independent risk factor for post-operative mortality after both elective open surgical repair (OSR) and EVAR[2]. As a result of an ageing population[3], the number of patients over 80 years (octogenarians) who qualify for elective AAA repair is increasing[4,5]. However, the mortality and morbidity after AAA surgery for octogenarians is increased[6–9], which is important in the decision making process of when and how to intervene in this usually frailer population.

In current literature that reports on octogenarians, meta-analyses that include mainly observational studies have not described outcomes with details for octogenarians[7–9], while RCTs barely enrolled patients over 80 years[6]. Peri-operative mortality of octogenarians after primary AAA repair in 11 countries was assessed by the Vascunet collaboration. However, the morbidity of these patients was not described[4]. Therefore, there is a paucity of real life clinical data concerning mortality and morbidity after AAA surgery for octogenarians. Moreover, published studies scarcely report on the peri-operative mortality of subgroups of octogenarians with either low or high peri-operative risks. The recent ESVS guideline state that it is reasonable to consider elective AAA repair of octogenarians with reasonable life expectancy and quality of life after informing them of the pros and cons of different treatment strategies including conservative treatment[10]. However, no statements were made which octogenarians have high perioperative risks. The aim of this study was to provide peri-operative mortality and major complication rates of octogenarians versus non-octogenarians following intact AAA repair. This was assessed following both open surgical and endovascular aneurysm repair including separate subanalyses for elective and urgent intact repair using a nationwide prospective registry. Furthermore, which octogenarians have low and high perioperative risks was identified, examining the influence of age and the presence of comorbidities on peri-operative mortality.

MATERIALS AND METHODS

Data sources and study design

The dataset was retrieved from the Dutch Surgical Aneurysm Audit (DSAA), a nationwide prospective and compulsory quality registry that registers all patients undergoing aortic aneurysm surgery in the Netherlands. The DSAA was initiated in 2013, and includes all patients who underwent surgical repair of an infrarenal or juxtarenal AAA without previous aortic surgery. Since 2016, patients undergoing revisional aneurysm surgery and/or patients undergoing thoracic or thoraco-abdominal aortic aneurysm repair have been

registered as well. Data verification took place through a random sample of hospitals[11]. The data were analysed retrospectively and reported following the STROBE guidelines[12].

Participants

For this study, all patients who were registered in the DSAA undergoing primary repair (EVAR or OSR) for an intact AAA between January 2013 and December 2018 were included for analysis, provided that sex, date of birth, date of surgery, survival status at the time of discharge or 30 days post-operatively were registered. Data analyses were per-formed on an anonymised dataset. Ethical approval was not needed according to Dutch law.

Definitions

Patients were considered octogenarians when turning 80 years old or older in the year of surgery. EVAR procedures followed by immediate conversion were categorised by intention to treat. Intact aneurysm repairs included pooled data of both elective repair and urgent intact AAA repair. "Cardiac comorbidity" was defined as the use of diuretic or digoxin, antianginal or antihypertensive therapy, peripheral oedema, warfarin therapy, raised jugular venous pressure, or cardiomegaly[13]. "Abnormality on ECG" was defined as atrial fibrillation, ischaemia or any other ECG abnormalities[13]. Because of possible confounding caused by the variables "Cardiac comorbidity" and "Abnormality on ECG", it was decided to combine these variables into the variable "Cardiac comorbidity including abnormality on ECG" in the analyses. "Pulmonary comorbidity" was defined as dyspnoea on exertion, limiting dyspnoea, dyspnoea at rest, or visible consolidations or fibrosis on chest imaging[13]. "Renal comorbidity" was defined as an eGFR<60 mL/min/1.73m^2, which is categorised as "chronic kidney disease" by the International Society of Nephrology[14]. The eGFR was estimated using the CKD-EPI equation[15] and the variables "creatinine", "sex", and "age".

Outcomes

All outcomes of octogenarians were compared with the results of non-octogenarians. The primary outcome was peri-operative mortality, which was defined as intra-operative mortality, mortality ≤30 days after surgery, or during admission (in hospital mortality). The secondary outcomes were peri-operative major complications (≤30 days), defined as either an intra-operative or post-operative complications that needed a re-intervention, induced pro-longed stay, or caused death[16] and the peri-operative mortality in patients with and without comorbidities. Furthermore, subgroup analyses were performed to compare outcomes of octogenarians and non-octogenarians treated in elective and urgent intact settings.

Statistical methods

Descriptive analysis was performed using t tests for para-metrically distributed data, chi square tests and Fisher exact tests. Baseline characteristics, as well as peri-operative outcomes, were compared between octogenarians and non-octogenarians undergoing either EVAR or OSR. Missing values were shown as separate categories. A p value of <.05 was considered statistically significant.

To investigate whether age ≥ 80 was associated with peri-operative mortality, multivariable logistic regression analyses were performed for both EVAR and OSR. Patient and aneurysm related variables, based on the V(p)-POSSUM predictive score[13,17], that were potential confounders and available in the DSAA were included as covariates: age ≥ 80, sex, pulmonary comorbidity, cardiac comorbidity including results of last pre-operative electrocardiogram, renal comorbidity, pre-operative haemoglobin, urgency, location, and diameter of the aneurysm. Factors with a p value of <.10 in univariable analysis were selected for multivariable analysis. Finally, the peri-operative mortality rates of octogenarians and non-octogenarians with no comorbidities, cardiac comorbidity (including abnormality on the ECG), pulmonary comorbidity, and renal comorbidity were shown.

Missing data

The data for this study contained some variables with missing values. If patients with any missing data had been excluded from the analyses, information on 2477 (19.1%) patients including 538 octogenarians who underwent EVAR and 685 (18.0%) patients including 74 octogenarians who underwent OSR would have been lost. To prevent such loss of information, a state of the art method of multiple imputation using chained equations (MICE) was used[18].

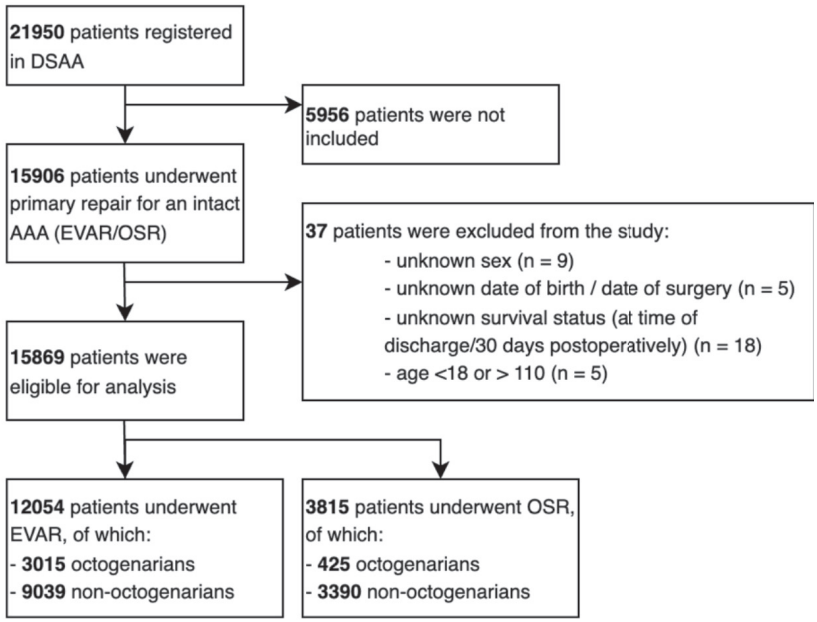
Missing data were imputed separately for EVAR and OSR patients. The outcome peri-operative mortality was not imputed, and the following variables were used in the imputation process: age, sex, cardiac and pulmonary co-morbidity, results of the last electrocardiogram, haemoglobin, creatinine, diameter, location, urgency, peri-operative mortality, pre- and post-operative complications, length of ICU stay, length of hospital stay, re-intervention, and re-admission. Twenty-five completed datasets we regenerated (each with 10 iterations) for both EVAR and OSR patients[18]. Values that were imputed were compared with values that were observed using scatter and density plots. For the multivariable regression models, the results of the imputed datasets were combined to produce a final result Rubin's rules[18]. For comparison, multivariable regression analyses using the subsets of complete cases were performed.

All analyses were performed using R version 3.6.1.

RESULTS

Between January 2013 and December 2018, 21950 consecutive patients were registered in the DSAA. Of these patients, 15906 underwent primary AAA repair for an intact aneurysm, of whom 15 869 (99.8%) were eligible for analysis (**Figure 1**). In total, 12054 EVAR patients including 3015 (25%) octogenarians, and 3815 OSR patients including 425 (11%) octogenarians, were included.

Figure 1: Study flow chart of included octogenarians and non-octogenarians who were registered in the Dutch Surgical Aneurysm Audit (DSAA) and who underwent primary repair of an intact abdominal aortic aneurysm (AAA) by endovascular aneurysm repair (EVAR) or open surgical repair (OSR).



Patient characteristics, aneurysm morphology, and operative data

Patient characteristics, aneurysm morphology, and operative data comparing octogenarians and non-octogenarians who received either EVAR or OSR are shown in **Table 1**. In both groups, octogenarians were more often female, had larger aneurysm diameters, and more often had pulmonary and renal comorbidity compared with younger patients. In the EVAR group and after multiple imputation in the OSR group, octogenarians suffered more often from cardiac comorbidity. In both the EVAR and OSR groups, octogenarians were more often treated for urgent intact aneurysms compared with non-octogenarians.

Table 1: Patient characteristics, aneurysm morphology and operative data for octogenarians vs. non-octogenarians who underwent either endovascular aneurysm repair (EVAR) or open surgical repair (OSR) of an intact abdominal aortic aneurysm

	EVAR			OSR		
	< 80 y (n = 9039)	**≥ 80 y (n = 3015)**	**p value**	**< 80 y (n = 3390)**	**≥ 80 y (n = 425)**	**p value**
Female sex	1095 (12.1) [12.1]	495 (16.4) [16.4]	<.001 [<.001]	624 (18.4) [18.4]	108 (25.4) [25.4]	.001 [<.001]
Age - y	70.76 ± 5.95	83.30 ± 2.91	N.A.	69.27 ± 6.85	82.18 ± 2.21	N.A.
Cardiac comorbidity including abnormalities on ECG			<.001 [<.001]			<.001 [.11]
No	2556 (33.2) [28.3]	678 (25.2) [22.5]		981 (32.1) [28.9]	104 (27.9) [24.5]	
Yes	5810 (66.8) [64.3]	2190 (74.8) [72.6]		2244 (67.9) [66.2]	295 (72.1) [69.4]	
Unknown/missing	673 (-) [7.4]	147 (-) [4.9]		165 (-) [4.9]	26 (-) [6.1]	
Pulmonary comorbidity			<.001 [.014]			<.001 [.028]
No	6623 (74.5) [73.3]	2143 (72.7) [71.1]		2521 (76.3) [74.4]	296 (72.9) [69.6]	
Yes	2263 (25.5) [25.0]	802 (27.3) [26.6]		781 (23.7) [23.0]	110 (27.1) [25.9]	
Unknown/missing	153 (-) [1.7]	70 (-) [2.3]		88 (-) [2.6]	19 (-) [4.5]	
Renal comorbidity			<.001 [<.001]			<.001 [<.001]
No, eGFR ≥ 60 mL/min/1.73m^2	6603 (74.8) [73.1]	1477 (50.2) [49.0]		2371 (72.6) [69.9]	209 (50.6) [49.2]	
Yes, eGFR <60 mL/min/1.73m^2	2224 (25.2) [24.6]	1471 (49.8) [48.8]		893 (27.4) [26.3]	206 (49.4) [48.5]	
Unknown / missing	212 (-) [2.3]	67 (-) [2.2]		126 (-) [3.7]	10 (-) [2.4]	
Haemoglobin - mmol/L	8.75 ± 1.00	8.36 ± 1.02	<.001 [<.001]	8.65 ± 1.01	8.25 ± 0.99	<.001 [<.001]
Missing	228 (-) [2.5]	74 (-) [2.5]		87 (-) [2.6]	8 (-) [1.9]	
Urgency: urgent intact	606 (6.7) [6.7]	274 (9.1) [9.1]	<.001 [<.001]	425 (12.5) [12.5]	92 (21.6) [21.6]	<.001 [<.001]

Table 1: *Continued.*

	EVAR			OSR		
	< 80 y (n = 9039)	**≥ 80 y (n = 3015)**	**p value**	**< 80 y (n = 3390)**	**≥ 80 y (n = 425)**	**p value**
Location: aortoiliac aneurysm	600 (6.6) [6.6]	160 (5.3) [9.1]	.010 [<.001]	208 (6.1) [6.1]	16 (3.8) [3.8]	<.001 [.064]
Aneurysm diameter - mm	58.97 ± 10.73	61.41 ± 11.51	<.001 [<.001]	62.68 ± 13.99	67.31 ± 15.48	<.001 [<.001]
Missing	109 (-) [1.2]	33 (-) [1.1]		72 (-) [2.1]	10 (-) [2.4]	
Procedure			<.001 [.003]			
EVAR	8484 (93.9) [93.9]	2878 (95.5) [95.5]				
Conversion	26 (0.3) [0.3]	10 (0.3) [0.3]				
Complex endovascular	529 (5.8) [5.8]	127 (4.2) [4.2]				

Data are presented as n (%) [%] and for continuous variables as mean ± standard deviation. Values in parentheses "(%)" are percentages after multiple imputation (25 datasets for EVAR patients, 25 datasets for OSR patients). Values in square brackets "[%]" are percentages including missing data with p values presented in square brackets as well.

Perioperative outcomes

Mortality

As shown in **Table 2** octogenarians had statistically significantly higher peri-operative mortality rates than non-octogenarians after surgery for all intact AAA. The odds ratio for peri-operative mortality in octogenarians compared to non-octogenarians was 2.5 for EVAR (1.9% vs. 0.8%, p <.001, OR 2.51) and 2.7 for OSR respectively (11.8% vs. 4.7%, p < .001, OR 2.73). **Table S1** shows the distribution of 30 day mortality and in hospital mortality in the composite outcome peri-operative mortality. In subgroup analyses of electively treated AAA patients (both EVAR and OSR), mortality rates were higher for octogenarians compared with non-octogenarians as well (EVAR: 1.4% vs. 0.6%, p <.001, OR 2.28; OSR: 9.3% vs 4.4%, p <.001, OR 2.24). In patients treated for urgent intact AAAs, octogenarians had higher mortality rates compared with non-octogenarians (EVAR: 6.6% vs. 2.6%, p = .007, OR 2.59; OSR: 20.7% vs. 6.6%, p <.001, OR 3.69).

Table 2: Peri-operative mortality rates and major complication rates for octogenarians vs. non-octogenarians who underwent either endovascular aneurysm repair (EVAR) or open surgical repair (OSR) of abdominal aortic aneurysm in intact, elective, and intact urgent setting

	Patients		Perioperative mortality*				Major complications**			
	<80 y	≥80 y	<80 y (ref.)	≥80 y	P	OR (95% CI)	<80 y (ref.)	≥80 y	P	OR (95% CI)
EVAR										
Intact	9039 (75.0)	3015 (25.0)	69 (0.8)	57 (1.9)	<.001	2.51 (1.75 – 3.56)	700 (7.7)	375 (12.4)	<.001	1.69 (1.47 – 1.92)
Elective	8433	2741	53 (0.6)	39 (1.4)	<.001	2.28 (1.50 – 3.45)	600 (7.1)	298 (10.9)	<.001	1.59 (1.37 – 1.83)
Urgent intact	606	274	16 (2.6)	18 (6.6)	.009	2.59 (1.30 – 5.22)	100 (16.5)	77 (28.1)	<.001	1.98 (1.41 – 2.79)
OSR										
Intact	3390 (88.9)	425 (11.1)	158 (4.7)	50 (11.8)	<.001	2.73 (1.93 – 3.79)	672 (19.8)	119 (28.0)	<.001	1.58 (1.25 – 1.98)
Elective	2965	333	130 (4.4)	31 (9.3)	<.001	2.24 (1.46 – 3.33)	580 (19.6)	86 (25.8)	.012	1.44 (1.10 – 1.86)
Urgent intact	425	92	28 (6.6)	19 (20.7)	<.001	3.69 (1.94 – 6.92)	92 (21.6)	33 (35.9)	.006	2.02 (1.24 – 3.27)

Data are presented as n (%) unless stated otherwise.

** Peri-operative mortality including intra-operative, 30 day and in hospital mortality. ** Major complication: post-operative death or a peri- or post-operative complication leading to a re-intervention or prolonged hospital stay*

Major complications

Table 2 shows that octogenarians more often developed major complications compared with non-octogenarians following both intact EVAR and OSR, as well as following elective and urgent intact repair. Major complication rates of octogenarians in intact setting were 12.4% after EVAR and 28.0% for OSR patients.

Associations with mortality

After univariable analyses, the factor "location" (EVAR) was not selected for multivariable analysis because of a p value >.10 (**Table 3**). The factor "age ≥ 80" was statistically significantly associated with higher mortality rates after adjusting for confounding factors after both EVAR and OSR (**Tables 3 and 4**). Sensitivity analysis involving multivariable analysis using complete cases showed a similar association of "age ≥ 80", with mortality after EVAR (OR 1.67, 95% CI 1.09 - 2.56) and OSR (OR 1.99, 95% CI 1.34 - 2.92) (**Table S2**).

Table 3: Multivariable logistic regression analyses to examine the association of age ≥ 80 and peri-operative mortality in patients with endovascular repair of abdominal aortic aneurysm. Missing data were completed by multiple imputation.

	Univariable analysis		Multivariable analysis	
	OR (95%-CI)	**P**	**aOR (95%-CI)**	**P**
Age ≥ 80	2.51 (2.33 – 2.69)	<.001	1.66 (1.54 – 1.79)	<.001
Female sex	1.48 (1.35 – 1.62)	<.001	1.16 (1.06 – 1.28)	.002
Cardiac comorbidity including abnormalities on ECG	2.43 (2.21 – 2.67)	<.001	1.69 (1.53 – 1.86)	<.001
Pulmonary comorbidity	3.98 (3.46 – 3.98)	<.001	3.18 (2.96 – 3.42)	<.001
Renal comorbidity, eGFR <60 mL/min/1.73m2	2.66 (2.48 – 2.86)	<.001	1.84 (1.70 – 1.98)	<.001
Haemoglobin	0.62 (0.60 – 0.64)	<.001	0.75 (0.73 – 0.78)	<.001
Urgent intact	4.84 (4.47 – 5.24)	<.001	3.89 (3.57 – 4.24)	<.001
Aortoiliac location of aneurysm	1.01 (0.90 – 1.16)	.92	-	-
Aneurysm diameter per 10 mm	1.28 (1.25 – 1.32)	<.001	1.10 (1.07 – 1.13)	<.001

OR = odds ratio; aOR = adjusted odds ratio, CI = confidence interval

Table 4: Multivariable logistic regression analyses to examine the association of age ≥ 80 and perioperative mortality in patients with open surgical repair of abdominal aortic aneurysm. Missing data was completed by multiple imputation.

	Univariable analysis		Multivariable analysis	
	OR (95% CI)	**P**	**aOR (95% CI)**	**P**
Age ≥ 80	2.73 (2.55 – 2.92)	<.001	2.02 (1.88 – 2.17)	<.001
Female sex	1.73 (1.62 – 1.84)	<.001	1.42 (1.33 – 1.52)	<.001
Cardiac comorbidity including abnormalities on ECG	1.99 (1.86 – 2.13)	<.001	1.76 (1.64 – 1.89)	<.001
Pulmonary comorbidity	1.98 (1.87 – 2.10)	<.001	1.78 (1.67 – 1.89)	<.001
Renal comorbidity, eGFR <60 mL/min/1.73m2	2.30 (2.18 – 2.44)	<.001	1.85 (1.75 – 1.96)	<.001
Haemoglobin	0.74 (0.72 – 0.76)	<.001	0.85 (0.83 – 0.88)	<.001
Urgent intact	1.95 (1.82 – 2.08)	<.001	1.81 (1.68 – 1.95)	<.001
Aortoiliac location of aneurysm	0.38 (0.32 – 0.45)	<.001	0.48 (0.40 – 0.58)	<.001
Aneurysm diameter per 10 mm	1.07 (1.05 – 1.09)	<.001	0.99 (0.97 – 1.01)	.25

OR = odds ratio; aOR = adjusted odds ratio, CI = confidence interval

Observed comorbidities and corresponding peri-operative mortality

Only 317 (10.5% in original data; 12.0% in imputed data) and 42 (9.9% in original data; 12.8% in imputed data) octogenarians undergoing EVAR and OSR had no comorbidities, respectively **(Table 5)**. Observed peri-operative mortality rates following intact AAA repair in patients with no comorbidity, cardiac, pulmonary, or renal comorbidity are shown in **Table 5**. After EVAR, the mortality rates of octogenarians with a cardiac, pulmonary, or renal co-morbidity reached 2.4%, 4.2%, or 2.5%, respectively, while octogenarians with no comorbidities had a rate of 0.4% (all percentages are based on imputed data). After OSR, the mortality rates of octogenarians with cardiac, pulmonary, or renal comorbidity reached 13.4%, 13.6%, and 14.8%, while octogenarians with no comorbidities had a mortality rate of 3.8% (based on imputed data).

Table 5: Perioperative mortality rates for octogenarians and non-octogenarians who underwent either EVAR and OSR in intact setting, stratified by the presence of comorbidities

	EVAR		OSR	
	< 80 y (n = 9039)	**≥ 80 y (n = 3015)**	**< 80 y (n = 3390)**	**≥ 80 y (n = 425)**
Comorbidities				
No comorbidities*	1654 (22.2) [18.3]	317 (12.0) [10.5]	612 (21.0) [18.1]	42 (12.8) [9.9]
Cardiac comorbidity including abnormalities on ECG	5810 (66.8) [64.3]	2190 (74.8) [72.6]	2244 (67.9) [66.2]	295 (72.1) [69.4]
Pulmonary comorbidity	2263 (25.5) [25.0]	802 (27.3) [26.6]	781 (23.7) [23.0]	110 (27.1) [25.9]
Renal comorbidity	2224 (25.2) [24.6]	1471 (49.8) [48.8]	893 (27.4) [26.3]	206 (49.4) [48.5]
Peri-operative mortality				
All patients	69 (0.8) [0.8]	57 (1.9) [1.9]	158 (4.7) [4.7]	50 (11.8) [11.8]
No comorbidities*	4 (0.3) [0.2]	1 (0.4) [0.3]	11 (1.9) [1.8]	2 (3.8) [4.8]
Cardiac comorbidity including abnormalities on ECG	51 (0.9) [0.9]	51 (2.4) [2.3]	234 (5.5) [5.5]	38 (13.4) [12.9]
Pulmonary comorbidity	35 (1.6) [1.5]	32 (4.2) [4.0]	60 (7.8) [7.7]	14 (13.6) [12.7]
Renal comorbidity	31 (1.4) [1.4]	36 (2.5) [2.4]	67 (7.5) [7.5]	30 (14.8) [14.6]

*Data are presented as n (%; %). Values in parentheses "(%)" are percentages after multiple imputation (25 datasets for EVAR patients, 25 datasets for OSR patients). Values in square brackets "[%]" are percentages including missing data. *No comorbidities: based on no pulmonary comorbidity, no cardiac comorbidity including no abnormalities on ECG, and no renal dysfunction (eGFR <60 mL/min/1.73m2)*

DISCUSSION

The octogenarians in this study were at risk of significantly higher peri-operative mortality and major complication rates after both EVAR and OSR for intact AAA compared with younger patients. Furthermore, the effect of comorbidities in this age group was more pronounced and was clearly associated with impaired survival. In octogenarians, mortality after OSR exceeded 10%, especially when comorbidities were present. After EVAR, octogenarians with pulmonary comorbidities had a mortality rate of approximately 4%. In contrast, mortality was 1.9% for all octogenarians in the EVAR group.

Surgical risk is at the heart of clinical (shared) decision making, especially when prophylactic surgery is performed on asymptomatic patients such as in elective AAA care[19]. To inform patients appropriately before undergoing high risk surgery, robust data are needed concerning morbidity and mortality. The DSAA is a mandatory national verified quality registry, set up to monitor and improve the quality of AAA care by providing benchmarked information to vascular surgeons. Since 2013, all patients undergoing primary abdominal aortic aneurysm surgery in the Netherlands have been registered, providing objective, real world data. Because of its scale and in contrast to other published studies, it enables relevant subanalyses such as the analysis described in this paper[8,9]. Additionally, local data on out-comes of octogenarians could be valuable to inform patients and family accurately, for example because of a potential hospital related volume outcome relationship for OSR[20]. Since 2019, a specific dashboard called the Codman Dashboard has enabled all Dutch vascular surgeons to analyse their registered outcomes of particular subgroup[21].

This study describes a mortality rate of 11.8% for all octogenarians after OSR, and this seems to exceed the yearly rupture risks of smaller aneurysms. Moreover, octogenarians with comorbidities have mortality rates > 10% after OSR, in contrast to the mortality rate of 3.6% in the(small) group of octogenarians without comorbidities (12.8% of all octogenarians in this cohort, based on imputed data). In the literature, a mortality rate of 7.5% for octogenarians who were treated electively by OSR was described in a meta-analysis[7]. For intact aneurysm repair, a mortality rate of 9.5% for octogenarians was described in an international study by Budtz-Lilly et al., which combined the results of 11 vascular registries[4], similar to the results from the present study. However, mortality rates in these studies were rarely specified for either high or low risk octogenarians[22]. In previous studies that examined the safety of surveillance for small aneurysms up to 5.5 cm, 30 day operative mortality rates of only 5.5%[23] and 2.1%[24] were described. This poses the question of whether operative mortality rates exceeding these numbers are acceptable, in particular in elderly patients undergoing preventive aneurysm repair at relatively small diameters that are at low risk of rupture.

After EVAR, this study reports a mortality rate of 1.9% for octogenarians. This is in line with the previously mentioned international study by Budtz-Lilly et al., which reported a mortality rate of 1.8% of octogenarians after EVAR. Meta-analyses that included older studies have described mortality rates for octogenarians of 3.7%[9] and 4.6%[7] after EVAR. The impact of improved device technology (lower profile devices), peri-operative management including better anaesthetic techniques[25], and cardioprotective medication[26] might play a role in improved survival of octogenarians in this study compared to the meta-analyses with older data[4]. In the present study, a peri-operative mortality rate of 4.2% was observed for octogenarians with a pulmonary comorbidity. This mortality rate was low compared with the mortality rate of 7.3% reported in the EVAR-2 study in patients who were considered not physically fit enough to undergo OSR[27].

Apart from the mortality rates following intact AAA repair, other outcomes for octogenarians are important as well and could assist in the clinical decision making process. First, to deal with the heterogeneity in the group of intact AAA repairs, subanalyses were performed for elective and urgent intact repair including adjustment for urgent intact repair in the multivariable analyses. Furthermore, in the present study, major complication rates were examined. As expected, octogenarians had higher major complication rates compared with non-octogenarians. Obviously, other outcome parameters, such as quality of life[28], re-intervention rate[6], long term outcomes[29], and costs[30], are also important to consider in the clinical decision making process for octogenarians, but these are not captured in the DSAA registry.

In this study, no association between aneurysm size and mortality was found in OSR patients, which might suggest that postponing OSR does not result in higher mortality rates. Remarkably, in EVAR patients, aneurysm size was associated with mortality. The diameter threshold for elective abdominal aneurysm repair is based on both peri-operative risk and the risk of rupture. However, the risk of rupture according to aneurysm diameter was not investigated. In the literature, little is known about the diameters of ruptured aneurysms between octogenarians and non-octogenarians[31]. In studies up to 2010, the mean annual risk of rupture of a 5 cm aneurysm was 0.6% in men and 2.9% in women. It is stated that the mean diameter of ruptured aneurysms in all patients has increased during the last decade, possibly because of increased statin therapy[26]. A previous study demonstrated that some patients with severe comorbidities and large aneurysms could be managed conservatively with acceptable results for long periods (7-76 months)[32]. Therefore, the question remains of whether the diameter threshold at which to intervene should be increased for octogenarians because of a much higher peri-operative risk, in particular when octogenarians experience comorbidities and OSR is considered to be the treatment modality.

Despite the relatively large number of octogenarians in this cohort, this study has some limitations. First, the DSAA includes only patients who were considered fit enough to undergo surgery, which was a clinical decision by the surgeon. Because of this selection bias, predictions of mortality rates based on the number of comorbidities of octogenarians who could be incorporated in the decision making process could not be made, as the decision to perform surgery had already been made. Therefore, the reported peri-operative outcomes of octogenarians in this study will probably be better than peri-operative outcomes of all octogenarians with an intact AAA. Second, information bias might have taken place, as age was calculated as the year of surgery minus the year of birth. This calculation included some patients of age 79 in the group "octogenarians", which might have led to an underestimation of the out-comes of octogenarians. Furthermore, this was a retrospective study of a retrieved dataset from the DSAA, a prospectively maintained national quality registry. As this audit is not designed purely for scientific research, information on some potential confounders such as peripheral artery obstructive disease[33], type of anaesthetic, anatomical details, surgeon experience, or frailty were not available. It would be interesting to examine the influence of frailty, as it has been reported that frailty is associated with age as well as with peri-operative mortality[34]. Furthermore, Joseph et al. stated that a frailty index was better for predicting mortality compared with age in emergency general surgery in the elderly[35], while age was a predictor of mortality in vascular studies that did not report on frailty[36,37]. Another limitation of this study is that the specific categories in the groups cardiac and pulmonary comorbidity were potentially not equally weighted between octogenarians and non-octogenarians, which might have caused heterogeneity in the groups of octogenarians vs. non-octogenarians and thus, these groups were not compared. Finally, the dataset had some missing data and thus, for multivariable logistic regression analyses and analyses stratified for the presence of comorbidities, missing data were imputed using multiple imputation. Sensitivity analyses using complete cases were performed for the multivariable analyses that examined the association of age ≥ 80 with mortality, with similar results.

In conclusion, age ≥ 80 and comorbidities are significantly associated with mortality after endovascular and open repair for abdominal aortic aneurysms. Mortality after OSR in octogenarians is exceedingly high, especially in the presence of comorbidities. Reported observed rates in this study can be used by everyone involved in the decision making process considering optimal care for aneurysm patients. More research focused on optimal treatment thresholds for elective AAA repair in both low and high risk subgroups of octogenarians is needed. For now, awareness of the presence of comorbidities is key in the decision making process.

Conflicts of interest
HV: consultant for Medtronic, WL Gore, Terumo, Endologix, and Arsenal AAA.

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LITERATURE

1 Lilja F, Mani K, Wanhainen A. Editor's Choice – Trend-break in Abdominal Aortic Aneurysm Repair With Decreasing Surgical Workload. *Eur J Vasc Endovasc Surg* 2017;**53**(6):811–9. Doi: 10.1016/j.ejvs.2017.02.031.

2 Arhuidese IJ, Salami A, Obeid T, Qazi U, Abularrage CJ, Black JH, et al. The age effect in increasing operative mortality following delay in elective abdominal aortic aneurysm repair presented at the society for clinical vascular surgery 42nd Annual Symposium, Carlsbad, CA, March 18-22, 2014. *Ann Vasc Surg* 2015;**29**(6):1181–7. Doi: 10.1016/j.avsg.2015.03.041.

3 CBS. Bevolkingspiramide. https://www.cbs.nl/nl-nl/visualisaties/bevolkingspiramide. 05/11/2020.

4 Budtz-Lilly J, Venermo M, Debus S, Behrendt CA, Altreuther M, Beiles B, et al. Editor's Choice – Assessment of International Outcomes of Intact Abdominal Aortic Aneurysm Repair over 9 Years. *Eur J Vasc Endovasc Surg* 2017;**54**(1):13–20. Doi: 10.1016/j.ejvs.2017.03.003.

5 Mani K, Lees T, Beiles B, Jensen LP, Venermo M, Simo G, et al. Treatment of abdominal aortic aneurysm in nine countries 2005-2009: A vascunet report. *Eur J Vasc Endovasc Surg* 2011;**42**(5):598–607. Doi: 10.1016/j.ejvs.2011.06.043.

6 Powell JT, Sweeting MJ, Ulug P, Blankensteijn JD, Lederle FA, Becquemin JP, et al. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. *Br J Surg* 2017;**104**(3):166–78. Doi: 10.1002/bjs.10430.

7 Henebiens M, Vahl A, Koelemay MJW. Elective surgery of abdominal aortic aneurysms in octogenarians: A systematic review. *J Vasc Surg* 2008;**47**(3):676–81. Doi: 10.1016/j.jvs.2007.09.004.

8 Biancari F, Catania A, D'Andrea V. Elective endovascular vs. open repair for abdominal aortic aneurysm in patients aged 80 years and older: Systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2011;**42**(5):571–6. Doi: 10.1016/j.ejvs.2011.07.011.

9 Han Y, Zhang S, Zhang J, Ji C, Eckstein HH. Outcomes of Endovascular Abdominal Aortic Aneurysm Repair in Octogenarians: Meta-analysis and Systematic Review. *Eur J Vasc Endovasc Surg* 2017;**54**(4):454–63. Doi: 10.1016/j.ejvs.2017.06.027.

10 Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *Eur J Vasc Endovasc Surg* 2019;**57**(1):8–93. Doi: 10.1016/j.ejvs.2018.09.020.

11 Dutch Institute for Clinical Auditing. Eindrapport dataverificatie DSAA. https://dica.nl/media/660/Eindrapport_dataverificatie_DSAA_2016.pdf. 05/11/2020.

12 STROBE Statement- checklist of items that should be included in reports of observational studies. https://www.strobe-statement.org/fileadmin/Strobe/uploads/checklists/STROBE_checklist_v4_combined.pdf. 08/11/2020.

13 Copeland GP, Jones D, Walters M. POSSUM: A scoring system for surgical audit. *Br J Surg* 1991;**78**(3):355–60. Doi: 10.1002/bjs.1800780327.

14 Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl* 2013;(3):1–150. Doi: 10.3182/20140824-6-za-1003.01333.

15 Levey, A.S; Stevens, L.A.; Schmid, C.H.; Zhang, Y; Castro III, A. F.; Feldman, H.I.; Kusek, J.W.; Eggers, P.; Van Lente, F.; Greene, T.; Coresh J. A new equation to estimate the glomeraulr filtration rate. *Ann Intern Med* 2009;**150**:604–12.

16 Lijftogt N, Karthaus EG, Vahl A, van Zwet EW, van der Willik EM, Tollenaar RAEM, et al. Failure to Rescue – a Closer Look at Mortality Rates Has No Added Value for Hospital Comparisons but Is Useful for Team Quality Assessment in Abdominal Aortic Aneurysm Surgery in The Netherlands. *Eur J Vasc Endovasc Surg* 2018;**56**(5):652–61. Doi: 10.1016/j.ejvs.2018.06.062.
17 Smith J, Tekkis P. Risk Prediction in surgery. http://www.riskprediction.org.uk/vasc-index.php. 08/11/2020.
18 White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med* 2011;**30**(4):377–99. Doi: 10.1002/sim.4067.
19 de Mik SML, Stubenrouch FE, Balm R, Ubbink DT. Systematic review of shared decision-making in surgery. *Br J Surg* 2018;**105**(13):1721–30. Doi: 10.1002/bjs.11009.
20 Gray WK, Day J, Horrocks M. Volume e Outcome Relationships in Elective Abdominal Aortic Aneurysm Surgery : Analysis of the UK Hospital Episodes Statistics Database for the Getting It Right First Time (GIRFT) Programme. *Eur J Vasc Endovasc Surg* 2020;(xxxx). Doi: 10.1016/j.ejvs.2020.07.069.
21 Beck N, van Bommel AC, Eddes EH, van Leersum NJ, Tollenaar RA, Wouters MW. The Dutch Institute for Clinical Auditing: Achieving Codman's Dream on a Nationwide Basis. *Ann Surg* 2020;**271**(4):627–31. Doi: 10.1097/SLA.0000000000003665.
22 Berry AJ, Smith RB, Weintraub WS, Chaikof EL, Dodson TF, Lumsden AB, et al. Age versus comorbidities as risk factors for complications after elective abdominal aortic reconstructive surgery. *J Vasc Surg* 2001;**33**(2):345–52. Doi: 10.1067/mva.2001.111737.
23 Brady AR, Brown LC, Fowkes FGR, Greenhalgh RM, Powell JT, Ruckley C V., et al. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002;**346**(19):1445–52. Doi: 10.1056/NEJMoa013527.
24 Lederle FA, Samuel EW, Johnson GR, Reinke DB, Littooy FN, Acher CW, et al. Immediate repair compared with surveillance of small aortic aneurysms. *N Engl J Med* 2002;**346**(19):1437–44. Doi: 10.1177/096721099900700502.
25 Armstrong RA, Squire YG, Rogers CA, Hinchliffe RJ, Mouton R. Type of Anesthesia for Endovascular Abdominal Aortic Aneurysm Repair. *J Cardiothorac Vasc Anesth* 2019;**33**(2):462–71. Doi: 10.1053/j.jvca.2018.09.018.
26 Salata K, Syed M, Hussain MA, Mestral C De, Greco E, Mamdani M, et al. Statins reduce abdominal aortic aneurysm growth, rupture, and perioperative mortality: A systematic review and meta-analysis. *J Am Heart Assoc* 2018;**7**(19). Doi: 10.1161/JAHA.117.008657.
27 United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG ED. Endovascular Repair of Abdominal Aortic Aneurysm in Patients Physically Ineligible for Open Repair. *N Engl J Med* 2010;**362**:1872–80. Doi: 10.1097/SLA.0000000000002392.
28 Prinssen M, Buskens E, Blankensteijn JD, Buth J, Tielbeek A V., Verhoeven ELG, et al. Quality of life after endovascular and open AAA repair. Results of a randomised trial. *Eur J Vasc Endovasc Surg* 2004;**27**(2):121–7. Doi: 10.1016/j.ejvs.2003.11.006.
29 Li B, Khan S, Salata K, Hussain MA, de Mestral C, Greco E, et al. A systematic review and meta-analysis of the long-term outcomes of endovascular versus open repair of abdominal aortic aneurysm. *J Vasc Surg* 2019;**70**(3):954-969.e30. Doi: 10.1016/j.jvs.2019.01.076.
30 Burgers LT, Vahl AC, Severens JL, Wiersema AM, Cuypers PWM, Verhagen HJM, et al. Cost-effectiveness of Elective Endovascular Aneurysm Repair Versus Open Surgical Repair of Abdominal Aortic Aneurysms. *Eur J Vasc Endovasc Surg* 2016;**52**(1):29–40. Doi: 10.1016/j.ejvs.2016.03.001.
31 Sweeting MJ, Thompson SG, Brown LC, Powell JT. Meta-analysis of individual patient data to examine factors affecting growth and rupture of small abdominal aortic aneurysms. *Br J Surg* 2012;**99**(5):655–65. Doi: 10.1002/bjs.8707.

32 Tanquilut EM, Veith FJ, Ohki T, Lipsitz EC, Shaw PM, Suggs WD, et al. Nonoperative management with selective delayed surgery for large abdominal aortic aneurysms in patients at high risk. *J Vasc Surg* 2002;**36**(1):41–6. Doi: 10.1067/mva.2002.122889.
33 Pini R, Gallitto E, Faggioli G, Mascoli C, Vacirca A, Fenelli C, et al. Predictors of perioperative and late survival in octogenarians undergoing elective endovascular abdominal aortic repair. *J Vasc Surg* 2019;**69**(5):1405–11. Doi: 10.1016/j.jvs.2018.07.059.
34 Houghton JSM, Nickinson ATO, Morton AJ, Nduwayo S, Pepper CJ, Rayt HS, et al. Frailty Factors and Outcomes in Vascular Surgery Patients: A Systematic Review and Meta-analysis. *Ann Surg* 2020;**272**(2):266–76. Doi: 10.1097/SLA.0000000000003642.
35 Joseph B, Zangbar B, Pandit V, Fain M, Mohler MJ, Kulvatunyou N, et al. Emergency General Surgery in the Elderly: Too Old or Too Frail? Presented orally at the Surgical Forum of the American College of Surgeons 100th Annual Clinical Congress, San Francisco, CA, October 2014. *J Am Coll Surg* 2016;**222**(5):805–13. Doi: 10.1016/j.jamcollsurg.2016.01.063.
36 Ambler GK, Gohel MS, Mitchell DC, Loftus IM, Boyle JR. The abdominal aortic aneurysm statistically corrected operative risk evaluation (AAA SCORE) for predicting mortality after open and endovascular interventions. *J Vasc Surg* 2015;**61**(1):35-43.e1. Doi: 10.1016/j.jvs.2014.06.002.
37 Grant SW, Hickey GL, Grayson AD, Mitchell DC, McCollum CN. National risk prediction model for elective abdominal aortic aneurysm repair. *Br J Surg* 2013;**100**(5):645–53. Doi: 10.1002/bjs.9047.

SUPPLEMENTARY MATERIALS

Table S1: Specifications of perioperative morality which is a combined outcome measure of intraoperative mortality, 30-day mortality and in-hospital mortality

EVAR – intact	<80 (n= 9039)	≥80 (n = 3015)
Perioperative mortality	**69 (0.8)**	**57 (1.9)**
Intraoperative mortality	0 (0.0)	0 (0.0)
30-day mortality	59 (0.7)	56 (1.9)
In-hospital mortality	55 (0.6)	37 (1.2)
OSR - intact	**<80 (n = 3390)**	**≥80 (n = 425)**
Perioperative mortaliy	**158 (4.7)**	**50 (11.8)**
Intraoperative mortality	0 (0.0)	0 (0.0)
30-day mortality	142 (4.2)	40 (9.4)
In-hospital mortality	151 (4.5)	49 (11.5)

Data are presented as n (%).

Table S2: Multivariable logistic regression analyses using complete cases to examine the association of age ≥ 80 and individual comorbidities with perioperative mortality, separately analysed for EVAR patients and OSR patients

Association of age and individual comorbidities with perioperative mortality for EVAR patients (complete cases)						
	Univariable analysis			**Multivariable analysis**		
Factor	**OR**	**95%-CI**	**P**	**aOR**	**95%-CI**	**P**
Age: ≥ 80	2.56	1.70 – 2.84	<.001	1.67	1.09 – 2.56	.018
Sex: female	1.53	0.89 – 2.51	.106	-	-	-
Cardiac comorbidity including abnormalities on ECG	3.10	1.76 – 5.99	<.001	2.12	1.19 – 4.14	0.017
Pulmonary comorbidity	3.99	2.66 – 6.06	<.001	3.30	2.18 – 5.05	<.001
Renal comorbidity (eGFR <60)	2.93	1.95 – 4.43	<.001	1.85	1.21 – 2.87	.005
Haemoglobin	0.56	0.47 – 0.67	<.001	0.67	0.56 – 0.81	<.001
Urgency: urgent intact	3.59	2.10 – 5.84	<.001	2.62	1.48 – 4.41	<.001
Location: aorto-iliac aneurysm	1.19	0.50 – 2.39	.666	-	-	-
Aneurysm diameter (per 10 mm)	1.29	1.10 – 1.49	<.001	1.13	0.96 – 1.32	0.135

Association of age and individual comorbidities with perioperative mortality for OSR patients (complete cases)						
	Univariable analysis			Multivariable analysis		
Factor	**OR**	**95%-CI**	**P**	**aOR**	**95%-CI**	**P**
Age: ≥ 80	2.64	1.80 – 3.81	<.001	1.99	1.34 – 2.92	<.001
Sex: female	1.91	1.35 – 2.66	<.001	1.62	1.13 – 2.28	.007
Cardiac comorbidity including abnormalities on ECG	2.08	1.43 – 3.13	<.001	1.88	1.28 – 2.85	.002
Pulmonary comorbidity	1.84	1.33 – 2.54	<.001	1.64	1.17 – 2.28	.003
Renal comorbidity (eGFR <60)	2.07	1.51 – 2.83	<.001	1.68	1.21 – 2.32	.002
Haemoglobin	0.76	0.66 – 0.89	<.001	0.88	0.75 – 1.03	.102
Urgency: urgent intact	1.67	1.08 – 2.49	.016	1.56	0.99 – 2.38	.045
Location: aorto-iliac aneurysm	0.50	0.18 – 1.11	0.133	-	-	-
Aneurysm diameter (per 10 mm)	1.01	0.89 – 1.12	0.920	-	-	-

CHAPTER

4

NATIONWIDE OUTCOMES OF OCTOGENARIANS FOLLOWING OPEN OR ENDOVASCULAR MANAGEMENT AFTER RUPTURED ABDOMINAL AORTIC ANEURYSMS

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ABSTRACT

Purpose

Octogenarians are known to have less-favorable outcomes following ruptured abdominal aortic aneurysm (rAAA) repair compared with their younger counterparts. Accurate information regarding perioperative outcomes following rAAA-repair is important to evaluate current treatment practice. The aim of this study was to evaluate perioperative outcomes of octogenarians and to identify factors associated with mortality and major complications after open surgical repair (OSR) or endovascular aneurysm repair (EVAR) of a rAAA using nationwide, real-world, contemporary data.

Methods

All patients that underwent EVAR or OSR of an infrarenal or juxtarenal rAAA between January 1, 2013, and December 31, 2018, were prospectively registered in the Dutch Surgical Aneurysm Audit (DSAA) and included in this study. The primary outcome was the comparison of perioperative outcomes of octogenarians versus non-octogenarians, including adjustment for confounders. Secondary outcomes were the identification of factors associated with mortality and major complications in octogenarians.

Results

The study included 2879 patients, of which 1146 were treated by EVAR (382 octogenarians, 33%) and 1733 were treated by OSR (410 octogenarians, 24%). Perioperative mortality of octogenarians following EVAR was 37.2% versus 14.8% in non-octogenarians (adjusted OR=2.9, 95% CI=2.8–3.0) and 50.0% versus 29.4% following OSR (adjusted OR=2.2, 95% CI=2.2–2.3). Major complication rates of octogenarians were 55.4% versus 31.8% in non-octogenarians following EVAR (OR=2.7, 95% CI=2.1–3.4), and 68% versus 49% following OSR (OR=2.2, 95% CI=1.8–2.8). Following EVAR, 30.6% of the octogenarians had an uncomplicated perioperative course (UPC) versus 49.5% in non-octogenarians (OR=0.5, 95% CI=0.4–0.6), while following OSR, UPC rates were 20.7% in octogenarians versus 32.6% in non-octogenarians (OR=0.5, 95% CI=0.4–0.7). Cardiac or pulmonary comorbidity and loss of consciousness were associated with mortality and major complications in octogenarians. Interestingly, female octogenarians had lower mortality rates following EVAR than male octogenarians (adjusted OR=0.7, 95% CI=0.6–0.8).

Conclusion

Based on this nationwide study with real-world registry data, mortality rates of octogenarians following ruptured AAA-repair were high, especially after OSR. However, a substantial proportion of these octogenarians following OSR and EVAR had an uneventful recovery. Known preoperative factors do influence perioperative outcomes and reflect current treatment practice.

INTRODUCTION

A ruptured abdominal aortic aneurysm (rAAA) represents a highly lethal condition, especially in older patients. In patients undergoing surgical treatment for a rAAA, 30-day mortality rates of 24.5% (95% CI=23.4–25.7) following endovascular aneurysm repair (EVAR) and 37.8% (95% CI=36.4–39.2) following open surgical repair (OSR) are described[1]. Advanced age is associated with increased in-hospital mortality[2,3]. A meta-analysis which included studies up to 2010 reported perioperative mortality rates of 59.2% for octogenarians treated with OSR after rAAA[4] and a more recent meta-analysis which included studies from centers of excellence, (nationwide) vascular registries, an administrative database, and an insurance database published 30-day mortality rates of 27% (95% CI=18–38) for octogenarians after EVAR and 52% (95% CI=44–60) after OSR, respectively[5]. Although these perioperative mortality rates are high, AAA repair is the only option for these patients to survive a rAAA. Long-term outcomes of octogenarians who were successfully treated appeared to be rea-sonable as in the Swedish Vascular Registry, the survival of octogenarians treated for rAAAs and who survived the first 90 days after surgery was similar to non-octogenarians[6]. Furthermore, in the recent meta-analysis, 1-year mortality rates in octogenarians of 35% (95% CI=18–56) following EVAR and 54% (95% CI=47–60) following OSR were reported[5].

A swift decision regarding treatment is vital in patients with rAAAs. Current predictive models were developed using data up to 2012 and have limited value in predicting mortality or major complications following rAAA repair[7–9].

However, this information is essential for decision-making regarding treatment or palliation, especially in elderly patients. The identification of patient factors associated with perioperative mortality in a nationwide cohort of octogenarians could evaluate the current selection of octogenarians to be treated for a rAAA. However, specific contemporary perioperative outcomes in octogenarians following rAAA repair based on a nationwide data reflecting real-world practice are scarce.

This study aimed to evaluate perioperative outcomes of octogenarians compared with non-octogenarians after OSR or EVAR of a ruptured infrarenal or juxtarenal AAA using nationwide, real-world, contemporary data. Furthermore, we identified factors associated with mortality and major complications in octogenarians and assessed time-trends of applied surgical techniques. Finally, we investigated the impact of complications on mortality and length of hospital stay based on a validated nationwide and mandatory clinical registry.

This study aimed to evaluate perioperative outcomes of octogenarians compared to non-octogenarians after OSR or EVAR of a ruptured infrarenal or juxtarenal AAA using nationwide, real-world, contemporary data. Furthermore, we identified factors associated with mortality and major complications in octogenarians and assessed time-trends of applied surgical techniques. Finally, we investigated the impact of complications on mortality and length of hospital stay based on a validated nationwide and mandatory clinical registry.

