Evaluating abdominal aortic aneurysm and carotid artery surgery in the Netherlands: variations in indication, treatment and outcomes measures

Karthaus, E.G.

EVALUATING ABDOMINAL AORTIC ANEURYSM AND CAROTID ARTERY SURGERY IN THE NETHERLANDS

VARIATION IN INDICATION, TREATMENT AND OUTCOME MEASURES

ELEONORA GEZINA KARTHAUS

EVALUATING ABDOMINAL AORTIC ANEURYSM AND CAROTID ARTERY SURGERY IN THE NETHERLANDS

VARIATION IN INDICATION, TREATMENT AND OUTCOME MEASURES

Evaluating abdominal aortic aneurysm and carotid artery surgery in the Netherlands:
variation in indication, treatment and outcome measures

ISBN: 978-94-6423-979-9
Cover Design: ProefschriftMaken || Proefschriftmaken.nl
Lay-out and printing: ProefschriftMaken || Proefschriftmaken.nl

Printing of this thesis was financially supported by:
Dutch Institute for Clinical Auditing; SOLV Advocaten; Universiteitsbibliotheek Leiden; Stichting ReSurge, vakgroep Chirurgie Gelre Ziekenhuizen

Evaluating abdominal aortic aneurysm and carotid artery surgery in the Netherlands variation in indication, treatment and outcome measures

Proefschrift

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof.dr.ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op dinsdag 11 oktober 2022
klokke 16.15 uur

door
Eleonora Gezina Karthaus
geboren te Deventer
in 1988

Promotores
Prof. Dr. J.F. Hamming
Prof Dr. G.J. de Borst (Universitair Medisch Centrum Utrecht, Utrecht)

Co-promotor
Dr. A.C. Vahl (Onze Lieve Vrouwe Gasthuis, Amsterdam)

Promotiecommissie
Prof. Dr. J.A. van der Hage
Prof. Dr. R.H. Geelkerken (Medisch Spectrum Twente, Enschede)
Prof. Dr. H.J.M. Verhagen (Erasmus Medisch Centrum, Rotterdam)
Prof. Dr. H. Putter
Dr. A. Schepers

Voor mijn ouders

Contents

CHAPTER 1

Introduction & outline of this thesis

INTRODUCTION

Due to the growing demand for openness about quality of healthcare and tools to improve healthcare during the beginning of this century, multiple clinical audits have been initiated in several medical specialties in the Netherlands and other Western countries. Clinical audits were first introduced by Codman in 1916 and are nowadays frequently used as an instrument to measure and improve quality of healthcare.[1] A clinical audit is defined as 'a quality improvement process that seeks to improve patient care and outcomes through systematic review of care against explicit criteria and the implementation of change'.[2]
In 2011 the Dutch Institute for Clinical Auditing (DICA) was founded to organize and facilitate the initiation of nationwide audits in the Netherlands, offering a uniform format.[3] In accordance with the original idea of Codman, audits were formed based on a cycle. It starts with the collection of information on a certain topic, followed by evaluating the results in order to identify areas for improvement. Subsequently changes can be implemented and in the following period one can evaluate whether the changes had the desired effect. An essential part of this quality assessment is that performance is compared to the performance of other healthcare providers, as this would stimulate providers to improve their performance. Through these audits, doctors intend to improve the outcomes of Dutch healthcare and, as a result, to contribute to the reduction of healthcare costs.

The Dutch Surgical Aneurysm Audit

The Dutch Surgical Aneurysm Audit (DSAA) was initiated by the Dutch Society for Vascular Surgery (Nederlandse Vereniging voor Vaatchirurgie: NVvV) in 2012 and was facilitated by the Dutch Institute for Clinical Auditing (DICA).[3,4] From 2013, all hospitals performing abdominal aortic aneurysm (AAA) surgery in the Netherlands were obligated to register all patients undergoing AAA surgery in the nationwide DSAA. Following the Donabedian model, information on the structure, process and outcomes of surgical aneurysm care were collected.[5] By registering this information quality of care could now be monitored and vascular surgeons could be provided of benchmarked information about their care.

Stakeholders

Although the DSAA was initially formed by and for vascular surgeons for quality improvement reasons, other stakeholders also contributed to the development of the audit so that it could serve several purposes. For the Dutch Healthcare Inspectorate (Inspectie Gezondheidszorg en Jeugd: IGJ) and the Dutch National Institute for Healthcare (Zorginstituut Nederland: ZIN), the DSAA could be used to supply information for quality indicators, necessary for the monitoring of patient safety.[6,7] The patient association for cardiovascular diseases (Hartenraad) intended to use the information from the DSAA to support individual patients in choosing a healthcare provider.[8] Finally, Dutch healthcare insurers were interested in the comparison of hospitals outcomes, so they could well informed purchase care for their policyholders.[9]

Quality indicators

During the formation of the DSAA, the NVvV collaborated with these stakeholders to decide which information needed to be registered and to eventually form a set of quality indicators of care.[10] The indicators were categorized by structure, process and outcomes of care and would be measured for each individual hospital. The questions which surgical outcomes best reflect quality of care and in which hospital volumes AAA surgery should be annually performed were important discussions when forming these indicators. The primary outcome measure of the DSAA was decided to be postoperative mortality within 30 days after surgery or during the initial admission (30-days/in-hospital mortality). Additionally, postoperative complication, postoperative reinterventions and readmissions were also registered.

The development of quality indicators is a continuous process in which the variables registered in the audit and the set of quality indicators is annually evaluated and adjusted if needed. After the first 3 years of auditing, the quality outcome indicators were first made public via a transparency portal.[11]

First results from the DSAA

With the DSAA being fully operational from January 2013 and all 65 hospitals performing AAA surgery participating, roughly 3350 AAA patients were annually registered between 2013-2014, of which 78% undergoing elective surgery, 6.3% undergoing surgery because of an acute symptomatic AAA and 16% because of a ruptured AAA.[12] The majority (75%) of elective patients was undergoing the more minimal invasive Endovascular Aneurysm Repair (EVAR) and the remaining 25% conventional Open Surgical Repair (OSR). In patients with an acute symptomatic and ruptured AAAs the percentage of treatment with EVAR was respectively 54% and 34%.

In accordance with other European countries, postoperative mortality after elective EVAR was 0.7%. Postoperative mortality after elective OSR however, was slightly higher with 5% (compared to 3.2% in Sweden).[12]

Since the outcomes of the DSAA are intended to be used for benchmarking hospitals as objective as possible, taking into account differences in patient characteristics between hospitals, Lijftogt et al. have conducted research into case-mix models for AAA surgery.[13,14] In the design of the DSAA it was decided to record variables from the VP POSSUM prediction model, a widely used and extensive model for prediction of postoperative mortality in various surgical procedures.[15] Lijftogt et al. concluded that a minimal set of patient characteristics, including sex, age, pulmonary comorbidities, urgency of surgery, aneurysm diameter, CGS, preoperative hemoglobin, creatinine and ECG, was sufficient.[14] Furthermore, they concluded that the added value of case mix correction is small in the case of an outcome measure with a low event rate and little variation between hospitals, as is the case with postoperative mortality in elective EVAR. Despite that, it has been decided to apply case-mix correction with this smaller set of variables in the DSAA to minimize the possibility of a hospital being disadvantaged in the comparison of outcomes.

Outline of the thesis

Due to the previously mentioned low mortality in elective AAA surgery, it turned out to be difficult to distinguish between hospitals on this outcome measure. In addition, the lack of variation in postoperative mortality also did not offer any leads for improvement initiatives. For the purpose of internal quality improvement, additional quality measures had to be sought and explored. From the start of the DSAA in 2013, extensive information was collected about patient characteristics, care processes and outcomes. With this sea of data, new facts came to light and, above all, new questions regarding the variation in indication, treatment and outcome measures of AAA surgery in the Netherlands arose, forming the basis of this thesis.

Indication

To prevent aortic rupture, international guidelines recommend elective surgery in patients with an AAA with a diameter of 55 mm or more in males and 50 mm or more in females.[16,17] These thresholds have been studied extensively and early elective surgery is not beneficial for patients with diameters below these cut-off values.[18-22] In the DSAA 17% of elective AAA patients was reported to have a smaller diameter than these thresholds, with variation between hospitals. In **chapter 2** we evaluated patient and disease characteristics associated with performing surgery on patients with smaller aneurysm diameters than recommended. We additionally performed a survey under Dutch vascular surgical units (VSUs) in order to investigate reasons for deviation from the diameter guidelines, with a focus on how VSUs expect to deviate from the guidelines compared to their actual deviation.

The diameter guidelines are based on the risk of rupture in fusiform shaped AAAs, which accounts for 95% of all AAAs. It suggests that elective surgical treatment in the less commonly presented saccular shaped AAAs is indicated at smaller diameters, as there is a longstanding believe that the asymmetrical shape of a saccular AAA might predispose them to rupture. However, guidelines fail to give a threshold for elective treatment in saccular AAAs, since no large case series of cohort studies have been performed. In **chapter 3** we aimed to present an overview of the experience with saccular AAAs in the Netherlands, evaluating differences between patients with a saccular and fusiform AAA in patient characteristics, clinical presentation, treatment and outcomes in order to substantiate a treatment threshold.

Treatment

EVAR has become standard of care in the treatment of elective abdominal aortic aneurysms, being performed in the majority of elective patients with a postoperative mortality decreased to 0.7%.[12,23] This in contrast to the relatively high postoperative mortality in elective OSR of 5% being performed in a selected group of patients, mostly not suitable for EVAR for anatomic reasons. As fewer patients are treated with EVAR, experience in this procedure could decrease and hospitals may not perform the surgical procedure sufficiently to maintain good quality of care.[24,25] However, today no minimum volume standard for elective OSR exist in the Netherlands.

In **chapter 4** we first evaluate patient characteristics associated with postoperative mortality after elective OSR in the current Dutch population to improve patient selection for elective OSR. Secondly, the association of hospital volume of OSR and postoperative mortality was investigated in order to explore a possible minimum volume standard for elective OSR.
Whereas randomized controlled trials (RCT) in elective AAA patients showed lower postoperative mortality and morbidity after EVAR compared to OSR, several RCTs could not demonstrate the superiority of EVAR over OSR in patients with a ruptured AAA.[26-29] RCTs contain a selected, relatively homogeneous population, which might hamper the generalizability of the results.[30] Large observational studies that investigated the same topic suggest a lower postoperative mortality in patients with a ruptured AAA treated with EVAR.[31-33] However, observational studies can be biased and adjustment of confounders can be incomplete.[34] An instrumental variable analysis is a pseudo-randomization technique, which is developed to control for unobserved confounders when comparing treatments in observational data.[35] In **chapter 5** we compared postoperative mortality of all consecutive RAAA patients treated with EVAR or OSR registered in the DSAA, using standard statistical methods and instrumental variable analysis.

Outcome measures

When measuring quality of care, there is an ongoing debate about which indicators best reflect quality of care. As previously mentioned, single outcomes indicators in aneurysm surgery often have a low event rate, which result in little variation and does not incite improvements. Furthermore, a single indicator generally seems to give a one-sided perspective and does not reflect the multidimensional aspect of the surgical process.[36]
Textbook Outcomes is a composite measure that was first described in surgical gastro-intestinal oncology.[36,37] As it includes all desirable outcomes of the surgical process, it gives a better impression of the overall quality of care and it increased the variation between hospitals.[38] In **Chapter 6** we define and test Textbook Outcome for elective AAA surgery.
In the evaluation of effectiveness of surgical AAA care, it is important to take, in addition to (postoperative) mortality and complications, long-term secondary aortic reinterventions (SARs) into account. Where elective endovascular aneurysm repair (EVAR) is known to have lower postoperative mortality than elective open repair, it appears that EVAR entails more SARs.[39-41] As mentioned, the use of EVAR has continuously increased over the past decades and is currently used in the vast majority of elective patients, which thereby will eventually also influence the number of SARs. However, it is unclear what the current extent of this problem is on a national scale and what the consequences are for patients. Since January 2016 all patients undergoing a SAR (endovascular or open) following a primary AAA repair are also included in the DSAA. As all data in the audit is collected on a procedural level, information on the primary procedures and corresponding SARs could now be merged. In **chapter 7** we aimed to provide insight in to the national number of SARs following primary AAA repairs in

the Netherlands. Secondly, we have described patient aneurysm and treatment characteristics and outcomes of patients undergoing SAR.

The Dutch Audit for Carotid interventions

Following the example of DSAA, the NVvV also initiated the Dutch Audit for Carotid Interventions (DACI). From June 2013, all patients undergoing carotid artery intervention were registered in this mandatory audit. The structure of the audit was similar to that of the DSAA, with variables for structure process and outcome indicators. There was a national minimum required volume of 20 carotid interventions per hospital. As in the Netherlands carotid stenting is only done in exceptional cases, it is primarily an audit of carotid endarterectomy (CEA). A CEA is primarily performed in patients with a symptomatic high-grade carotid stenosis, to prevent a recurrent transient ischemic attack (TIA) or ischemic stroke.[42,43] Based on studies from Rothwell we learned that a CEA is more effective in preventing a stroke in the first two weeks after the index-event.[44,45] International guidelines therefore recommend performing a CEA in patients with symptomatic carotid stenosis within two weeks after the index event.[46] When forming the DACI, it was important to be able to provide insight into the waiting time for carotid endarterectomy, nationally and also between hospital. The percentage of patients with a symptomatic carotid stenosis undergoing surgery within 2 weeks after the index event became a quality process indicator, in which initially 80% was the minimal standard.[47] As quality outcome indicators, postoperative mortality and, in accordance with international literature, the combined outcome (major) measure stroke and/or death were used. Additionally, rebleeding and cerebral nerve injury were also registered and included in the quality indicators. As in the DSAA, case-mix correction of the postoperative outcomes was performed using the variables of the VP-Possum prediction model.[15]

In **chapter 8** we describe the results of patients with symptomatic carotid artery stenosis undergoing CEA and registered in the DACI during the first years of auditing, in which overall quality is evaluated, as well as the variation between hospitals in process and outcomes indicators. Additionally, patient characteristics associated with major stroke and/or death have been identified. In **chapter 9** we discuss the origin and formation of the 'time-to-intervention' guideline and how it should be interpreted.

REFERENCES

1. Codman EA. A Study in Hospital Efficiency. *Privately printed.* 1916.
2. NICE. *Principles for Best Practice in Clinical Audit.* 2002.
3. Dutch Institute for Clinical Auditing (DICA). http://www.dica.nl/.
4. Nederlandse Vereniging voor Vaatchirurgie (NVvV). http://nvvv-vaatchirurgie.nl/.
5. Donabedian A. Evaluating the quality of medical care. *Milbank Mem Fund Q.* 1966;44(3):Suppl:166-206.
6. Inspectie Gezondheidszorg en Jeugd (IGJ). https://www.igz.nl/.
7. Zorginstituut Nederland (ZIN). https://www.zorginstituutnederland.nl/.
8. Harteraad. http://www.harteraad.nl/.
9. Zorgverzekeraars Nederland (ZN). https://www.zn.nl/.
10. Kwaliteitsindicatoren DSAA. 2019; https://dica.nl/media/1863/DSAA 2019.2 Factstheet indicatoren extern 2019 DEF.pdf.
11. Transparantieportaal. https://dica.nl/dica/Transparantieportaal. Accessed 22-12-2019.
12. Lijftogt N, Vahl AC, Wilschut ED, et al. Adjusted Hospital Outcomes of Abdominal Aortic Aneurysm Surgery Reported in the Dutch Surgical Aneurysm Audit. *Eur J Vasc Endovasc Surg.* 2017;53(4):520-532.
13. Lijftogt N, Luijnenburg TWF, Vahl AC, et al. Systematic review of mortality risk prediction models in the era of endovascular abdominal aortic aneurysm surgery. *Br J Surg.* 2017;104(8):964-976.
14. Lijftogt N, Vahl A, van der Willik EM, et al. Toward Optimizing Risk Adjustment in the Dutch Surgical Aneurysm Audit. *Ann Vasc Surg.* 2019;60:103-111.
15. Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. *Br J Surg.* 1991;78(3):355-360.
16. Chaikof EL, Dalman RL, Eskandari MK, 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 e72.
17. Moll FL, Powell JT, Fraedrich G, et al. Management of abdominal aortic aneurysms clinical practice guidelines of the European society for vascular surgery. *Eur J Vasc Endovasc Surg.* 2011;41 Suppl 1:S1-S58.
18. Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med.* 2002;346(19):1437-1444.
19. Powell JT, Brown LC, Forbes JF, et al. Final 12-year follow-up of surgery versus surveillance in the UK Small Aneurysm Trial. *Br J Surg.* 2007;94(6):702-708.
20. Ouriel K, Clair DG, Kent KC, Zarins CK, Positive Impact of Endovascular Options for treating Aneurysms Early I. Endovascular repair compared with surveillance for patients with small abdominal aortic aneurysms. *J Vasc Surg.* 2010;51(5):1081-1087.
21. Filardo G, Powell JT, Martinez MA, Ballard DJ. Surgery for small asymptomatic abdominal aortic aneurysms. *Cochrane Database Syst Rev.* 2015(2):CD001835.
22. United Kingdom Small Aneurysm Trial P, Powell JT, Brady AR, et al. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med.* 2002;346(19):1445-1452.
23. EG Karthaus AV, BHP Elsman. *Jaarrapport DSAA 2015.* 2016.
24. Phillips P, Poku E, Essat M, et al. Procedure Volume and the Association with Short-term Mortality Following Abdominal Aortic Aneurysm Repair in European Populations: A Systematic Review. *Eur J Vasc Endovasc Surg.* 2017;53(1):77-88.
25. Trenner M, Kuehnl A, Salvermoser M, 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. *Eur J Vasc Endovasc Surg.* 2018;55(2):185-194.
26. Reimerink JJ, Hoornweg LL, Vahl AC, et al. Endovascular repair versus open repair of ruptured abdominal aortic aneurysms: a

multicenter randomized controlled trial. *Ann Surg.* 2013;258(2):248-256.

27. Investigators IT, Powell JT, Sweeting MJ, et al. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ.* 2014;348:f7661.
28. Hinchliffe RJ, Bruijstens L, MacSweeney ST, Braithwaite BD. A randomised trial of endovascular and open surgery for ruptured abdominal aortic aneurysm–results of a pilot study and lessons learned for future studies. *Eur J Vasc Endovasc Surg.* 2006;32(5):506-513; discussion 514-505.
29. Desgranges P, Kobeiter H, Katsahian S, et al. Editor's Choice–ECAR (Endovasculaire ou Chirurgie dans les Anevrysmes aorto-iliaques Rompus): A French Randomized Controlled Trial of Endovascular Versus Open Surgical Repair of Ruptured Aorto-iliac Aneurysms. *Eur J Vasc Endovasc Surg.* 2015;50(3):303-310.
30. Badger S, Forster R, Blair PH, Ellis P, Kee F, Harkin DW. Endovascular treatment for ruptured abdominal aortic aneurysm. *Cochrane Database Syst Rev.* 2017;5:CD005261.
31. Giles KA, Hamdan AD, Pomposelli FB, Wyers MC, Dahlberg SE, Schermerhorn ML. Population-based outcomes following endovascular and open repair of ruptured abdominal aortic aneurysms. *J Endovasc Ther.* 2009;16(5):554-564.
32. Giles KA, Pomposelli FB, Hamdan AD, Wyers MC, Schermerhorn ML. Comparison of open and endovascular repair of ruptured abdominal aortic aneurysms from the ACS-NSQIP 2005-07. *J Endovasc Ther.* 2009;16(3):365-372.
33. McPhee J, Eslami MH, Arous EJ, Messina LM, Schanzer A. Endovascular treatment of ruptured abdominal aortic aneurysms in the United States (2001-2006): a significant survival benefit over open repair is independently associated with increased institutional volume. *J Vasc Surg.* 2009;49(4):817-826.
34. Stukel TA, Fisher ES, Wennberg DE, Alter DA, Gottlieb DJ, Vermeulen MJ. Analysis of observational studies in the presence of treatment selection bias: effects of invasive cardiac management on AMI survival using propensity score and instrumental variable methods. *JAMA.* 2007;297(3):278-285.
35. Baiocchi M, Cheng J, Small DS. Instrumental variable methods for causal inference. *Stat Med.* 2014;33(13):2297-2340.
36. Kolfschoten NE, Kievit J, Gooiker GA, et al. Focusing on desired outcomes of care after colon cancer resections; hospital variations in 'textbook outcome'. *Eur J Surg Oncol.* 2013;39(2):156-163.
37. Busweiler LAD, Schouwenburg MG, van Berge Henegouwen MI, et al. 'Textbook outcome': what we should strive for in oesophagogastric cancer surgery. *Br J Surg.* 2017;in press.
38. Dimick JB, Staiger DO, Hall BL, Ko CY, Birkmeyer JD. Composite measures for profiling hospitals on surgical morbidity. *Ann Surg.* 2013;257(1):67-72.
39. De Bruin JL, Baas AF, Buth J, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1881-1889.
40. United Kingdom ETI, Greenhalgh RM, Brown LC, et al. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1863-1871.
41. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM, investigators Et. 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. *Lancet.* 2016;388(10058):2366-2374.
42. Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med.* 1998;339(20):1415-1425.
43. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet.* 1998;351(9113):1379-1387.
44. Rothwell PM, Eliasziw M, Gutnikov SA, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *Lancet.* 2003;361(9352):107-116.

45. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ, Carotid Endarterectomy Trialists C. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet.* 2004;363(9413):915-924.
46. Writing G, Naylor AR, Ricco JB, et al. Management of Atherosclerotic Carotid and Vertebral Artery Disease: 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg.* 2017.
47. *Kwaliteitsindicatoren DACI.*

Abdominal aortic aneurysm surgery

CHAPTER 2

Variation in Surgical Treatment of Abdominal Aortic Aneurysms with Small Aortic Diameters in the Netherlands

E.G. Karthaus, A.C. Vahl, L.R. van der Werf, B.H.P Elsman, J.A. Van Herwaarden, M.W.J.M. Wouters, J.F. Hamming

Annals of Surgery 2020

ABSTRACT

Background and objective

Guidelines recommend surgical treatment for asymptomatic abdominal aortic aneurysms (AAA) with a diameter of at least 55mm for men and 50mm for women. We evaluate reasons to deviate from these guidelines and focus on the difference in how Dutch vascular surgical units (VSU) perceive their deviation and their actual deviation.

Methods

All patients undergoing elective AAA-repair between 2013-2016 registered in the Dutch Surgical Aneurysm Audit (DSAA) were included. Surgery at diameters of <55mm for men and <50mm for women were considered guideline deviations. National deviation and hospital variation in deviation were evaluated over time. Questionnaires were distributed among all Dutch VSUs, inquiring for acceptable reasons for guideline deviation. VSUs were asked to estimate the guideline deviation percentage in their hospital which were then compared with their DSAA-percentage.

Results

9039 patients were included. In 15% we found guideline deviation, varying from 2-40% between VSUs. Over time, 21 VSUs were identified with a lower percentage of deviation than the national mean each year and 8 VSUs with a higher percentage. 44/60 VSUs completed the questionnaire. Most commonly reported reasons to deviate were concomitant large iliac diameter (91%) and saccular aneurysm (82%). The majority of the VSUs (77%) estimated their guideline deviation to be <5%. 11 VSUs (25%) estimated their deviation concordant with their DSAA-percentage, but 75% of VSUs underestimated their deviation.

Conclusion

Dutch VSUs regularly deviate from the guidelines regarding aneurysm diameter, with variation between VSUs. Consensus exists amongst VSUs on acceptable reasons for guideline deviations, however the majority underestimates their actual deviation percentage.

INTRODUCTION

The indication for elective surgical treatment in patients with an asymptomatic abdominal aortic aneurysm (AAA) depends on multiple factors, of which the diameter of the aneurysm is the most important one, as the risk of rupture increases with the diameter of the aneurysm.[1] International guidelines recommend surgical treatment in patients with an asymptomatic abdominal aortic aneurysm with a diameter of 55 mm or more in males and 50 mm or more in females.[2,3] These diameter thresholds for intervention have been studied extensively and early intervention in asymptomatic patients with a small abdominal aortic aneurysm (<55mm in males, <50mm in females) has not proven to be beneficial compared to watchful waiting.[4-8] Since 2013, all patients undergoing aortic aneurysm surgery in the Netherlands are registered in a nationwide audit, the Dutch Surgical Aneurysm Audit (DSAA)[9]. This audit reported previously that 17% of all patients undergoing elective aneurysm surgery is operated with a smaller diameter than recommended in the guidelines, with variation between hospitals.[10] Other studies have also confirmed variation in practice regarding the aneurysm diameter, nationally and internationally.[11-13] There are reasons why surgeons could decide to deviate from this guideline, for example a saccular-shaped aneurysm, a large iliac component, rapid growth etc.[14] However, unnecessarily large variation in clinical practice is undesirable, because it can result in unnecessary adverse outcomes for patients[13] and will lead to unnecessary costs.[15,16] To minimize differences in practice, to improve quality of care and to use health care more efficiently, it is important to have more insight into the reasons for this variation in clinical practice.

The aim of this study is first to evaluate patient and disease characteristics associated with performing surgical therapy on patients with a smaller aortic diameter than recommended in the guideline and secondly to investigate reasons to deviate from this guideline with a focus on how often Dutch vascular surgical units (VSUs) think they deviate from the guidelines and actually do.

METHODS

This study consists of three parts:

1. Analysis of national data from the DSAA
2. Survey questionnaire among Dutch Vascular Surgeons
3. Comparison of the outcomes of the survey questionnaire and DSAA data

Part 1 – Analysis of national data from the Netherlands

Data source and patient selection

The dataset is derived from the DSAA. This compulsory nationwide audit was initiated in 2013 and prospectively registers all patients undergoing surgery for an aortic aneurysm or dissection. Data are registered via a web-based survey or provided by the hospitals as a batch data file. All patients with a juxta- or infrarenal abdominal aortic aneurysm undergoing primary elective surgery between January 2013 and December 2016 were included. All patients with symptomatic or ruptured abdominal aortic aneurysms, isolated iliac artery aneurysms, thoracic aortic aneurysms or/and dissections, undefined aneurysms and patients undergoing revision surgery were excluded. Additionally, patients operated in hospitals that stopped performing aneurysm surgery after the first year of the study period were also excluded.

Aneurysm diameter

In the survey of the DSAA, the largest measured aortic aneurysm diameter, anterior-posterior measured with ultrasound or computed tomography angiography (CTA) and extracted from the radiology report, is registered. The diameter thresholds for surgical treatment in asymptomatic abdominal aortic aneurysms according to the Dutch national guideline are used: 55mm or more for males, 50 mm or more for females. We have made a distinction between 'any deviations' from this guideline (diameter <55mm in males, diameter <50mm in females), 'small deviations' (diameter from 50-54mm in males, 45-49mm in females) and 'large deviations' (diameter <50mm in males, diameter <45mm in females).

Dutch health care policies regarding elective AAA surgery.

For the treatment of elective AAA, there is an annual minimum volume standard of 20 elective AAA repairs per hospital in the Netherlands. This minimum volume standard is monitored with the use of DSAA-data. All patients undergoing elective AAA surgery are pre-operatively discussed in a multidisciplinary team or vascular meeting. This is also a quality indicator that is monitored in the DSAA.

Analysis

Using descriptive analysis (T-test and chi-square tests), patient, disease and treatment characteristics were compared between two separate groups: all patients treated according to the national guidelines and all patients in which was ''deviated from the guidelines". Patient, treatment and hospital characteristics independently associated with any deviation from the guidelines were evaluated using a multivariable logistic regression analysis with p-value of 0.05 using an enter model. Co-variables used in this multivariable logistic regression analysis were: sex, age, pulmonary state, cardiac state, results of last preoperative electrocardiogram, malignancy, pre-operative hemoglobin and creatinine, type of surgical procedure and hospital

volume. Additionally, variation in surgical treatment of small aneurysms (diameter <55mm in males, diameter <50mm in females) between hospitals was evaluated over time, by comparison of the percentage of deviation from the guideline per hospital over the years 2013-2016. All statistical analyses were performed using SPSS statistical software (version 24; IBM Corp, Armonk, NY).

Part 2 – Survey questionnaire among Dutch Vascular Surgeons

In order to obtain insight in the reasons why vascular surgeons decide to operate patients with a small abdominal aortic aneurysm diameter, an online survey questionnaire was distributed among VSUs in the 60 hospitals that perform AAA surgery in the Netherlands. The contact person for the DSAA of each VSU, chief of the department of vascular surgery, was contacted to fill in the questionnaire for his/her VSU. The survey consisted of 14 questions (appendix 1). In the first section, units were asked to estimate how often they perform surgery on patients with a small aortic aneurysm diameter in 2 multiple choice questions. Subsequently, they were asked what they thought to be acceptable reasons to deviate from the guideline, in which multiple reasons were proposed. Finally, they were asked to estimate to what extent these 11 reasons were applicable to or did occur in their hospital, by using a Likert scale. In order to compare the results of the questionnaire with the DSAA data, units were asked to report the name of their hospital, making the questionnaire not anonymous.
Descriptive analyses were used to evaluate outcomes.

Part 3 – Comparison of the outcomes of the survey questionnaire and DSAA data

Results of de survey questionnaire were compared with the DSAA data on hospital level. Discrepancies between the estimated percentage of guideline deviation by the VSUs and their actual practice were evaluated, as well as the differences in reasons to deviate from guidelines between hospitals with high and low guideline adherence.

RESULTS

Part 1 – Analysis of national data from the Netherlands

Between January 2013 and December 2016, 10186 patients underwent elective aneurysm surgery in the Netherlands. After exclusion of 546 patients with an isolated iliac aneurysm, 212 with a (concomitant) thoracic aneurysm/dissection, 209 with an undefined aneurysm, 166 with revision surgery and 14 patients operated in hospitals that stopped performing AAA surgery, a total of 9039 patients was included for analysis. Out of these patients, 15% (1324 patients) had a smaller abdominal aortic diameter than in which surgical treatment

is recommended by the national guideline, 16% of all male patients and 9.0% of all female patients. In 11% (969) this concerned a small deviation from the guideline and in 3.9% (355) a large deviation.

Compared to the group of patients treated according to the guideline, there were more male patients in the group in which was deviated from the guideline (91% versus 85%, p<0.001) and this group was on average 3 years younger (mean 70.9 SD 8.0 versus 73.5 SD 7.5, p<0.001). Additionally, pulmonary state, cardiac state, pre-operative ECG, malignancies, preoperative hemoglobin and type of surgical procedure were unequally distributed between the two groups (table 1).

Characteristics associated with deviation from the guideline

Characteristics independently associated with deviation from the guideline were: male gender (odds ratio [confidence interval]: 1.709[1.386-2.109]) and treatment with EVAR (1.432[1.232-1.664]). (table 2) Characteristics with a low odds ratio for deviation from the guideline were: age (0.958[0.950-0.966], per additional year), peripheral edema (0.644[0.510-0.864]), current malignancy (0.560[0.399-0.786]), and hospital volume (0.998[0.997-0.999], per additional procedure).

Hospital variation

Between hospitals, the percentage deviations from the guideline varied between 2-40% (median: 13%). (0-33% small deviations; 0-17% large deviations) (figure 1). When the variation in surgical treatment of small abdominal aortic aneurysms was evaluated over time, 21 hospitals could be identified with a lower percentage of deviations than the national mean (15%) of deviations every year (Appendix 2). Respectively, twelve, six and fourteen hospitals had a higher percentage deviations than the national mean of deviations in 1, 2 or 3 years. Finally, seven hospitals could be identified that had a higher percentage of deviations than the national mean in every year.

Part 2 – Survey questionnaire among Dutch Vascular Surgical teams

A total of 44 (out of 60) VSUs completed the online survey questionnaire (73% response rate). The majority of the units (n=34, 77%) estimated to deviate from the guideline in less than 5% of their patients. The remaining 9 (21%) and 1 (2%) estimated to deviate from the guidelines in respectively 5-15% and >15% of their patients. Additionally, 42 (95.5%) and 2 (4.5%) units answered that they perform surgery on patients with an aneurysm of more 5 mm smaller than the recommended threshold (large deviation) in respectively <5% and 5-15% of their patient.