MATERIALS AND METHODS

Data sources and study design

Data were collected from the Dutch Surgical Aneurysm Audit (DSAA), a mandatory nationwide clinical registry. All Dutch vascular surgeons performing aortic aneurysm interventions register their aortic aneurysm interventions in the DSAA. Since the establishment of the DSAA in 2013, the DSAA includes all patients that underwent repair of an infrarenal or juxtarenal aneurysm without previous aortic surgery and, thus, all rAAA repairs performed in the Netherlands were included in the DSAA. Data verification took place through a random sample of hospitals, concluding that the data had a high degree of reliability, with very few discrepancies detected and showing a case ascertainment of 98.4%[10,11]**.** The data derived from this registry were anonymized and were retrospectively analysed. The study followed the STROBE statement[12].

Participants

All consecutive patients that were registered in the DSAA undergoing primary repair (EVAR or OSR) of a ruptured infrarenal or juxtarenal AAA between January 1, 2013 and December 31, 2018 were included for analysis. Patients with missing date of birth, sex, or survival status at the time of discharge or 30-days postoperatively were excluded. No ethical approval or informed consent was required for this study according to Dutch law.

Definitions

Age was calculated as year of surgery minus year of birth. Patients were considered octogenarians when their age was 80 years or older at the time of surgery. EVAR procedures followed by immediate conversion were categorized by intention-to-treat.

Outcomes

The primary outcome was the comparison of perioperative outcomes (perioperative mortality, major complications, and the desirable composite outcome "uncomplicated peri-operative course" [UPC]) of octogenarians with non-octogenarians. Secondary outcomes were the identification of factors associated with perioperative mortality and

major complications in octogenarians and the influence of complications on perioperative mortality and length of hospital stay of living patients. Finally, time-trends per year regarding applied surgical techniques were evaluated.

Perioperative mortality was defined as death within 30-days or in-hospital. Major complications were defined as either intraoperative or postoperative complications that resulted in a prolonged length of stay, needed a reintervention, or caused mortality[13] and described the perioperative period (first 30 days) following rAAA-repair. Prolonged length of stay was defined as the length of stay exceeding the 75th percentile of the length of stay of all living patients. The UPC was achieved when no perioperative mortality, no intraoperative complications, no postoperative surgical complications (for details, see **Table S1**), no reinterventions, no readmission, and no prolonged length of stay occurred, and was based on the composite outcome Textbook Outcome, which was previously described for elective AAA repairs[14].

Statistical methods

Baseline characteristics were stratified by EVAR and OSR and were compared between octogenarians and non-octogenarians. Categorical variables were compared between groups using Chi-square tests and Fisher exact tests, when appropriate. Continuous variables were compared using t-tests were used for normally distributed variables and Mann–Whitney U tests otherwise.

Differences in perioperative outcomes were examined with univariable logistic regression analyses with odds ratios including 95% confidence intervals. The associations between age ≥80 and mortality and major complications were examined for EVAR and OSR patients with multivariable logistic regression analyses using covariates and the fac-tor "age ≥ 80." In these analyses, patient characteristics based on both the V(p)-possum score[15] and the Hardman index[16] were included as covariates to adjust for confounding. Covariates used for analysis were gender, pulmonary comorbidity, cardiac comorbidity, abnormalities on preoperative electrocardiogram (ECG), preoperative renal dysfunction (creatine ≥190μmol/L), systolic blood pressure (per 10mmHg), loss of consciousness (Glasgow Coma Scale <12), anemia (hemoglobin <5.6mmol/L), aneurysm diameter (per 10mm), and location of the aneurysm (abdominal aortic or aortoiliac). Factors with a $p<0.10$ in univariable analysis were selected for multivariable logistic regression analysis.

Factors associated with mortality and major complications were examined for octogenarians who underwent EVAR and OSR using logistic regression analyses. For this analysis, covariates mentioned earlier and age (as a continuous variable) were included.

Factors with a p <0.10 in univariable analysis and factors considered clinically relevant (age and sex) were selected for multivariable logistic regression analysis.

Furthermore, we examined whether the proportion of applied surgical techniques and the proportion of octogenarians versus non-octogenarians decreased or increased linearly, using univariable logistic regression analyses. The impact of subgroups of complications, as registered in the DSAA, on mortality and median hospital-stay length of living patients was examined using descriptive statistics. For all analyses, statistical significance was defined as a p<0.05.

Missing data

The data of this subset from the DSAA contained variables with missing values (**Table S2**). If patients with any missing data had been excluded from the multivariable analyses, information of 237 octogenarians (62%) that received EVAR and 290 octogenarians (71%) that received OSR would have been lost. In all variables with missing data, 7.8% and 10.1% of the information was missing for EVAR and OSR, respectively. No patterns of missing data were found. Therefore, missing data were assumed to be missing at random for all covariates allowing to impute missing data[17].

In order to deal with the missing data, the method of multiple imputation using chained equations (MICE) was per-formed for both EVAR and OSR patients[18]. Outcomes, as perioperative mortality, were not imputed. To account for the variation in completing the data set with multiple imputation, 60 data sets were used for EVAR patients and 70 data sets were used for OSR patients (each with 20 iterations)[18]. Further details are shown in **Table S2**. After imputation, values that were imputed were compared with values that were observed using scatter plots and plots of the densities. For the multivariable logistic regression models, the results of the imputed data sets were combined to produce a final result using the Rubin's rules[19]. For comparison, multivariable logistic regression models using the subsets of complete cases were performed.

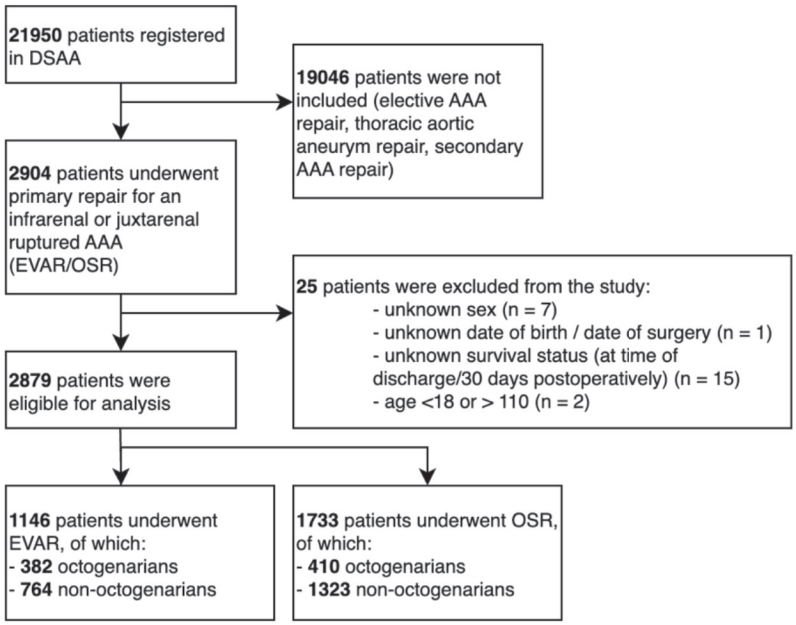
All analyses were performed using R version 3.6.1.

RESULTS

Between January 2013 and December 2018, 2904 patients from 61 hospitals who underwent primary repair for an infrarenal or juxtarenal rAAA were registered in the DSAA database. Of these patients, 2879 (99.1%) were eligible for analysis (**Figure 1**). In total, 792 octogenarians and 2087 non-octogenarians were included. Of all included patients, 1146 patients were treated with EVAR (382 octogenarians [33.3%] and 764 non-octogenarians

(66.7%)), while 1733 patients were treated with OSR (410 octogenarians [23.7%] and 1323 non-octogenarians (76.3%)). In the EVAR group, 34 EVAR procedures (3.0%) were followed by immediate conversion. Of all 792 octogenarians in this study, 382 (48.2%) received EVAR, while of all 2087 non-octogenarians, 764 (36.6%) received EVAR (p<0.001).

Figure 1: Flow diagram of included octogenarians and non-octogenarians following rAAA-repair. DSAA, Dutch Surgical Aneurysm Audit; EVAR, endovascular aneurysm repair; OSR, open surgical repair; rAAA, ruptured abdominal aortic aneurysm.



Patient characteristics, aneurysm morphology, and operative data

Original data and percentages of imputed data of patient characteristics, aneurysm morphology, and operative data, are shown in **Table 1**. Octogenarians were more often female compared to non-octogenarians, especially in the OSR group. Furthermore, octogenarians had more cardiac comorbidities, pulmonary comorbidities, or abnormalities on ECG, and presented with lower baseline hemoglobin and higher baseline creatinine levels. Octogenarians undergoing EVAR and OSR more often had a loss of consciousness (GCS <12) compared to non-octogenarians. From 2013 up to 2015, the exact location of the aneurysm relative to the renal arteries and information of referral patterns were not registered in the DSAA. From 2016-2018, 210/750 (28.0%) AAAs registered following OSR were juxtarenal AAAs (46 octogenarians, 164 non-octogenarians), and 7/638 (1.1%) AAAs registered following EVAR had a juxtarenal location. Most patients were presented at the

emergency department of the hospital in which they received treatment (465/638 (72.9%) following EVAR, 586/791 (74.1%) following OSR), while some patients were first presented in another hospital (60/638 (9.4%) following EVAR, 67/791 (8.5%) following OSR). It was not registered in the DSAA whether patients were suitable for EVAR. More procedural data (intraoperative blood loss, use of cell saver, intraoperative complications, admission to ICU, and length of ICU-stay) can be found in **Table S3**.

Table 1: Patient characteristics, aneurysm morphology and operative data for octogenarians versus non-octogenarians undergoing endovascular aneurysm repair (EVAR) and open surgical repair (OSR)

	EVAR			OSR		
	< 80	**≥ 80**	**P**	**< 80**	**≥ 80**	**P**
Number of patients	764	382		1323	410	
Sex: female	87 (11.4) [11.4]	60 (15.7) [15.7]	<0.001 [0.049]	175 (13.2) [13.2]	106 (25.9) [25.9]	<0.001 [<0.001]
Age, years	70.33 ± 6.69	84.52 ± 3.40	N.A. [N.A.]	70.46 ± 6.22	83.35 ± 2.93	N.A. [N.A.]
Preoperative cardiac comorbidity			<0.001 [<0.001]			<0.001 [0.053]
None	337 (50.3) [44.1]	119 (36.3) [31.2]		581 (52.7) [43.9]	151 (47.1) [36.8]	
Medication for hypertension, angina pectoris, diuretics, or digoxin	276 (40.9) [36.1]	166 (49.9) [43.5]		431 (39.1) [32.6]	137 (43.0) [33.4]	
Peripheral edema, coumarins, borderline cardiomyopathy	44 (6.8) [5.8]	39 (12.0) [10.2]		74 (6.7) [5.6]	26 (8.2) [6.3]	
Elevated central venous pressure, cardiomegaly	12 (2.0) [1.6]	6 (1.9) [1.6]		15 (1.5) [1.1]	5 (1.7) [1.2]	
Unknown / missing	95 (-)[12.4]	52 (-) [13.6]		222 (-) [16.8]	91 (-) [22.2]	
Preoperative pulmonary comorbidity			<0.001 [0.002]			<0.001 [0.006]
No dyspnea	504 (77.5) [66.0]	205 (67.7) [53.7]		810 (79.4) [61.2]	219 (72.5) [53.4]	
Dyspnea during exercise	105 (16.8) [13.7]	71 (24.3) [18.6]		159 (16.0) [12.0]	70 (23.4) [17.1]	
Invalidating dyspnea	19 (3.1) [2.5]	13 (4.6) [3.4]		25 (2.9) [1.9]	9 (3.1) [2.2]	
Dyspnea at rest, consolidation, fibrosis	16 (2.6) [2.1]	8 (3.3) [2.1]		17 (1.7) [1.3]	1 (1.0) [0.2]	
Unknown / missing	120 (-) [15.7]	85 (-) [22.3]		312 (-) [23.6]	111 (-) [27.1]	

Table 1: *Continued.*

	EVAR			OSR		
	< 80	**≥ 80**	**P**	**< 80**	**≥ 80**	**P**
Preoperative ECG			<0.001 [<0.001]			<0.001 [0.005]
No abnormalities	259 (52.2) [33.9]	91 (36.2) [23.8]		403 (51.3) [30.5]	104 (46.0) [25.4]	
Atrial fibrillation	29 (6.0) [3.8]	40 (17.4) [10.5]		47 (6.6) [3.6]	31 (13.7) [7.6]	
Ischemia	26 (5.3) [3.4]	12 (5.2) [3.1]		45 (6.8) [3.4]	11 (6.1) [2.7]	
Other deviating results	186 (36.5) [24.3]	104 (41.1) [27.2]		271 (35.2) [20.5]	83 (34.2) [20.2]	
Not performed / missing	264 (-) [34.6]	135 (-) [35.3]		557 (-) [42.1]	181 (-) [44.1]	
Preoperative haemoglobin, mmol/L	7.40 ± 1.40	6.90 ± 1.30	<0.001 [<0.001]	7.40 ± 1.39	6.85 ± 1.34	<0.001 [<0.001]
Preoperative haemoglobin, mmol/L			<0.001 [0.172]			<0.001 [0.017]
≥ 5.6	657 (89.1) [86.0]	315 (85.0) [82.5]		1136 (89.9) [85.9]	334 (84.8) [81.5]	
< 5.6	81 (10.9) [10.6]	55 (15.0) [14.4]		125 (10.1) [9.4]	59 (15.2) [14.4]	
Unknown / missing	26 (-) [3.4]	12 (-) [3.1]		62 (-) [4.7]	17 (-) [4.1]	
Preoperative creatinine, µmol/L	106 [85.75 - 129.25]	116.00 [92.00 – 146.00]	<0.001 [<0.001]	106.00 [86.00 – 131.00]	113.00 [90.00 – 138.00]	0.001 [<0.001]
Preoperative creatinine, µmol/L			<0.001 [0.459]			0.240 [0.629]
up to 189	655 (90.9) [85.7]	317 (88.5) [83.0]		1132 (93.3) [85.6]	358 (93.5) [87.3]	
≥ 190	65 (9.1) [8.5]	40 (11.5) [10.5]		79 (6.7) [6.0]	23 (6.5) [5.6]	
Unknown / missing	44 (-) [5.8]	25 (-) [6.5]		112 (-) [8.5]	29 (-) [7.1]	
Preoperative systolic blood pressure, mmHg	110 [89.00 – 135.0]	109 [85.50 – 130.00]	<0.001 [0.201]	106.00 [82.00 – 135.00]	100.00 [80.00 – 124.00]	<0.001 [0.007]
Unknown / missing	55 (-) [7.2]	31 (-) [8.1]		134 (-) [10.1]	44 [-] (10.7)	

Table 1: *Continued.*

	EVAR			OSR		
	< 80	**≥ 80**	**P**	**< 80**	**≥ 80**	**P**
Preoperative Glascow Coma Scale (GCS)			<0.001 [0.007]			0.001 [0.899]
Normal GCS (GCS ≥ 12)	671 (95.9) [87.8]	318 (91.3) [83.2]		1021 (87.3) [77.2]	314 (86.6) [76.6]	
Loss of consciousness (GCS < 12)	26 (4.1) [3.4]	29 (8.7) [7.6]		141 (12.7) [10.7]	47 (13.4) [11.5]	
Unknown / missing	67 (-) [8.8]	35 (-) [9.2]		161 (-) [12.2]	49 (-) [12.0]	
Location			<0.001 [0.578]			<0.001 [0.008]
Abdominal	718 (94.0) [94.0]	355 (91.3) [91.3]		1269 (95.9) [95.9]	404 (98.5) [98.5]	
Aortoiliac	46 (6.0) [6.0]	27 (7.1) [7.1]		54 (4.1) [4.1]	6 (1.5) [1.5]	
Diameter	76.37 ± 17.11	75.35 ± 17.40	<0.001 [0.362]	79.25 ± 17.25	79.03 ± 18.73	0.222 [0.833]
Unknown / missing	41 (-) [5.4]	33 (-) [8.6]		109 (-) [8.2]	35 (-) [8.5]	

Abbreviations: EVAR, endovascular aneurysm repair; GCS, Glasgow Coma Scale; OSR, open surgical repair. Data are presented as n (%) and for continuous variables as mean ± standard deviation (SD) or median with IQR. Values in parentheses "(%)" are percentages after multiple imputation (60 data sets for EVAR patients, 70 data sets for OSR patients). Values in square brackets "[%]" are percentages including missing data. p-values without parentheses are calculated from data after multiple imputation and p-values in square brackets "[%]" are calculated from data including missing data.

Perioperative mortality

The perioperative mortality rate of all octogenarians was 43.8% compared to 24.1% in all non-octogenarians (p<0.001). **Table 2** shows that octogenarians following EVAR had a mortality rate of 37.2% compared with 14.8% in non-octogenarians (OR=3.41, 95% CI=2.56–4.55). The mortality rate of octogenarians following OSR was 50.0% compared with 29.4% in non-octogenarians (OR=2.40, 95% CI=1.91–3.01).

Moreover, after adjustment for confounders, octogenarians had a significantly higher mortality rate compared with non-octogenarians following both EVAR and OSR (EVAR: aOR 2.87, 95%-CI 2.76-2.99, OSR: aOR 2.21, 95%-CI 2.15–2.28). We found similar results using the subsets with complete cases following both EVAR (aOR 2.93, 95%-CI 1.74–4.98, p<0.001) and OSR (aOR 2.20, 95%-CI 1.39–3.48).

Table 2: Perioperative outcomes of octogenarians versus non-octogenarians after both endovascular aneurysm repair (EVAR) and open surgical repair (OSR)

	EVAR					OSR				
	< 80 (ref.)	**≥ 80**	**OR (95% CI)[a]**	**OR (95% CI)[b]**	**aOR (95% CI)[c]**	**< 80 (ref.)**	**≥ 80**	**OR (95% CI)[a]**	**OR (95% CI)[b]**	**aOR (95% CI)[c]**
Number of patients	764	382				1323	410			
Perioperative mortality (intraoperative, 30-day and in-hospital)	113 (14.8)	142 (37.2)	3.41 (2.56 – 4.55)	3.41 (3.28 – 3.54)	2.87 (2.76 – 2.99)	389 (29.4)	205 (50.0)	2.40 (1.91 – 3.01)	2.40 (2.34 – 2.47)	2.21 (2.15 – 2.28)
Major complicationsd	242 (31.8)	211 (55.4)	2.66 (2.07 – 3.43)			652 (49.3)	279 (68.2)	2.21 (1.75 – 2.80)		
Textbook Outcome	378 (49.5)	117 (30.6)	0.45 (0.35 – 0.58)			431 (32.6)	85 (20.7)	0.54 (0.41 – 0.70)		
No perioperative mortality	651 (85.2)	240 (62.8)				934 (70.6)	205 (50.0)			
No complications during surgery	679 (88.9)	310 (81.2)				1078 (81.5)	308 (75.1)			
No surgical complications	591 (77.4)	262 (68.6)				782 (59.1)	239 (58.3)			
No reintervention	646 (84.6)	327 (85.6)				1024 (77.4)	322 (78.5)			
No readmission	650 (85.1)	334 (87.4)				1152 (87.1)	354 (86.3)			

Table 2: *Continued.*

	EVAR					OSR				
	< 80 (ref.)	**≥ 80**	**OR (95% CI)[a]**	**OR (95% CI)[b]**	**aOR (95% CI)[c]**	**< 80 (ref.)**	**≥ 80**	**OR (95% CI)[a]**	**OR (95% CI)[b]**	**aOR (95% CI)[c]**
No prolonged stay	585 (76.6)	289 (75.7)				1052 (79.5)	323 (78.8)			

Data are presented as n (%). Abbreviations: CI, confidence interval; EVAR, endovascular aneurysm repair; OR, odds ratio; OSR, open surgical repair. [a]OR using original data. [b]OR using original data completed by multiple imputation. [c]OR using original data completed by multiple imputation, adjusted for gender, age ≥ 80, cardiac comorbidity, pulmonary comorbidity, abnormalities on ECG, creatinine ≥ 190, systolic blood pressure (per 10 mmHg), haemoglobin <5.6, aortoiliac location, diameter (per 10 mm). [d]Major complication: post-operative death or a peri- or post-operative complication leading to a re-intervention or prolonged hospital stay (EVAR > 13 days, OSR > 24 days).

Major complications and uncomplicated perioperative course

Table 2 shows that octogenarians develop major complications more often, compared with non-octogenarians, following both EVAR (55.4% vs 31.8%, OR=2.66, 95% CI=2.07–3.43) and OSR (68.2% vs 49.3%, OR=2.21, 95% CI=1.75- 2.80). In octogenarians who underwent EVAR and developed major complications, cardiac complications were most common (28.9%), while abdominal complications were most common in octogenarians following OSR (28.7%). More details of cardiac and abdominal complications are provided in **Table S4**. Octogenarians with major complications that survived perioperatively had a median length of hospital stay of 18 days (IQR=15–31) following EVAR and 31 days (IQR=26–41) following OSR (**Table 3**). Furthermore, octogenarians had less often an UPC than non-octogenarians following both EVAR (30.6% vs 49.5%, OR=0.45, 95% CI=0.35–0.58) and OSR (20.7% vs 32.6% (OR=0.54, 95% CI=0.41–0.70).

Factors associated with perioperative mortality and major complications in octogenarians

Figure 2 and **Table S5** show patient-related risk factors that are associated with mortality in octogenarians. Following EVAR, an increase in age was associated with mortality, while female sex was associated with less mortality. Following OSR, both an increase in age and gender were not associated with mortality. Moreover, creatinine ≥190 was associated with less mortality, as well as hemoglobin <5.6. Loss of consciousness, abnormalities on ECG, and pulmonary and cardiac comorbidity were associated with mortality in both groups. Analysis on a subgroup of patients to assess patient-related risk factors including aneurysm location (infrarenal or juxtarenal) in octogenarians that underwent OSR showed that a juxtarenal aneurysm location was associated with less mortality compared with an infrarenal location (aOR=0.93, 95% CI=0.89–0.98).

Figure 2: Forest plots showing the results of multivariable logistic regression analyses for EVAR (A) and OSR (B) to assess the association of patient-related risk factors with perioperative mortality in octogenarians (using original data completed by multiple imputation). OR>1 indicates higher mortality. EVAR, endovascular aneurysm repair; OSR, open surgical repair

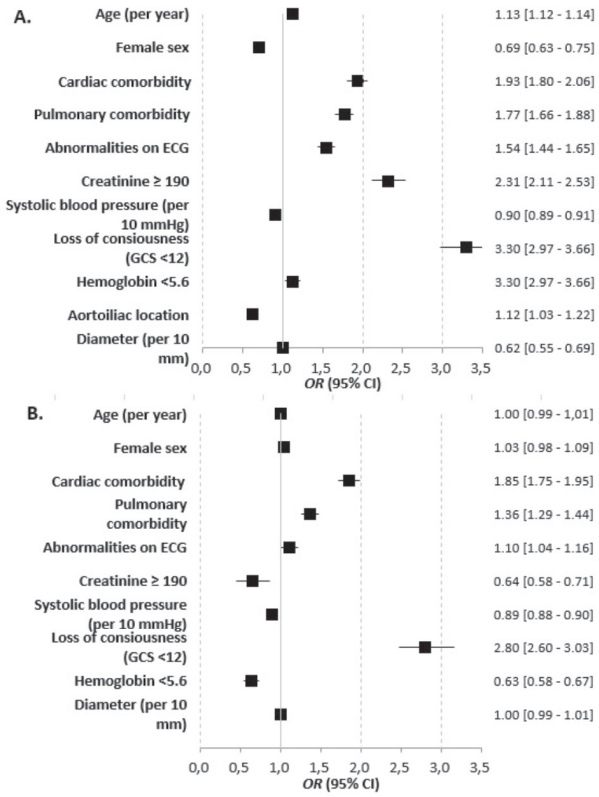
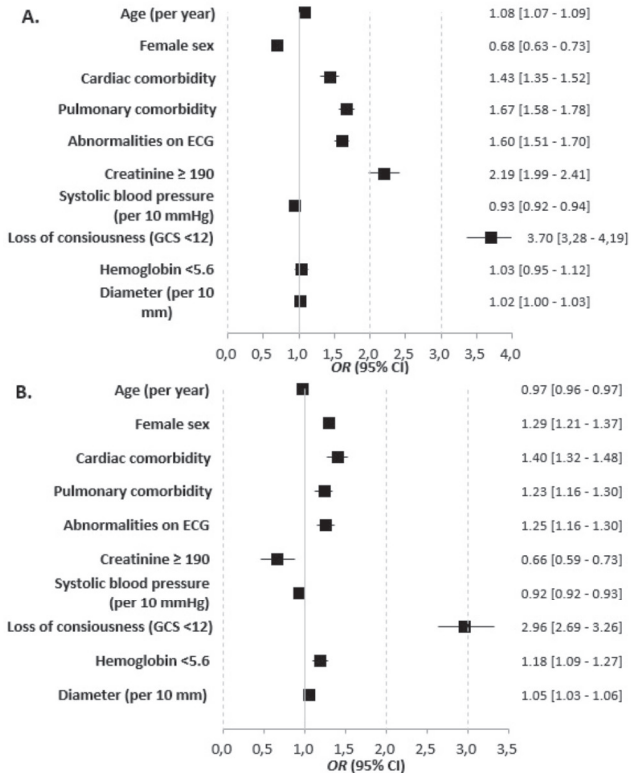


Figure 3 and **Table S6** show that in octogenarians, an increase in age was associated with more major complications following EVAR, while female sex was associated with fewer major complications. Following OSR, an increase in age was associated with fewer complications, while female sex was associated with more major complications. Abnormalities on ECG, pulmonary, cardiac comorbidity, and loss of consciousness were associated with major complications in both groups.

Figure 3: Forest plots showing the results of multivariable logistic regression analyses for EVAR (A) and OSR (B) to assess the association of patient-related risk factors with major complications in octogenarians (using original data completed by multiple imputation). OR>1 indicates more major complications. EVAR, endovascular aneurysm repair; OSR, open surgical repair



Time trends of applied surgical technique, number of hospitals, perioperative mortality and proportion of octogenarians

In all patients and in the subgroup of octogenarians, EVAR was increasingly applied compared with OSR (all patients: OR=1.15, 95% CI=1.10–1.21; octogenarians: OR=1.18, 95% CI=1.09–1.29). In all patients, the percentage of EVAR increased from 29% in 2013 to 47% in 2018, while in octogenarians, the percentage of EVAR increased from 39% in 2013 to 55% in 2018. In 2013, 36 hospitals performed EVAR in ruptured setting, while in 2018, 47 hospitals performed EVAR in ruptured setting. The number of hospitals that performed OSR in ruptured setting was 55 in 2013 and 52 in 2018. The perioperative mortality remained stable over the years in all patients, and in the subgroup of octogenarians (all patients: OR=0.98, 95% CI=0.94–1.03; octogenarians: OR=1.02, 95% CI=0.94–1.11), despite a higher proportion of patients treated with EVAR. During the study period, the proportion of octogenarians

versus non-octogenarians was stable in all patients (OR=0.98, 95% CI=0.93–1.03), OSR patients (OR=0.95, 95% CI=0.89–1.02), and EVAR patients (OR=0.97, 95% CI=0.91–1.05).

The impact of complications on perioperative outcomes in octogenarians

Table 3 shows that some octogenarians with specific com-plications have high perioperative mortality rates (EVAR: abdominal complication 81.1%, re-bleeding 93.8%; OSR: re-bleeding 82.1%, and renal complication: 64.9%). Moreover, an abdominal complication or an arterial occlusion following EVAR, and an abdominal or a neurologic complication following OSR have the highest median length of hospital-stay of living patients.

Table 3: Perioperative outcomes (perioperative mortality and length of hospital-stay of living patients) of all octogenarians, octogenarians with no postoperative complications, octogenarians with specific postoperative complications, octogenarians with major complications, stratified for EVAR and OSR.

	No. of octogenarians n (%)	**Perioperative mortality n (%)**	**Length of hospital-stay of living patients median [IQR]**
EVAR			
All octogenarians	382 (100)	142 (37.2)	9 [6-15]
Octogenarians with no postoperative complications	132 (34.6)	8 (6.1)	7 [5-10]
Octogenarians with one or more postoperative complications	249 (65.2)	133 (53.4)	13 [8-21]
Octogenarians with specific postoperative complications			
Abdominal	53 (13.9)	43 (81.1)	26.5 [18.75 – 33.50]
Cardiac	68 (17.8)	47 (69.1)	15 [6 – 18.5]
Pulmonary	73 (19.1)	27 (37.0)	15 [11 – 27.5]
Arterial occlusion	22 (5.8)	13 (59.1)	25 [18-32]
Reconstruction	20 (5.2)	8 (40.0)	6.50 [4.75 – 10.50]
Re-bleeding	16 (4.2)	15 (93.8)	NA
Wound	8 (2.1)	1 (12.5)	8 [7 – 13.5]
Neurologic	28 (7.3)	12 (42.9)	16.5 [8.75 – 31.5]
Renal	42 (11.0)	28 (66.7)	17 [13-21]
Other	73 (19.1)	41 (56.2)	15 [9 – 21]

Table 3: *Continued.*

	No. of octogenarians n (%)	Perioperative mortality n (%)	Length of hospital-stay of living patients median [IQR]
Octogenarians no major complications	170 (44.5)	0 (0.0)	8 [5-10]
Octogenarians with major complications	211 (55.2)	142 (67.3)	18 [15-31]
OSR			
All octogenarians	410 (100)	205 (50.0)	19 [12-28]
Octogenarians with no postoperative complications	90 (22.0)	26 (28.9)	11.5 [7.25-16.75]
Octogenarians with one or more postoperative complications	319 (77.8)	178 (55.8)	21 [15.5-32]
Octogenarians with specific postoperative complications			
Abdominal	84 (20.5)	54 (64.3)	31.5 [19 – 39.75]
Cardiac	82 (20.0)	49 (59.8)	21 [17 – 30]
Pulmonary	85 (20.7)	28 (32.9)	22.5 [16.75 – 37.25]
Arterial occlusion	34 (8.3)	19 (55.9)	30 [22 – 40]
Reconstruction	3 (0.7)	3 (100.0)	NA
Re-bleeding	28 (6.8)	23 (82.1)	17 [16 – 19]
Wound	10 (2.4)	3 (30.0)	25 [20 – 30.75]
Neurologic	40 (9.8)	12 (30)	31 [20.25 – 37.5]
Renal	74 (18.0)	48 (64.9)	27 [17 – 38]
Other	106 (25.9)	57 (53.8)	21 [16 – 36]
Octogenarians with no major complications	130 (31.7)	0 (0.0)	14 [9 – 19]
Octogenarians with major complications	279 (68.0)	205 (73.5)	31 [26 – 41]

Abbreviations: EVAR, endovascular aneurysm repair; OSR, open surgical repair. Data are presented as n (%) and for continuous variables as median with IQR. Patients can suffer from more than 1 postoperative complication simultaneously and thus can fall into more than 1 postoperative complication category. Thus, the perioperative outcomes can also be caused by another complication than by the complication of the reported group.

DISCUSSION

This study showed that perioperative mortality rates of octogenarians following both EVAR and OSR were high (37.2% after EVAR; 50.0% after OSR) and significantly unfavorable compared with younger patients, similar to the existing literature[24]. However, a substantial proportion of the octogenarians had an uneventful recovery after surgery (1/3 after EVAR and 1/5 after OSR). The preoperative risk factors pulmonary or cardiac comorbidity and loss of consciousness were associated with mortality and major com-plications in octogenarians following both EVAR and OSR for rAAAs, while an increased age was not associated with mortality following OSR, and female sex was associated with less mortality following EVAR.

The recently published ESVS guidelines state that acceptable results of treatment for rAAA can be achieved in patients aged >80 years[20]. A recent meta-analysis regarding the outcome of rAAA-repair in octogenarians, which included besides a study from the nationwide Swedish Vascular Registry, studies from expert centers, (non-nationwide) vascular registries, an administrative database, and an insurance database, found pooled 30-day mortality rates of 27% (95% CI=18–38) following EVAR and 52% (95% CI=44–60)[5] following OSR. Interestingly, our perioperative mortality rates following OSR were similar compared with the rates reported in the meta-analysis, while our perioperative mortality rates following EVAR were increased. In our study, "age ≥ 80" was associated with mortality following both EVAR (aOR=2.87) and OSR (aOR=2.21), while a recent nationwide study using administrative data from Japan reported that "age ≥ 80" was not associated with mortality in patients that underwent EVAR (aOR=1.13, 95% CI=0.77–1.66) and described mortality rates of 24.7% in octogenarians and 23.5% in younger patients following EVAR[21]. Furthermore, 55% of the octogenarians did not undergo OSR or EVAR in this Japanese study. In contrast, a recent Dutch multicentre cohort study reported a turndown rate for rAAA treatment of only 29.9%[22], suggesting that the Japanese octogenarians were more strictly selected. Therefore, although we could not report the turndown rate of our nationwide cohort, we hypothesize that the increased perioperative mortality rates after EVAR in our study may suggest that relatively many high-risk octogenarians in the Netherlands underwent EVAR for rAAAs as a last resort.

Moreover, we described major complications and UPC rates in octogenarians compared with non-octogenarians. As expected, major complication rates were higher, and UPC rates were lower in octogenarians compared with non-octogenarians. The UPC was based on Textbook Outcome, which is usually used for reporting the Quality of Care in an elective setting of abdominal aneurysm treatment[14]. We chose to describe UPC rates to clarify the proportion of octogenarians that achieves a desirable outcome following

rAAA-repair, which was not described before. As is shown in **Table 2**, it is important to note that about 1/3 of octogenarians with rAAA undergoing EVAR and 1/5 undergoing ORS had a completely uneventful recovery, arguing that the current selection process for surgery is quite acceptable. Although we did not have information on turndown rates, better outcomes of octogenarians could probably be achieved with stricter selection for treatment. However, in our opinion, our UPC results suggest that turning down patients solely based on their age should be avoided since some octogenarians do have acceptable results. Besides, it is described that a substantial proportion of the octogenarians that survive rAAA repair (>80%) returned to their home after rehabilitation[22]. Moreover, it is hard to predict patients that definitely will perish after surgery, and it remains questionable whether current prediction models are sufficient to do this in this patient category reliably[8].

Without an almost perfect prediction, patients will not be withheld from treatment using a scoring system[7]. Although current prediction models, using a cohort with patients up to 2015, could not reliably predict mortality in preoperative setting with area under the receiver operating characteristic curves (AUCs) varying from 0.59 to 0.72[7], we did not develop a new predictive model since our database does not include patients turned down for surgery and lacks morpho-logical or anatomical details. In 2016, the Dutch Aneurysm Score (DAS) was developed, which reported an externally validated AUC of 0.77[9]. However, we could not externally validate the DAS using our nationwide cohort since the DSAA does not include information on cardiopulmonary resuscitation. Therefore, our study described preoperative patient risk factors associated with perioperative mortality and major complications in octogenarians, reflecting their current real-life treatment practice. Loss of consciousness was highly associated with mortality and major complications following both EVAR and OSR, suggesting that few octogenarians with loss of consciousness survive rAAA-repair. Interestingly, we found that females had lower mortality following EVAR, but not following OSR. Usually, higher 30-day mortality rates in women following rAAA-repair have been reported[23]. Therefore, our results could suggest that female octogenarians potentially were strictly selected for EVAR. Moreover, we found that in both treatment groups, lower systolic blood pressure was associated with less mortality, which was not in line with another study that reported on predictors of mortality after repair of rAAAs[24]. This somewhat contradictory result may be due to higher turndown rates for octogenarians with low systolic blood pressure. In octogenarians, increased age was associated with mortality following EVAR, but was not associated with mortality following OSR. Moreover, elevated preoperative creatinine and decreased preoperative hemoglobin, a predictor for mortality in the DAS[9], were associated with less mortality in octogenarians following OSR. In addition, a juxtarenal aneurysm location was associated with less mortality compared with an infrarenal location following OSR, which was in contrast with the results of the IMPROVE trial in which a short aneurysm neck of rAAAs was associated with mortality following

OSR[25]. We hypothesize that all these counterintuitive findings could be a reflection of selection bias and that octogenarians with elevated preoperative creatinine, decreased preoperative hemoglobin, or a juxtarenal aneurysm who received OSR were more strictly selected for surgery, resulting in a selection of relatively fit octogenarians with low general frailty. For Dutch vascular surgeons, this information reflects the current treatment practice of octogenarians. This information could serve as a first step to evaluate the selection of octogenarians for surgery. However, it will be essential to have additional information on octogenarians who were not selected for surgery to assess the entire selection process of octogenarians for surgery. Moreover, survival after aneurysm repair is not the sole parameter of clinical success and should be complemented by patient-centered outcomes such as health-related quality of life and postoperative living situation[22].

This study shows that octogenarians underwent EVAR more frequently than non-octogenarians (48.2% vs 36.6%) and that EVAR was increasingly applied during the study period in both octogenarians and non-octogenarians. Our study showed that the endovascular treatment of rAAAs in all patients increased from 29% in 2013 to 47% in 2018. This percentage has increased over the years since physicians became more familiar with the EVAR technique and a stock of stent-grafts became more widely available[26]. However, the actual clinical decision in octogenarians regarding the surgical procedure when both EVAR and OSR are suitable could be dependent on local or regional setting as well[27]. Surprisingly, our study showed that despite the increased use of EVAR, the perioperative mortality rates of octogenarians and all patients were stable over the years, which was in contrast with previous studies[28]. A possible explanation for these stable mortality rates could be that due to the increased application of EVAR, relatively more frail patients have received treatment for an rAAA during the study period, which could have influenced perioperative mortality rates[29]. Although the proportion of octogenarians did not change over the years in our study, we could not objectify an increasing frailty rate with the data registered in the DSAA. The decreasing numbers of OSR in ruptured setting should have our attention in upcoming years, as a study that included data from 11 vascular registries reported lower in-hospital mortality rates in hospitals with high volumes of OSR in ruptured setting[30].

For a correct interpretation of our findings, it is important to note that the results of OSR patients are not directly comparable with the results of EVAR patients since the characteristics of patients included in both groups were not similar. Octogenarians that underwent OSR had more often loss of consciousness and were more frequently female, compared with the octogenarians that underwent EVAR. It was described that in intact setting, only 34% of the female were morphologically suitable for EVAR within the instructions for use (IFU) due to short and angulated proximal aneurysm necks or

unsuitable iliac arteries (access vessels) compared with 54% in male[31], which could clarify our high proportion of females undergoing OSR. Moreover, in our study, the OSR group included several juxtarenal AAAs, while only a few juxtarenal AAAs were treated with EVAR, which was probably due to a lack of suitable endovascular treatment options for juxtarenal AAAs. Future solutions with physician-modified grafts, chimney technique or off-the-shelf solutions might change these numbers[32–34]. Besides the differences in measured characteristics, which could be a reflection of selection bias and could influence outcomes, unmeasured characteristics were probably also different between the two groups. Therefore, we refrained from a direct comparison between both groups (EVAR vs OSR) and propensity score matching.

A limitation of this study is that our data was retrieved from a nationwide quality registry that contains limited data. Consequently, we could not correct for all potential confounders in our multivariable analyses—for example, as mentioned before, we could not correct for frailty since frailty was not registered in our registry. Frailty is described as an independent predictor of in-hospital mortality in emergency general surgery[29] and could influence perioperative mortality rates. Moreover, the variable aneurysm location (infrarenal or juxtarenal) was not available in the entire study period. Therefore, we could only perform an analyses on a subgroup of patients to assess the influence of aneurysm location on perioperative mortality. Finally, no information is available of patients not eligible for surgical repair since only patients who were stable enough to reach the hospital and underwent surgery were included. Therefore, our findings could be a reflection of selection bias and we could not report on all patients with rAAAs. An important strength of our study is the mandatory nationwide setup.

CONCLUSION

This nationwide study provides us with valuable real-life contemporary data on outcomes after repair of rAAA in octogenarians that could serve as a first step to evaluate the selection of octogenarians for surgery. Although aneurysm repair is associated with high mortality in this patient cate-gory, especially after OSR, it is important to realize that a substantial proportion of these patients (1/3 after EVAR and 1/5 after OSR) had an uneventful recovery. Known preoperative risk factors do influence these outcomes and reflect current treatment practice.

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Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: J.J.W.: consultant for Cordis/Cardinal Health, former con-sultant for Baxter. J.v.H.: is or has been consultant for Cook Medical, Gore Medical, Medtronic, Philips Medical Systems and Terumo Aortic. H.V.: consultant for Medtronic, WL Gore, Terumo, Endologix, Arsenal AAA, and Philips. Speakers bureau: Abbott.

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REFERENCES

1 Kontopodis N, Galanakis N, Antoniou SA, Tsetis D, Ioannou C v., Veith FJ, et al. Meta-Analysis and Meta-Regression Analysis of Outcomes of Endovascular and Open Repair for Ruptured Abdominal Aortic Aneurysm. *European Journal of Vascular and Endovascular Surgery* 2020;**59**(3):399–410. Doi: 10.1016/j.ejvs.2019.12.023.

2 Han Y, Zhang S, Zhang J, Ji C, Eckstein HH. Outcomes of Endovascular Abdominal Aortic Aneurysm Repair in Octogenarians: Meta-analysis and Systematic Review. *European Journal of Vascular and Endovascular Surgery* 2017;**54**(4):454–63. Doi: 10.1016/j.ejvs.2017.06.027.

3 Locham S, Lee R, Nejim B, Dakour Aridi H, Malas M. Mortality after endovascular versus open repair of abdominal aortic aneurysm in the elderly. *Journal of Surgical Research* 2017;**215**(February):153–9. Doi: 10.1016/j.jss.2017.03.061.

4 Biancari F, Mazziotti MA, Paone R, Laukontaus S, Venermo M, Lepäntalo M. Outcome after Open Repair of Ruptured Abdominal Aortic Aneurysm in Patients >80 Years Old: A Systematic Review and Meta-analysis. *World J Surg* 2011;**35**(7):1662–70. Doi: 10.1007/s00268-011-1103-x.

5 Roosendaal LC, Kramer GM, Wiersema AM, Wisselink W, Jongkind V. Outcome of Ruptured Abdominal Aortic Aneurysm Repair in Octogenarians: A Systematic Review and Meta-Analysis. *European Journal of Vascular and Endovascular Surgery* 2019;(xxxx). Doi: 10.1016/j.ejvs.2019.07.014.

6 Mani K, Björck M, Lundkvist J, Wanhainen A. Improved long-term survival after abdominal aortic aneurysm repair. *Circulation* 2009;**120**(3):201–11. Doi: 10.1161/CIRCULATIONAHA.108.832774.

7 Vos CG, de Vries JPPM, Werson DAB, van Dongen EPA, Schreve MA, Ünlü Ç. Evaluation of five different aneurysm scoring systems to predict mortality in ruptured abdominal aortic aneurysm patients. *J Vasc Surg* 2016;**64**(6):1609–16. Doi: 10.1016/j.jvs.2016.05.099.

8 Thompson PC, Dalman RL, Harris EJ, Chandra V, Lee JT, Mell MW. Predictive models for mortality after ruptured aortic aneurysm repair do not predict futility and are not useful for clinical decision making. *J Vasc Surg* 2016;**64**(6):1617–22. Doi: 10.1016/j.jvs.2016.07.121.

9 von Meijenfeldt GCI, van Beek SC, Bastos Gonçalves F, Verhagen HJM, Zeebregts CJ, Vahl AC, et al. Development and External Validation of a Model Predicting Death After Surgery in Patients With a Ruptured Abdominal Aortic Aneurysm: The Dutch Aneurysm Score. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(2):168–74. Doi: 10.1016/j.ejvs.2016.10.024.

10 Dutch Institute for Clinical Auditing. Eindrapport dataverificatie DSAA. https://dica.nl/media/660/Eindrapport_dataverificatie_DSAA_2016.pdf. 05/11/2020.

11 van der Werf LR, Voeten SC, van Loe CMM, Karthaus EG, Wouters MWJM, Prins HA. Data verification of nationwide clinical quality registries. *BJS Open* 2019;**3**(6):857–64. Doi: 10.1002/bjs5.50209.

12 STROBE Statement- checklist of items that should be included in reports of observational studies. https://www.strobe-statement.org/fileadmin/Strobe/uploads/checklists/STROBE_checklist_v4_combined.pdf. 08/11/2020.

13 Lijftogt N, Karthaus EG, Vahl A, van Zwet EW, van der Willik EM, Tollenaar RAEM, et al. Failure to Rescue – a Closer Look at Mortality Rates Has No Added Value for Hospital Comparisons but Is Useful for Team Quality Assessment in Abdominal Aortic Aneurysm Surgery in The Netherlands. *European Journal of Vascular and Endovascular Surgery* 2018;**56**(5):652–61. Doi: 10.1016/j.ejvs.2018.06.062.

14 Karthaus EG, Lijftogt N, Busweiler LAD, Elsman BHP, Wouters MWJM, Vahl AC, et al. Textbook Outcome: A Composite Measure for Quality of Elective Aneurysm Surgery. *Ann Surg* 2017;**266**(5):898–904. Doi: 10.1097/SLA.0000000000002388.
15 Copeland GP, Jones D, Walters M. POSSUM: A scoring system for surgical audit. *British Journal of Surgery* 1991;**78**(3):355–60. Doi: 10.1002/bjs.1800780327.
16 Acosta S, Ögren M, Bergqvist D, Lindblad B, Dencker M, Zdanowski Z. The Hardman index in patients operated on for ruptured abdominal aortic aneurysm: a systematic review. *J Vasc Surg* 2006;**44**(5):949–54. Doi: 10.1016/j.jvs.2006.07.041.
17 Sterne JAC, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, et al. Multiple imputation for missing data in epidemiological and clinical research: Potential and pitfalls. *BMJ (Online)* 2009;**339**(7713):157–60. Doi: 10.1136/bmj.b2393.
18 White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med* 2011;**30**(4):377–99. Doi: 10.1002/sim.4067.
19 Rubin DB. Multiple Imputation for Nonresponse in Surveys 1987. Doi: 10.2307/3172772.
20 Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(1):8–93. Doi: 10.1016/j.ejvs.2018.09.020.
21 Yamaguchi T, Nakai M, Sumita Y, Nishimura K, Nagai T, Anzai T, et al. Impact of Endovascular Repair on the Outcomes of Octogenarians with Ruptured Abdominal Aortic Aneurysms: A Nationwide Japanese Study. *European Journal of Vascular and Endovascular Surgery* 2020;**59**(2):219–25. Doi: 10.1016/j.ejvs.2019.07.016.
22 Roosendaal LC, Wiersema AM, Yeung KK, Ünlü Ç, Metz R, Wisselink W, et al. Survival and Living Situation After Ruptured Abdominal Aneurysm Repair in Octogenarians. *European Journal of Vascular and Endovascular Surgery* 2021;**61**:375–81. Doi: 10.1016/j.ejvs.2020.11.023.
23 Zommorodi S, Bottai M, Hultgren R. Sex differences in repair rates and outcomes of patients with ruptured abdominal aortic aneurysm. *British Journal of Surgery* 2019;**106**(11):1480–7. Doi: 10.1002/bjs.11258.
24 Garland BT, Danaher PJ, Desikan S, Tran NT, Quiroga E, Singh N, et al. Preoperative risk score for the prediction of mortality after repair of ruptured abdominal aortic aneurysms. *J Vasc Surg* 2018;**68**(4):991–7. Doi: 10.1016/j.jvs.2017.12.075.
25 Powell JT, Sweeting MJ, Thompson MM, Hinchliffe RJ, Ashleigh R, Bell R, et al. The effect of aorticmorphology on peri-operative mortality of ruptured abdominal aortic aneurysm. *Eur Heart J* 2015;**36**(21):1328–34. Doi: 10.1093/eurheartj/ehu521.
26 Melillo AM, Trani JL, Gaughan JP, Carpenter JP, Lombardi J V. Assessing trends, morbidity, and mortality in ruptured abdominal aortic aneurysm repair with 9 years of data from the National Surgical Quality Improvement Program. *J Vasc Surg* 2020;**71**(2):423–31. Doi: 10.1016/j.jvs.2019.04.462.
27 Karthaus EG, Lijftogt N, Vahl A, van der Willik EM, Amodio S, van Zwet EW, et al. Patients with a Ruptured Abdominal Aortic Aneurysm Are Better Informed in Hospitals with an "EVAR-preferred" Strategy: An Instrumental Variable Analysis of the Dutch Surgical Aneurysm Audit. *Ann Vasc Surg* 2020;**69**:332–44. Doi: 10.1016/j.avsg.2020.06.015.
28 Dias-Neto M, Castro-Ferreira R, Mani K, Freitas A, Leite-Moreira A, Sampaio SM. Nationwide Analysis of Ruptured Abdominal Aortic Aneurysm in Portugal (2000–2015). *European Journal of Vascular and Endovascular Surgery* 2020;**60**(1):27–35. Doi: 10.1016/j.ejvs.2020.02.024.
29 Joseph B, Zangbar B, Pandit V, Fain M, Mohler MJ, Kulvatunyou N, et al. Emergency General Surgery in the Elderly: Too Old or Too Frail? Presented orally at the Surgical Forum of the American College of Surgeons 100th Annual Clinical Congress, San Francisco, CA, October 2014. *J Am Coll Surg* 2016;**222**(5):805–13. Doi: 10.1016/j.jamcollsurg.2016.01.063.

30 Scali ST, Beck AW, Sedrakyan A, Mao J, Venermo M, Faizer R, et al. Hospital Volume Association With Abdominal Aortic Aneurysm Repair Mortality: Analysis of the International Consortium of Vascular Registries. *Circulation* 2019;**140**(15):1285–7. Doi: 10.1161/CIRCULATIONAHA.119.042504.

31 Ulug P, Sweeting MJ, von Allmen RS, Thompson SG, Powell JT, Ulug P, et al. Morphological suitability for endovascular repair, non-intervention rates, and operative mortality in women and men assessed for intact abdominal aortic aneurysm repair: systematic reviews with meta-analysis. *The Lancet* 2017;**389**(10088):2482–91. Doi: 10.1016/S0140-6736(17)30639-6.

32 Juszczak MT, Vezzosi M, Khan M, Mascaro J, Claridge M, Adam D. Endovascular repair of acute juxtarenal and thoracoabdominal aortic aneurysms with surgeon-modified fenestrated endografts. *J Vasc Surg* 2020;**72**(2):435–44. Doi: 10.1016/j.jvs.2019.10.056.

33 Dias N V., Jabr A Bin, Sveinsson M, Björses K, Malina M, Kristmundsson T. Impact of renal chimney grafts on anatomical suitability for endovascular repair in ruptured abdominal aortic aneurysm. *Journal of Endovascular Therapy* 2015;**22**(1):105–9. Doi: 10.1177/1526602814564384.

34 Kristmundsson T, Sveinsson M, Björses K, Törnqvist P, Dias N. Suitability of the Zenith p-branch standard fenestrated endovascular graft for treatment of ruptured abdominal aortic aneurysms. *Journal of Endovascular Therapy* 2015;**22**(5):760–4. Doi: 10.1177/1526602815601096.

SUPPLEMENTARY MATERIALS

Table S1

The following complications were defined as a surgical complications:

- any abdominal complication (abdominal abscess, abdominal sepsis, ileus, spleen injury, bowel ischemia, bowel injury, stoma placement, other abdominal complications)
- any arterial occlusion ((major) amputation, renal artery arterial occlusion, other arterial occlusion (including trash foot))
- any prosthesis-/reconstruction related complication (prosthesis infection, prosthesis migration, other prosthesis-/reconstruction related complications)
- any wound complication (deep wound infection, fascia dehiscence, other wound complications)
- any renal complication (renal insufficiency (without hemodialysis or requiring hemodialysis))
- any rebleeding
- pulmonary complication: pneumothorax
- neurologic complication: paraplegia

Table S2

Variables used for multiple imputation, including the number of records for which each variable is missing and the imputation method that was used; for binary data logistic regression was used and for unordered categorical data polytomous logistic regression (polyreg) was used. Bayesian linear regression (norm) was used for normal-distributed numeric data (norm), and data predictive mean matching (pmm) was used for non-normal distributed numeric data[1].

	Missing - EVAR (n, (%)	Missing - OSR (n, %)	Imputation method
Cardiac history	147 (12.8)	313 (18.1)	Polyreg*
Pulmonary history	205 (17.9)	423 (24.4)	Polyreg*
ECG abnormalities	399 (34.8)	738 (42.6)	Polyreg*
Hemoglobin	38 (3.3)	79 (4.6)	Norm**
Creatinine	69 (6.0)	141 (8.1)	Pmm***
GCS	102 (8.9)	210 (12.1)	Polyreg*

1 https://www.rdocumentation.org/packages/mice/versions/3.10.0/topics/mice

Table S2 *(continued)*

	Missing - EVAR (n, (%)	Missing - OSR (n, %)	Imputation method
Systolic blood pressure	86 (7.5)	178 (10.3)	Pmm***
Diameter of the aneurysm	74 (6.4)	144 (8.3)	Norm**
Perioperative complications	10 (0.9)	7 (0.4)	Polyreg*
Length of stay at ICU	12 (1.0)	29 (1.7)	Pmm***
Length of hospital stay	27 (2.4)	36 (2.1)	Pmm***
Reinterventions	3 (0.3)	5 (0.3)	Logreg****
Readmission	77 (6.7)	145 (8.4)	Logreg****
Complications	2 (0.2)	3 (0.2)	Logreg****
Also included as complete data: year of surgery, age, gender, location of the aneurysm, survival status and procedure			

** Polytomous logistic regression ** Bayesian linear regression *** Predictive mean matching **** Logistic regression*

Datasets of EVAR and OSR patients were separately imputed. All variables were included in the multiple imputation as predictor, except the variables 'Length of stay at ICU' and 'Length of hospital stay' that were not included as predictor due to strong correlations.

In the complete dataset, 451 (39.4%) EVAR patients and 527 (30.4%) OSR patients had no missing data.

Table S3

	EVAR 80- (n = 764)	EVAR 80+ (n = 382)	P-value
Intraoperative blood loss			0.206
0-100 ml	208 (27.2)	82 (21.5)	
101-500 ml	271 (35.5)	146 (38.2)	
501-999 ml	28 (3.7)	18 (4.7)	
>1000 ml	58 (7.6)	37 (9.7)	
NA/missing	199 (26.0)	99 (25.9)	
Use of cell saver*	37/417 (8.9)	24/221 (10.9)	0.502
Intraoperative complications			<0.001
No	679 (88.9)	310 (81.2)	

Table S3 *(continued)*

	EVAR 80- (n = 764)	EVAR 80+ (n = 382)	P-value
Cardiopulmonary resuscitation / myocardial infarction	17 (2.2)	28 (7.3)	
Other	57 (7.5)	40 (10.5)	
Death	4 (0.5)	1 (0.3)	
NA/missing	7 (0.9)	3 (0.8)	
Admission to ICU			0.932
No	96 (12.6)	51 (13.4)	
Yes	660 (86.4)	327 (85.6)	
NA/missing	8 (1.0)	4 (1.0)	
Length of ICU-stay (median [IQR])	1 [1, 3]	1 [1, 3]	0.664

** data from 2016 is shown*

	OSR 80- (n = 1323)	OSR 80+ (n = 410)	P-value
Intraoperative blood loss			0.025
0-100 ml	5 (0.4)	5 (1.2)	
101-500 ml	45 (3.4)	18 (4.4)	
501-999 ml	92 (7.0)	31 (7.6)	
>1000 ml	899 (68.0)	248 (60.5)	
NA/missing	282 (21.3)	108 (26.3)	
Use of cell saver*			0.062
No	120/613 (19.6)	48/178 (27.0)	
Yes	492/613 (80.3)	130/178 (73.0)	
NA/missing	1/613 (0.2)	0/613 (0.0)	
Intraoperative complications			0.005
No	1078 (81.5)	308 (75.1)	
Cardiopulmonary resuscitation / myocardial infarction	82 (6.2)	34 (8.3)	
Other	154 (11.6)	59 (14.4)	
Death	4 (0.3)	7 (1.7)	
NA/missing	5 (0.4)	2 (0.5)	
Admission to ICU			0.932
No	68 (5.1)	46 (11.2)	
Yes	1231 (93.0)	359 (87.6)	
NA/missing	24 (1.8)	5 (1.2)	
Length of ICU-stay (median [IQR])	3 [2, 8]	3 [1, 8]	0.664

** data from 2016 is shown*

	EVAR 80+, patients who survived perioperatively (n = 240)	EVAR 80+, patients who died perioperatively (n = 142)	P-value
Intraoperative blood loss			0.001
0-100 ml	57 (23.8)	25 (17.6)	
101-500 ml	102 (42.5)	44 (31.0)	
501-999 ml	11 (4.6)	7 (4.9)	
>1000 ml	13 (5.4)	24 (16.9)	
NA/missing	57 (23.8)	42 (29.6)	
Use of cell saver*	13/135 (9.6)	11/86 (12.8)	0.607
Intraoperative complications			<0.001
No	224 (93.3)	86 (60.6)	
Cardiopulmonary resuscitation / myocardial infarction	2 (0.8)	26 (18.3)	
Other	11 (4.6)	29 (29.4)	
Death	0 (0.0)	1 (0.7)	
NA/missing	3 (1.2)	0 (0.0)	
Admission to ICU			
No	28 (11.7)	23 (16.2)	0.100
Yes	221 (87.9)	116 (81.7)	
NA/missing	1 (0.4)	3 (2.1)	
Length of ICU-stay (median [IQR])	1 [1, 3]	1 [1, 3]	0.939

** data from 2016 is shown*

	OSR 80+, patients who survived perioperatively (n = 205)	OSR 80+, patients who died perioperatively (n = 205)	P-value
Intraoperative blood loss			0.054
0-100 ml	2 (1.0)	3 (1.5)	
101-500 ml	10 (4.9)	8 (3.9)	
501-999 ml	22 (10.7)	9 (4.4)	
>1000 ml	126 (61.5)	122 (59.5)	
NA/missing	45 (22.0)	63 (30.7)	
Use of cell saver*	57/80 (71.2)	73/98 (74.5)	0.753
Intraoperative complications			< 0.001
No	178 (86.8)	130 (63.4)	
Cardiopulmonary resuscitation / myocardial infarction	1 (0.5)	33 (16.1)	
Other	25 (12.2)	34 (16.6)	
Death	0 (0.0)	7 (3.4)	
NA/missing	1 (0.5)	1 (0.5)	
Admission to ICU			< 0.001
No	6 (2.9)	40 (19.5)**	
Yes	197 (96.1)	162 (79.0)	
NA/missing	2 (1.0)	3 (1.5)	
Length of ICU-stay (median [IQR])	5 [3, 11]	1 [1, 5]	<0.001

** data from 2016 is shown. ** Of these patients: 21 patients received cardiopulmonary resuscitation or had a myocardial infarction during surgery, and 7 patients died during surgery.*

Table S4

Overview of complications included in cardiac and abdominal complications:

Cardiac complications: myocardial infarction, heart failure, cardiac rhythm disturbances, other cardiac complications

Abdominal complications: abdominal abscess, abdominal sepsis, ileus, spleen injury, bowel ischemia, bowel injury, stoma placement, other abdominal complications.

Table S5

Univariable and multivariable logistic regression analyses using original data completed by multiple imputation for EVAR and OSR to assess the association of patient-related risk factors with perioperative mortality in octogenarians

EVAR	**Univariable analysis**			**Multivariable analysis**		
Factor	**OR**	**95%-CI**	**P-value**	**aOR**	**95%-CI**	**P-value**
Age (per year)	1.12	1.11 – 1.13	<0.001	1.13	1.12 – 1.14	<0.001
Female sex	0.75	0.69 – 0.81	<0.001	0.69	0.63 – 0.75	<0.001
Cardiac comorbidity	2.16	2.03 – 2.29	<0.001	1.93	1.80 – 2.06	<0.001
Pulmonary comorbidity	2.12	2.00 – 2.24	<0.001	1.77	1.66 – 1.88	<0.001
Abnormalities on ECG	2.22	2.09 – 2.35	<0.001	1.54	1.44 – 1.65	<0.001
Creatinine ≥ 190	2.51	2.32 – 2.73	<0.001	2.31	2.11 – 2.53	<0.001
Systolic blood pressure (per 10 mmHg)	0.89	0.88 – 0.90	<0.001	0.90	0.89 – 0.91	<0.001
GCS <12	3.89	3.53 – 4.29	<0.001	3.30	2.97 – 3.66	<0.001
Hemoglobin <5.6	1.40	1.30 – 1.51	<0.001	1.12	1.04 – 1.22	0.006
Aortoiliac location	0.69	0.62 – 0.77	<0.001	0.62	0.55 – 0.69	<0.001
Diameter (per 10 mm)	1.03	1.02 – 1.05	<0.001	0.99	0.97 – 1.01	0.209
OSR	**Univariable analysis**			**Multivariable analysis**		
Factor	**OR**	**95%-CI**	**P-value**	**aOR**	**95%-CI**	**P-value**
Age (per year)	1.00	0.99 – 1.01	0.672	1.00	0.99 – 1.01	0.451
Female sex	1.05	1.00 – 1.11	0.059	1.03	0.98 – 1.09	0.267
Cardiac comorbidity	1.76	1.68 – 1.85	<0.001	1.85	1.75 – 1.95	<0.001
Pulmonary comorbidity	1.42	1.34 – 1.49	<0.001	1.36	1.29 – 1.44	<0.001
Abnormalities on ECG	1.45	1.38 – 1.52	<0.001	1.10	1.04 – 1.16	<0.001
Creatinine ≥ 190	0.64	0.58 – 0.71	<0.001	0.64	0.58 – 0.71	<0.001
Systolic blood pressure (per 10 mmHg)	0.90	0.89 – 0.90	<0.001	0.89	0.88 – 0.90	<0.001
GCS <12	2.60	2.42 – 2.80	<0.001	2.80	2.60 – 3.03	<0.001
Hemoglobin <5.6	0.88	0.82 – 0.94	<0.001	0.63	0.58 – 0.67	<0.001
Aortoiliac location	1.00	0.82 – 1.21	1.000	-		
Diameter (per 10 mm)	0.99	0.98 – 1.00	0.065	1.00	0.99 – 1.01	0.841

Table S6

Univariable and multivariable logistic regression analyses using original data completed by multiple imputation for EVAR and OSR to assess the association of patient-related risk factors with major complications in octogenarians

EVAR	**Univariable analysis**			**Multivariable analysis**		
Factor	**OR**	**95%-CI**	**P-value**	**aOR**	**95%-CI**	**P-value**
Age (per year)	1.09	1.08 – 1.10	<0.001	1.08	1.07 – 1.09	<0.001
Female sex	0.66	0.62 – 0.71	<0.001	0.68	0.63 – 0.73	<0.001
Cardiac comorbidity	1.70	1.61 – 1.80	<0.001	1.43	1.35 – 1.52	<0.001
Pulmonary comorbidity	2.00	1.89 – 2.12	<0.001	1.67	1.58 – 1.78	<0.001
Abnormalities on ECG	2.10	1.98 – 2.21	<0.001	1.60	1.51 – 1.70	<0.001
Creatinine ≥ 190	2.47	2.26 – 2.71	<0.001	2.19	1.99 – 2.41	<0.001
Systolic blood pressure (per 10 mmHg)	0.92	0.92 – 0.93	<0.001	0.93	0.92 – 0.94	<0.001
GCS <12	4.34	3.86 – 4.90	<0.001	3.70	3.28 – 4.19	<0.001
Hemoglobin <5.6	1.27	1.18 – 1.37	<0.001	1.03	0.95 – 1.12	0.494
Aortoiliac location	1.01	0.92 – 1.12	0.788	-		
Diameter (per 10 mm)	1.04	1.02 – 1.05	<0.001	1.02	1.00 – 1.03	0.059
OSR	**Univariable analysis**			**Multivariable analysis**		
Factor	**OR**	**95%-CI**	**P-value**	**aOR**	**95%-CI**	**P-value**
Age (per year)	0.97	0.96 – 0.98	<0.001	0.96	0.96 – 0.97	<0.001
Female sex	1.27	1.20 – 1.34	<0.001	1.29	1.21 – 1.37	<0.001
Cardiac comorbidity	1.43	1.36 – 1.51	<0.001	1.40	1.32 – 1.48	<0.001
Pulmonary comorbidity	1.27	1.20 – 1.34	<0.001	1.23	1.16 – 1.30	<0.001
Abnormalities on ECG	1.46	1.39 – 1.54	<0.001	1.25	1.18 – 1.32	<0.001
Creatinine ≥ 190	0.69	0.63 – 0.76	<0.001	0.66	0.59 – 0.73	<0.001
Systolic blood pressure (per 10 mmHg)	0.92	0.91 – 0.92	<0.001	0.92	0.92 – 0.93	<0.001
GCS <12	3.11	2.84 – 3.42	<0.001	2.96	2.69 – 3.26	<0.001
Hemoglobin <5.6	1.44	1.34 – 1.55	<0.001	1.18	1.09 – 1.27	<0.001
Aortoiliac location	0.94	0.77 – 1.15	0.532	-		
Diameter (per 10 mm)	1.02	1.01 – 1.03	0.007	1.05	1.03 – 1.06	<0.001

CHAPTER

5

MORTALITY FOLLOWING ELECTIVE ABDOMINAL AORTIC ANEURYSM REPAIR IN WOMEN

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ABSTRACT

Background

Previous studies have focused on patient-related risk factors to explain the higher mortality risk in women undergoing elective abdominal aortic aneurysm (AAA) repair. The aim of this study was to evaluate whether hospital-related factors influence outcomes following AAA repair in women.

Methods

Patients undergoing elective AAA repair in 61 hospitals in the Netherlands were identified from the Dutch Surgical Aneurysm Audit registry (2013–2018). A mixed-effects logistic regression analysis was conducted to assess the effect of sex on in-hospital and/or 30-day mortality. This analysis accounted for possible correlation of outcomes among patients who were treated in the same hospital, by adding a hospital-specific random effect to the statistical model. The analysis adjusted for patient-related risk factors and hospital volume of open surgical repair (OSR) and endovascular aneurysm repair (EVAR).

Results

Some 12 034 patients were included in the analysis. The mortality rate was higher in women than among men: 53 of 1780 (3.0per cent) versus 152 of 10 254 (1.5 per cent) respectively. Female sex was significantly associated with mortality after correction for patient- and hospital-related factors (odds ratio 1.68, 95 per cent c.i. 1.20 to 2.37). OSR volume was associated with lower mortality (OR 0.91 (0.85 to 0.95) per 10-procedure increase) whereas no such relationship was identified with EVAR volume (OR 1.03 (1.01 to1.05) per 10-procedure increase).

Conclusion

Women are at higher risk of death after abdominal aortic aneurysm repair irrespective of patient- and hospital-related factors.

INTRODUCTION

Patients with an abdominal aortic aneurysm (AAA) can be treated electively by open surgical repair (OSR) or endovascular aneurysm repair (EVAR)[1]. Previous studies[2–5] have shown that excess perioperative mortality is evident among women following both types of repair. Well known patient-related risk factors are associated with increased mortality risk, including age, cardiac and pulmonary co-morbidity, and impaired renal function[6–9]. Despite correction for such factors, female sex has persistently been associated with increased mortality[2,8].

Hospital-level factors such as expertise in AAA surgery may in-fluence patient outcomes. Volume can be used as a proxy for expertise and has been found to have an inverse relationship with mortality[1,10,11]. However, previous studies[2,8,12] have focused only on patient-related factors. The aim of this study was to establish whether hospital-level factors could explain some of the differences in outcome associated with women after AAA surgery.

METHODS

Study Design and Data Source

A retrospective study from the Dutch Surgical Aneurysm Audit (DSAA) was conducted in accordance with the STROBE statement[13]. The DSAA is a nationwide and mandatory quality registry that was initiated in 2013, and obtains data on all patients who undergo surgery for an aortic aneurysm in the Netherlands across 61 hospitals.

Study Population

Patients eligible for the present study were female and male patients registered in the DSAA who underwent primary elective OSR or EVAR for an asymptomatic AAA between January 2013 – December 2018.

Variables and Definitions

Patient- and hospital-related factors considered to have an im-pact on mortality from a clinical point of view and/or known from the literature were assessed before the analysis by means of a directed acyclic graph to minimize bias (**Table S1**). The patient-related risk factors age, AAA diameter, cardiac and pulmonary co-morbidity, serum creatinine levels, and type of repair were extracted from the registry. Cardiac and pulmonary co-morbidities were registered in the DSAA in accordance with POSSUM[14]. This score is used to predict 30-day mortality and morbidity rates after surgery, and was designed specifically for surgical audit purposes[15,16]. The hospital-related factor hospital volume was divided into OSR and EVAR volume, as the separate volumes can be differently associated with

mortality[17]. The volumes of both types of repair were calculated as the total number of primary elective repairs in each hospital throughout the 6-year study period. The total number of patients who had surgery for an aortic aneurysm per hospital was used to calculate hospital volume, regardless of whether patients had missing values on patient-related risk factors as all of the registered repairs add to the cumulative hospital expertise.

Outcome

The primary outcome of interest for this study was the effect of sex on perioperative mortality, comprising in-hospital mortality during primary admission and 30-day mortality.

Statistical Analysis

Baseline characteristics of both the total study cohort and complete cases are reported, along with hospital characteristics including the percentage of women treated with OSR and EVAR per hospital. Continuous variables, stratified by sex, are reported as mean (s.d.) or median (i.q.r.), depending on the distribution. Categorical variables are reported as absolute numbers with percentages.

The data can be regarded to have a clustered structure as they were obtained from 61 hospitals, whereby patients from the same hospital formed a single cluster (group). It is possible that patients treated in the same hospital have correlated outcomes[18,19]. A wide variety of factors may lead to higher or lower mortality rates in particular hospitals. To deal with possible correlated out-comes, a mixed-effects logistic regression model was used. The following were used as fixed effects in the analysis: OSR volume, EVAR volume, age, sex, AAA diameter, cardiac and pulmonary co-morbidity, serum creatinine levels, and type of repair. The random effect in the statistical model was a hospital-specific offset, which was assumed to follow a normal distribution with a mean of zero. To assess the degree of correlation between patients treated in the same hospital, the intraclass correlation coefficient (ICC) was calculated[19]. The ICC is calculated by dividing the random-effect variance (between-hospital variance) by the total unexplained variance (between-hospital variance and assumed within-hospital variance; fixed value of $\pi^2/3$ in standard logistic distribution)[19,20].

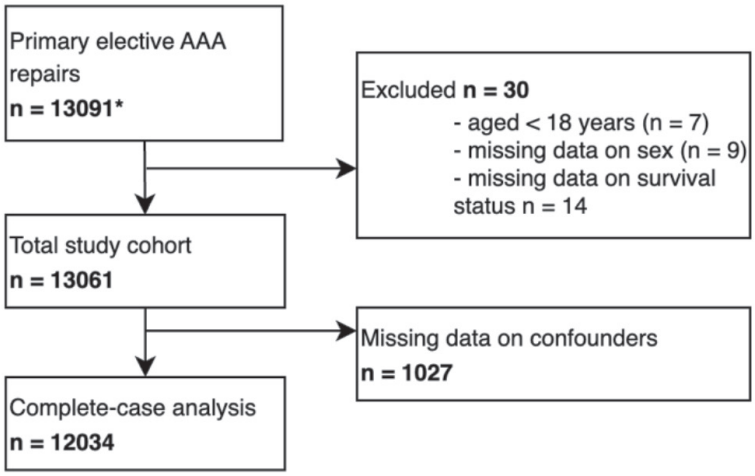
The analysis included patients with complete data on patient-related risk factors (complete-case analysis). The association be-tween variables and perioperative mortality was expressed as odds ratios (ORs) with the corresponding 95 per cent confidence intervals. $P<0.050$ was considered statistically significant. Statistical analyses were conducted with SPSS®25 (IBM, Armonk, NY, USA) and R studio version 1.3.959 (The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Participants and Descriptive Data

Some 13 091 patients who underwent elective primary AAA repair in 61 hospitals were registered in the DSAA (**Fig. 1**). These data were used to calculate hospital volume. After exclusion of 30 patients aged 18 years or under, or for whom information on sex or mortality was missing, the total study cohort comprised 13 061 patients. Data were considered to be missing completely at random as patients with missing values on patient-related factors were not treated at specific hospitals. Hence, no hospital was excluded from the analysis. Ultimately, 12 034 patients were included in the complete case-analysis. A total of 2827 patients were treated with OSR (550 women, 19.5 per cent) and 9207 with EVAR (1230 women, 13.4 per cent). Women were older than men at the time of surgery: mean (s.d.) 74.1(7.7) versus 73.1(7.6) years respectively (P,0.001) (**Table 1**).

Figure 1: Study flow diagram.



*Used in calculation of hospital volume. AAA, abdominal aortic aneurysm

Table 1: Baseline characteristics of patients undergoing primary elective abdominal aortic aneurysm repair in the Netherlands (2013–2018)

	Total study cohort		Complete cases	
	Women (n = 1916)	**Men (n = 11145)**	**Women (n = 1780)**	**Men (n = 10254)**
Age (years)*	74.1 (7.7)	73.1 (7.6)	74.1 (7.7)	73.1 (7.6)
AAA diameter (mm) **	55 (52-60)	58 (55-65)	55 (52-60)	58 (55-65)
missing	30 (1.6)	125 (1.1)		
Preoperative cardiac status				
no cardiac history	820 (43.9)	4702 (43.7)	780 (43.8)	4492 (43.8)
medication for hypertension, angina pectoris, diuretics, digoxin	883 (47.3)	4889 (45.4)	841 (47.2)	4631 (45.2)
peripheral oedema, anticoagulation (vitamin K antagonist), borderline cardiomyopathy	144 (7.7)	995 (9.2)	138 (7.8)	957 (9.3)
increased central venous pressure, cardiomegaly	21 (1.1)	182 (1.7)	21 (1.2)	174 (1.7)
missing	48 (2.5)	377 (3.4)		
Preoperative pulmonary status				
no dyspnoea	1313 (69.6)	8280 (75.4)	1232 (69.2)	7715 (75.2)
dyspnoea on exertion	476 (25.2)	2281 (20.8)	457 (25.7)	2145 (20.9)
disabling dyspnoea	72 (3.8)	318 (2.9)	69 (3.9)	302 (2.9)
dyspnoea at rest, consolidation, fibrosis	26 (1.4)	100 (0.9)	22 (1.2)	92 (0.90)
missing	29 (1.5)	166 (1.5)		
Creatinine (µmol/L)**	76 (65-92)	92 (79-110)	76 (64-92)	92 (79-109)
missing	44 (2.3)	305 (2.7)		

*Values in parentheses are percentages unless indicated otherwise; values are *mean (s.d.) and **median (i.q.r.). Baseline characteristics are shown for 13061 patients who underwent primary elective abdominal aortic aneurysm (AAA) repair after exclusion of those aged 18 years or less, or with missing values on sex or mortality, and for 12 034 patients after excluding those whose data set was incomplete.*

Hospital Characteristics

The median total number of elective AAA repairs over 6 years was 243 (i.q.r. 187–320) per hospital. The median OSR volume was 55 (39–78) and median EVAR volume was 193 (140–240). Some 18.8 per cent of all patients treated by OSR per hospital, and 12.9 percent of all those treated by EVAR per hospital, were women (**Table 2**).

Table 2: Type of repair and proportion of women treated per hospital across 61 hospitals in the Netherlands (2013-2018)

	Total study cohort (n = 13061)	**Complete cases (n = 12034)**
% OSR per hospital	23.2 (16.5-30.0)	23.1 (16.3-29.1)
% women treated per hospital	14.8 (12.6-16.2)	14.6 (12.7-16.0)
% women treated by OSR per hospital	18.2 (14.7-21.8)	18.8 (15.2-22.9)
% women treated by EVAR per hospital	12.6 (10.5-15.2)	12.9 (10.7-15.4)

Values are median (interquartile range). OSR, open surgical repair. EVAR, endovascular aneurysm repair.

Mortality Data

The overall mortality rate was higher in women than men (53 of 1780 (3.0 per cent) versus 152 of 10 254 (1.5 per cent); P=0.001). Mortality rates were higher in women than in men after both OSR (38 of 550 (6.9 per cent) versus 104 of 2277 (4.6 per cent); P=0.024) and EVAR (15 of 1230 (1.2 per cent) versus 48 of 7977 (0.6 per cent); P=0.014).

Mixed-effects Logistic Regression Analysis

After adjusting for patient- and hospital-related factors, female sex was significantly associated with perioperative mortality (OR 1.68, 95 per cent c.i. 1.20 to 2.37). Advanced age, cardiac and pulmonary comorbidity, higher serum creatinine levels, and OSR as type of repair were also associated with an increased mortality risk (**Table 3**). Higher hospital OSR volume was associated with a lower risk of mortality (OR 0.91 (0.85 to 0.95) per 10-procedure increase), whereas higher hospital EVAR volume was associated with a higher risk of death (OR 1.03 (1.01 to 1.05) per 10-procedure increase).

The estimated hospital-specific offset variance across hospitals was 0.08. An ICC of 0.024 (2.4 per cent) suggested that the out-comes of patients treated in the same hospital were only slightly correlated.

Table 3: Mixed-effects logistic regression analysis to determine the effect of sex on 30-day and/or in-hospital mortality following elective abdominal aortic aneurysm repair in the Netherlands

	Odds ratio	P
Sex (F versus M)	1.68 (1.20, 2.37)	0.003
Age (per year)	1.07 (1.05, 1.10)	<0.001
AAA diameter (per 10 mm)	1.04 (0.91, 1.18)	0.577
Cardiac co-morbidity		
no cardiac history	1.00 (reference)	
medication for hypertension, angina pectoris, diuretics, digoxin	1.31 (0.94, 1.83)	0.108
peripheral oedema, anticoagulation (vitamin K antagonist), borderline cardiomyopathy	1.86 (1.17, 2.95)	0.009
increased central venous pressure, cardiomegaly	2.64 (1.12, 6.23)	0.026
Pulmonary co-morbidity		
no dyspnoea	1.00 (reference)	
dyspnoea on exertion	2.36 (1.73, 3.21)	<0.001
disabling dyspnoea	2.12 (1.03, 4.36)	0.042
dyspnoea at rest, consolidation, fibrosis	8.33 (3.86, 17.99)	<0.001
Creatinine (per 100-µmol/l increase)	1.61 (1.33, 1.96)	<0.001
Type of repair (OSR versus EVAR)	12.23 (8.69, 17.23)	<0.001
Hospital volume OSR (per 10 procedures	0.91 (0.85, 0.95)	0.002
Hospital volume EVAR (per 10 procedures)	1.03 (1.01, 1.05)	0.017

Values in parentheses are 95 per cent confidence intervals. OSR, open surgical repair; EVAR, endovascular aneurysm repair. These are the results of the analysis investigating the effect of sex on perioperative mortality, with correction for confounders.

DISCUSSION

The associations between both patient- and hospital-related factors and mortality in AAA surgery have been well reported previously. In the investigation of the higher mortality rate in women following elective AAA repair, contemporary studies[2,3,5] have focused foremost on patient-related risk factors. As hospital-level factors can affect outcomes as well, a study combining both factors was conducted to find an explanation beyond patient-related factors for why women are at higher risk. Using nationwide data on aortic aneurysm repair in the Netherlands, the present study found that female sex was associated with mortality after additional correction for interhospital variation.

These findings corroborated those of a recent study[21] that investigated sex as a modifier in the volume–outcome relationship. The authors concluded that female sex was associated with increased mortality and that hospital volume did not have a consistent effect in women[21]. Another study[11] that investigated various hospital-level variables showed that institutional practice patterns had a relatively minor impact on mortality in comparison to patient-level risk factors. These reports suggest that factors at patient level may be more important in explaining the higher mortality risk among women. The patient-level risk factors advanced age, cardiac and pulmonary co-morbidity, high serum creatinine levels, and OSR as type of repair were associated with mortality in the present study, in agreement with previous studies[6,22,23]. Further in-depth research on other patient-related risk factors, such as anatomical, genetic or biological differences between women and men, are needed to identify potential explanations for the sex-specific mortality risk.

Hospital volume as a measurable parameter at hospital level was used as a proxy to express possible variation in expertise in AAA surgery and other hospital-related processes, such as re-sources for dealing with postoperative complications. Cumulative number of OSR or EVAR procedures performed over 6 years in each hospital was used as hospital volume, which can be considered to correspond to the average annual volume used in previous studies[24–26]. The focus of the present analysis was the mortality risk among patients who underwent elective re-pair. As such, ruptured AAA procedures were not taken into the calculation of hospital volume, which may not have done justice to tertiary referral centres that performed more repairs for ruptured AAA than other centres and may potentially have affected outcomes. Although different definitions of volume have been used, higher hospital volume is reported to be associated with lower mortality after AAA repair[27–29]. However, there seems to be a difference in strength of the association of OSR and EVAR volume with mortality. Previous research[17] has shown that the association between OSR volume and mortality is stronger than that for EVAR volume. Although higher OSR volume was associated with lower mortality as identified previously[24,30], EVAR volume was associated with a slightly higher mortality risk in the present study. As EVAR has a relatively low mortality rate and EVAR volume has been reported to have no or little relationship with mortality, a possible explanation for this surprising observation is that selection bias had occurred[24,25]. EVAR as a less invasive operation is often the procedure of choice in older patients with more co-morbidity, and/or offered to a broader selection of patients[31–34]. Alternatively, heterogeneity in definitions of hospital volume may also have had an impact on differences in out-comes. For example, some analyses[24–26]used the average annual hospital volume, whereas another study[35] used the annual hospital volume. Although these studies revealed similar outcomes for OSR (volume–outcome association), a minor difference was noted for EVAR (minor volume–outcome association or no association). Notably, the interpretation of the volume–outcome relationship in the present study

is different from that in studies that investigated the effect of hospital volume on the mortality risk of patients undergoing OSR or EVAR[25,26,35]. As such, the hospital volume–outcome relationship can be investigated in various ways, reflecting the complexity of the underlying mechanisms.

The study aimed to control for possible unexplained interhospital variation that may have affected patient outcomes, by accounting for possible correlation between outcomes of patients treated in the same hospital. Hospital parameters that may vary included the concept of heterogeneity in differences in surgical experience with type of repair or differences in experience with postoperative AAA care in women. As a secondary finding, the analysis showed that there was no heterogeneity between hospitals after correction for the fixed effects; all hospitals performed equally. Although the study aimed to capture these unmeasured hospital-related parameters, there is a possibility that the authors could not have accounted for all such factors.

The study showed that female sex is associated with high mortality after elective AAA repair. The high mortality risk in women may in part be due to a minor delay in treatment, reflected by a median AAA diameter of 5.5 cm, with potentially more advanced AAA disease and need for complex repair. However, as women are at higher risk of perioperative mortality, perhaps the trade-off of treating women with surgery should be re-evaluated. The thresh-old for treating AAA in women is currently set at an aortic diameter of 5.0 cm, which is lower than the threshold of 5.5 cm in men, possibly because women have a higher risk of aneurysm rupture than men[1,36]. Yet, perhaps the perioperative mortality risk exceeds the rupture risk at the lower AAA diameter threshold. As further studies are warranted to investigate this trade-off, a more dynamic approach to treatment may be suggested meanwhile. For women undergoing open repair, the threshold should perhaps be increased until as-yet unidentified risk factors for mortality have been elucidated, whereas a lower threshold maybe indicated for EVAR considering the low mortality risk. It is clear that a tailormade decision is required, by incorporating the patient's preference into shared decision-making[37].

There were some limitations to this study. First, potential risk factors that were not registered in the DSAA could not be taken into account. These include both patient- and hospital-related factors; the former include AAA parameters such as aneurysm anatomy and operative complexity, and the latter surgeon volume (number of procedures performed per surgeon) which has been proposed to be associated with mortality[38,39]. Social factors such as caregiver status may also influence outcomes, which could not be taken into account in the present analysis. Second, this retrospective study used data from a quality registry that was not primarily designed for research and could have missing

values. The percentage of missing values for each co-morbidity was less than 4 per cent and the incomplete data were distributed over approximately 8 per cent of the patients. The information bias of the extracted variables was therefore considered to be acceptable.

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Disclosure
The authors declare no conflict of interest.

REFERENCES

1 Wanhainen A, Verzini F, van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(1):8–93. Doi: 10.1016/j.ejvs.2018.09.020.

2 Sidloff DA, Saratzis A, Sweeting MJ, Michaels J, Powell JT, Thompson SG, et al. Sex differences in mortality after abdominal aortic aneurysm repair in the UK. *British Journal of Surgery* 2017;**104**(12):1656–64. Doi: 10.1002/bjs.10600.

3 Deery SE, Soden PA, Zettervall SL, Shean KE, Bodewes TCF, Pothof AB, et al. Sex differences in mortality and morbidity following repair of intact abdominal aortic aneurysms. Journal of Vascular Surgery, vol. 65. Mosby Inc.; 2017. pp. 1006–13.

4 Desai M, Choke E, Sayers RD, Nath M, Bown MJ. Sex-related trends inmortality after elective abdominal aortic aneurysmsurgery between 2002 and 2013 at National Health Service hospitals in England: Less benefit for women compared with men. *Eur Heart J* 2016;**37**(46):3452–60. Doi: 10.1093/eurheartj/ehw335.

5 Lo RC, Bensley RP, Hamdan AD, Wyers M, Adams JE, Schermerhorn ML. Gender differences in abdominal aortic aneurysm presentation, repair, and mortality in the Vascular Study Group of New England. *J Vasc Surg* 2013;**57**(5):1261-1268.e5. Doi: 10.1016/j.jvs.2012.11.039.

6 Grant SW, Grayson AD, Purkayastha D, Wilson SD, McCollum C. Logistic risk model for mortality following elective abdominal aortic aneurysm repair. *British Journal of Surgery* 2011;**98**(5):652–8. Doi: 10.1002/bjs.7463.

7 Chaikof EL, Dalman RL, Eskandari MK, Jackson BM, Lee WA, Mansour MA, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg* 2018;**67**(1):2-77.e2. Doi: 10.1016/j.jvs.2017.10.044.

8 Mehta M, Byrne WJ, Robinson H, Roddy SP, Paty PSK, Kreienberg PB, et al. Women derive less benefit from elective endovascular aneurysm repair than men. *J Vasc Surg* 2012;**55**(4):906–13. Doi: 10.1016/j.jvs.2011.11.047.

9 Nathan DP, Brinster CJ, Jackson BM, Wang GJ, Carpenter JP, Fairman RM, et al. Predictors of decreased short- and long-term survival following open abdominal aortic aneurysm repair. *J Vasc Surg* 2011;**54**(5):1237–43. Doi: 10.1016/j.jvs.2011.05.028.

10 Holt PJE, Poloniecki JD, Gerrard D, Loftus IM, Thompson MM. Meta-analysis and systematic review of the relationship between volume and outcome in abdominal aortic aneurysm surgery. *British Journal of Surgery* 2007;**94**(4):395–403. Doi: 10.1002/bjs.5710.

11 Hicks CW, Canner JK, Arhuidese I, Obeid T, Black JH, Malas MB. Comprehensive assessment of factors associated with in-hospital mortality after elective abdominal aortic aneurysm repair. JAMA Surgery, vol. 151. American Medical Association; 2016. pp. 838–45.

12 Indrakusuma R, Jalalzadeh H, Vahl AC, Koelemay MJW, Balm R. Editor's Choice – Sex Related Differences in Peri-operative Mortality after Elective Repair of an Asymptomatic Abdominal Aortic Aneurysm in the Netherlands: a Retrospective Analysis of 2013 to 2018. *European Journal of Vascular and Endovascular Surgery* 2019;**58**(6):813–20. Doi: 10.1016/j.ejvs.2019.05.017.

13 von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *International Journal of Surgery* 2014;**12**(12):1495–9. Doi: 10.1016/j.ijsu.2014.07.013.

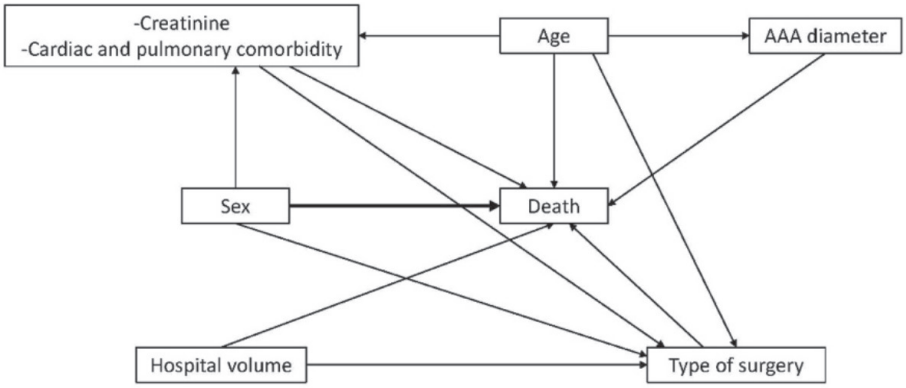
14 DICA. Jaarrapportage 2014 DSAA Aneurysma Chirurgie. https://dica.nl/jaarrapportage-2014/dsaa.html. 10/07/2020.

15 Copeland GP, Jones D, Walters M. POSSUM: A scoring system for surgical audit. *British Journal of Surgery* 1991;**78**(3):355–60. Doi: 10.1002/bjs.1800780327.
16 Copeland GP. The POSSUM System of Surgical Audit. n.d.
17 Landon BE, O'Malley AJ, Giles K, Cotterill P, Schermerhorn ML. Volume-outcome relationships and abdominal aortic aneurysm repair. *Circulation* 2010;**122**(13):1290–7. Doi: 10.1161/CIRCULATIONAHA.110.949172.
18 Berlin JA, Kimmel SE, ten Have TR, Sammel MD. An empirical comparison of several clustered data approaches under confounding due to cluster effects in the analysis of complications of coronary angioplasty. *Biometrics* 1999;**55**(2):470–6. Doi: 10.1111/j.0006-341X.1999.00470.x.
19 Austin PC, Merlo J. Intermediate and advanced topics in multilevel logistic regression analysis. *Stat Med* 2017;**36**(20):3257–77. Doi: 10.1002/sim.7336.
20 Wu S, Crespi CM, Wong WK. Comparison of methods for estimating the intraclass correlation coefficient for binary responses in cancer prevention cluster randomized trials. *Contemp Clin Trials* 2012;**33**(5):869–80. Doi: 10.1016/j.cct.2012.05.004.
21 Trenner M, Salvermoser M, Busch A, Reutersberg B, Eckstein HH, Kuehnl A. Effect modification of sex and age for the hospital volume-outcome relationship in abdominal aortic aneurysm treatment: Secondary data analysis of the nationwide german diagnosis related groups statistics from 2005 to 2014. *J Am Heart Assoc* 2020;**9**(6). Doi: 10.1161/JAHA.119.014534.
22 Becquemin JP, Chemla E, Chatellier G, Allaire E, Mellière D, Desgranges P. Perioperative factors influencing the outcome of elective abdominal aorta aneurysm repair. *European Journal of Vascular and Endovascular Surgery* 2000;**20**(1):84–9. Doi: 10.1053/ejvs.2000.1102.
23 Steffen M S-RTJGBDGRT. [The DIGG risk score : A risk predictive model of perioperative mortality after elective treatment of intact abdominal aortic aneurysms in the DIGG register]. *Chirurg* 2019;**90**:913–20.
24 Scali ST, Beck AW, Sedrakyan A, Mao J, Venermo M, Faizer R, et al. Hospital Volume Association With Abdominal Aortic Aneurysm Repair Mortality: Analysis of the International Consortium of Vascular Registries. *Circulation* 2019;**140**(15):1285–7. Doi: 10.1161/CIRCULATIONAHA.119.042504.
25 Zettervall SL, Schermerhorn ML, Soden PA, McCallum JC, Shean KE, Deery SE, et al. The effect of surgeon and hospital volume on mortality after open and endovascular repair of abdominal aortic aneurysms. Journal of Vascular Surgery, vol. 65. Mosby Inc.; 2017. pp. 626–34.
26 Gray WK, Day J, Horrocks M. Editor's Choice – Volume–Outcome Relationships in Elective Abdominal Aortic Aneurysm Surgery: Analysis of the UK Hospital Episodes Statistics Database for the Getting It Right First Time (GIRFT) Programme. *European Journal of Vascular and Endovascular Surgery* 2020;**60**(4):509–17. Doi: 10.1016/j.ejvs.2020.07.069.
27 Trenner M, Kuehnl A, Salvermoser M, Reutersberg B, Geisbuesch S, Schmid V, et al. Editor's Choice – High Annual Hospital Volume is Associated with Decreased in Hospital Mortality and Complication Rates Following Treatment of Abdominal Aortic Aneurysms: Secondary Data Analysis of the Nationwide German DRG Statistics from 2005 to 2013. *European Journal of Vascular and Endovascular Surgery* 2018;**55**(2):185. Doi: 10.1016/j.ejvs.2017.11.016.
28 Phillips P, Poku E, Essat M, Woods HB, Goka EA, Kaltenthaler EC, et al. Procedure Volume and the Association with Short-term Mortality Following Abdominal Aortic Aneurysm Repair in European Populations: A Systematic Review. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(1):77–88. Doi: 10.1016/j.ejvs.2016.10.007.
29 Holt PJE, Poloniecki JD, Khalid U, Hinchliffe RJ, Loftus IM, Thompson MM. Effect of endovascular aneurysm repair on the volume-outcome relationship in aneurysm repair. *Circ Cardiovasc Qual Outcomes* 2009;**2**(6):624–32. Doi: 10.1161/CIRCOUTCOMES.109.848465.

30 Scali ST, Beck A, Sedrakyan A, Mao J, Behrendt CA, Boyle JR, et al. Editor's Choice – Optimal Threshold for the Volume–Outcome Relationship After Open AAA Repair in the Endovascular Era: Analysis of the International Consortium of Vascular Registries. *European Journal of Vascular and Endovascular Surgery* 2021;**61**(5):747–55. Doi: 10.1016/j.ejvs.2021.02.018.
31 Anderson PL, Arons RR, Moskowitz AJ, Gelijns A, Magnell C, Faries PL, et al. A statewide experience with endovascular abdominal aortic aneurysm repair: Rapid diffusion with excellent early results. *J Vasc Surg* 2004;**39**(1):10–8. Doi: 10.1016/j.jvs.2003.07.020.
32 United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG ED. Endovascular Repair of Abdominal Aortic Aneurysm in Patients Physically Ineligible for Open Repair. *New England Journal of Medicine* 2010;**362**:1872–80. Doi: 10.1097/SLA.0000000000002392.
33 Dias-Neto M, Norton L, Sousa-Nunes F, Silva JR, Rocha-Neves J, Teixeira JF, et al. Impact of Gradual Adoption of EVAR in Elective Repair of Abdominal Aortic Aneurysm: A Retrospective Cohort Study from 2009 to 2015. *Ann Vasc Surg* 2021;**70**:411–24. Doi: 10.1016/j.avsg.2020.06.029.
34 Dias-Neto M, Mani K, Leite-Moreira A, Freitas A, Sampaio S. Nationwide Analysis of Intact Abdominal Aortic Aneurysm Repair in Portugal from 2000 to 2015. *Ann Vasc Surg* 2020;**66**:54-64.e1. Doi: 10.1016/j.avsg.2019.12.013.
35 Tong T, Aber A, Chilcott J, Thokala P, Walters SJ, Maheswaran R, et al. Volume-outcome relationships in open and endovascular repair of abdominal aortic aneurysm: Administrative data 2006-2018. *British Journal of Surgery* 2021;**108**(5):521–7. Doi: 10.1002/bjs.11919.
36 Skibba AA, Evans JR, Hopkins SP, Yoon HR, Katras T, Kalbfleisch JH, et al. Reconsidering gender relative to risk of rupture in the contemporary management of abdominal aortic aneurysms. Journal of Vascular Surgery, vol. 62. Mosby Inc.; 2015. pp. 1429–36.
37 Ubbink DT, Koelemay MJW. Shared Decision Making in Vascular Surgery. Why Would You? *European Journal of Vascular and Endovascular Surgery* 2018:749–50. Doi: 10.1016/j.ejvs.2018.06.042.
38 Arnaoutakis DJ, Scali ST, Neal D, Giles KA, Huber TS, Powell RJ, et al. Surgeon experience association with patient selection and outcomes after open abdominal aortic aneurysm repair. Journal of Vascular Surgery, vol. 72. Mosby Inc.; 2020. pp. 1325-1336.e2.
39 Scali ST, Arnaoutakis DJ, Neal D, Giles KA, Goodney PP, Suckow BD, et al. Association between surgeon case volume and years of practice experience with open abdominal aortic aneurysm repair outcomes. Journal of Vascular Surgery, vol. 73. Mosby Inc.; 2021. pp. 1213-1226.e2.

SUPPLEMENTAL MATERIALS

Table S1: Directed Acyclic Graph



Display of causal assumptions between the variables. The primary interest is the effect of sex on death. Creatinine, cardiac and pulmonary comorbidity, age, AAA diameter, type of surgery and hospital volume were confounders in the statistical model.

CHAPTER

6

SHORT-TERM OUTCOMES OF OPEN SURGICAL ABDOMINAL AORTIC ANEURYSM REPAIR FROM THE DUTCH SURGICAL ANEURYSM AUDIT

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ABSTRACT

Background

The sharp decrease in open surgical repair (OSR) for abdominal aortic aneurysm (AAA) has raised concerns about con-temporary postoperative outcomes. The study was designed to analyse the impact of complications on clinical outcomes within30 days following OSR.

Methods

Patients who underwent OSR for intact AAA registered prospectively between 2016 and 2019 in the Dutch Surgical Aneurysm Audit were included. Complications and outcomes (death, secondary interventions, prolonged hospitalization) were evaluated. The adjusted relative risk (aRR) and 95 per cent confidence intervals were computed using Poisson regression. Subsequently, the population-attributable fraction (PAF) was calculated. The PAF reflects the expected percentage reduction of an outcome if a com-plication were to be completely prevented.

Results

A total of 1657 patients were analysed. Bowel ischaemia and renal complications had the largest impact on death (aRR 12.44 (95 per cent c.i. 7.95 to 19.84) at PAF 20 (95 per cent c.i. 8.4 to 31.5) per cent and aRR 5.07 (95 per cent c.i. 3.18 to 8.07) at PAF14 (95 per cent c.i. 0.7 to 27.0) per cent, respectively). Arterial occlusion had the greatest impact on secondary interventions (aRR 11.28 (95 per cent c.i. 8.90 to 14.30) at PAF 21 (95 per cent c.i. 14.7 to 28.1) per cent), and pneumonia (aRR 2.52 (95 per cent c.i. 2.04 to 3.10) at PAF 13 (95 per cent c.i. 8.3 to 17.8) per cent) on prolonged hospitalization. Small effects were observed on outcomes for other complications.

Conclusion

The greatest clinical impact following OSR can be made by focusing on measures to reduce the occurrence of bowel ischaemia, arterial occlusion and pneumonia.

INTRODUCTION

In the field of vascular surgery, registry data are being used increasingly as a tool for quality improvement[1]. Since 2013, all patients undergoing abdominal aortic aneurysm (AAA) surgery in the Netherlands have been recorded in the Dutch Surgical Aneurysm Audit (DSAA) to monitor and improve the quality of care[2,3]. Nowadays, AAA is predominantly treated by endovascular aortic aneurysm repair (EVAR) rather than open surgical repair (OSR)[4]. In about 25 per cent of elective infrarenal AAA repairs, OSR is still the preferred method[5,6]. Previous studies have shown the initial benefits of lower morbidity and mortality rates after EVAR, but this early advantage disappears during follow-up[5,7–9]. Quality improvement of perioperative care in vascular patients has become an important topic to prevent complications[10]. Yet, concerns have arisen that as OSR is now performed so infrequently, patient outcomes may be less favourable[11]. In order to optimize the current short-term outcomes after OSR, it is necessary to improve the quality of surgical postoperative care. Therefore, those postoperative complications that most affect outcomes need to be highlighted. Previous literature has demonstrated the prevalence of complications and out-comes after open AAA repair[5,7–9,12]. However, just reporting the prevalence of outcomes is not enough to measure the overall im-pact of complications on the population.