Table 1. Comparison of patient characteristics between patients with guideline adherence and guideline deviation

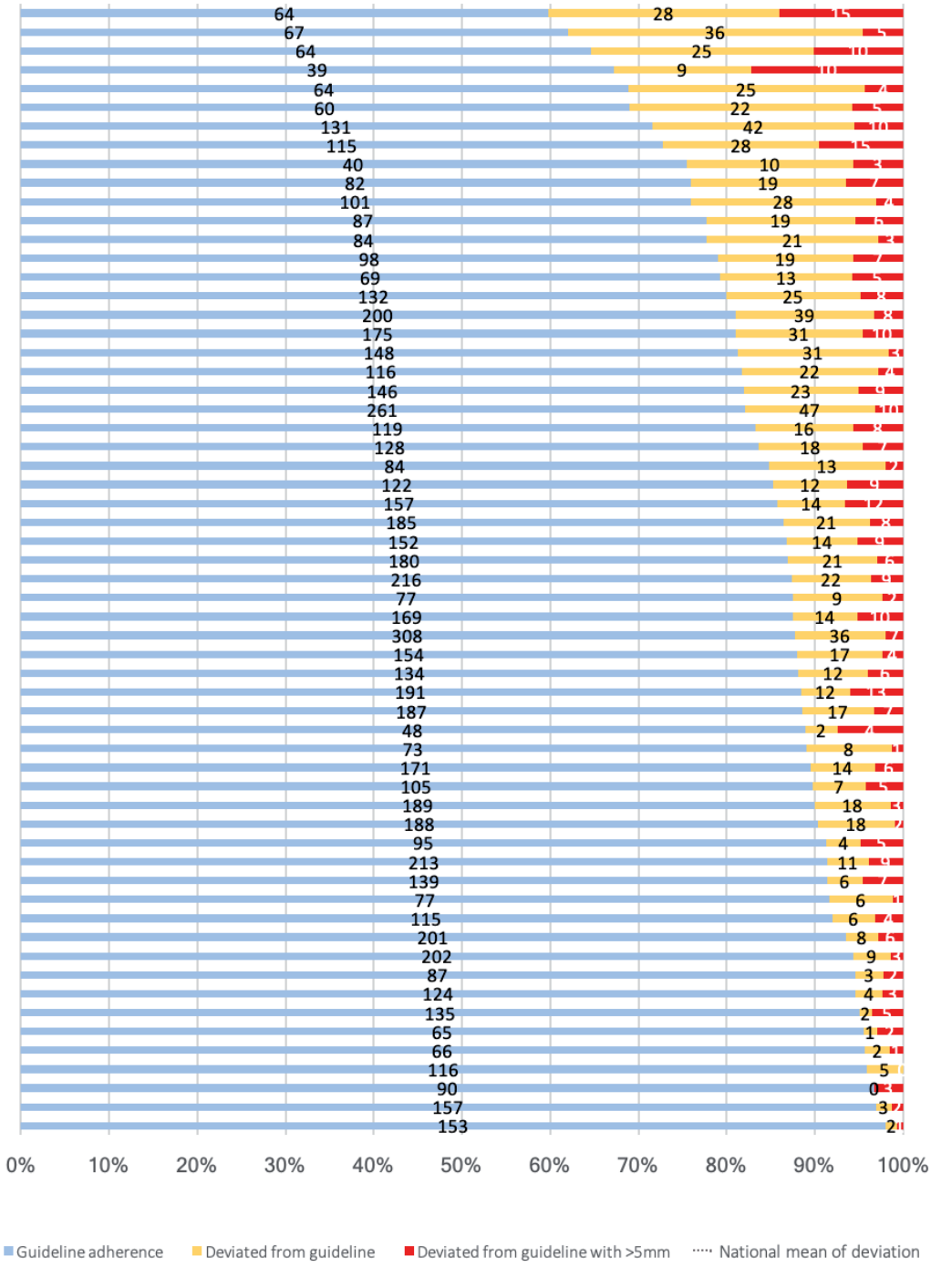
	Guideline adherence		**Guideline deviation**		
	Aneurysm diameter s(males ≥55 mm, female ≥50 mm)		Aneurysm diameter (males <55 mm, female <50 mm)		
	N	%	N	%	P value
Number of patients	7715	85%	1324	15%	
Age (mean, years)	73.5 SD 7.5		70.9 SD 8.0		<.001
Sex					<.001
Male	6532	85%	1207	91%	
Female	1183	15%	117	8.8%	
Year of surgery					.009
2013	1636	21%	332	25%	
2014	2090	27%	361	27%	
2015	1964	26%	318	24%	
2016	2025	26%	313	24%	
Cardiac state					<.001
No abnormalities	3511	46%	670	51%	
Peripheral edema	672	8.7%	75	5.7%	
Raised CVP	119	1.5%	22	1.7%	
Antihypertensive medication	3103	40%	503	38%	
Unknown	310	4.0%	54	4.1%	
Pulmonary state					.044
No dyspnea	5633	73%	1015	77%	
Dyspnea	1655	22%	242	18%	
Severe dyspnea	314	4.1%	51	3.9%	
Unknown	113	1.5%	16	1.2%	
Malignancy					.002
None	6217	81%	1102	83%	
Current	392	5.1%	39	2.9%	
History of malignancy	1106	14%	183	14%	
Last pre-operative ECG					.021
No abnormalities	4235	55%	781	59%	
Abnormalities	2731	35%	429	32%	
No ECG performed/Unknown ECG	749	9.7%	114	8.6%	
Hart rate (mean, BPM)	73 SD 13		73 SD 14		.174
Systolic blood pressure (mean, mmHg)	140 SD 20		140 SD 20		.930
Preoperative laboratory results					
Hemoglobin (mmol/L)	8.6 SD 1.0		8.8 SD 1.0		<.001
Leukocytes (10^9/L)	8.5 SD 2.8		8.4 SD 3.0		.284
Creatinine (mmol/L)	90 IQR 77-107		89 IQR 77-104		.183
Sodium					.555
Normal sodium (135-145 mmol/L)	7294	95%	1257	95%	
Hypo/hypernatremia	421	5.5%	67	5.1%	
Potassium					.160
Normal potassium (3.5-5.0 mmol/L)	7256	94%	1232	93%	
Hypo/hyperpotassemia	459	5.9%	92	6.9%	
Treatment					.002
OSR	1808	23%	258	20%	
EVAR	5907	77%	1066	81%	

Table 2. Patient and hospital characteristics independently associated with deviation from the guideline

	Deviation from the guideline	
	0dds Ratio	95% CI
Number of patients	9039	
Age (mean, years)	0.958	0.950-0.966
Sex		
Female	Ref.	
Male	1.709	1.386-2,109
Pulmonary state		
No dyspnea	Ref.	
Dyspnea	0.895	0.767-1.045
Severe dyspnea	1.017	0.746-1.386
Unknown	0.870	0.508-1.491
Cardiac state		
No abnormalities	Ref.	
Peripheral edema	0.664	0.510-0.864
Raised CVP	1.042	0.647-1.679
Antihypertensive medication	0.899	0.789-1.023
Unknown	0.988	0.724-1.348
Last pre-operative ECG		
No abnormalities	Ref.	
Abnormalities	0.994	0.868-1.138
No ECG performed	0.862	0.692-1.074
Malignancy		
None	Ref.	
Current	0.560	0.399-0.786
History of malignancy	1.024	0.861-1.216
Preoperative laboratory results		
Hemoglobin (mmol/L)		
<7.5	Ref.	
7.5-8.5	1.096	0.869-1.382
8.6-9.5	1.112	0.893-1.386
>9.5	1.136	0.896-1.441
Creatinine (mmol/L)		
<80	Ref.	
80-100	1.062	0.916-1.230
101-120	1.043	0.867-1.255
>120	0.994	0.814-1.214
Treatment		
OSR	Ref.	
EVAR	1.432	1.232-1.664
Hospital volume 2013-2016*	0.998	0.997-0.999

* Volume of elective AAA repairs between 2013-2016.

Figure 1. Percentage deviations from guideline per vascular surgical unit



Acceptable reasons mentioned to deviate from the guideline were aorto-iliac aneurysm with large iliac diameter (n=40, 91%), saccular aortic aneurysm (n=36, 82%), rapid aneurysm growth (n=35, 80%) and a chronic painful aneurysm (non-acute mild abdominal pain during physical examination) (n=27, 61%) (Appendix 3). Other suggested reasons were patients desire to undergo aneurysm surgery (n=15, 34%), a connective tissue disorder (n=10, 23%), younger age of the patient (n=6, 14%), a positive family history for aortic aneurysm rupture (n=5, 11%), afraid that treatment with EVAR would not be possible when the aneurysm would grow further (n=1, 2%), other reasons (n=3, 7%) and no good reasons (n=0, 0%). The reasons to deviate from the guideline that were reported to in fact occur in their own practice were (Appendix 4): 'concomitant large iliac aneurysm' (regularly 39%, often 39%), 'saccular aneurysm' (regularly 39%, often 30%) and 'rapid aneurysm growth' (regularly 32%, often 25%). 'Space on the operating room schedule' and 'achieving volume standard' were never (0, 0%) reported. 'Afraid that EVAR would not be possible when the aneurysm grows', 'young age of the patient' and 'positive family history' were answered to never occur in respectively 93%, 61% and 57% of the units.

Part 3 – Comparison of survey questionnaire and DSAA data

The percentage of deviations from the guideline per vascular surgical unit as registered in the DSAA (figure 2 left column) were compared to the in the survey estimated percentage of deviations per unit (figure 2 right column). Eleven units had an estimated percentage concordant (green) to their actual practice registered in the DSAA and 33 had not (red). Of the 33 units with non-concordant estimations, 11 units estimated to deviate from the guideline in <5% of the patients while doing that in >15%. The percentage of large deviations from the guideline per unit as registered in the DSAA compared to the estimated percentage deviations per unit is given in figure 3. There were 31 units with concordant estimations of large deviations and 13 with non-concordant estimations. Not responding to the survey (hospitals in grey) does not seem to be associated with higher percentage deviations from the guideline. Differences in patient and hospital characteristics between units that did and did not respond to the survey are shown in table 3. In the group of non-responders, there were more high-volume hospitals and an EVAR procedure was more common.

DISCUSSION

Dutch VSUs regularly decide to deviate from the guideline regarding aneurysm diameter. Male gender, young age, absence of peripheral edema and current malignancy, treatment with EVAR and lower hospital volume are factors that are independently associated with performing elective aneurysm repair on patients with a smaller aneurysm diameter than recommended in the guidelines. Guideline deviation varied considerably between units, both

Figure 2. Comparison of actual percentage deviations and estimated percentage per vascular surgical unit.

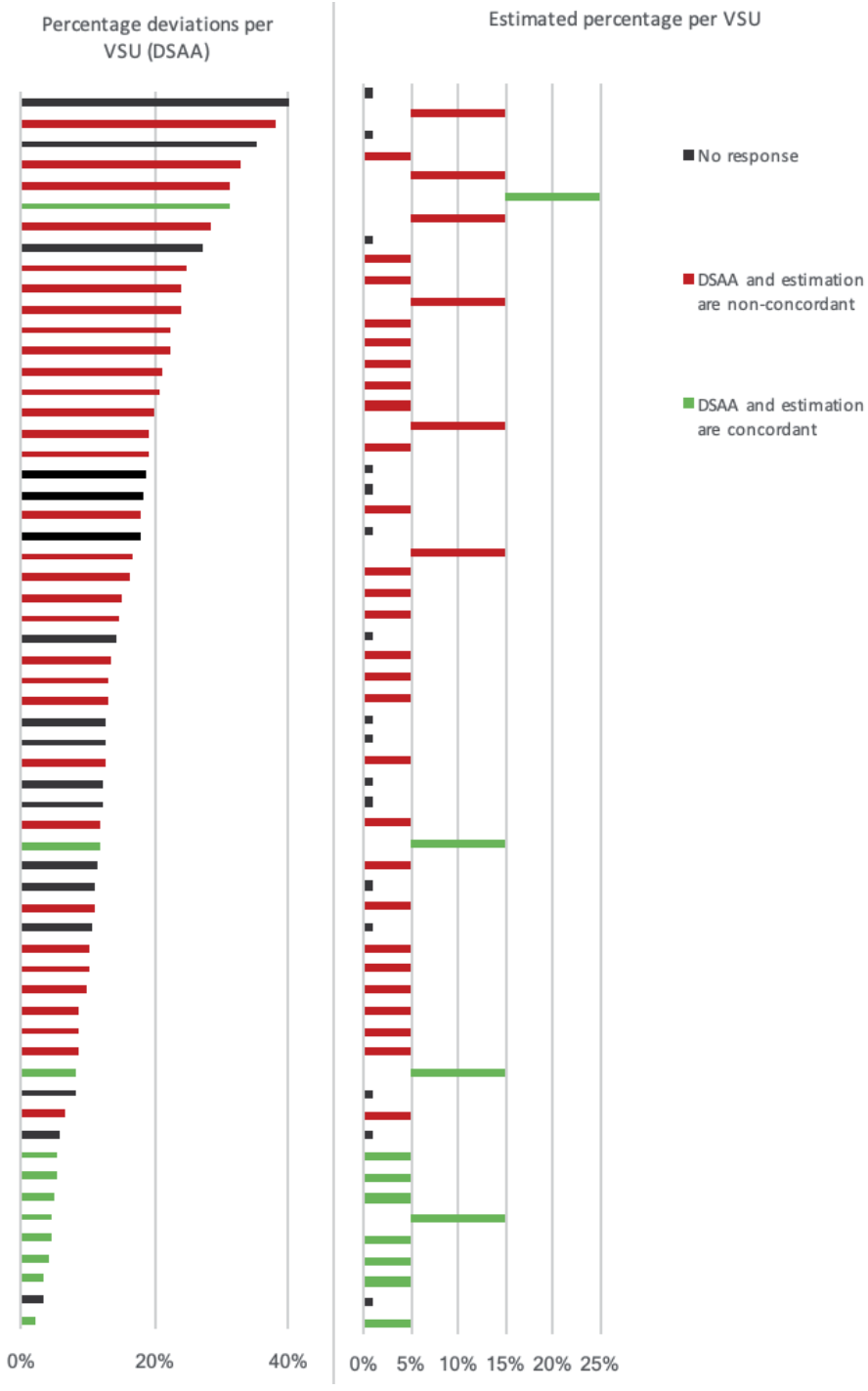


Figure 3. Comparison of actual percentage large deviations and estimated percentage per vascular surgical unit.

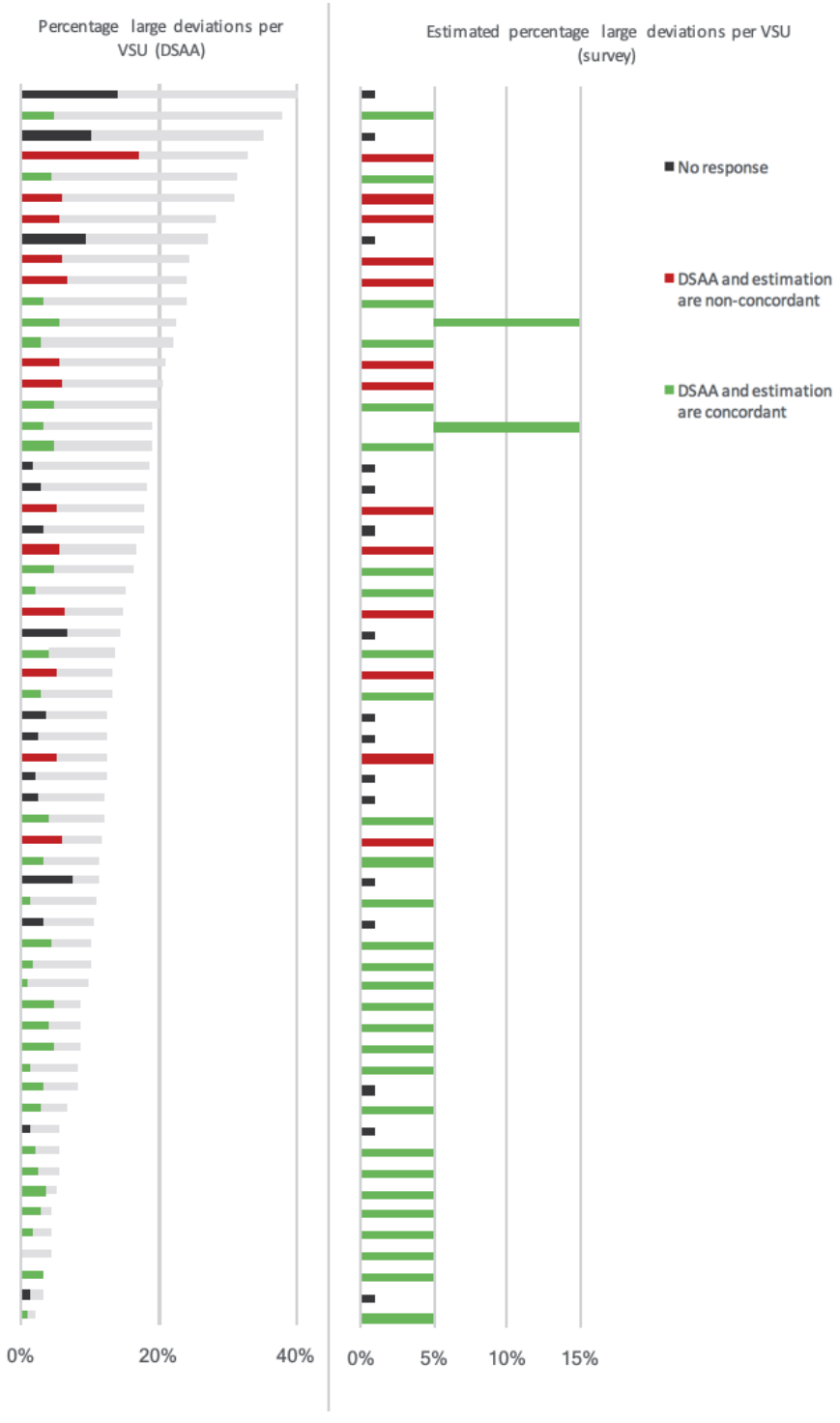


Table 3. Differences in patient and hospital characteristics between VSUs that responded and did not respond to the questionnaire

	Units that responded		Units that did not respond		
	N	%	N	%	
Number of patients	6243	69%	2796	31%	
Age (mean, years)	73,1 SD 7.7		73,2 SD 7.2		.519
Sex					.051
Male	5315	85%	2424	87%	
Female	928	15%	372	13%	
Treatment					.000
OSR	1496	24%	570	20.4%	
EVAR	4747	76%	2226	79.6%	
Hospital volume*					.000
<100	965	16%	241	9%	
100-150	1594	26%	374	13%	
150-200	1507	24%	1051	38%	
>200	2177	35%	1130	40%	
Guideline adherence					.387
Guideline adherence	5342	86%	2373	85%	
Deviation from guideline	901	14%	423	15%	

* Volume of elective AAA repairs between 2013-2016.

for small and large deviations. When the variation in surgical treatment of small abdominal aortic aneurysms was evaluated over time, units that rarely deviate from the guideline could be identified, as well as units that structurally did. Among Dutch VSUs there is agreement on acceptable reasons to perform elective surgery on patients with a small aortic aneurysm. However, there is considerable variation in the extent to which these reasons occur in actual practice. The estimated percentage of guideline deviations of each unit was often non-concordant and much lower than the actual practice as registered in the DSAA.

Since the publication of a retrospective review about the incidence of AAA and AAA rupture in nonspecific autopsies, the maximum aneurysm diameter is generally regarded as an important measure of risk for rupture.[17] International guidelines recommend an aneurysm diameter threshold for elective aneurysm repair of >55 mm in male and >50mm in female, based on the balance between the risk of aneurysm rupture and postoperative mortality in elective aneurysm repair.[2,3,18]

Two large randomized controlled trails, the UKSAT and ADAM trail, have evaluated potential benefit of elective aneurysm repair in asymptomatic patients with a diameter between 40-54mm, compared to watchful waiting.[4,8] In both trials, the postoperative mortality was significantly higher than the rupture rate. Therefore, early intervention is not beneficial. With the advent of EVAR, post-operative mortality in elective aneurysm surgery has strongly decreased. However, more recent studies comparing early EVAR and surveillance, have again not shown a mortality benefit for early intervention.[5,6,14] Therefore, the current

diameter thresholds for intervention in patients with asymptomatic aortic aneurysms have not changed.[2,3]

Nevertheless, this study shows that in reality Dutch VSUs regularly decide to perform surgery on patients with smaller aneurysm diameters than the thresholds, with a wide variation between units. Generally, a saccular shape of the aneurysm or an AAA with a large iliac aneurysm component are accepted for early surgical treatment, but high level of evidence is lacking.[2,3] Moreover, it is suggested that patients with rapid expansion of a small aortic aneurysm may benefit from early repair.[2,19,20] Patients with connective tissue diseases have an increased risk to develop aortic pathology and therefore it is understandable to perform early intervention on these patients.[21,22] However, an isolated abdominal aortic aneurysms is rare in patients with connective tissue diseases and therefore it does not seem to be a good reason to deviate from the guideline.[23,24] The benefit of early intervention for other reasons as young age and positive family history have not been demonstrated or investigated.[3]
Except for connective tissue diseases, mostly treated in centers of expertise, it is plausible that patient and aneurysm characteristics and the occurrence of reasons to deviate from the guideline are about equally distributed among hospitals. However, the questionnaire did show some variation between vascular units in how often these reasons resulted in guideline deviation. Indications as saccular aneurysm or aorto-iliac aneurysms with a large iliac component are relatively uncommon, nevertheless in this study, of all reasons they were most frequently reported as 'regularly' of 'often' occurring.[25,26]

Male gender and treatment with EVAR were independently associated with deviation from the guideline, whereas increasing age, peripheral edema, current malignancy, and high hospital volume were independently associated with adherence. These characteristics do not necessarily correspond to the generally accepted indications, as the mean age of patients with a saccular aneurysm or aorto-iliac aneurysm with large iliac component is comparable with the mean age of aneurysm patients or even higher.[25] Additionally, as female gender is associated with a higher risk of rupture, it would be expected that guideline deviation would happen more often in female patients than in males.[27,28] This suggest that in relatively young males with little to no co-morbidities that are eligible for treatment with EVAR, surgical treatment is more often chosen for smaller aneurysm diameters than recommended in the guideline. Another interesting finding is that hospitals with lower volumes performed surgery more often on patients with smaller diameter than hospitals with higher volumes. Besides achieving volume standards, financial incentives may also play a role in deviating from the guideline.[11]
When evaluating deviation from the guideline over time between units, units with a lower percentage of deviations than the national mean could be identified, as well as units with a higher percentage of deviations than the national mean in every year. Apparently, there is a certain consistency in the behavior of VSUs to perform surgery or not on patients with a smaller aortic diameter. Remarkably, VSUs with a higher total percentage of guideline

deviations more often had an estimation non-concordant with their actual practice than VSUs with a lower total percentage of deviations. It seems that VSUs that frequently deviate from the guideline are apparently not aware that they are doing this.

This study has several limitations. To evaluate the national performance and difference between surgical teams regarding surgical treatment for small abdominal aortic aneurysms, it would have been useful to know the exact reason to deviate from the guideline for each patient. Unfortunately, this information was not captured in the DSAA. By combining information about the incidence of deviation from the DSAA and information about the reasons and occurrence of these reasons from our questionnaire, we have tried to approach the proportion of different reason per vascular surgical unit in order to get more insight into variation in practice between units.
Secondly, the measurement of aneurysm diameter registered in the DSAA is not standardized. For the surveillance of patients with an asymptomatic AAA ultrasound is the imaging modality of preference. However, it may be possible that diameters measured with Computed Tomography Angiography (CTA) are registered as well. It is known that a diameter of an aneurysm is often larger when measured with CTA compared to ultrasound. This could result in an underestimation of the actual percentage of guideline deviation.[3] As we mainly focus on the decision-making following the measurement, this problem probably is not relevant.
Lastly, although a 73% response rate on a national questionnaire is quite good, we were not able provide information on the reported reasons of all Dutch VSUs. However, as the percentage of guideline deviation was not associated with not responding to the questionnaire and not responding appears to be coincidental, we consider the sample representative.

Guideline deviations happen often and extensively, and most hospitals that frequently deviate from the guideline do not seem to be aware of the fact that they are doing so. Therefore, providing good feedback information to vascular units is important for their process of quality of care improvement. The DSAA has an online portal in which vascular units can review their performance on multiple domains and compare this to other units. From January 2018, the percentage of guideline deviation regarding aneurysm diameter in elective AAA patients, compared to the national mean and the percentage of all other vascular units, will be fed back to the units. Consequently teams will be more aware how they perform and hopefully variation in practice will decrease.[29]

CONCLUSION

Deviations from the guideline regarding aneurysm diameter threshold for repair in the Netherlands is frequent, with a wide variety between vascular surgical teams. Discrepancies between what Dutch vascular surgical teams think they do and they actually do, might be an

explanation for the frequent and wide variation in guideline deviations. Introducing feedback by clinical auditing might create awareness of occurrence of deviation in VSUs.

ACKNOWLEDGEMENTS

The authors would like to thank all surgeons, registrars, physician assistants and administrative nurses that registered all the patients in the DSAA, the Dutch Surgical Aneurysm Audit group and all vascular surgical units that have responded to the survey questionnaire.

REFERENCES

1. Lo RC, Lu B, Fokkema MT, et al. Relative importance of aneurysm diameter and body size for predicting abdominal aortic aneurysm rupture in men and women. *J Vasc Surg.* 2014;59(5):1209-1216.
2. Chaikof EL, Dalman RL, Eskandari MK, 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 e72.
3. Moll FL, Powell JT, Fraedrich G, et al. Management of abdominal aortic aneurysms clinical practice guidelines of the European society for vascular surgery. *Eur J Vasc Endovasc Surg.* 2011;41 Suppl 1:S1-S58.
4. Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med.* 2002;346(19):1437-1444.
5. Powell JT, Brown LC, Forbes JF, et al. Final 12-year follow-up of surgery versus surveillance in the UK Small Aneurysm Trial. *Br J Surg.* 2007;94(6):702-708.
6. Ouriel K, Clair DG, Kent KC, Zarins CK, Positive Impact of Endovascular Options for treating Aneurysms Early I. Endovascular repair compared with surveillance for patients with small abdominal aortic aneurysms. *J Vasc Surg.* 2010;51(5):1081-1087.
7. Filardo G, Powell JT, Martinez MA, Ballard DJ. Surgery for small asymptomatic abdominal aortic aneurysms. *Cochrane Database Syst Rev.* 2015(2):CD001835.
8. United Kingdom Small Aneurysm Trial P, Powell JT, Brady AR, et al. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med.* 2002;346(19):1445-1452.
9. Lijftogt N, Vahl AC, Wilschut ED, et al. Adjusted Hospital Outcomes of Abdominal Aortic Aneurysm Surgery Reported in the Dutch Surgical Aneurysm Audit. *Eur J Vasc Endovasc Surg.* 2017;53(4):520-532.
10. https://www.dica.nl/jaarrapportage-2014/assets/uploads/DICA-JAAR-OFFLINE-2014.pdf.
11. Beck AW, Sedrakyan A, Mao J, et al. Variations in Abdominal Aortic Aneurysm Care: A Report From the International Consortium of Vascular Registries. *Circulation.* 2016;134(24):1948-1958.
12. Zettervall SL, Buck DB, Soden PA, et al. Regional variation exists in patient selection and treatment of abdominal aortic aneurysms. *J Vasc Surg.* 2016;64(4):921-927 e921.
13. Karthikesalingam A, Vidal-Diez A, Holt PJ, et al. Thresholds for Abdominal Aortic Aneurysm Repair in England and the United States. *N Engl J Med.* 2016;375(21):2051-2059.
14. Cao P, De Rango P, Verzini F, et al. Comparison of surveillance versus aortic endografting for small aneurysm repair (CAESAR): results from a randomised trial. *Eur J Vasc Endovasc Surg.* 2011;41(1):13-25.
15. Birkmeyer JD, Reames BN, McCulloch P, Carr AJ, Campbell WB, Wennberg JE. Understanding of regional variation in the use of surgery. *Lancet.* 2013;382(9898):1121-1129.
16. Tomee SM, Bastiaannet E, Schermerhorn ML, Golledge J, Hamming JF, Lindeman JH. The Consequences of Real Life Practice of Early Abdominal Aortic Aneurysm Repair: A Cost-Benefit Analysis. *Eur J Vasc Endovasc Surg.* 2017;54(1):28-33.
17. Darling RC, Messina CR, Brewster DC, Ottinger LW. Autopsy study of unoperated abdominal aortic aneurysms. The case for early resection. *Circulation.* 1977;56(3 Suppl):II161-164.
18. Scott RA, Wilson NM, Ashton HA, Kay DN. Is surgery necessary for abdominal aortic aneurysm less than 6 cm in diameter? *Lancet.* 1993;342(8884):1395-1396.
19. Powell JT, Sweeting MJ, Brown LC, Gotensparre SM, Fowkes FG, Thompson SG. Systematic review and meta-analysis of growth rates of small abdominal aortic aneurysms. *Br J Surg.* 2011;98(5):609-618.
20. Thompson SG, Brown LC, Sweeting 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;17(41):1-118.

21. Ho NC, Tran JR, Bektas A. Marfan's syndrome. *Lancet.* 2005;366(9501):1978-1981.
22. Roberts WC, Honig HS. The spectrum of cardiovascular disease in the Marfan syndrome: a clinico-morphologic study of 18 necropsy patients and comparison to 151 previously reported necropsy patients. *Am Heart J.* 1982;104(1):115-135.
23. Hagerty T, Geraghty P, Braverman AC. Abdominal Aortic Aneurysm in Marfan Syndrome. *Ann Vasc Surg.* 2017;40:294 e291-294 e296.
24. Takayama T, Miyata T, Nagawa H. True abdominal aortic aneurysm in Marfan syndrome. *J Vasc Surg.* 2009;49(5):1162-1165.
25. Shang EK, Nathan DP, Boonn WW, et al. A modern experience with saccular aortic aneurysms. *J Vasc Surg.* 2013;57(1):84-88.
26. Kristmundsson T, Dias N, Resch T, Sonesson B. Morphology of Small Abdominal Aortic Aneurysms Should be Considered before Continued Ultrasound Surveillance. *Ann Vasc Surg.* 2016;31:18-22.
27. Brown LC, Powell JT. Risk factors for aneurysm rupture in patients kept under ultrasound surveillance. UK Small Aneurysm Trial Participants. *Ann Surg.* 1999;230(3):289-296; discussion 296-287.
28. Sweeting MJ, Thompson SG, Brown LC, Powell JT, collaborators R. Meta-analysis of individual patient data to examine factors affecting growth and rupture of small abdominal aortic aneurysms. *Br J Surg.* 2012;99(5):655-665.
29. Jamtvedt G, Young JM, Kristoffersen DT, O'Brien MA, Oxman AD. Audit and feedback: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev.* 2006(2):CD000259.

Appendix 1. Survey questionnaire that wat send to all VSUs performing aneurysm surgery in the Netherlands.

1. *What percentage of patients, undergoing elective abdominal aortic aneurysm surgery in your hospital,* ***do you think*** *has a* ***smaller*** *aneurysm diameter than in which surgical treatment is recommended by the guideline (males <55mm and female <50mm)?*
   - □ <5%
   - □ 5-15%
   - □ >15%

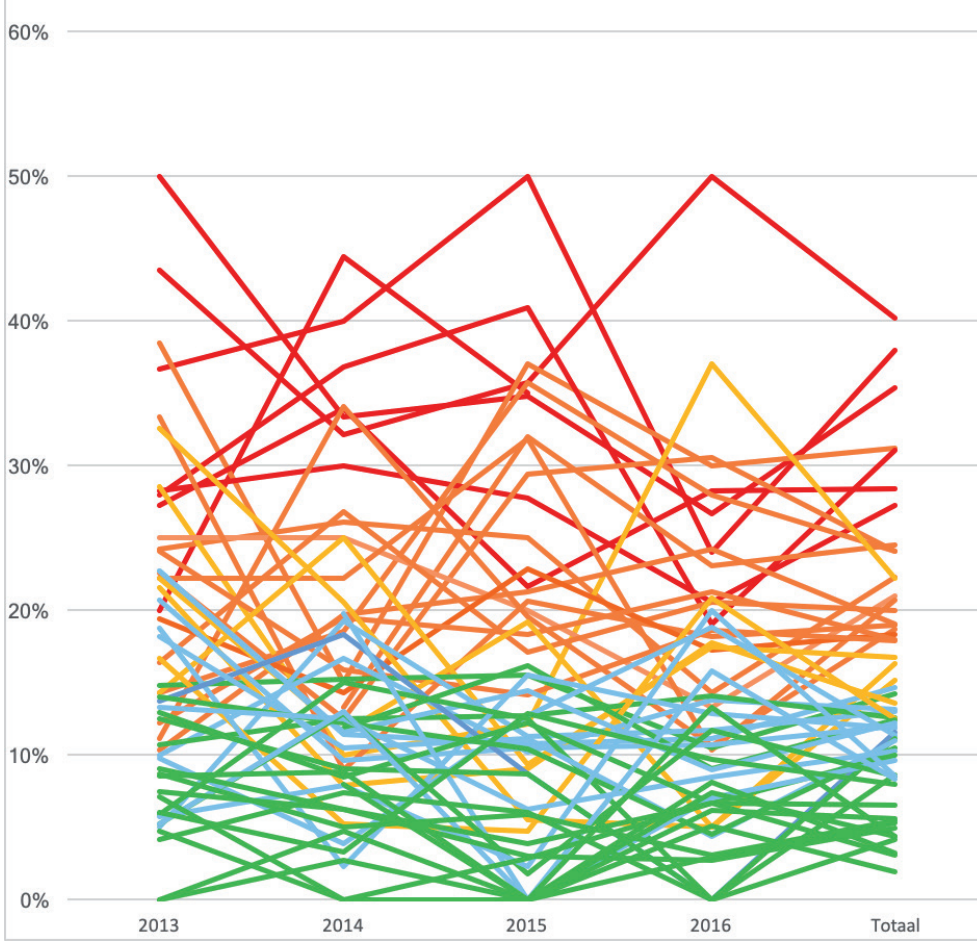
2. *What percentage of patients, undergoing elective abdominal aortic aneurysm surgery in your hospital,* ***do you think*** *has an aneurysm diameter* ***of more than 5mm smaller*** *than in which surgical treatment is recommended by the guideline (males <50mm and female <45mm)?*
   - □ <5%
   - □ 5-15%
   - □ >15%

3. *Which of the patient related factors mentioned below is in your opinion an acceptable reason to deviate from the national guideline regarding aneurysm diameters? (Possible to fill in multiple reasons)*
   - □ *Desire of patient to undergo surgical treatment*
   - □ *Rapid aneurysm growth*
   - □ *Chronical painful aneurysm*
   - □ *Connective tissue disorder*
   - □ *Positive family history of aortic aneurysm rupture*
   - □ *Patient with a young age*
   - □ *Saccular shaped aneurysm*
   - □ *Iliac aneurysm of >40mm*
   - □ *Afraid that EVAR would not be possible when the aneurysm would grow further*
   - □ *None*
   - □ *Other, namely…*

4. *To which extend do the reasons mentioned below play a role in the decision to deviate from the guideline?*

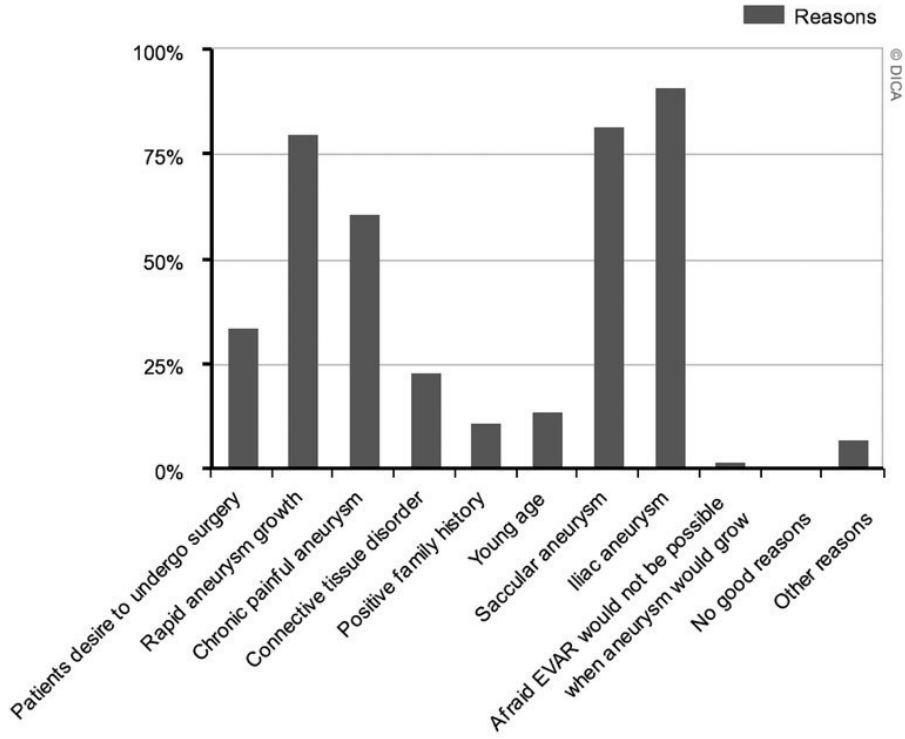
	Never		*Sometimes*		*Always*
Desire of patient to undergo surgical treatment	o	o	o	o	o
Rapid aneurysm growth	o	o	o	o	o
Chronical painful aneurysm	o	o	o	o	o
Connective tissue disorder	o	o	o	o	o
Positive family history for aortic aneurysm rupture	o	o	o	o	o
Patient with a young age	o	o	o	o	o
Saccular shaped aneurysm	o	o	o	o	o
Iliac aneurysm of >40mm	o	o	o	o	o
Afraid that EVAR would not be possible when the aneurysm would grow further	o	o	o	o	o
Space on the operating room schedule	o	o	o	o	o
Achieving the annual volume threshold	o	o	o	o	o

Appendix 2. Percentage deviations from the guideline per vascular surgical unit over time (2013-2016).