In order to define those complications most relevant to OSR, and to assess their impact on postoperative outcomes and the consequences of avoidance of a certain complication, the population-attributable fraction (PAF) can be used. The PAF is the pro-portion of events in the population that are attributable to the risk factor. The PAF is defined by the reduction of a disease (for example lung cancer) in the population that would occur if a certain risk factor was completely removed (for example no to-bacco use)[13,14]. Furthermore, the PAF is a useful tool to assess the impact on public health of complications of several outcomes (such as death and secondary interventions), as it includes the frequency of a complication as well as the relative risk of a certain outcome related to that complication[14]. Complications after OSR lead to an increase in mortality rate and duration of hospital stay and significant increase in medical costs[15,16]. Furthermore, the 30-day intervention rate after OSR has been associated with increased postoperative mortality rate[16]. Reduction of complications is likely to result in lower postoperative morbidity and mortality rates, especially if those complications with the largest impact on mortality rate can be prevented.

The aim of this DSAA registry study was to identify the most frequently occurring complications following OSR, and subsequently to evaluate the impact of these complications on predetermined outcomes within 30 days by using the PAF.

METHODS

Study design

This observational study used data accessed from the DSAA, a mandatory national vascular audit in which every vascular medical centre has registered all AAA repairs in the Netherlands since 2013. The DSAA is one of the healthcare quality registries of the Dutch Institute of Clinical Auditing[2]. Verification of the DSAA data was executed in 2015 through a random sample of hospitals[17]. This study was approved by the scientific board of the DSAA (DSAA201907) and performed in accordance with the STROBE guidelines for observational studies[18].

Patients

All consecutive patients were eligible for inclusion if they had undergone a primary OSR for a non-ruptured (elective and symptomatic) infrarenal AAA between January 2016 and December 2019 at one of 60 medical centres in the Netherlands. Patients were excluded if predefined variables such as sex, age or 30-dayor in-hospital death were missing.

Definitions

Baseline patient characteristics included age, sex, preoperative AAA diameter, cardiac co-morbidities (such as angina pectoris, hypertension), pulmonary co-morbidities (such as dyspnoea, chronic pulmonary diseases), and haemoglobin and creatinine concentrations. The definitions of registered co-morbidities can be found in **Table S1**. Up to 2018, baseline patient characteristics and co-morbidities were registered in the DSAA in accordance with the categorizations of the Physiological and Operative Severity Score for the enumeration of Mortality and morbidity (POSSUM) score, a mortality-risk-prediction model for surgical patients[19]. From 2019 onwards, the registration of co-morbidities has been based on International Classification of Diseases (ICD) codes. Postoperative complications registered in the DSAA are listed in **Table S2**. Postoperative morbidity was assessed, and the complications were distributed into the following categories: abdominal sepsis or abscess, bowel ischaemia, arterial occlusion (for example amputation, renal or other artery occlusion, trash foot), wound complications (such as deep wound infection), myocardial infarction or arrhythmia, congestive heart failure, pneumonia, other pulmonary complications (pulmonary embolism, pneumothorax), renal insufficiency (scored at surgeon's discretion; without or requiring haemodialysis), significant rebleeding (need for packed cells transfusion or secondary intervention), neurological complications (cerebrovascular accident or paraplegia), and other.

The primary outcome measure was the impact of postoperative complications within 30 days on mortality rate, secondary interventions and prolonged hospital stay. Postoperative

death was defined as death within 30 days after the primary OSR, or within the same period of hospital admission. Secondary interventions were defined as all secondary interventions following primary OSR within 30 days that were registered in the DSAA. Prolonged hospital stay was specified as length of hospital stay of the surviving patients above the 75th percentile, registered in the DSAA and stratified by elective or urgent intact repair.

Statistical analysis

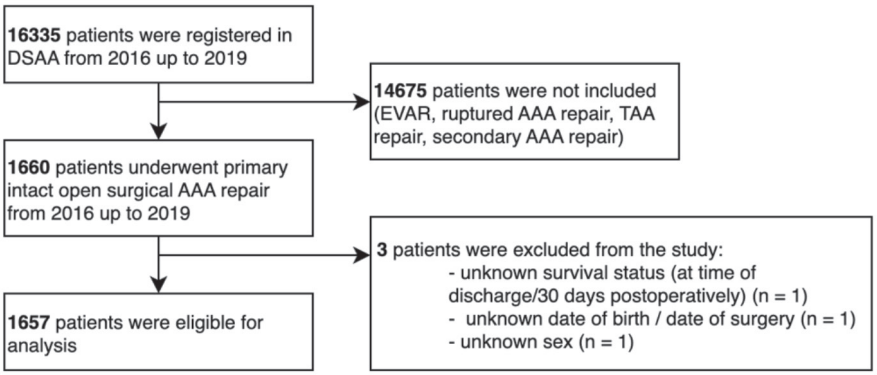
Patient characteristics were analysed by means of descriptive statistics. Normal distribution of the data was tested with histograms and Q-Q plots. Normally distributed continuous data were reported as mean with standard deviation. Data were reported as median with interquartile range if they did not follow normal distribution. Categorical variables were presented as proportions, and differences in proportions were assessed with the χ^2 test and Fisher's exact test, when appropriate. A two-sided $P<0.050$ was considered to be statistically significant. The frequencies of all complications and outcomes were calculated. First, the adjusted relative risk (aRR) with 95 per cent confidence intervals was calculated for each complication–outcome pair using Poisson regression models with log link (exponentiates linear predictors) and robust error variance (to narrow confidence intervals) to estimate risk ratios for binary outcomes, while adjusting for con-founders. Possible confounders included: age, sex, preoperative AAA diameter, cardiac status, pulmonary status, haemoglobin, creatinine and urgency of repair (elective or urgent intact). Subsequently, the PAF was determined to measure the impact of the complications. The PAF model takes into account the frequency and relative risk of a specific outcome whilst correcting for confounders and other complications. All PAF calculations were executed with the attributable fraction (AF) package in R software to estimate the adjusted attributable fraction in cohort studies[20]. In this study, the risk-adjusted PAF accounts for the proportional reduction in outcome (postoperative death, secondary intervention, prolonged hospital stay), if a given complication could be completely eliminated from the study population. All statistical calculations were performed with R (R Foundation for statistical computing, Vienna, Austria) version 4.0.2.

RESULTS

Study population

In total, 16 335 patients were registered in the DSAA by 60 hospitals in the Netherlands between 1 January 2016 and 31 December 2019 (**Figure 1**).

Figure 1: Flow chart of included patients



DSAA, Dutch Surgical Aneurysm Audit; AAA, abdominal aortic aneurysm; EVAR, endovascular aortic aneurysm repair; TAA, thoracic aortic aneurysm

Some 1660 patients (10.2 per cent) underwent primary OSR for an intact infrarenal AAA, of which 1657 (99.8 percent) were eligible for inclusion. The majority of patients were male (1310 patients, 78.2 per cent) and the mean (s.d.) age was 70.6 (7.51) years. The majority of the patients had cardiac co-morbidities (1074 patients, 64.8 per cent). Patient characteristics and co-morbidities are specified in **Table 1**.

Table 1: Baseline characteristics

Variables	Overall (n = 1657)	Missing
Sex, female	327 (20.9)	0
Age (years)	70.62 (7.51)	0
Cardiac co-morbidity	1074 (64.8)	30 (1.8)
Pulmonary co-morbidity	1231 (74.3)	30 (1.8)
Haemoglobin (mmol/l)	8.59 (1.03)	40 (2.4)
Creatinine (µmol/l)	87 (74.00, 106.00)	57 (3.4)
Aneurysm diameter (mm)	62.61 (13.13)	10 (0.6)
Urgency of repair, urgent intact	225 (13.6)	0
Year of surgery		0
2016	394 (23.8)	
2017	403 (24.3)	
2018	420 (25.3)	
2019	440 (26.6)	

Postoperative clinical outcomes

All postoperative complications and clinical outcomes are shown in **Table 2**. Pneumonia (13.0 per cent), renal insufficiency (6.7 per cent) and myocardial infarction or arrhythmia (5.6 per cent) were the most common complications after OSR. There were 72 deaths (4.3 per cent) within 30 days or in-hospital, 306 (18.5 percent) patients had a prolonged hospital stay and 162 patients (9.8 per cent) underwent secondary intervention. Most of the secondary interventions were carried out via an open surgical procedure, that is relaparotomy (116 patients, 71.6 per cent). No differences were found between men and women in the incidence of specific complications (**Table S3**).

Table 2: Postoperative complications and clinical outcomes in 1657 patients

	Patients (n = 1657)	**Missing**
Postoperative complications		
Abdominal sepsis or abscess	14 (0.8)	4 (0.2)
Bowel ischemia (transmural)	47 (2.8)	4 (0.2)
Arterial occlusion	52 (3.1)	2 (0.1)
Wound infection	52 (3.1)	5 (0.3)
Myocardial infarction or arrhythmia	92 (5.6)	6 (0.4)
Congestive heart failure	46 (2.8)	6 (0.4)
Pneumonia	215 (13.0)	2 (0.1)
Pulmonary (embolism, pneumothorax)	39 (2.4)	2 (0.1)
Renal insufficiency	111 (6.7)	2 (0.1)
Requiring haemodialysis	39 (2.4)	
Rebleeding	29 (1.8)	0
Cerebrovascular accident or paraplegia	11 (0.7)	2 (0.1)
Outcomes		
Death	72 (4.3)	0
Secondary interventions	162 (9.8)	1 (0.1)
Endovascular	9 (0.5)	
Percutaneous	6 (0.4)	
Endoscopic	1 (0.1)	
Thoracolaparoscopic	2 (0.1)	
Open	116 (7.0)	
Other	28 (1.7)	
Prolonged hospital stay	306 (18.5)	19 (1.1)

The risk-adjusted associations between postoperative complications and outcomes (death, secondary interventions, prolonged hospitalization) are shown in **Tables 3–5**. Most patients died with the complication abdominal sepsis or abscess (50 per cent). The occurrence of rebleeding most often led to a secondary intervention (90 per cent) and abdominal sepsis or abscess (71 per cent) to prolonged hospitalization. Abdominal sepsis or abscess, and bowel ischaemia were associated with the greatest relative risk of postoperative death (aRR 12.44 (95 per cent c.i. 7.95–19.48) and 8.87 (95 per cent c.i. 5.51 to 14.25) respectively). Apart from wound complications and pneumonia, all postoperative complications were significantly related to death. Arterial occlusion and bowel ischaemia were associated with the greatest relative risk of undergoing a secondary intervention (aRR 11.28 (95 per cent c.i.8.90 to 14.30) and 10.21 (95 per cent c.i. 7.57 to 13.75) respectively). All postoperative complications were significantly associated with prolonged hospitalization, with the highest association for abdominal sepsis or abscess (aRR 3.84 (95 per cent c.i. 2.58 to 5.73)) and wound complications (aRR 3.58 (95 per cent c.i. 2.74 to 4.70)).

Table 3: Risk-adjusted associations and population-attributable fraction between postoperative deaths and complications after open surgical repair of abdominal aortic aneurysm

Postoperative complication	No. died/ survived*	Risk-adjusted association ***		Risk adjusted PAF ****	
		aRR **	P	PAF **	P
Abdominal sepsis or abscess	7/7 (50)	12.44 (7.95, 19.48)	<0.001	7.19 (1.05-13.34)	0.022
Bowel ischemia	20/27 (43)	8.87 (5.51, 14.25)	<0.001	19.97 (8.40, 31.53)	<0.001
Arterial occlusion	11/41 (21)	6.92 (3.99, 11.97)	<0.001	11.05 (2.85, 19.25)	0.008
Wound infection	2/50 (4)	1.08 (0.27, 4.35)	0.909		
Myocardial infarction or arrhythmia	14/78 (15)	3.44 (1.98, 6.00)	<0.001	12.90 (2.15, 23.65)	0.019
Congestive heart failure	11/35 (24)	4.21 (2.14, 8.29)	<0.001	10.95 (1.80, 20.11)	0.019
Pneumonia	16/199 (7)	1.51 (0.86, 2.64)	0.147		
Pulmonary	12/27 (31)	6.94 (3.88, 12.41)	<0.001	12.19 (3.65, 20.72)	0.005
Renal	23/88 (21)	5.07 (3.18, 8.07)	<0.001	13.86 (0.69, 27.02)	0.039
Rebleeding	6/23 (21)	4.83 (2.07, 11.27)	<0.001	3.89 (-2.24, 10.02)	0.214

Table 3: *Continued.*

Postoperative complication	No. died/ survived*	Risk-adjusted association ***		Risk adjusted PAF ****	
		aRR **	P	PAF **	P
Cerebrovascular accident or paraplegia	4/7 (36)	5.64 (2.07, 15.34)	<0.001	3.91 (-1.23, 9.05)	0.136

**Values in parentheses are percentage that died; **Values in parentheses are 95 per cent confidence intervals. Patients can have multiple complications and thus fall into multiple categories. P values were obtained via Multivariable Poisson regression. ***Multivariable Poisson regression. ****Logistic regression-based estimate of confounder-adjusted attributable fractions. aRR, adjusted relative risk; PAF, population-attributable fraction.*

Table 4: Risk-adjusted associations and population-attributable fraction between secondary interventions and complications after open surgical repair of abdominal aortic aneurysm

Postoperative complication	No. with/without intervention*	Risk-adjusted association ***		Risk adjusted PAF ****	
		aRR **	P	PAF **	P
Abdominal sepsis or abscess	12/2 (86)	9.84 (7.40, 13.08)	<0.001	5.01 (1.47, 8.56)	0.006
Bowel ischemia	33/14 (70)	10.21 (7.57, 13.75)	<0.001	13.66 (7.99, 19.34)	<0.001
Arterial occlusion	42/10 (81)	11.28 (8.90, 14.30)	<0.001	21.36 (14.66, 28.06)	<0.001
Wound infection	31/21 (60)	7.95 (5.94, 10.65)	<0.001	13.11 (7.53, 18.69)	<0.001
Myocardial infarction or arrhythmia	15/77 (16)	1.64 (0.98, 2.75)	0.057		
Congestive heart failure	9/37 (20)	2.02 (1.05, 3.90)	0.036	0.34 (-1.60, 2.29)	0.729
Pneumonia	26/189 (12)	1.31 (0.89, 2.0)	0.184		
Pulmonary	9/30 (23)	2.64 (1.44, 4.82)	0.002	1.33 (-1.26, 3.91)	0.314
Renal	29/82 (26)	3.12 (2.16, 4.54)	<0.001	0.14 (-5.31, 5.59)	0.961
Rebleeding	26/3 (90)	9.65 (7.43, 12.53)	<0.001	11.32 (6.39, 16.25)	<0.001
Cerebrovascular accident or paraplegia	4/7 (36)	3.31 (1.43, 7.63)	0.005	1.09 (-1.57, 3.76)	0.422

**Values in parentheses are percentage that had intervention; **Values in parentheses are 95 per cent confidence intervals. Patients can have multiple complications and thus fall into multiple categories. P values were obtained via Multivariable Poisson regression. ***Multivariable Poisson regression. ****Logistic regression-based estimate of confounder-adjusted attributable fractions. aRR, adjusted relative risk; PAF, population-attributable fraction.*

Table 5: Risk-adjusted associations and population-attributable fraction between prolonged hospitalization and complications after open surgical repair of abdominal aortic aneurysm

Postoperative complication	No. with/without prolonged hospitalization*	Risk-adjusted association ***		Risk adjusted PAF ****	
		aRR **	P	PAF **	P
Abdominal sepsis or abscess	10/4 (71)	3.84 (2.58. 5.73)	<0.001	1.23 (-0.14, 2.59)	0.079
Bowel ischemia	26/21 (55)	2.72 (2.05, 3.61)	<0.001	2.59 (0.27, 4.91)	0.029
Arterial occlusion	20/32 (39)	2.31 (1.58, 3.37)	<0.001	0.92 (-1.38, 3.21)	0.434
Wound infection	33/19 (64)	3.58 (2.74, 4.70)	<0.001	4.84 (2.44, 7.25)	<0.001
Myocardial infarction or arrhythmia	48/43 (53)	2.75 (2.17, 3.48)	<0.001	7.04 (3.93, 10.15)	<0.001
Congestive heart failure	25/20 (56)	2.65 (1.94, 3.63)	<0.001	3.28 (0.76, 5.79)	0.011
Pneumonia	88/125 (41)	2.52 (2.04, 3.10)	<0.001	13.05 (8.29, 17.81)	<0.001
Pulmonary	19/19 (50)	2.46 (1.70, 3.59)	<0.001	2.18 (-0.04, 4.42)	0.055
Renal	63/47 (57)	3.25 (2.59, 4.06)	<0.001	5.86 (2.19, 9.53)	0.002
Rebleeding	15/14 (52)	2.36 (1.61, 3.46)	<0.001	1.21 (-0.28, 2.70)	0.112
Cerebrovascular accident or paraplegia	5/6 (46)	2.24 (1.12, 4.50)	0.022	0.05 (-1.04, 1.14)	0.926

**Values in parentheses are percentage that had prolonged hospitalization; **Values in parentheses are 95 per cent confidence intervals. Patients can have multiple complications and thus fall into multiple categories. ***Multivariable Poisson regression. ****Logistic regression-based estimate of confounder-adjusted attributable fractions. P values were obtained via Multivariable Poisson regression. aRR, adjusted relative risk; PAF, population-attributable fraction.*

Population attributable fraction

Risk-adjusted PAFs were estimated for each complication–out-come pair (for example, complication–death, complication–secondary intervention) to characterize the effect of each complication of the respective outcome measure (see **Tables 3–5**). In the study population, bowel ischaemia and renal complications had the greatest overall impact on short-term postoperative death. Prevention of these complications would result in a decrease in mortality rate of 19.97 (95 per cent c.i. 8.40 to 31.53) per cent due to bowel ischaemia, and 13.86 (95 per cent c.i. 0.69 to 27.02) percent for renal complications. Elimination of arterial occlusion and bowel ischaemia would result in a reduction of secondary interventions of 21.36 (95 per cent c.i. 14.66 to 28.06) per cent and13.66 (95 per cent c.i. 7.99 to 19.34) per cent, respectively. Postoperative complications such as congestive heart failure and renal complications had the least impact on undergoing a secondary intervention, 0.34 and 0.14 per cent respectively. Pneumonia had the highest overall impact on prolonged hospital stay at 13.05 (95 per cent c.i. 8.29 to 1781) per cent. The other postoperative complications were observed to have less impact on prolonged hospital stay.

DISCUSSION

This registry cohort study provided an overview of current morbidity and mortality rates following OSR in the Netherlands. The impact of relevant postoperative complications on clinical out-comes was assessed by means of the PAF. Bowel ischaemia and renal complications had the strongest association with postoperative death. Arterial occlusion and bowel ischaemia were shown to have the highest impact on secondary interventions, and pneumonia on prolonged hospitalization.

Originally PAF was used to define contributory risk factors and the impact of medical interventions on the health status of a population[13,14]. The strength of PAF is that it merges the frequency of the risk factor with the relative risk of a certain outcome relating to that risk factor. PAFs have already been shown to be useful in analysis of the impact of postoperative complications on clinical outcomes after major vascular surgery[21]. Complications such as bleeding and pneumonia were found to have the largest overall impact, and it was suggested they should be prioritized as targets for improvement of the quality of surgical vascular care[21]. This emphasizes the relevance of using the PAF in gaining understanding of the current outcomes after OSR, as the PAF identifies opportunities for prevention of a disease in patients and the incidence of exposure in the population.

The postoperative mortality rate was 4.3 per cent in this registry for open repair of intact AAA and comparable to the 4.4 percent from vascular registries in 11 countries[22]. Complete

elimination of bowel ischaemia would lead to a reduction of 20per cent, and prevention of renal insufficiency to a reduction of14 per cent in mortality rate following OSR. The 2.8 per cent incidence of bowel ischaemia following OSR is in line with the 1.9–3.6 per cent reported in previous studies[23,24]. Although the PAF of bowel ischaemia was lower than that of arterial occlusion after secondary interventions, it showed the highest clinical impact on two of the three outcomes in the present study. The origin of postoperative bowel ischaemia is multifactorial, but patient factors (age, female gender, hypertension) as well as longer operating time, and increased blood loss are proven risk factors[20,24,25]. Surgical quality-improvement programmes should prioritize the prevention of these risk factors. This can be achieved by initiating AAA repair quality-improvement programmes where the continued focus should be on associated risk factors such as blood loss and operating time[23–26].

Postoperative renal failure is also a well known risk factor for death following open AAA repair[27,28]. Multiple reasons for the development of renal insufficiency following OSR have already been explored: several types of medication[29], patients with AAA with a history of smoking resulting in atherosclerosis which leads to cardiovascular and renal disease[30], and clamping time during OSR[31]. Preoperative assessment by a nephrologist can be helpful for risk prediction of postoperative renal insufficiency[28,31]. Further research is necessary to analyse whether concentration of care should be considered at least for OSR, because proficiency in OSR is declining due to the ever-increasing use of EVAR. Therefore, the European Society for Vascular Surgery guidelines recommend 30 elective AAA repairs per year per centre[31].

Prevention of arterial occlusion would lead to a reduction of 21 per cent of secondary interventions within 30 days of OSR. Prophylactic perioperative heparinization is routine in open AAA surgery, yet the evidence that this has a beneficial effect is not compelling[32] and is currently being investigated[33]. Wound infections were also found to have a large impact on the need for secondary intervention. Several studies have recorded possible risk factors for wound infections after major vascular surgery and suggested strategies for preventing this[34,35]. Perioperative recommendations to prevent this were use of chlorhexidine, antibiotic prophylaxis, maintenance of normothermia and glucose control[35].

Finally, pneumonia had the greatest effect on prolonged hospitalization with a PAF rate of 13 per cent. Open repair of AAA increases the risk of postoperative complications, and has also been proven to be an important cause of prolonged hospitalization[36]. Enhanced recovery after surgery may contribute to pre-venting pulmonary complications, as improvements following OSR have been previously observed in duration of hospital stay, intake and ambulation[36].

A recent international Delphi study among vascular surgeons analysed the nature and severity of complications following surgery for AAA, carotid artery disease and peripheral artery disease[37]. For patients undergoing open AAA repair, bowel ischaemia and acute myocardial infarction were the two major complications on which consensus was reached. This finding is in concordance with the present study, as these complications (bowel ischaemia, 20 per cent, and myocardial infarction or arrhythmia, 13 per cent) had a great impact on mortality rate.

There are some limitations that apply to this study. First, the DSAA is a national registry, and the possibility of under-reporting of complications exists (registration bias). However, the DSAA registry is mandatory for all national medical centres, and each mandatory variable should be registered before completing a patient's record. Variables to prevent complications, such as antiplatelet medication and postoperative physiotherapy, unfortunately could not be assessed in this study, as the DSAA registry contains no information on these. Second, it was not absolutely evident if a particular complication (for example, arterial occlusion) resulted in a particular outcome (prolonged hospitalization). Third, long-term outcomes (greater than 30 days) were not examined and thus could have underestimated the number of postoperative complications that occur later, such as wound infections.

The strengths of this cohort study are its prospectively registered population-based nationwide set-up, the use of the PAF model while correcting for confounders, large sample size and a complete and validated database.

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Disclosure
H.V. is a consultant for Medtronic, WL Gore, Terumo, Endologix, and Arsenal AAA. Speakers bureau: Abbott. The remaining authors (AG, AA, MK, AV, RB) declare no conflict of interest.

REFENCES

1 Mani K, Lees T, Beiles B, Jensen LP, Venermo M, Simo G, et al. Treatment of abdominal aortic aneurysm in nine countries 2005-2009: A vascunet report. *European Journal of Vascular and Endovascular Surgery* 2011;**42**(5):598–607. Doi: 10.1016/j.ejvs.2011.06.043.

2 Dutch Institute for Clinical Auditing. Dutch Surgical Aneurysm Audit . https://dica.nl/dsaa/home. 04/03/2020.

3 Lijftogt N, Vahl AC, Wilschut ED, Elsman BHP, Amodio S, van Zwet EW, et al. Adjusted Hospital Outcomes of Abdominal Aortic Aneurysm Surgery Reported in the Dutch Surgical Aneurysm Audit. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(4):520–32. Doi: 10.1016/j.ejvs.2016.12.037.

4 Dua A, Kuy S, Lee CJ, Upchurch GR, Desai SS. Epidemiology of aortic aneurysm repair in the United States from 2000 to 2010. *J Vasc Surg* 2014;**59**(6):1512–7. Doi: 10.1016/j.jvs.2014.01.007.

5 Schermerhorn ML, Buck DB, O'Malley AJ, Curran T, McCallum JC, Darling J, et al. Long-Term Outcomes of Abdominal Aortic Aneurysm in the Medicare Population. *New England Journal of Medicine* 2015;**373**(4):328–38. Doi: 10.1056/nejmoa1405778.

6 Karthaus EG, Vahl A, van der Werf LR, Elsman BHP, van Herwaarden JA, Wouters MWJM, et al. Variation in Surgical Treatment of Abdominal Aortic Aneurysms with Small Aortic Diameters in the Netherlands. *Ann Surg* 2020;**271**(4):781–9. Doi: 10.1097/SLA.0000000000003050.

7 Patel R, Sweeting MJ, Powell JT, Greenhalgh RM. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. *The Lancet* 2016;**388**(10058):2366–74. Doi: 10.1016/S0140-6736(16)31135-7.

8 van Schaik TG, Yeung KK, Verhagen HJ, de Bruin JL, van Sambeek MRHM, Balm R, et al. Long-term survival and secondary procedures after open or endovascular repair of abdominal aortic aneurysms. *J Vasc Surg* 2017;**66**(5):1379–89. Doi: 10.1016/j.jvs.2017.05.122.

9 Lederle FA, Kyriakides TC, Stroupe KT, Freischlag JA, Padberg FT, Matsumura JS, et al. Open versus Endovascular Repair of Abdominal Aortic Aneurysm. *New England Journal of Medicine* 2019;**380**(22):2126–35. Doi: 10.1056/NEJMoa1715955.

10 Ploeg AJ, Flu HC, Lardenoye JHP, Hamming JF, Breslau PJ. Assessing the quality of surgical care in vascular surgery; Moving from outcome towards structural and process measures. *European Journal of Vascular and Endovascular Surgery* 2010;**40**(6):696–707. Doi: 10.1016/j.ejvs.2010.05.010.

11 Dua A, Koprowski S, Upchurch G, Lee CJ, Desai SS. Progressive shortfall in open aneurysm experience for vascular surgery trainees with the impact of fenestrated and branched endovascular technology. Journal of Vascular Surgery, vol. 65. Mosby Inc.; 2017. pp. 257–61.

12 Siracuse JJ, Schermerhorn ML, Meltzer AJ, Eslami MH, Kalish JA, Rybin D, et al. Comparison of outcomes after endovascular and open repair of abdominal aortic aneurysms in low-risk patients. *British Journal of Surgery* 2016;**103**(8):989–94. Doi: 10.1002/bjs.10139.

13 Rockhill B, Newman B, Weinberg C. Use and Misuse of Population Attributable Fractions. *Am J Public Health* 2008;**98**:15–9.

14 Poole C. A history of the population attributable fraction and related measures. *Ann Epidemiol* 2015;**25**(3):147–54. Doi: 10.1016/j.annepidem.2014.11.015.

15 Dimick JB, Pronovost PJ, Cowan JA, Lipsett PA. Complications and costs after high-risk surgery: Where should we focus quality improvement initiatives? *J Am Coll Surg* 2003;**196**(5):671–8. Doi: 10.1016/S1072-7515(03)00122-4.

16 Deery SE, O'Donnell TFX, Bodewes TCF, Dalebout BA, Pothof AB, Shean KE, et al. Early reintervention after open and endovascular abdominal aortic aneurysm repair is associated with high mortality. *J Vasc Surg* 2018;**67**(2):433-440.e1. Doi: 10.1016/j.jvs.2017.06.104.

17 Dutch Institute for Clinical Auditing. Dutch Surgical Aneurysm Audit, Eindrapport dataverificatie DSAA. https://dica.nl/media/660/Eindrapport_dataverificatie_DSAA_2016.pdf. 11/06/2022.
18 von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. vol. 370. 2007.
19 Tomee SM, Lijftogt N, Vahl A, Hamming JF, Lindeman JHN. A registry-based rationale for discrete intervention thresholds for open and endovascular elective abdominal aortic aneurysm repair in female patients. *J Vasc Surg* 2018;**67**(3):735–9. Doi: 10.1016/j.jvs.2017.07.123.
20 Dahlqwist E, Zetterqvist J, Pawitan Y, Sjölander A. Model-based estimation of the attributable fraction for cross-sectional, case–control and cohort studies using the R package AF. *Eur J Epidemiol* 2016;**31**(6):575–82. Doi: 10.1007/s10654-016-0137-7.
21 Bennett KM, Kent KC, Schumacher J, Greenberg CC, Scarborough JE. Targeting the most important complications in vascular surgery. *J Vasc Surg* 2017;**65**(3):793–803. Doi: 10.1016/j.jvs.2016.08.107.
22 Budtz-Lilly J, Venermo M, Debus S, Behrendt CA, Altreuther M, Beiles B, et al. Editor's Choice – Assessment of International Outcomes of Intact Abdominal Aortic Aneurysm Repair over 9 Years. *European Journal of Vascular and Endovascular Surgery* 2017;**54**(1):13–20. Doi: 10.1016/j.ejvs.2017.03.003.
23 Perry RJT, Martin MJ, Eckert MJ, Sohn VY, Steele SR. Colonic ischemia complicating open vs endovascular abdominal aortic aneurysm repair. *J Vasc Surg* 2008;**48**(2):272–7. Doi: 10.1016/j.jvs.2008.03.040.
24 Ultee KHJ, Zettervall SL, Soden PA, Darling J, Bertges DJ, Verhagen HJM, et al. Incidence of and risk factors for bowel ischemia after abdominal aortic aneurysm repair. Journal of Vascular Surgery, vol. 64. Mosby Inc.; 2016. pp. 1384–91.
25 Jalalzadeh H, van Leeuwen CF, Indrakusuma R, Balm R, Koelemay MJW. Systematic review and meta-analysis of the risk of bowel ischemia after ruptured abdominal aortic aneurysm repair. *J Vasc Surg* 2018:900–15. Doi: 10.1016/j.jvs.2018.05.018.
26 Willemsen SI, ten Berge MG, Statius van Eps RG, Veger HTC, van Overhagen H, van Dijk LC, et al. Nationwide Study to Predict Colonic Ischemia after Abdominal Aortic Aneurysm Repair in The Netherlands. *Ann Vasc Surg* 2021;**73**:407–16. Doi: 10.1016/j.avsg.2020.11.015.
27 Dariane C, Coscas R, Boulitrop C, Javerliat I, Vilaine E, Goeau-Brissonniere O, et al. Acute Kidney Injury after Open Repair of Intact Abdominal Aortic Aneurysms. *Ann Vasc Surg* 2017:294–300. Doi: 10.1016/j.avsg.2016.09.010.
28 Grant SW, Grayson AD, Grant MJ, Purkayastha D, McCollum CN. What are the risk factors for renal failure following open elective abdominal aortic aneurysm repair? *European Journal of Vascular and Endovascular Surgery* 2012;**43**(2):182–7. Doi: 10.1016/j.ejvs.2011.11.018.
29 Segal R, Lubart E, Leibovitz A, Berkovitch M, Habot B, Yaron M, et al. Early and late effects of low-dose aspirin on renal function in elderly patients. *American Journal of Medicine* 2003;**115**(6):462–6. Doi: 10.1016/S0002-9343(03)00436-4.
30 Lloyd GM, Newton JD, Norwood MGA, Franks SC, Bown MJ, Sayers RD. Patients with abdominal aortic aneurysm: Are we missing the opportunity for cardiovascular risk reduction? *J Vasc Surg* 2004;**40**(4):691–7. Doi: 10.1016/j.jvs.2004.06.039.
31 Wanhainen A, Verzini F, van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(1):8–93. Doi: 10.1016/j.ejvs.2018.09.020.

32 Wiersema AM, Jongkind V, Bruijninckx CMA, Reijnen MMPJ, Vos JA, van Delden OM, et al. CAPPAStudy Group Consensus on Arterial PeriProcedural Anticoagulation. Prophylactic perioperative anti-thrombotics in open and endovascular abdominal aortic aneurysm (AAA) surgery: A systematic review. *European Journal of Vascular and Endovascular Surgery* 2012:359–67. Doi: 10.1016/j.ejvs.2012.06.008.
33 Clinical Trials. ACT Guided Heparinization During Open Abdominal Aortic Aneursym Repair (ACTION-1). https://clinical trials.gov/ct2/show/NCT04061798. 03/03/2021.
34 Wiseman JT, Fernandes-Taylor S, Barnes ML, Saunders RS, Saha S, Havlena J, et al. Predictors of surgical site infection after hospital discharge in patients undergoing major vascular surgery Presented at the 2015 Vascular Annual Meeting of the Society for Vascular Surgery, Chicago, Ill, June 17-20, 2015. Journal of Vascular Surgery, vol. 62. Mosby Inc.; 2015. pp. 1023-1031.e5.
35 Dua A, Desai SS, Seabrook GR, Brown KR, Lewis BD, Rossi PJ, et al. The effect of Surgical Care Improvement Project measures on national trends on surgical site infections in open vascular procedures. Journal of Vascular Surgery, vol. 60. Mosby Inc.; 2014. pp. 1635–9.
36 McGinigle KL, Eldrup-Jorgensen J, McCall R, Freeman NL, Pascarella L, Farber MA, et al. A systematic review of enhanced recovery after surgery for vascular operations. *J Vasc Surg* 2019:629-640.e1. Doi: 10.1016/j.jvs.2019.01.050.
37 de Mik SML, Stubenrouch FE, Legemate DA, Balm R, Ubbink DT, Becquemin JP, et al. Delphi Study to Reach International Consensus Among Vascular Surgeons on Major Arterial Vascular Surgical Complications. *World J Surg* 2019;**43**(9):2328–36. Doi: 10.1007/s00268-019-05038-3.

SUPPLEMENTAL MATERIALS

Table S1: Overview of the registered comorbidities in 2014 up to 2018 and in 2019

Pulmonary comorbidity	Variables
2014-2018	Dyspnea during exercise, invalidating dyspnea, dyspnea at rest, consolidation, fibrosis
2019	Chronic pulmonary diseases, COPD, CARA, emphysema, chronic bronchitis, fibrosis

Cardiac comorbidity	Variables
2014-2018	Medication for hypertension, angina pectoris, diuretics, or digoxin, peripheral edema, coumarins, borderline cardiomyopathy, elevated central venous pressure, cardiomegaly
2019	Hypertension, angina pectoris, myocardial infarction, PTCA, CABG, valvular heart disease, heart valve replacement, atrial fibrillation, heart rhythm disorders, heart failure, congestive heart failure, cardiomyopathy

Table S2: Definitions of complications registered in the DSAA registry

Abdominal	Abdominal abscess, abdominal sepsis, ileus, spleen injury, bowel ischemia, bowel injury, stoma placement, other abdominal complications
Arterial occlusion	(major) amputation, renal artery arterial occlusion, other arterial occlusion (including trash foot)
Prosthesis-/ reconstruction related	Prosthesis infection, Prosthesis migration, other prosthesis-/ reconstruction related complications
Wound	Deep wound infection, fascia dehiscence, other wound complications
Cardiac	Myocardial infarction, cardiac decompensation (failure), cardiac rhythm disturbances, other cardiac complications
Pulmonary	Pneumonia, pulmonary embolism, pneumothorax, other pulmonary complications
Neurological	Cerebrovascular accident, paraplegia, delirium, other neurological complications
Renal	Renal insufficiency (without hemodialysis or requiring hemodialysis)
Rebleeding	Rebleeding
Infection	Infections other than pulmonary and surgical
Other	Other postoperative complications

Table S3: Postoperative complications divided by gender

Complications	Male (%)	Female (%)	P Value
Abdominal sepsis or abscess	10 (0.8)	4 (1.2)	0.764
Bowel ischemia (transmural)	34 (2.6)	13 (3.7)	0.506
Arterial occlusion	39 (3.0)	13 (3.7)	0.457
Wound infection	45 (3.4)	7 (2.0)	0.403
Myocardial infarction or arrhythmia	68 (5.2)	24 (6.9)	0.446
Congestive heart failure	32 (2.4)	14 (4.0)	0.268
Pneumonia	166 (12.7)	49 (14.1)	0.598
Pulmonary (embolism, pneumothorax)	26 (2.0)	13 (3.7)	0.121
Renal insufficiency	85 (6.5)	26 (7.5)	0.478
Rebleeding	19 (1.5)	10 (2.9)	0.115
Cerebrovascular accident or paraplegia	11 (0·8)	0	0.139

PART 2

COMPLEX AORTIC ANEURYSM TREATMENT OUTCOMES

CHAPTER

7

ASSOCIATION OF HOSPITAL VOLUME WITH PERIOPERATIVE MORTALITY OF ENDOVASCULAR REPAIR OF COMPLEX AORTIC ANEURYSMS: A NATIONWIDE COHORT STUDY

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ABSTRACT

Objective

We evaluate nationwide perioperative outcomes of complex EVAR and assess the volume-outcome association of complex EVAR.

Summary Background Data

Endovascular treatment with fenestrated (FEVAR) or branched (BEVAR) endografts is progressively used for excluding complex aortic aneurysms (complex AAs). It is unclear if a volume-outcome association exists in endovascular treatment of complex AAs (complex EVAR).

Methods

All patients prospectively registered in the Dutch Surgical Aneurysm Audit who underwent complex EVAR (FEVAR or BEVAR) between January 2016 and January 2020 were included. The effect of annual hospital volume on perioperative mortality was examined using multivariable logistic regression analyses. Patients were stratified into quartiles based on annual hospital volume to determine hospital volume categories.

Results

We included 694 patients (539 FEVAR patients, 155 BEVAR patients). Perioperative mortality following FEVAR was 4.5% and 5.2% following BEVAR. Postoperative complication rates were 30.1% and 48.7%, respectively. The first quartile hospitals performed <9 procedures/yr; second, third, and fourth quartile hospitals performed 9-12, 13-22, and ≥23 procedures/yr. The highest volume hospitals treated the significantly more complex patients. Perioperative mortality of complex EVAR was 9.1% in hospitals with a volume of <9, and 2.5% in hospitals with a volume of ≥13 (P=0.008). After adjustment for confounders, an annual volume of ≥13 was associated with less perioperative mortality compared to hospitals with a volume of <9.

Conclusions

Data from this nationwide mandatory quality registry shows a significant effect of hospital volume on perioperative mortality following complex EVAR, with high volume complex EVAR centers demonstrating lower mortality rates.

INTRODUCTION

Since the inception of endovascular treatment of abdominal aortic aneurysms (AAAs), endovascular management of complex aortic aneurysms has been of interest, as open surgical procedures are associated with significant mortality and morbidity[1,2]. Complex aortic aneurysms are defined as those including the renal or visceral segment of the aorta[3]. Traditionally, complex aortic aneurysms were treated with open surgical repair (OSR), including suprarenal or supravisceral clamping, since the first generation endografts were unsuitable to treat these aneurysms[3]. Due to reduced mortality and morbidity[3,4], treatment with fenestrated (FEVAR) or branched (BEVAR) endovascular aneurysm repair is progressively used for excluding complex aortic aneurysms[5,6]. Nowadays, many patients with complex aortic aneurysms, including those who are unfit for OSR, are successfully treated with FEVAR or BEVAR (complex EVAR)[7]. Vascular registry data are essential to assess outcomes of new procedures[8]. This is especially relevant for complex EVAR, since randomized controlled trials have not been performed on this matter. Literature on data of FEVAR/BEVAR exists, albeit predominantly from centres of excellence[2,9]. Nationwide outcomes of FEVAR or BEVAR reflecting daily clinical practice have not been reported yet.

FEVAR and BEVAR are considered technically complex procedures, performed in a fragile patient category. The potential influence of hospital volume on perioperative outcomes of these interventions is, therefore, a subject of interest[4,10], especially since an increase in hospital volume has been shown to improve outcomes in other aortic interventions[11–13]. In contrast to AAA repair, both the most recent European Society for Vascular Surgeon (ESVS) guidelines and Society for Vascular Surgery (SVS) guidelines do not advise a minimum caseload per year for complex EVAR[14–17]. Research has established that a volume-outcome relationship exists in open juxtarenal AAA repair[18] and in thoracoabdominal aortic aneurysm repair[19,20], but it is unclear if a volume-outcome relationship exists in FEVAR[4,10] or BEVAR patients.

This study evaluated the nationwide perioperative outcomes of patients who underwent complex EVAR (FEVAR or BEVAR) using data from a mandatory nationwide quality registry. Furthermore, we assessed the association of hospital volume with perioperative mortality of complex EVAR.

METHODS

Study design and data source

The dataset was retrieved from the Dutch Surgical Aneurysm Audit (DSAA), which is a mandatory and prospective quality registry of aneurysm surgery performed by vascular

surgeons. Since 2013, the DSAA prospectively registers all primary abdominal aortic interventions in the Netherlands. Since 2016, endovascular complex aortic aneurysm repair (complex EVAR), including FEVAR and BEVAR, secondary aortic surgery, and/or thoracic or thoracoabdominal aortic aneurysm repair are registered as well. Data verification was conducted through a random sample of hospitals, indicating high reliability of the data[21,22]. Case-ascertainment was 98.4% in a subgroup of 14 hospitals investigated, and completeness of data was verified including mortality and complications[21,22]. The steering committee of the DSAA approved the study protocol. Ethical approval or informed consent was not required for this study according to Dutch law as the data were anonymised. The data in our study was retrospectively analysed and reported according to the STROBE Statement[23].

Study population

All patients that underwent endovascular repair (FEVAR and BEVAR) for an intact complex aortic aneurysm and who were registered in the DSAA between January 1st 2016 and December 31st 2019 were included in this study. Patients that underwent endovascular aortic arch repair were not included in this study. Patients were excluded when data was missing in variables date of birth, date of surgery, sex, and survival status at the time of discharge or 30-days postoperatively. For analyses regarding the total hospital volume of EVAR, all endovascular aortic interventions that were performed in those hospitals that performed complex EVAR between January 1st 2016 and December 31st 2019 were included as well.

Definitions

A patient receiving surgery in two planned stages was included twice in the DSAA and was allocated to the group (FEVAR or BEVAR) of the first intervention. For patient characteristics, length of hospital stay and length of stay at the ICU, the details of the first intervention were reported, for other perioperative outcomes, the outcomes of both stages were reported as one outcome. Variables 'Cardiac comorbidity' and 'Pulmonary comorbidity' were based on the V-POSSUM[24] from 2016 – 2018, and were based on ICD-10 codes in 2019 (**Table S1**). The details in these variables were stratified per patient into the categories 'absent' or 'present'.

Hospital volume

Hospital volume of complex EVAR (FEVAR and BEVAR) was calculated per year and over the 4-year study period, and was reported as the number of patients that underwent an intervention. Hospital volume of total endovascular aortic interventions (per year and over the 4-year study period) was defined as the number of patients that underwent FEVAR and BEVAR, and the total number of all endovascular aortic interventions (which

included all endovascular repairs for ruptured aortic aneurysms, and conventional EVARs and TEVARs). Patients were stratified into quartiles based on the (annual) volume of the hospital in which they underwent complex EVAR to determine the cut-off points for the categories of hospital volumes.

Outcomes

The primary outcome of this study was perioperative mortality. Perioperative mortality was defined as 30-day mortality and in-hospital mortality and included mortality following both stages of complex EVAR when applicable. Secondary outcomes were other perioperative outcomes that occurred within 30 days after complex EVAR (postoperative complications, intraoperative complications, length of stay at ICU, length of hospital stay, reinterventions, readmissions, major complication, and failure to rescue), the association between hospital volume and perioperative mortality, and other factors associated with perioperative mortality. Major complications were defined as either intraoperative or perioperative complications that caused a prolonged stay (threshold: FEVAR: >7 days, BEVAR: >9 days), reintervention, or death[25]. Failure to rescue was defined as the number of patients that died perioperatively divided by the number of patients with a major complication[25]. The annual and overall hospital volume of complex EVAR, all endovascular aortic interventions, FEVAR, and BEVAR, were examined to assess the association between hospital volume and perioperative mortality.

Statistical methods

Patients and aneurysm characteristics and outcomes of both FEVAR and BEVAR were analysed using descriptive statistics. Patients and aneurysm characteristics and outcomes were stratified according to the quartiles of the annual hospital volume of complex EVAR. Differences in categorical variables were tested with Chi-square tests or Fisher's exact tests. The distribution of continuous variables was examined with histograms and Q-Q plots. T-tests were used for normally distributed variables and Mann-Whitney U-tests otherwise. A P-value of ≤0.050 was considered statistically significant.

Univariable and multivariable logistic regression analyses were performed to examine the association between annual hospital volume (based on quartiles) of complex EVAR and perioperative mortality and to identify factors associated with mortality. Covariates used for this analysis were age, sex, pulmonary and cardiac comorbidity, creatinine, haemoglobin, referral, aneurysm diameter, location of the aneurysm, type of surgery, urgency, procedure, number of targeted vessels, and annual hospital volume. The lowest quartile of hospital volume was used as the reference category. Variables with a P-value ≤0.010 in univariable analysis and variables that were considered clinically relevant were included in the multivariable analysis, and outcomes were reported in (adjusted) odds

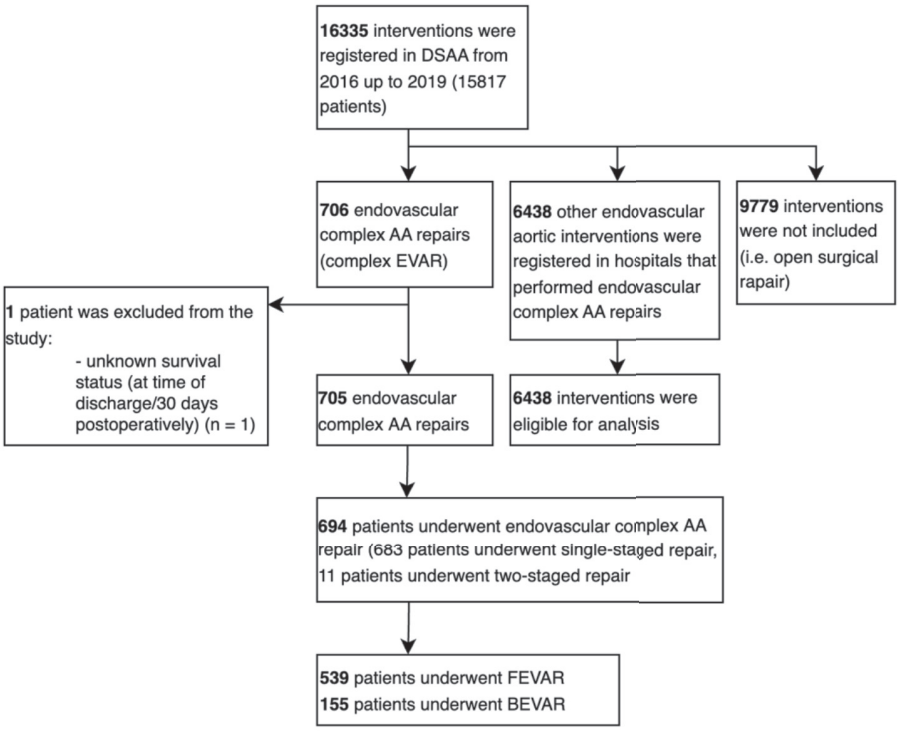
ratios with 95%-CI confidence intervals. Moreover, a multivariable logistic regression model with a restricted cubic spline using 4 knots that account for a non-linear relationship was created to visualize the association between annual hospital volume of complex EVAR and mortality[26]. The associations between hospital volume (continuous and based on quartiles) of all endovascular aortic interventions, hospital volume of FEVAR, hospital volume of BEVAR, and perioperative mortality were examined with univariable analyses.

All analyses were carried out using R, version 4.0.2.

RESULTS

In total, 15817 patients that underwent 16335 interventions in 61 Dutch hospitals were registered in the DSAA between January 1st 2016 and December 31st 2019. In these patients, 706 complex EVAR repairs were registered. After excluding one patient with an unknown survival status, 705 complex EVAR repairs from 28 hospitals were included in this study. In 11 patients, two interventions were registered (median time between these two interventions was 70 days, IQR 33.5 – 118 days), and thus 694 patients were included for further analysis. Of these patients, 539 underwent FEVAR, and 155 underwent BEVAR. For analyses regarding the overall hospital volume of endovascular aortic interventions, 6438 other endovascular aortic interventions were included (**Figure 1**).

Figure 1: Flow chart of included patients



Patient and aneurysm characteristics

An overview of the patient characteristics of all patients as well as stratified for FEVAR and BEVAR is shown in **Table 1**. The mean age of the FEVAR patients was 73.8 years, and the mean age of BEVAR patients was 72.3 years. In FEVAR patients, 12.8% were female, and in BEVAR patients, 38.1% were female. Most patients had cardiac comorbidity (FEVAR: 75.9%, BEVAR; 79.9%). The majority of the patients were referred by another hospital (FEVAR: 50.3%, BEVAR: 67.7%). In the FEVAR group, most patients (70.6%) were treated for a juxtarenal or infrarenal aneurysm, and in the BEVAR group, most patients were treated for a thoracoabdominal aneurysm (84.5%). Of all patients, 75.9% underwent a primary repair, mainly due to atherosclerosis (87.3%).

Table 1: Patient characteristics, aneurysm morphology and operative data of patients following complex EVAR (FEVAR and BEVAR)

	Complex EVAR*	FEVAR	BEVAR
Number of patients	694	539	155
Number of interventions	705	545	160
Number of hospitals	28		
Age, years	73.5 ± 6.6	73.8 ± 6.7	72.3 ± 6.2
Sex: female	128 (18.4)	69 (12.8)	59 (38.1)
Preoperative pulmonary comorbidity			
Absent	453 (66.3)	362 (68.2)	91 (59.9)
Present	230 (33.7)	169 (31.8)	61 (40.1)
Unknown / missing	11	8	3
Preoperative cardiac comorbidity			
Absent	160 (23.2)	129 (24.1)	31 (20.1)
Present	530 (76.8)	407 (75.9)	123 (79.9)
Unknown / missing	4	3	1
Preoperative creatinine, µmol/L	95 [79 – 114]	96 [82 – 114]	88 [72 – 115]
Unknown / missing	26	23	3
Preoperative hemoglobin, mmol/L	8.5 ± 1.0	8.6 ± 1.0	8.3 ± 1.0
Unknown / missing	21	20	1
Aneurysm diameter, mm	63.7 ± 9.4	62.8 ± 9.2	66.8 ± 9.5
Unknown / missing	6	5	1
Location of the aneurysm			
Abdominal: juxtarenal or infrarenal	396 (57.2)	379 (70.6)	17 (11.0)
Abdominal: suprarenal	65 (9.4)	58 (10.8)	7 (4.5)
Thoracoabdominal	231 (33.4)	100 (18.6)	131 (84.5)
Abdominal: unspecified / aorto-iliac	2	2	0
Type of surgery			
Primary	527 (75.9)	409 (75.9)	118 (76.1)
Secondary aortic intervention	167 (24.1)	130 (24.1)	37 (23.9)
Pathogenesis: primary repair			
Atherosclerosis	460 (87.3)	358 (87.5)	102 (86.4)
Inflammatory	4 (0.8)	4 (1.0)	0 (0.0)
Infectious	4 (0.8)	2 (0.5)	2 (1.7)
Dissection	12 (2.3)	7 (1.7)	5 (4.2)

Table 1: *Continued.*

	Complex EVAR*	FEVAR	BEVAR
Connective tissue disease	2 (0.4)	2 (0.5)	0 (0.0)
Unknown	45 (8.5)	36 (8.8)	9 (7.6)
Pathogenesis: secondary aortic intervention			
Infected prosthesis	2 (1.2)	1 (0.8)	1 (2.7)
Endoleak	88 (52.7)	77 (59.2)	11 (29.7)
False aneurysm	7 (4.2)	7 (5.4)	0 (0.0)
New aneurysm**	18 (10.8)	12 (9.2)	6 (16.2)
Progression of aneurysmatic disease	52 (31.1)	33 (25.4)	19 (51.4)
Urgency			
Elective	682 (98.3)	536 (99.4)	146 (94.1)
Urgent intact	12 (1.7)	3 (0.6)	9 (5.9)
Number of targeted vessels			
1-2	136 (19.6)	126 (23.4)	10 (6.5)
3	252 (36.4)	218 (40.5)	34 (21.9)
≥ 4	305 (44.0)	194 (36.1)	111 (71.6)
Unknown / missing	1	1	0

*Values are presented as n (%), mean (SD), or median [interquartile range]. * Complex EVAR: FEVAR and BEVAR. ** Aneurysm on different anatomical location than for which the primary procedure was done.*

Perioperative outcomes

Table 2 shows that the perioperative mortality was 4.5% following FEVAR and 5.2% following BEVAR. Postoperative complication rates were 30.1% following FEVAR and 45.2% following BEVAR. Of all FEVAR patients, 5.9% had a neurological complication (2.4% paraplegia, 0.7% stroke), while 14.8% had a neurological complication following BEVAR (5.2% paraplegia, 1.9% stroke). Intraoperative complications occurred in 11.9% following FEVAR and in 17.4% following BEVAR. The median length of hospital stay was 4 days following FEVAR and 6 days following BEVAR. The reintervention rate was 8.9% following FEVAR and 21.3% following BEVAR.

Table 2: Perioperative outcomes of patients following complex EVAR (FEVAR and BEVAR)

	Complex EVAR*	FEVAR	BEVAR
Number of patients	694	539	155
Perioperative mortality	32 (4.6)	24 (4.5)	8 (5.2)
Postoperative complication	232 (33.4)	162 (30.1)	70 (45.2)
Abdominal complication	30 (4.3)	25 (4.6)	5 (3.2)
Pulmonary complicaton	59 (8.5)	44 (8.2)	15 (9.7)
Cardiac complication	30 (4.3)	22 (4.1)	8 (5.2)
Neurological complication	55 (7.9)	32 (5.9)	23 (14.8)
Paraplegia	21 (3.0)	13 (2.4)	8 (5.2)
Stroke	7 (1.0)	4 (0.7)	3 (1.9)
Prosthesis-/ reconstruction related	17 (2.4)	11 (2.0)	6 (3.9)
Rebleeding	21 (3.0)	13 (2.4)	8 (5.2)
Renal	36 (5.2)	30 (5.6)	6 (3.9)
Wound	14 (2.0)	9 (1.7)	5 (3.2)
Arterial occlusion	26 (3.7)	16 (3.0)	10 (6.5)
Infection	22 (3.2)	10 (1.9)	12 (7.7)
Other	56 (8.1)	39 (7.2)	17 (11.0)
Intraoperative complication	91 (13.1)	64 (11.9)	27 (17.4)
Cardiopulmonary resuscitation / MI	1 (0.1)	0 (0.0)	1 (0.6)
Occlusion of side branch	15 (2.2)	12 (2.2)	3 (1.9)
Type 1 endoleak	17 (2.5)	13 (2.4)	4 (2.6)
Type 3 endoleak	7 (1.0)	4 (0.7)	3 (1.9)
Other	49 (7.1)	35 (6.5)	16 (10.3)
Intra-operative mortality	1 (0.1)	1 (0.2)	0 (0.0)
Missing	1	1	0
Length of stay at ICU	1 [0 - 2]	1 [0 - 1]	2 [1 - 3]
Missing	2	2	0
Length of hospital stay	5 [3 - 7]	4 [3 - 7]	6 [4 - 10]
Missing	9	7	2
Reinterventions	81 (11.7)	48 (8.9)	33 (21.3)
Endovascular	21 (3.0)	12 (2.2)	9 (5.8)
Percutaneous	6 (0.9)	3 (0.6)	3 (1.9)
Endoscopic	1 (0.1)	1 (0.2)	0 (0.0)
Thoraco-laparoscopic	28 (4.0)	16 (3.0)	12 (7.7)

Table 2: *Continued.*

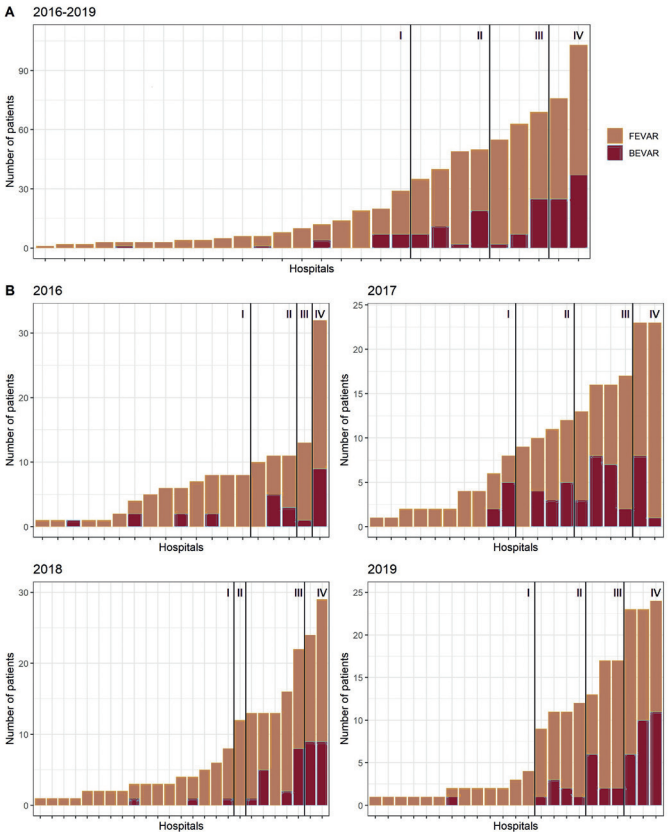
	Complex EVAR*	FEVAR	BEVAR
Open	69 (9.9)	16 (3.0)	9 (5.8)
Readmission	69 (9.9)	52 (9.6)	17 (11.0)
Major complication	159 (22.9)	112 (20.8)	47 (30.3)
Failure to rescue	32/159 (20.1)	24/112 (21.4)	8/47 (17.0)

*Values are presented as n (%), or median [interquartile range]. The specific complications included in the categories of postoperative complications are shown in Table S2.*Complex EVAR: FEVAR and BEVAR*

Hospital volumes

Figure 2 shows the number of patients that underwent FEVAR and BEVAR per hospital. The median annual hospital volume of complex EVAR was 13 patients [IQR 9-23], and the median hospital volume during the 4-year study period was 55 patients [IQR 35-76]. **Figure S1** shows the number of endovascular aortic interventions in hospitals that performed FEVAR and BEVAR. The median overall hospital volume of all endovascular aortic interventions was 304 interventions (IQR 207-357), and the median annual hospital volume was 72 interventions (IQR 52-90). Details regarding volume of FEVAR and BEVAR per hospital are shown in **Table S3.**

Figure 2: (A) Overall number of patients per hospital that underwent complex EVAR (FEVAR and BEVAR), including quartiles of overall hospital volume (I: < 35, II: 35-54, III: 55-75, IV: ≥ 76). (B) Annual number of patients per hospital that underwent complex EVAR (FEVAR and BEVAR), including quartiles of annual hospital volume (I: < 9, II: 9-12, III: 13-22, IV: 23))



Patient and aneurysm characteristics and perioperative outcomes, stratified per quartile of annual hospital volume of complex EVAR

Patient and aneurysm characteristics and perioperative outcomes, stratified per quartile of annual hospital volume of complex EVAR, are shown in **Table S4.** In 2019, 13/23 hospitals treated less than 9 patients. In hospitals with an annual volume of <9, 9.5% of the patients were female, while in hospitals with an annual volume of ≥23, 24.9% were female. The percentage of cardiac comorbidity was higher in hospitals with a higher annual volume. In hospitals with an annual volume of ≥23, 66.2% of the patients were referred by another hospital. Hospitals with a higher annual volume performed more BEVAR and more secondary aortic interventions than lower-volume hospitals. Perioperative mortality rates were 9.1% in hospitals with an annual volume <9, 5.4% in hospitals with an annual volume of 9-12, and 2.5% in hospitals with an annual volume of 13-22 and ≥23 (p = 0.008)

(shown in **Figure S2**). The percentage of postoperative complication rates did not differ between the hospital volume categories (35.2%, 31.0%, 33.7%, and 33.3% in hospitals with an annual volume of <9, 9-12, 13-12, and ≥23). Also, the percentage of major complications and failure to rescue did not differ statistically significantly between the hospital volume categories (**Table S4**).

Association of annual hospital volume of complex EVAR with mortality

Factors associated with mortality following univariable and multivariable analysis are shown in **Table 3**. An annual volume of complex EVAR of 13-22 and ≥23 was significantly associated with less mortality compared to an annual volume of <9 after adjustment for confounders (13-22: aOR 0.11, 95%-CI 0.02-0.37, ≥23: aOR 0.14, 95%-CI 0.04-0.42, ref: <9). Other factors associated with mortality were female sex (aOR 3.37, 95%-CI 1.77-6.43) and aneurysm diameter (aOR 1.05, 95%-CI 1.00-1.09). **Figure 3** shows the restricted cubic spline, which visualizes the non-linear association between annual hospital volume and mortality of complex EVAR after adjustment for confounders.

Table 3: Univariable and multivariable analyses to assess whether annual hospital volume of complex EVAR (FEVAR + BEVAR) is associated with increased perioperative mortality of complex EVAR

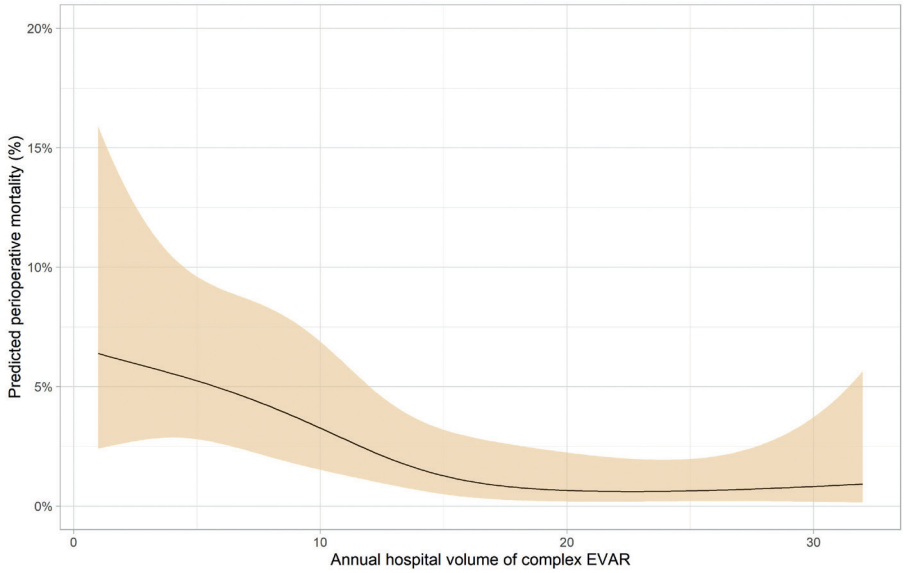
	No. of patients	Univariable analysis		Multivariable analysis	
		OR (95%-CI)	P	aOR (95%-CI)	P
Annual volume of complex EVAR					
<9	165	Ref.		Ref.	
9-12	129	0.57 (0.21 – 1.41)	0.24	0.44 (0.16 – 1.12)	0.096
13-22	199	0.26 (0.08 – 0.68)	0.010	0.11 (0.02 – 0.37)	0.001
≥ 23	201	0.26 (0.08 – 0.67)	0.010	0.14 (0.04 – 0.42)	<0.001
Age, years		1.03 (0.98 – 1.09)	0.256		
Sex					
Male	566	Ref.		Ref.	
Female	128	2.30 (1.35 – 3.85)	0.002	3.37 (1.77 – 6.43)	<0.001
Pulmonary comorbidity					
Absent	453	Ref.			
Present	230	1.91 (0.92 – 3.94)	0.081	1.75 (0.79 – 3.85)	0.164
Missing	11				
Cardiac comorbidity					
Absent	160	Ref.			
Present	530	1.04 (0.46 – 2.65)	0.935		
Missing	4				
Preoperative creatinine		1.003 (0.998 – 1.007)	0.151		
Preoperative haemoglobin		0.85 (0.53 – 1.04)	0.085	0.77 (0.53 – 1.13)	0.177
Referral					
General practitioner	124	Ref.			
Emergency department	10	1.86 (0.09 – 12.22)	0.582		

Table 3: *Continued.*

	No. of patients	Univariable analysis		Multivariable analysis	
		OR (95%-CI)	P	aOR (95%-CI)	P
Other hospital	373	0.80 (0.34 – 2.11)	0.625		
Medical specialist in own hospital	181	0.67 (0.22 – 2.01)	0.469		
Missing	6				
Aneurysm diameter		1.03 (0.996 – 1.07)	0.074	1.05 (1.00 – 1.09)	0.024
Location of the aneurysm					
Abdominal: juxtarenal or infrarenal	396	Ref.			
Abdominal: suprarenal	65	0.75 (0.11 – 2.74)	0.711		
Thoracoabdominal	231	1.53 (0.72 – 3.21)	0.256		
Type of surgery					
Primary	522	Ref.			
Secondary aortic intervention	167	0.72 (0.26 – 1.66)	0.473		
Urgency					
Elective	682	Ref.			
Urgent intact	12	1.91 (0.10 – 10.29)	0.542		
Procedure*					
FEVAR	539	Ref.			
BEVAR	155	1.17 (0.48 – 2.55)	0.711	0.71 (0.24 – 1.82)	0.492
Number of targeted vessels					
1 - 2	136	Ref.			
3	252	0.45 (0.14 - 1.38)	0.158		
≥ 4	305	1.22 (0.52 – 3.20)	0.656		
Missing	1				

*OR indicates Odds Ratio, CI indicates confidence interval. *Included in multivariable analysis due to clinical relevance.*

Figure 3: Association between annual hospital volume and perioperative mortality for complex EVAR (FEVAR and BEVAR): restricted cubic spline (4 knots), including adjustment for confounders



Association of (annual and overall) hospital volume of FEVAR, BEVAR, and all endovascular aortic interventions with mortality

Table S5 shows that an overall volume of complex EVAR of 35-54, 55-75, and ≥76 in 4 years was associated with less mortality compared to an overall volume of <35. In FEVAR patients, a higher overall volume, as well as a higher annual volume, were associated with less mortality in FEVAR patients. In BEVAR patients, no associations between hospital volume and mortality were found, likely due to a low number of BEVAR patients. An overall volume of 207-303 total endovascular aortic interventions was associated with less perioperative mortality of complex EVAR compared to an overall volume of <207, while higher overall volumes (304-346, ≥347) were not associated with less mortality compared to an overall volume of 207-303. Moreover, a higher annual volume of total endovascular aortic interventions was not associated with less mortality of complex EVAR.

DISCUSSION

This population-based study that includes data from a nationwide mandatory quality registry describes the association between hospital volume and mortality in patients that underwent complex EVAR (FEVAR and BEVAR). In the entire cohort, the perioperative mortality rate was 4.6%. In the Dutch setting, perioperative mortality rates of complex

EVAR were 2.5% in hospitals with an annual volume of complex EVAR of 13 or more, while perioperative mortality rates were 9.1% in hospitals with an annual volume of less than 9. After adjustment for confounders, an annual hospital volume of complex EVAR of 13-22 and ≥23 was significantly associated with lower perioperative mortality compared to an annual hospital volume of <9.

The perioperative mortality as reported in our study appears to be consistent with the literature. However, no results of complex EVAR from a mandatory nationwide quality registry have been published previously, which makes it challenging to make a valid comparison with other studies as smaller cohort studies are more prone to selection bias and heterogeneity in reporting. Furthermore, these former studies mainly describe outcomes from centers of excellence. A meta-analysis reporting on endovascular TAAA repair (branched or fenestrated endografts) described hospital mortality or 30-day mortality of 7.4%[27], and a meta-analysis describing FEVAR of juxtarenal aneurysms reported a pooled early postoperative mortality of 3.3%[28]. Recent published large observational cohort studies, not included in the meta-analyses, reported perioperative mortality rates of 1.8-3.9% following FEVAR[9,24,29] and 2.7% following a physician modified endograft[29], while mortality rates of F/BEVAR for thoracoabdominal aortic aneurysms as reported by German administrative data were 9.2%[19]. Although our study also includes less favourable results of low-volume hospitals, the 4.6% overall mortality rate is in line with previous literature but could potentially improve further with centralisation of care.

Previous studies reporting the association between hospital volume and mortality in complex EVAR (FEVAR and BEVAR) did not show any hospital volume-outcome relationship. One observational study that compared low-volume (<4 FEVAR/year) and high-volume (4-6 FEVAR/year) hospitals did not demonstrate a hospital volume-outcome relationship of FEVAR[4], and a recent systematic review found no evidence of whether hospital volume affects mortality in FEVAR patients[10]. Our study describes the results of complex EVAR from a mandatory nationwide registry and examines the association between hospital volume and perioperative mortality of complex EVAR. This nationwide study design is important in revealing the association between hospital volume and mortality as no minimum number of complex EVAR was required in the Netherlands during the study period, and consequently, many low-volume hospitals were included. Furthermore, the substantial risk of complex EVAR on perioperative mortality might also have played a role in revealing a volume-outcome relationship[30]. Other studies reporting on thoracic aortic aneurysms (TAAs) and thoracoabdominal aortic aneurysms (TAAAs) did describe the influence of hospital volume on perioperative outcomes. A high annual hospital volume (≥13) of thoracic aortic aneurysms (TAAs), treated with FEVAR/BEVAR, open surgical repair, or hybrid, was significantly associated with less mortality[19]. Moreover, lower morbidity and

mortality was shown in high volume hospitals (annual volume >22) performing complex EVAR including TEVAR for thoracoabdominal aortic aneurysms [20]. Also, a low annual hospital volume (<9) of open juxtarenal repair was associated with higher perioperative mortality[18].

Several studies have shown associations between the number of aortic interventions and outcomes[31–33]. Since infrarenal endovascular aneurysm repair has been centralized in the United Kingdom, mortality rates following these interventions have dropped from 1.5% to 0.9% following EVAR and from 5.4% to 4.0% following OSR[11]. Defining the optimal threshold or cut-off is difficult and might differ between countries[34–36]. Therefore, it is vital to investigate the volume-outcome associations of complex EVAR in specific healthcare systems. Other countries (USA, UK, Germany) do not have any specific requirements for a minimum hospital volume of complex EVAR[37,38]. The reason for this is that there is no scientific data on this subject, as our paper is the first describing a volume-outcome relationship for complex endovascular aortic procedures. The data derived from this study seems to indicate that one should not perform fewer than nine complex procedures per hospital annually in the Netherlands and that an annual volume of at least 13 complex EVAR procedures appears to result in better outcomes. Furthermore, in our spline diagram the reduction of mortality is even observed until 20 cases per year. Therefore, as in many surgical procedures and outcomes: annual caseload does matter. Above this volume, there is very little incremental benefit in perioperative mortality by increasing center volume. In addition, a minimum number of total endovascular aortic interventions does not seem to be essential for low mortality rates of complex EVAR. Complex EVAR procedures are technically complex procedures, and it could be hypothesized that specific expertise from the vascular surgeon and team in treating complex EVAR is more important than a high institutional knowledge created by a high volume of standard EVAR. Finally, although failure to rescue appeared higher in low-volume hospitals (38.5%), the difference in failure to rescue between the volume categories was not statistically significant. This could be a result of treating more complex aneurysmal disease as well as patients with more comorbidities in higher volume hospitals masking the true effect of failure to rescue on hospital mortality. It is described that in intact AAA-repairs, an increase in hospital volume is significantly associated with less failure to rescue, which could be caused due to prompt recognition and management of complications in large volume hospitals[33].

Spinal cord ischemia as well as cerebral embolism are the most feared complications following management of thoracic aortic aneurysms[15] and complex aortic aneurysms[39]. Previous studies have reported paraplegia rates of 4.1% and 5.2% following FEVAR and BEVAR[27,40], which is in accordance with our present results. Also, the stroke rates following FEVAR and BEVAR reported by this study were consistent with the literature[41,42]. The

reintervention rate is frequently reported when endovascular repair is compared with open surgical repair. Interestingly, this study reported a considerable number of reinterventions within 30 days following BEVAR (21.3%). Although the DSAA included some details regarding the nature of the reinterventions, the exact cause of the reinterventions remains unclear. Future improvement seems possible, given the high rate of reinterventions. Multivariable analysis showed that female sex was associated with higher perioperative mortality following complex EVAR, which was not consistent with current literature that describes that females have similar mortality rates as males following fenestrated-branched EVAR for treatment of TAAA[43]. Although we found that high-volume hospitals treated more female patients than low-volume hospitals, mortality rates were lower in high-volume hospitals. The number of targeted vessels was not associated with mortality, which was in agreement with previous studies[44,45], but contrary to another study that suggests that incorporating additional visceral vessels is significantly associated with increased mortality[46]. Our study showed that low-volume hospitals treated aneurysms with less targeted vessels than high-volume hospitals, suggesting that low-volume hospitals treat less extensive aneurysms. Furthermore, as previously reported[47], our study did not find an association between preoperative creatinine and perioperative mortality. Future studies are needed to verify factors associated with perioperative mortality.

The strength of this study is the unique nationwide study design using data from a mandatory quality registry. One limitation is that our data is retrieved from a nationwide quality registry, which is not primarily designed for scientific purposes and registers a limited number of variables. Consequently, the description of clinical and aneurysm characteristics is limited, and therefore, we could not report this study according to the reporting standards of endovascular aortic repair of aneurysm involving the renal-mesenteric arteries[48]. Secondly, the definitions of variables 'location of the aneurysm', 'FEVAR', and 'BEVAR' in the DSAA might have been interpreted differently by treating physicians, which could have induced selection bias. The reported location of the aneurysm might have been influenced by interobserver variability as some clinicians could have reported the location of the aneurysm by the anatomic extent of the aortic disease, while others might have reported it by the extent of the repair. Moreover, patients who received an endograft with a combination of fenestrations and branches are registered in either the FEVAR or BEVAR category, based on local clinical opinion, although this probably includes very few patients. Therefore, we choose to report the volume-outcome association of the entire cohort of FEVAR and BEVAR patients. Thirdly, we could only report on hospital volume and not on surgeon volume, as surgeon volume is not registered in the DSAA. For open AAA surgery, a lower surgeon annual volume was associated with higher 30-day mortality[11].

In conclusion, this nationwide population-based study with data from 539 FEVAR and 155 BEVAR patients provides an unique overview of perioperative outcomes following FEVAR and BEVAR, including a significant effect of hospital volume of complex EVAR on perioperative mortality with high volume complex EVAR centers showing lower mortality. An annual caseload of at least 9 complex EVAR procedures seems to be the minimum requirement to significantly reduce mortality in this group of patients, while an annual volume of at least 13 appears to result in better outcomes. At 20 cases, the optimum annual caseload and mortality is achieved, suggesting this should be our national threshold.

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Disclosures

Conflicts of interest: JW: Consultant for Cordis/Cardinal Health, former consultant for Baxter; JvH: Consultant/ proctor for Terumo Aortic, Cook, Microport, WL Gore and Philips; BM: Consultant for Philips; CZ: Consultant for Terumo Aortic; GS: Consultant for Cook and Philips; HV: Consultant for Medtronic, WL Gore, Terumo, Endologix, and Philips

REFERENCES

1 Latz CA, Boitano L, Schwartz S, Swerdlow N, Dansey K, Varkevisser RRB, et al. Editor's Choice – Mortality is High Following Elective Open Repair of Complex Abdominal Aortic Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2021;**61**(1):90–7. Doi: 10.1016/j.ejvs.2020.09.002.

2 Varkevisser RRB, O'Donnell TFX, Swerdlow NJ, Liang P, Li C, Ultee KHJ, et al. Fenestrated endovascular aneurysm repair is associated with lower perioperative morbidity and mortality compared with open repair for complex abdominal aortic aneurysms. *J Vasc Surg* 2019;**69**(6):1670–8. Doi: 10.1016/j.jvs.2018.08.192.

3 Swerdlow NJ, Wu WW, Schermerhorn ML. Open and endovascular management of aortic aneurysms. *Circ Res* 2019;**124**(4):647–61. Doi: 10.1161/CIRCRESAHA.118.313186.

4 Davis FM, Albright J, Battaglia M, Eliason J, Coleman D, Mouawad N, et al. Fenestrated repair improves perioperative outcomes but lacks a hospital volume association for complex abdominal aortic aneurysms. *J Vasc Surg* 2020;**73**(2):417-425.e1. Doi: 10.1016/j.jvs.2020.05.039.

5 Suckow BD, Goodney PP, Columbo JA, Kang R, Stone DH, Sedrakyan A, et al. National trends in open surgical, endovascular, and branched-fenestrated endovascular aortic aneurysm repair in Medicare patients. *J Vasc Surg* 2018;**67**(6):1690-1697.e1. Doi: 10.1016/j.jvs.2017.09.046.

6 Cross J, Richards T. Current practice of aneurysm management in the UK. *Ann R Coll Surg Engl* 2014;**96**(1):27–31. Doi: 10.1308/003588414X13824511650416.

7 Tran K, Lee AM, McFarland GE, Sgroi MD, Lee JT. Complex endovascular aneurysm repair is associated with higher perioperative mortality but not late mortality compared with infrarenal endovascular aneurysm repair among octogenarians. *J Vasc Surg* 2019;**69**(2):327–33. Doi: 10.1016/j.jvs.2018.04.064.

8 de Guerre L, Venermo M, Mani K, Wanhainen A, Schermerhorn M. Paradigm shifts in abdominal aortic aneurysm management based on vascular registries. *J Intern Med* 2020:1–13. Doi: 10.1111/joim.13051.

9 Pini R, Giordano J, Ferri M, Palmieri B, Solcia M, Michelagnoli S, et al. The Italian Multicentre Registry of Fenestrated Anaconda™ Endografts for Complex Abdominal Aortic Aneurysms Repair. *European Journal of Vascular and Endovascular Surgery* 2020;**60**(2):181–91. Doi: 10.1016/j.ejvs.2020.04.032.

10 Saricilar EC, Iliopoulos J, Ahmad M. A systematic review of the effect of surgeon and hospital volume on survival in aortic, thoracic and fenestrated endovascular aneurysm repair. *J Vasc Surg* 2021;**74**(1):287–95. Doi: 10.1016/j.jvs.2020.12.104.

11 Gray WK, Day J, Horrocks M. Volume e Outcome Relationships in Elective Abdominal Aortic Aneurysm Surgery : Analysis of the UK Hospital Episodes Statistics Database for the Getting It Right First Time (GIRFT) Programme. *European Journal of Vascular & Endovascular Surgery* 2020;(xxxx). Doi: 10.1016/j.ejvs.2020.07.069.

12 Landon BE, O'Malley AJ, Giles K, Cotterill P, Schermerhorn ML. Volume-outcome relationships and abdominal aortic aneurysm repair. *Circulation* 2010;**122**(13):1290–7. Doi: 10.1161/CIRCULATIONAHA.110.949172.

13 Holt PJE, Poloniecki JD, Gerrard D, Loftus IM, Thompson MM. Meta-analysis and systematic review of the relationship between volume and outcome in abdominal aortic aneurysm surgery. *British Journal of Surgery* 2007;**94**(4):395–403. Doi: 10.1002/bjs.5710.

14 Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(1):8–93. Doi: 10.1016/j.ejvs.2018.09.020.
15 Riambau V, Böckler D, Brunkwall J, Cao P, Chiesa R, Coppi G, et al. Editor's Choice – Management of Descending Thoracic Aorta Diseases: Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). *European Journal of Vascular and Endovascular Surgery* 2017;**53**(1):4–52. Doi: 10.1016/j.ejvs.2016.06.005.
16 Oderich GS, Forbes TL, Chaer R, Davies MG, Lindsay TF, Mastracci T, et al. Reporting standards for endovascular aortic repair of aneurysms involving the renal-mesenteric arteries. *J Vasc Surg* 2021;**73**(1):4S-52S. Doi: 10.1016/j.jvs.2020.06.011.
17 Chaikof EL, Dalman RL, Eskandari MK, Jackson BM, Lee WA, Mansour MA, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg* 2018;**67**(1):2-77.e2. Doi: 10.1016/j.jvs.2017.10.044.
18 O'Donnell TFX, Boitano LT, Deery SE, Lancaster RT, Siracuse JJ, Schermerhorn ML, et al. Hospital Volume Matters: The Volume-Outcome Relationship in Open Juxtarenal AAA Repair. *Ann Surg* 2020;**271**(1):184–90. Doi: 10.1097/SLA.0000000000002873.
19 Geisbüsch S, Kuehnl A, Salvermoser M, Reutersberg B, Trenner M, Eckstein HH. Editor's Choice – Hospital Incidence, Treatment, and In Hospital Mortality Following Open and Endovascular Surgery for Thoraco-abdominal Aortic Aneurysms in Germany from 2005 to 2014: Secondary Data Analysis of the Nationwide German DRG Microdata. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(4):488–98. Doi: 10.1016/j.ejvs.2018.10.030.
20 Locham S, Hussain F, Dakour-Aridi H, Barleben A, Lane JS, Malas M. Hospital Volume Impacts the Outcomes of Endovascular Repair of Thoracoabdominal Aortic Aneurysms. *Ann Vasc Surg* 2020;**67**(October 2019):232-241.e2. Doi: 10.1016/j.avsg.2019.09.018.
21 Dutch Institute for Clinical Auditing. Eindrapport dataverificatie DSAA. https://dica.nl/media/660/Eindrapport_dataverificatie_DSAA_2016.pdf. 05/11/2020.
22 van der Werf LR, Voeten SC, van Loe CMM, Karthaus EG, Wouters MWJM, Prins HA. Data verification of nationwide clinical quality registries. *BJS Open* 2019;**3**(6):857–64. Doi: 10.1002/bjs5.50209.
23 STROBE Statement- checklist of items that should be included in reports of observational studies. https://www.strobe-statement.org/fileadmin/Strobe/uploads/checklists/STROBE_checklist_v4_combined.pdf. 08/11/2020.
24 Copeland GP, Jones D, Walters M. POSSUM: A scoring system for surgical audit. *British Journal of Surgery* 1991;**78**(3):355–60. Doi: 10.1002/bjs.1800780327.
25 Lijftogt N, Karthaus EG, Vahl A, van Zwet EW, van der Willik EM, Tollenaar RAEM, et al. Failure to Rescue – a Closer Look at Mortality Rates Has No Added Value for Hospital Comparisons but Is Useful for Team Quality Assessment in Abdominal Aortic Aneurysm Surgery in The Netherlands. *European Journal of Vascular and Endovascular Surgery* 2018;**56**(5):652–61. Doi: 10.1016/j.ejvs.2018.06.062.
26 Gauthier J, Wu Q V., Gooley TA. Cubic splines to model relationships between continuous variables and outcomes: a guide for clinicians. *Bone Marrow Transplant* 2020;**55**(4):675–80. Doi: 10.1038/s41409-019-0679-x.
27 Rocha R V., Lindsay TF, Friedrich JO, Shan S, Sinha S, Yanagawa B, et al. Systematic review of contemporary outcomes of endovascular and open thoracoabdominal aortic aneurysm repair. *J Vasc Surg* 2020;**71**(4):1396-1412.e12. Doi: 10.1016/j.jvs.2019.06.216.
28 Jones AD, Waduud MA, Walker P, Stocken D, Bailey MA, Scott DJA. Meta-analysis of fenestrated endovascular aneurysm repair versus open surgical repair of juxtarenal abdominal aortic aneurysms over the last 10 years. *BJS Open* 2019;**3**(5):572–84. Doi: 10.1002/bjs5.50178.

29 O'Donnell TFX, Patel VI, Deery SE, Li C, Swerdlow NJ, Liang P, et al. The state of complex endovascular abdominal aortic aneurysm repairs in the Vascular Quality Initiative. *J Vasc Surg* 2019;**70**(2):369–80. Doi: 10.1016/j.jvs.2018.11.021.
30 Halm EA, Lee C, Chassin MR. Is volume related to outcome in health care? A systematic review and methodologic critique of the literature. *Ann Intern Med* 2002;**137**:511–20. Doi: 10.7326/0003-4819-137-6-200209170-00012.
31 Landon BE, O'Malley AJ, Giles K, Cotterill P, Schermerhorn ML. Volume-outcome relationships and abdominal aortic aneurysm repair. *Circulation* 2010;**122**(13):1290–7. Doi: 10.1161/CIRCULATIONAHA.110.949172.
32 Holt PJE, Poloniecki JD, Gerrard D, Loftus IM, Thompson MM. Meta-analysis and systematic review of the relationship between volume and outcome in abdominal aortic aneurysm surgery. *British Journal of Surgery* 2007;**94**(4):395–403. Doi: 10.1002/bjs.5710.
33 D'Oria, Mario; Scali, Salvatore; Mao, Jialin; Stone, David; Sedrakya, Art; Eldrup, Nikolaj; Venermo, Maarit; Cassar, Kevin; Altreuther, Martin; Boyle, Jonathan R; Behrent, Christian-Alexander; Beck, Adam. W.; Mani K. Association between Hospital Volume and Failure to Rescue after Open or Endovascular Repair of Intact Abdominal Aortic Aneurysms in the VASCUNET and International Consortium of Vascular Registries. *Ann Surg* 2021. Doi: 10.1097/SLA.0000000000005044.
34 Beck AW, Sedrakyan A, Mao J, Venermo M, Faizer R, Debus S, et al. Variations in Abdominal Aortic Aneurysm Care: A Report from the International Consortium of Vascular Registries. *Circulation* 2016;**134**(24):1948–58. Doi: 10.1161/CIRCULATIONAHA.116.024870.
35 Phillips P, Poku E, Essat M, Woods HB, Goka EA, Kaltenthaler EC, et al. Procedure Volume and the Association with Short-term Mortality Following Abdominal Aortic Aneurysm Repair in European Populations: A Systematic Review. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(1):77–88. Doi: 10.1016/j.ejvs.2016.10.007.
36 Scali ST, Beck A, Sedrakyan A, Mao J, Behrendt CA, Boyle JR, et al. Optimal Threshold for the Volume–Outcome Relationship After Open AAA Repair in the Endovascular Era: Analysis of the International Consortium of Vascular Registries. *European Journal of Vascular and Endovascular Surgery* 2021;(xxxx). Doi: 10.1016/j.ejvs.2021.02.018.
37 Debus ES. S3-Leitlinie zum Screening, Diagnostik Therapie und Nachsorge des Bauchaortenaneurysmas. *Gefässchirurgie* 2018;**23**(6):402–3. Doi: 10.1007/s00772-018-0452-2.
38 Waton S, Johal A, Birmpili P, Li Q, Cromwell D, Pherwani A, O'Neill R BJ. National Vascular Registry: 2020 Annual report. *London: The Royal College of Surgeons of England* 2020;(November).
39 Spanos K, Kölbel T, Kubitz JC, Wipper S, Konstantinou N, Heidemann F, et al. Risk of spinal cord ischemia after fenestrated or branched endovascular repair of complex aortic aneurysms. *J Vasc Surg* 2019;**69**(2):357–66. Doi: 10.1016/j.jvs.2018.05.216.
40 Spanos K, Kölbel T, Kubitz JC, Wipper S, Konstantinou N, Heidemann F, et al. Risk of spinal cord ischemia after fenestrated or branched endovascular repair of complex aortic aneurysms. *J Vasc Surg* 2019;**69**(2):357–66. Doi: 10.1016/j.jvs.2018.05.216.
41 Westin GG, Rockman CB, Sadek M, Ramkhelawon B, Cambria MR, Silvestro M, et al. Increased ischemic complications in fenestrated and branched endovascular abdominal aortic repair compared with standard endovascular aortic repair. *J Vasc Surg* 2020;**72**(1):36–43. Doi: 10.1016/j.jvs.2019.09.044.
42 Diamond KR, Simons JP, Crawford AS, Arous EJ, Judelson DR, Aiello F, et al. Effect of thoracoabdominal aortic aneurysm extent on outcomes in patients undergoing fenestrated/branched endovascular aneurysm repair. *J Vasc Surg* 2021. Doi: 10.1016/j.jvs.2021.01.062.

43 Edman NI, Schanzer A, Crawford A, Oderich GS, Farber MA, Schneider DB, et al. Sex-related outcomes after fenestrated-branched endovascular aneurysm repair for thoracoabdominal aortic aneurysms in the U.S. Fenestrated and Branched Aortic Research Consortium. *J Vasc Surg* 2021:1–10. Doi: 10.1016/j.jvs.2021.02.046.
44 Katsargyris A, Oikonomou K, Kouvelos G, Mufty H, Ritter W, Verhoeven ELG. Comparison of outcomes for double fenestrated endovascular aneurysm repair versus triple or quadruple fenestrated endovascular aneurysm repair in the treatment of complex abdominal aortic aneurysms. *J Vasc Surg* 2017;**66**(1):29–36. Doi: 10.1016/j.jvs.2016.11.043.
45 Oikonomou K, Kasprzak P, Schierling W, Kopp R, Pfister K. Graft complexity-related outcomes of fenestrated endografting for abdominal aortic aneurysms. *Journal of Endovascular Therapy* 2017;**24**(2):230–6. Doi: 10.1177/1526602817691752.
46 Patel SD, Constantinou J, Simring D, Ramirez M, Agu O, Hamilton H, et al. Results of complex aortic stent grafting of abdominal aortic aneurysms stratified according to the proximal landing zone using the Society for Vascular Surgery classification. *J Vasc Surg* 2015;**62**(2):319-325.e2. Doi: 10.1016/j.jvs.2015.03.035.
47 Cajas-Monson L, D'Oria M, Tenorio E, Mendes BC, Oderich GS, DeMartino RR. Effect of renal function on patient survival after endovascular thoracoabdominal and pararenal aortic aneurysm repair. *J Vasc Surg* 2021:1–7. Doi: 10.1016/j.jvs.2020.11.040.
48 Oderich GS, Forbes TL, Chaer R, Davies MG, Lindsay TF, Mastracci T, et al. Reporting standards for endovascular aortic repair of aneurysms involving the renal-mesenteric arteries. *J Vasc Surg* 2021;**73**(1):4S-52S. Doi: 10.1016/j.jvs.2020.06.011.

SUPPLEMENTAL MATERIAL

Figure S1: Number of FEVAR, BEVAR, and other endovascular aortic interventions per hospital (2016-2019)

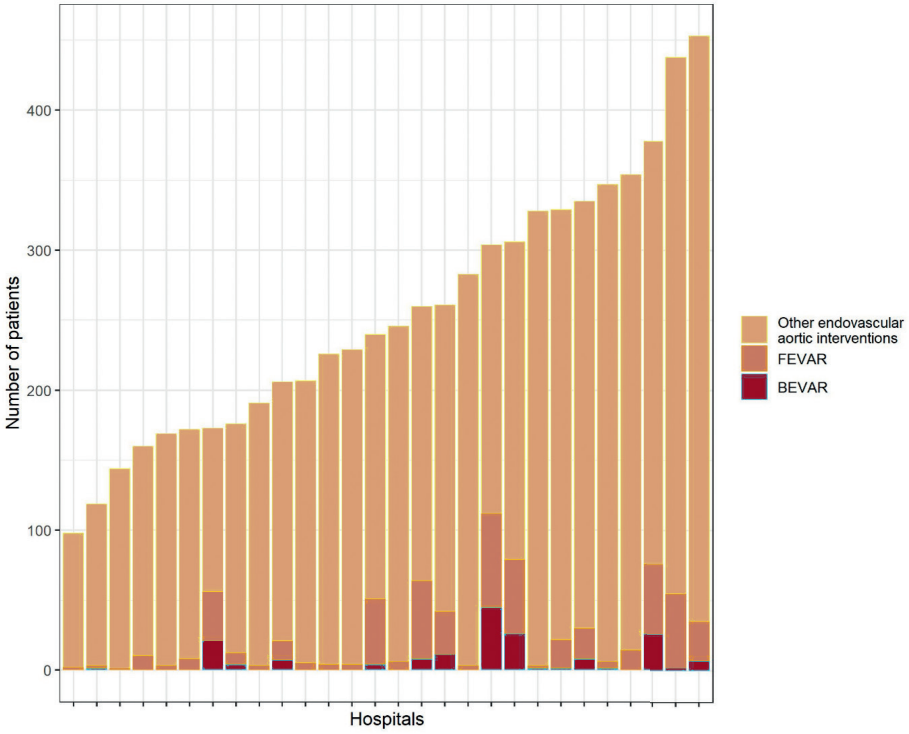

Figure S2: Perioperative mortality, stratified per quartile of annual hospital volume of complex EVAR (FEVAR and BEVAR)

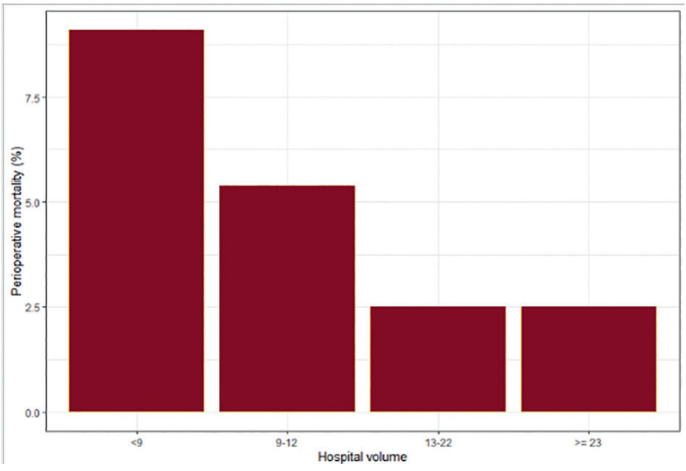

Table S1

Pulmonary comorbidity	Variables
2014-2018	Dyspnea during exercise, invalidating dyspnea, dyspnea at rest, consolidation, fibrosis
2019	Chronic pulmonary diseases, COPD, CARA, emphysema, chronic bronchitis, fibrosis

Cardiac comorbidity	Variables
2014-2018	Medication for hypertension, angina pectoris, diuretics, or digoxin, peripheral edema, coumarins, borderline cardiomyopathy, elevated central venous pressure, cardiomegaly
2019	Hypertension, angina pectoris, myocardial infarction, PTCA, CABG, valvular heart disease, heart valve replacement, atrial fibrillation, heart rhythm disorders, heart failure, congestive heart failure, cardiomyopathy

Table S2

Categories of postoperative complications	Specific complications
Abdominal	Abdominal abscess, abdominal sepsis, ileus, spleen injury, bowel ischemia, bowel injury, stoma placement, other abdominal complications
Pulmonary	Pneumonia, pulmonary embolism, pneumothorax, other pulmonary complications
Cardiac	Myocardial infarction, cardiac decompensation (failure), cardiac rhythm disturbances, other cardiac complications
Neurological	Stroke, paraplegia, delirium, other neurological complications
Prosthesis-/ reconstruction related	Prosthesis infection, Prosthesis migration, other prosthesis-/ reconstruction related complications
Rebleeding	Rebleeding
Renal	Renal insufficiency (without hemodialysis or requiring hemodialysis)
Wound	Deep wound infection, fascia dehiscence, other wound complications
Arterial occlusion	(major) amputation, renal artery arterial occlusion, other arterial occlusion (including trash foot)
Infection	Infections other than pulmonary and surgical
Other	Other postoperative complications

Table S3: Hospital volumes of complex EVAR, FEVAR, BEVAR, and total endovascular aortic interventions in complex EVAR hospitals

	Complex EVAR (FEVAR + BEVAR)	**FEVAR**	**BEVAR**	**Total endovascular aortic interventions including complex EVAR in complex EVAR hospitals**
Number of hospitals	28	28	14	28
Number of patients	694	539	155	
Number of interventions	705	545	160	7096
Median number of patients per hospital [IQR]	55 [35 -76]	47 [28–53]	25 [11-25]	304 [207-347]
Median number of patients per hospital per year [IQR]	13 [9-23]	11 [7-15]	7 [3-9]	72 [52 – 90]

Total endovascular aortic interventions were reported as median [IQR] number of interventions per hospital

Table S4: Patient characteristics, aneurysm characteristics, operative characteristics, and perioperative outcomes of patients following FEVAR and BEVAR, stratified per quartile of annual hospital volume of complex EVAR

	Complex EVAR (FEVAR + BEVAR)	Annual volume				P-value
		<9	9-12	13-22	≥ 23	
Number of patients	694	165 (23.8)	129 (18.6)	199 (28.7)	201 (29.0)	
Number of hospitals						
2016	19	14	3	1	1	
2017	20	10	4	4	2	
2018	25	17	1	5	2	
2019	23	13	4	3	3	
Patient characteristics						
Age, years	73.5 ± 6.6	74.1 ± 6.8	73.4 ± 6.2	73.5 ± 6.9	73.0 ± 6.3	.410
Sex: female	128 (18.4)	19 (11.5)	19 (14.7)	40 (20.1)	50 (24.9)	.006
Preoperative pulmonary comorbidity	230 (33.1)	46 (28.2)	56 (44.1)	65 (33.5)	63 (61.7)	.033
Preoperative cardiac comorbidity	530 (76.4)	101 (62.0)	98 (76.0)	160 (81.2)	171 (85.1)	<.001
Preoperative creatinine, µmol/L	95 [79 - 114]	98 [82 - 102]	98 [81 - 122]	91 [78 - 110]	95 [76 - 113]	.072
Preoperative hemoglobin, mmol/L	8.5 ± 1.0	8.7 ± 1.0	8.5 ± 1.0	8.5 ± 1.0	8.5 ± 1.1	.232
Referral						
General practitioner	124 (17.9)	50 (31.1)	26 (20.2)	26 (13.2)	22 (10.9)	<.001
Emergency department	10 (1.4)	4 (2.5)	1 (0.8)	3 (1.5)	2 (1.0)	
Other hospital	373 (53.7)	56 (34.8)	62 (48.1)	122 (61.9)	133 (66.2)	
Medical specialist in own hospital	181 (26.1)	51 (31.7)	40 (31.0)	46 (23.4)	44 (21.9)	
Aneurysm characteristics						

Table S4: *Continued.*

	Complex EVAR (FEVAR + BEVAR)	Annual volume				P-value
		<9	9-12	13-22	≥ 23	
Aneurysm diameter	63.7 ± 9.4	62.4 ± 8.8	64.1 ± 9.1	62.3 ± 8.7	65.8 ± 10.3	.001
Location of the aneurysm						<.001
Abdominal: juxtarenal or infrarenal	396 (57.2)	122 (74.4)	69 (53.5)	116 (58.6)	89 (44.3)	
Abdominal: suprarenal	65 (9.4)	10 (6.1)	22 (17.1)	17 (8.6)	16 (8.0)	
Thoracoabdominal	231 (33.4)	32 (19.5)	38 (29.5)	65 (32.8)	96 (47.8)	
Type of surgery						.041
Primary	527 (75.9)	139 (78.9)	101 (78.3)	158 (79.4)	138 (68.7)	
Secondary aortic intervention	167 (24.1)	35 (21.2)	28 (21.7)	41 (20.6)	63 (31.3)	
Operative characteristics						
Urgency						.101
Elective	682 (98.3)	164 (99.4)	129 (100.0)	194 (97.5)	195 (97.0)	
Urgent intact	12 (1.7)	1 (0.6)	0 (0.0)	5 (2.5)	6 (3.0)	
Procedure						<.001
FEVAR	539 (77.7)	147 (89.1)	102 (70.1)	152 (76.4)	138 (68.7)	
BEVAR	155 (22.3)	18 (10.9)	27 (20.9)	47 (23.6)	63 (31.3)	
Number of targeted vessels						<.001
1 – 2	136 (19.6)	56 (34.1)	27 (20.9)	25 (12.6)	28 (13.9)	
3	252 (36.4)	57 (34.8)	47 (36.4)	87 (43.7)	61 (30.3)	
≥ 4	305 (44.0)	51 (31.1)	55 (42.6)	87 (43.7)	112 (55.7)	

Table S4: *Continued.*

	Complex EVAR (FEVAR + BEVAR)	Annual volume				P-value
		<9	9-12	13-22	≥ 23	
Unknown / missing	1					
Perioperative outcomes						
Perioperative mortality	32 (4.6)	15 (9.1)	7 (5.4)	5 (2.5)	5 (2.5)	.008
Postoperative complications	232 (33.4)	58 (35.2)	40 (31.0)	67 (33.7)	67 (33.3)	.904
Intraoperative complications	89 (12.8)	16 (9.8)	17 (13.3)	35 (17.6)	21 (10.4)	.092
Length of stay at ICU	1 [0-2]	1 [0-2]	1 [0-2]	1 [0-2]	1 [0-2]	.381
Length of hospital stay	5 [3-7]	5 [3-7]	4 [3-7]	4 [3-7]	6 [3-8]	.251
Reinterventions	80 (11.5)	21 (12.7)	20 (15.5)	19 (9.5)	20 (10.0)	.322
Readmissions	68 (9.8)	18 (10.9)	10 (7.8)	26 (23.1)	14 (7.0)	.167
Major complication	159 (22.9)	39 (23.6)	32 (24.8)	46 (23.1)	42 (20.9)	.855
Failure to rescue	32/159 (20.1)	15/39 (38.5)	7/32 (21.9)	5/46 (10.9)	5/42 (11.9)	.060

Values are presented as n (%), mean (SD), or median [interquartile range].