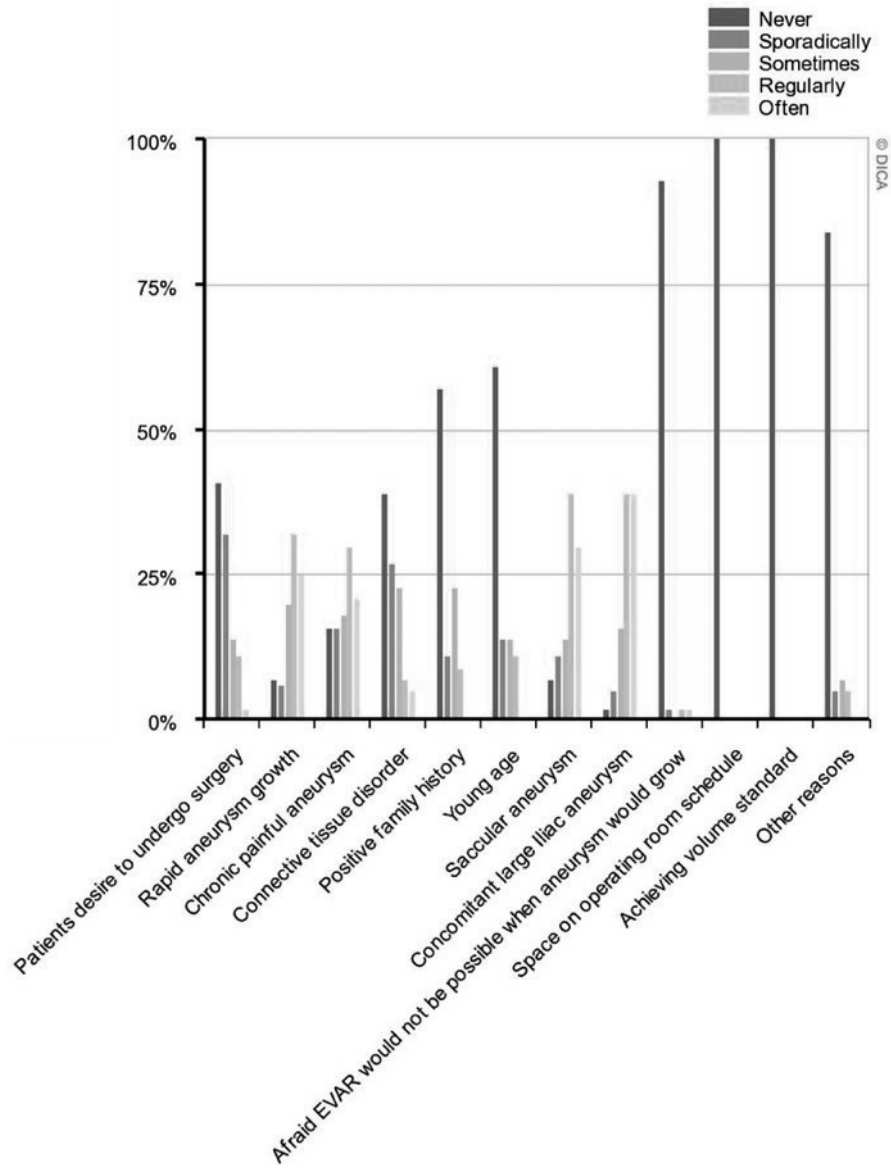


Explanation of figure: The green lines represents the VSUs with a lower percentage of deviations than the national mean (15%) of deviations every year. The blue, yellow and orange lines represents VSUs with a higher percentage deviations than the national mean of deviations in respectively 1, 2 or 3 years. The red lines represent the VSUs with a higher percentage of deviations than the national mean in every year.

Appendix 3. Reported acceptable reasons to deviate from the guidelines



Appendix 4. The extent to which the reasons to deviate from the guideline occur in practice.



CHAPTER 3

Saccular Abdominal Aortic Aneurysms: Patient Characteristics, Clinical Presentation, Treatment and Outcomes in the Netherlands

E.G. Karthaus, T.M.L. Tong, A.C. Vahl, J.F. Hamming

Annals of Surgery 2019

ABSTRACT

Background and objective

Based on the assumption that SaAAAs are more prone to rupture, guidelines suggest early elective treatment. However, little is known about the natural history of SaAAAs and the threshold for intervention is not substantiated. The objective is to analyze differences between saccular (SaAAAs) and fusiform abdominal aortic aneurysms (FuAAAs) regarding patient characteristics, treatment and outcome, to advise a threshold for intervention for SaAAAs.

Methods

Observational study including primary repairs of degenerative AAAs in the Netherlands between 2016-2018 in which the shape was registered, registered in the Dutch Surgical Aneurysm Audit (DSAA). Patients were stratified by urgency of surgery; elective versus acute (symptomatic/ruptured). Patient characteristics, treatment and outcome were compared between SaAAAs and FuAAAs.

Results

7659 primary AAA-patients were included, 6.1% (n=471) SaAAAs and 93.9% (n=7188) FuAAAs. There were 5945 elective patients (6.5% SaAAA) and 1714 acute (4.8% SaAAA). Acute SaAAA-patients were more often female (28.9% vs 17.2%, p=0.007) compared to acute FuAAA-patients. SaAAAs had smaller diameters than FuAAAs, in elective (53.0mm vs 61mm, p=0.000) and acute (68mm vs 75mm, p=0.002) patients, even after adjusting for gender. Additionally, 25.2% of acute SaAAA-patients presented with diameters <55mm and 8.4% <45mm, versus 8.1% and 0.6% of acute FuAAA-patients (p=0.000). Postoperative outcomes did not significantly differ between shapes in both elective and acute patients.

Conclusion

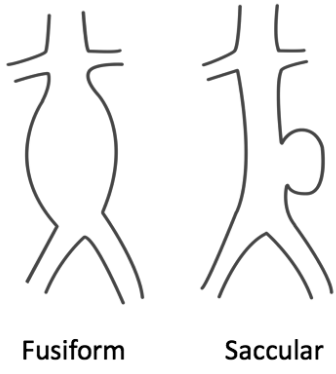
SaAAAs become acute at smaller diameters than FuAAAs in DSAA patients. This study therefore supports the current idea that SaAAAs should be electively treated at smaller diameters than FuAAAs. The exact diameter threshold for elective treatment of SaAAAs is difficult to determine, but a diameter of 45mm seems to be an acceptable threshold.

INTRODUCTION

A saccular shaped abdominal aortic aneurysm (SaAAA), a focally spherical asymmetric dilatation of the aorta, is not common, and is reported to account for about 5% of all abdominal aortic aneurysms (AAAs) (figure 1).[1,2] The vast majority of all AAAs is fusiform shaped (FuAAAs). According to current international guidelines, elective AAA surgery is indicated in aneurysms with a maximum aortic diameter of at least 55mm in men and 50mm in women.[3] However, this only concerns the frequently presenting FuAAAs. The most recent American and European guidelines suggest that elective surgical treatment of SaAAAs is indicated at even smaller diameters, but fail to give an exact threshold for intervention in these patients.[3,4] There is a long-standing belief that SaAAAs should be treated at smaller diameters, as the unique asymmetrical shape might predispose them to rupture.[5-7] Additionally, Kristmundsson et al. showed that small ruptured AAAs (<5.5cm) were more often saccular shaped.[2] However, Shang et al. found no significantly increased risk of rupture in patients with a SaAAA, compared to patients with a FuAAA based on radiologic findings.[8]

Currently no large case series or cohort studies of patients with SaAAAs have been reported. The natural history of patients with SaAAAs is actually unknown and the question remains whether a different treatment diameter threshold should be applied. This study aims to present an overview of the experience with patients with SaAAAs in the Netherlands. Using data from the Dutch Surgical Aneurysm Audit (DSAA) differences are analyzed between SaAAAs and FuAAAs regarding patient characteristics, clinical presentation, treatment and outcome, to substantiate a threshold for operative correction.

Figure 1. Saccular and fusiform shaped abdominal aortic aneurysm



METHODS

Data source

The Dutch Surgical Aneurysm Audit (DSAA) is a nationwide and compulsory quality registry, that registers all patients undergoing aortic surgery in the Netherlands. The DSAA was started in 2013 as an audit for primary AAA surgery and from 2016 all aortic aneurysm/dissection surgical procedures were included. Since 2016 the shape of degenerative aneurysms (fusiform or saccular) is registered in the DSAA. In other pathologies, the shape is not registered. The final responsibility for the registered patient data lies with the vascular surgeon. Verification of the DSAA data was carried out in 2015 by a third trusted party, through a random sample of hospitals and will be continued in the future.[9]

Patient selection

All patients undergoing primary AAA repair in the Netherlands between January 2016 and December 2018 and registered in the DSAA were selected for this study. To consider a patient eligible for analysis the date of birth, date of surgery, type of surgical procedure, urgency of surgical procedure and survival status at time of discharge and 30-days postoperatively had to be known. Furthermore, only patients with a degenerative AAA, in which the aneurysm shape (fusiform/saccular) was specified, were included for analysis.

Definitions and statistical analyzes

A saccular shaped AAA was defined as a focally spherical asymmetric dilatation of the abdominal aorta and fusiform as a coil-shaped dilatation (figure 1). Patients were stratified by the urgency of surgery; elective versus acute presentations. We assume that surgery is indicated in all acute presentations in order to prevent rupture and/or death. As we are interested in a diameter thresholds for elective surgery of SaAAA, all patients with an acute symptomatic or ruptured AAA were grouped and classified as ''acute". Aneurysm shape and diameter registered in the DSAA are extracted from the radiology report and confirmed by a vascular surgeon. In FuAAAs this concerns the largest measured aneurysm diameter, anterior-posterior with ultrasound or computed tomography angiography (CTA) and in SaAAAs the largest diameter measured on axial CTA coupe. Postoperative mortality was defined as mortality within 30-days after surgery or during admission (30-days/in-hospital). Postoperative complication (30-days/in-hospital) were categorized by surgical and non-surgical complications. Descriptive analyses were performed comparing patient characteristics, clinical presentation, treatment and postoperative outcomes between SaAAA and FuAAA patients. Postoperative outcomes were analyzed separately for acute symptomatic and ruptured patients.

Continuous variables were analyzed with a T-test or Mann-Whitney U test when appropriate. Categorical variables were analyzed with a chi-square test. A p-value of <0.05 was considered as significant. To evaluate diameter thresholds for elective repair, the relative risk (RR) for acute presentation between SaAAA and FuAAA was determined per diameter category in

acute patients. All statistical analyses were performed using SPSS statistical software (version 24; IBM Corp, Armonk, NY).

RESULTS

Between January 2016 and December 2018, 9089 patients underwent a primary AAA repair in the Netherlands and were registered in the DSAA, of which 9035 (99.4%) were eligible for analysis. The AAA had a degenerative pathology in 7668 (84.9%) of patients. In the remaining 1367 patients, the AAA was caused by infection or inflammation (n=222, 2.5%), dissection (n=62, 0.7%), trauma (n=5, 0.1%), connective tissue diseases (n=86, 1.0%) and unknown pathology (n=992, 11.0%). All 7659 (99.9%) patients with a degenerative AAA, in which the shape was specified, were included in this study: 6.1% (n=471) had a SaAAA and 93.9% (n=7188) a FuAAA. The elective group consisted of 5945 patients and the acute group of 1714 patients. Stratified by the urgency of surgery there were 6.5% (n=388) SaAAAs in elective group and 4.8% (n=83) in the acute (symptomatic/ruptured) group.

Patient characteristics

Patient characteristics, stratified by urgency of surgery and compared between patients with a SaAAA and FuAAA, are presented in table 1. The cohort consisted predominantly of males (84.8% elective, 82.2% acute). In the elective group, distribution of sex was comparable between patients with SaAAA and FuAAA. In the acute group, patients with a SaAAA were more often female, compared to patients with a FuAAA (28.9% vs 17.2%; p=0.007). Baseline characteristics were similar regarding age, cardiac status, pulmonary status, preoperative laboratory results and Glasgow Coma Scale.

Aneurysm and treatment characteristics

In the elective group, patients with SaAAAs were treated at smaller diameters than patients with FuAAAs (mean 53.0 SD 11.4 vs 61.0 SD 9.5; p=0.000) (table 1). Adjusted for gender, the differences in mean diameter between aortic shapes remained (table 2a). Additionally, when dividing maximum aneurysm diameters into categories, patients with SaAAAs were more often undergoing elective surgery at diameters of <45mm, 45-49mm or 50-55mm compared to patients with FuAAAs (<45mm: 20.1% vs 0.7%, 45-49mm: 14.7% vs 1.6% and 50-55mm 19.6%-13.4%; p=0.000). There were no significant differences in type of AAA and type of surgical procedures between the elective SaAAA and FuAAA patients. In the acute setting, patients with SaAAAs had also a smaller mean maximum aneurysm diameter compared to patients with FuAAAs (mean 70.7 SD 23.1 vs 76.5 SD 17.3; p=0.000), also when adjusted for gender (table 2b). When analyzed in categories, a different distribution of maximum diameters between SaAAAs and FuAAAs was seen: acute SaAAA patients more often had a maximum diameter <55mm compared to patients with FuAAAs (25.2%

Table 1. Patient and treatment characteristics

	Elective AAA					**Acute AAA**				
	Fusiform		**Saccular**		***P-value***	**Fusiform**		**Saccular**		***P-value***
	N	%	N	%		N	%	N	%	
Number of patients	5558	93.5%	388	6.5%		1631	95%	83	4.8%	
Age (mean, years)	73.5 SD 7.3		74.0 SD 7.4		*0.175*	74.2 SD 8.0		74.3 SD 8.0		*0.856*
Sex					*0.110*					*0.007*
Male	4722	85%	318	82.0%		1350	83%	59	71%	
Female	835	15%	70	18.0%		281	17%	24	29%	
Cardiac comorbidity					*0.991*					*0.258*
None	2052	37%	142	36.6%		629	39%	29	35%	
Yes	3390	61%	238	61.3%		833	51%	49	59%	
Unknown	115	2.1%	8	2.1%		169	10%	5	6.0%	
Pulmonary comorbidity					*0.406*					*0.679*
None	3961	71%	265	68.3%		988	61%	50	60%	
Yes	1520	27%	116	29.9%		320	20%	19	23%	
Unknown	76	1.4%	7	1.8%		323	20%	14	17%	
Preoperative laboratory results										
Hemoglobin (mean, mmol/L)	8.7 SD 1.0		8.7 SD 1.0		*0.779*	7.7 SD 1.4		7.8 SD 1.4		*0.511*
Creatinine (median, mmol/L)	90 IQR 77-108		90 IQR 77-108		*0.896*	100 IQR 80-125		89 IQR 74.5-107		*0.028*
Glasgow Coma Scale										*0.217*
Normal GCS						1310	80%	72	87%	
Lowered GCS						228	14%	6	7.2%	
GCS unknown						93	5.7%	5	6.0%	
Aneurysm diameter (mean, mm)	61.0 SD 9.5		53.0 SD 11.4		*0.000*	76.5 SD 17.3		70.7 SD 23.1		*0.033*
Aneurysm diameter (median, mm)						75 IQR 62-89		68 IQR 53-82		*0.002*
Min-max (mm)	31-140		31-9			32-150		32-140		
Aneurysm diameter categories					*0.000*					*0.000*
<45mm	37	0.7%	78	20%		9	0.6%	7	8.4%	
45-49mm	88	1.6%	57	15%		38	2.3%	8	9.6%	
50-54mm	742	13%	76	20%		85	5.2%	6	7.2%	
55-64mm	3364	61%	111	29%		302	19%	13	16%	
65-75mm	797	14%	33	8.5%		310	19%	14	17%	
>=75mm	509	9.2%	19	4.9%		824	51%	30	36%	
Missing	20	0.4%	14	3.6%		63	3.9%	5	6.0%	
Type of AAA					*0.309*					*0.438*
Infrarenal	4888	88%	351	91%		1380	85%	74	89%	
Juxtarenal	615	11%	35	9.0%		237	15%	9	11%	
Suprarenal	52	0.9%	2	0.5%		14	0.9%	0	0.0%	
Missing	3	0.1%	0	0.0%		0	0.0%	0	0.0%	
Urgency of surgery										*0.001*
Acute symptomatic						527	34%	42	51%	
Acute rupture						1084	67%	41	49%	
Missing						0	0.0%	0	0.0%	
Treatment					*0.080*					*0.526*
EVAR	4333	78%	313	81%		836	51%	47	57%	
OSR	5	0.1%	1	0.3%		766	47%	35	42%	
Converted to OSR	1188	21%	69	18%		10	0.6%	1	1.2%	
Other	31	0.6%	5	1.3%		19	1.2%	0	0.0%	
Missing	1	0.0%	0	0.0%		0	0.0%	0	0.0%	

Table 2a. Mean abdominal aortic diameter adjusted for gender and shape in elective patients

					95% Confidence Interval for B	
	B	Std. Error	Beta	Sig.	Lower Bound	Upper Bound
(Constant)	73,709	0,675		0,000	72,387	75,032
Sex	-4,236	0,344	-0,155	0,000	-4,909	-3,562
Aneurysm shape	-7,861	0,507	-0,195	0,000	-8,854	-6,868

Table 2b. Mean abdominal aortic diameter adjusted for gender and shape in acute patients

					95% Confidence Interval for B	
	B	Std. Error	Beta	Sig.	Lower Bound	Upper Bound
(Constant)	92,776	2,436		0,000	87,999	97,553
Sex	-9,979	1,114	-0,216	0,000	-12,164	-7,794
Aneurysm shape	-4,639	1,997	-0,056	0,020	-8,556	-0,721

vs. 8.1%; p=0.000), which results in a RR for an acute presentation of 3.1 (95%CI 2.1-4.7) in SaAAA with a diameter <55mm, compared to FuAAAs of the same size (table 3). Additionally, 8.4% (n=7) of SaAAA patients was presented with a diameter <45mm versus 0.6% (n=9) in FuAAA (RR 15.3, 95%CI 5.8-40.0). SaAAAs were presented more often as acute symptomatic (50.6% vs 32.1%) and less frequent as an acute rupture compared to the FuAAAs (49.4% vs 66.5%; p=0.002). Additionally, there were no significant differences in type of surgical procedures performed in the acute setting between the SaAAA and FuAAA.

Surgical outcomes

Regarding perioperative and postoperative complications there were no significant differences between the SaAAA and FuAAA groups (table 4), in elective, acute symptomatic and ruptured patients. In respectively 16.3% (5.7% surgical) and 20.2% (8.8% surgical) of elective SaAAA and FuAAA patients, a postoperative complication occurred. In acute symptomatic patients,

Table 3. Relative risk for acute presentation between saccular and fusiform AAAs

	Fusiform		Saccular		Relative Risk for acute presentation	95% Confidence Interval
	N	%	N	%		
	1631		83			
Aneurysm diameter						
<45mm	9	0.6%	7	8.4%	15.3	5.8–40.0
≥45mm	1622	99.4%	76	91.%		
<50mm	47	2.9%	15	18.0%	6.3	3.7–10.7
≥50mm	1584	97.1%	68	82.0%		
<55mm	132	8.1%	21	25.2%	3.1	2.1–4.7
≥55mm	1499	91.9%	62	74.8%		
<65mm	434	26.6%	34	40.9%	1.5	1.2–2.0
≥65mm	1197	73.4%	49	59.1%		

Table 4. Postoperative outcomes

	Elective					Acute Symptomatic					Ruptured				
	Fusiform		Saccular		P	Fusiform		Saccular		P	Fusiform		Saccular		P
	N	%	N	%		N	%	N	%		N	%	N	%	
Perioperative complication					*0.662*					0.157					0.441
No complication	5247	94.5%	365	94.1%		515	94.1%	41	97.6%		897	82.7%	34	82.9%	
Reanimation/MI	11	0.2%	1	0.3%		0	0.%	0	0%		55	5.1%	1	2.4%	
Occlusion of side branch	46	0.8%	6	1.5%		6	1.1%	0	0%		20	1.8%	0	0%	
Type 1 endoleak	92	1.7%	4	1.0%		11	2.0%	0	0%		11	1.0%	2	4.9%	
Type 3 endoleak	10	0.2%	0	0.0%		1	0.2%	1	2,40%		4	0.4%	0	0%	
Bowel injury	8	0.1%	0	0.0%		1	0.2%	0	0%		9	0.8%	0	0%	
Ureter injury	2	0.0%	0	0.0%		0	0.0%	0	0%		3	0.3%	0	0%	
Other	139	2.5%	12	3.1%		13	2.4%	0	0%		85	7.8%	4	9.8%	
Postoperative complication					*0.172*					0.228					0.096
No complication	4434	79.8%	325	83.8%		390	71.3%	26	61.9%		351	32.4%	20	48.8%	
Surgical complication	314	5.7%	17	4.4%		33	6.0%	1	2.4%		131	12.1%	4	9.8%	
General complication	631	11.4%	41	10.6%		95	17.4%	12	28.6%		383	35.3%	7	17.1%	
Surgical and general complication	170	3.1%	5	1.3%		29	5.3%	3	7.1%		213	19.6%	10	24.4%	
Unknown complication	8	0.1%	0	0.0%		0	0%	0	0%		6	0.6%	0	0%	
Reintervention	261	4.7%	15	3.5%	*0.248*	33	6.0%	3	7.1%	0.772	218	20.1%	10	24.4%	0.721
Length of hospital stay (mean, days)	5.1 SD 13.5		4.3 SD 7.42		*0.247*	8.0 SD 18.6		8.0 SD 12.3		0.985	16.1 SD 21.4		21.8 SD 24.0		0.183
Re-admission	325	5.8%	21	5.4%	*0.723*	41	7.5%	5	11.9%	0.305	65	6.0%	5	12.2%	0.107
Death	99	1.8%	7	1.8%	*0.974*	24	4.4%	1	2.4%	0.534	332	30.6%	7	17.1%	0.063

this was seen in 38.1% (9.5% surgical) of the SaAAA group and 28.7% (11.3% surgical) of the FuAAA group and in 51.2% (34.2% surgical) versus 67.6% (31.7% surgical) in ruptured patients. Postoperative mortality was similar between SaAAA and FuAAA in elective (1.8% vs 1.8%; p=0.974), acute symptomatic (2.4% vs. 4.4%, p=0.534) and ruptured patients (17.3% vs. 30.6%, p=0.063).

DISCUSSION

Of all patients undergoing primary AAA surgery because of degenerative AAA in the Netherlands between 2016 and 2018, 6.1% had a SaAAA (6.5% elective, 4.8% acute). Patient characteristics were comparable between SaAAAs and FuAAAs, except that acute SaAAA patients were more often female compared to acute FuAAA patients. The accepted threshold for surgery is 55mm in FuAAAs (50mm in women).[3,4] As expected, elective patients with a SaAAA were operated at smaller diameters than elective FuAAA patients and the

majority of elective SaAAA patients were undergoing surgery with a diameter <55mm. Also, acute SaAAA patients were more often presented with smaller diameters than acute FuAAA patients: 25.2% of the acute SaAAAs had a diameter <55mm and 8.4% <45mm, while this was only 8.1% and 0.6% of the FuAAA group respectively. This resulted in a RR on an acute presentation of >3 in SaAAAs with diameters <55mm compared to FuAAAs of the same size and >15 in SaAAAs <45mm. This suggests a threshold of at least 45mm. Both SaAAAs and FuAAAs had similar treatment ratios with EVAR and OSR in the elective and acute setting, there were no differences in postoperative outcomes.

SaAAAs have been described as a relatively rare condition since early in the 20th century.[10] Since then, mainly case reports and small case series have been published on their clinical presentation and etiology.[11-14] Where FuAAAs often occurs as a result of degeneration of the arterial wall, SaAAAs appear to have a more varied etiology, including trauma, aortic infection, inflammatory diseases, degeneration of a penetrating atherosclerotic ulcer and previous aortic surgery.[15-17] With the development of imaging techniques, larger cohorts of patients with a saccular aortic aneurysm are identified.[1,2,8] Reported incidences of SaAAAs vary from 1.5%-5.0%, which corresponds to our finding 6.1% in the Dutch population.[1,2,8] Shang et al. described the largest cohort so far: 284 patients with a saccular thoracic or abdominal aortic aneurysm.[8] The majority of saccular aneurysms in this cohort were located in the descending thoracic aorta and only 24.2% (n=78) in the abdominal aorta. While case-series suggested a varied etiology of SaAAAs, Shang et al. found that the majority (81.1%) of saccular aortic aneurysms was caused by atherosclerosis (degeneration) and only 3.7% followed after trauma, 1.2% was caused by infection, 1.0% by arteritis and in 13.1% the etiology was unclear. Comparable data about the etiology for specifically SaAAA alone is not available to date.

Despite the fact that little is known about the natural course of SaAAAs, the assumption prevails that SaAAAs are more prone to rupture than those with a fusiform shape. The association between aneurysm shape and risk of rupture is based on the case-control study from Szilagyi et al in 1966 in which aneurysm characteristics were compared between patients with surgical and nonsurgical treatment.[7] It was thought that the asymmetrical shape of a SaAAA predisposes to rupture.[7,18] While there was no hard evidence for the association between shape and rupture, this association is mentioned in many case-series ever since.[1,2,6,8,19] In 1992, the subcommittee of the Joint Council of the Society for Vascular Surgery published a report recommending surgical treatment of saccular aneurysms regardless the size or symptom status.[5] Although this recommendation is only suggested in the current guidelines of the American and European Society for Vascular Surgery, it seems that it is still met by many vascular surgeons.[4,20] Apparently this recommendation is also followed by vascular surgeons in the Netherlands as more than half of elective patients with a SaAAA in our series was operated at a diameter <55mm. Although early surgical treatment is performed in the majority of elective SaAAAs in the Netherlands, still 17.6% of all SaAAAs presented in an

acute setting. Additionally, patients with acute SaAAAs presented with significantly smaller diameters than acute FuAAAs, even when adjusted for gender. These findings are consistent with Kristmundsson et al, who reported that small ruptured AAAs (<5.5cm) were more often saccular shaped, particularly in women.[2] Remarkably enough 8.4% of acute SaAAAs in our cohort had a smaller diameter than 45mm and the smallest diameter even 32mm. Furthermore, when looking at all AAAs <55mm, we found a RR of 3.1 for SaAAA patients to become acute compared to FuAAA patients. When lowering the diameter threshold this RR increased to even 15.3 for SaAAAs <45mm. This supports the current idea that SaAAAs should be electively treated at smaller aortic diameters than FuAAAs.[2]
On the contrary, Shang et al., found similar aneurysm growth rates between saccular and fusiform aneurysms and did not find any relation between shape and risk of rupture. However, this study included all types of aortic aneurysms, not only abdominal, and all pathologies.[8]

As cohorts of patients with a SaAAA are rarely described, little is known about the treatment and its outcomes, therefore we compared the treatment and outcomes of SaAAAs with their fusiform counterparts. In the Netherlands, SaAAAs are treated with EVAR in respectively in 80.7% of elective and 56.6% of acute patients, which is comparable with FuAAA patients. Comparing crude peri- and postoperative outcomes between patients with SaAAAs and FuAAAs, in elective, acute symptomatic and ruptured setting we found no significant differences.

This study has some limitations. The Dutch Surgical Aneurysm Audit only registers patients who underwent surgical repair of an aortic aneurysm. Patients with an AAA who are not (yet) operated or acute patients that died before they reached the hospital or could be operated, are not included in this dataset. Secondly, the DSAA was primarily set up as a quality registry for aortic surgery in the Netherlands and was not specifically designed for scientific purposes. Therefore, more detailed anatomic information or other measurements than maximum aneurysm diameters were not available. Furthermore, the measurement of maximum diameters in ruptured aneurysms can be difficult. In both the SaAAA and FuAAA group we found very small maximum aortic diameters. FuAAAs sometimes involve the iliac arteries, in these cases the indication for surgical repair can be based on the maximum iliac diameter instead of maximum aortic diameter, which may have resulted in unjustified lower diameters in the FuAAA group. This will not occur in the SaAAA group and may have influenced our comparison of diameters between the two shapes. The difference in diameters between SaAAA and FuAAA could actually be greater.

Until now this seems to be the largest cohort of exclusively SaAAAs and comparing the characteristics and results to fusiform counterparts. As our findings support the idea that SaAAAs should be surgically treated at smaller diameters than FuAAAs, it would be important to know what the threshold for elective surgery should be in saccular patients. Ideally, a

trial could test the effectivity of a newly proposed threshold. However, considering the low incidence of SaAAAs this is not an easily feasible option. Since only observational data are available, a threshold could be chosen based on the smallest diameters is which acute patients were presented. In our cohort of 83 patients with an acute SaAAA, 25.2% was presented with a diameter < 55mm, 8.4% <45mm and the smallest diameter in an acute patient was 32mm. Associated RR makes it clear that SaAAAs have a considerably greater chance to become acute at smaller diameters than FuAAAs. However, this based on a relative small cohort and does not provide an exact threshold. Pooling of observational data on SaAAAs could help to eventually determine a threshold for intervention.

CONCLUSION

SaAAAs become acute at smaller aortic diameters than FuAAAs in the Dutch Surgical Aneurysm Audit database. This study therefore supports the current idea that SaAAAs should be electively treated at smaller aortic diameters than FuAAAs. The exact diameter thresholds for elective treatment of SaAAAs is difficult to determine, but a minimum of at least 45mm seems to be an acceptable threshold.

REFERENCES

1. Iwai T, Sato S, Muraoka Y, Inoue Y, Sugano N, Endo M. Atherosclerotic abdominal aorta saccular protrusion. *Int Surg.* 1996;81(2):189-194.
2. Kristmundsson T, Dias N, Resch T, Sonesson B. Morphology of Small Abdominal Aortic Aneurysms Should be Considered before Continued Ultrasound Surveillance. *Ann Vasc Surg.* 2016;31:18-22.
3. Wanhainen A, Verzini F, Van Herzeele I, 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.
4. Chaikof EL, Dalman RL, Eskandari MK, 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 e72.
5. Hollier LH, Taylor LM, Ochsner J. Recommended indications for operative treatment of abdominal aortic aneurysms. Report of a subcommittee of the Joint Council of the Society for Vascular Surgery and the North American Chapter of the International Society for Cardiovascular Surgery. *J Vasc Surg.* 1992;15(6):1046-1056.
6. Taylor BV, Kalman PG. Saccular aortic aneurysms. *Ann Vasc Surg.* 1999;13(6):555-559.
7. Szilagyi DE, Smith RF, DeRusso FJ, Elliott JP, Sherrin FW. Contribution of abdominal aortic aneurysmectomy to prolongation of life. *Ann Surg.* 1966;164(4):678-699.
8. Shang EK, Nathan DP, Boonn WW, et al. A modern experience with saccular aortic aneurysms. *J Vasc Surg.* 2013;57(1):84-88.
9. Dataverification Dutch Surgical Aneurysm Audit 2015. [PDF]. http://dica.nl/media/660/Eindrapport_dataverificatie_DSAA_2016.pdf, 2016.
10. Baird IM. Saccular aneurysms of the abdominal aorta; report of three cases and review. *AMA Arch Intern Med.* 1953;91(5):626-632.
11. Kelemen E, Jr., Balogh J. Saccular aneurysm of the abdominal aorta due to medianecrosis. *Angiology.* 1966;17(4):247-251.
12. Yasuhara H, Muto T. Infected abdominal aortic aneurysm presenting with sudden appearance: diagnostic importance of serial computed tomography. *Ann Vasc Surg.* 2001;15(5):582-585.
13. Owen RP, Chan C. Saccular abdominal aortic aneurysm: clear cause of exquisite back pain. *BMJ Case Rep.* 2012;2012.
14. Minor ME, Menzoian JO, Raffetto JD. Noninfectious saccular abdominal aortic aneurysm—a report of two cases. *Vasc Endovascular Surg.* 2003;37(5):353-358.
15. Brown SL, Busuttil RW, Baker JD, Machleder HI, Moore WS, Barker WF. Bacteriologic and surgical determinants of survival in patients with mycotic aneurysms. *J Vasc Surg.* 1984;1(4):541-547.
16. Coady MA, Rizzo JA, Hammond GL, Pierce JG, Kopf GS, Elefteriades JA. Penetrating ulcer of the thoracic aorta: what is it? How do we recognize it? How do we manage it? *J Vasc Surg.* 1998;27(6):1006-1015; discussion 1015-1006.
17. Benrashid E, McCoy CC, Rice HE, Shortell CK, Cox MW. Mycotic Saccular Abdominal Aortic Aneurysm in an Infant after Cardiac Catheterization: A Case Report. *Ann Vasc Surg.* 2015;29(7):1447 e1445-1447 e1411.
18. Vorp DA, Raghavan ML, Webster MW. Mechanical wall stress in abdominal aortic aneurysm: influence of diameter and asymmetry. *J Vasc Surg.* 1998;27(4):632-639.
19. Pappu S, Dardik A, Tagare H, Gusberg RJ. Beyond fusiform and saccular: a novel quantitative tortuosity index may help classify aneurysm shape and predict aneurysm rupture potential. *Ann Vasc Surg.* 2008;22(1):88-97.
20. Moll FL, Powell JT, Fraedrich G, et al. Management of abdominal aortic aneurysms clinical practice guidelines of the European society for vascular surgery. *Eur J Vasc Endovasc Surg.* 2011;41 Suppl 1:S1-S58.

CHAPTER 4

Dutch Surgical Aneurysm Audit: Volume and Outcome of Elective Open Aneurysm Repair

E.G. Karthaus, A.C. Vahl, E.M. van der Willik, E.W. van Zwet, R. Balm, G.J. de Borst, J.F. Hamming

Submitted to Annals of Vascular Surgery

ABSTRACT

Background and objectives

Endovascular aneurysm repair (EVAR) has become standard of care in the treatment of elective abdominal aortic aneurysms (AAA), with a decrease in procedural mortality to <1%. Consequently, elective open surgical repair (OSR) is performed only in a minority of patients with a mortality of around 5%. Aiming to improve procedural outcomes, we determined the patient characteristics associated with mortality after elective OSR for AAA in the Dutch population and evaluated the association between hospital volume of elective OSR and adjusted mortality in order to explore a possible volume standard.

Methods

In this observational retrospective study**,** all patients undergoing elective OSR for an AAA between 2013-2018 in the Netherlands and prospectively registered in the compulsory Dutch Surgical Aneurysm Audit (DSAA) were included. The primary outcome was mortality (30-days/in-hospital). To evaluate a possible association between patient characteristics and mortality, a multivariable logistic regression analysis was performed. Next the case-mix adjusted postoperative mortality over the period 2013-2018 was calculated per hospital and displayed in a funnel plot. Additionally, the association between hospital volume and mortality after OSR was investigated with a generalized linear mixed model, adjusted for patient characteristics.

Results

In a six-year timeframe, 3100 patients with an AAA underwent elective OSR, which represents 23% of all electively repaired AAA. The overall mortality was 5.0% (n=156). Patient characteristics independently associated with mortality were: female sex [OR 1.676, 95% CI 1.132-2.483], age (OR 1.067, 95% CI 1.040-1.096) pulmonary state (dyspnea OR 1.756, 95% CI 1.230-2.508), preoperative hemoglobin (OR 0.836, 95% CI 0.702-0.996) and creatinine level (OR 1.004, 95% CI 1.001-1.008).
Elective OSR was performed in 59 hospitals, with a volume in 6 years varying from 1-141 elective OSR procedures and a case-mix adjusted mortality varying from 0-16%(mean 5%). Fourteen hospitals had a significantly lower mortality than the national mean mortality while none performed significantly worse. Adjusted for patient characteristics, hospital volume was not significantly associated with postoperative mortality after elective OSR.

Conclusion

In the Netherlands, annual hospital volume of elective OSR is not significantly associated with adjusted postoperative mortality. Female sex, increasing age, pulmonary state, preoperative hemoglobin and creatinine were significantly associated with mortality after elective OSR.

INTRODUCTION

Endovascular aneurysm repair (EVAR) has become standard of care in the treatment of elective abdominal aortic aneurysms (AAA). Since the landmark trials, postoperative mortality after elective EVAR has even decreased to less than 1%.[1] This is in contrast to elective open surgical repair (OSR) where postoperative mortality remained unchanged: 5% mortality in the Netherlands and varying from 2.0% to 5.6% between other European countries.[2-5]

With EVAR as the preferred surgical treatment, almost 80% of all Dutch elective aneurysm patients is now undergoing EVAR.[2] This percentage of elective EVAR is comparable to other European countries.[6] Patients, not suitable for treatment with EVAR, undergoing elective OSR have therefore become a selected group of patients mostly with a more difficult anatomy of the aneurysm. Also, this group may include more patients at a greater risk for postoperative mortality, due to changed patient selection. So, the unchanged mortality rate of 5% after OSR might reflect an improvement of care of AAA patients treated by OSR.

A possible factor for improving postoperative outcomes after elective OSR is the hospital volume in which this procedure is performed. Previous studies showed a relationship between hospital volume and postoperative mortality in AAA surgery.[7,8] In the Netherlands, there is a minimum volume standard of 20 elective abdominal aortic aneurysm procedures (EVAR and OSR) a year per hospital. However, this minimum volume standard dates from the time that OSR was mainly performed. With the increased use of EVAR over the last decades, the use of OSR simultaneously has decreased. Due to this decrease, hospitals may not perform the surgical procedure sufficiently to maintain good quality of care, which may possible influence postoperative mortality.[9] However, although the American minimum standard has been set at 10 OSR procedures a year, the Dutch minimum standard has yet not been changed or stratified by type of surgical procedure.[10,11]

The aim of our study was to analyze the association between hospital volume of elective OSR and postoperative mortality, in order to explore a possible minimum volume standard for elective OSR. Furthermore, we evaluate which patient characteristics are associated with postoperative mortality after elective OSR in the current Dutch population

METHODS

Data source and patient selection

The dataset was derived from the Dutch Surgical Aneurysm Audit (DSAA). This compulsory nationwide audit was initiated in 2013 and prospectively registers all patients undergoing surgery for an aortic aneurysm or dissection. Data were registered via a web-based survey or

provided by the hospital via a batch file. All patients with a juxta- or infrarenal abdominal aortic aneurysm undergoing primary elective open surgical repair between January 2013 and December 2018 were included for analyses. All patients with a thoracic or thoracoabdominal aortic aneurysm or dissection, a ruptured or acute symptomatic abdominal aortic aneurysm, elective abdominal aortic aneurysm undergoing EVAR and secondary aortic reintervention following a primary AAA repair were excluded. A minimal set of variables had to be registered to consider a patient eligible for further analysis: date of birth, date of surgery, type of surgical procedure and patient survival status (30 days/in-hospital). Verification of the DSAA data was carried out in 2015 by a third trusted party, through a random sample of hospitals and will be repeated in the near future.[12,13]

Primary outcome measure

The primary outcome of this study was postoperative mortality, 30-days and/or in-hospital. Patient characteristics were compared between patients with postoperative mortality and patients who survived after OSR, using T-tests for continuous variables and chi-square tests for categorical variables.

Multivariable logistic regression analysis

In order to evaluate possible associations between patient characteristics and postoperative mortality, a multivariable logistic regression analysis (enter model) at a p value of 0.05, was performed.

Patient characteristics included in this analysis were based on the elements of the V(p)-POSSUM predictive score: sex, age, maximal aneurysm diameter, pulmonary state, cardiac state, results of last preoperative electrocardiogram, preoperative hemoglobin and preoperative creatinine level.[14]

In case of missing data in continuous variables, the mean of each variable was imputed. Data was most frequently missing in preoperative creatinine (3.5%) and hemoglobin (2.6%). If data was missing in categorical variables, a category 'unknown' was added.

Additionally, to demonstrate the influence of certain patient characteristics and make them more useful to clinicians, mortality rates were stratified by the subgroups of combined patient characteristics that were most strongly associated with mortality.

Hospital selection: hospital volume

The annual volume of elective OSR was measured per hospital during a period of 6 years (2013-2018). Additionally, the ratio of elective OSR and EVAR volumes per hospital in this period was calculated. To evaluate the variation in postoperative mortality between hospitals, hospital volume of OSR was plotted against case-mix adjusted mortality rates in a funnel plot. The association between hospital volume of OSR per year and postoperative mortality was evaluated with a generalized linear mixed regression model, adjusted for all patient characteristics previously proven to be associated with postoperative mortality. As patients

treated in the same hospital share many experiences, we have to account for the resulting correlation. Therefore, a random effect per hospital was added to the model. Patients operated in hospitals that stopped performing elective OSR (4 hospitals, N=41, 0.03%) were excluded from this analysis.

All statistical analyzes regarding the association between patient characteristics and mortality were performed using SPSS statistical software (version 24; IMB Corp, Armonk, NY). All statistical analyzes regarding the association between hospital volume and postoperative mortality were performed using R statistical software (version 3.4.0)

RESULTS

Between January 2013 and December 2018, 14364 patients underwent elective abdominal aortic aneurysm repair in the Netherlands and were registered in the DSAA. After exclusion of all patients undergoing revision surgery (n=692, 4.8%), patients undergoing EVAR (10567, 74%) and patients with incomplete data (n=5, 0.03%), 3100 patients with an AAA undergoing primary elective open surgical repair and eligible for analyses were included in the study.

The majority of the cohort consisted of males (n=2505, 80.8%) with a mean age of 70.8 years (SD 7.3). Of all patients undergoing elective OSR between 2013-2018, 156 (5.0%) patients died within 30 days postoperatively and/or during their initial hospital stay, with a highest mortality (7.1%) in 2015 and the lowest (3.8%) in 2017. Patient characteristic, compared between patients with postoperative mortality and patients who remained alive after elective OSR, are shown in table 1. Patients with postoperative mortality were more often female (27.6% vs 18.8%, p = 0.006) and on average 3.6 years older (p =<0.001) than patients who survived. Additionally, cardiac state, preoperative electrocardiogram, pulmonary state, preoperative hemoglobin and preoperative creatinine levels were significantly different between the two groups.

Patient characteristics associated with postoperative mortality

The multivariable logistic regression analysis for postoperative mortality after elective OSR is shown in table 2. Patient characteristics independently associated with postoperative mortality after elective OSR were: female sex [odds ratio (OR) 1.676, 95% confidence interval (CI) 1.132-2.483], age per year (OR 1.067, 95% CI 1.040-1.096) pulmonary state (dyspnea OR 1.756, 95% CI 1.230-2.508), preoperative hemoglobin (OR 0.836, 95% CI 0.702-0.996) and preoperative creatinine per unit (OR 1.004, 95% CI 1.001-1.008).

Table 1. Comparison of patient characteristics between patients with and without postoperative mortality

	Patients survived		**Patients with postoperative mortality**		
	N	%	N	%	P-value
Sex					0.006
Male	2392	81%	113	72%	
Female	552	19%	43	28%	
Age (mean, years)	70.6 SD 7.3		74.2 SD 6.6		<0.001
Year of surgery					0.193
2013	524	96%	23	4.2%	
2014	530	94%	32	5.7%	
2015	435	93%	33	7.1%	
2016	470	95%	26	5.2%	
2017	478	96%	19	3.8%	
2018	507	96%	23	4.3%	
Cardiac state					0.010
No failure	1235	42%	50	32%	
Hypertension, angina pectoris, use of diuretics/digoxin	1387	47%	77	49%	
Peripheral edema, use of coumarin, cardiomyopathy	200	6.8%	21	14%	
Raised CVP, cardiomegaly	39	1.3%	3	1.9%	
Unknown	83	2.8%	5	3.2%	
Preoperative ECG					0.021
No abnormalities	1662	57%	67	43%	
Atrial fibrillation	156	5.3%	12	7.7%	
Ischemia	67	2.3%	5	3.2%	
Other abnormalities	870	30%	61	39%	
Unknown ECG /No ECG performed	189	6.4%	11	7.1%	
Pulmonary state					<0.001
No dyspnea	2238	76 %	95	61%	
Mild dyspnea	616	21%	53	34%	
Severe dyspnea	90	3.1%	8	5.1%	
Aneurysm diameter					0.327
<55mm	536	18%	20	13%	
55-64mm	1471	50%	84	54%	
65-74mm	457	16%	27	17%	
>75mm	438	15%	21	14%	
Missing	42	1.4%	4	2.6%	
Preoperative laboratory results					
Hemoglobin (mean, mmol/L)	8.7 SD 0.98		8.3 SD 0.97		<0.001
Creatinine (median, mmol/L)	90 IQR 76-107		98 IQR 78-131		<0.001

Table 2. Patient characteristics independently associated with postoperative mortality

	Odds Ratio	95% Confidence interval
Sex		
Male	Ref.	
Female	1.676	1.132–2.483
Age (years)	1.067	1.040–1.096
Aneurysm diameter (mm)	1.002	0.988–1.016
Cardiac state		
No failure	Ref.	
Hypertension, angina pectoris, use of diuretics/digoxin	1.228	0.845–1.787
Peripheral edema, use of coumarin, cardiomyopathy	1.669	0.952–2.925
Raised CVP, cardiomegaly	1.154	0.329–4.047
Unknown	1.269	0.484–3.328
Preoperative ECG		
No abnormalities	Ref.	
Abnormalities	1.416	0.989–2.026
Unknown ECG /No ECG performed	1.553	0.796–3.030
Pulmonary state		
No dyspnea	Ref.	
Mild dyspnea	1.756	1.230–2.508
Severe dyspnea	1.792	0.823–3.901
Hemoglobin (mmol/L)	0.836	0.702–0.996
Creatinine (mmol/L)	1.004	1.001–1.008

Table 3 demonstrates, as a practical example, the differences in mortality rates between patients with and without patient characteristics most strongly associated with mortality. For example, the combined characteristics 'age of 75 years and higher' and 'pulmonary comorbidity' resulted in a mortality of 11.0% in males and 13.1% in females.

Hospital volume

Between 2013-2018 elective OSR was performed in 59 hospitals, in which the total volumes of OSR in this period varied from 1 to 141 procedures. Figure 1 shows the volume of OSR per hospital per 2-year period. The majority of hospitals is performing on average less then 10 elective OSR procedures a year and only 20 hospitals perform on average more than 10 elective OSR a year. Figure 2 shows the ratio of OSR and EVAR per hospital between 2013-2018. Out of all hospitals, 7 hospitals performed on average less than 20 AAA procedures (EVAR and/or OSR) a year. Four of these hospitals stopped performing elective OSR after 2015. The crude mortality percentages varied from 0-13.9% between hospitals. In figure 3, postoperative mortality is plotted against total hospital volume of OSR between 2013-2018, adjusted for patient characteristics. Case-mix adjusted mortality varied from 0-16% between hospitals, with the majority of hospitals performing within the confidence intervals no hospitals with a significantly higher postoperative mortality than the national mean of 5.0%. Fourteen hospitals had a significantly lower postoperative mortality than the national

Table 3. Postoperative mortality after elective OSR stratified by subgroups of patients.

Dead	Male (n=2505) 4.5% (n=113)							Female (n=595) 7.3% (n=43)							p = 0.006
Dead	Age < 75 years (n=1706) 2.9% (n=50)			Age 75 years and older (n=799) 7.9% (n=63)			p = 0.000	Age < 75 years (n=361) 5.8% (n=21)			Age 75 years and older (n=234) 9.4% (n=22)			p = 0.099	
Dead	No pulmonary comorbidity (n=1330) 2.3% (n=31)	Pulmonary comorbidity (n=376) 5.1% (n=19)	p = 0.006	No pulmonary comorbidity (n=581) 6.7% (n=39)	Pulmonary comorbidity (n=218) 11.0% (n=24)	p = 0.045		No pulmonary comorbidity (n=249) 4.4% (n=11)	Pulmonary comorbidity (n=112) 8.9% (n=10)	p = 0.090	No pulmonary comorbidity (n=173) 8.1% (n=14)	Pulmonary comorbidity (n=61) 13.1% (n=8)	p = 0.248		

Figure 1. Volume of elective OSR procedures per hospital in 2013-2018

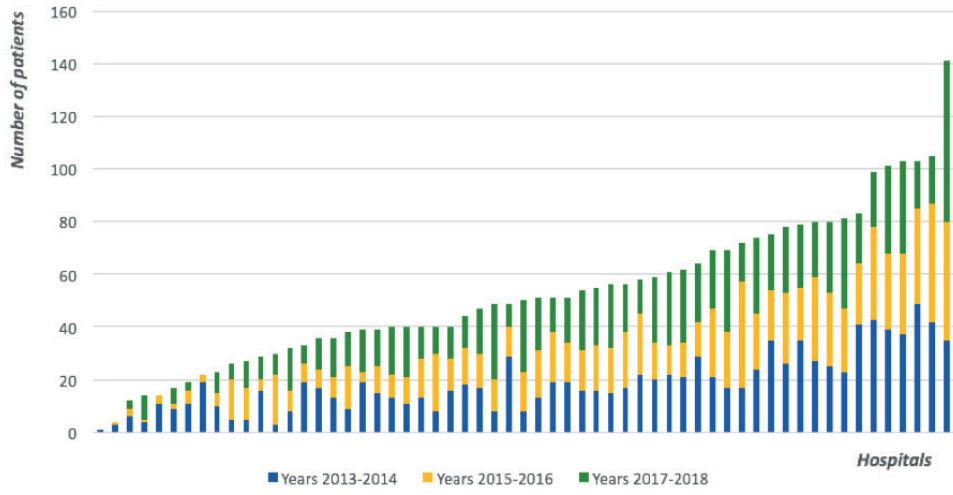
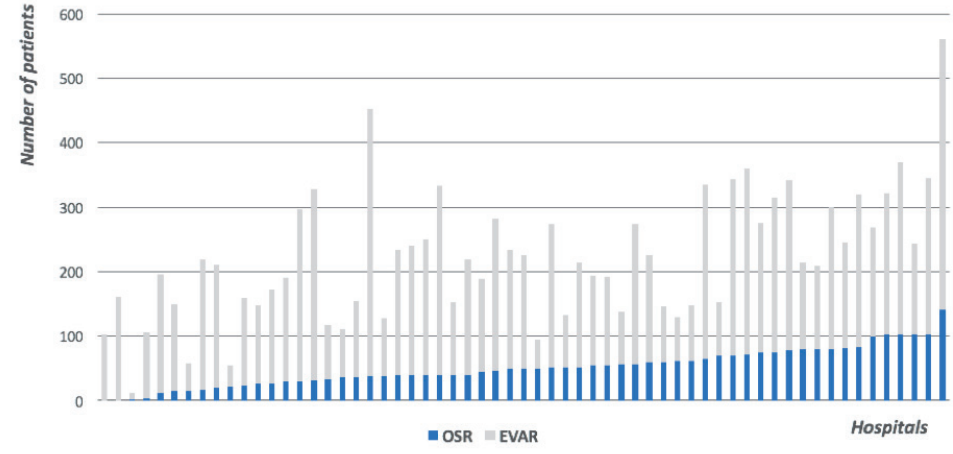


Figure 2. Ratio of elective OSR and EVAR per hospital between 2013-2018



mean, of which 6 hospitals had a total case load of less than 20 procedures in 6 years and a corresponding mortality of 0% and should therefore be left outside consideration. Using a generalized linear mixed model adjusting for sex, age, pulmonary state, preoperative hemoglobin and preoperative creatinine, we found no association between annual hospital volume and postoperative mortality (table 4).

Figure 3. Relation between hospital volume of OSR and case-mix adjusted postoperative mortality

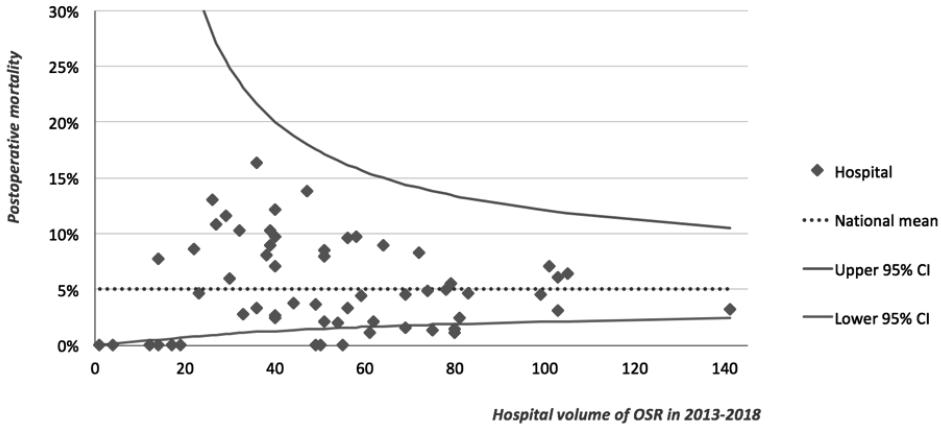


Table 4. The association between hospital volume of OSR per year and postoperative mortality.

Random effects	Variance	SD		
(intercept)	0.09895	0.3146		
Fixed effects	Estimate	SE	Z-value	P
(intercept)	-3.317	0.230	-14.397	<0.001
Volume	-0.009	0.015	-0.589	0.556
Age	0.066	0.013	4.952	<0.001
Gender				
Male	Ref.			
Female	0.439	0.200	2.198	0.028
Pulmonary state				
No dyspnea	Ref.			
Mild dyspnea	0.602	0.186	3.234	0.001
Severe Dyspnea	0.722	0.396	1.823	0.068
Preoperative hemoglobin	-0.191	0.090	-2.131	0.033
Preoperative creatinine	0.004	0.002	2.563	0.010

DISCUSSION

In the Netherlands, elective OSR was performed with a postoperative mortality of 5% (n=156) in 6 consecutive years. Patients with postoperative mortality were more often female, on average 3.6 years older, and had more cardiac and pulmonary co-morbidities, as well as preoperative elevated creatinine and decreased hemoglobin levels. Female sex, increasing age, pulmonary co-morbidities, preoperative hemoglobin and preoperative creatinine levels were independently associated with postoperative mortality after elective OSR. Elective OSR was performed in 59 hospitals in the Netherlands, in which the total elective OSR volume varied from 1 to 141. Although the adjusted postoperative mortality ranged from

0-16%, no hospitals had a significantly higher postoperative mortality. In a generalized linear mixed regression model, annual hospital volume of elective OSR was not associated with postoperative mortality after elective OSR in the current Dutch population.

Studies dated from the pre-EVAR era reported a postoperative mortality after elective OSR varying from 2.7-6.1%.[15-18] Since the introduction of EVAR, the use of elective OSR has decreased over time and as reported in this study is now only performed 22% of elective patients. In the current Dutch population, this group will predominantly consist of AAA patients not suitable for EVAR. With the emerge of national quality registries, nowadays trends in the use of surgical techniques and their outcomes can be monitored on a national level.[2,19] The current postoperative mortality after elective OSR is comparable to the reported mortality prior to the introduction of EVAR. This is remarkable considering that much progress has been made in surgical and perioperative care in the past 25 years. On the other hand, nowadays the OSR group consist of more patients with complex juxta and supra renal aneurysms. However, today one may question whether 5% is an acceptable mortality risk for an elective procedure.

Aiming to further reduce postoperative mortality after elective OSR, a possible solution could be found in the improvement of the selection of patients. Already in the pre-EVAR era, several models were formed, in which patient characteristics were used to predict postoperative mortality after (elective) open AAA surgery.[14,20-22] The widely-used Glasgow Aneurysm Score contained only a small selection of variables where other models, such as the POSSUM and Leiden score, were more extensive. Patient characteristics corresponding in these models were: age, myocardial disease, and renal failure. Notable is that the Leiden score was the only one that included sex as a predictive factor. As we hypothesized that the introduction of EVAR made patients undergoing elective OSR a select group of patients, we were interested in the factors associated with postoperative mortality in this current population. In addition to age and renal failure, sex, pulmonary comorbidities and preoperative hemoglobin were found to be associated with postoperative mortality.

The declining use of elective OSR and the absence of a minimum volume standard specific for elective OSR, has led to the situation in the Netherlands that 59 hospitals perform elective OSR with an annual volume that ranges between 1-33 procedures between hospitals. Since previous studies have demonstrated a relationship between hospital volume and outcomes, hospital volume seemed a logical variable to investigate for quality improvement within the DSAA.[23,24] Additionally, a minimum standard of 10 elective OSR per hospital per year is added in the latest SVS guideline.[10] In contrast to the previous studies, we found no statistically significant association between hospital volume of OSR per year and postoperative mortality in all (n = 3100) Dutch elective OSR patients operated in 59 hospitals over a 6-year period. A possible explanation for this difference is that in some previous studies

single regression analysis were used, where in our opinion, mixed models would be more appropriate, as it accounts for the unmeasured factors corresponding between patients treated in the same hospital.[25] Additionally, the difference could be explained by the fact that some studies used the total procedural volume of OSR (elective and acute) as the OSR hospital volume, as the performance of acute OSR would contribute to the experience with OSR.[24] We have deliberately chosen to use only the number of elective OSR because we believe hospitals should perform OSR sufficiently in an elective setting to be able to perform OSR in ruptured patients. Furthermore, we have not included the number of EVAR procedure in this analysis, because this is a completely different intervention and the ratio of OSR/EVAR differs greatly between hospitals, as illustrated in figure 2.

The lack of a significant association between volume of OSR and postoperative mortality, could not substantiate a new volume standard for elective OSR for the Netherlands. However, this does not alter the fact that hospital volume is still an important topic of discussion within quality measurement. When a surgical procedure is performed relatively infrequently by a hospital, mortality or the absence of it says little about whether the next patient can be treated safely. A funnel plot might give the impression that all hospitals perform well, namely not significantly different from the national average, but actually we are not really sure. When lowering the mortality standard to an imaginary mortality of 3% (appendix 1), the confidence intervals only shift slightly downwards, so that fewer hospitals perform significantly better. However, the differences in outcome between hospitals do not change.

In the search for a suitable volume standard for elective OSR, we additionally turned the question around. Instead of looking at what volume is needed for better postoperative outcomes, we looked for the volume needed to show that hospitals are doing well enough and to be able to detect significant worsening of outcomes. As an example, appendix 2. shows the number of cases (per hospital) needed on the x-axis versus the power of detecting a difference in mortality, in which the lines represent the alternative mortality (6%, 7%, etc.) in a hospital compared to the average national mortality of 5%. The values at which the limits of such a statistical model should be set, remain to be discussed. Though, even with this method, the hospital volumes needed to observe differences in outcome are not feasible in the current practice, not even with more centralization of OSR care. Nevertheless, in a more centralized situation, with higher volume of OSR per hospital, it may be possible that an association between volume and postoperative mortality can be found. Additionally, in a shift towards more centralization of OSR surgery, it may also be conceivable that not all vascular surgeons within a team will still perform OSR, but only by those with sufficient exposure. However, as the DSAA focuses solely on the numbers results of the entire team rather than the individual surgeon, we have no data to support this notion.

CONCLUSION

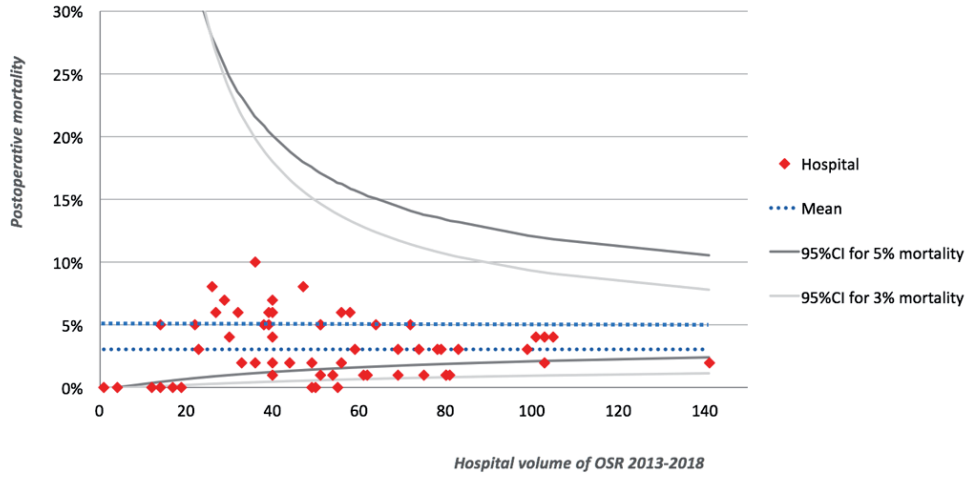
In the Netherlands, elective OSR for AAA has a mortality of 5%. Female sex, increasing age, pulmonary state, preoperative hemoglobin and creatinine were independently associated with postoperative mortality. Annual hospital volume of elective OSR was not associated with postoperative mortality in the current population of the DSAA. Based on this study we cannot substantiate a minimum volume standard for elective OSR.

REFERENCES

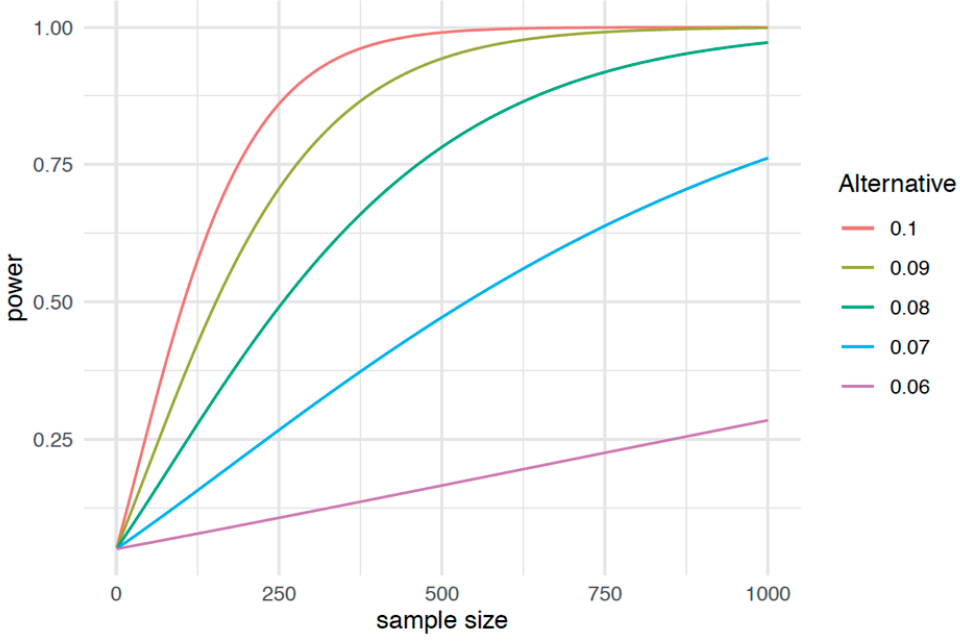
1. Lijftogt N, Vahl AC, Wilschut ED, et al. Adjusted Hospital Outcomes of Abdominal Aortic Aneurysm Surgery Reported in the Dutch Surgical Aneurysm Audit. *Eur J Vasc Endovasc Surg.* 2017;53(4):520-532.
2. http://www.dica.nl/.
3. NVR-VSQIP. https://www.vsqip.org.uk/reports/2017-annual-report/.
4. Trenner M, Kuehnl A, Reutersberg B, Salvermoser M, Eckstein HH. Nationwide analysis of risk factors for in-hospital mortality in patients undergoing abdominal aortic aneurysm repair. *Br J Surg.* 2018;105(4):379-387.
5. Budtz-Lilly J, Venermo M, Debus S, 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.
6. Swedvasc. http://www.ucr.uu.se/swedvasc/arsrapporter/swedvasc-2018/viewdocument.
7. Phillips P, Poku E, Essat M, et al. Procedure Volume and the Association with Short-term Mortality Following Abdominal Aortic Aneurysm Repair in European Populations: A Systematic Review. *Eur J Vasc Endovasc Surg.* 2017;53(1):77-88.
8. Trenner M, Kuehnl A, Salvermoser M, 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. *Eur J Vasc Endovasc Surg.* 2018;55(2):185-194.
9. Eckstein HH, Bruckner T, Heider P, et al. The relationship between volume and outcome following elective open repair of abdominal aortic aneurysms (AAA) in 131 German hospitals. *Eur J Vasc Endovasc Surg.* 2007;34(3):260-266.
10. Chaikof EL DR, Eskandari MK, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg.* 2018;67:p2-77.e72.
11. Moll FL, Powell JT, Fraedrich G, et al. Management of abdominal aortic aneurysms clinical practice guidelines of the European society for vascular surgery. *Eur J Vasc Endovasc Surg.* 2011;41 Suppl 1:S1-S58.
12. Dataverification Dutch Surgical Aneurysm Audit 2015. [PDF]. http://dica.nl/media/660/Eindrapport_dataverificatie_DSAA_2016.pdf, 2016.
13. van der Werf LR, Voeten SC, van Loe CMM, Karthaus EG, Wouters M, Prins HA. Data verification of nationwide clinical quality registries. *BJS Open.* 2019;3(6):857-864.
14. Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. *Br J Surg.* 1991;78(3):355-360.
15. Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med.* 2002;346(19):1437-1444.
16. Bradbury AW, Adam DJ, Makhdoomi KR, et al. A 21-year experience of abdominal aortic aneurysm operations in Edinburgh. *Br J Surg.* 1998;85(5):645-647.
17. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. The UK Small Aneurysm Trial Participants. *Lancet.* 1998;352(9141):1649-1655.
18. Prinssen M, Verhoeven EL, Buth J, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med.* 2004;351(16):1607-1618.
19. DSAA annual report 2017. 2017; http://dica.nl/jaarrapportage-2017/home.
20. Patterson BO, Holt PJ, Hinchliffe R, Loftus IM, Thompson MM. Predicting risk in elective abdominal aortic aneurysm repair: a systematic review of current evidence. *Eur J Vasc Endovasc Surg.* 2008;36(6):637-645.
21. Samy AK, Murray G, MacBain G. Glasgow aneurysm score. *Cardiovasc Surg.* 1994;2(1):41-44.
22. Steyerberg EW, Kievit J, de Mol Van Otterloo JC, van Bockel JH, Eijkemans MJ, Habbema JD. Perioperative mortality of elective abdominal aortic aneurysm surgery. A clinical prediction rule based on literature and individual patient data. *Arch Intern Med.* 1995;155(18):1998-2004.

23. Hicks CW, Canner JK, Arhuidese I, Obeid T, Black JH, 3rd, Malas MB. Comprehensive Assessment of Factors Associated With In-Hospital Mortality After Elective Abdominal Aortic Aneurysm Repair. *JAMA Surg.* 2016;151(9):838-845.
24. Zettervall SL, Schermerhorn ML, Soden PA, et al. The effect of surgeon and hospital volume on mortality after open and endovascular repair of abdominal aortic aneurysms. *J Vasc Surg.* 2017;65(3):626-634.
25. Kim W, Wolff S, Ho V. Measuring the Volume-Outcome Relation for Complex Hospital Surgery. *Appl Health Econ Health Policy.* 2016;14(4):453-464.

Appendix 1. Relation between hospital volume of OSR and case-mix adjusted postoperative mortality compared to the national mean of 3% and 5% mortality.



Appendix 2. Number of cases needed per hospital to detect alternative mortality rates compared to the current national mean of 5%



CHAPTER 5

Patients with a Ruptured Abdominal Aortic Aneurysm are Better Informed in Hospitals with an 'EVAR-preferred' Strategy: An Instrumental Variable Analysis of the DSAA

E.G. Karthaus, N. Lijftogt, A.C. Vahl, E.M.van der Willik, S. Amodio, E.W. van Zwet, J.F. Hamming

Annals of Vascular Surgery 2020

ABSTRACT

Background and objective

While several observational studies suggested a lower postoperative mortality after minimal invasive endovascular aneurysm repair (EVAR) in RAAA-patients compared to conventional open surgical repair (OSR), landmark RCTs have not been able to prove the superiority of EVAR over OSR. RCTs contain a selected, homogeneous population, influencing external validity. Observational studies are biased and adjustment of confounders can be incomplete. Instrumental variable (IV)-analysis (pseudo-randomization) may help to answer the question if ruptured abdominal aortic aneurysm (RAAA) patients have lower postoperative mortality when undergoing EVAR compared to OSR.

Methods

Observational study including all RAAA-patients, registered in the Dutch Surgical Aneurysm Audit between 2013-2017. The risk difference (RD) in postoperative mortality (30-days/in-hospital) between patients undergoing EVAR and OSR was estimated, in which adjustment for confounding was performed in 3 ways: linear model adjusted for observed confounders, propensity-score-model (multivariable-logistic-regression analysis) and IV-analysis (two-stage-least-square regression), adjusting for observed and unobserved confounders, with the variation in percentage of EVAR per hospital as the IV-instrument.

Results

2419 RAAA-patients (1489 OSR, 930 EVAR) were included. Unadjusted postoperative mortality was 34.9% after OSR and 22.6% after EVAR (RD 12.3%, 95%CI 8.5-16%). The RD, adjusted for observed confounders using linear regression analysis and propensity score analysis was respectively 12.3% (95%CI 9.6-16.7%) and 13.2% (95%CI 9.3-17.1%) in favor of EVAR. Using IV-analysis, adjusting for observed and unobserved confounders, RD was 8.9% (95%CI -1.1-18.9%) in favor of EVAR.

Conclusion

Adjusting for observed confounders, RAAA-patients undergoing EVAR had a significant better survival compared to OSR in a consecutive large cohort. Adjustment for unobserved confounders resulted in a clinical relevant RD. An 'EVAR-preference-strategy' in RAAA-patients could result in lower postoperative mortality.

INTRODUCTION

In the elective treatment of abdominal aortic aneurysms (AAA), minimal invasive endovascular aneurysm repair (EVAR) has proven to be superior to conventional open surgical repair (OSR) in the short/mid-term, with a lower postoperative mortality and morbidity.[1] Several randomized controlled trials (RCTs) failed however to establish superiority of EVAR in patients with a life-threatening ruptured abdominal aortic aneurysm (RAAA), and no significant differences in immediate postoperative survival were found.[2-5] A drawback of these trials is that they might contain only a selected population of RAAA patients, which hampers the external validity (generalizability) of the results.[6] Additionally, randomization methods were different between these trials and some were underpowered, affecting the internal validity.[6] Large observational studies, adjusting for known confounders, suggested a lower postoperative mortality in RAAA patients treated with EVAR.[7-9]. However, observational studies suffer from indication bias by important prognostic baseline differences between patients and the adjustment of confounders can be incomplete as clinical and social interactions in the diagnostic-treatment pathway are often not measured.[10] For example, anatomic characteristics of the aneurysm or the surgeon's preference for one or the other surgical procedure may influence the choice of treatment in RAAA patients. Using large databases with consecutive patients and different treatment preferences of hospitals, treatments, as applied in daily practice, can be compared with pseudo-randomization techniques. Instrumental variable (IV) analysis is such a technique, as it is developed to control the unobserved and/or unmeasured bias between different treatment groups and tries to find a randomized experiment embedded in an observational study, to subsequently estimate the difference in treatment effect.[11]

The aim of this study was to investigate if patients with a RAAA registered in the nationwide and compulsory Dutch Surgical Aneurysm Audit (DSAA) have a better postoperative survival when treated with EVAR compared to OSR, correcting for observed confounders with standard statistical methods and unobserved confounders with IV analysis (pseudo-randomization). Secondly, the postoperative mortality between hospitals with a high and low preference for EVAR were compared.

METHODS

Study design

This is a prospective observational study, which examines if patients with a RAAA have a lower postoperative mortality after EVAR compared to OSR, adjusting for observed and unobserved confounders.