Table S5: Univariable analyses to assess whether hospital volume of complex EVAR, FEVAR, BEVAR and total endovascular aortic interventions is associated with increased perioperative mortality

A

Volume of complex EVAR*	No. of patients (complex EVAR*)	Mortality of complex EVAR*	
		OR (95%-CI)	**P-value**
Overall volume of complex EVAR*			
Continuous		0.98 (0.97 – 0.995)	**0.009**
Categorical (based on quartiles)			
< 35	154	Ref.	
35-54	174	0.52 (0.20 – 1.28)	**0.162**
55 - 75	187	0.36 (0.12 – 0.93)	**0.043**
≥ 76	179	0.31 (0.10 – 0.85)	**0.030**
Annual volume of complex EVAR*			
Continuous		0.93 (0.89 – 0.98)	**0.007**
Categorical (based on quartiles)			
<9	165	Ref.	
9-12	129	0.57 (0.21 – 1.41)	0.241
13-22	199	0.26 (0.08 – 0.68)	**0.010**
≥ 23	201	0.26 (0.08 – 0.67)	**0.010**

*OR indicates Odds Ratio, CI indicates confidence interval. * Complex EVAR: FEVAR and BEVAR*

B

Volume of FEVAR	No. of patients (FEVAR)	Mortality of FEVAR	
		OR (95%-CI)	**P-value**
Overall volume of FEVAR			
Continuous		0.97 (0.95 – 0.99)	**0.006**
Categorical (based on quartiles)			
<28	134	Ref.	
28 – 46	132	0.53 (0.18 – 1.44)	0.228
47-52	98	0.35 (0.08 – 1.17)	0.118
≥ 53	175	0.26 (0.07 – 0.78)	**0.024**
Annual volume of FEVAR			
Continuous		0.89 (0.81 – 0.96)	**0.004**
Categorical (based on quartiles)			
<7	129	Ref.	
7 – 10	139	0.44 (0.15 – 1.17)	0.111
11-14	114	0.45 (0.14 – 1.25)	0.143
≥ 15	157	0.06 (0.003 – 0.32)	**0.008**

OR indicates Odds Ratio, CI indicates confidence interval.

C

Volume of BEVAR	No. of patients (BEVAR)	Mortality of BEVAR	
		OR (95%-CI)	**P-value**
Overall volume of BEVAR			
Continuous		1.00 (0.93 – 1.06)	0.886
Categorical (based on quartiles)			
<11	38	Ref.	
11-24	30	0.62 (0.03 – 6.79)	0.703
25	50	1.57 (0.29 – 11.75)	0.616
≥ 26	37	0.50 (0.02 – 5.44)	0.578

Annual volume of BEVAR			
Continuous		0.94 (0.74 – 1.19)	0.609
Categorical (based on quartiles)			
<3	28	Ref.	
3-6	48	0.18 (0.01 – 1.47)	0.142
7-8	31	0.57 (0.07 – 3.73)	0.561
≥ 9	48	0.36 (0.05 – 2.32)	0.283

OR indicates Odds Ratio, CI indicates confidence interval.

D

Volume of total endovascular aortic interventions	No. of patients (complex EVAR*)	Mortality of complex EVAR*	
		OR (95%-CI)	**P-value**
Overall volume of total endovascular aortic interventions			
Continuous		1.00 (0.997 – 1.01)	0.673
Categorical (based on quartiles)			
< 207	111	Ref.	
207 – 303	174	0.26 (0.10 – 0.70)	**0.007**
304 – 346	230	1.23 (0.36 – 3.77)	0.722
≥ 347	179	0.67 (0.26 – 1.74)	0.402
Annual volume of total endovascular aortic interventions			
Continuous		1.00 (0.98 – 1.01)	0.842
Categorical (based on quartiles)			
<52	117	Ref.	
52-71	170	0.80 (0.29 – 2.29)	0.665
72-89	240	0.43 (0.14 – 1.33)	0.140
≥ 90	167	1.00 (0.37 – 2.83)	0.999

*OR indicates Odds Ratio, CI indicates confidence interval. *Complex EVAR: FEVAR and BEVAR*

CHAPTER

8

RESULTS FROM A NATIONWIDE PROSPECTIVE REGISTRY ON OPEN SURGICAL OR ENDOVASCULAR REPAIR OF JUXTARENAL ABDOMINAL AORTIC ANEURYSMS

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ABSTRACT

Background

Juxtarenal abdominal aortic aneurysms (JRAAAs) can be treated either with open surgical repair (OSR) including suprarenal clamping or by complex endovascular aneurysm repair (cEVAR). In this study, we present the comparison between the short-term mortality and complications of the elective JRAAA treatment modalities from a national database reflecting daily practice in The Netherlands.

Methods

All patients undergoing elective JRAAA open repair or cEVAR (fenestrated EVAR or chimney EVAR) between January 2016 and December 2018 registered in the Dutch Surgical Aneurysm Audit (DSAA) were eligible for inclusion. Descriptive perioperative variables and outcomes were compared between patients treated with open surgery or endovascularly. Adjusted odds ratios for short-term outcomes were calculated by logistic regression analysis.

Results

In all, 455 primary treated patients with JRAAAs could be included (258 OSR, 197 cEVAR). Younger patients and female patients were treated more often with OSR vs cEVAR (72 ± 6.1 vs 76 ± 6.0; P< .001 and 22% vs 15%; P= .047, respectively). Patients treated with OSR had significantly more major and minor complications as well as a higher chance of early mortality (OSR vs cEVAR, 45% vs 21%; P< .001; 34% vs 23%; P= .011; and 6.6% vs 2.5%; P= .046, respectively). After logistic regression with adjustment for confounders, patients who were treated with OSR showed an odds ratio of 3.64 (95% confidence interval [CI], 2.25-5.89; P< .001) for major complications compared with patients treated with cEVAR, and for minor complications, the odds ratios were 2.17 (95% CI, 1.34-3.53; P= .002) higher. For early mortality, the odds ratios were 3.79 (95% CI, 1.26-11.34; P= .017) higher after OSR compared with cEVAR.

Conclusions

In this study, after primary elective OSR for JRAAA, the odds for major complications, minor complications, and short-term mortality were significantly higher compared with cEVAR.

INTRODUCTION

Due to the lower mortality and its minimal invasive character, endovascular aneurysm repair (EVAR) has been widely implemented in daily practice and is the preferred method of treatment of abdominal aortic aneurysms (AAAs) in most practices[1]. Since the introduction of EVAR almost three decades ago, an increasing amount of research has focused on the differences between open surgery and EVAR to treat AAA[2–5]. Several trials on elective infrarenal aneurysm showed a survival advantage for EVAR in the short-term[6]. This advantage was, however, lost after 3 years of follow-up.

The Dutch Surgical Aneurysm Audit (DSAA) is a mandatory nationwide audit for all patients treated for an aortic aneurysm in The Netherlands and was introduced in 2013[7]. Previous research from this database between 2013 and 2015 showed a combined mortality for open surgery and EVAR of 1.9% for infrarenal and juxtarenal aortic aneurysms (JRAAAs) combined. So far, little specific data is published on outcomes of JRAAA repair when JRAAAs account for roughly 15% of all AAAs[8]. As JRAAAs demand a different, more complex approach in open surgery (suprarenal clamping) and in complex endovascular repair (cEVAR; chimney EVAR [CHEVAR] or fenestrated EVAR [FEVAR]), outcomes after JRAAA treatment are most likely different from treatment of infrarenal aneurysms. Therefore, JRAAAs should be evaluated separately in observational research as well as in a randomized trial. Consequently, this study evaluates the most recent short-term outcomes after elective juxtarenal aortic repair in a consecutive cohort from a nationwide database reflecting daily practice in The Netherlands.

METHODS

This is a retrospective study performed on a prospectively collected registry. We followed the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines reporting this study.

Data source

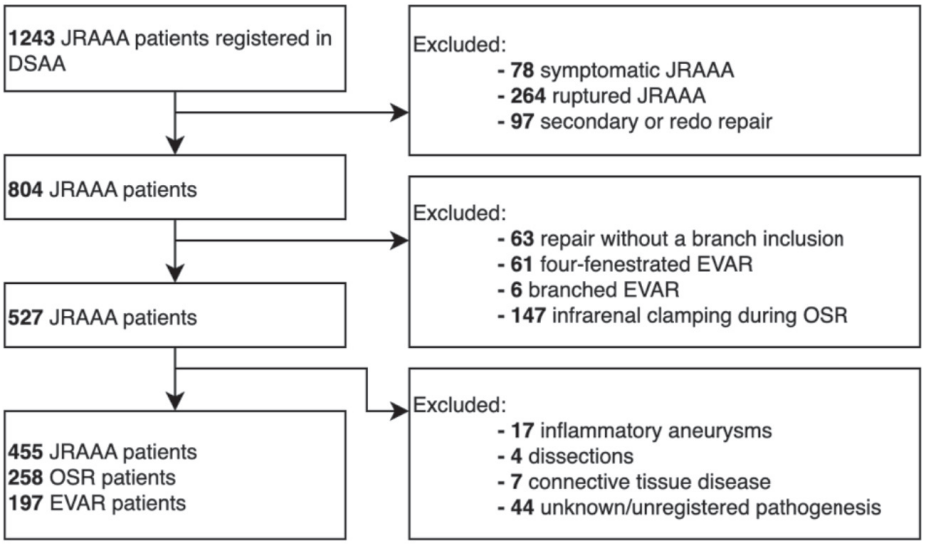
The dataset was derived from the DSAA. The DSAA is a compulsory nationwide audit that was initiated in 2013 and prospectively registers all patients treated for an aortic aneurysm (infrarenal, juxtarenal, suprarenal aneurysms) either with OSR or cEVAR. The purpose of the DSAA is to monitor quality and improve outcomes after aortic aneurysm treatment. Surgeons register their data via a web-based survey or deliver the data as a data file. Our research group was granted permission by the DSAA scientific and ethical committee after submitting a research proposal to evaluate all patients with JRAAAs treated in The Netherlands between January 2016 and December 2018. Patient consent was not necessary

according to the ethical committee, as the DSAA database we received was anonymized data. The study complied with the Declaration of Helsinki.

Study population

Between 2016 and 2018, 12,194 patients were registered in the DSAA with an aortic aneurysm. In this dataset, 1243 patients were registered as having a JRAAA. Elective, primary, and atherosclerotic JRAAAs were included. The exact flow diagram of patient inclusion and exclusion is shown in **Figure 1**. The final database consisted of 455 electively and primarily treated patients with JRAAAs in 44 Dutch hospitals; 258 patients treated with OSR and 197 with cEVAR.

Figure 1: Patient selection



Abbreviations: JRAAA: Juxtarenal abdominal aortic aneurysm, DSAA: Dutch Surgical Aneurysm Audit, OSR: open surgical repair, EVAR: endovascular aneurysm repair.

Definitions

A JRAAA is generally defined as an aortic aneurysm extending up to but not involving the renal arteries (ie, a short infrarenal aortic neck <10 mm), necessitating inter-renal, suprarenal below the superior mesentery artery, or infra- or supracoeliac clamping[9,10]. The DSAA database included all patients who were marked as segment C AAAs and JRAAAs by the registering clinicians. Segment C aneurysm was defined as an aortic aneurysm distally from the superior mesenteric artery. Suprarenal clamping was defined as clamping

above one or both renal arteries. As the DSAA database did not provide us with anatomical features to check if all included patients met the formal definition of a juxtarenal aneurysm, we used operation characteristics to approximate the formal anatomical definition. We excluded all patients with infrarenal clamping in the OSR treatment group, because when infrarenal clamping is used, it is more likely to be an infrarenal aneurysm, and therefore, misclassification is likely. If patients were endovascularly treated, they had to have undergone some type of branch inclusion in the reconstruction (i.e., CHEVAR or FEVAR), and therefore at least one targeted vessel. Patients treated with FEVAR with four fenestrations and branched EVAR (BEVAR) were excluded, because in most cases BEVAR was used for suprarenal aneurysms, and therefore, misclassification is most likely. The DSAA database does not specify which arteries were targeted per patient. Study variables included all preoperative and perioperative variables, which are compulsory to submit for every patient with aneurysm in the DSAA registration. Some study variables included the option 'unknown.'

Preoperative cardiac status was recorded in the DSAA registry as the presence of: (1) no cardiac history; (2) medication for hypertension, angina pectoris, diuretics, or digoxin; (3) presence of peripheral edema or use of vitamin K antagonists or borderline cardiomyopathy; (4) presence of an elevated central venous pressure or cardiomegaly; and (5) unknown. Preoperative pulmonary status was recorded in the registry as the presence of: (1) no pulmonary history; (2) presence of dyspnea during exercise; (3) presence of severe dyspnea, including invalidating dyspnea, dyspnea at rest, consolidation and lung fibrosis; and (4) unknown. Electrocardiogram (ECG) abnormalities consisted of atrial fibrillation, ischemia, or any other abnormalities on ECG.

A cardiac complication is recorded as yes if myocardial infarction, decompensated heart failure, cardiac arrhythmias, or other cardiac complications occurred. Pulmonary complications are recorded as yes if pneumonia, pulmonary embolism, pneumothorax, or other pulmonary complications occurred. Renal complications are recorded as yes if renal insufficiency not requiring hemodialysis or renal insufficiency requiring hemodialysis occurred. Neurologic complications are recorded as yes if cerebrovascular accident, paraplegia, delirium, or other neurologic complications occurred. Abdominal complications are recorded as yes if abdominal abscess, abdominal sepsis, ileus, spleen injury, bowel ischemia, bowel injury, stoma placement, or other abdominal complications occurred. Arterial occlusions are recorded as yes if (major) amputation, renal artery arterial occlusion, or other arterial occlusion (including trash foot) occurred. Reconstruction and prosthesis-related complications are recorded as yes if prothesis infection, prothesis migration, or other reconstruction and prosthesis-related complications occurred. Wound complications are recorded as yes if deep wound infection, fascia dehiscence,

or other wound complications occurred. Postoperative bleeding was marked as yes if a postoperative bleeding occurred. Infection (nonsurgical) was marked as yes when an infection occurred that was not a surgical or pulmonary infection. The category 'other' complications is any other complication that occurred within 30 days or within hospital admission and did not fit any of the other categories.

The primary endpoint was early mortality, and secondary endpoints were major and minor complications within 30 days, reintervention/reoperations within 30 days, and unplanned readmission within 30 days after discharge. Early mortality was defined as death within 30 days after treatment or within initial hospital admission. A major complication was defined as any postoperative adverse event causing a prolonged hospital stay, reintervention, or early mortality, with a maximum of one major complication[11]. A minor complication was defined as any postoperative adverse event that did not lead to a prolonged hospital stay, reintervention, permanent injury, or early mortality. The definition of major or minor complication is therefore not based on the specific complication but on the consequence the complication had. A prolonged hospital stay was defined as the length of hospital stay beyond the 75th percentile of length of stay per treatment group. Complications that occurred within 30 days after treatment or within initial hospital admission causing permanent injury, like permanent dialysis after kidney failure, were marked as complications <30 days causing permanent injury. Patients who underwent a reoperation or reintervention within 30 days after initial treatment or within hospital admission were marked as reoperation or reintervention <30 days. Unplanned readmissions were admissions within 30 days after discharge of the initial admission that did not involve a planned admission.

Statistical analysis.

Categorical variables were described by frequency distribution and compared across patient groups treated with OSR or cEVAR. Continuous variables were tested for normality and linearity by one-sample Kolmogorov-Smirnov testing and then compared across treatment groups using one-way analysis of variance. This was done for preoperative variables as well as intraoperative variables and outcomes. Adjusted odds ratios were estimated by a multivariable logistic regression model adjusting for age, sex, cardiac status, result of last ECG, pulmonary status, preoperative hemoglobin level, preoperative creatinine level, and largest diameter of the aneurysm. If variables contained missing data, this is acknowledged in the Tables. All P-values are two-tailed, with values <.05 considered statistically significant. All analysis were performed using STATA 14.1MP statistical software (College Station, Tex).

RESULTS

From the included 455 electively primarily treated patients with JRAAAs from 44 Dutch hospitals, 258 patients were treated with OSR and 197 with cEVAR. In the OSR group, patients were significantly younger compared with the cEVAR group (72 ± 6.1 vs 76 ± 6.0 years, respectively; P< .001; **Table 1**). Female patients were more often treated with OSR compared with male patients (OSR: female vs male, 22% vs 78%; cEVAR: female vs male, 14% vs 86%; P= .047). No difference was seen between comorbidities or preoperative laboratory values. The number of patients treated over the years remained stable also in the distribution between the treatment groups and sex.

Table 1: Preoperative characteristics of elective primary JRAAA repairs

	Total (N = 455)	**OSR (n = 258; 57%)**	**cEVAR (n = 197; 43%)**	***P***
Age, years	74 ± 6.2	72 ± 6.1	76 ± 6.0	< .001
Sex				.047
Male	369 (81)	201 (78)	168 (85)	
Female	86 (19)	57 (22)	29 (15)	
Year of treatment				.431
2016	163 (36)	95 (37)	68 (35)	
2017	147 (32)	77 (30)	70 (35)	
2018	145 (32)	86 (33)	59 (30)	
Cardiac status				.850
No abnormalities	151 (33)	90 (35)	61 (31)	
Antihypertensive medication	254 (56)	139 (54)	115 (58)	
Peripheral edema	33 (7)	20 (8)	13 (7)	
Raised central venous pressure	5 (1)	3 (1)	2 (1)	
Unknown	12 (3)	6 (2)	6 (3)	
Pulmonary status				.564
No dyspnea	343 (69)	181 (70)	162 (68)	
Dyspnea	123 (25)	66 (26)	57 (24)	
Severe dyspnea	23 (5)	9 (3)	14 (6)	
Unknown	6 (1)	2 (1)	4 (2)	
Last preoperative ECG				.037
No abnormalities	200 (44)	123 (48)	77 (39)	
Abnormalities	226 (49)	126 (49)	100 (51)	

Table 1: *Continued.*

	Total (N = 455)	OSR (n = 258; 57%)	cEVAR (n = 197; 43%)	*P*
No ECG performed/unknown ECG	29 (6)	9 (3)	20 (10)	
Hemoglobin, mmol/L	8.6 ± 0.98	8.6 ± 0.96	8.7 ± 1.01	.228
Creatinine, mmol/L	101 ± 44	101 ± 53	101 ± 28	.926
GFR, mL/min/1.73 m2	70 ± 22	72 ± 23	68 ± 20	.139
Largest diameter aneurysm when treated, mm	60 [11]	60 [12]	61 [10]	.877

cEVAR, Complex endovascular aneurysm repair (fenestrated EVAR or chimney EVAR); ECG, electrocardiogram; GFR, glomerular filtration rate; IQR, interquartile range; JRAAA, juxtarenal abdominal aortic aneurysm; OSR, open surgical repair.
Data are presented as n (%), mean ± standard deviation, or median [IQR]. Boldface P represents statistically significant data.

During OSR, a tube prosthesis was used in 139 of 258 cases (54%), and in 45% of cases, a bifurcated prosthesis was used (**Table 2**). In 55% of cases, the aortic clamp was placed above both renal arteries, and in 37% above one of the renal arteries. For cEVAR, fenestrated grafts were mostly used (125/197; 69%); the remaining cEVAR cases were treated with chimney EVAR. Almost 90% of procedures involved two or three target vessels.

Table 2: Intraoperative characteristics of elective primary JRAAA repairs

	Total (n= 455)	OSR (n= 258; 57%)	cEVAR (n= 197; 43%)	P
Intraoperative characteristics, OSR	NA		NA	NA
Type of prosthesisa				
Tube prosthesis		139 (54)		
Bifurcation prosthesis		117 (45)		
Unknown		2 (1)		
Clamping above renal arteriesa				
Above 1 renal artery		95 (37)		
Above 2 renal arteries		143 (55)		
Unknown		20 (8)		
Intraoperative characteristics, cEVAR	NA	NA		NA

Table 2: *Continued.*

	Total (n= 455)	OSR (n= 258; 57%)	cEVAR (n= 197; 43%)	P
Endovascular procedurea				
Chimney EVAR			54 (27)	
Fenestrated EVAR			143 (73)	
Amount or target vessels				
One target vessel			24 (12)	
Two target vessels			82 (42)	
Three target vessels			91 (46)	
Intraoperative complication				.088
None	421 (93)	241 (93)	180 (92)	
Cardiac arrest or resuscitation	1 (0)	1 (0)	0	
Unintended occlusion branch	5 (1)	2 (1)	3 (1)	
Type I endoleak	5 (1)	NA	5 (3)	
Type III endoleak	0	NA	0	
Iatrogenic bowel damage	3 (1)	3 (1)	NA	
Iatrogenic ureter damage	1 (0)	1 (0)	NA	
Other	19 (4)	10 (5)	9 (4)	
Blood loss, mL				**<.001**
<100	56 (13)	2 (1)	54 (27)	
101-500	106 (23)	23 (9)	83 (42)	
501-999	65 (14)	45 (17)	20 (10)	
1000 or more	200 (44)	173 (67)	27 (14)	
Unknown	28 (6)	15 (6)	13 (7)	
Peritoneal contamination	NA		NA	NA
None		234 (92)		
Minimal fluid		19 (7)		
Abscess		0		
Peritonitis, fecal contamination[a]		2 (1)		
Amount of initial procedures				.826
One procedure	406 (89)	229 (89)	177 (90)	
Two procedures	43 (10)	26 (10)	17 (9)	
More than two procedures	6 (1)	3 (1)	3 (1)	

cEVAR, Complex endovascular aneurysm repair (fenestrated EVAR or chimney EVAR); JRAAA, juxtarenal abdominal aortic aneurysm; NA, not applicable; OSR, open surgical repair. Data are presented as n (%). Boldface P values represent statistical significance. [a]Missing data <5%.

OSR showed similar intraoperative complications compared with cEVAR (7% vs 8%; P¼ .088), which was mainly due to the occurrence of a type I endoleak in 5 patients (3%) in the cEVAR group. Blood loss was significantly different in favor of cEVAR, in which most patients had blood loss between 101 and 500 mL compared with mostly more than 1000 mL in the OSR group (P< .001).

Postoperative characteristics are described in **Table 3**. Almost one-half of the OSR-treated patients had some type of complication within 30 days compared with one-third of the cEVAR-treated patients (no missing data). After OSR, patients more often underwent a reintervention within 30 days after initial JRAAA treatment due to a third of the relatively high amount of re-laparotomies. Unfortunately, the database does not provide data on the reasons for these re-laparotomies. More abdominal and renal complications occurred after OSR compared with after cEVAR, but for the different categories of complications, more than one-half of the data was missing. After treatment with cEVAR, patients had a significantly shorter intensive care unit stay and hospital stay compared with OSR (both P< .001).

Table 3: Postoperative characteristics of elective primary JRAAA repairs

	Total (N = 455)	**OSR (n = 258; 57%)**	**cEVAR (n = 197; 43%)**	***P***
Intensive care admission, days	1 [0-2]	2 [1-3]	0 [0-1]	<.001
Hospital admission, days	7 [4-10]	8 [6-12]	4 [3-7]	<.001
Patients with a complication within 30 days[a]	192 (42)	127 (49)	65 (33)	<.001
Category complications within 30 days[b]				
Cardiac	39 (13)	31 (15)	8 (9)	.057
Pulmonary	59 (19)	38 (18)	21 (23)	.683
Renal	35 (11)	30 (14)	5 (5)	.010
Neurologic	39 (13)	24 (11)	15 (16)	.382
Abdominal	30 (10)	26 (12)	4 (4)	.004
Arterial occlusion	22 (7)	16 (8)	6 (7)	.659
Reconstruction/prosthesis-related	10 (3)	5 (2)	5 (5)	.127
Wound	15 (5)	12 (6)	3 (3)	.277
Postoperative bleeding	9 (3)	5 (2)	4 (4)	.492
Infection (non-surgical)	14 (4)	9 (4)	5 (5)	.879
Other	36 (12)	18 (8)	18 (19)	.023

Table 3: *Continued.*

	Total (N = 455)	**OSR (n = 258; 57%)**	**cEVAR (n = 197; 43%)**	***P***
Patients with a reintervention or reoperation within 30 days[a]	50 (11)	34 (13)	16 (8)	.188
Endovascular procedure	6 (12)	1 (3)	5 (31)	.046
Percutaneous procedure	2 (4)	1 (3)	1 (6)	.848
Endoscopic procedure	2 (4)	1 (3)	1 (6)	.848
Reoperation open procedure	27 (55)	22 (67)	5 (31)	.007
Opening wound only	2 (7)	1 (5)	1 (20)	.848
Re-laparotomy	15 (56)	15 (68)	0	
Other open procedure	10 (37)	6 (27)	4 (80)	.832
Other procedure	12 (25)	8 (24)	4 (26)	.480

cEVAR, Complex endovascular aneurysm repair (fenestrated EVAR or chimney EVAR); IQR, Interquartile range; JRAAA, juxtarenal abdominal aortic aneurysm; OSR, open surgical repair. Data are presented as n (%) or median [IQR]. Boldface P values represent statistical significance. [a] *No missing data.* [b]*Missing data 50%-60%.*

Looking at the outcomes within 30 days, patients treated with OSR had significantly more complications, both major and minor, as well as a higher risk of early mortality (**Table 4**). The number of targeted vessels were not associated with the occurrence of major or minor complications (P= .542 and P= .648, respectively). Also, it was not associated with early mortality (P = .569). After adjustment for age, sex, cardiac status, result of the last ECG, pulmonary status, preoperative hemoglobin level, preoperative creatinine level, and largest diameter aneurysm, the odds ratios for major complications within 30 days after treatment were 3.64 (95% confidence interval [CI], 2.25-5.89) higher when treated with OSR. For minor complications, the odds ratios were 2.17 (95% CI, 1.34-3.53) higher after treatment with OSR relative to cEVAR, and for early mortality, the odds ratios were higher with 3.79 (95% CI, 1.26-11.34).

Table 4: Adjusted early outcomes after primary elective JRAAA repair

	Total (N = 455)	OSR (n = 258; 57%)	cEVAR (n = 197; 43%)	OR[a]	95% CI
Major complications <30 days	157 (34.5)	116 (45.0)	41 (20.8)	3.64	2.25-5.89
Minor complications <30 days	132 (29.0)	87 (33.7)	45 (22.8)	2.17	1.34-3.53
Complications <30 days causing permanent injury	34 (7.5)	21 (8.1)	13 (6.6)	1.05	0.91-1.22
Reoperation or reintervention <30 days	50 (10.9)	34 (13.2)	16 (8.1)	1.69	0.85-3.40
Unplanned readmission <30 days after discharge	34 (7.5)	14 (5.4)	20 (10.2)	0.55	0.25-1.20
Early mortality	22 (4.8)	17 (6.6)	5 (2.5)	3.79	1.26-11.34

cEVAR, Complex endovascular aneurysm repair (fenestrated EVAR or chimney EVAR); CI, confidence interval; JRAAA, juxtarenal abdominal aortic aneurysm; OR, odds ratio; OSR, open surgical repair. Data are presented as n (%). ORs are given for OSR compared with EVAR. Boldface values represent statistical significance. [a]Logistic regression is performed for each outcome measure, adjusting for age, sex, cardiac status, result of last electrocardiogram, pulmonary status,preoperative hemoglobin level, preoperative creatinine level, largest diameter aneurysm, hospital operation volume for juxtarenal aneurysms, and year of operation.

DISCUSSION

This study provides data on real-life daily practice in The Netherlands treating JRAAAs. More major and minor complications occurred after OSR compared with cEVAR, as well as a significantly higher 30-day mortality. After adjustment for confounders, the odds ratios for major complications as well as early mortality were over 3.5-fold higher after OSR compared with cEVAR, and minor complications showed a 2-fold higher odds ratio. The generalizability of this study is influenced by patient selection based on the available data (ie, type of treatment), and the number of patients included, which should be taken into account when interpreting this study.

A recent meta-analysis discussing the trials for elective infrarenal abdominal aneurysm treatment showed significantly lower early mortality for patients treated with EVAR[12]. For more complex aortic aneurysms, such as JRAAAs, two high-quality meta-analyses have been published, both showing no significant differences in early mortality between OSR and FEVAR[13,14]. OSR did show a higher number of postoperative complications compared with FEVAR in both studies. These results were also taken into account by the European

Society of Vascular Surgery guideline, which recommends that the preferred treatment option for JRAAAs is an endovascular solution with fenestrated endografts when feasible because the mortality is equal but the morbidity is less[10]. Within this guideline, the use of CHEVAR is only recommended in the acute setting or as an endovascular bailout option and is ideally restricted to a maximum of two chimneys. This is due to the advantage of CHEVAR not being a custom-made device, and therefore, it can be used in an emergency setting. The disadvantage is that postoperative type Ia endoleaks and chimney graft occlusion occur more often compared with FEVAR[10,15,16]. Our registry did include patients treated with CHEVAR in the elective setting between 2016 and 2018, which was before the newest guideline publication.

The lack of significant difference in mortality in the meta-analyses of Rao et al and Jones et al was possibly caused by including patients in the endovascular group with more comorbidities[13,14]. In accordance with the previously published literature, in this study, major complications occurred more often in patients treated with OSR compared with cEVAR, especially renal and abdominal complications. This is probably also the explanation for more reinterventions within 30 days after treatment with OSR and could very well have affected the shortterm mortality. Although suprarenal clamping in the OSR group does skew the chances of postoperative renal impairment, previous studies found no effect on the occurrence of permanent dialysis and mortality, and this is therefore probably not a complete explanation for the mortality difference in this study[17–19]. In patients treated for infrarenal aneurysms, it is known that a short neck is associated with higher mortality in patients treated with OSR, whereas EVAR is not possible in this group[20,21]. The generally broader range of anatomical characteristics that are accepted for OSR compared with cEVAR could therefore also be a factor contributing to a higher mortality after OSR in this study.

In this registry, the choice of treatment modality was left to the surgeons' discretion. Therefore, some patients may have undergone OSR because cEVAR was not available in that hospital, whereas other patients may have been offered an endovascular solution only in a hospital with an "endovascular-first" strategy for JRAAA. Even when both treatments are equally enrolled in the concerning hospital and the patient's anatomy is suited for both, it can be difficult to decide which patient to offer which treatment. A methodically well-developed preoperative risk model specifically made for JRAAAs could be of value to give more preoperative guidance. A recent study of the Vascular Quality Initiative data did show that acute kidney injury after JRAAA treatment with OSR was associated with increased comorbidities preoperatively and also was associated with worse short- and long-term mortality[16]. Further risk stratification of preoperative comorbidities and also information on the impact of the different treatment modalities on quality of life could

aid in the decision-making process[10]. Unfortunately, no randomized controlled trial has been performed comparing treatment outcomes of OSR vs cEVAR for JRAAA, although that would be the best way to truly compare these treatment modalities[6]. Because the choice of a surgical approach is multifactorial, a randomized trial would be the most appropriate method that corrects by default for confounding by indication[10].

Limitations

This study must be interpreted in the context of its design. Patient selection was done on operation technique only, as there was no information on anatomical configurations, inevitably causing selection bias. Some pararenal or suprarenal AAAs may have been included in the endovascular group and treated with three-fenestrated EVAR. Also, in the OSR group, selection bias could also be present; patients with anatomically true JRAAAs could have been treated using an infrarenal clamp anyway and were therefore excluded from analysis in this study. Also, the local availability of cEVAR and the preference of the surgeon or patient is an influence on the decision of whether to treat the JRAAA endovascularly or openly, which were unknown parameters in this study.

The retrospective analysis of prospectively collected data was done using data from the DSAA registry. As with all registries, it depends on the registering physician reporting on perioperative characteristics, which may lead to errors in interpretation of the data before reporting, errors during data input, or missing data. The DSAA is a prospective quality registry system and provides us with crucial variables to include patients with JRAAAs as adequately as possible (ie, suprarenal clamping during OSR or the usage of branch inclusion in the reconstruction during cEVAR). Despite this, the registry did not provide us the anatomical configurations of the infrarenal neck lengths or aneurysm involvement of the renal arteries or extension above the renal arteries.

CONCLUSIONS

This study provides the data on current practice of the treatment of JRAAAs in The Netherlands. In this study, after primary elective OSR for JRAAAs, the odds for major complications, minor complications, and short-term mortality were all significantly higher compared with cEVAR. Though this study reflects daily practice in The Netherlands, selection bias and number of included patients should be taken into account when interpreting the generalizability of this study. For future research, development of a preoperative risk model would be a valuable tool to preoperatively identify patients most likely to survive treatment, preferably in a prospective cohort including anatomical configurations to prevent the issue of selection bias.

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REFERENCES

1 von Meijenfeldt GCI, Ultee KHJ, Eefting D, Hoeks SE, ten Raa S, Rouwet E v., et al. Differences in mortality, risk factors, and complications after open and endovascular repair of ruptured abdominal aortic aneurysms. *European Journal of Vascular and Endovascular Surgery* 2014;**47**(5):479–86. Doi: 10.1016/j.ejvs.2014.01.016.

2 Becquemin JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, et al. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients. *J Vasc Surg* 2011;**53**(5):1167-1173.e1. Doi: 10.1016/j.jvs.2010.10.124.

3 Blankensteijn JD, de Jong SECA, Prinssen M, van der Ham AC, Buth J, van Sterkenburg SMM, et al. Two-Year Outcomes after Conventional or Endovascular Repair of Abdominal Aortic Aneurysms. *New England Journal of Medicine* 2005;**352**(23):2398–405. Doi: 10.1056/nejmoa051255.

4 Greenhalgh R, Brown L, Kwong G, Powell J, Thompson S, EVAR trial participants. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet* 2004;**364**:843–8.

5 Lederle FA, Freischlag JA, Kyriakides TC, Matsumura JS, Padberg FT, Kohler TR, et al. Long-Term Comparison of Endovascular and Open Repair of Abdominal Aortic Aneurysm. *New England Journal of Medicine* 2012;**367**(21):1988–97. Doi: 10.1056/nejmoa1207481.

6 Powell JT, Sweeting MJ, Ulug P, Blankensteijn JD, Lederle FA, Becquemin JP, et al. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. *British Journal of Surgery* 2017;**104**(3):166–78. Doi: 10.1002/bjs.10430.

7 Karthaus EG, Vahl A, van der Werf LR, Elsman BHP, van Herwaarden JA, Wouters MWJM, et al. Variation in Surgical Treatment of Abdominal Aortic Aneurysms with Small Aortic Diameters in the Netherlands. *Ann Surg* 2020;**271**(4):781–9. Doi: 10.1097/SLA.0000000000003050.

8 Jongkind V, Yeung KK, Akkersdijk GJM, Heidsieck D, Reitsma JB, Tangelder GJ, et al. Juxtarenal aortic aneurysm repair. *J Vasc Surg* 2010:760–7. Doi: 10.1016/j.jvs.2010.01.049.

9 Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM, et al. Reporting standards for endovascular aortic aneurysm repair. *J Vasc Surg* 2002;**35**(5):1048–60. Doi: 10.1067/mva.2002.123763.

10 Wanhainen A, Verzini F, van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(1):8–93. Doi: 10.1016/j.ejvs.2018.09.020.

11 Lijftogt N, Karthaus EG, Vahl A, van Zwet EW, van der Willik EM, Tollenaar RAEM, et al. Failure to Rescue – a Closer Look at Mortality Rates Has No Added Value for Hospital Comparisons but Is Useful for Team Quality Assessment in Abdominal Aortic Aneurysm Surgery in The Netherlands. *European Journal of Vascular and Endovascular Surgery* 2018;**56**(5):652–61. Doi: 10.1016/j.ejvs.2018.06.062.

12 Stather PW, Sidloff D, Dattani N, Choke E, Bown MJ, Sayers RD. Systematic review and meta-analysis of the early and late outcomes of open and endovascular repair of abdominal aortic aneurysm. *Br J Surg* 2013:863–72. Doi: 10.1002/bjs.9101.

13 Jones AD, Waduud MA, Walker P, Stocken D, Bailey MA, Scott DJA. Meta-analysis of fenestrated endovascular aneurysm repair versus open surgical repair of juxtarenal abdominal aortic aneurysms over the last 10 years. *BJS Open* 2019;**3**(5):572–84. Doi: 10.1002/bjs5.50178.

14 Rao R, Lane TRA, Franklin IJ, Davies AH. Open repair versus fenestrated endovascular aneurysm repair of juxtarenal aneurysms. *J Vasc Surg* 2015:242-255.e5. Doi: 10.1016/j.jvs.2014.08.068.
15 Li Y, Hu Z, Bai C, Liu J, Zhang T, Ge Y, et al. Fenestrated and Chimney Technique for Juxtarenal Aortic Aneurysm: A Systematic Review and Pooled Data Analysis. *Sci Rep* 2016;**6**. Doi: 10.1038/srep20497.
16 O'Donnell TFX, Patel VI, Deery SE, Li C, Swerdlow NJ, Liang P, et al. The state of complex endovascular abdominal aortic aneurysm repairs in the Vascular Quality Initiative. *J Vasc Surg* 2019;**70**(2):369–80. Doi: 10.1016/j.jvs.2018.11.021.
17 Chong T, Nguyen L, Owens CD, Conte MS, Belkin M. Suprarenal aortic cross-clamp position: A reappraisal of its effects on outcomes for open abdominal aortic aneurysm repair. *J Vasc Surg* 2009;**49**(4):873–80. Doi: 10.1016/j.jvs.2008.10.057.
18 Hoshina K, Nemoto M, Shigematsu K, Nishiyama A, Hosaka A, Miyahara T, et al. Effect of suprarenal aortic cross-clamping – Juxtarenal vs. infrarenal short and/or large neck abdominal aortic aneurysm –. *Circulation Journal* 2014;**78**(9):2219–24. Doi: 10.1253/circj.CJ-14-0384.
19 Samoila G, Williams IM. Anatomical Considerations and Open Surgery to Treat Juxtarenal Abdominal Aortic Aneurysms. *Vasc Endovascular Surg* 2018:349–54. Doi: 10.1177/1538574418762004.
20 IMPROVE Trial Investigators. The effect of aortic morphology on peri-operativemortality of ruptured abdominal aortic aneurysm. *Eur Heart J* 2015:1328–34. Doi: 10.1093/eurheartj/ehv096.
21 van Beek SC, Reimerink JJ, Vahl AC, Wisselink W, Reekers JA, Legemate DA, et al. Outcomes after open repair for ruptured abdominal aortic aneurysms in patients with friendly versus hostile aortoiliac anatomy. *European Journal of Vascular and Endovascular Surgery* 2014;**47**(4):380–7. Doi: 10.1016/j.ejvs.2014.01.003.

PART 3

NEW OPPORTUNITIES FOR FEEDBACK AND OUTCOME MEASUREMENT

CHAPTER

9

ADMINISTRATIVE HEALTHCARE DATA AS AN ADDITION TO THE DUTCH SURGICAL ANEURYSM AUDIT TO EVALUATE MID-TERM REINTERVENTIONS FOLLOWING ABDOMINAL AORTIC ANEURYSM REPAIR: A PILOT STUDY

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ABSTRACT

Background

The Dutch Surgical Aneurysm Audit (DSAA) is a nationwide mandatory quality registry that evaluates the perioperative outcomes of abdominal aortic aneurysms (AAAs). The DSAA includes perioperative outcomes that occur up to 30 days, but various complications following AAA repair occur after this period. Administrative healthcare data yield the possibility to evaluate later occurring outcomes such as reinterventions, without increasing the registration burden. The aim of this study is to assess the feasibility and the potential benefit of administrative healthcare data to evaluate mid-term reinterventions following intact AAA repair.

Method

All patients that underwent primary endovascular aneurysm repair (EVAR) or open surgical repair (OSR) for an intact infrarenal AAA between January 2017 and December 2018 were selected from the DSAA. Subsequently, these patients were identified in a database containing reimbursement data. Healthcare activity codes that refer to reinterventions following AAA repair were examined to assess reinterventions within 12 and 15 months following EVAR and OSR.

Results

We selected 4043 patients from the DSAA, and 2059 (51%) patients could be identified in the administrative healthcare database. Reintervention rates of 10.4% following EVAR and 9.5% following OSR within 12 months ($p = 0.719$), and 11.5% following EVAR and 10.8% following OSR within 15 months ($p = 0.785$) were reported.

Conclusion

Administrative healthcare data as an addition to the DSAA is potentially beneficial to evaluate mid- term reinterventions following intact AAA repair without increasing the registration burden for clinicians. Further validation is necessary before reliable implementation of this tool is warranted.

INTRODUCTION

The Dutch Surgical Aneurysm Audit (DSAA) is a nationwide mandatory quality registry that monitors and evaluates the perioperative outcomes of the treatment of abdominal aortic aneurysms (AAAs), performed by Dutch vascular surgeons in all Dutch hospitals[1]. Data of the DSAA, prospectively collected by vascular surgeons, reflect real-world practice and are mainly used for quality indicators to provide feedback to hospitals on their performances. Secondary, the data of the DSAA is used for scientific research that evaluates the quality of the Dutch AAA-care on a national level[2].

The DSAA includes perioperative outcomes that occur up to 30 days postoperatively or during the same hospital admission. However, com- plications and reinterventions that occur after 30-days are not scarce following EVAR and OSR[3]. Several patients treated with endovascular aortic aneurysm repair (EVAR) experience long-term endograft complications resulting in reintervention[3,4], while patients treated with open surgical repair (OSR) are at-risk for reinterventions for complications related to the laparotomy[3,5]. Therefore, as most patients survive multiple years following an AAA-repair[6,7], reliable data on long-term results, especially the durability of EVAR, are of utmost importance. Available data that evaluates mid and long-term reinterventions especially describes data from randomized controlled trail[6,7]. Observational studies often contain data from centers of excellence[4], while nationwide data on mid and long-term reinterventions to evaluate the nationwide impact of reinterventions are scarce.

A limited registration burden is crucial for quality registries[2]. Therefore, it might be valuable to add administrative healthcare data to the DSAA to evaluate the number and percentage of mid-term reinterventions following intact AAA repair without increasing the registration burden for clinicians. However, research that is performed with administrative healthcare data may be subject to several limitations[8]. Thus, the aim of this study is to assess the feasibility and the potential benefit of using administrative healthcare data to evaluate the frequency and type of mid-term reinterventions (reinterventions within 12 and 15 months) following intact AAA repair.

METHODS

Study design and data sources

This study serves as a pilot study to explore adding mid-term reinterventions following AAA repair to the Dutch Surgical Aneurysm Audit using administrative healthcare data. For this observational multicenter retrospective cohort study, two separate datasets were constructed. The first dataset was retrieved from the Dutch Surgical Aneurysm Audit

(DSAA-dataset), a mandatory nationwide quality registry in the Netherlands. The DSAA was established in 2013, and from that year forward, each hospital started registering all patients that underwent repair of an infrarenal or juxtarenal aneurysm without previous aortic surgery performed by vascular surgeons. Data verification of the DSAA was performed in a random sample of hospitals, indicating high reliability of data[9]. The administrative healthcare data, the second dataset, was retrieved from the 'Benchmark Database' serviced by LOGEX, a Dutch healthcare analytics company. This database is primarily used for reimbursement purposes and contains information on diagnosis and specific healthcare activity codes developed by the Dutch Healthcare Authority (NZA)[10]. Both AAA repairs and reinterventions are represented in specific healthcare activities codes. Healthcare insurance is mandatory in the Netherlands, and invoices to insurance companies are based on healthcare declaration codes that include specific healthcare activity codes. Dutch administrative healthcare data has previously been used for scientific purposes[11,12] and is considered accurate[12]. The administrative healthcare dataset was constructed using specific healthcare activity codes that described EVAR and OSR. This dataset also included information on reinterventions following an aneurysm repair, as well as limited information regarding patient and treatment characteristics.

Patient selection

For this study, the following in and exclusion criteria were used: all patients that underwent primary EVAR or OSR with clamping below the renal arteries for an intact infrarenal AAA between January 2017 and December 2018 were selected from the DSAA and included in the DSAA- dataset. Patients who were attempted to be treated endovascular but were converted from EVAR to OSR during surgery were not included in this study. Patients with an age below 20 or above 90 years were excluded. Subsequently, the administrative healthcare data was extracted from the administrative healthcare database by selecting patients with healthcare activity codes corresponding to EVAR or OSR (without reconstruction of one or two renal arteries) and the diagnosis code 'aneurysm of the aorta and arteries', whereafter these patients were included in the administrative healthcare dataset. The date of surgery noted in these specific healthcare activities that describe EVAR or OSR (shown in **Table 1**) determined the start of the follow-up periods of 12 and 15 months. Due to privacy restrictions, patient data in the administrative healthcare database was fully anonymized and could not be linked on patient-level to the DSAA dataset. Also, reintervention rates per hospital could not be assessed. Only patients that underwent a reintervention in the same hospital as their primary AAA-repair could be identified in the administrative healthcare database and were included in the administrative healthcare dataset. This study was conducted in 2020 and 2021.

Definitions and outcomes

Definitions

Reinterventions were selected from the administrative healthcare database using codes for specific care activities. The codes representing the reinterventions were selected based on clinical relevance. The selected reinterventions were divided into 'vascular-related reinterventions', which included aneurysm-related reinterventions, peripheral vessel-related reinterventions, amputations, and other vascular reinterventions, and 'abdominal reinterventions' that included laparotomies and corrections of incisional hernias. Within each category, reinterventions that described similar procedures were summarized into one subcategory. A complete overview of included reinterventions is presented in **Table S2–6**. Due to privacy re- strictions, the exact time in months or days between the primary intervention and the reintervention could not be extracted from the administrative healthcare database.

Outcomes

Outcomes of this study were the number and percentage of reinterventions (reinterventions per category and individual reinterventions) within 12 months and 15 months following intact AAA repair, stratified for EVAR and OSR, and the number of specific reinterventions that occurred in the administrative healthcare dataset. Both reinterventions within 12 and 15 months following AAA repair were examined to provide insight into the possible risk of selection bias that could be caused due to clinical follow-up moments with computed tomography angiography (CTA) scanning that most patients undergo at 12 months after surgery[13].

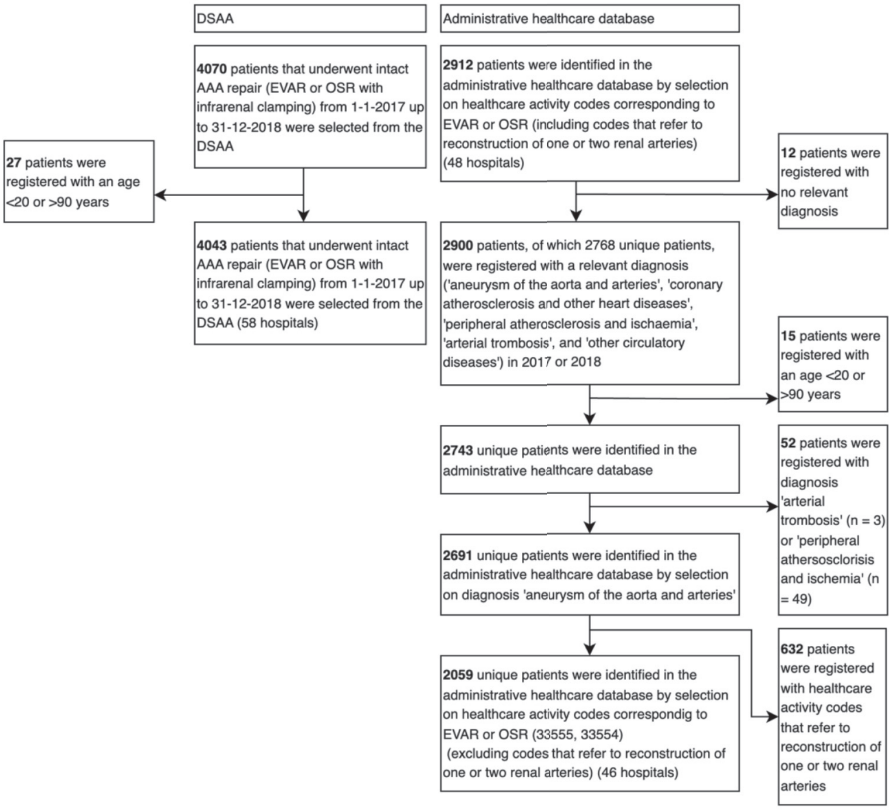
Statistical methods

Categorical variables were presented in numbers (%), and continuous variables that followed a normal distribution were presented as mean and standard deviation (SD). Differences in patient characteristics that were present in both the DSAA-dataset and the administrative healthcare dataset were examined between the DSAA-dataset and administrative healthcare dataset stratified for EVAR and OSR using chi-square and Fisher exact tests when appropriate. Differences in continuous variables were examined between the groups by independent- samples t-tests. In order to evaluate the frequency and type of mid- term reinterventions (reinterventions within 12 and 15 months) following intact AAA repair, differences in the overall number of reinterventions within 12 and 15 months following EVAR and OSR were examined between EVAR and OSR, stratified for 12 and 15 months, using chi-square and Fisher exact tests when appropriate. Similar analyses were performed to assess differences between EVAR and OSR within the categories of reinterventions.