Data source, participants and setting

The dataset was retrieved from the Dutch Surgical Aneurysm Audit (DSAA). This nationwide and compulsory audit started in 2013 and registers all patients, including patient and treatment characteristics, with an aortic aneurysm and/or dissection undergoing surgical treatment in the Netherlands. We included all patients with a primary RAAA registered in the DSAA between January 2013 and December 2017. All patients with a thoracic aortic aneurysm/dissection, undefined aneurysm/dissection and all patients with a secondary reintervention of a previous aortic aneurysm repair were excluded.
Verification of the DSAA data was carried out in 2015 by a third trusted party, through a random sample of hospitals.[12,13]

Primary outcome

The primary outcome of this study was postoperative mortality, which was defined as mortality within 30 days after surgery or during admission (30-days/in-hospital).

Statistical analysis

Patients were divided in two groups, EVAR or OSR, based on 'start-of-treatment'. Patient characteristics and hospital related factors were compared between the groups, using T-tests and chi-square tests.
Crude postoperative mortality rates between patients treated with EVAR and OSR were compared, using a linear regression model. When considering a binary outcome, it is standard practice to use logistic regression. The effect of EVAR versus OSR will then be estimated as a (log) odds ratio. As we prefer to estimate the effect as a risk difference (RD), we used linear regression.
Subsequently, we used 3 different methods to adjust for confounding when estimating the RD: a linear model adjusted for confounders, a propensity score, i.e. the probability of getting a certain treatment, adjusted for observed confounders, and an IV analysis adjusted for observed and unobserved confounders.

Adjusted linear regression analysis

In order to correct for observed confounders we used a linear regression model to compare adjusted mortality rates between patients treated with EVAR and OSR. Patient characteristics based on V(p)-POSSUM variables, year of surgery and hospital volume of RAAA patients, were entered as co-variables in this model.[14,15]

Propensity score analysis

The propensity score (PS) analysis was carried out in two successive steps. In the first step, a multivariable logistic regression analysis (ENTER model with a p-value at 0.05) for the 'choice of treatment' was performed. The same patient and hospitals characteristics as used in the adjusted linear regression analysis were entered as co-variables in this model.

In the second step a RD was estimated, using a multivariable linear regression analysis for the primary outcome 'postoperative mortality', adjusted for the PS obtained in step 1 and the choice of treatment as co-variables.

Instrumental variable analysis

First, we divided all hospitals in 2 groups with the median %EVAR per hospital as a cut-off point: those with a low %EVAR in RAAA patients (0-37% EVAR) and those with a high %EVAR (38-100% EVAR). We demonstrate the distribution of measured possible confounders between these two groups.

An IV-analysis can be used to estimate the effect of a treatment in observational data, corrected for unobserved confounders. The IV is a factor that highly influences the choice of treatment, but has no independent influence on patient outcome. The IV is thus not related to the prognosis of the patient. An IV-analysis behaves as a pseudo-randomization, in which patients are weighed based on the probability of getting a certain treatment. When using an IV-analysis, one does not compare individual patients with different treatments, but one compares the outcomes of patients with a different chance of getting a certain treatment. The methods of IV-analysis have also been described in detail elsewhere.[11]

When using an IV-analysis to compare postoperative mortality after OSR and EVAR in patients with a RAAA, we had to make two assumptions:

1. There is no association between patient characteristics and the hospital where patients are treated. In the Netherlands, patients with a RAAA are admitted to nearest hospital performing acute AAA surgery.
2. As the Netherlands has a homogeneous care landscape with an overall high quality standard, quality of care is comparable between hospitals performing acute AAA surgery

Based on these assumptions the following analysis was performed. The percentage of RAAA patients treated with EVAR per hospital (%EVAR) (i.e. treatment preference of the hospital), was chosen as the IV. The strength of the IV was tested with a partial F statistic. Subsequently the IV-analysis was performed with a Two-Stage least square (2SLS) model. The co-variables used in this model were the same as in the first step of the PS-analysis. Outcome was reported in a RD between EVAR and OSR. Finally, the IV-model itself was tested with a 'test for weak instruments' and a 'Wu-Hausman test'.

All statistical analyses were performed using R statistical software (version 3.4.0). When data were missing for continues variables used in the regression analyzes, the mean was imputed. Data were most frequently missing for preoperative heart rate (13%) and systolic blood pressure (9.0%).

RESULTS

Participants and descriptive analysis

We identified 2660 RAAA patients operated between January 2013 and December 2017. All patients with a thoracic aneurysm (76, 2.8%), undefined aneurysm (45, 1.7%), revision of a previous aortic aneurysm repair (80, 3.0%) or incomplete data (40, 1.5%) were excluded. A total of 2419 patients were included for analyses, of which 1489 (61.6%) were treated with OSR and 930 (38.4%) with EVAR. Twenty-seven (1.1%) of EVAR patients were converted to OSR and remained in the EVAR group for analysis. The EVAR group consisted of 86% males, compared to 84% of males in the OSR group (p=0.075). EVAR patients were significantly older than OSR patients (75.3 SD 8.8 versus 73.6 SD 7.8, p<.001) and had significantly more often a normal Glasgow Coma Scale (GCS) (72% versus 63%, p<.001). Other differences in co-morbidity and clinical presentation are displayed in table 1. Over the years 2013-2017 there was an increase in the use EVAR from 29% to 46%.

Outcome data and main results

The unadjusted postoperative mortality after OSR was 34.9% (n=519) and 22.6% (n=210) after EVAR. Using an unadjusted linear regression, the RD in postoperative mortality after OSR and EVAR was 12.3%, with a 95% confidence interval (CI) of 8.5-16%.

Case-mix adjusted linear regression analysis

The mortality difference, adjusted for measured confounders was 12.3% (95%CI 9.6-16.7%), in favor of RAAA patients treated with EVAR (table 2.).

Propensity score analysis

Step 1**:** Patient characteristics of RAAA patients associated with receiving EVAR were increased age (odds ratio (OR) 1.03, 95%CI 1.02-1.04), leukocytes between $10.0x10^9$/L-$14.9x10^9$/L (OR 1.26, 95%CI 1.00-1.59) or more than $20x10^9$/L (OR 1.55, 95%CI 1.23-2.14) and current malignancy (OR 1.67, 95%CI 1.02-2.74) (table 3a). Patients with female gender (OR 0.64, 95%CI 0.49-0.83), GCS of 9-11 (OR 0.59, 95%CI 0.35-0.98), GCS <9 (OR 0.34, 95%CI 0.21-0.54) or an unknown GCS (OR 0.67, 95%CI 0.50-0.91), increased aneurysm diameter (OR 0.99, 95%CI 0.98-0.99), systolic blood pressure of <80mmHg (OR 0.73, 95%CI 0.55-0.96), and/or unknown pulmonary status (OR 0.75, 95%CI 0.59-0.97) were less likely to receive EVAR. Additionally, patients operated in hospitals with a higher volume and patients operated in later years of the study were significantly more likely to receive EVAR. Step 2: In RAAA patients the RD, adjusted for the probability of treatment with EVAR (PS for EVAR calculated in step 1), was 13.2% (95%CI 9.3-17.1%) in favor of treatment with EVAR (table 3b).

Table 1. Patient characteristics per surgical treatment

	EVAR		OSR		
	N	%	N	%	
Number of patients	930		1489		
Age (mean, years)	75.3 SD 8.8		73.6 SD 7.8		.000
Sex					.075
Male	802	86%	1244	84%	
Female	128	14%	245	17%	
Year of surgery					.000
2013	122	13%	301	13%	
2014	198	21%	325	21%	
2015	192	21%	321	21%	
2016	205	22%	293	22%	
2017	213	23%	249	17%	
Cardiac state					.039
No abnormalities	385	41%	659	44%	
Peripheral edema, cardiomegaly	68	7.3%	82	5.5%	
Raised CVP, use of coumarin, borderline cardiomyopathy	15	1.5%	18	1.2%	
Medication for hypertension, angina pectoris, diuretics or digoxin	324	35%	465	31%	
Unknown	138	15%	265	18%	
Pulmonary state					.002
No dyspnea	580	62%	904	61%	
Dyspnea	141	15%	205	14%	
Severe Dyspnea	48	5.2%	45	3.0%	
Unknown	161	17%	335	23%	
Malignancy					.002
None	816	88%	1367	92%	
Current	40	4.3%	33	2.2%	
History of malignancy	74	8.0%	89	6.0%	
Last pre-operative ECG					.001
No abnormalities	274	30%	421	28%	
Atrial fibrillation	59	6.3%	68	4.6%	
Ischemia	33	3.5%	43	2.9%	
Other abnormalities	222	24%	292	20%	
Unknown/No ECG performed	342	37%	665	45%	
Diameter (mean, mm)	76 SD 16.0		80 SD 16.6		.000
Hart rate (mean, BPM)	87 SD 21		87 SD 22		.852
Systolic blood pressure (mean, mmHg)	112 SD 33		109 SD 34		.007
Glasgow Coma Scale					.000
GCS 15	673	72%	931	63%	
GCS 12-14	127	14%	206	14%	
GCS 9-11	24	2.6%	56	3.8%	
GCS <9	26	2.6%	114	7.7%	
Unknown	80	9.3%	182	12%	
Preoperative laboratory results					
Hemoglobin (mmol/L)	7.2 SD 1.4		7.3 SD 1.4		.613
Leukocytes (10^9/L)	14.2 SD 5.5		13.6 SD 5.4		.013
Creatinine (mmol/L)	112 IQR 91-133		111 IQR 88-131.5		.195
Sodium					.077

Table 1 continued

	EVAR		OSR		
	N	%	N	%	
Normal sodium	725	78%	1205	81%	
Hypo/hypernatremia	205	22%	284	19%	
Potassium					.493
Normal potassium	763	82%	1205	81%	
Hypo/hyperpotassemia	167	18%	284	19%	

Table 2. Linear regression analysis for postoperative mortality in RAAA patients

	Estimate	SE	p-value
Procedure			
OSR			
EVAR	-0.131	0.018	<0.001
Gender			
Male			
Female	0.025	0.025	0.313
Age			
Age	0.010	0.001	<0.001
Glasgow Coma Scale			
GCS 15			
GCS 12-14	0.089	0.026	0.001
GCS 9-11	0.232	0.049	<0.001
GCS <9	0.190	0.038	<0.001
GCS unknown	0.168	0.029	<0.001
Year of surgery			
2013			
2014	-0.068	0.028	0.013
2015	0.000	0.028	0.990
2016	0.010	0.028	0.724
2017	0.042	0.029	0.148
Volume of ruptured patients in hospital of treatment			
<25			
25-40	-0.005	0.036	0.881
40-55	0.016	0.027	0.546
55-70	-0.021	0.031	0.477
>70	-0.975	0.001	0.014
Aneurysm diameter			
Diameter	-0.001	0.001	0.061
Preoperative systolic blood pressure			
110-139			
>140	-0.035	0.025	0.156
80-109	0.025	0.022	0.258
<80	0.078	0.027	0.004
Preoperative heart rate			
70-79			
80-99	0.010	0.027	0.713
>100	0.013	0.029	0.655
<70	-0.016	0.030	0.596

Table 2 continued

	Estimate	SE	p-value
Creatinine			
<90			
90-109	0.007	0.025	0.790
110-139	0.083	0.024	0.001
>140	0.101	0.028	<0.001
Hemoglobin			
>8.50			
7.5-8.49	-0.038	0.026	0.148
6.0-7.49	-0.022	0.025	0.386
<6	0.026	0.031	0.404
Leukocytes			
<10.0			
10.0-14.9	-0.001	0.022	0.978
15.0-19.9	-0.024	0.027	0.375
>20.0	-0.014	0.032	0.673
Sodium			
Normal sodium			
Hyponatremia	0.023	0.022	0.301
Hypernatremia	0.231	0.071	0.001
Potassium			
Normal potassium			
Hypokalemia	-0.019	0.027	0.489
Hyperkalemia	0.027	0.034	0.418
Malignancy			
None			
Current Malignancy	0.095	0.050	0.059
History of malignancy, curatively treated	0.065	0.034	0.058
Preoperative ECG			
No abnormalities			
Atrial fibrillation (60-90 bpm)	0.084	0.042	0.045
Ischemia (ST depression >2mm at rest)	0.209	0.051	<0.001
Other abnormalities	0.029	0.025	0.252
No preoperative ECG performed	0.080	0.022	<0.001
Cardiac status			
None			
Peripheral edema, cardiomegaly	0.069	0.038	0.070
Raised CVP, use of coumarin, borderline cardiomyopathy	0.050	0.075	0.502
Medication for hypertension, angina pectoris, diuretics or digoxin	0.058	0.020	0.004
Unknown	0.081	0.027	0.003
Pulmonary status			
No dyspnea			
Dyspnea	0.050	0.026	0.038
Severe dyspnea	0.198	0.046	<0.001
Unknown	0.061	0.024	0.013

Table 3a. Propensity score for treatment with EVAR

	Odds	95% CI
Gender		
Male	Ref	
Female	0.64	0.49-0.83
Age		
Age	1.03	1.02-1.04
Glasgow Coma Scale		
GCS 15	Ref.	
GCS 12-14	0.83	0.64-1.08
GCS 9-11	0.59	0.35-0.98
GCS <9	0.34	0.21-0.54
GCS unknown	0.67	0.50-0.91
Year of surgery		
2013	Ref.	
2014	1.48	1.11-1.97
2015	1.45	1.09-1.95
2016	1.61	1.20-2.15
2017	2.15	1.60-2.90
Volume of ruptured patients in hospital of treatment		
<25	Ref.	
25-40	1.26	0.86-1.84
40-55	1.64	1.23-2.18
55-70	1.81	1.32-2.50
>70	1.48	1.08-2.04
Aneurysm diameter		
Diameter	0.99	0.98-0.99
Preoperative systolic blood pressure		
110-139	Ref.	
>140	0.94	0.73-1.20
80-109	0.93	0.75-1.15
<80	0.73	0.55-0.96
Preoperative heart rate		
80-99	Ref.	
>100	0.89	0.68-1.18
70-79	0.99	0.74-1.32
<70	0.98	0.72-1.32
Creatinine		
<90	Ref.	
90-109	1.08	0.84-1.40
110-139	1.13	0.89-1.44
>140	1.12	0.85-1.48
Hemoglobin		
>8.50	Ref.	
7.5-8.49	0.89	0.70-1.26
6.0-7.49	0.88	0.61-1.10
<6	1.05	0.64-1.30
Leukocytes		
<10.0	Ref.	
10.0-14.9	1.26	1.00-1.59

Table 3a continued

	Odds	95% CI
15.0-19.9	1.08	0.82-1.41
>20.0	1.55	1.23-2.14
Sodium		
Normal sodium	Ref.	
Hypo/hypernatremia	1.14	0.94-1.39
Potassium		
Normal potassium	Ref.	
Hypo/hyperkalemia	0.99	0.85-1.15
Malignancy		
None	Ref.	
Current Malignancy	1.67	1.02-2.74
History of malignancy, curatively treated	1.15	0.82-1.61
Preoperative ECG		
No abnormalities	Ref.	
Atrial fibrillation (60-90 bpm)	1.21	0.80-1.83
Ischemia (ST depression >2mm at rest)	1.23	0.74-2.05
Other abnormalities	1.05	0.82-1.34
No preoperative ECG performed	0.86	0.69-1.07
Cardiac status		
None	Ref.	
Peripheral edema, cardiomegaly	1.24	0.85-1.82
Raised CVP, use of coumarin, borderline cardiomyopathy	1.22	0.58-2.57
Medication for hypertension, angina pectoris, diuretics or digoxin	1.07	0.87-1.31
Unknown	1.11	0.84-1.47
Pulmonary status		
No dyspnea	Ref.	
Dyspnea	0.86	0.67-1.11
Severe dyspnea	1.51	0.96-2.37
Unknown	0.75	0.59-0.97

Table 3b. Comparison of mortality in patient treated with OSR and EVAR, corrected for the propensity score

	Beta	Lower 95% CI	Upper 95% CI
Surgical Procedure			
OSR	Ref.		
EVAR	-0.13	-0.17	-0.09
Propensity score for treatment with EVAR	-0.11	-0.03	0.24

Instrumental variable analysis

The percentage of treatment with EVAR in RAAA patients ranged from 0-100% (median: 37% EVAR) between 61 hospitals. 1220 patients were operated in hospitals with a low %EVAR and 1199 patients in hospitals with a high %EVAR. The mean %EVAR in hospitals with a low %EVAR was 25.2% (0-37%) compared to mean of 52.0% (38-100%) in hospitals with a high %EVAR in RAAA patients (p<.001).

Table 4 shows the distribution of observed possible confounders between the two groups

of hospitals. The crude mortality in hospitals with a low %EVAR was 31.1% (380/1220) versus 29.1% (349/1199) in hospitals with a high %EVAR: RD 2.0% (95%CI -1.6–5.7%). To adjust also for unobserved confounders, we used the %EVAR per hospital as an IV (partial F statistic >10). The estimated RD in RAAA patients treated with EVAR, using an IV-analysis (2SLS model), was 8.9% (95%CI -1.1-18.9%) compared to RAAA patients treated with OSR.

Table 4. Distribution of measured confounders between hospitals with a low and high percentage of treatment with EVAR, divided by the median of 37% as cut-off point

	Hospitals with low % EVAR (0-37%)		Hospitals with high % EVAR (38-100%)		
	N = 1220	%	N = 1199	%	P
Surgical procedure					.000
OSR	913	75%	576	48%	
EVAR	307	25%	623	52%	
Year of surgery					.143
2013	218	18%	205	17%	
2014	259	21%	264	22%	
2015	277	23%	236	20%	
2016	254	21%	244	20%	
2017	212	17%	250	21%	
Volume of ruptured patients in hospital of treatment					.000
<25	192	16%	147	12%	
25-40	124	10%	100	8.3%	
40-55	518	43%	426	36%	
55-70	124	10%	301	25%	
>70	262	22%	225	19%	
Gender					.375
Male	1024	84%	1022	85%	
Female	196	16%	177	15%	
Age					.466
Age	74.1 SD 7.9		74.4 SD 8.6		
Pulmonary status					.140
No dyspnea	743	61%	741	62%	
Dyspnea	168	14%	178	15%	
Severe dyspnea	40	3.3%	53	4.4%	
Unknown	269	22%	227	19%	
Cardiac status					.001
None	520	43%	524	44%	
Peripheral edema, cardiomegaly	62	5.1%	88	7.3%	
Raised CVP, use of coumarin, borderline cardiomyopathy	16	1.3%	17	1.4%	
Medication for hypertension, angina pectoris, diuretics or digoxin	384	32%	405	34%	
Unknown	238	20%	165	14%	
Preoperative ECG					.000
No abnormalities	341	28%	354	30%	
Atrial fibrillation (60-90 bpm)	58	4.8%	69	5.8%	
Ischemia (ST depression >2mm at rest)	34	2.8%	42	3.5%	

Table 4 continued

	Hospitals with low % EVAR (0-37%)		**Hospitals with high % EVAR (38-100%)**		
	N = 1220	**%**	**N = 1199**	**%**	**P**
Other abnormalities	224	18%	290	24%	
No preoperative ECG performed	563	46%	444	37%	
Malignancy					.477
None	1108	91%	1075	90%	
Current Malignancy	32	2.6%	41	3.4%	
History of malignancy, curatively treated	80	6.6%	83	6.9%	
Aneurysm diameter (mm)					.253
Diameter	78,7 SD 16,3		78,0 SD 16,4		
Glasgow Coma Scale					.157
GCS 15	789	65%	806	67%	
GCS 12-14	158	13%	175	15%	
GCS 9-11	39	3.2%	41	3.4%	
GCS <9	80	6.6%	60	5.0%	
GCS unknown	145	12%	117	9.8%	
Preoperative systolic blood pressure (mmHg)					.253
110-139	396	33%	387	32%	
>140	260	21%	225	19%	
80-109	385	32%	383	32%	
<80	179	15%	204	17%	
Preoperative heart rate (BPM)					.751
70-79	158	13%	165	14%	
80-99	498	41%	466	39%	
>=100	327	27%	336	28%	
<70	327	19%	232	19%	
Hemoglobin (mmol/L)					.541
>8.50	240	20%	215	18%	
7.5-8.49	310	25%	328	27%	
6.0-7.49	469	38%	450	38%	
<6	201	17%	206	17%	
Leukocytes (10^9/L)					.955
<10.0	273	22%	259	22%	
10.0-14.9	561	46%	558	47%	
15.0-19.9	254	21%	247	21%	
>20.0	132	11%	135	11%	
Creatinine (mmol/L)					.359
<90	306	25%	305	25%	
90-109	280	23%	256	21%	
110-139	401	33%	377	31%	
>140	233	19%	261	22%	
Sodium					.894
Normal sodium	969	79%	961	80%	
Low sodium	233	19%	220	18%	
High sodium	18	1.5%	18	1.5%	
Potassium					.347
Normal potassium	983	81%	985	82%	
Low potassium	150	12%	125	10%	
High potassium	87	7.1%	89	7.4%	

Finally, the test for weak instrument was not rejected, which suggests that the %EVAR per hospital is not a weak instrument. The Wu-Hausman test was rejected, from which we can conclude that the IV-analysis can be used additional to a standard linear regression.

DISCUSSION

Between 2013-2017, 2419 patients underwent RAAA surgery in the Netherlands, of which 62% was treated with OSR and 38% with EVAR. Patients were treated in 61 hospitals, and percentage of treatment with EVAR varied from 0-100%. The crude postoperative mortality after OSR was 34.9% and 22.6% after EVAR. With standard linear regression analysis and PS-analysis adjusting for observed confounders a significant 30 days/in-hospital survival benefit of 12.3% and 13.2% respectively, could been demonstrated for RAAA patients undergoing EVAR, compared to RAAA patients undergoing OSR. Using IV-analysis (pseudo-randomization) to adjust for observed and unobserved confounders, a postoperative survival benefit of approximately 8.9% was seen in EVAR patients. Additionally, patients operated in hospitals with a high %EVAR in RAAA patients had a 2.0% lower crude postoperative mortality compared to patients operated in hospitals with a low %EVAR in RAAA patients.

The landmark trials evaluating treatment strategies in RAAA patients could not show a significant survival benefit after treatment with EVAR compared OSR.[2-5] Respectively for the AJAX, ECAR and IMPROVE trial, mortality differences of 4.0% (OSR 25% vs EVAR 21%, p=0.66), 6.0% (OSR 25% vs EVAR 18%, p=ns), and 2.0% (OSR 37.4% vs EVAR 35.4%, p=0.62) were found. The inclusion of patients and randomization methods turned out to be obstacles in these trials. The AJAX and ECAR trial only included RAAA patients suitable for both surgical techniques, which led to the exclusion of respectively 61% and 80% of all presented RAAA patients.[2-5] Also, the inclusion seemed to be rather conservative. The IMPROVE trial, on the other hand, included all RAAA patients and randomized patients by treatment strategy, which led to many cross-overs especially from the EVAR to OSR group.[3] Some observational studies, using standard statistical methods, comparing mortality between both techniques in RAAA patients, demonstrated significant survival benefits after treatment EVAR, varying from 6% to 33%.[7-9,16,17] These results are in line with the 12.3% adjusted mortality difference in our study. However, other observational studies did not establish a significant mortality difference between OSR and EVAR.[18-20] The results of observational studies can be biased due to missing or incomplete adjustment for confounding. PS-methods are previously used to control for the selection bias in RAAA patients, which confirmed a postoperative survival benefit for RAAA patients treated with EVAR.[21,22] Gunnarsson et al. suggested that besides differences in baseline characteristics, the primary treatment strategy of a hospital in RAAA patients could influence the results of the comparison between EVAR

and OSR.[23] However, they found no association with outcome and EVAR preference, but they only used conventional logistic regression analysis adjusting for observed confounders. IV-methods have long been used in economic studies and are being increasingly used in health studies.[11] In studies of various medical specialties, this technique has been used to control for unobserved confounders, such as treatment preference of a physician, when comparing treatments.[10,24-27] IV-analysis is particularly useful when large differences in treatment strategy exists. This applies for instance to RAAA care in the Netherlands, where the percentage of treatment with EVAR varied from 0 to 100% between hospitals.

With the use of IV-analysis in RAAA patients undergoing surgical treatment in the Netherlands, a survival benefit of 8.9% in EVAR patients compared to OSR patients was established. However, the CIs were wide (-1.1%-18.9%) resulting in a non-significant RD. Wide CIs are inherent to IV-analysis, as it compares the outcome of patients with a different chance of getting a certain treatment, instead of comparing the outcome of individual patients. In our study, we used the %EVAR per hospital as the IV, by which data was aggregated on the level of the 61 RAAA hospitals in the Netherlands and therefore resulted in a RD with broad CIs. IV-analyzes are particularly useful in larger cohorts, in which more patients with a different chance of receiving a certain treatment (i.e. hospitals) can be identified. International collaboration and the merging of national datasets might be useful for repeating this analysis and could possibly result in a more precise estimation.

The mortality difference resulting from our IV-analysis, represents the difference in mortality between the situation when all patients were treated with EVAR compared to the situation where all patients were treated with OSR. The daily practice is obviously more differentiated, as not all RAAAs are anatomically suitable for treatment with EVAR.

The current mean treatment ratio in RAAA patients in the Dutch population is 37% EVAR versus 63% OSR. The EVAR percentage is relatively high compared to Denmark (8.2%) and Norway (21%), and more comparable to Sweden (30%) and the United Kingdom (41%).[28,29] Moreover, the VASCUNET collaboration reported that 23% of RAAA patients was treated with EVAR in the 11 participating countries between 2010-2013.[30] Over time, the percentage of EVAR increased from 29% in 2013 to 46% in 2017. This numbers gives the impression that experience with EVAR in ruptured AAAs and adaptation of the care system to be able to use EVAR in an acute setting, could play a role in the choice for EVAR in these patients. As OSR is less and less performed in the elective setting, there are concerns that experience with the OSR declines. The survival benefit we found in RAAA-patients treated with EVAR could therefore also be the result of the loss of experience with OSR. However, when comparing mortality rates of OSR in RAAA patients of the DSAA, SWEDVASC and the Cochrane review of the trials, respectively 30%, 34% and 37%, the outcome of OSR did not decline over time.[6,23] Moreover, the lower mortality of EVAR in the DSAA (22%) and SWEDVASC (22%) compared to the trials (34%) indicates a possible improvement of EVAR results in RAAA patients. One can speculate that the trials came to early, where the EVAR technique for RAAA was still in development.

When comparing surgical procedures, it is also important to evaluate long-term survival. A meta-analysis of the three randomized trials showed a non-significant trend to lower mortality in EVAR patients after 1-year follow-up.[31] Additionally, the IMPROVE Trial investigators reported a lower overall mortality in EVAR patients at 3-year follow-up (EVAR 48% vs OSR 56%, hazard ratio 0.92, 95%CI 0.75-1.13) and a comparable overall mortality of approximately 60% at 7-years follow-up.[32] Unfortunately, the DSAA cannot provide information on long-term survival. In the future, this may be possible through a link with other population databases.

As the DSAA only registers patients that received surgical intervention, it does not provide information on the number of patients presented with an RAAA who were denied for surgery or died before surgical intervention could take place. When evaluating the outcomes of RAAA care, it would be useful to have this information, as the decision for surgical intervention can differ between hospitals and might be associated with EVAR preference, or not. Hospitals could potentially influence their outcomes by selecting patients for surgical treatment.
In order to use an IV-analysis, two assumptions were made. When comparing two pharmaceutical treatments you can safely state that the quality of the treatment is equal in all hospitals. When comparing surgical treatments, this is more uncertain, as surgeon's skills affects the quality of the treatment. The broad CIs around the RD, which are previously mentioned and inherent to the use of IV-methods, are another limitation. Randomization remains the golden standard, but has other obstacles in comparing results in RAAA patients. Therefore, the IV-method can be a good alternative for this research question, as it tries to find a randomized experiment embedded in an observational study.

Our findings suggest that an EVAR-first strategy in RAAA patients may improve postoperative survival. An EVAR-team must then be available 24/7. This has substantial implications for the organization of RAAA care. Currently there are 61 hospitals in the Netherlands that perform RAAA surgery and improvement of care necessitates further concentration of RAAA care. A new volume standard of at least 40 interventions (elective and/or acute) yearly is set by our National Healthcare Institute and Inspectorate of Healthcare, which will contribute to concentration of RAAA care with 24/7 availability of an EVAR-team.

CONCLUSION

Using standard statistical methods, the postoperative 30-day/in-hospital survival of RAAA patients undergoing EVAR was approximately 12% lower than in those undergoing OSR in a large consecutive series of unselected patients in the DSAA. Additionally, an IV-analysis showed a clinical relevant mortality difference in favor of EVAR patients. By taking both

results into account, it is plausible to think that a strategy with a preference for EVAR in RAAA patients will result in a decreased postoperative mortality.

REFERENCES

1. Lijftogt N, Vahl AC, Wilschut ED, et al. Adjusted Hospital Outcomes of Abdominal Aortic Aneurysm Surgery Reported in the Dutch Surgical Aneurysm Audit. *Eur J Vasc Endovasc Surg.* 2017;53(4):520-532.
2. Reimerink JJ, Hoornweg LL, Vahl AC, et al. Endovascular repair versus open repair of ruptured abdominal aortic aneurysms: a multicenter randomized controlled trial. *Ann Surg.* 2013;258(2):248-256.
3. Investigators IT, Powell JT, Sweeting MJ, et al. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ.* 2014;348:f7661.
4. Hinchliffe RJ, Bruijstens L, MacSweeney ST, Braithwaite BD. A randomised trial of endovascular and open surgery for ruptured abdominal aortic aneurysm–results of a pilot study and lessons learned for future studies. *Eur J Vasc Endovasc Surg.* 2006;32(5):506-513; discussion 514-505.
5. Desgranges P, Kobeiter H, Katsahian S, et al. Editor's Choice–ECAR (Endovasculaire ou Chirurgie dans les Anevrysmes aorto-iliaques Rompus): A French Randomized Controlled Trial of Endovascular Versus Open Surgical Repair of Ruptured Aorto-iliac Aneurysms. *Eur J Vasc Endovasc Surg.* 2015;50(3):303-310.
6. Badger S, Forster R, Blair PH, Ellis P, Kee F, Harkin DW. Endovascular treatment for ruptured abdominal aortic aneurysm. *Cochrane Database Syst Rev.* 2017;5:CD005261.
7. Giles KA, Hamdan AD, Pomposelli FB, Wyers MC, Dahlberg SE, Schermerhorn ML. Population-based outcomes following endovascular and open repair of ruptured abdominal aortic aneurysms. *J Endovasc Ther.* 2009;16(5):554-564.
8. Giles KA, Pomposelli FB, Hamdan AD, Wyers MC, Schermerhorn ML. Comparison of open and endovascular repair of ruptured abdominal aortic aneurysms from the ACS-NSQIP 2005-07. *J Endovasc Ther.* 2009;16(3):365-372.
9. McPhee J, Eslami MH, Arous EJ, Messina LM, Schanzer A. Endovascular treatment of ruptured abdominal aortic aneurysms in the United States (2001-2006): a significant survival benefit over open repair is independently associated with increased institutional volume. *J Vasc Surg.* 2009;49(4):817-826.
10. Stukel TA, Fisher ES, Wennberg DE, Alter DA, Gottlieb DJ, Vermeulen MJ. Analysis of observational studies in the presence of treatment selection bias: effects of invasive cardiac management on AMI survival using propensity score and instrumental variable methods. *JAMA.* 2007;297(3):278-285.
11. Baiocchi M, Cheng J, Small DS. Instrumental variable methods for causal inference. *Stat Med.* 2014;33(13):2297-2340.
12. Dataverification Dutch Surgical Aneurysm Audit 2015. [PDF]. http://dica.nl/media/660/Eindrapport_dataverificatie_DSAA_2016.pdf, 2016.
13. van der Werf LR, Voeten SC, van Loe CMM, Karthaus EG, Wouters M, Prins HA. Data verification of nationwide clinical quality registries. *BJS Open.* 2019;3(6):857-864.
14. Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. *Br J Surg.* 1991;78(3):355-360.
15. http://www.riskprediction.org.uk/vasc-index.php.
16. Mehta M, Byrne J, Darling RC, 3rd, et al. Endovascular repair of ruptured infrarenal abdominal aortic aneurysm is associated with lower 30-day mortality and better 5-year survival rates than open surgical repair. *J Vasc Surg.* 2013;57(2):368-375.
17. Nedeau AE, Pomposelli FB, Hamdan AD, et al. Endovascular vs open repair for ruptured abdominal aortic aneurysm. *J Vasc Surg.* 2012;56(1):15-20.
18. Ockert S, Schumacher H, Bockler D, Megges I, Allenberg JR. Early and midterm results after open and endovascular repair of ruptured abdominal aortic aneurysms in a comparative analysis. *J Endovasc Ther.* 2007;14(3):324-332.
19. Visser JJ, Bosch JL, Hunink MG, et al. Endovascular repair versus open surgery in patients with ruptured abdominal aortic aneurysms: clinical outcomes with 1-year follow-up. *J Vasc Surg.* 2006;44(6):1148-1155.

20. Saqib N, Park SC, Park T, et al. Endovascular repair of ruptured abdominal aortic aneurysm does not confer survival benefits over open repair. *J Vasc Surg.* 2012;56(3):614-619.
21. Holt PJ, Karthikesalingam A, Poloniecki JD, Hinchliffe RJ, Loftus IM, Thompson MM. Propensity scored analysis of outcomes after ruptured abdominal aortic aneurysm. *Br J Surg.* 2010;97(4):496-503.
22. Edwards ST, Schermerhorn ML, O'Malley AJ, et al. Comparative effectiveness of endovascular versus open repair of ruptured abdominal aortic aneurysm in the Medicare population. *J Vasc Surg.* 2014;59(3):575-582.
23. Gunnarsson K, Wanhainen A, Djavani Gidlund K, Bjorck M, Mani K. Endovascular Versus Open Repair as Primary Strategy for Ruptured Abdominal Aortic Aneurysm: A National Population-based Study. *Eur J Vasc Endovasc Surg.* 2016;51(1):22-28.
24. Johnston SC. Combining ecological and individual variables to reduce confounding by indication: case study—subarachnoid hemorrhage treatment. *J Clin Epidemiol.* 2000;53(12):1236-1241.
25. Sheetz KH, Norton EC, Regenbogen SE, Dimick JB. An Instrumental Variable Analysis Comparing Medicare Expenditures for Laparoscopic vs Open Colectomy. *JAMA Surg.* 2017;152(10):921-929.
26. Tsuchiya A, Yasunaga H, Tsutsumi Y, Matsui H, Fushimi K. Mortality and Morbidity After Hartmann's Procedure Versus Primary Anastomosis Without a Diverting Stoma for Colorectal Perforation: A Nationwide Observational Study. *World J Surg.* 2018;42(3):866-875.
27. Brooke BS, Goodney PP, Kraiss LW, Gottlieb DJ, Samore MH, Finlayson SR. Readmission destination and risk of mortality after major surgery: an observational cohort study. *Lancet.* 2015;386(9996):884-895.
28. NVR-VSQIP. https://www.vsqip.org.uk/reports/2017-annual-report/.
29. Swedvasc. http://www.ucr.uu.se/swedvasc/arsrapporter/swedvasc-2018/viewdocument.
30. Budtz-Lilly J, Bjorck M, Venermo M, et al. The Impact of Centralisation and Endovascular Aneurysm Repair on Treatment of Ruptured Abdominal Aortic Aneurysms Based on International Registries. *Eur J Vasc Endovasc Surg.* 2018.
31. Sweeting MJ, Ulug P, Powell JT, Desgranges P, Balm R, Ruptured Aneurysm T. Ruptured Aneurysm Trials: The Importance of Longer-term Outcomes and Meta-analysis for 1-year Mortality. *Eur J Vasc Endovasc Surg.* 2015;50(3):297-302.
32. Investigators IT. Comparative clinical effectiveness and cost effectiveness of endovascular strategy v open repair for ruptured abdominal aortic aneurysm: three year results of the IMPROVE randomised trial. *BMJ.* 2017;359:j4859.

CHAPTER 6

Textbook Outcome: A Composite Measure for Quality of Elective Aneurysm Surgery

E.G. Karthaus, N. Lijftogt, L.A.D. Busweiler, B.H.P. Elsman, M.W.J.M. Wouters, A.C. Vahl, J.F. Hamming

Annals of Surgery 2017

ABSTRACT

Background and objective

Single quality indicators in vascular surgery are often not distinctive and insufficiently reflect the quality of care. The aim was to investigate a new composite quality measurement, which comprises a desirable outcome for elective aneurysm surgery, called 'Textbook Outcome' (TO).

Methods

All patients undergoing elective abdominal aortic aneurysm (AAA) repair, registered in the Dutch Surgical Aneurysm Audit (DSAA) between 2014-2015 were included. TO was defined as the percentage of patients who had AAA-repair without intraoperative complications, postoperative surgical complications, re-interventions, prolonged hospital stay (endovascular aneurysm repair (EVAR) ≤4 days, open surgical repair (OSR) ≤10 days), re-admissions and postoperative mortality (≤30 days after surgery / at discharge). Case-mix adjusted TO rates were used to compare hospitals and to compare individual hospital results for different procedures.

Results

5170 patients were included, of which 4039 were treated with EVAR and 1131 with OSR. TO was achieved in 71% of EVAR and 53% of OSR. Important obstacles for achieving TO were a prolonged hospital stay, postoperative complications, and re-admissions. Adjusted TO rates varied from 38%-89% (EVAR) and 0%-97% (OSR) between individual hospitals. Hospitals with a high TO for OSR also had a high TO for EVAR, however a high TO for EVAR did not implicate a high TO for OSR.

Conclusion

TO generates additional information to evaluate the overall quality of the care of elective aneurysm surgery, which subsequently can be used by hospitals to improve the quality of their care.

INTRODUCTION

Since 2013, all patients undergoing aneurysm surgery in the Netherlands are registered in the Dutch Surgical Aneurysm Audit (DSAA) to monitor and improve quality of care.[1,2] By registering parameters on structure, process and outcome, surgeons can be provided with benchmarked information on the quality of their care, which subsequently can be used for quality improvement.[3] However, it remains unclear which indicators best reflect quality of care. Single outcome indicators in aneurysm surgery like mortality after endovascular aneurysm repair (EVAR) often have a low event rate, which results in little variation and does not incite improvements. Moreover, a single indicator generally seems to give a one-sided perspective and does not reflect the multidimensional aspect of the surgical process.[4]

'Textbook Outcome' (TO), a composite measure including all desirable outcomes, has first been described in gastro-intestinal cancer surgery.[4,5] Since TO covers the most important parameters of the surgical process, it gives a better impression of the overall quality of care and most likely reflects the desires of patients more closely. Secondly, TO increases the event rate and hence the variation between hospitals. Therefore TO could also be used for hospital comparison in order to recognize 'best-practice' that could serve as an example for participants in the registry.[6,7]

The objective of this study was to define and test TO for elective aneurysm surgery. Hospital variation in (adjusted) outcomes on this composite measure were investigated, as well as the association with the operative technique.

METHODS

Data source

The dataset was retrieved from the DSAA, a national outcome registry initiated in 2013 including all patients who underwent surgery for an abdominal aortic aneurysm (AAA). During the first years of registration, only patients with a primary infra- or juxta-renal AAA were registered. As of 2016, all patients with an aneurysm in the thoracic aorta or aortic arch and all patients with a revision of their aneurysm repair are registered as well.[1]

Patient selection

All patients undergoing elective AAA repair between January 2014 and December 2015 registered in the DSAA, were included provided that date of birth, date of surgery, type of surgical procedure and patient survival status 30 days after surgery and at time of discharge were registered. Patients with a ruptured or acute symptomatic AAA were excluded.

Definitions

When defining TO for elective AAA repair, a difference in definition should be made for patients treated with EVAR or open surgical repair (OSR), since the choice of treatment will influence both the surgical and postoperative process. Patients were categorized by intention to treat. The scientific committee of the DSAA made a selection of relevant process and outcome parameters for desirable patient outcome: no intraoperative complications (1), no postoperative surgical complications (2), no re-interventions (3), no prolonged length of hospital stay (LOS) (EVAR ≤ 4 days, OSR ≤ 10 days) (4), no re-admissions ≤ 30 days after discharge (5) and no postoperative mortality ≤30 days after surgery / at discharge. (6). When all 6 desired outcomes were realized TO was achieved.

Only surgical complications were included in the parameter 'postoperative complications'. All serious non-surgical complications, which had a disadvantageous effect on patient recovery, would have automatically led to a prolonged LOS. Since a prolonged LOS is included in the definition of TO, patients with severe non-surgical complications are captured as well. A re-intervention was defined as any surgical or radiological intervention related to the primary intervention. To determine the cut-off point for prolonged LOS for each surgical procedure a questionnaire was distributed among 20 vascular surgeons, all from different hospitals. The mean reported number of days was chosen. Postoperative mortality was defined as mortality during the initial hospital stay or within 30 days after surgery.

Analysis

All analyses were performed for EVAR and OSR separately. The overall percentages of TO and percentages of patients for each independent outcome parameter were calculated. Parameters were placed in chronological order. When data were missing for one of the selected parameters, TO could not be achieved.

Patient characteristics were compared between patients with and those without TO using the T-test and Chi-square test. Based on the V(p)-POSSUM score, patient characteristics included in this analysis were: gender, age, aneurysm diameter, systolic blood pressure, heart rate, pulmonary status, cardiac status, prior or current malignancies, preoperative electrocardiogram and preoperative laboratory results.[8]

Possible associations between patient characteristics and TO were analyzed to subsequently adjust hospitals TO rates for the case-mix of their patients. Therefore, all previously mentioned patient characteristics were entered in a multivariable logistic regression model at a p-value of 0.05 using an ENTER model.

Funnel plots with confidence intervals (CIs) of 95% and 99% were used to show hospital variation for adjusted TO rates. In case data were missing for continuous variables, the mean of each variable was imputed. Data were missing most frequently for preoperative heart rate (5.8% EVAR, 6.6% OSR) and sodium (9.6% EVAR, 5.8% OSR). In other continuous variables missing data were not exceeding 5% of the total.

TO rates for EVAR and OSR per hospitals were compared with the national mean and plotted in a four quadrants figure. Additionally, the association between TO, hospital volume and EVAR/OSR ratio was assessed. Hospitals where only one of the procedures was performed were excluded in this analysis.
Since prolonged LOS is quite a 'soft' measure, we performed a sensitivity analysis with different cut-off points for prolonged LOS to investigate the influence of the chosen cut-off point on TO. Statistical analyses were performed in PASW Statistics version 21.0 (SPSS inc, Chicago, IL).

RESULTS

A total of 5172 patients underwent elective AAA repair and were registered in the DSAA, of which 5168 (99.9%) were eligible for analyses. 4039 patients were treated with EVAR (78%) and 1129 with OSR (22%). (Appendix 1., Flowchart) Ten patients (0.02%) that were initially planned for EVAR, were converted to OSR. TO was realized in 71% of EVAR patients and in 53% of OSR patients (Figure 1). In both surgical procedures, a prolonged LOS (EVAR 17%, OSR 37%) resulted in a decrease of TO. In addition, 11% of EVAR patients was re-admitted after discharge and 17% of OSR patients had a postoperative surgical complication. In 5.4% of EVAR and in 5.3% of OSR TO was not realized because data were missing for one of the selected parameters.

Univariable Analysis

Patient characteristics are shown in Table 1. Patients with TO were more often male and on average one year younger of age, compared to patients without TO. Furthermore, the distribution of cardiac state, pulmonary state and preoperative hemoglobin levels was significantly different between patients with and without a TO, for EVAR and OSR.

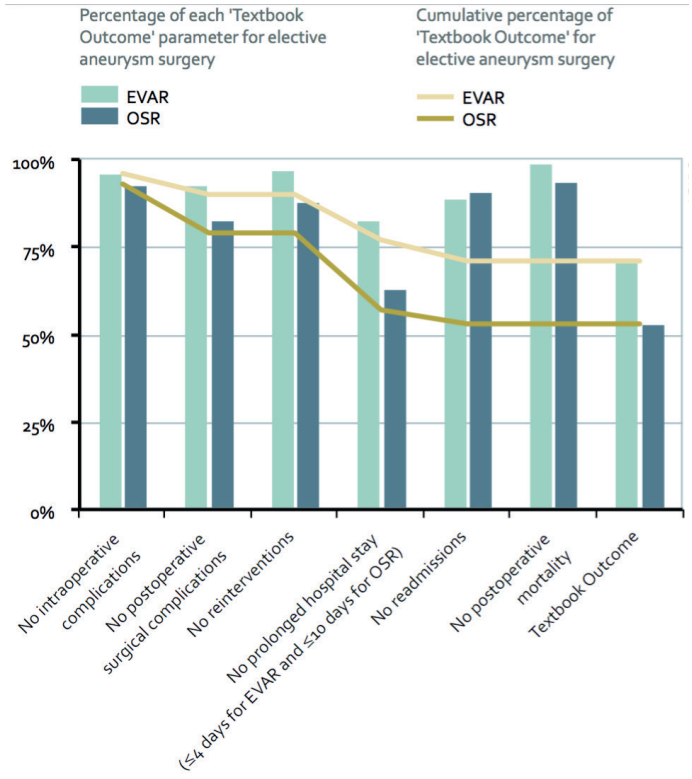
Multivariable Analysis

Younger age (EVAR and OSR (odds ratio[95%CI]), 0.98[0.97-0.99] and 0.97[0.96-0.99]), male gender (OR 1.61[1.32-1.97] and OR 1.73[1.24-2.42]), and higher preoperative hemoglobin (1.17[1.08-1.26] and 1.16[1.01-1.34]) were significantly associated with achieving TO in EVAR and OSR patients. Patients with dyspnea during exercise were less likely to achieve TO. Additionally, this also applies to EVAR patients with peripheral edema and OSR patients with medically treated hypertension. (Appendix 2., which demonstrates the associations between patient characteristics and TO.)

Textbook outcome by hospital

Figure 2a and 2b show the case-mix adjusted percentages of TO for EVAR and OSR by hospital volume for individual hospitals. The adjusted TO varied between hospitals from

Figure 1. Textbook Outcome in EVAR and OSR.



39%-92% and 0%-100%, respectively in EVAR and OSR patients. (Appendix 3., which demonstrates the unadjusted percentage achieved TO-parameters per hospital.) In both surgical procedures, five hospitals had a significantly lower TO rate compared to the mean. No hospitals performed significantly better than the mean in both EVAR and OSR.

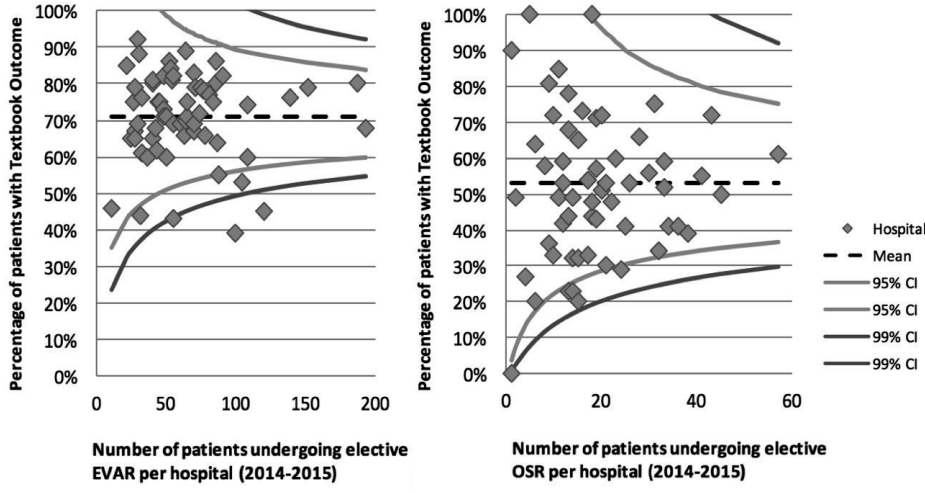
Textbook Outcome EVAR and OSR

Figure 3 shows adjusted TO rates for EVAR and OSR by hospital, compared to the national mean. Hospitals were divided into 4 groups; desirable outcome for both procedures (green), high TO in EVAR and low in OSR (blue), high TO in OSR and low in EVAR (orange) and a low TO in both procedures (red). Most hospitals had a higher TO in EVAR patients than in OSR. Additionally, most hospitals with a high TO for OSR did also had a high TO for EVAR. However, a high TO for EVAR did not automatically result in a high TO for OSR. The variation in hospital volume, TO rates and EVAR/OSR ratio within the different quadrants is shown in table 3.

Table 1. Patient characteristics

	EVAR					OSR				
	No TO		TO		P	No TO		TO		P
	N	%	N	%		N	%	N	%	
Number of patients	1174	29%	2865	71%		536	47%	593	53%	
Age (mean, years)	74.8 ± 7.7		73.5 ± 7.4		.000	71.7 ± 7.3		69.8 ± 7.4		.000
Gender					.000					.000
Male	961	82%	2542	89%		414	77%	508	86%	
Female	213	18%	323	11%		122	23%	85	14%	
Aneurysm diameter (mm)	59.7 ± 10.8		59.0 ± 10.4		.048	62.7 ± 13.3		61.5 ± 13.5		.129
Heart rate (BPM)	73.4 ± 13.3		72.4 ± 12.9		.020	74.4 ± 13.5		74.1 ± 13.5		.698
Systolic blood pressure (mmHg)	139.5 ± 19.7		140.0 ± 20.1		.429	141.2 ± 20.4		140.9 ± 18.9		.744
Cardiac State					.000					.006
No abnormalities	487	42%	1340	47%		208	39%	289	49%	
Peripheral edema	124	11%	238	8.3%		43	8.0%	29	4,90%	
Raised CVP	17	1.4%	28	1,00%		7	1.3%	6	1.0%	
Antihypertensive med	460	39%	1186	41%		251	47%	250	42%	
Unknown	86	7.3%	73	2.5%		27	5.0%	19	3.2%	
Pulmonary State					.002					.001
No dyspnea	824	70%	2189	76%		377	70%	480	81%	
Dyspnea during exercise	278	24%	537	19%		133	25%	91	15%	
Disabling dyspnea	43	3.7%	78	2.7%		8	1.5%	10	1.7%	
Dyspnea at rest	14	1.2%	27	0.9%		6	1.1%	4	0.7%	
Unknown	15	1.3%	34	1.2%		12	2.2%	8	1.3%	
Malignancy					.562					.485
None	941	80%	2272	79%		456	85%	512	86%	
Current	66	5.6%	150	5.2%		18	3.4%	13	2.2%	
History of Malignancy, curative treated	167	14%	443	16%		62	12%	68	12%	
Last preoperative ECG					.272					.212
No abnormalities	620	53%	1574	55%		304	57%	337	57%	
Atrial fibrillation	75	6.4%	197	6.9%		33	6.2%	24	4.0%	
Ischemia	21	1.8%	33	1.2%		9	1.7%	5	0.8%	
Other abnormalities	314	27%	751	26%		150	28%	169	29%	
No ECG performed	144	12%	310	11%		40	7.5%	58	9.8%	
Preoperative laboratory results										
Hemoglobin	8.5 ± 1.0		8.8 ± 1.0		.000	8.5 ± 1.0		8.7 ± 0.9		.000
Sodium					.102					.735
Normal Sodium	1105	94%	2732	95%		506	94%	557	94%	
Hypo/Hypernatremia	69	5.9%	133	4.6%		20	6.1%	36	6.1%	
Potassium					.555					.563
Normal	1102	94%	2703	94%		497	93%	555	94%	
Hypo/ hyperpotassemia	72	6.1%	162	5.7%		39	7.3%	38	6.4%	
Creatinine	100.7 ± 44.5		98.2 ± 43.1		.101	96.7 ± 35.7		93.6 ± 29.5		.116

Figure 2. Influence of volume on the adjusted TO in patients after EVAR and OSR per hospital.



Length of hospital stay and Textbook Outcome

Changing the cut-off point for prolonged LOS to ≥5, ≥6 and ≥7 days in the definition of TO for EVAR resulted in a TO of respectively 75%, 76% and 78%. A cut-off point for prolonged LOS of ≥11, ≥12, ≥13 and ≥14 days in the definition of TO for OSR resulted in a TO of respectively 56%, 59%, 60% and 61%. When comparing hospitals, changing prolonged LOS to ≥7 days for EVAR and ≥14 days for OSR did not lead to a difference in hospital variation of TO. (Appendix 4., which demonstrates TO with LOS ≥7 days for EVAR and ≥14 days for OSR)

DISCUSSION

To our knowledge this is the first article on a composite quality measure for desired patient outcome in elective aneurysm surgery. TO provides information on the overall quality of care, in which the key elements of the surgical process, as defined by the vascular surgical community of the Netherlands, are included. TO was realized in 71% of EVAR patients and 53% of OSR patients. The main reasons why TO was not achieved were a prolonged LOS in both surgical procedures, re-admissions after discharge for EVAR patients and postoperative complications for OSR patients. Variation in hospital outcomes was more pronounced using TO then using single outcome parameters.[2] A wider hospital variation in adjusted TO is seen in OSR, compared to EVAR. The majority of hospitals had a higher TO in EVAR than in OSR. This could be expected, because other audits and trials reported less mortality and postoperative complications in EVAR patients, compared to OSR.[9,10]

Figure 3. Percentage TO for EVAR versus OSR per hospital.

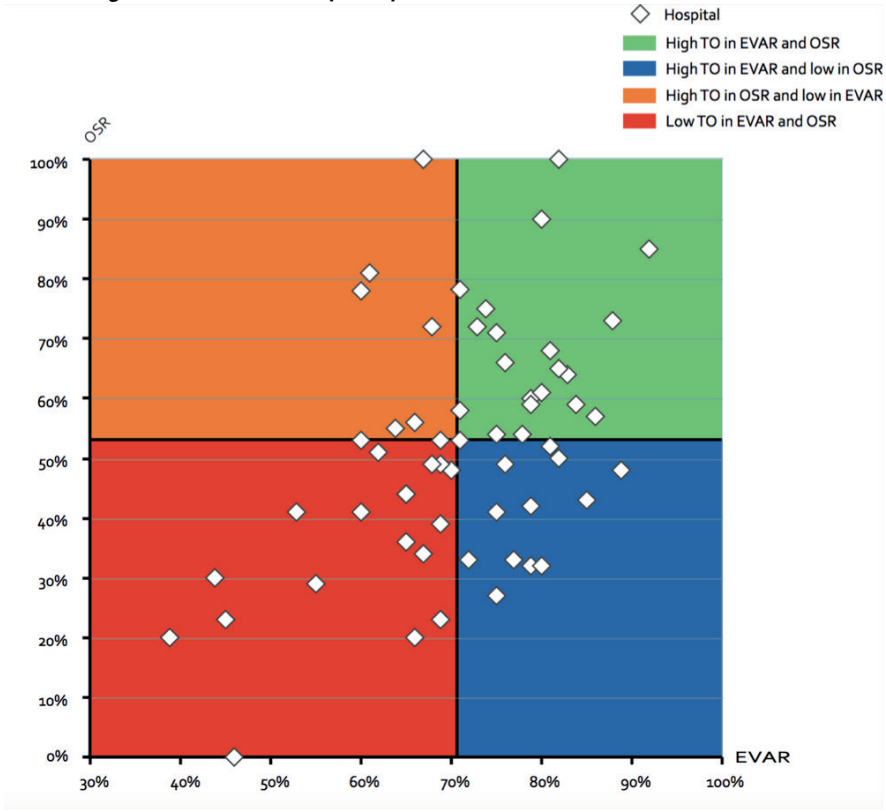


Table 2. TO for EVAR and OSR in relation with volume and the EVAR/OSR ratio

	Mean Volume EVAR (range)	Textbook Outcome EVAR	Mean Volume OSR (range)	Textbook Outcome OSR	EVAR/OSR ratio
Favorable TO for EVAR and OSR both	63 (27-187)	71%–92%	20 (1–57)	53%–100%	76%/ 24%
Favorable TO for EVAR only	75 (22-152)	72%–89%	19 (2-45)	27%–52%	80%/ 20%
Favorable TO for OSR only	53 (28-87)	61%–69%	19 (9-41)	53%–100%	73%/ 27%
Unfavorable TO for EVAR and OSR both	69 (11-193)	39%–70%	18 (1–38)	0%–51%	79%/ 21%

Quality of care has been primarily focused on mortality and morbidity rates. However, mortality and morbidity alone do not reflect the quality of care completely.[11,12] When only single indicators are taken into account, a hospital might perform well in one and worse in the another, as those are often not related.[4,13] Additionally, when the incidence of mortality and morbidity decreases or variation is lacking, it hampers the discriminative ability of single quality indicators.[14] Dimick et al previously described that only 8% of the American hospitals met the minimum caseload for AAA repairs, necessary to detect a doubling of the mortality rate and therefore mortality alone should not be used as a quality indicator.[15]

The Society for Thoracic Surgeons was one of the first to start a clinical audit to monitor their results.[16] In order to measure quality more accurately and to overcome issues with single quality indicators, a task force was formed to develop methods for combining multiple care domains into a comprehensive composite quality measure.[17] On behalf of this task force, O'Brien et al analyzed four methods of composite scoring for cardiac surgery.[18] He describes that the 'all-or-none' method, which we used for TO, increases the variability between hospitals and therefore may be helpful to compare performance between hospitals. Additionally, Nolan et al. stated that an all-or-none scoring system reflects the interests and desires of patients more closely.[19]
Where quality indicators as mortality, morbidity and re-interventions are directly related to desirable outcome, the ideal LOS as quality indicator is more debatable. In the literature, the mean LOS after elective aneurysm surgery is varying from discharge at the same day to 4 days for EVAR, and 5 to 10 days for OSR.[20-28] Our additional sensitivity analysis showed that prolonging the maximal LOS in the definition of TO for both surgical procedures resulted in a gradual increase in TO, but did not lead to a change in hospital variation. Based on this analysis, combined with literature and the questionnaire, the cut-off points we chose in our original definition of TO (EVAR ≥ 4, OSR ≥ 10), seems to provide a reasonable margin.

For both surgical procedures, there is a wide variation in TO with the majority of hospitals performing within the CIs around the mean. When TO rates for EVAR and OSR by hospital are compared with the mean, a different distribution is seen (Figure 3). Most hospitals performing well for OSR also did for EVAR (green), but hospitals with a high TO in EVAR patients did not necessarily do well in OSR (blue). Hypothetically, there is an ideal ratio of EVAR to OSR, so that every patient receives the surgical procedure suiting the anatomy of the aneurysm. Subsequently, the choice of surgical procedure might influence outcomes; surgeons who have a preference to choose to perform EVAR (also on difficult anatomy) will only perform OSR on the most difficult aneurysms. They will perform EVAR on patients where OSR might have been a better choice, resulting in relatively less favorable outcomes than possible in both groups (red). On the other hand, performing OSR in patients who are suitable for EVAR may result in a desirable TO for OSR, however patients are withhold from a potential less invasive operation with less postoperative mortality. So, TO must be considered at least together with postoperative mortality and the ratio EVAR/OSR. In this study EVAR/OSR ratios in the green and red quadrant were comparable and did not seem to explain the difference in TO. Remarkably, the proportion of EVAR is the largest in the blue quadrant and the smallest in the orange quadrant. The question rises if volume of OSR is an important factor. Few hospitals perform well in OSR and less good in EVAR (orange), but this might be confounded by indication. One might expect that hospital volume would influence hospital performance, but procedure volume was varying within the quadrants and did not seem to have effect on TO (table 3). Hospitals with low TO for both procedures

(red) should probably look for the more structural problems in their care process to improve outcomes for both procedures.

There are several limitations to this study. The dataset is retrieved from a national clinical audit and has some missing data. When data were missing on the selected parameters for TO, it was consequently not possible to achieve TO, therefore the percentage TO is possibly higher than described, overall and per hospital.
Secondly, because the audit is not designed for scientific purposes purely, the choice of desired parameters for TO was limited.
Thirdly, TO does not consider the unequal influence of different parameters on patient outcome and patient experience. Therefore, TO is not designed to replace single quality indicators, but is meant as an addition.

Since there is a wide variation in TO between hospitals within the CIs, it is difficult to recognize 'best practices'. But more important, individual hospitals can see where they can improve to achieve desired outcomes. Therefore, TO is initially particularly suitable as an instrument for internal quality improvement and not for hospital comparison. In the future, TO can be implemented in the DSAA feedback system for hospitals, to help identify areas for improvement.

CONCLUSION

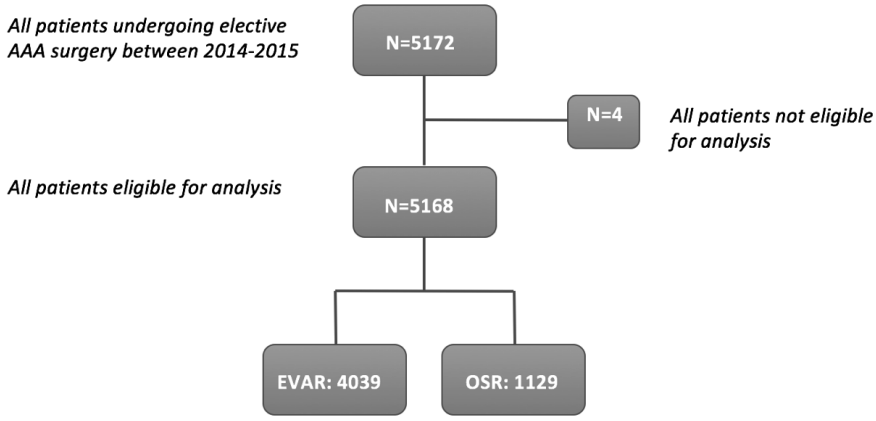
This first study about TO in elective AAA surgery shows that a composite measure provides additional information on the overall quality of surgical care, which subsequently can be used for internal quality improvement. Overall, a TO was realized in 71% of EVAR patients and 53% of OSR patients, with a wide variation between hospitals.

REFERENCES

1. http://www.dica.nl/.
2. Lijftogt N, Vahl AC, Wilschut ED, et al. Adjusted Hospital Outcomes of Abdominal Aortic Aneurysm Surgery Reported in the Dutch Surgical Aneurysm Audit. *Eur J Vasc Endovasc Surg.* 2017;in press.
3. Donabedian A. Evaluating the quality of medical care. *Milbank Mem Fund Q.* 1966;44(3):Suppl:166-206.
4. Kolfschoten NE, Kievit J, Gooiker GA, et al. Focusing on desired outcomes of care after colon cancer resections; hospital variations in 'textbook outcome'. *Eur J Surg Oncol.* 2013;39(2):156-163.
5. Busweiler LAD, Schouwenburg MG, van Berge Henegouwen MI, et al. 'Textbook outcome': what we should strive for in oesophagogastric cancer surgery. *Br J Surg.* 2017;in press.
6. Dimick JB, Staiger DO, Hall BL, Ko CY, Birkmeyer JD. Composite measures for profiling hospitals on surgical morbidity. *Ann Surg.* 2013;257(1):67-72.
7. Dijs-Elsinga J, Otten W, Versluijs MM, et al. Choosing a hospital for surgery: the importance of information on quality of care. *Med Decis Making.* 2010;30(5):544-555.
8. Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. *Br J Surg.* 1991;78(3):355-360.
9. Malas M, Arhuidese I, Qazi U, Black J, Perler B, Freischlag JA. Perioperative mortality following repair of abdominal aortic aneurysms: application of a randomized clinical trial to real-world practice using a validated nationwide data set. *JAMA Surg.* 2014;149(12):1260-1265.
10. Mani K, Bjorck M, Wanhainen A. Changes in the management of infrarenal abdominal aortic aneurysm disease in Sweden. *Br J Surg.* 2013;100(5):638-644.
11. Siracuse JJ, Schermerhorn ML, Meltzer AJ, et al. Comparison of outcomes after endovascular and open repair of abdominal aortic aneurysms in low-risk patients. *Br J Surg.* 2016;103(8):989-994.
12. Prinssen M, Verhoeven EL, Buth J, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med.* 2004;351(16):1607-1618.
13. Parina RP, Chang DC, Rose JA, Talamini MA. Is a low readmission rate indicative of a good hospital? *J Am Coll Surg.* 2015;220(2):169-176.
14. Birkmeyer JD, Dimick JB, Birkmeyer NJ. Measuring the quality of surgical care: structure, process, or outcomes? *J Am Coll Surg.* 2004;198(4):626-632.
15. Dimick JB, Welch HG, Birkmeyer JD. Surgical mortality as an indicator of hospital quality: the problem with small sample size. *JAMA.* 2004;292(7):847-851.
16. Clark RE. The development of The Society of Thoracic Surgeons voluntary national database system: genesis, issues, growth, and status. *Best Pract Benchmarking Healthc.* 1996;1(2):62-69.
17. Shahian DM, Edwards FH, Ferraris VA, et al. Quality measurement in adult cardiac surgery: part 1—Conceptual framework and measure selection. *Ann Thorac Surg.* 2007;83(4 Suppl):S3-12.
18. O'Brien SM, Shahian DM, DeLong ER, et al. Quality measurement in adult cardiac surgery: part 2—Statistical considerations in composite measure scoring and provider rating. *Ann Thorac Surg.* 2007;83(4 Suppl):S13-26.
19. Nolan T, Berwick DM. All-or-none measurement raises the bar on performance. *JAMA.* 2006;295(10):1168-1170.
20. Moscato VP, O'Brien-Irr MS, Dryjski ML, Dosluoglu HH, Cherr GS, Harris LM. Potential clinical feasibility and financial impact of same-day discharge in patients undergoing endovascular aortic repair for elective infrarenal aortic aneurysm. *J Vasc Surg.* 2015;62(4):855-861.
21. Lachat ML, Pecoraro F, Mayer D, et al. Outpatient endovascular aortic aneurysm repair: experience in 100 consecutive patients. *Ann Surg.* 2013;258(5):754-758; discussion 758-759.
22. Edwards MS, Andrews JS, Edwards AF, et al. Results of endovascular aortic aneurysm repair with general, regional, and local/monitored anesthesia care in the American College of Surgeons National Surgical Quality Improvement Program database. *J Vasc Surg.* 2011;54(5):1273-1282.

23. Mehaffey JH, LaPar DJ, Tracci MC, Cherry KJ, Kern JA, Upchurch GR, Jr. Targets to prevent prolonged length of stay after endovascular aortic repair. *J Vasc Surg.* 2015;62(6):1413-1420.
24. Dillavou ED, Muluk SC, Makaroun MS. Improving aneurysm-related outcomes: nationwide benefits of endovascular repair. *J Vasc Surg.* 2006;43(3):446-451; discussion 451-442.
25. Pasin L, Nardelli P, Landoni G, et al. Enhanced recovery after surgery program in elective infrarenal abdominal aortic aneurysm repair. *J Cardiovasc Surg (Torino).* 2016.
26. Teixeira PG, Woo K, Abou-Zamzam AM, Zettervall SL, Schermerhorn ML, Weaver FA. The impact of exposure technique on perioperative complications in patients undergoing elective open abdominal aortic aneurysm repair. *J Vasc Surg.* 2016;63(5):1141-1146.
27. Chang JK, Calligaro KD, Lombardi JP, Dougherty MJ. Factors that predict prolonged length of stay after aortic surgery. *J Vasc Surg.* 2003;38(2):335-339.
28. de la Motte L, Jensen LP, Vogt K, Kehlet H, Schroeder TV, Lonn L. Outcomes after elective aortic aneurysm repair: a nationwide Danish cohort study 2007-2010. *Eur J Vasc Endovasc Surg.* 2013;46(1):57-64.