RESULTS

In total, 4 043 patients from 58 hospitals that underwent EVAR or OSR with infrarenal clamping for an intact infrarenal AAA between January 2017 and December 2018 were selected from the Dutch Surgical Aneurysm Audit and included in the DSAA-dataset (**Figure 1**). A total of 2 059 patients from 46 hospitals were identified in the administrative healthcare database. The specific healthcare activities that describe EVAR and OSR and which were used to construct the administrative healthcare dataset are described in **Table S1.** In total, 3 372 patients that underwent EVAR were included in the DSAA-dataset, compared to 1 734 (51.4%) patients which were included in the administrative healthcare dataset. Furthermore, 671 patients that underwent OSR were included in the DSAA-dataset, compared to 325 (48.4%) which were included in the administrative healthcare dataset.

Figure 1: Flow chart of patients included in the DSAA dataset and administrative healthcare dataset



Patient characteristics

Characteristics of the patients included in the DSAA-dataset, as well as the patient characteristics that are detailed in the administrative healthcare dataset, are shown in **Table 1**. No differences in age and sex were seen between patients included in the DSAA-dataset and the administrative healthcare dataset.

Table 1: Characteristics of patients included in the DSAA dataset and characteristics of patients included in the administrative healthcare dataset. Characteristics were chosen based on relevance and availability of information in the datasets. Information that was not available in the DSAA-dataset or administrative healthcare dataset was displayed as 'n.a.'.

	EVAR			OSR		
	DSAA	**Administrative healthcare dataset**	**P-value**	**DSAA**	**Administrative healthcare dataset**	**P-value**
Number of patients	3372	1734		671	325	
Number of hospitals	58	44		55	45	
Sex: female	482 (14.3%)	240 (13.8%)	0.691	136 (20.3%)	65 (20.0%)	0.988
Age, years			0.602			0.826
≤ 62	203 (6.0%)	119 (6.9%)		92 (13.7%)	42 (12.9%)	
63-72	1139 (33.8%)	592 (34.1%)		298 (44.4%)	142 (43.7%)	
73-82	1574 (46.7%)	785 (45.3%)		247 (36.8%)	120 (36.9%)	
83-90	456 (13.5%)	238 (13.7%)		34 (5.1%)	21 (6.5%)	
ASA						
0	n.a.	450 (25.7%)		n.a.	78 (24.0%)	
1	n.a.	8 (0.5%)		n.a.	3 (0.9%)	
2	n.a.	413 (23.8%)		n.a.	78 (24.0%)	
3	n.a.	749 (43.2%)		n.a.	146 (44.9%)	
4	n.a.	119 (6.9%)		n.a.	22 (6.2%)	
Charlson comorbidity index						
1	n.a.	1 (0.1%)		n.a.	2 (0.6%)	
2	n.a.	35 (2.0%)		n.a.	16 (4.9%)	

Table 1: *Continued.*

	EVAR			OSR	
	DSAA	**Administrative healthcare dataset**	**P-value**	**DSAA**	**Administrative healthcare dataset**
3	n.a.	211 (12.2%)		n.a.	64 (19.7%)
4	n.a.	495 (28.5%)		n.a.	10195 (29.2%)
5	n.a.	391 (22.5%)		n.a.	57 (17.5%)
6	n.a.	601 (34.7%)		n.a.	91 (28.0%)
Pulmonary comorbidity					
No	2447 (72.6%)	n.a.		502 (74.8%)	n.a.
Yes	851 (25.2%)	n.a.		155 (23.1%)	n.a.
Missing	74 (2.2%)	n.a.		14 (2.1%)	n.a.
Cardiac comorbidity					
No	1161 (34.4%)	n.a.		237 (35.3%)	n.a.
Yes	2149 (63.7%)	n.a.		427 (63.6%)	n.a.
Missing	62 (1.8%)	n.a.		7 (1.0%)	n.a.
Creatinine	90 [77, 108]	n.a.		90.0 [74, 107]	n.a.
Aneurysm diameter (mean ± sd)	59.9 ± 10.5	n.a.		62.9 ± 13.1	n.a.

Reinterventions within 12 months and 15 months following EVAR and OSR

Table 2 shows an overview of the reinterventions detected within 12 and 15 months following EVAR and OSR. The percentages of reinterventions within 12 and 15 months following EVAR compared to OSR did not differ. More vascular reinterventions were detected within 12 months following EVAR compared to OSR (9.2% vs. 4.6%; p = 0.009). In addition, more abdominal reinterventions were detected within 12 months following OSR compared to EVAR (6.2% vs. 1.6%; p <0.001). Similar results were found when examining the reinterventions that occurred within 15 months.

Reinterventions within the subcategories and the identification of reinterventions in the administrative healthcare database

Tables 3A-E show an overview of subcategories of reinterventions and individual reinterventions within 12 and 15 months following EVAR and OSR. **Table S2–6** show all healthcare activity codes that were selected from the administrative healthcare database.

Aneurysm related reinterventions

Table 3A shows the reinterventions that took place at the central vessels. In this category, 21 healthcare activity codes that describe reinterventions at the central vessels were selected from the administrative healthcare database. From these healthcare activity codes, 7 different healthcare activity codes were present in the administrative healthcare dataset, while some healthcare activity codes did not occur in this dataset. Most reinterventions that occurred within 12 months were registered in the subcategory 'Reconstruction of the aorta or side branches' (2.4% following EVAR, 1.2% following OSR).

Table 2: Overview of total reinterventions and reinterventions per category within 12 months and within 15 months following EVAR and OSR

	<12 months			<15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Total*	180 (10.4)	31 (9.5)	0.719	199 (11.5)	35 (10.8)	0.785
Vascular	159 (9.2)	15 (4.6)	0.009	178 (10.3)	15 (4.6)	0.002
Central vessels	53 (3.1)	7 (2.2)	0.473	64 (3.7)	7 (2.2)	0.187
Peripheral vessels	63 (3.6)	6 (1.8)	0.129	70 (4.0)	6 (1.8)	0.055
Amputation	7 (0.4)	0 (0.0)	0.605	7 (0.4)	0 (0.0)	0.605
Other	87 (5.0)	7 (2.2)	0.020	96 (5.5)	7 (2.2)	0.008
Abdominal	27 (1.6)	20 (6.2)	<0.001	28 (1.6)	24 (7.4)	<0.001

** Total: both vascular and abdominal reinterventions*

Table 3A: Reinterventions that took place at the central vessels within 12 and 15 months following intact AAA repair

	<12 months			< 15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n= 1734)**	**OSR (n = 325)**	**P-value**
Central vessels	53 (3.1)	7 (2.2)	0.473	64 (3.7)	7 (2.2)	0.187
Embolectomy of blood vessels of the abdomen (open or endovascular procedure) (35501, 35502)	8 (0.5)	2 (0.6)		9 (0.5)	2 (0.6)	
Percutaneous transluminal angioplasty of the (non coronary) central vessels excluding the renal artery (33351)	10 (0.6)	1 (0.3)		13 (0.7)	1 (0.3)	
Reconstruction of the aorta or side branches such as renal arteries, iliac arteries, or subclavian artery (open or endovascular procedure) (33554, 33555, 33342)	41 (2.4)	4 (1.2)		48 (2.8)	4 (1.2)	
Insertion of an aortic bifurcation prosthesis and reconstruction of both renal arteries, open procedure (33561)	1 (0.1)	1 (0.3)		1 (0.1)	1 (0.3)	

Peripheral vessel-related reinterventions

Table 3B shows the reinterventions that took place at the peripheral vessels. In total, 15 healthcare activity codes that describe reinterventions at the peripheral vessels were selected from the administrative healthcare database. From these healthcare activity codes, 11 different healthcare activity codes were present in the administrative healthcare dataset.

Amputations

Amputations following AAA repair are shown in **Table 3C**. Four healthcare activity codes that describe amputations were selected from the administrative healthcare database. From these healthcare activity codes, 3 different healthcare activity codes were present in the administrative healthcare dataset. No amputations were detected following OSR

Other vascular reinterventions

Table 3D shows other vascular reinterventions. In this category, 5 healthcare activity codes that describe other vascular reinterventions were selected from the administrative healthcare database. All these 5 healthcare activity codes were present in the administrative healthcare dataset. Following EVAR, a percutaneous transluminal angioplasty for stenosis or occlusion was most common (3.1%) in the dataset that included reinterventions within 12 months.

Abdominal reinterventions

Abdominal reinterventions are shown in **Table 3E**. In this category, 14 healthcare activity codes that describe abdominal reinterventions were selected from the administrative healthcare database. From these healthcare activity codes, 9 different healthcare activity codes were present in the administrative healthcare dataset. Following OSR, an exploratory laparotomy was most often present in both datasets representing reinterventions within 12 and 15 months (4.6%).

Table 3B: Reinterventions that took place at the peripheral vessels within 12 and 15 months following intact AAA repair

	< 12 months			< 15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Peripheral vessels	63 (3.6)	6 (1.8)	0.129	70 (4.0)	6 (1.8)	0.055
Percutaneous transluminal angioplasty of the peripheral arteries (33672)	10 (0.6)	1 (0.3)		11 (0.6)	1 (0.3)	
Embolectomy of peripheral blood vessels (33600)	19 (1.1)	2 (0.6)		21 (1.2)	2 (0.6)	
Axillobifemoral bypass graft (33673)	1 (0.1)	0 (0.0)		1 (0.1)	0 (0.0)	
Carotid-subclavian bypass graft or femorofemorol bypass graft (33677, 33678)	20 (1.2)	1 (0.3)		22 (1.3)	1 (0.3)	
Femoro-crural bypass graft, open procedure (33680)	2 (0.1)	0 (0.0)		2 (0.1)	0 (0.0)	
Endovascular treatment of femoro-crural or femoropopliteal traject (33681, 33679)	3 (0.2)	1 (0.3)		4 (0.2)	1 (0.3)	
Endovascular reconstruction of open repair of a peripheral artery (33668, 33669, 33670)	24 (1.4)	3 (0.9)		27 (1.6)	3 (0.9)	

Table 3C: Amputations within 12 and 15 months following intact AAA repair

	<12 months			<15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Amputations	7 (0.4)	0 (0.0)	0.605	7 (0.4)	0 (0.0)	0.605
Transfemoral amputation (38590)	1 (0.1)	0 (0.0)		1 (0.0)	0 (0.0)	
Transtibial amputation (38690)	3 (0.2)	0 (0.0)		3 (0.2)	0 (0.0)	
Amputation or exarticulation of a toe (38791)	4 (0.2)	0 (0.0)		4 (0.2)	0 (0.0)	

Table 3D: Other vascular reinterventions within 12 and 15 months following intact AAA-repair

	<12 months			<15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Vascular; other	87 (5.0)	7 (2.2)	0.020	96 (5.5)	7 (2.2)	0.008
Percutaneous transluminal angioplasty for stenosis or occlusion at other non-coronary vessels (80821, 80822)	54 (3.1)	6 (1.8)		59 (3.4)	6 (1.8)	
Trombolysis using medication (i.e. urokinase, streptokinase) (80829)	29 (1.7)	0 (0.0)		32 (1.8)	0 (0.0)	
Embolisation of vessels (80828, 80028)	22 (1.3)	1 (0.3)		28 (1.6)	1 (0.3)	

Table 3E: Abdominal reinterventions within 12 and 15 months following intact AAA-repair

	<12 months			<15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Abdominal	27 (1.6)	20 (6.2)	<0.001	28 (1.6)	24 (7.4)	<0.001
Exploratory laparotomy (35512)	6 (0.3)	15 (4.6)		6 (0.3)	15 (4.6)	
Small bowel resection, open procedure (34638)	2 (0.1)	2 (0.6)		2 (0.1)	2 (0.6)	
Colon resection, with or without coecostomy, open or endoscopic procedure (34738, 34739)	14 (0.8)	1 (0.3)		15 (0.9)	2 (0.6)	
Colostomy or ileostomy creation following laparotomy, open procedure (34752)	3 (0.2)	1 (0.3)		3 (0.2)	1 (0.3)	
Ileus that requires surgery, without resection or anastomosis, open or endoscopic procedure (34880, 34881)	4 (0.2)	3 (0.9)		4 (0.2)	3 (0.9)	
Incisional hernia (open / laparoscopic procedure), or incarcerated hernia without bowel resection (35740, 35741, 35702)	5 (0.3)	5 (1.3)		5 (0.3)	8 (2.5)	

DISCUSSION

In this study, we evaluate the feasibility and the potential benefit of using administrative healthcare data as a source for mid-term outcomes for patients undergoing EVAR and OSR to evaluate reinterventions within 12 and 15 months following intact AAA repair. By first selecting patients that underwent an intact AAA repair from the DSAA, whereafter patients were selected from the administrative healthcare database, we could estimate the proportion of patients that were identified in the administrative healthcare database. Moreover, multiple detailed reinterventions were present in the administrative healthcare database, and thus, many reinterventions following intact AAA repair could be evaluated. However, within our study design, it was not possible to link the administrative healthcare data directly to the DSAA on a patient-level due to privacy restrictions.

Our study reported reintervention rates of 10.4% following EVAR and 9.5% following OSR within 12 months following AAA repair. Unfortunately, available follow-up data was limited, and therefore, we could not include reinterventions that occurred after 15 months following AAA repair. As far as we know, only one other quality registry, the Vascular Quality Initiative, in which hospitals participate electively[14], has studied reinterventions following EVAR after linkage of Medicare claims data[8,15] and another claims database[16], and demonstrated a 1-year reintervention rate of 6% following EVAR[8]. Furthermore, a meta-analysis reported higher long-term reinterventions rates following EVAR compared to OSR using data from 4 randomized controlled trials[17]. Another meta-analysis that included both RCTs and observational cohort studies reported long-term reintervention rates (5 to 9 years) of 17.6% following EVAR and 14.9% following OSR[4]. However, interestingly, a population-based matched cohort study using administrative healthcare data described that long-term reintervention rates did not differ following EVAR and OSR[18]. Despite the considerable number of performed studies, the exact percentages of reinterventions in literature and our study are hardly comparable since each study used other criteria for describing reinterventions[17] and reported other follow-up periods. Nevertheless, reporting reinterventions at the national level might be valuable to evaluate the nationwide impact of the reinterventions following EVAR and OSR, especially since reinterventions significantly raise the costs of AAA repair[19,20]. Although we could only report on a large sample of nationwide data within this study design, which had similar patient characteristics (age and sex) when comparing the administrative healthcare data with the DSAA, this study revealed that about 1 in 10 patients received a reintervention within 12 months following EVAR and OSR.

The development of quality registries should not be inherent with an increase in registration burden[21]. One advantage of adding administrative healthcare data to our

quality registry is that this method does not impose an extra registration burden on physicians since the administrative healthcare data is collected routinely within the hospital information systems[22]. However, within this pilot study, it was not feasible to link the administrative data to the DSAA patients due to privacy restrictions under Dutch law. Patients included in the DSAA are registered by all 58 hospitals that perform intact AAA repair in the Netherlands. Due to this high number of hospitals that register patients in the DSAA, we chose to examine the potential of adding healthcare administrative data to the DSAA. However, linkage of data, which could be achieved by asking permission to all 58 hospitals, will be needed to optimally use the additional information regarding reinterventions provided by the administrative healthcare data. With a linkage of the administrative healthcare dataset to the DSAA-dataset, it will be possible to examine whether specific patient or aneurysm-related factors registered in the DSAA are associated with particular reinterventions or reinterventions in general. Moreover, when evaluating the number of reinterventions following OSR compared to the number of reinterventions following EVAR, it will be necessary to adjust for potential confounders since the crude number of reinterventions might be influenced by selection bias[22] as EVAR could be performed in patients that were unfit for OSR[23] or had more comorbidities[4]. Therefore, the results of this study could serve as a preview of the additional information that could be added to the DSAA when a combined data source is available.

With a combined data source, further research could also focus on the percentages of reinterventions within 12 or 15 months per hospital. These percentages might be relevant feedback to hospitals since the percentage of reinterventions could reflect long-term complication rates of individual hospitals. The individual hospital percentages of reinterventions could depend on local follow-up schemes to detect complications requiring a reintervention[13] and the degree of failure of surveillance[24]. Therefore, it could be valuable to evaluate whether significant variation in the number of reinterventions between hospitals exists using funnel plots that detect hospitals performing below or above the national average percentage of reinterventions within 12 or 15 months. Interestingly, it has been studied that although patients that are compliant with surveillance following EVAR may have an increased reintervention rate, compliance with surveillance does not appear to be associated with survival[25]. More recently, no difference in overall survival was described between patients that underwent secondary intervention following a type 2 endoleak and those who did not undergo secondary intervention[13]. Therefore, it would be interesting to examine the cause of increased reintervention rates in hospitals and to assess whether reinterventions influence long-term survival in future studies. Therefore, it would be interesting to examine the cause of increased reintervention rates in hospitals and to assess whether reinterventions influence long-term survival in future studies.

Although healthcare administrative data is potentially valuable to add to our quality registry, it is important to realize that administrative data has several limitations. First, data validity is crucial when data is used for evaluating quality of healthcare[26]. Another study describing administrative data linkage with registry data validated whether reintervention rates following AAA repair were accurately reflected in the administrative healthcare data[8]. Due to the previously mentioned privacy restrictions, we could not verify whether the described reintervention rates correspond with the data as registered in hospital charts. However, Dutch routinely collected claims data was considered accurate for patients with an acute myocardial infarction[12]. Secondly, since all healthcare activity codes within 12 or 15 months following AAA-repair that occurred in the administrative healthcare database were included and no additional details were provided within the descriptions of the reintervention, we could not determine whether the reinterventions were related to complications of the AAA-repair, or whether the reinterventions were related to another complication. Moreover, due to the limited information included in the description of the reinterventions, we could not determine which specific complication caused the reintervention. Also, only patients who underwent a reintervention in the same hospital as where their primary AAA repair was performed could be identified in the administrative healthcare dataset. Although we hypothesized that most patients underwent a reintervention in the same hospital as their primary intervention, the administrative healthcare data potentially did not provide a complete overview of the number of reinterventions that occurred. The VQI, which indirectly linked their data with a claims database could not capture all reinterventions as well, since data on care performed at Veteran's Association hospitals were not included in the claims database[16].

Also, our study design has certain limitations. First, the administrative healthcare database has a near nationwide coverage which means that not all hospitals that perform AAA repair are present in the administrative healthcare dataset. Therefore, the results of our study represented a large sample from a nationwide cohort instead of a nationwide cohort. Secondly, extensive analysis examining the influence of patient characteristics on reintervention rates or analysis on when reinterventions occur was not possible since the administrative health- care data was not linked to the DSAA. Also, since there was no linkage of data, we could not verify whether reinterventions that were registered in the DSAA (reinterventions within 30 days) corresponded with reinterventions within 30 days that were registered in the administrative healthcare data. An important strength of this study was its simple study design in which the potential benefit of adding administrative health- care data retrospectively to the DSAA could be examined.

In conclusion, adding administrative healthcare data to the DSAA is potentially beneficial to evaluate mid-term reinterventions following intact AAA repair without increasing the

registration burden for clinicians. However, the administrative healthcare data should be linked with the DSAA to further validate this data before reliable implementation of this tool is warranted.

Conflict of interest

HV: Consultant for Medtronic, WL Gore, Terumo, Endologix, and Philips. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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REFERENCES

1 Lijftogt N, Vahl AC, Wilschut ED, Elsman BHP, Amodio S, van Zwet EW, et al. Adjusted Hospital Outcomes of Abdominal Aortic Aneurysm Surgery Reported in the Dutch Surgical Aneurysm Audit. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(4):520–32. Doi: 10.1016/j.ejvs.2016.12.037.

2 Beck N, van Bommel AC, Eddes EH, van Leersum NJ, Tollenaar RA, Wouters MW. The Dutch Institute for Clinical Auditing: Achieving Codman's Dream on a Nationwide Basis. *Ann Surg* 2020;**271**(4):627–31. Doi: 10.1097/SLA.0000000000003665.

3 Schermerhorn ML, Buck DB, O'Malley AJ, Curran T, McCallum JC, Darling J, et al. Long-Term Outcomes of Abdominal Aortic Aneurysm in the Medicare Population. *New England Journal of Medicine* 2015;**373**(4):328–38. Doi: 10.1056/nejmoa1405778.

4 Li B, Khan S, Salata K, Hussain MA, de Mestral C, Greco E, et al. A systematic review and meta-analysis of the long-term outcomes of endovascular versus open repair of abdominal aortic aneurysm. *J Vasc Surg* 2019;**70**(3):954-969.e30. Doi: 10.1016/j.jvs.2019.01.076.

5 Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(1):8–93. Doi: 10.1016/j.ejvs.2018.09.020.

6 Patel R, Sweeting MJ, Powell JT, Greenhalgh RM. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. *The Lancet* 2016;**388**(10058):2366–74. Doi: 10.1016/S0140-6736(16)31135-7.

7 van Schaik TG, Yeung KK, Verhagen HJ, de Bruin JL, van Sambeek MRHM, Balm R, et al. Long-term survival and secondary procedures after open or endovascular repair of abdominal aortic aneurysms. *J Vasc Surg* 2017;**66**(5):1379–89. Doi: 10.1016/j.jvs.2017.05.122.

8 Columbo JA, Kang R, Hoel AW, Kang J, Leinweber KA, Tauber KS, et al. A comparison of reintervention rates after endovascular aneurysm repair between the Vascular Quality Initiative registry, Medicare claims, and chart review. *J Vasc Surg* 2019;**69**(1):74-79.e6. Doi: 10.1016/j.jvs.2018.03.423.

9 van der Werf LR, Voeten SC, van Loe CMM, Karthaus EG, Wouters MWJM, Prins HA. Data verification of nationwide clinical quality registries. *BJS Open* 2019;**3**(6):857–64. Doi: 10.1002/bjs5.50209.

10 Open data van de Nederlandse Zorgauthoriteit. https://www.opendisdata.nl/. 10/05/2021.

11 Salet N, Bremmer RH, Verhagen MAMT, Ekkelenkamp VE, Hansen BE, De Jonge PJF, et al. Is Textbook Outcome a valuable composite measure for short-term outcomes of gastrointestinal treatments in the Netherlands using hospital information system data? A retrospective cohort study. *BMJ Open* 2018;**8**(2). Doi: 10.1136/bmjopen-2017-019405.

12 Eindhoven DC, van Staveren LN, van Erkelens JA, Ikkersheim DE, Cannegieter SC, Umans VAWM, et al. Nationwide claims data validated for quality assessments in acute myocardial infarction in The Netherlands. *Netherlands Heart Journal* 2018;**26**(1):13–20. Doi: 10.1007/s12471-017-1055-3.

13 Mulay S, Geraedts ACM, Koelemay MJW, Balm R, Balm R, Elshof JW, et al. Type 2 Endoleak With or Without Intervention and Survival After Endovascular Aneurysm Repair. *European Journal of Vascular and Endovascular Surgery* 2021;**61**(5):779–86. Doi: 10.1016/j.ejvs.2021.01.017.

14 Dansey KD, de Guerre LEVM, Swerdlow NJ, Li C, Lu J, Patel PB, et al. A comparison of administrative data and quality improvement registries for abdominal aortic aneurysm repair. *J Vasc Surg* 2021;**73**(3):874–88. Doi: 10.1016/j.jvs.2020.06.105.

15 Tsougranis G, Eldrup-Jorgensen J, Bertges D, Schermerhorn M, Morales P, Williams S, et al. The Vascular Implant Surveillance and Interventional Outcomes (VISION) Coordinated Registry Network: An effort to advance evidence evaluation for vascular devices. *J Vasc Surg* 2020;**72**(6):2153–60. Doi: 10.1016/j.jvs.2020.04.507.
16 Columbo JA, Sedrakyan A, Mao J, Hoel AW, Trooboff SW, Kang R, et al. Claims-based surveillance for reintervention after endovascular aneurysm repair among non-Medicare patients. *J Vasc Surg* 2019;**70**(3):741–7. Doi: 10.1016/j.jvs.2018.11.031.
17 Powell JT, Sweeting MJ, Ulug P, Blankensteijn JD, Lederle FA, Becquemin JP, et al. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. *British Journal of Surgery* 2017;**104**(3):166–78. Doi: 10.1002/bjs.10430.
18 Salata K, Hussain MA, De Mestral C, Greco E, Aljabri BA, Mamdani M, et al. Comparison of Outcomes in Elective Endovascular Aortic Repair vs Open Surgical Repair of Abdominal Aortic Aneurysms. *JAMA Netw Open* 2019;**2**(7):1–14. Doi: 10.1001/jamanetworkopen.2019.6578.
19 Columbo JA, Goodney PP, Gladders BH, Tsougranis G, Wanken ZJ, Trooboff SW, et al. Medicare costs for endovascular abdominal aortic aneurysm treatment in the Vascular Quality Initiative. *J Vasc Surg* 2021;**73**(3):1056–61. Doi: 10.1016/j.jvs.2020.06.109.
20 Bulder RMA, Eefting D, Vriens PWHE, van Tongeren RB, Matsumura JS, van den Hout WB, et al. Editor's Choice – A Systemic Evaluation of the Costs of Elective EVAR and Open Abdominal Aortic Aneurysm Repair Implies Cost Equivalence. *European Journal of Vascular and Endovascular Surgery* 2020;**60**(5):655–62. Doi: 10.1016/j.ejvs.2020.07.012.
21 Zegers M, Veenstra GL, Gerritsen G, Verhage R, van der Hoeven HJG, Welker GA. Perceived Burden Due to Registrations for Quality Monitoring and Improvement in Hospitals: A Mixed Methods Study. *Int J Health Policy Manag* 2020;(x):1–14. Doi: 10.34172/ijhpm.2020.96.
22 Clarke GM, Conti S, Wolters AT, Steventon A. Evaluating the impact of healthcare interventions using routine data. *The BMJ* 2019;**365**(June):1–7. Doi: 10.1136/bmj.l2239.
23 United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG ED. Endovascular Repair of Abdominal Aortic Aneurysm in Patients Physically Ineligible for Open Repair. *New England Journal of Medicine* 2010;**362**:1872–80. Doi: 10.1097/SLA.0000000000002392.
24 Grima MJ, Karthikesalingam A, Holt PJ, Kerr D, Chetter I, Harrison S, et al. Multicentre Post-EVAR Surveillance Evaluation Study (EVAR-SCREEN). *European Journal of Vascular and Endovascular Surgery* 2019;**57**(4):521–6. Doi: 10.1016/j.ejvs.2018.10.032.
25 Grima MJ, Boufi M, Law M, Jackson D, Stenson K, Patterson B, et al. Editor's Choice – The Implications of Non-compliance to Endovascular Aneurysm Repair Surveillance: A Systematic Review and Meta-analysis. *European Journal of Vascular and Endovascular Surgery* 2018;**55**(4):492–502. Doi: 10.1016/j.ejvs.2017.11.030.
26 Venermo M, Mani K, Kolh P. The quality of a registry based study depends on the quality of the data – without validation, it is questionable. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(5):611–2. Doi: 10.1016/j.ejvs.2017.03.017.

SUPPLEMENTAL MATERIAL

Table S1: Overview of specific care activity codes that were used to construct the administrative healthcare database and number of patients that could be included

EVAR	Number of patients	OSR	Number of patients
Reconstruction of the aorta or side branches as renal arteries or iliac artery, endovascular aneurysm repair (33555)	1734	Reconstruction of the aorta or side branches as renal arteries or iliac artery, open repair (33554)	325

Table S2

	<12 months			< 15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n= 1734)**	**OSR (n = 338)**	**P-value**
Vascular: central vessels	53 (3.1)	7 (2.2)	0.473	64 (3.7)	7 (2.2)	0.187
Embolectomy of blood vessels of the abdomen (open or endovascular procedure) (35501, 35502)	8 (0.5)	2 (0.6)		9 (0.5)	2 (0.6)	
Embolectomy of blood vessels of the abdomen, open procedure (35501)	2 (0.1)	1 (0.3)		3 (0.2)	1 (0.3)	
Embolectomy of blood vessels of the abdomen, endovascular procedure (35502)	6 (0.3)	1 (0.3)		6 (0.3)	1 (0.3)	
Percutaneous transluminal angioplasty of the (non coronary) central vessels (33350)	0	0		0	0	
Percutaneous transluminal angioplasty of the (non coronary) central vessels excluding the renal artery (33351)	10 (0.6)	1 (0.3)		13 (0.7)	1 (0.3)	
Percutaneous transluminal angioplasty of the renal artery (33360)	0	0		0	0	
Percutaneous transluminal angioplasty of the renal artery, from 1 kidney (88126)	0	0		0	0	
Reconstruction of the aorta or side branches such as renal arteries, iliac arteries, or subclavian artery (open or endovascular procedure (33554, 33555, 33342)	41 (2.4)	4 (1.2)		48 (2.8)	4 (1.2)	

Table S2 *Continued.*

	<12 months			< 15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n= 1734)**	**OSR (n = 338)**	**P-value**
Reconstruction of the aorta or side branches such as renal arteries or iliac arteries, open surgical procedure (33554)	10 (0.6)	0 (0.0)		11 (0.6)	0 (0.0)	
Reconstruction of the aorta or side branches such as renal arteries or iliac arteries, endovascular (33555)	32 (1.8)	4 (1.2)		40 (2.3)	4 (1.2)	
Reconstruction of the aorta or side branches such as artery subclavia, endovascular procedure (33342)	1 (0.1)	0 (0.0)		1 (0.1)	0 (0.0)	
Reconstruction of the aorta or side branches such as renal renal arteries or iliac arteries (33556)	0	0		0	0	
Reconstruction of the aorta or side branches such as subclavian artery (33340)	0	0		0	0	
Reconstruction of the aorta or side branches such as subclavian artery, open procedure (33341)	0	0		0	0	
Aortic bifurcated or straight graft with concomitant reconstruction of one renal artery, open procedure (33559)	0	0		0	0	
Insertion of an aortic bifurcation prosthesis and reconstruction of one renal artery, endovascular procedure (33560)	0	0		0	0	

Table S2 *Continued.*

	<12 months			< 15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n= 1734)**	**OSR (n = 338)**	**P-value**
Insertion of an aortic bifurcation prosthesis and reconstruction of both renal arteries, open procedure (33561)	1 (0.1)	1 (0.3)		1 (0.1)	1 (0.3)	
Insertion of an aortic bifurcation prosthesis and reconstruction of both renal arteries, endovascular procedure (33562)	0	0		0	0	
Insertion of an aortic bifurcation prosthesis and reconstruction of one renal artery (33557)	0	0		0	0	
Aortic bifurcated or straight graft with a concomitant reconstruction of one renal artery, open procedure (33558)	0	0		0	0	
Operative treatment of ruptured AAA (33531)	0	0		0	0	

The underlined reinterventions are also shown in table 3A.

Table S3

	< 12 months			< 15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Vascular: peripheral vessels	63 (3.6)	6 (1.8)	0.129	70 (4.0)	6 (1.8)	0.055
Percutaneous transluminal angioplasty of the peripheral arteries (33672)	10 (0.6)	1 (0.3)		11 (0.6)	1 (0.3)	
Percutaneous transluminal angioplasty of the peripheral vessels (33699)	0	0		0	0	
Embolectomy of peripheral blood vessels (33600)	19 (1.1)	2 (0.6)		21 (1.2)	2 (0.6)	
Axillobifemoral bypass graft (33673)	1 (0.1)	0 (0.0)		1 (0.0)	0 (0.0)	
Axillofemoral bypass graft (33674)	0	0		0	0	
Carotid-subclavian bypass graft or femorofemorol bypass graft (33677, 33678)	20 (1.2)	1 (0.3)		22 (1.3)	1 (0.3)	
Carotid-subclavian bypass graft or femorofemorol bypass graft (33677)	11 (0.6)	0 (0.0)		13 (0.7)	0 (0.0)	
Femorofemorol bypass graft, open procedure (33678)	9 (0.5)	1 (0.3)		9 (0.5)	1 (0.3)	
Femoro-crural bypass graft, open procedure (33680)	2 (0.1)	0 (0.0)		2 (0.1)	0 (0.0)	
Femoropopliteal bypass graft (33675)	0	0		0	0	
Femoro-crural bypass graft (33676)	0	0		0	0	
Endovascular treatment of femoro-crural or femoropopliteal traject (33681, 33679)	3 (0.2)	1 (0.3)		4 (0.2)	1 (0.3)	

Table S3 *Continued.*

	< 12 months			< 15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Endovascular treatment of femoro-crural traject (33681)	1 (0.1)	0 (0.0)		1 (0.1)	0 (0.0)	
Endovascular treatment of femoropopliteal traject (33679)	2 (0.1)	1 (0.3)		3 (0.2)	1 (0.3)	
Endovascular reconstruction of open repair of a peripheral artery (33668, 33670, 33669)	24 (1.4)	3 (0.9)		27 (1.6	3 (0.9)	
Endovascular reconstruction of peripheral artery using transplant, endarteriectomy, endostent or patch (33668)	2 (0.1)	(0.0)		2 (0.1)	(0.0)	
Open repair of a peripheral artery using transplant, endarteriectomy, endostent or patch (33670)	21 (1.2)	3 (0.9)		23 (1.3)	3 (0.9)	
Open repair of a peripheral artery using transplant, endarteriectomy, endostent or patch, using a microscope (33669)	1 (0.1)	0 (0.0)		2 (0.1)	0 (0.0)	

The underlined reinterventions are also shown in table 3B.

Table S4

	<12 months			<15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Vascular: amputations	7 (0.4)	0 (0.0)	0.605	7 (0.4)	0 (0.0)	0.605
Transfemoral amputation (38590)	1 (0.1)	0 (0.0)		1 (0.1)	0 (0.0)	
Transtibial amputation (38690)	3 (0.2)	0 (0.0)		3 (0.2)	0 (0.0)	
Transmetatarsal amputation (38790)	0	0		0	0	
Amputation or exarticulation of a toe (38791)	4 (0.2)	0 (0.0)		4 (0.2)	0 (0.0)	

The underlined reinterventions are also shown in table 3C.

Table S5

	<12 months			<15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Vascular: other	87 (5.0)	7 (2.2)	0.020	96 (5.5)	7 (2.2)	0.008
Percutaneous transluminal angioplasty for stenosis or occlusion at other non-coronary vessels (80821, 80822)	54 (3.1)	6 (1.8)		59 (3.4)	6 (1.8)	
Percutaneous transluminal angioplasty for stenosis at other non-coronary vessels (80821)	36 (2.1)	6 (1.8)		39 (2.2)	6 (1.8)	
Percutaneous transluminal angioplasty for occlusion at other non-coronary vessels (80822)	23 (1.3)	0 (0.0)		25 (1.4)	0 (0.0)	
Trombolysis using medication (i.e. urokinase, streptokinase) (80829)	29 (1.7)	0 (0.0)		32 (1.8)	0 (0.0)	

Table S5 *Continued.*

	<12 months			<15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Embolisation of vessels (80828, 80028)	22 (1.3)	1 (0.3)		28 (1.6)	1 (0.3)	
Embolisation of vessels (80828)	20 (1.1)	1 (0.3)		26 (1.5)	1 (0.3)	
Non-elective embolisation of vessels (80028)	2 (0.1)	0 (0.0)		2 (0.1)	0 (0.0)	

The underlined reinterventions are also shown in table 3D.

Table S6

	<12 months			<15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Abdominal	27 (1.6)	20 (6.2)	<0.001	28 (1.6)	24 (7.4)	<0.001
Exploratory laparotomy (35512)	6 (0.3)	15 (4.6)		6 (0.3)	15 (4.6)	
Small bowel resection, open procedure (34638)	2 (0.1)	2 (0.6)		2 (0.1)	2 (0.6)	
Small bowel resection, endoscopic procedure (34639)	0	0		0	0	
Incarcerated hernia and bowel resection (34633)	0	0		0	0	
Colon resection, with or without coecostomy, open or endoscopic procedure (34738, 34739)	14 (0.8)	1 (0.3)		15 (0.9)	2 (0.6)	
Colon resection, with or without coecostomy, open procedure (34738)	9 (0.5)	1 (0.3)		9 (0.5)	1 (0.3)	

Table S6 *Continued.*

	<12 months			<15 months		
	EVAR (n = 1734)	**OSR (n = 325)**	**P-value**	**EVAR (n = 1734)**	**OSR (n = 325)**	**P-value**
Colon resection, with or without coecostomy, endoscopic procedure (34739)	5 (0.3)	0 (0.0)		6 (0.3)	1 (0.3)	
Colostomy or ileostomy creation following laparotomy, open procedure (34752)	3 (0.2)	1 (0.3)		3 (0.2)	1 (0.3)	
Colostomy or ileostomy creation following laparotomy, endoscopic procedure (34753)	0	0		0	0	
Ileus that requires surgery, without resection or anastomosis, open or endoscopic procedure (34880, 34881)	4 (0.2)	3 (0.9)		4 (0.2)	3 (0.9)	
Ileus that requires surgery, without resection or anastomosis, open proecedure (34880)	3 (0.1)	2 (0.6)		3 (0.1)	2 (0.6)	
Ileus that requires surgery, without resection or anastomosis, endoscopic proecedure (34881)	1 (0.1)	1 (0.3)		1 (0.1)	1 (0.3)	
Therapeutic laparoscopy (35588)	0	0		0	0	
Incisional hernia (open / laparoscopic procedure), or incarcerated hernia without bowel resection (35740, 35741, 35702)	5 (0.3)	6 (1.8)		5 (0.3)	8 (2.5)	
Incisional hernia, open procedure (35740)	3 (0.2)	5 (1.5)		3 (0.2)	7 (2.1)	
Incisional hernia, laporascopic procedure (35741)	2 (0.1)	0 (0.0)		2 (0.1)	1 (0.3)	
Incarcerated hernia without bowel resection, open procedure (35702)	0	0		0	0	
Incarcerated hernia without bowel resection, endoscopic procedure (35712)	0	0		0	0	

The underlined reinterventions are also shown in table 3E.

CHAPTER

11

GENERAL DISCUSSION

GENERAL DISCUSSION

Quality registries, including the Dutch Surgical Aneurysm Audit (DSAA), reflect nationwide real-world treatment outcomes and can be used to evaluate and improve the actual quality of care[1]. Although randomised controlled trials (RCTs) are considered the gold standard to assess or compare two different treatment modalities, insights from quality registries can be complementary to RCTs, as RCTs do not always reflect clinical reality[2]. Therefore, this thesis aims to gain insight into the quality and true real-world outcomes of the current practice of aortic aneurysm treatment in the Netherlands. Furthermore, we investigated new opportunities to develop the DSAA further.

Abdominal aortic aneurysm treatment outcomes

One of the aims of the DSAA is to improve treatment outcomes over time. Therefore, since the introduction of the DSAA in 2013, hospital feedback on abdominal aortic aneurysm treatment outcomes has been provided using funnel plots that compare individual hospital results with the national average. In this thesis, we demonstrate that since 2014, several perioperative outcomes (mortality, major complications, and textbook outcome) of EVAR and OSR for intact AAA had improved, except for perioperative mortality following EVAR, which remained unchanged (**Chapter 2**). The perioperative mortality following OSR decreased, from 6.1% in 2014 to 4.7% in 2019, in line with rates described in international registries[3]. Although the exact cause of these improvements is hard to be determined as it is probably multifactorial, the establishment of the DSAA likely plays an important role in this improvement[4].

RCT results can be misleading when applied in clinical reality due to an unrepresentative selection of patients. Therefore, we used data reflecting real-world results which could provide vital information when evaluating treatment outcomes for patients not included in RCTs. Octogenarians are barely enrolled in current RCTs[5], while in our nationwide cohort study, +/- 25% of the patients that underwent EVAR had an age above 80. Moreover, we revealed that mortality rates of octogenarians following OSR exceeded 10%, especially when comorbidities were present. Interestingly, in the (small) group of octogenarians without comorbidities that underwent OSR, the mortality was only 3.6% (**Chapter 3**). In the literature, a meta-analysis that included octogenarians electively treated by OSR for an AAA reported a mortality of 7.5%[6], and a study that showed the combined results of 11 vascular registries of intact aneurysm repair reported a mortality rate of 9.5%[3]. It should be realised that in an elective setting, the perioperative risks versus the risk of aneurysm rupture should be considered. Studies that examined the safety of surveillance for aneurysms up to 5.5 cm reported 30-day mortality rates of only 2.1% in the immediate repair group[7] and 5.5% in the early elective surgery group[8], which is significantly lower compared to

our observations in octogenarians. Recently, a study reported annual rupture rates that were much lower than previously reported rates, including a 3-year cumulative incidence of rupture of 4.5% for men and 12.8% for women with AAA diameters between 6.1 and 7.0 cm[9]. This poses the question whether current reported surgical risks for octogenarians are acceptable, especially for elderly patients with small aneurysm diameters with a low risk of rupture. Due to the high perioperative risks and relatively low risks of rupture, the threshold diameter for open surgical repair may need to be increased up to 6.5 or 7.0 cm in male octogenarians with comorbidities. Further research should be performed to examine the optimal cutoff point for aneurysm repair in male and female octogenarians with and without comorbidities while considering the risk of rupture, the patient's estimated life expectancy, and perioperative risks.

Perioperative mortality rates of octogenarians following ruptured AAA repair are also substantial, especially following OSR, after which perioperative mortality rates of 50% are reported (**Chapter 4**). This percentage was in accordance with a recently published meta-analysis[10]. Our results following ruptured AAA repair could reflect selection bias since only patients who were stable enough to reach the hospital and underwent surgery are included in our registry. Moreover, patients with fragile preoperative conditions might not undergo surgery anymore. The potential selection bias was reflected in our multivariable analysis, which counterintuitively showed that factors such as 'increased age' and 'elevated preoperative creatinine' were associated with less mortality in octogenarians following OSR. For Dutch vascular surgeons, our results reflect the current national practice of treatment of octogenarians. This information could be a first step in evaluating the selection of octogenarians for surgery. However, turndown rates are not reported in the DSAA. Therefore, we could not gain insight into preoperative patient selection, which is essential to assess the entire selection process of octogenarians for surgery. Interestingly, a recent multi-centre cohort study from the Netherlands reported a turndown rate for ruptured AAA of only 29.9%. In comparison, a study including octogenarians receiving OSR from Japan reported a turndown of 54.7%[11]. Survival after aneurysm repair is not the sole parameter of clinical success. Therefore, mortality rates should be complemented by patient-centred outcomes such as health-related quality of life and postoperative living situations[12]. The measurement of quality of life in octogenarians requires further investigation since, in literature, information on the quality of life of octogenarians following ruptured AAA repair is not available[12]. Moreover, in elective patients, current aneurysm-specific questionaries measuring the quality of life following elective AAA require extension and further validation[13].

Women have increased perioperative mortality rates following EVAR and OSR for an intact AAA[14,15]. This difference in mortality rates persists despite correction for well-known

patient-related factors[16,17]. Besides patient-related factors, factors on hospital level could affect treatment outcomes as well. However, it was not studied yet whether these factors may explain the difference in mortality rates between women and men. **Chapter 5** show that even after correction for interhospital variation, the female sex was still associated with increased mortality following elective EVAR or OSR. Further in-depth studies on patient-related factors, such as anatomical, genetic, and biological differences, are needed to identify potential declarations for this difference. This information could be collected by observational cohort studies that include longitudinal data, information on biomarkers, and imaging, such as the multicenter Dutch AAA bank[18].

Since the introduction of EVAR in 1991, the number of patients treated by EVAR has increased, which resulted in a reduction in the number of performed OSR[19,20]. Consequently, concerns have arisen about whether the current number of performed OSRs is enough to achieve and maintain the best outcomes. In recent years, perioperative mortality rates following OSR decreased from 6.1% to 4.6% (**Chapter 2**), but a worrisome variation between hospitals is seen. Perioperative outcomes could be further improved by a reduction of complications. Following major vascular surgery, including OSR, EVAR, open lower extremity bypass graft, or lower extremity amputations, complications such as bleeding and pneumonia were found to have the most significant overall impact[21]. To provide more insight into the consequences of complications following OSR, we identify the complications that most affect the outcomes of perioperative mortality, secondary intervention, and prolonged hospitalisation for this group of patients. Bowel ischemia and renal complications had the highest impact on perioperative mortality, while arterial occlusion and bowel ischemia were shown to have the highest impact on secondary interventions. Pneumonia had the highest impact on prolonged hospital admissions (**Chapter 6**). Surgical quality improvement programs should prioritise the prevention of these complications.

Complex aortic aneurysm treatment outcomes

An increase in hospital volume has been shown to improve outcomes of basically all surgical procedures, including aortic interventions like open juxtarenal AAA repair[22] and thoracoabdominal aortic aneurysm repair[23,24]. Previous studies reporting on a volume-outcome relation in complex EVAR (FEVAR and BEVAR) did not show any hospital volume-outcome relationship[23,24]. In **Chapter 7,** we report that perioperative mortality rates following FEVAR were 4.5%, and 5.2% following BEVAR. Moreover, we revealed that an increase in annual hospital volume of complex EVAR (FEVAR and BEVAR) was significantly associated with lower perioperative mortality. The nationwide design of our study was important in revealing the association between hospital volume and mortality as no minimum number of complex EVAR was required in the Netherlands during the study

period. Therefore, many low-volume hospitals were included in our study. The data from our research suggest that an annual hospital volume of less than 9 complex EVAR procedures is too low to expect satisfactory results, whereas an annual volume of at least 13 complex EVAR procedures appears to result in better outcomes. However, in a spline diagram, the mortality reduction was even observed until 20 cases per year, suggesting that an annual volume requirement for complex EVAR procedures per hospital should be set around 20. The influence of surgeon volume could not be examined in our study, as this information is not registered in the DSAA. Recently, the Dutch Society of Vascular Surgery has decided to set minimum volume requirements for complex endovascular aneurysm treatment (at least 20 chimney EVAR, FEVAR, BEVAR, or TEVAR per year, or at least 10 per category)[25]. Interestingly, these volume thresholds of 10 and 20 per year do not fully match the results of our study as the types of surgery differ. The optimal threshold might vary between countries[26–28] and might be influenced by surgeons' learning curves. Therefore, it is important to continue investigating the volume-outcome associations of complex EVAR.

In contrast to the treatment results of abdominal aortic aneurysms, no RCTs have been performed to compare outcomes of OSR versus fenestrated EVAR and chimney EVAR for complex aortic aneurysms, including juxtarenal aortic aneurysms. A multicenter prospective registry in which patients received f/b-EVAR if they were considered at high risk for open surgery reported that there was no difference in 30-day mortality between f/b-EVAR and OSR[29]. In this thesis, it is reported that crude national perioperative mortality rates for juxtarenal AAAs were 6.6% following open surgical repair and 2.5% following complex endovascular repair, including fenestrated EVAR and Chimney EVAR. Also, after adjustment for confounders, there was more perioperative mortality after OSR compared with fenestrated and chimney EVAR for juxtarenal aortic aneurysms in an elective setting. In this study, using data from the DSAA, the choice of treatment modality was left to the preference of the local surgeon, similar to most other performed observational cohort studies. Therefore, some patients may have undergone endovascular treatment due to an 'endovascular-first' strategy of the hospital. In contrast, other patients may have been offered OSR because FEVAR/ChEVAR was not available in their hospital (**Chapter 8**). Another limitation of our study was the limited amount of anatomical aneurysm details included in the DSAA. The higher perioperative mortality following OSR in this thesis contrasts with the results of two meta-analyses that included case series and retrospective cohort studies. These meta-analyses showed no significant differences in early mortality between FEVAR and OSR[30,31]. The lack of differences in mortality in these meta-analyses was potentially caused by including patients in the endovascular group with more comorbidities. In addition, the meta-analyses reported that major complications occurred more often following OSR, which is in accordance with the results described in this thesis. The results of the meta-analyses were taken into account by the ESVS guideline, which

states that an endovascular solution with fenestrated endografts for juxtarenal aortic aneurysms should be considered the preferred treatment option when feasible[32]. However, since current observational cohort studies are all prone to selection bias, it should be realised that an RCT is needed to truly compare the treatment outcomes of FEVAR/ChEVAR versus OSR for juxtarenal AAAs.

New opportunities for feedback and outcome measurement and future perspectives for the Dutch Surgical Aneurysm Audit

Although various nationwide cohort studies were performed in this thesis using data from the DSAA, it should be realised that the principle aim of the Dutch Surgical Aneurysm Audit is to provide hospitals feedback using the principles of clinical auditing. Therefore, the amount of data to be registered is a consideration between the minimum required data needed for the clinical auditing process and more extensive data collection to register data that is useful for scientific purposes. Furthermore, although registering in the DSAA has made clinicians aware that their results could become public, which could have induced improvement the aneurysmal care, it is essential to think about the further development of the DSAA to achieve further improvement of both the monitoring and outcomes of aortic aneurysm care. For the further development of the DSAA, the following considerations should be taken into account.