Appendix 1. Flowchart patient selection



Appendix 2. Patient characteristics associated with 'Textbook Outcome'

	EVAR		OSR	
	Odds	95% CI	Odds	95% CI
Number of patients				
Age (years)	0.983	0.974-0.993	0.976	0.959-0.993
Gender				
Female	Ref		Ref	
Male	1.611	1.317-1.971	1.732	1.238-2.422
Aneurysm diameter (mm)	0.996	0.990-1.003	0.996	0.987-1.006
Heart rate (BPM)	0.994	0.989-1.000	0.999	0.990-1.008
Systolic blood pressure (mmHg)	1.002	0.998-1.005	0.997	0.991-1.004
Cardiac State				
No abnormalities	Ref		Ref	
Peripheral edema	0.730	0.562-0.947	0.579	0.332-1.008
Raised CVP	0.696	0.370-1.312	0.836	0.268-2.603
Antihypertensive med	0.966	0.827-1.129	0.731	0.563-0.948
Unknown	0.301	0.214-0.423	0.553	0.290-1.053
Pulmonary State				
No dyspnea	Ref		Ref	
Dyspnea during exercise	0.775	0.653-0.921	0.570	0.418-0.776
Disabling dyspnea	0.755	0.510-1.118	1.173	0.443-3.102
Dyspnea at rest	0.898	0.460-1.754	0.476	0.129-1.755
Unknown	1.067	0.560-2.032	0.595	0.230-1.543
Malignancy				
None	Ref		Ref	
Current	1.060	0.776-1.446	0.716	0.366-1.527
History of Malignancy, curative treated	1.183	0.970-1.444	1.010	0.685-1.487
Last preoperative ECG				
No abnormalities	Ref		Ref	
Atrial fibrillation	1.348	0.993-1.830	0.904	0.494-1.656
Ischemia	0.694	0.391-1.232	0.588	0.187-1.855
Other abnormalities	1.018	0.858-1.208	1.124	0.845-1.495
No ECG performed	0.953	0.759-1.197	1.330	0.849-2.085
Preoperative laboratory results				
Hemoglobin	1.166	1.082-1.256	1.164	1.013-1.338
Sodium				
Normal Sodium	ref		ref	
Hypo- or hypernatremia	0.958	0.703-1.306	1.299	0.769-2.192
Potassium				
Normal potassium	ref		ref	
Hypo- or hyperpotassemia	0.986	0.734-1.324	1.049	0.647-1.701
Creatinine	1	0.998-1.001	0.998	0.994-1.002

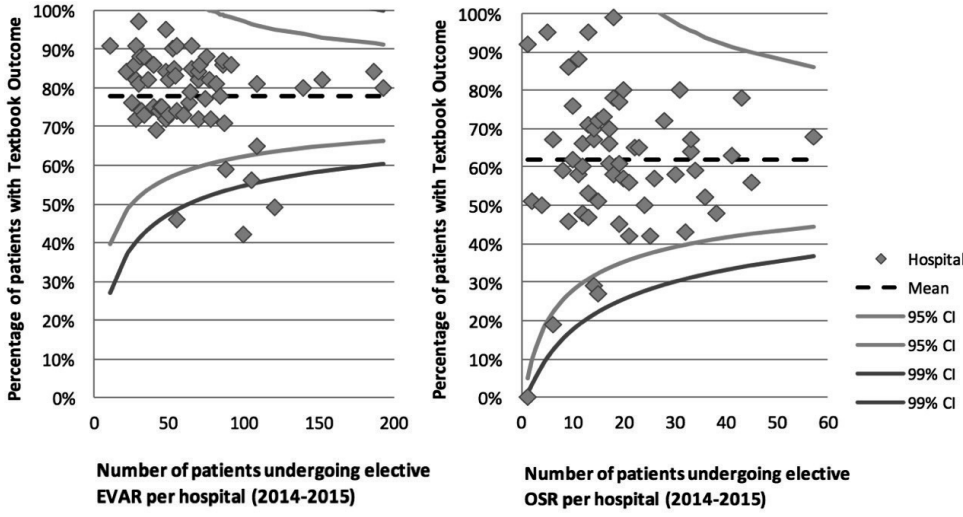
Appendix 3. the unadjusted percentage achieved TO-parameters per hospital

	EVAR								OSR							
Hospital	Hospital volume (n=4039)	TO	No Peroperative complications	No surgical complications	No reinterventions	No prolonged LOS	No readmission	No mortality	Hospital volume (n=1129)	TO	No Peroperative complications	No surgical complications	No reinterventions	No prolonged LOS	No readmission	No mortality
1	30	90%	100%	100%	100%	93%	97%	100%	11	91%	100%	100%	100%	91%	100%	100%
2	91	80%	99%	95%	99%	89%	92%	100%	5	100%	100%	100%	100%	100%	100%	100%
3	40	80%	98%	100%	100%	85%	98%	100%	1	100%	100%	100%	100%	100%	100%	100%
4	31	90%	97%	97%	100%	94%	97%	100%	16	75%	100%	81%	81%	81%	94%	94%
5	40	83%	100%	100%	100%	88%	95%	98%	13	77%	100%	92%	92%	85%	92%	85%
6	44	77%	91%	91%	93%	84%	91%	98%	19	79%	95%	84%	89%	84%	100%	100%
7	53	85%	100%	94%	98%	98%	91%	100%	12	67%	92%	75%	75%	75%	92%	92%
8	42	71%	90%	90%	93%	88%	88%	98%	10	80%	80%	90%	90%	80%	100%	90%
9	70	81%	99%	97%	97%	87%	96%	100%	6	67%	100%	100%	100%	67%	100%	100%
10	65	74%	97%	95%	97%	77%	100%	98%	43	74%	100%	91%	91%	79%	91%	98%
11	28	64%	100%	100%	100%	64%	100%	100%	18	83%	100%	89%	89%	83%	100%	100%
12	109	76%	98%	94%	95%	86%	91%	100%	31	71%	94%	90%	94%	74%	100%	97%
13	86	88%	100%	94%	98%	93%	95%	99%	19	58%	95%	68%	79%	63%	100%	79%
14	50	60%	96%	84%	98%	66%	94%	100%	13	85%	100%	100%	100%	85%	100%	100%
15	187	79%	94%	94%	98%	91%	93%	99%	57	65%	93%	84%	88%	72%	96%	93%
16	33	79%	97%	97%	100%	85%	97%	100%	28	64%	86%	100%	100%	71%	93%	96%
17	48	73%	98%	94%	96%	81%	94%	100%	20	70%	100%	95%	95%	70%	100%	95%
18	75	80%	100%	97%	97%	83%	96%	100%	33	61%	100%	85%	88%	70%	94%	100%
19	71	79%	99%	96%	97%	87%	90%	100%	23	57%	100%	87%	87%	70%	87%	87%
20	54	83%	94%	93%	98%	94%	94%	100%	33	52%	97%	85%	85%	55%	100%	94%
21	50	72%	98%	92%	92%	82%	88%	100%	8	63%	63%	75%	75%	88%	100%	88%
22	78	71%	92%	95%	97%	83%	86%	99%	30	63%	90%	90%	93%	83%	83%	93%
23	55	84%	100%	96%	98%	87%	95%	98%	45	49%	87%	73%	80%	58%	96%	93%
24	27	78%	96%	96%	96%	85%	96%	100%	17	53%	100%	82%	94%	59%	100%	94%
25	77	78%	96%	92%	94%	87%	96%	99%	17	53%	100%	100%	100%	53%	94%	94%
26	48	69%	100%	88%	96%	79%	94%	100%	15	60%	87%	80%	93%	60%	100%	100%
27	22	86%	100%	91%	91%	100%	86%	100%	19	42%	95%	68%	74%	68%	84%	95%

Appendix 3 continued

28	139	76%	94%	91%	93%	83%	94%	100%	2	50%	100%	100%	100%	100%	50%	100%
29	48	73%	94%	85%	98%	88%	92%	100%	26	50%	85%	85%	96%	81%	92%	96%
30	64	77%	98%	98%	98%	81%	98%	100%	22	45%	95%	77%	77%	55%	95%	95%
31	70	69%	100%	96%	99%	74%	93%	100%	21	52%	86%	71%	95%	52%	95%	95%
32	87	63%	94%	94%	95%	84%	78%	100%	41	54%	93%	85%	85%	63%	83%	90%
33	84	75%	93%	94%	96%	87%	89%	100%	36	42%	92%	78%	92%	56%	81%	97%
34	86	81%	98%	99%	99%	85%	99%	100%	15	33%	100%	87%	93%	40%	93%	93%
35	40	68%	93%	85%	98%	85%	90%	100%	13	46%	85%	85%	100%	69%	85%	92%
36	64	70%	97%	86%	94%	86%	89%	98%	18	44%	94%	89%	89%	61%	89%	100%
37	43	63%	93%	91%	93%	63%	98%	98%	20	50%	95%	75%	85%	60%	95%	85%
38	81	78%	96%	94%	98%	86%	94%	100%	17	35%	88%	88%	88%	53%	94%	94%
39	74	73%	97%	97%	100%	85%	88%	100%	10	40%	100%	70%	80%	50%	100%	80%
40	28	71%	89%	89%	100%	79%	96%	100%	12	42%	100%	75%	75%	42%	100%	92%
41	30	67%	97%	97%	100%	67%	97%	100%	11	45%	91%	73%	82%	64%	91%	82%
42	193	69%	96%	93%	95%	76%	93%	100%	14	43%	100%	64%	86%	43%	100%	79%
43	36	61%	100%	97%	100%	64%	97%	97%	12	50%	100%	83%	100%	58%	83%	100%
44	152	80%	97%	92%	95%	84%	95%	97%	14	29%	93%	79%	93%	36%	71%	93%
45	28	64%	93%	82%	96%	79%	96%	100%	18	44%	89%	94%	4%	50%	94%	100%
46	55	69%	91%	87%	93%	84%	91%	98%	38	37%	95%	68%	71%	42%	89%	92%
47	70	69%	3%	90%	97%	84%	89%	99%	32	34%	84%	78%	81%	63%	75%	94%
48	65	77%	100%	100%	100%	77%	100%	100%	4	25%	100%	100%	100%	25%	100%	100%
49	109	60%	88%	83%	96%	79%	90%	98%	34	41%	94%	79%	94%	50%	91%	94%
50	25	64%	100%	92%	96%	68%	92%	100%	9	33%	100%	78%	78%	33%	100%	89%
51	60	70%	97%	90%	95%	82%	83%	98%	14	21%	86%	57%	57%	29%	79%	86%
52	52	88%	100%	98%	100%	88%	100%	100%	0	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
53	88	57%	95%	93%	94%	83%	68%	98%	24	29%	92%	88%	92%	42%	79%	100%
54	63	68%	86%	94%	98%	84%	95%	100%	6	17%	83%	67%	100%	50%	100%	100%
55	45	76%	96%	93%	96%	82%	96%	100%	0	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
56	32	44%	94%	100%	100%	47%	94%	97%	21	29%	100%	81%	90%	33%	90%	86%
57	33	61%	91%	79%	85%	79%	88%	100%	9	9%	100%	89%	89%	89%	100%	100%
58	120	38%	93%	93%	97%	83%	48%	99%	13	23%	85%	92%	100%	54%	77%	92%
59	100	39%	89%	91%	99%	89%	50%	99%	15	20%	87%	87%	93%	60%	40%	100%
60	105	52%	98%	93%	94%	81%	66%	100%	25	0%	84%	88%	88%	84%	72%	92%
61	11	45%	100%	100%	100%	45%	91%	100%	1	0%	0%	0%	0%	0%	100%	100%
62	55	44%	100%	96%	100%	84%	58%	98%	0	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Total	4039	71%	96%	93%	97%	83%	89%	99%	1129	53%	93%	83%	88%	63%	91%	94%

Appendix 4. Percentage of adjusted Textbook Outcome (EVAR Length of stay ≤ 7 days, OSR length of stay ≤ 14 days) in patients after EVAR and OSR per hospital, identified by volume.



CHAPTER 7

National Numbers of Secondary Aortic Reinterventions after Primary Abdominal Aortic Aneurysm Surgery from the Dutch Surgical Aneurysm Audit

E.G. Karthaus, A.C. Vahl, B.H.P. Elsman, M.W.J.M. Wouters, G.J. de Borst, J.F. Hamming

Annals of Vascular Surgery 2020

ABSTRACT

Background and objective

Long term secondary aortic reinterventions (SARs) can be a sing of (lack of) effectiveness of abdominal aortic aneurysm (AAA) surgery. This study provides insight into the national number of SAR after primary AAA repair by EVAR or by OSR in the Netherlands.

Methods

Observational study including all patients undergoing SAR between 2016-2017, registered in the compulsory Dutch Surgical Aneurysm Audit (DSAA). The DSAA started in 2013, SARs are registered from 2016. Characteristics of SAR and postoperative outcomes (mortality/complications) were analyzed, stratified by urgency of SAR. Data of SARs were merged with data of their preceded primary AAA-repair, registered in the DSAA after January 2013. In these SAR-patients, treatment characteristics of the preceded primary AAA-repair were additionally described, with focus on differences between stent grafts.

Results

Between 2016-2017, 691 patients underwent SAR, this concerned 9.3% of all AAA-procedures (infrarenal/juxtarenal/suprarenal) in the Netherlands (77% elective/11% acute symptomatic/12% ruptured). Endoleak (60%) was the most frequent indication for SAR. SARs were performed with EVAR in 66%. Postoperative mortality after SAR was 3.4%, 11% and 29% in elective, acute symptomatic and ruptured patients respectively.
In 26% (n=181) of the SAR-patients their primary AAA-repair was performed after January 2013 and data of primary and SAR procedures could be merged. In 93% (n=136), primary AAA-repair was EVAR. Endografts that primarily were used were nitinol/Polyester (62%), nitinol/PFTE (8%), endovascular sealing (21%) and others (9%), compared to their national market share of respectively 76% (OR 0.52[95%CI 0.38-0.71]), 15% (0.50[0.29-0.89]), 4.9% (5.04[3.44-7.38]), and 4.1% (2.81[1.66-4.74]).

Conclusion

In the Netherlands, about one-tenth of the annual AAA-procedures concerns a SAR. A quarter of this cohort had a SAR within 1-5 years after their primary AAA-repair. Most SARs followed after primary EVAR-procedures, in which an overrepresentation of endovascular sealing grafts was seen. Postoperative mortality after SAR is comparable with primary AAA-repair.

INTRODUCTION

The choice of surgical technique in primary abdominal aortic aneurysm (AAA) repairs is mainly based on patient and aneurysm-related characteristics. Because of lower postoperative mortality and morbidity after treatment with endovascular aneurysm repair (EVAR) compared to conventional open surgical repair (OSR), EVAR has become the preferred procedure in the elective setting and in many centers even in the acute setting.[1-3] However, when choosing a treatment strategy, it is also important to take long-term outcomes into account, such as surgical secondary reinterventions. Secondary reinterventions are undesirable for the patient and additionally contributes to higher costs of care. Follow-up studies of the Endovascular Aneurysm Repair 1 (EVAR-1) trial and Dutch Randomized Endovascular Aneurysm Management (DREAM) trial, comparing EVAR and OSR in elective AAA patients, demonstrated a similar long-term survival but a significantly higher overall secondary reintervention rate in patients treated with EVAR.[4-6] After the DREAM (12 years) and EVAR-1 trial (15 years), the secondary reintervention rate was respectively 38% and 26% in EVAR patients, compared to 21% and 12% in OSR patients.[6,7] Over time, endovascular devices and techniques have been further developed aiming to improve its safety and durability, which possibly affects the generalizability of these results for today practice.[8] Additionally, the use of EVAR has continued to increase over the past decades and is currently used in almost 80% of all patients undergoing elective AAA surgery in the Netherlands.[9] Presumably both factors will influence the amount of secondary aortic reinterventions (SARs) that is carried out in daily practice. However, it is unclear what the current extent of this problem is on a national scale and what the consequences are for patients.

With the use of the nationwide Dutch Surgical Aneurysm Audit (DSAA), which registers all SAR procedures since 2016, we aimed to provide insight into the national number of open surgical and endovascular SARs following primary OSR or primary EVAR. Secondly, we aimed to describe patient, aneurysm and treatment characteristics and outcomes of patients undergoing SAR.

METHODS

Data source and patient selection

The dataset is retrieved from the Dutch Surgical Aneurysm Audit (DSAA). This mandatory and nationwide audit was initiated in 2013 and prospectively registers all patients undergoing surgery for an aortic aneurysm or dissection. Initially, only patients undergoing a primary abdominal aortic (infrarenal and juxtarenal) repair were registered in the DSAA. Since January 2016, all primary aortic procedures (EVAR and OSR) for an infrarenal/juxtarenal/suprarenal AAA and all SARs (endovascular or open procedure) following a primary AAA repair were also included in the audit. Data are registered via a web-based survey or provided via a batch data

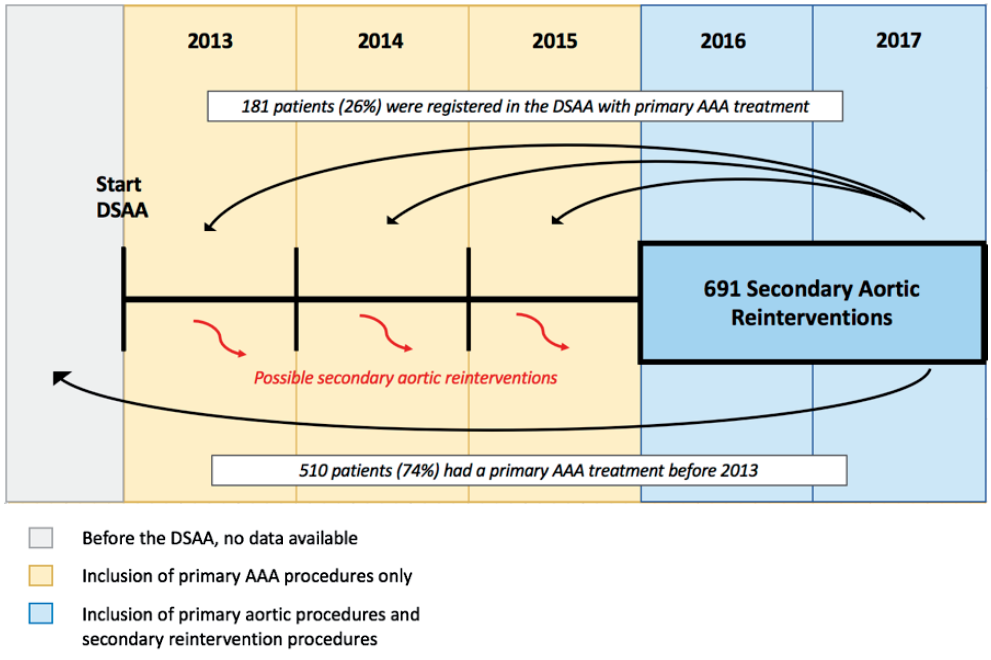
file per hospital and is collected on procedural level. Of each individual surgical procedure, corresponding patient characteristics, procedure characteristics and 30-days or in hospital postoperative outcome are registered. With each procedure, the vascular surgeon must then indicate whether it concerns a primary AAA procedure or an SAR. Patients undergoing multiple surgical aortic procedures are thereby re-registered in each case.

In this study, we included all patients undergoing SAR, concerning the iliac and/or abdominal aorta, after the start of registration in January 2016 until December 2017. To consider a patient eligible for analysis the date of birth, date of surgery, type of surgical procedure, urgency of surgical procedure and survival status at time of discharge and 30-days postoperatively had to be known. In these SAR patients (i.e. individual procedural records) we have no standard information about the primary AAA procedure. However, when SAR patients had undergone their primary AAA-repair between January 2013 (start of the DSAA) and December 2017 and were registered in the DSAA, data of the primary AAA repair and SAR were merged (figure 1) and formed a sub-cohort. When the primary AAA repair was performed before January 2013, data on the primary AAA repair were not available and could not be merged with the SAR data.

All patients undergoing thoracic aortic surgery were excluded from this study.

Verification of the DSAA data was carried out in 2015 by a third trusted party, through a random sample of hospitals and will be continued in the future.[10]

Figure 1. Flow chart of patients included in this study



Definitions

All surgical secondary aortic reinterventions (SAR) following primary AAA repair concerning the iliac and/or abdominal aorta are considered as a SAR. All reintervention procedures occurring within 30 days after primary AAA repair or during initial admission were considered as postoperative reinterventions and not as SAR. Secondary reinterventions performed by other specialties, such as interventional radiologists, and all other secondary reintervention procedures not related to the aorta were not registered in the DSAA and therefore not included as a SAR in this study. Postoperative mortality was defined as mortality within 30 days after SAR or during admission (30-day/in-hospital). Postoperative complications were categorized by surgical and non-surgical complications. A hybrid procedure is defined as a procedure in which open and endovascular technique are combined.

Statistical analysis

Patient and aneurysm characteristics, treatment and outcomes of the total cohort of patients undergoing SAR were stratified by the urgency of SAR (i.e., elective, acute symptomatic and acute ruptured) and analyzed with descriptive statistics. Additionally, postoperative outcomes of SARs were compared with outcomes of primary AAA repairs with T-tests and chi-square tests.

In case of missing data in a categorical or continues variable was exceeding 5%, a category 'missing/unknown' was added. In the sub-cohort of patients with both data on the primary AAA procedure and the SAR, combined treatment characteristics, time to SAR and outcomes were described using descriptive statistics. The ratio of different types of stent grafts, used at primary AAA repair, in patients undergoing SAR were compared with the ratio of the national market share of these grafts. All statistical analyses were performed using SPSS statistical software (version 24; IMB Corp, Armonk, NY).

RESULTS

Between January 2016 and December 2017, 8234 patients were registered in the Dutch Surgical Aneurysm Audit and eligible for analysis, of which 7425 (90%) patients were undergoing AAA surgery, 718 (8.7%) thoracic aortic aneurysm (TAA) surgery and in 91 (1.1%) patients the location of the aneurysm was unspecified. Of all patients undergoing AAA surgery, 691 patients (9.3%) underwent a SAR following primary AAA surgery, of which 21 patients (3.0%) also underwent a second SAR. These 691 SAR-patients were included in this study.

All patients undergoing secondary aortic reconstruction surgery

The total SAR-cohort consisted predominantly of males (n=613, 89%) and had a mean age of 75 years (SD 7.8). Patient characteristics are showed in table 1.

The majority of patients (n=530, 76.7%) was undergoing SAR in elective setting and respectively 10.9% (n=75) and 12.4% (n=86) were undergoing a SAR because of an acute symptomatic or ruptured AAA. Endoleak after EVAR (n= 412, 60%) were most often the indication for SAR, followed by progression of aneurysmatic disease (n=185, 26.8%), false aneurysm (n=49, 7.1%) and infected prostheses (n=42, 6.1%). In the majority of patients (n=453, 65.6%), SAR was performed with an endovascular procedure, 21% (n=145) with an open procedure, in 3.2% (n=22) the SAR was converted from endovascular to open procedure and in 1.3% (n=9) a hybrid procedure was performed. In the remaining 8.9% (n=62) of SARs, the procedure was unspecified.

Postoperative complications following SAR occurred in 26.5% (n=141) of elective patients, in 48.7% (n=29) of acute symptomatic patients and in 62.7% (n=54) of patients with a ruptured aneurysm (table 2). In respectively, 7.2%, 10.7% and 25.6% postoperative reintervention was necessary within 30 days after the SAR or during hospital stay. More than 50% of these postoperative reinterventions were open procedures, most of them following an open SAR. Postoperative mortality (30-days/in-hospital) was 3.4%, 10.7% and 29.1% in elective, acute symptomatic and ruptured aneurysm patients respectively. Table 3 shows how the observed (unadjusted) postoperative outcomes of SARs compared to the outcomes of primary AAA procedures in the same period. Postoperative mortality after SAR comparable to primary AAA repair in all urgency settings. There were more postoperative complications after elective SARs compared to elective primary AAA repairs.

Patients undergoing SAR matched to their primary AAA repair registered in the DSAA

Of all patients undergoing a SAR, 26% (n=181) was registered in the DSAA with their primary AAA repair between January 2013 and December 2017 and could be evaluated for the combined treatment characteristics of the primary AAA repair and of the SAR (figure 1). In the remaining 74% (n= 510) of SAR patients the primary AAA was not registered in the DSAA, which implies that they, in all probability, had undergone their primary AAA repair before 2013. The primary procedure in these patients is thereby unknown.

In the matched sub-cohort of 181 patients, the median maximum AAA diameter at the moment of primary AAA repair was 60mm (IQR 55-73mm). The median time from primary AAA procedure until SAR was 25 months (IQR 11-35 months).

Out of the 181 patients, 93% (n=169) was primarily treated with EVAR, 6.1% (n=11) with OSR and 0.6% (n=1) with a hybrid procedure. Figure 2 provides an overview of the surgical technique used in the primary AAA procedures and the following SARs. Types of endovascular grafts that were most frequently used in the primary EVAR procedures were nitinol/polyester stent grafts (n=104; 62%), nitinol/PFTE stent grafts (n=14; 8%), endovascular sealing stent grafts (n=35; 21%) and others (n=16; 9%). Table 4 specifies the indications for SAR per type of endovascular stent and the market share per type in the Netherlands. The proportion of

Table 1. Patient and treatment characteristics of patients undergoing SAR between 2016-2017

	Elective		**Acute–Symptomatic**		**Acute- Ruptured**		**Total**	
	N	%	N	%	N	%	N	%
Number of patients	530		75		86		691	
Age (mean, years)	74.9 SD 7.4		75.9 SD 8.9		74.4 SD 9.3		74.9 SD 7.8	
Sex								
Male	478	90%	59	79%	76	88%	613	89%
Female	52	9.8%	16	21%	10	12%	78	11%
Year of surgery								
2016	211	40%	31	41%	45	52%	287	42%
2017	319	60%	44	59%	41	48%	404	59%
Pulmonary state								
No dyspnea	348	66%	42	56%	49	57%	439	64%
Dyspnea	147	28%	20	27%	17	19%	184	27%
Severe Dyspnea	25	4.7%	4	5.3%	3	3.5%	32	4.6%
Unknown	10	1.9%	9	12%	17	20%	36	5.2%
Cardiac state								
No abnormalities	189	36%	19	25%	31	36%	239	35%
Peripheral edema	54	10%	13	17%	11	13%	78	11%
Raised CVP	14	2.6%	4	5.3%	0	0%	18	2.6%
Antihypertensive medication	261	49%	35	47%	38	44%	334	48%
Unknown	12	2.3%	4	5.3%	6	7.0%	22	3.2%
Last pre-operative ECG								
No abnormalities	209	39%	21	28%	29	34%	259	38%
Atrial fibrillation	56	10%	8	11%	9	11%	73	11%
Ischemia	22	4.2%	0	0%	1	1.2%	23	3.3%
Other abnormalities	185	35%	34	45%	25	29%	244	35%
No ECG performed	58	11%	12	16%	22	26%	92	13%
Type of aneurysm								
Infrarenal	295	56%	46	61%	54	63%	395	57%
Juxtarenal	87	16%	6	8.0%	9	11%	102	15%
Suprarenal	19	3.6%	2	2.7%	2	2.3%	23	3.3%
Unknown	129	24%	21	28%	21	24%	171	25%
Pathogenesis								
Infected prosthesis	24	4.5%	8	11%	10	12%	42	6.1%
Endoleak	329	62%	41	55%	42	49%	412	60%
False aneurysm	32	6.0%	6	8.0%	11	13%	49	7.1%
Progression of aneurysmatic disease	143	27.%	18	25%	23	27%	185	27%
Unknown	2	0.4%	1	1.3%	0	0.0%	3	0.4%
Surgery								
Endovascular	365	69%	41	55%	47	55%	453	66%
Open	93	18%	20	27%	32	37%	145	21%
Converted to open	16	3.0%	4	5.3%	2	2.3%	22	3.2%
Hybrid	3	0.6%	4	5.3%	2	2.3%	9	1.3%
Other	53	10%	6	8.0%	3	3.5%	62	8.9%

Table 2. Postoperative outcomes of patients undergoing SAR

	Elective		Acute–Symptomatic		Acute–Ruptured		Total	
	N	%	N	%	N	%	N	%
Postoperative complications								
No complication	389	73.4%	46	61.3%	31	36.0%	466	67.4%
Surgical complication	40	7.5%	5	6.7%	13	15.1%	58	8.4%
Non-surgical complication	72	13.5%	17	22.7%	26	30.2%	115	16.6%
Surgical and non- surgical complication	29	5.5%	7	9.3%	15	17.4%	51	7.4%
Unknown complication	0	0.0%	0	0.0%	1	1.2%	1	0.1%
Permanent injury due to complication*								
No	100	70.9%	17	58.6%	20	36.4%	137	61.2%
Yes	29	20.6%	8	27.6%	28	50.9%	65	29.0%
Unknown	12	8.5%	4	13.8%	7	12.7%	23	10.3%
Re-intervention within 30 days/in hospital								
No	492	92.8%	66	88.0%	63	73.3%	621	89.9%
Yes	38	7.2%	8	10.7%	22	25.6%	68	9.8%
unknown	0	0.0%	1	1.3%	1	1.2%	2	0.3%
Type of re-intervention**								
Endovascular procedure	8	21.1%	3	37.5%	6	27.3%	17	25.0%
Percutaneous procedure	1	2.6%	0	0,00%	1	4.5%	2	2.9%
Endoscopic procedure	1	2.6%	0	0,00%	0	0.0%	1	1.5%
Reoperation open procedure	21	55.3%	4	50.0%	14	63.6%	39	57.4%
Other	7	18.4%	1	12.5%	1	4.5%	9	13.2%
Re-admission (within 30 days after discharge)	30	5.70%	9	12.0%	7	7.0%	46	6.7%
Postoperative mortality (30-days/ in-hospital)	18	3.4%	8	10.7%	25	29.1%	51	7.4%

*Calculated in all patients with a postoperative complication
**Calculated in all patients with a re-intervention

primary endovascular sealing stent grafts in patients with a SAR is significant (21% vs. 4.9%, [OR 5.04, 95%CI 3.44-7.38]). All other types of stent grafts were equally represented in the SAR-group, relative to their market share.

In the twelve patients (6.7%) with a primary OSR or hybrid procedure, the indications for SAR were progression of aneurysmatic disease (n=5, 45%), infected prosthesis (n=4, 36%), false aneurysm (n=1, 9.1%) and other unspecified reasons (n=2, 18.2%).

The majority of the sub-cohort (n=136, 75.1%) was primary treated in an elective setting, 10.5% (n=19) in acute symptomatic and 14.4% (n=26) in ruptured setting. Figure 3 shows the urgency settings of the primary procedures and following SARs. 80% of patients with an elective primary AAA repair did undergo their SAR in an elective setting as well (n=109, 80.1%). The remaining 8.1% (n=11) and 11.8% (n=16) of primary elective patients underwent a SAR in an acute symptomatic or ruptured setting. Of these 27 patients 6 (22%) died of complications of the SAR procedure.

Table 3. Surgical treatment and outcomes of SAR compared to primary AAA repairs 2016-2017

	Elective					**Acute - Symptomatic**					**Acute - Ruptured**				
	Primary repair		SAR			Primary repair		SAR			Primary repair		SAR		
	N	%	N	%	p-value	N	%	N	%	P-value	N	%	N	%	P-value
Surgical procedure					0.000					0.000					0.003
Endovascular	3974	77%	365	69%		370	65%	41	55%		403	41%	47	55%	
Converted to open	5	0.1%	16	3.0%		3	0.5%	4	5.3%		7	0.7%	2	2,3%	
Open	1102	22%	93	18%		195	34%	20	27%		556	56%	32	37%	
Hybrid	24	0.5%	3	0.6%		2	0.3%	4	5.3%		11	1.1%	2	2.3%	
Other	31	0.6%	53	10%		4	0.7%	6	8.0%		10	1.0%	3	3.5%	
Postoperative complications					0.001					0.623					0.855
No complication	4100	80%	389	73%		386	67%	46	61%		315	32%	31	36%	
Surgical complication	284	5.5%	40	7.5%		38	6.6%	5	6.7%		134	14%	13	15%	
Non-surgical complication	586	11%	72	14%		116	20%	17	23%		334	34%	26	30%	
Surgical and non- surgical complication	155	3.0%	29	5.5%		34	5.9%	7	9.3%		197	20%	15	17%	
Unknown complication	11	0.2%	0	0.0%		0	0.0%	0	0.0%		7	0.7%	1	1.2%	
Permanent injury due to complication*					0.014					0.282					0.388
No	839	81%	100	71%		136	72%	17	59%		307	46%	20	36%	
Yes	129	13%	29	21%		38	20%	8	28%		296	44%	28	51%	
Unknown	65	6.3%	12	8.5%		14	7.4%	4	14%		67	10%	7	13%	
Reintervention within 30 days/in hospital					0.015					0.166					0.315
No	4896	96%	492	93%		536	94%	66	89%		789	80%	63	73%	
Yes	228	4.4%	38	7.2%		37	6.5%	8	10,8%		192	20%	22	26%	
Unknown	5	0.1%	0	0.0%		0	0.0%	0	0.0%		6	0.6%	1	1.2%	
Re-admission (within 30 days after discharge)	301	5.9%	30	5.7%	0.855	46	8.0%	9	12.2%	0.230	60	6.1%	6	7.1%	0.718
Postoperative mortality (30-days/in-hospital)	86	1.7%	18	3.4%	0.005	35	6.1%	8	10.7%	0.135	313	32%	25	29%	0.613

*Calculated in all patients with a postoperative complication

Figure 2. Type of primary surgical procedure followed by type of SAR in patients undergoing a primary AAA procedure after 2013 and a SAR between 2016-2017.

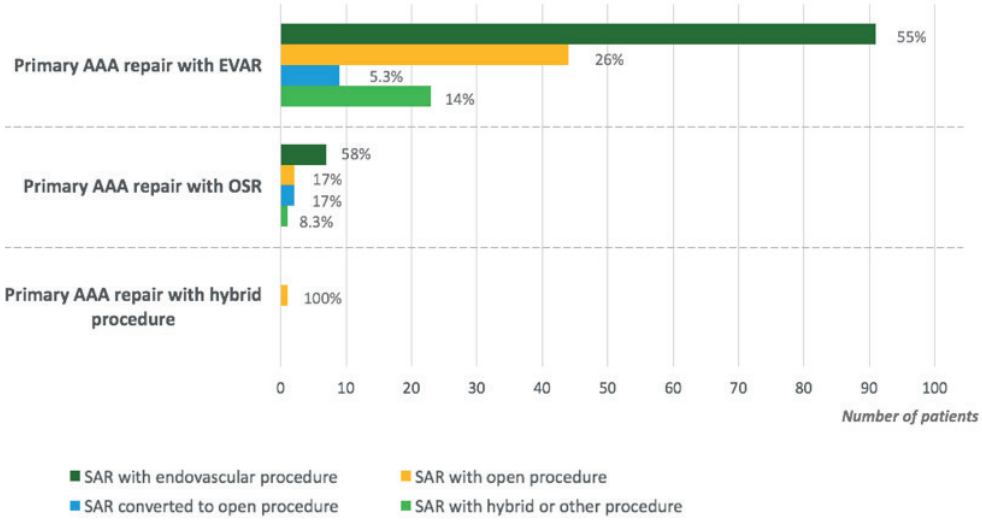
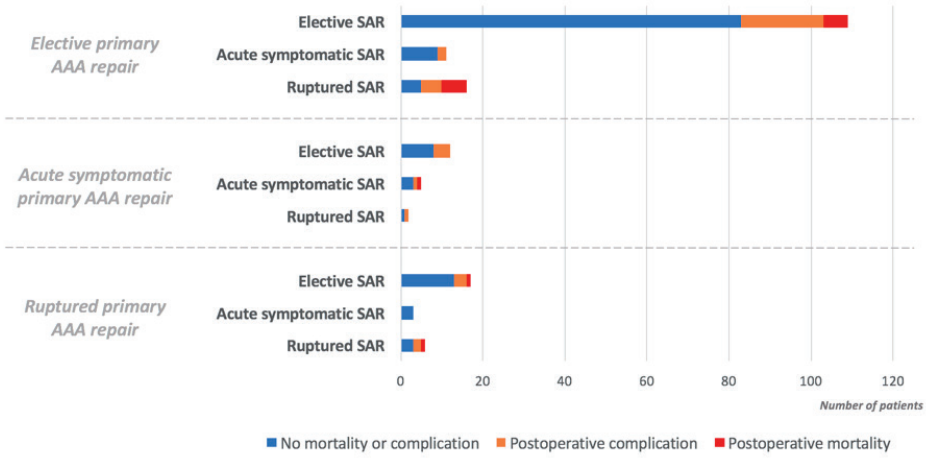


Table 4. The indication for secondary aortic reintervention per type of endovascular graft used in the primary AAA procedure

	Infected prosthesis		Endoleak		Progression of aneurysmatic disease		Unknown		Total	%	Use of endovascular prosthesis in the Netherlands 2013-2017
Nitinol/polyester	2	1.9%	87	84%	15	14.9%	0	0%	104	62%	76%
Nitinol/PTFE	3	21%	10	71%	1	7.1%	0	0%	14	8%	15%
Endovascular sealing	0	0%	28	80%	7	20%	0	0%	35	21%	4.9%
Other	0	0%	13	81%	2	13%	1	6.3%	16	9%	4.1%
	5	3.0%	138	82%	25	14.8%	1	0.6%	169	100%	100%

Figure 3. Urgency of primary surgical procedure followed by urgency of SAR in patients undergoing a primary AAA procedure after 2013 and a SAR between 2016-2017



DISCUSSION

Between January 2016 and December 2017, 691 patients underwent a SAR in the Netherlands, which counts for 9.3% of all AAA procedures performed. Endoleak was the most frequent indication for SAR. The majority of SARs was performed in an elective setting and more than half with an endovascular procedure. Postoperative mortality after SAR was 3.4%, 11% and 29% in respectively elective, acute symptomatic and ruptured AAA patients, which is in line with the results after primary procedures. About a quarter of the patients was previously registered in the DSAA for their primary AAA repair between 2013-2017 (=short/midterm SAR). This implies that the remaining three quarters had their primary AAA repair before the start of the audit and therefore information on their primary AAA repair (=long term SAR) is lacking.
The vast majority of SARs followed after primary DSAA registered EVAR procedures (169/181), in which an overrepresentation of endovascular sealing stents grafts was seen. Only half of these primary EVAR procedures could be treated with again an endovascular procedure during SAR. Furthermore, one-fifth of patients with a primary elective AAA procedure underwent an acute symptomatic or ruptured SAR.