Assessing the reliability of the data using data verification

Since data managers or clinicians register the data in the DSAA, it is essential that the registered data is verified to check whether it is complete and accurate. In the past (2015), data verification was performed manually by employees trained by DICA. In this data verification project performed in 14 out of the 60 participating hospitals, the completeness of the DSAA was evaluated, and the accuracy of data was assessed. The completeness of the registration was found to be 99.8%, while the accuracy on mortality and complications was 100% and 92.6%, respectively. Although this method for data verification had promising results, the technique was very time-consuming and expensive[33]. Therefore, a new automatic data verification method was applied recently. This method was based on detecting discrepancies between reimbursement data and the data as registered in the registries. Although this method has promising results, it is not yet performed in all DSAA hospitals, which should be improved in the future.

Decreasing the registration burden for clinicians

One of the biggest challenges of the DSAA is the registration burden for clinicians. Although electronic health records are implemented in all Dutch hospitals, most clinicians and data managers still have to fill in the DSAA registry manually, which is extremely time-consuming. The project 'Registratie aan de bron' evaluated whether information

that needs to be filled in in the DSAA is also registered in the electronic medical record systems and how this information is registered in several hospitals. Furthermore, it was examined whether the information registered in the quality registries could be translated into standardised definitions ('zorginformatiebouwstenen' (zibs)). In the near future, it should be discussed with all stakeholders (clinicians, hospitals, and suppliers of electronic medical records systems) how automatic registering in the DSAA and other registries could be implemented nationally[34,35]. Some hospitals have already implemented an automatic filling of the DSAA from their electronic medical record system. However, this filling often is not reliable enough.

Follow-up data in the DSAA

The DSAA includes perioperative outcomes that occur up to 30 days following surgery or during the same hospital admission. However, complications and reinterventions after this perioperative period are not scarce following EVAR and OSR[36]. As most patients survive multiple years following an AAA repair, reliable data on long-term results, especially the durability of EVAR are essential. Available data that evaluate mid and long-term reinterventions especially describe data from randomized controlled trials or from observational studies that contain data from centres of excellence. A limited registration burden is crucial for quality registries, and therefore, we assessed the feasibility and potential benefit of using administrative healthcare data to evaluate the frequency and type of mid-term reinterventions following intact AAA repair. Detailed information regarding reinterventions was present in the administrative healthcare data, and thus, many reinterventions following intact AAA repair could be evaluated. Unfortunately, within our study design, it was not possible to link the administrative healthcare data directly to the DSAA on a patient level due to privacy restrictions (**Chapter 9**). Linkage of data from the DSAA with administrative healthcare data, which could be achieved by asking permission from all 58 hospitals that register their patients in the DSAA, will be needed to optimally use and validate the additional information regarding reinterventions provided by the administrative healthcare data. Moreover, future research should examine whether the percentages of reinterventions per hospital within 12 or 15 months following AAA repair are relevant information to use for feedback, as these percentages of reinterventions could depend on local follow-up schema to detect complications requiring a reintervention[37] and the degree of failure of surveillance[38]. The reported reintervention rates of our study (10.4% following EVAR and 9.5% following OSR within 12 months following AAA repair) are hardly comparable with the data reported in the literature since each study used different criteria for describing reinterventions[5]. Nevertheless, reporting reinterventions at a national level might be valuable to evaluate the nationwide impact of reinterventions following EVAR and OSR, especially since reinterventions significantly raise the costs of AAA repair[39,40].

Providing feedback

Besides collecting data, data analysis is another important step in the clinical audit cycle[41]. The DSAA provides feedback using funnel plots that evaluate individual hospital clinical outcomes, including clinical outcomes of the last 36 months, against a yearly benchmark. It is challenging to determine whether hospital clinical outcome rates improve or deteriorate over shorter periods. When funnel plots include clinical outcomes from fewer patients due to a shorter period, the power of the funnel plots will decrease[42]. In industrial processes, real-time process control systems are widely applied. In medical contexts, the application of real-time process control, for example, the CUSUM method, is rising. The CUSUM method monitors real-time trends in outcome rates set off against control limits based on baseline data and adjusted for patients' risk factors. With the application of control limits, the CUSUM method can distinguish common cause variation, which is the natural variation present in all outcome events, from special cause variation, which is an unexpected variation that could result from a system's failure.

In this thesis, we describe how the CUSUM method could provide feedback to vascular surgeons that treat AAA patients using data from the DSAA. We found that median-sized hospitals with substantially deviating results were detected within two years using the CUSUM method (**Chapter 10**). Although a comparison of the statistical performance of the CUSUM with the funnel plots was not performed as the CUSUM method was not comparable with funnel plots, we assumed that CUSUM charts could complement the feedback provided by the currently used funnel plots. Physicians who register their patients in the DSAA already have access to the Codman Dashboard. This dynamic monitoring dashboard could be used to implement the Log-likelihood CUSUM for internal usage. Future research should examine whether implementing CUSUM charts would significantly improve outcomes.

Quality indicators

The quality of care can be improved by reducing variation in clinical outcomes between hospitals[1]. To encourage clinicians to improve the quality of their delivered care, the quality indicators used for feedback should be able to demonstrate significant variation in outcomes between hospitals. However, the DSAA indicators that report on the outcomes of AAA repair show limited variation in hospital results. Based on these results, it was concluded by the scientific committee of the DSAA that the quality of care as measured by current quality indicators is predominantly sufficient. However, it is questionable whether current quality indicators have enough power to detect actual significant differences between hospitals since patient numbers per hospital are relatively low[42]. When one of the funnel plots shows that the results of a hospital are significantly worse compared to the national average, the audit committee of the Dutch Society for Surgery (NVVH) can

decide to perform an audit. Through this audit, the hospital is encouraged to analyse patients who suffered from (major) complications or died perioperatively[43].

To strive for further improvement, both hospitals with unacceptable and acceptable results could also be challenged more to improve their results, for example, by learning from best practices. One example of learning from each other is from the Dutch upper gastrointestinal surgeons. These surgeons organise best practice meetings annually. At these meetings, surgeons from all hospitals present their results using their quality registry and show used operative techniques, including video presentations. After this, an open discussion follows to improve each other's operative techniques. It is expected that this program will lead to much improvement. However, the effectiveness of this program should be evaluated[44].

Current quality indicators mainly provide feedback on perioperative outcomes. Therefore, the development of new quality indicators, for example, quality indicators that monitor perioperative processes, could be an option for further evaluation of the quality of aneurysm care. In addition, it should be discussed with vascular surgeons whether quality indicators reporting on long-term outcomes could have additional value in evaluating variation between hospitals. Recently, a linkage of DSAA data with data from VEKTIS that include long-term mortality has been completed for scientific purposes. Although these VEKTIS data still have disadvantages, such as missing data, it should be discussed whether, for example, 1-year mortality is helpful in monitoring the quality of aneurysmal care since many patients that undergo AAA surgery will die from other causes than the AAA[45].

Case-mix correction for comparison of hospital performances

The characteristics of treated patients may differ between hospitals and could influence hospital results. Case-mix correction is ideally applied on quality indicators to adjust for these differences. However, case-mix correction should only adjust for relevant patient factors and patient factors that differ between hospitals[46]. In 2021, the scientific committee of the DSAA concluded that the applied case-mix correction on DSAA indicators (consisting of age, gender, cardiac comorbidity, pulmonary comorbidity, creatinine, and aneurysm diameter) did not represent the characteristics of the treated patients sufficiently, whereafter it was decided to remove the case mix correction from the quality indicators. Although the case-mix correction was extensively examined before implementation and was based on the V-POSSUM[47], it would be valuable to evaluate which specific information was missing in the former case-mix correction to try to revise the case-mix correction model.

Monitoring of hospital volumes and outcomes

In September 2022, the 'Integraal zorgakkoord' was published by the Dutch ministry of health[48]. In this paper, it is stated that in the near future, a volume requirement will be implemented. This volume requirement requires that hospitals have to perform 50 up to 100 vascular procedures (treatment of abdominal aortic aneurysms, carotid endarterectomies, and surgical interventions for peripheral artery disease) annually to improve the quality of care. The DSAA could be an ideal database to evaluate nationwide AAA outcomes after the implementation of the volume requirements and to monitor changes in numbers and outcomes of AAA treatment per hospital.

Comparing our national results with international collaborations

Comparing our results with the results of registries in other countries could be valuable to put the Dutch nationwide results in an international perspective. VASCUNET is an international collaboration of vascular quality registries[49] and has performed several studies, for example, on regional differences in patient selection[50]. One of the challenges for performing valid comparisons between different countries is the heterogeneity between data sets[51]. To be able to perform valid comparisons between different countries, definitions of outcomes and other variables should be harmonized. VASCUNET has planned to launch a project in order to reduce this heterogeneity. Moreover, it should be realised that most quality registries do not have nationwide coverage, and not all are verified, which could induce selection bias contrary to the DSAA.

'Samen beslissen' using the Codman Dashboard

Besides stimulating quality improvement, the Dutch Institute for Clinical Auditing strives to use the data of the quality registries to support the clinical decision-making process for patients and clinicians. Recently, a dashboard has been developed for patients suffering from colorectal tumours[52]. With this dashboard, patients can be informed by their clinicians about the results of patients with similar characteristics to compare their treatment options. A similar dashboard could be helpful for patients suffering from an AAA. However, for patients considering treatment for an AAA or a conservative approach, it should be realised that with current DSAA data, the choice between an aortic intervention versus watchful waiting can not be supported with data as only patients who receive an intervention are registered in the DSAA. Moreover, the DSAA might not be suitable yet to support clinical decision-making between treatment with EVAR versus OSR, as the reason for the choice for EVAR or OSR, including anatomical details, is not registered in the DSAA. This is essential information as the choice for EVAR or OSR also depends on patient-specific aneurysmal characteristics since not all patients are suitable to be treated with EVAR.

CONCLUSIONS

This thesis shows that the DSAA provides valuable insights into the quality and true real-world outcomes of the current practice of aortic aneurysm treatment in the Netherlands. Our results include the outcomes of octogenarians additional to existing RCTs, show an improvement in treatment outcomes over time, and reveal a volume-outcome relationship for complex EVAR. Moreover, our results show the impact of complications following OSR, demonstrate the outcomes of OSR versus complex EVAR for juxtarenal AAs, demonstrate the feasibility and potential benefit of administrative healthcare data to evaluate mid-term reinterventions, and identify the value of providing real-time feedback to hospitals using CUSUM charts. It is essential to think about the next steps of the DSAA to achieve further improvement in the monitoring and outcomes of aortic aneurysm care.

REFERENCES

1 Beck N, van Bommel AC, Eddes EH, van Leersum NJ, Tollenaar RA, Wouters MW. The Dutch Institute for Clinical Auditing: Achieving Codman's Dream on a Nationwide Basis. *Ann Surg* 2020;**271**(4):627–31. Doi: 10.1097/SLA.0000000000003665.

2 Paraskevas KI, de Borst GJ, Veith FJ. Why randomized controlled trials do not always reflect reality. *J Vasc Surg* 2019:607-614.e3. Doi: 10.1016/j.jvs.2019.01.052.

3 Budtz-Lilly J, Venermo M, Debus S, Behrendt CA, Altreuther M, Beiles B, et al. Editor's Choice – Assessment of International Outcomes of Intact Abdominal Aortic Aneurysm Repair over 9 Years. *European Journal of Vascular and Endovascular Surgery* 2017;**54**(1):13–20. Doi: 10.1016/j.ejvs.2017.03.003.

4 Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, et al. Audit and feedback: Effects on professional practice and healthcare outcomes. *Cochrane Database of Systematic Reviews* 2012;**2012**(6). Doi: 10.1002/14651858.CD000259.pub3.

5 Powell JT, Sweeting MJ, Ulug P, Blankensteijn JD, Lederle FA, Becquemin JP, et al. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. *British Journal of Surgery* 2017;**104**(3):166–78. Doi: 10.1002/bjs.10430.

6 Henebiens M, Vahl A, Koelemay MJW. Elective surgery of abdominal aortic aneurysms in octogenarians: A systematic review. *J Vasc Surg* 2008;**47**(3):676–81. Doi: 10.1016/j.jvs.2007.09.004.

7 Lederle FA, Samuel EW, Johnson GR, Reinke DB, Littooy FN, Acher CW, et al. Immediate repair compared with surveillance of small aortic aneurysms. *N Engl J Med* 2002;**346**(19):1437–44. Doi: 10.1177/096721099900700502.

8 THE UNITED KINGDOM SMALL ANEURYSM TRIAL PARTICIPANTS*, Powell JT, Brady AR, Brown LC, Fowkes FG, Greenhalgh RM, et al. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *New England Journal of Medicine* 2002;**346**(19):1445–52. Doi: 10.1056/NEJMoa013527.

9 Lancaster EM, Gologorsky R, Hull MM, Okuhn S, Solomon MD, Avins AL, et al. The natural history of large abdominal aortic aneurysms in patients without timely repair. Journal of Vascular Surgery, vol. 75. Elsevier Inc.; 2022. pp. 109–17.

10 Roosendaal LC, Kramer GM, Wiersema AM, Wisselink W, Jongkind V. Outcome of Ruptured Abdominal Aortic Aneurysm Repair in Octogenarians: A Systematic Review and Meta-Analysis. *European Journal of Vascular and Endovascular Surgery* 2020;**59**(1):16–22. Doi: 10.1016/j.ejvs.2019.07.014.

11 Yamaguchi T, Nakai M, Sumita Y, Nishimura K, Nagai T, Anzai T, et al. Impact of Endovascular Repair on the Outcomes of Octogenarians with Ruptured Abdominal Aortic Aneurysms: A Nationwide Japanese Study. *European Journal of Vascular and Endovascular Surgery* 2020;**59**(2):219–25. Doi: 10.1016/j.ejvs.2019.07.016.

12 Roosendaal LC, Wiersema AM, Yeung KK, Ünlü Ç, Metz R, Wisselink W, et al. Survival and Living Situation After Ruptured Abdominal Aneurysm Repair in Octogenarians. *European Journal of Vascular and Endovascular Surgery* 2021;**61**:375–81. Doi: 10.1016/j.ejvs.2020.11.023.

13 Bulder RMA, Hamming JF, van Schaik J, Lindeman JHN. Towards Patient Centred Outcomes for Elective Abdominal Aortic Aneurysm Repair: A Scoping Review of Quality of Life Scales. *European Journal of Vascular and Endovascular Surgery* 2021:630–41. Doi: 10.1016/j.ejvs.2021.06.026.

14 Sidloff DA, Saratzis A, Sweeting MJ, Michaels J, Powell JT, Thompson SG, et al. Sex differences in mortality after abdominal aortic aneurysm repair in the UK. *British Journal of Surgery* 2017;**104**(12):1656–64. Doi: 10.1002/bjs.10600.

15 Desai M, Choke E, Sayers RD, Nath M, Bown MJ. Sex-related trends inmortality after elective abdominal aortic aneurysmsurgery between 2002 and 2013 at National Health Service hospitals in England: Less benefit for women compared with men. *Eur Heart J* 2016;**37**(46):3452–60. Doi: 10.1093/eurheartj/ehw335.
16 Mehta M, Byrne WJ, Robinson H, Roddy SP, Paty PSK, Kreienberg PB, et al. Women derive less benefit from elective endovascular aneurysm repair than men. *J Vasc Surg* 2012;**55**(4):906–13. Doi: 10.1016/j.jvs.2011.11.047.
17 Grant SW, Grayson AD, Purkayastha D, Wilson SD, McCollum C. Logistic risk model for mortality following elective abdominal aortic aneurysm repair. *British Journal of Surgery* 2011;**98**(5):652–8. Doi: 10.1002/bjs.7463.
18 Jalalzadeh H, Indrakusuma R, Blankensteijn JD, Wisselink W, Yeung KK, Lindeman JHN, et al. Design and protocol of a comprehensive multicentre biobank for abdominal aortic aneurysms. *BMJ Open* 2019;**9**(8). Doi: 10.1136/bmjopen-2018-028858.
19 Wendt K, Kristiansen R, Krohg-Sørensen K, Gregersen FA, Fosse E. Trends in abdominal aortic and iliac aneurysm repairs in Norway from 2001 to 2013. *European Journal of Vascular and Endovascular Surgery* 2016;**51**(2):194–201. Doi: 10.1016/j.ejvs.2015.08.015.
20 Akkersdijk GJM, Prinssen M, Blankensteijn JD. The impact of endovascular treatment on in-hospital mortality following non-ruptured AAA repair over a decade: A population based study of 16,446 patients. *European Journal of Vascular and Endovascular Surgery* 2004. Doi: 10.1016/j.ejvs.2004.01.003.
21 Bennett KM, Kent KC, Schumacher J, Greenberg CC, Scarborough JE. Targeting the most important complications in vascular surgery. *J Vasc Surg* 2017;**65**(3):793–803. Doi: 10.1016/j.jvs.2016.08.107.
22 O'Donnell TFX, Boitano LT, Deery SE, Lancaster RT, Siracuse JJ, Schermerhorn ML, et al. Hospital Volume Matters: The Volume-Outcome Relationship in Open Juxtarenal AAA Repair. *Ann Surg* 2020;**271**(1):184–90. Doi: 10.1097/SLA.0000000000002873.
23 Geisbüsch S, Kuehnl A, Salvermoser M, Reutersberg B, Trenner M, Eckstein HH. Editor's Choice – Hospital Incidence, Treatment, and In Hospital Mortality Following Open and Endovascular Surgery for Thoraco-abdominal Aortic Aneurysms in Germany from 2005 to 2014: Secondary Data Analysis of the Nationwide German DRG Microdata. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(4):488–98. Doi: 10.1016/j.ejvs.2018.10.030.
24 Locham S, Hussain F, Dakour-Aridi H, Barleben A, Lane JS, Malas M. Hospital Volume Impacts the Outcomes of Endovascular Repair of Thoracoabdominal Aortic Aneurysms. *Ann Vasc Surg* 2020;**67**(October 2019):232-241.e2. Doi: 10.1016/j.avsg.2019.09.018.
25 Akkersdijk A: Revisie Aortadocument Nederlandse Vereniging voor Vaatchirurgie Versie 3 Oktober 2021. n.d.
26 Beck AW, Sedrakyan A, Mao J, Venermo M, Faizer R, Debus S, et al. Variations in Abdominal Aortic Aneurysm Care: A Report from the International Consortium of Vascular Registries. *Circulation* 2016;**134**(24):1948–58. Doi: 10.1161/CIRCULATIONAHA.116.024870.
27 Phillips P, Poku E, Essat M, Woods HB, Goka EA, Kaltenthaler EC, et al. Procedure Volume and the Association with Short-term Mortality Following Abdominal Aortic Aneurysm Repair in European Populations: A Systematic Review. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(1):77–88. Doi: 10.1016/j.ejvs.2016.10.007.
28 Scali ST, Beck A, Sedrakyan A, Mao J, Behrendt CA, Boyle JR, et al. Optimal Threshold for the Volume–Outcome Relationship After Open AAA Repair in the Endovascular Era: Analysis of the International Consortium of Vascular Registries. *European Journal of Vascular and Endovascular Surgery* 2021;(xxxx). Doi: 10.1016/j.ejvs.2021.02.018.

29 Michel M, Becquemin JP, Clément MC, Marzelle J, Quelen C, Durand-Zaleski I. Editor's Choice - Thirty day Outcomes and Costs of Fenestrated and Branched Stent Grafts versus Open Repair for Complex Aortic Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2015;**50**(2):189–96. Doi: 10.1016/j.ejvs.2015.04.012.
30 Rao R, Lane TRA, Franklin IJ, Davies AH. Open repair versus fenestrated endovascular aneurysm repair of juxtarenal aneurysms. *J Vasc Surg* 2015:242-255.e5. Doi: 10.1016/j.jvs.2014.08.068.
31 Jones AD, Waduud MA, Walker P, Stocken D, Bailey MA, Scott DJA. Meta-analysis of fenestrated endovascular aneurysm repair versus open surgical repair of juxtarenal abdominal aortic aneurysms over the last 10 years. *BJS Open* 2019;**3**(5):572–84. Doi: 10.1002/bjs5.50178.
32 Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(1):8–93. Doi: 10.1016/j.ejvs.2018.09.020.
33 van der Werf LR, Voeten SC, van Loe CMM, Karthaus EG, Wouters MWJM, Prins HA. Data verification of nationwide clinical quality registries. *BJS Open* 2019;**3**(6):857–64. Doi: 10.1002/bjs5.50209.
34 DICA. Slimmer gegevensgebruik in de zorg is cruciaal. https://dica.nl/nieuws/slimmer-gegevensgebruik-in-de-zorg-is-cruciaal. 09/01/2022.
35 Nictiz. Implementatiestrategie Registratie aan de bron. https://amigo.nictiz.nl/implementatiestrategie-registratie-aan-de-bron. 09/01/2022.
36 Schermerhorn ML, Buck DB, O'Malley AJ, Curran T, McCallum JC, Darling J, et al. Long-Term Outcomes of Abdominal Aortic Aneurysm in the Medicare Population. *New England Journal of Medicine* 2015;**373**(4):328–38. Doi: 10.1056/nejmoa1405778.
37 Mulay S, Geraedts ACM, Koelemay MJW, Balm R, Balm R, Elshof JW, et al. Type 2 Endoleak With or Without Intervention and Survival After Endovascular Aneurysm Repair. *European Journal of Vascular and Endovascular Surgery* 2021;**61**(5):779–86. Doi: 10.1016/j.ejvs.2021.01.017.
38 Grima MJ, Karthikesalingam A, Holt PJ, Kerr D, Chetter I, Harrison S, et al. Multicentre Post-EVAR Surveillance Evaluation Study (EVAR-SCREEN). *European Journal of Vascular and Endovascular Surgery* 2019;**57**(4):521–6. Doi: 10.1016/j.ejvs.2018.10.032.
39 Columbo JA, Goodney PP, Gladders BH, Tsougranis G, Wanken ZJ, Trooboff SW, et al. Medicare costs for endovascular abdominal aortic aneurysm treatment in the Vascular Quality Initiative. *J Vasc Surg* 2021;**73**(3):1056–61. Doi: 10.1016/j.jvs.2020.06.109.
40 Bulder RMA, Eefting D, Vriens PWHE, van Tongeren RB, Matsumura JS, van den Hout WB, et al. Editor's Choice – A Systemic Evaluation of the Costs of Elective EVAR and Open Abdominal Aortic Aneurysm Repair Implies Cost Equivalence. *European Journal of Vascular and Endovascular Surgery* 2020;**60**(5):655–62. Doi: 10.1016/j.ejvs.2020.07.012.
41 Limb C, Fowler A, Gundogan B, Koshy K, Agha R. How to conduct a clinical audit and quality improvement project. *Int J Surg Oncol (N Y)* 2017;**2**(6):e24–e24. Doi: 10.1097/ij9.0000000000000024.
42 Seaton SE, Barker L, Lingsma HF, Steyerberg EW, Manktelow BN. What is the probability of detecting poorly performing hospitals using funnel plots? *BMJ Qual Saf* 2013;**22**(10):870–6. Doi: 10.1136/bmjqs-2012-001689.
43 NVVH. Audit. https://heelkunde.nl/themas/thema?dossierid=49250304&title=audit. 09/01/2022.
44 van der Werf L, Nieuwenhuijzen G, van Berge Henegouwen M. Betere zorg door veilig behandeluitkomsten te delen. *Med Contact (Bussum)* 2020;**39**:34–7.

45 de Bruin, JL.; Baas, AF; Buth, J; Prinssen, M; Verhoeven, ELG.; Cuypers, PWM; van Sambeek, MRHM; Balm, R; Grobbee, DE; Blankensteijn J. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm: The DREAM Study Group. The New England Journal of Medicine 2010; 362: 1881-1889. *New England Journal of Medicine* 2010;**362**:1881–9. Doi: 10.1177/1358863X10391839.

46 Elfrink AKE, van Zwet EW, Swijnenburg RJ, den Dulk M, van den Boezem PB, Mieog JSD, et al. Case-mix adjustment to compare nationwide hospital performances after resection of colorectal liver metastases. *European Journal of Surgical Oncology* 2021;**47**(3):649–59. Doi: 10.1016/j.ejso.2020.10.016.

47 Lijftogt N, Vahl AC, Wilschut ED, Elsman BHP, Amodio S, van Zwet EW, et al. Adjusted Hospital Outcomes of Abdominal Aortic Aneurysm Surgery Reported in the Dutch Surgical Aneurysm Audit. *European Journal of Vascular and Endovascular Surgery* 2017;**53**(4):520–32. Doi: 10.1016/j.ejvs.2016.12.037.

48 van Volksgezondheid M, en Sport W. Integraal Zorg Akkoord - Samen werken aan gezonde zorg. 2022.

49 Mitchell D, Venermo M, Mani K, Bjorck M, Troeng T, Debus S, et al. Quality improvement in vascular surgery: The role of comparative audit and vascunet. *European Journal of Vascular and Endovascular Surgery* 2015;**49**(1):1–3. Doi: 10.1016/j.ejvs.2014.08.026.

50 Mani K, Venermo M, Beiles B, Menyhei G, Altreuther M, Loftus I, et al. Regional Differences in Case Mix and Peri-operative Outcome After ElectiveAbdominal Aortic Aneurysm Repair in the Vascunet Database. *European Journal of Vascular and Endovascular Surgery* 2015:646–52. Doi: 10.1016/j.ejvs.2015.03.022.

51 Sutzko DC, Mani K, Behrendt CA, Wanhainen A, Beck AW. Big data in vascular surgery: registries, international collaboration and future directions. *J Intern Med* 2020:51–61. Doi: 10.1111/joim.13077.

52 Programma uitkomstgerichte zorg. DICA kijkt samen vooruit met dynamisch dashboard. https://platformuitkomstgerichtezorg.mett.nl/themas/inzicht+in+uitkomsten/1966827.aspx?t=DICA-kijkt-samen-vooruit-met-dynamisch-dashboard. 09/11/2022.

CHAPTER

12

SUMMARY IN ENGLISH AND DUTCH

SUMMARY IN ENGLISH

In this thesis, the quality and real-world outcomes of aortic aneurysm treatment in the Netherlands are examined as well as new opportunities to develop the DSAA further.

Part 1: Abdominal aortic aneurysm treatment outcomes

In **Chapter 2** the nationwide trends in perioperative outcomes of patients who underwent endovascular aneurysm repair (EVAR) or open surgical repair (OSR) for an intact abdominal aortic aneurysm (AAA) between 2014 and 2019 are provided. This information shows that for EVAR patients, perioperative mortality did not improve, while major complications decreased, and textbook outcome rates increased. For OSR patients, the perioperative mortality rates, as well as major complications, decreased, while the proportion of patients that achieved textbook outcome increased. Furthermore, the study shows that over the years, more patients with a cardiac comorbidity underwent treatment.

As a result of an aging population, and increasing possibilities for treatment with EVAR, the number of patients over 80 years (octogenarians) being treated is increasing. The perioperative outcomes of octogenarians vs. non-octogenarians who underwent EVAR and OSR for an intact AAA in a nationwide cohort are reported and the influence of comorbidities on perioperative mortality is studied in **Chapter 3**. Octogenarians had higher mortality and major complication rates following EVAR and OSR than younger patients. In octogenarians that underwent OSR, perioperative mortality rates exceeded 10%, especially when comorbidities were present.

A ruptured abdominal aortic aneurysm is a lethal condition, especially in older patients. In **Chapter 4**, we have evaluated the perioperative outcomes of EVAR or OSR for a ruptured AAA in octogenarians. We found that perioperative mortality rates of octogenarians were high (37% following EVAR and 50% following OSR). However, a substantial percentage of octogenarians had an uneventful recovery (31% following EVAR, 21% following OSR). Cardiac comorbidity, pulmonary comorbidity, and loss of consciousness at presentation were associated with perioperative mortality in octogenarians. Interestingly, female octogenarians had lower mortality rates following EVAR than male octogenarians.

In **Chapter 5**, it is discussed whether confounding factors at hospital level may declare the difference in mortality rates between women and men in patients that underwent EVAR and OSR for an intact AAA. It is shown that even after adjustment for patient and hospital-related factors, female sex was still significantly associated with higher perioperative mortality.

A reduction of complications can further improve perioperative outcomes following OSR. In **Chapter 6**, it is identified that bowel ischemia and renal complications had the highest impact on perioperative mortality, while arterial occlusion and bowel ischemia had the highest impact on secondary interventions. Pneumonia had the highest impact on prolonged hospital admissions.

Part 2: Complex aortic aneurysm treatment outcomes

Endovascular treatment with fenestrated (FEVAR) or branched (BEVAR) EVAR is increasingly used for excluding complex aortic aneurysms (complex AAs). Nationwide perioperative outcomes following FEVAR and BEVAR and whether an association between hospital volume and perioperative mortality exists for patients treated with these endovascular treatment modalities are examined in **Chapter 7**. First, it is reported that the perioperative mortality was 4.5% following FEVAR and 5.2% following BEVAR. Secondly, we have revealed that perioperative mortality decreased when the annual volume of a hospital increases: perioperative mortality was 9.1% in hospitals with a volume of <9 and 2.5% in hospitals with a volume of ≥13.

The outcomes of open surgical repair (including suprarenal clamping) versus complex EVAR (chimney EVAR and FEVAR) for elective juxtarenal aneurysms are studied in **Chapter 8**. Our research shows that even after adjusting for confounders, patients treated with OSR had higher perioperative mortality rates and more major and minor complications than patients treated with complex EVAR.

Part 3: New opportunities for feedback and outcome measurement

Multiple complications and reinterventions occur after 30 days following EVAR and open surgical repair. However, in our nationwide registry, only complications and reinterventions that occur within 30 days are registered. In **Chapter 9,** the feasibility and potential benefit of using administrative healthcare data to evaluate mid-term reinterventions following intact AAA repair are assessed, since a limited registration burden for clinicians is essential. We found that administrative healthcare data is potentially beneficial for evaluating mid-term reinterventions. However, within our study design, the administrative healthcare data could not be directly linked with the DSAA due to privacy restrictions. Linkage is needed to validate the data further.

In **Chapter 10**, the value of providing real-time feedback to hospitals on their clinical outcomes using Log-likelihood cumulative sum control (CUSUM) charts is examined. The number of treated patients that is needed to detect hospitals with a deviating risk in the achievement of textbook outcome is evaluated. It appeared that median-sized hospitals with deviating results were detected within two years using CUSUM charts. The feedback from CUSUM charts that evaluate performances ongoing complements the feedback provided by the currently used funnel plots.

SUMMARY IN DUTCH / NEDERLANDSE SAMENVATTING

In dit proefschrift worden de kwaliteit en 'real-world' uitkomsten van de aorta aneurysma behandelingen in Nederland onderzocht. Ook worden nieuwe mogelijkheden voor de doorontwikkeling van de Dutch Surgical Aneurysm Audit (DSAA) onderzocht.

Deel 1: Behandel uitkomsten van het abdominale aorta aneurysma
In **Hoofdstuk 2** worden de nationale trends in perioperatieve uitkomsten onderzocht van patiënten die een endovasculaire (EVAR) of open chirurgische behandeling voor een intact abdominaal aorta aneurysma (AAA) hebben ondergaan gedurende de periode 2014 tot en met 2019. De resultaten tonen dat in de groep patiënten die een endovasculaire behandeling ondergingen de perioperatieve mortaliteit niet verbeterde, maar dat voor deze groep het percentage grote complicaties afnam, en het percentage 'Textbook Outcome' toenam. In de groep patiënten die een open chirurgische behandeling ondergingen nam zowel de perioperatieve mortaliteit als het percentage grote complicaties af, terwijl het percentage 'Textbook Outcome' toenam. Daarnaast laten de resultaten zien dat gedurende de studieperiode, het aantal patiënten met een cardiale comorbiditeit dat een behandeling onderging toenam.

Doordat de Nederlandse bevolking veroudert, en de mogelijkheden voor een endovasculaire behandeling van een AAA zijn toegenomen, neemt het aantal patiënten van 80 jaar of ouder (tachtigplussers) dat behandeld wordt voor een AAA toe. In **Hoofdstuk 3** worden de perioperatieve uitkomsten van tachtigplussers versus tachtigminners die een endovasculaire behandeling danwel een open chirurgische behandeling voor een intact AAA ondergingen weergegeven. Daarnaast wordt de invloed van comorbiditeiten op de perioperatieve mortaliteit onderzocht. Tachtigplussers hebben een hogere mortaliteit en krijgen meer grote complicaties na een endovasculaire en open chirurgische behandeling dan jongere patiënten. De perioperatieve mortaliteit van tachtigplussers met comorbiditeiten die een open chirurgische behandeling ondergingen is zelfs meer dan 10%.

Een gebarsten AAA is vaak dodelijk, vooral voor oudere patiënten. In **Hoofdstuk 4**, worden de perioperatieve uitkomsten weergegeven van tachtigplussers die een endovasculaire danwel open chirurgische behandeling ondergaan vanwege een geruptureerd AAA. De resultaten laten zien dat de perioperatieve mortaliteit van tachtigplussers hoog is (37% na EVAR, 50% na een open chirurgische behandeling). Een substantieel deel van de tachtigplussers heeft echter een herstel zonder significante tegenslagen. Het hebben van een cardiale comorbiditeit, pulmonale comorbiditeit, en bewustzijnsverlies bij presentatie op de spoedeisende hulp is geassocieerd met perioperatieve mortaliteit bij

tachtigplussers. Het is opmerkelijk dat in de groep tachtigplussers die EVAR ondergingen, vrouwen een lagere mortaliteit hadden mannen.

In **Hoofdstuk 5** wordt onderzocht of confounders op ziekenhuisniveau het verschil in mortaliteit tussen vrouwen en mannen die behandeld worden voor een intact AAA kunnen verklaren. Het blijkt dat zelfs na correctie voor patiëntfactoren en confounders op ziekenhuisniveau, het vrouwelijke geslacht nog steeds geassocieerd is met een hogere perioperatieve mortaliteit.

Een reductie van complicaties kan de perioperatieve uitkomsten na een open chirurgische behandeling verder verbeteren. In **Hoofdstuk 6** wordt getoond dat darmischemie en renale complicaties de meeste impact op perioperatieve mortaliteit hebben, terwijl een arteriële occlusie en darmischemie de meeste impact hebben op re-interventies. Een pneumonie heeft de meeste impact op een verlengde opnameduur in het ziekenhuis.

Deel 2: Behandel uitkomsten van complexe aorta aneurysma

Een endovasculaire behandeling met gefenestreerde (FEVAR) of branched (BEVAR) EVAR wordt steeds vaak toegepast om complexe aorta aneurysmata uit te schakelen. In **Hoofdstuk 7** worden de nationale perioperatieve uitkomsten na FEVAR en BEVAR weergegeven. Daarnaast wordt onderzocht of er een associatie tussen het jaarlijks ziekenhuisvolume en perioperatieve mortaliteit bestaat. Het blijkt dat de perioperatieve mortaliteit na FEVAR 4.5%, en na BEVAR 5.2% is. Daarnaast wordt gezien dat de perioperatieve mortaliteit daalt wanneer het jaarlijks ziekenhuisvolume toeneemt: de perioperatieve mortaliteit was 9.1% in ziekenhuizen die jaarlijks <9 operaties uitvoeren, terwijl de perioperatieve mortaliteit 2.5% was in ziekenhuizen die jaarlijks ≥13 operaties uitvoeren.

In **Hoofdstuk 8** worden de uitkomsten onderzocht van een open chirurgische behandeling (door middel van het plaatsen van een suprarenale klem) versus een complexe endovasculaire behandeling middels chimney EVAR en FEVAR bij patiënten die in electieve setting worden behandeld aan een juxtarenaal aneurysma**.** Er wordt getoond dat, zelfs na het corrigeren voor confounders, patiënten die behandeld worden middels een open chirurgische behandeling een hogere perioperatieve mortaliteit, en meer grote en kleine complicaties hebben dan patiënten die behandeld worden middels een complexe endovasculaire behandeling.

Deel 3: Nieuwe mogelijkheden voor feedback en het meten van uitkomsten

Veel complicaties en re-interventies treden op na de eerste 30 dagen na een endovasculaire behandeling danwel open chirurgische behandeling. In de DSAA, onze nationale

kwaliteitsregistratie, worden echter alleen de complicaties en re-interventies die binnen 30 dagen na de behandeling plaatsvinden geregistreerd. Omdat een beperkte registratielast voor clinici essentieel is, wordt in **Hoofdstuk 9** de haalbaarheid en het mogelijke voordeel van het gebruik van administratieve data onderzocht om hiermee de re-interventies die op de middellange termijn plaatsvinden te evalueren. Er wordt getoond dat het gebruik van administratieve data mogelijk nuttig kan zijn om re-interventies die op middellange termijn plaatsvinden te evalueren. Vanwege privacy restricties was het binnen de gebruikte onderzoeksopzet niet mogelijk om de administratieve data te koppelen aan de DSAA. Voor het valideren van de administratieve data is een koppeling van de data echter nodig.

In **Hoofdstuk 10** wordt de waarde onderzocht van het verschaffen van real-time feedback aan ziekenhuizen over hun klinische uitkomsten met behulp van CUSUM-kaarten. Er wordt onderzocht hoeveel patiënten behandeld moeten worden om ziekenhuizen met een afwijkend risico in het behalen van 'Textbook Outcome' op te sporen. Het blijkt dat ziekenhuizen van een mediane grootte met afwijkende resultaten binnen 2 jaar opgespoord worden wanneer de CUSUM-kaarten worden gebruikt. De feedback van de CUSUM-kaarten die continu prestaties evalueren is een aanvulling op de feedback die verschaft worden met behulp van de funnel plots die op dit moment gebruikt worden.

A

APPENDICES

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LIST OF PUBLICATIONS

Publications in this thesis

Administrative healthcare data as an addition to the Dutch Surgical Aneurysm Audit to evaluate mid-term reinterventions following abdominal aortic aneurysm repair: a pilot study.
A.J. Alberga, V.A. Stangenberger, J.L. de Bruin, J.J. Wever, J.A. Wilschut, C.L. van den Brand, H.J.M. Verhagen, M.W.J.M. Wouters, in collaboration with the Dutch Society of Vascular Surgery, the Steering Committee of the Dutch Surgical Aneurysm Audit, and the Dutch Institute for Clinical Auditing.
International Journal of Medical Informatics, 2022

Nationwide outcomes of octogenarians following open or endovascular management after ruptured abdominal aortic aneurysms.
A.J. Alberga, J.L. de Bruin, F. Bastos Gonçalves, E.G. Karthaus, J.A. Wilschut, J.A. van Herwaarden, J.J. Wever, H.J.M. Verhagen, in collaboration with the Dutch Society of Vascular Surgery, the Steering Committee of the Dutch Surgical Aneurysm Audit and the Dutch Institute for Clinical Auditing.
Journal of Endovascular Therapy, 2022

Trends in outcomes of treatment of non-ruptured abdominal aortic aneurysms –a nationwide prospective cohort study.
A.J. Alberga, E.G. Karthaus, J. Wilschut, J.L. de Bruin, G.P. Akkersdijk, R.H. Geelkerken, J.F. Hamming, J.J. Wever, H.J.M. Verhagen, in collaboration with the Dutch Society of Vascular Surgery, the Steering Committee of the Dutch Surgical Aneurysm Audit and the Dutch Institute for Clinical Auditing. *European Journal of Vascular and Endovascular Surgery, 2022*

Mortality following elective abdominal aortic aneurysm repair in women.
V.N. Tedjawirja V.N., **A.J. Alberga,** M.H.P. Hof, A.C. Vahl, M.J.W. Koelemay, R. Balm.; Dutch Society of Vascular Surgery.
British Journal of Surgery, 2022

Results from a nationwide prospective registry on open surgical or endovascular repair of juxtarenal abdominal aortic aneurysms.
G.C.I. von Meijenfeldt, **A.J. Alberga**, R. Balm, A.C. Vahl, H.J.M. Verhagen, J.D. Blankensteijn, C.J. Zeebregts, M.J. van der Laan.
Journal of Vascular Surgery, 2022

Association of hospital volume with perioperative mortality of endovascular repair of complex aortic aneurysms.
A.J. Alberga, G.C.I. von Meijenfeldt, V. Rastogi, J.L. de Bruin, J.J. Wever, J.A. van Herwaarden, J.F. Hamming, Constantijn E.V.B. Hazenberg, J. van Schaik, B.M.E. Mees, M.J. van der Laan, C.J. Zeebregts, G.W.H. Schurink, H.J.M. Verhagen, in collaboration with the Dutch Society of Vascular Surgery, the Steering Committee of the Dutch Surgical Aneurysm Audit, and the Dutch Institute for Clinical Auditing.
Annals of Surgery, 2021

Outcomes of octogenarians and the effect of comorbidities after intact abdominal aortic aneurysm repair in The Netherlands – a Nationwide cohort study.
A.J. Alberga, E.G. Karthaus, E.W. van Zwet, J.L. de Bruin, J.A. van Herwaarden, J.J. Wever, H.J.M. Verhagen; Dutch Society of Vascular Surgery; Steering Committee of the Dutch Surgical Aneurysm Audit; Dutch Institute for Clinical Auditing.
European Journal of Vascular and Endovascular Surgery, 2021

Impact of postoperative complications on outcomes after open surgical repair of intact abdominal aortic aneurysms in the Netherlands.
A.C.M. Geraedts, **A.J. Alberga**, M.J.W. Koelemay, H.J.M. Verhagen, R. Balm, in collaboration with the Dutch Society for Vascular Surgery.
British Journal of Surgery Open, 2021

Real-time monitoring of hospital performances in the Dutch Surgical Aneurysm Audit by use of cumulative sum control charts.
A.J. Alberga, E.W. van Zwet, J.L. de Bruin, E.S. van Hattum, J.J. Wever, H.J.M. Verhagen, M.W.J.M. Wouters, J.A. Wilschut, in collaboration with the Dutch Society of Vascular Surgery, the Steering Committee of the Dutch Surgical Aneurysm Audit, and the Dutch Institute for Clinical Auditing. *Submitted*

Other publications

The influence of the COVID-19 pandemic on the surgical patterns of care in the Netherlands: a prospective, nationwide study.
M.R. de Graaff, R.N.M. Hogenbirk, Y.F. Janssen, A.K.E. Elfrink, R.S.L. Liem, S.W. Nienhuijs, J.P.M. de Vries, J.W. Elshof, E. Verdaasdonk, J. Melenhorst, H.L. van Westreenen, M.G. Besselink, J.R. Ruurda, M.I. van Berge Henegouwen, J.M. Klaase, M. den Dulk, M. van Heijl, J.H. Hegeman, J.Braun, D.M. Voeten, F.S. Würdemann, A.K. Warps, **A.J. Alberga**, J.A. Suurmeijer, E.O. Akpinar, N. Wolfhagen, AL van den Boom, M.J. Bolster-van Eenennaam, P. van Duijvendijk, D.J. Heineman, M.W.J.M. Wouters, S. Kruijff.
British Journal of Surgery, 2022

Outcomes after major surgical procedures in octogenarians: a nationwide cohort study.
A.K.E. Elfrink*, **A.J. Alberga***, M.I. van Berge Henegouwen, W.H. Scheurs, L.G.M. van der Geest, H.J.M. Verhagen, J.T. Dekker, D. J. Grünhagen, M.W.J.M. Wouters*, J.M. Klaase* (* Shared authorship).
World Journal of Surgery, 2022

Response to commentary on 'Treatment Outcome Trends for Non-Ruptured Abdominal Aortic Aneurysms: A Nationwide Prospective Cohort Study'.
A.J. Alberga, J.L. de Bruin, H.J.M. Verhagen.
European Journal of Vascular and Endovascular Surgery, 2022

Outcomes and Treatment Options for Duodenal Adenocarcinoma: A Systematic Review and Meta-Analysis.
L.L. Meijer, **A.J. Alberga**, J.K. de Bakker, H.J. van der Vliet, T.Y.S. Le Large, N.C.T. van Grieken, R. de Vries, F. Daams, B.M. Zonderhuis, G. Kazemier.
Annals of Surgical Oncology, 2018

Patient volumes of non-COVID-19 healthcare during the pandemic in the Netherlands: are there secondary victims? A population-based cohort study.
D.M. Voeten, L.J. Stolze, S. Brinkman, B.C.T. van Brussel, T. Hoekstra, M.B.A. Heemskerk, A.C. Hemke, G.A.W. Denissen, L.N. van Steenbergen, L. Derks, M.M. Roefs, M.L.S. Driessen, R.G.H.H. Nelissen, L. Broeders, M.I. van Berge Henegouwen, P.J, Nederkoorn, K.J. Nass, **A.J. Alberga**, A.K. Warps, F.S. Würdemann, M.D. Algera, A.K.E. Elfrink, M.R. de Graaff, N. Maliko, J.A. Suurmeijer, N. Wolfhagen, C.L. van den Brand, J.A. Wilschut, M.W.J.M. Wouters, on behalf of the COVID-19-impact group.
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Course	**Year**	**ECTS**
R-cursus (DICA)	2019	0.86
Practical biostatistics E-course (AMC)	2019	1.1
Klinische epidemiologie Schiermonnikoog (LUMC)	2020	2.1
Wetenschappelijke integriteit (EUR)	2020	0.3
Writing course (VU)	2020	3.0
eBROK cursus	2021	1.5
Seminars and workshops		
Educational lectures (DICA)	2019-2021	5.56
Research meetings (DICA)	2019-2021	5.56
(Inter)national conferences including presentations		
Vaatdagen (Noordwijkerhout)	2019	0.6
Chirurgendagen (Veldhoven)	2019	0.6
DICA congres (Amsterdam)	2019	0.3
Najaarsvergadering NVVV (Ermelo)	2019	0.3
Oral presentation 'Uitkomsten van octogenarians in de DSAA'		0.5
ESVS annual meeting (virtual)	2020	0.6
Oral presentation 'Outcomes of octogenarians following ruptured abdominal aortic aneurysm repair – a nationwide cohort study'		0.5
Poster presentation 'Improvement of outcomes after non-ruptured abdominal aortic aneurysm repair'		0.5
Charing cross (virtual)	2021	0.6
Oral presentation 'Outcomes of Octogenarians following ruptured abdominal aortic aneurysm repair – nationwide cohort study'		0.5
Vaatdag (virtual)	2021	0.3

Oral presentation 'Trends in behandeluitkomsten van niet-geruptureerde abdominale aorta aneurysmata – een Nederlandse nationale prospectieve cohortstudie'		0.5
Poster presentation 'Uitkomsten van octogenarians na een behandeling van geruptureerde abdominale aorta aneurysmata: een Nederlandse nationale cohortstudie'		0.5
Vascular rounds (Amsterdam UMC); oral presentation	2021	0.5
Impact congress (Amsterdam)	2021	0.3
ESVS annual meeting (Rotterdam)	2021	0.6
Oral presentation 'The application of cumulative sum control charts to monitor hospital performances over time in the Dutch Surgical Aneurysm Audit		0.5
Oral presentation 'Outcomes of FEVAR and BEVAR, and the influence of hospital volume on perioperative mortality'		0.5
Najaarsvergadering NVVV (Ermelo)	2021	0.3
Oral presentation 'Uitkomsten van FEVAR en BEVAR, en de invloed van ziekenhuisvolume op perioperative mortaliteit – een Nederlandse nationale cohortstudie'		0.5
Vascular Rounds (Rotterdam); oral presentation	2021	0.5
ESVS annual meeting (Rome)	2022	0.6
Oral presentation 'Administrative healthcare data as an addition to the Dutch Surgical Aneurysm Audit to evaluate mid-term reinterventions following abdominal aortic aneurysm repair'		0.5
Total		31.08

ABOUT THE AUTHOR

Anna Judith Alberga was born on the 11th of December 1991 in Eindhoven, the Netherlands. She graduated from secondary school at S.G. Augustinianum in Eindhoven in 2010, whereafter she moved to Amsterdam to start studying Medicine at the Vrije Universiteit (VU). In these years, she played violin in symphony orchestras, and she was a sailing instructor at a sailing school in Friesland. During her studies, Anna took an extracurricular minor Business Administration, and went to South Africa for a rotation in Pediatrics and Gynaecology at the University of Pretoria and to Suriname for a rotation at the Emergency Department at the Academisch Ziekenhuis Paramaribo.

After finishing her Master's degree in 2017, Anna started her career as a surgical resident not in training at the Department of Surgery at the VU Medical Center. In January 2019, she started as a PhD candidate at the Erasmus University Medical Center and the Dutch Institute for Clinical Auditing under the supervision of prof. dr. H.J.M. Verhagen (Erasmus University Medical Center), dr. J.J. Wever (Haga Teaching Hospital), and dr. J.L. de Bruin (Erasmus University Medical Center). Her research focused on aortic aneurysm treatment outcomes in the Netherlands. During her PhD period, Anna was awarded the 'Best Presentation' at the European Society for Vascular Surgery (ESVS) Annual Meeting in Rotterdam. At DICA, she coordinated the Dutch Surgical Aneurysm Audit (DSAA) and the Dutch Audit for Carotid Interventions (DACI). Furthermore, she represented her fellow PhD colleagues in management team meetings for two years.

After her fulltime PhD period, Anna worked as a resident not in training at the Intensive Care Unit at the Leiden University Medical Center and for the Dutch COVID-19 vaccination program. Anna continued her career as a resident not in training at 'Kliniek Eerste Constantijn Huygensstraat' of Mentrum, a mental healthcare institution for people with severe psychiatric disorders in Amsterdam. In September 2023, Anna will start the general practice training program in Amsterdam.

In her spare time, Anna likes doing sports such as running, road cycling, field hockey, surfing, sailing, and ice skating. Anna lives in Amsterdam together with her boyfriend Coen.