Where elective EVAR is known to have a lower postoperative mortality than elective OSR, this survival benefit disappears after about two years.[11] In addition, it appears that EVAR entails more SARs, which in turn leads to higher costs. Although the follow-up study of the Open Versus Endovascular Repair (OVER) trial did not demonstrate higher overall secondary reintervention rate in patients treated with EVAR compared to OSR, the first follow-up

studies of the DREAM and EVAR-1 trial did.[4,5,12] However, these two studies did not include all laparotomy related reinterventions. More recently, 12 and 15-year follow-up studies of these same trials included all secondary reinterventions directly and indirectly related to the primary AAA repair and confirmed a significantly higher overall secondary reintervention rate in elective patients treated with EVAR compared to OSR.[6,7]. The same results were seen in a large American observational study.[11] To evaluate how the outcomes of these studies relate to daily practice (real world), you would ideally follow a large cohort of primary AAA patients, such as registered in the DSAA, over time.

Because the DSAA was initially set up without the registration of SARs, which was added only three years after the start of the audit, it is not (yet) possible to make statements about the national incidence of SARs following primary AAA (figure 1). However, almost 10 percent of all AAA procedures performed in 2016-2017 concerns a SAR. No other national quality registry ever reported their national annual volume of SARs and let alone the outcome.[13-16] Since EVAR was introduced in 1991 and now performed in a steady percentage of approximately 80% of elective AAA patients, one can state that the national annual number of SARs provides a good insight into the extent of the problem in daily practice.[9,17]

There is a presumption that the number of patients treated with EVAR outside the instructions for use (IFU) is increasing. Unfortunately, this is information not yet registered in the DSAA. Today only small series are reported, comparing outcomes after EVAR within and outside instructions for use, which showed conflicting results in postoperative outcomes and reintervention rates.[18-20] However other studies have already demonstrated that anatomical characteristics of the AAA are predictive for reintervention after EVAR.[21,22] Although larger studies with longer follow-up periods are needed to evaluate the influence treatment outside IFU on SARs, the increasing use of EVAR outside IFU most likely affects the number of SARs.

Whereas a new aneurysm, graft infection and graft stenosis are reported indications for SAR in patients primarily treated with EVAR or OSR, endoleak and graft migration only occurs in EVAR patients.[7,8,23-25] In the majority of our patients, endoleak (60%) was the indication for SAR. So probably at least 60% of all SARs performed between 2016-2017 followed after a primary EVAR procedure.

By merging data of SARs with data on the corresponding primary AAA procedures, we were able to provide insight into combined treatment characteristics in 26% of the DSAA. Whereas we already concluded that at least 60% of SARs in the total cohort occurred after a primary EVAR procedure, this was actually the case in 93% of the sub-cohort. This high percentage may partly be explained by the fact that about 70% of all primary AAA repairs is performed with EVAR.[9] Furthermore, we only report on SARs, where part of secondary reinterventions following primary OSR is not related to the aorta (i.e. laparotomy related).[5,11] Lastly, the maximal follow-up of 5 years and the way the audit was set up (i.e. missing the early SARs in 2013-2015) could have influenced the proportion of primary EVAR in this sub-cohort,

as SARs after primary EVAR usually occur at a different time of follow-up than SARs after primary OSR.[6,7,26] Additionally, as three-quarters of the SARs occur at least more than four years after the primary AAA repair, long term follow up seems to be necessary.

The large proportion of nitinol/polyester stent grafts in SAR patients from the sub-group analysis, is in accordance with the high percentage of national use of these stents. However, 21% of primary endovascular sealing stent grafts in SAR patients was significantly higher than the national use. The endovascular sealing system was designed to overcome common issues with endovascular systems, such as endoleak and graft migration, by which more patients with a difficult anatomy of the aorta might be eligible for treatment with an endovascular technique. Where previous studies demonstrated that these endovascular sealing systems were safe and had low SAR rates, others raised their concerns about more reinterventions and risk of rupture.[27-30] Again, the missing early SARs of patients undergoing primary AAA repair between 2013-2015 in our study could have influenced the proportion of different stent grafts in our sub-cohort. Furthermore, it is unclear how many and which patients were treated outside instructions for use. Nevertheless, the significant overrepresentation of endovascular sealing stent grafts in national SARs is an important finding of this study and needs further attention.

This study has some limitations that need to be addressed. As the audit exclusively registers surgical aortic procedures, we were only able to evaluate surgical SARs. All laparotomy related secondary reinterventions, such as incisional hernia repair and bowel obstruction, that may be needed after primary OSR and all SAR performed by the interventional radiologist are therefore not included in this analysis. Both would probably have increased the number of secondary reinterventions performed after primary AAA surgery considerably. Secondly, as only patients undergoing surgery are registered, the number of SARs performed does not necessarily correspond to the number of SARs required. Possibly only patients that are fit enough (and did not die) undergo SAR, by which selection-bias might be present. The number of SARs presented in this study will, therefore, be an underestimation of the actual number of SARs that is performed (and possibly required) after primary AAA surgery in the Netherlands.

Where part of our analyzes are now hampered due to missing SARs in the period 2013-2015, with time the DSAA will be a complete registration of primary AAA repairs and subsequent SARs. With a few more years of auditing, it will be possible to provide a national incidence of SAR and to evaluate differences in national SAR-rates between surgical techniques and additionally between the type of EVAR stent grafts that are used. The latter is an important step forward, as the audit can serve to detect problems with specific stent grafts at an early stage. In addition, one-fifth of patients with an initial elective primary AAA repair underwent SAR in an urgent or acute setting, with the associated increased morbidity, which indicates

there might be room for improvement. Finally, as we know that SARs are frequently needed after EVAR, it is a challenge to find out how the optimal follow-up after EVAR should look like.

CONCLUSION

Data from the Dutch Surgical Aneurysm Audit shows that about one-tenth of the annual AAA procedures concerns a SAR. Endoleak was the most frequent reason for SAR. About a quarter of SAR patients had a SAR within 1-5 years after their primary AAA repair. The majority of SARs were performed after a primary EVAR procedure, in which an overrepresentation of endovascular sealing stent grafts was seen. Furthermore, only half of primary EVAR procedures could again be treated with an endovascular procedure during SAR. Postoperative mortality after SAR is comparable to primary AAA repair in all urgency settings. Additionally, there were more postoperative complications after elective SARs compared to elective primary AAA repairs.

REFERENCES

1. Greenhalgh RM, Brown LC, Kwong GP, Powell JT, Thompson SG, participants Et. 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(9437):843-848.
2. Lederle FA, Freischlag JA, Kyriakides TC, et al. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. *JAMA.* 2009;302(14):1535-1542.
3. Prinssen M, Verhoeven EL, Buth J, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med.* 2004;351(16):1607-1618.
4. De Bruin JL, Baas AF, Buth J, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1881-1889.
5. United Kingdom ETI, Greenhalgh RM, Brown LC, et al. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1863-1871.
6. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM, investigators Et. 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. *Lancet.* 2016;388(10058):2366-2374.
7. van Schaik TG, Yeung KK, Verhagen HJ, et al. Long-term survival and secondary procedures after open or endovascular repair of abdominal aortic aneurysms. *J Vasc Surg.* 2017;66(5):1379-1389.
8. Al-Jubouri M, Comerota AJ, Thakur S, et al. Reintervention after EVAR and open surgical repair of AAA: a 15-year experience. *Ann Surg.* 2013;258(4):652-657; discussion 657-658.
9. DSAA annual report 2017. 2017; http://dica.nl/jaarrapportage-2017/home.
10. Dataverification Dutch Surgical Aneurysm Audit 2015. [PDF]. http://dica.nl/media/660/Eindrapport_dataverificatie_DSAA_2016.pdf, 2016.
11. Schermerhorn ML, Buck DB, O'Malley AJ, et al. Long-Term Outcomes of Abdominal Aortic Aneurysm in the Medicare Population. *N Engl J Med.* 2015;373(4):328-338.
12. Lederle FA, Freischlag JA, Kyriakides TC, et al. Long-term comparison of endovascular and open repair of abdominal aortic aneurysm. *N Engl J Med.* 2012;367(21):1988-1997.
13. NVR-VSQIP. NVR-VSQIP annual report 2017. https://www.vsqip.org.uk/reports/2017-annual-report/.
14. Swedvasc. Swedvasc annual report 2017. http://www.ucr.uu.se/swedvasc/arsrapporter/swedvasc-2018/viewdocument.
15. GermanVasc. https://germanvasc.de/.
16. Karbase. Karbase annual report 2017. http://karbase.dk/onewebmedia/Karbase A%CC%8Arsrapport 2017 pdf.pdf.
17. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. *Ann Vasc Surg.* 1991;5(6):491-499.
18. Beckerman WE, Tadros RO, Faries PL, et al. No major difference in outcomes for endovascular aneurysm repair stent grafts placed outside of instructions for use. *J Vasc Surg.* 2016;64(1):63-74 e62.
19. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y. Outcomes following endovascular abdominal aortic aneurysm repair both within and outside of the instructions for use. *Ann Thorac Cardiovasc Surg.* 2014;20(1):61-66.
20. Nakai M, Sato M, Sato H, et al. Midterm results of endovascular abdominal aortic aneurysm repair: comparison of instruction-for-use (IFU) cases and non-IFU cases. *Jpn J Radiol.* 2013;31(9):585-592.
21. Pitoulias GA, Valdivia AR, Hahtapornsawan S, et al. Conical neck is strongly associated with proximal failure in standard endovascular aneurysm repair. *J Vasc Surg.* 2017;66(6):1686-1695.
22. Ohrlander T, Dencker M, Acosta S. Morphological state as a predictor for reintervention and mortality after EVAR for AAA. *Cardiovasc Intervent Radiol.* 2012;35(5):1009-1015.
23. Quinney BE, Parmar GM, Nagre SB, et al. Long-term single institution comparison of endovascular

aneurysm repair and open aortic aneurysm repair. *J Vasc Surg.* 2011;54(6):1592-1597; discussion 1597-1598.

24. Mehta M, Sternbach Y, Taggert JB, et al. Long-term outcomes of secondary procedures after endovascular aneurysm repair. *J Vasc Surg.* 2010;52(6):1442-1449.
25. Bartoli MA, Thevenin B, Sarlon G, et al. Secondary procedures after infrarenal abdominal aortic aneurysms endovascular repair with second-generation endografts. *Ann Vasc Surg.* 2012;26(2):166-174.
26. Krishnamoorthi H, Jeon-Slaughter H, Wall A, et al. Rate of Secondary Intervention After Open Versus Endovascular Abdominal Aortic Aneurysm Repair. *J Surg Res.* 2018;232:99-106.
27. Gossetti B, Martinelli O, Ferri M, Silingardi R, Verzini F, Investigators IG. Preliminary results of endovascular aneurysm sealing from the multicenter Italian Research on Nellix Endoprosthesis (IRENE) study. *J Vasc Surg.* 2018;67(5):1397-1403.
28. Carpenter JP, Cuff R, Buckley C, et al. One-year pivotal trial outcomes of the Nellix system for endovascular aneurysm sealing. *J Vasc Surg.* 2017;65(2):330-336 e334.
29. van den Ham LH, Holden A, Savlovskis J, et al. Editor's Choice–Occurrence and Classification of Proximal Type I Endoleaks After EndoVascular Aneurysm Sealing Using the Nellix Device. *Eur J Vasc Endovasc Surg.* 2017;54(6):729-736.
30. Harrison SC, Winterbottom AJ, Coughlin PA, Hayes PD, Boyle JR. Editor's Choice–Mid-term Migration and Device Failure Following Endovascular Aneurysm Sealing with the Nellix Stent Graft System–a Single Centre Experience. *Eur J Vasc Endovasc Surg.* 2018;56(3):342-348.

Carotid artery surgery

CHAPTER 8

The Dutch Audit for Carotid Interventions: Transparency in Quality of Carotid Endarterectomy in Symptomatic Patients in the Netherlands

E.G. Karthaus, A.C. Vahl, L.S. Kuhrij, B.H.P Elsman, R.H. Geelkerken, M.W.J.M. Wouters, J.F. Hamming, G.J. de Borst

European Journal for Vascular and Endovascular Surgery 2018

ABSTRACT

Background & objective

The Dutch Audit for Carotid Interventions (DACI) registers all patients undergoing interventions for carotid artery stenosis in the Netherlands. We describe the design of the DACI and results of patients with a symptomatic stenosis undergoing carotid endarterectomy (CEA). We aimed to evaluate variation between hospitals in process of care and (adjusted) outcomes, as well as predictors for major stroke/death after CEA.

Methods

We identified all patients with a symptomatic stenosis, undergoing CEA and registered in the DACI between 2014-2016. Descriptive analyses on patient characteristics, process of care and outcomes were performed. Case-mix adjusted hospital procedural outcomes as (30-day/in-hospital) mortality, stroke/death and major stroke/death, were compared with the national mean. A multivariable logistic regression model (backward elimination at $p>0.10$) was used to identify predictors for major stroke/death.

Results

6459 patients, registered by 52 hospitals, were included. The majority (4832, 75%) was treated <2 weeks after their first hospital consultation, varying from 40-93% between hospitals. Mortality, stroke/death and major stroke/death were respectively 1.1%, 3.6% and 1.8%. Adjusted major stroke/death rates for hospital comparison varied between 0-6.5%. Nine hospitals performed significantly better, none performed significantly worse. Predictors for major stroke/death were: sex, age, pulmonary disease, presenting neurologic symptoms and perioperative shunt.

Conclusion

CEA in the Netherlands is associated with an overall low mortality and (major) stroke/death. Whereas the indicator time-to-intervention varied between hospitals, mortality and (major) stroke/death are not significantly distinctive to identify worse practices and therefore unsuitable for hospital comparison in the Dutch setting. Additionally, predictors for major stroke/death on population level could be identified.

INTRODUCTION

In patients with a recent transient ischemic attack (TIA) or ischemic stroke in the presence of a high-grade ipsilateral carotid artery stenosis, recurrent stroke can be best prevented by carotid endarterectomy (CEA).[1] Optimal care for patients undergoing carotid artery surgery is summarized in guidelines, based on large randomized controlled trials.[1-4] However, actual daily practice is not always consistent with these guidelines, allowing practice and patient outcomes to vary between healthcare providers.[5] This variation could indicate a difference in quality of care on a national level.

The increasing demand for quality-control methods and the introduction of a minimum threshold on hospital volume of 20 CEA per year in the Netherlands has led to the initiation of the Dutch Audit for Carotid Interventions (DACI).[6] This nationwide audit was initiated in 2012 and mandatory since June 2013 for all vascular surgeons performing carotid artery interventions. The main objective of this audit is to measure and improve quality of care in carotid artery interventions in the Netherlands. By registering important parameters on process of care and patient outcomes, a comparison of hospitals can be made and surgeons can be provided with benchmarked information on their quality of care. Providing insight into possible variation between hospitals can subsequently incite quality improvement. Additionally, information from the DACI can be used to monitor national guideline adherence and outcomes in patients undergoing carotid interventions.

This report describes the design of the DACI and provides an overview of the results of patients with a symptomatic carotid artery stenosis undergoing CEA in the Netherlands in the first years of the audit. It was our aim to report evaluation of variation between hospitals in processes of care and (adjusted) patient outcome, as well as identification of independent predictors for major stroke and/or death related to CEA.

METHODS

DICA

The DACI is facilitated by the Dutch Institute for Clinical Auditing (DICA).[6] The DICA facilitates and organizes the initiation of nationwide audits for various medical professions and offers a uniform format. In collaboration with DICA, the Dutch Society for Vascular Surgery initiated the Dutch Audit for Carotid Interventions (DACI). The DACI is related to a scientific committee, which is responsible for the interpretation and accountability of the data.

DACI data source

Since June 2013, the DACI is mandatory for all vascular surgeons and registers all patients undergoing a carotid intervention because of a high-grade carotid artery stenosis in the Netherlands. This includes CEA with or without patch angioplasty, eversion CEA or carotid artery stenting (CAS). Of each registered patient 77 items, grouped into three categories, are scored (appendix 1.). The first category includes patient characteristics and clinical presentation required to enable an adjusted comparison of data between hospitals. The second category includes items regarding the process of care and surgical treatment. The postoperative period and patient outcomes (30-day/in-hospital) are registered in the third category. The data is prospectively collected via a web-based survey or provided by the hospitals via a batch data file. Hospitals may decide who registers the data (e.g. data managers, nurse practitioners or physician). However, in all participating hospitals the final responsibility for registration of patients lies with the physician. The content of the dataset is evaluated on an annual basis and if necessary alterations are made. Verification of the DACI data was carried out in 2015 by a third trusted party. The process of verification was coordinated by an independent data verification committee, which consisted of medical experts, a biostatistician, a deputy of the Dutch Health Care Inspectorate and a deputy from the Dutch patient federation. Data was verified through a random sample of 15 hospitals, and will be continuously repeated in the future.

Patient selection

All patients undergoing CEA for a symptomatic stenosis and registered in the DACI between January 2014 and December 2016 were included. Date of birth, date of surgery, type of surgical procedure performed and patient survival status (30-days/in-hospital) had to be known to consider a patient eligible for further analysis. In the Netherlands, asymptomatic patients usually do not receive surgical intervention outside the margins of randomized clinical trials and CAS is not performed as standard primary treatment for a symptomatic carotid stenosis, therefore asymptomatic patients and patients treated with CAS were excluded. Additionally, patients treated in a hospital that stopped performing CEA's during the first year of the study period were also excluded.

Definitions

Within the DACI, time-to-intervention was defined as the time from first consultation at the hospital until CEA, instead of the time from first neurological symptoms until intervention, because this is the timeframe that hospitals can influence themselves and can improve. Postoperative mortality was defined as mortality within 30 days after CEA and/or during the primary admission (30-day/in-hospital). A postoperative stroke was described as a new neurological deficit 30-day/in-hospital, which lasted longer than 24 hours. A stroke resulting in a decline of more than 2 points in postoperative modified Rankin Scale (mRS) was considered as a major stroke, all other strokes as a minor stroke.[7,8] The combined outcome

parameters stroke and/or death (stroke/death) and major stroke and/or death (major stroke/death) consists the patients who had a (major) stroke and/or death 30-day/in-hospital. Cranial nerve injury (CNI) was defined as the loss of function of a cranial nerve, measured 30-day/in-hospital. Only a postoperative wound hemorrhage that required a re-intervention was considered as a postoperative wound hemorrhage.

Analyses

Descriptive analyses for patient characteristics, process of care and patient outcomes were performed. The percentage of patients with a time-to-intervention of <2 weeks, was calculated per hospital and compared with the national mean in a funnel plot. The national mean was derived from this dataset.

Possible associations between patient characteristics and outcomes, as mortality and (major) stroke/death were evaluated with a multivariable logistic regression model at a p-value of 0.05 using an ENTER model. This analysis was used to adjust hospital outcomes for the case-mix of their patients. Patient characteristics included in this analysis were based on the V(p)-POSSUM predictive score: sex, age, pulmonary status, cardiac status, preoperative electrocardiogram, preoperative creatinine level and presenting symptoms.[9] A funnel plot with a confidence interval (CI) of 95% around the national mean was used to show hospital variation for case-mix adjusted outcomes. Hospitals with a significantly lower major stroke/death than the national mean were identified as 'hospitals with better outcomes' and hospitals with a higher major stroke/death as 'hospitals with worse outcome'. Hospital and practice related factors were compared between hospitals with better outcomes and the other hospitals using chi-square tests. Finally, to identify risk factors for postoperative major stroke/death, a prediction model was formed, using a multivariable logistic regression model at a p-value of 0.10 with backward elimination.

For missing data in continuous variables, the mean of each variable was imputed. Missing data in continuous variables were not exceeding 5% of the total of each variable.

RESULTS

Patient characteristics

From January 2014 to December 2016, 6861 patients with a carotid artery stenosis undergoing carotid intervention were registered by 52 hospitals in the Netherlands. After exclusion of all asymptomatic patients (274, 4.0%), all patients treated with CAS (122, 1.9%) and patients operated in a hospital that stopped performing CEA's during the study period (6, 0.9%), 6459 patients were eligible for analysis and included in this study. The cohort consisted predominantly of males (4479, 69%) and had a mean age of 72.1 years. Patient characteristics are shown in Table 1.

Table 1. Patient and disease characteristics

	2014-2016	
Number of patients	6459	
Age	72.1 ± 9.3	
Sex		
Male	4479	69%
Female	1980	31%
Comorbidity		
Malignancy		
None	5485	85%
Current malignancy	152	2.4%
History of malignancy, curatively treated	822	13%
Pulmonary status		
No dyspnea	5117	79%
Dyspnea during exercise	1079	17%
Disabling dyspnea	161	2.5%
Dyspnea at rest/fibrosis	34	0.5%
Unknown	68	1.1%
Cardiac status		
None	2155	33%
Medication for hypertension	3624	56%
Peripheral edema	589	9.1%
Raised CVP	71	1.1%
Unknown	20	0.3%
Preoperative ECG		
No abnormalities	3616	56%
Atrial fibrillation	428	6,60%
Ischemia	127	2.0%
Other abnormalities	2062	32%
No preoperative ECG performed	226	3.5%
Preoperative laboratory results		
Hemoglobin	8.6 ± 1.04	
Sodium	139 ± 3.00	
Potassium	4.2 ± 0.42	
Creatinine	86 IQR 31	
Preoperative systolic blood pressure	148 ± 23.0	
Preoperative heart rate	74 ± 13.7	
Side of carotid artery stenosis		
Left	3318	51%
Right	3103	48%
Unknown	38	0.6%
Presenting symptoms		
Ocular symptoms	1192	19%
Cortical symptoms	5158	79%
Vertebrobasilar and other	109	1.7%
Previous CEA		
None	6162	95%
Yes, ipsilateral	66	1.0%
Yes, contralateral	218	3.4%
Yes, both sides	13	0.2%

Clinical presentation and process of care.

The majority of patients presented with cortical symptoms (5158, 79%) (table 1). In 75% (4832) of patients the time-to-intervention was <2 weeks after the first hospital consultation. Figure 1a shows the hospital comparison of the percentage patients undergoing CEA <2 weeks after the first consultation. The median time-to-intervention varied between hospitals from 7-16 days.

A CEA with patch angioplasty was performed in the majority of patients (4958, 77%), followed by eversion CEA (808, 12%) or CEA without patch angioplasty (693, 11%) (table 2). General anesthesia during intervention was used in 94% of all patients, in which 93% intraoperative neurologic monitoring was used. Intraoperative shunting was used in 20% of all patients undergoing CEA, of which 69% was carried out with intra-operative neurologic monitoring and 31% was done without. A small minority of 16 patients (0.2%) received no intraoperative neurological monitoring and no shunt, while operated under general anesthesia.

Clinical Outcomes

The 30-day/in-hospital postoperative mortality was 1.1% (69) (table 3.). Mortality rates slightly differed between surgical procedures, but differences were not significant: CEA with patch angioplasty 0.4%, CEA without patch angioplasty 1.6% or eversion CEA 0.9% (P = 0.371). Of all patients, 3.2% (206) had a postoperative stroke, of which 62% (127) had a minor stroke and 38% (79) had a major stroke. The combined major stroke/death and any stroke/death rate were 1.8% (115) and 3.6% (235) respectively. CNI and postoperative wound hemorrhage were observed in 2.8% (183) and 4.1% (262) of patients respectively. A re-intervention was performed in 4.7% (305), of which the majority (86%) was indicated because of a postoperative wound hemorrhage and in 14% the indication was unknown.

Hospital comparison of outcomes

The multivariable logistic regression analyses for mortality, major stroke/death and stroke/death are displayed in table 4. Pulmonary state (severe dyspnea) and presenting with cortical symptoms were found to be significantly associated with all three outcome measures. Increasing age and female gender were associated with mortality and major stroke/death. Abnormalities on the last pre-operative electrocardiogram were associated with stroke/death.

Figure 1b-d shows the case-mix adjusted outcomes for respectively mortality, major stroke/death and any stroke/death by hospital volume for individual hospitals. The case-mix adjusted mortality, major stroke/death and any stroke/death rates varied respectively from 0-6.5%, 0-6.4% and 0-9.6% between hospitals. Five hospitals had a significantly lower adjusted percentage stroke/death, when compared to the national mean. Additionally, nine hospitals had a significantly lower adjusted percentage major stroke/death. No hospital performed significantly worse than the mean.

Figure 1a Hospital comparison of time to intervention

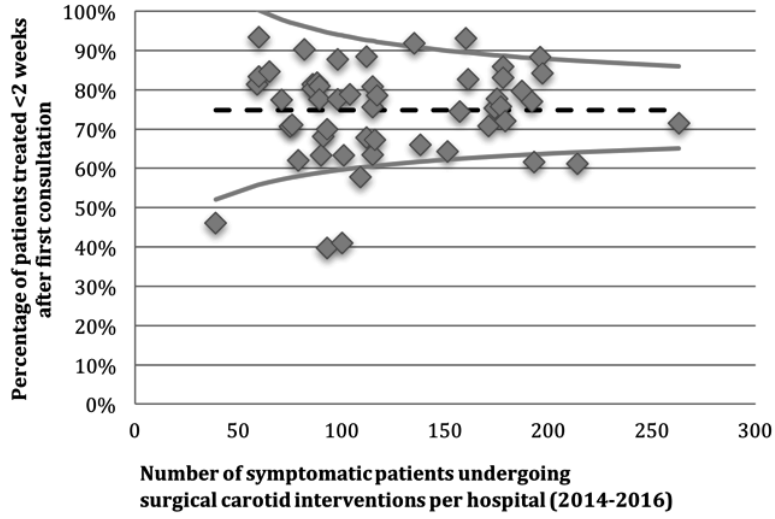


Figure 1b Hospital comparison for mortality

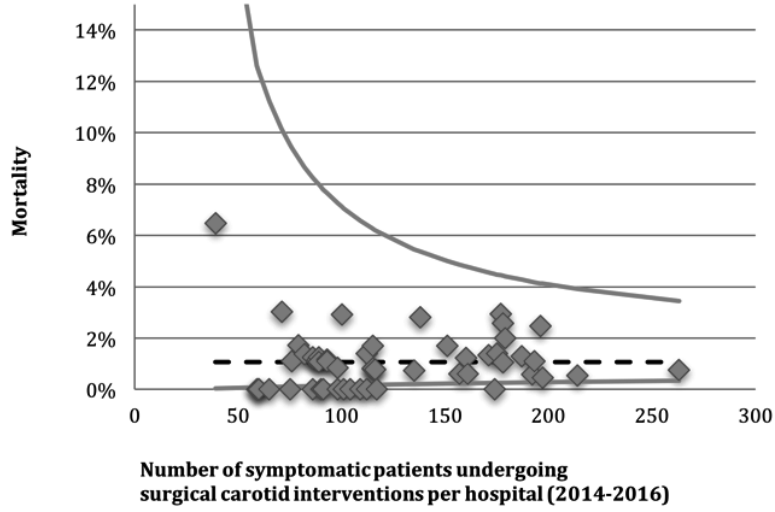


Figure 1c. Hospital comparison for Major Stroke and/or death

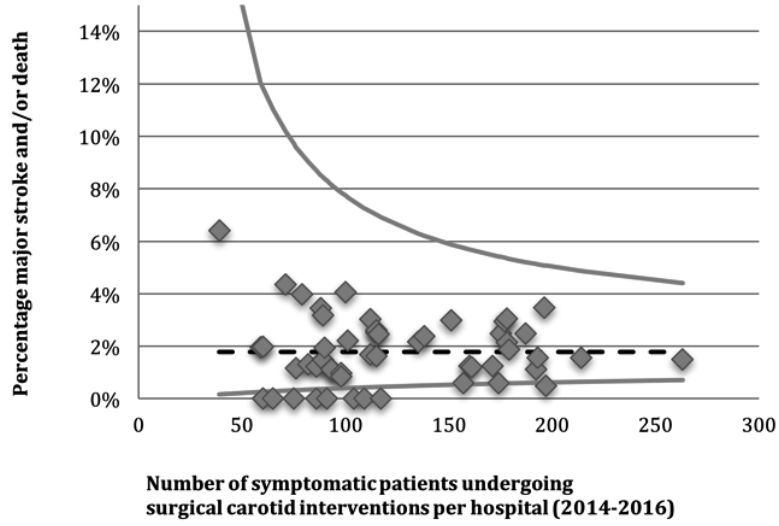


Figure 1d Hospital comparison for stroke and/or death

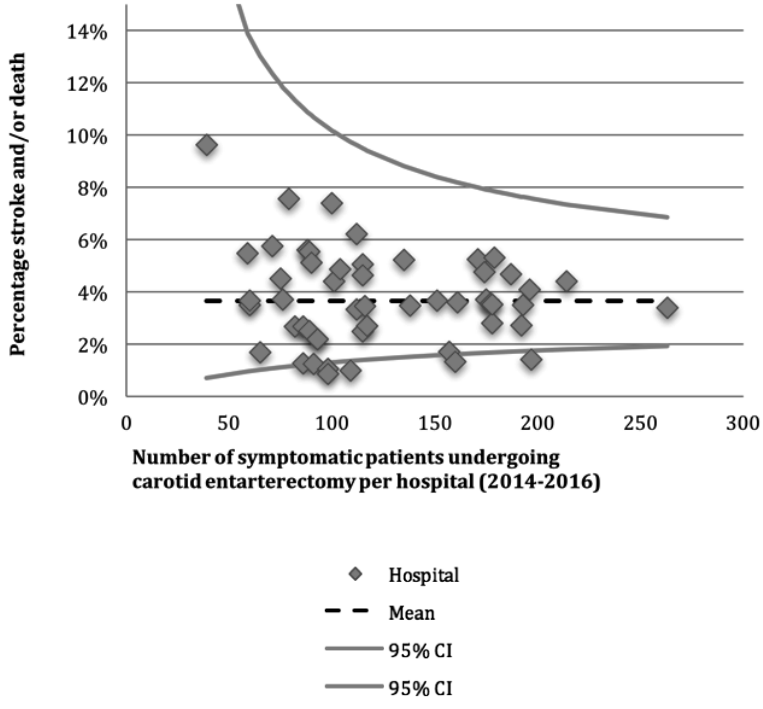


Table 2. Treatment characteristics.

	2014-2016	
Number of patients	6459	
Imaging*		
Duplex	6311	98%
CTA	4237	66%
MRA	1313	20%
DSA	35	0.5%
Referral		
Internally	5267	82%
Tertiary	1188	18%
Unknown	4	0.1%
Time until carotid intervention**		
< 2 weeks	4832	75%
> 2 weeks	1582	25%
Unknown	45	0.7%
Surgical procedure		
CEA without patch angioplasty	693	11%
CEA with patch angioplasty	4958	77%
Eversion CEA	808	12%
Anesthesia		
Local anesthesia	368	5.7%
General anesthesia	6084	94%
Unknown	7	0.1%
Neurologic monitoring		
No monitoring	435	6.7%
Awake patient	314	4.9%
EEG	2822	44%
Stump pressure	130	2.0%
EEG & TCD	2693	42%
Other combinations	65	1.0%
Shunting during surgery		
No shunting	4629	72%
Shunting	1262	20%
Unknown	568	8.8%
Postoperative medication		
Acetylsalicylic acid	2441	38%
Statin	5519	85%
Dipyridamole	851	13%
Coumarin	364	5.6%
Clopidogrel	4247	66%
Antihypertensive medication	4348	67%
New anticoagulants	90	1.4%
Heparin***	5378	83%

* In 79.9% a combination of diagnostic imaging was used.
** Time from first consultation at the hospital until CEA.
*** Postoperative use of heparin as venous thromboembolism prophylaxis is protocoled in the Netherlands

Table 3. Outcomes 30 days postoperatively and/or during admission

	2014-2016	
Number of patients	6459	
Postoperative period		
Stroke	206	3.2%
Cranial nerve injury	183	2.8%
Hemorrhage	262	4.1%
Complications		
Other surgical complication	109	1.7%
General complication	384	5.9%
Other	108	1.7%
Reintervention	305	4.7%
Death	69	1.1%
Major stroke and/or mortality	115	1.8%
Stroke and/or mortality	235	3.6%

Table 4. Patient characteristics predictive for Mortality, Stroke / Mortality and Major Stroke/ Mortality.

	Mortality		Major Stroke / Mortality		Stroke / Mortality	
	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Number of patients	6459		6459		6459	
Age	1.05	1.015-1.077	1.035	1.012-1.058	1.014	0.999-1.030
Sex						
Male	Ref		Ref		Ref	
Female	1.970	1.217-3.187	1.585	1.074-2.337	1.218	0.917-1.616
Pulmonary State						
No dyspnea	Ref		Ref		Ref	
Dyspnea	0.529	0.238-1.178	0.803	0.472-1.368	1.047	0.740-1.481
Severe dyspnea	3.978	1.907-8.298	3.013	1.567-5.795	2.323	1.373-3.930
Cardiac State						
No abnormalities*	Ref		Ref		Ref	
Cardiac co-morbidities	1.188	0.675-2.090	1.265	0.809-1.893	1.280	0.933-1.757
Last preoperative ECG						
No abnormalities	Ref		Ref		Ref	
Abnormalities (atrial fibrillation, ischemia and others)	1.402	0.848-2.317	1.282	0.868-1.893	1.470	1.116-1.936
Presenting symptoms						
Ocular symptoms	Ref		Ref		Ref	
Cortical symptoms	3.065	1.109-8.472	2.345	1.179-4.664	2.345	1.179-4.664
Vertebrobasilar or other symptoms	2.320	0.255-21.086	2.175	0.462-10.252	2.175	0.462-10.252
Preoperative laboratory results						
Creatinine			1.001	0.996-1.005	1.001	0.996-1.005

**Preoperative creatinine level not included in the multivariable logistic regression analysis for mortality because of the limited degrees of freedom.*

As shown in table 5, the patients operated in the 9 hospitals with better outcomes, were more frequently referred from other hospitals, compared to patients operated in hospitals with a major stroke/death within the CI's. In contrast, these 9 hospitals were more often hospitals with relatively lower volumes. The time-to- intervention did not differ between the two groups. General anesthesia and CEA without patch angioplasty were more frequently used in these 9 hospitals compared to the other hospitals. Additionally, perioperative shunting was less often performed in these 9 hospitals.

Patient, practice and hospital related factors predictive for major stroke/death

Sex, age, pulmonary state, neurologic presenting symptoms and perioperative shunting are predictive for major stroke/death, with an area under the curve of 0.691 (table 6). All

Table 5. Comparison of hospital related factors between hospital with a lower percentage major stroke/ death and hospitals performing within the CI's

	Not treated in 'best practice'		Treated in 'best practices'		
	N = 5555	%	N =904	%	P
Referral					
Internal	4633	83%	634	70%	.000
Tertiary	920	17%	268	30%	
Hospital volume (3 years)					.000
Low volume (0-110)	1668	30%	590	65%	
Normal volume (111-175)	2107	38%	117	13%	
High volume (176-263)	1780	32%	197	22%	
Time to intervention					
>2 weeks	1383	25%	199	22%	.170
<2 weeks	4134	74%	698	77%	
Unknown	38	0.7%	7	0.8%	
Anesthesia					.000
Local	363	6.5%	6	0.7%	
General	5193	94%	898	99%	
Surgical procedure					.000
CEA without patch	554	10%	139	15%	
CEA with patch	4303	78%	655	73%	
Eversion CEA	698	13%	110	12%	
Perioperative shunting					.000
No shunting	3901	70%	728	81%	
Shunting	1159	21%	103	11%	
Unknown	495	8.9%	73	8.1%	
Neuro-monitoring					.000
No monitoring	428	7.7%	7	0.8%	
EEG	2283	41%	539	60%	
Stump pressure	130	2.3%	0	0.0%	
Awake patient	314	5.7%	0	0.0%	
EEG / TCD	2342	42.2%	351	38.8%	
Other (combinations of) monitoring	58	1.0%	7	0.8%	

Table 6. Factors predictive for major stroke/death

	Odds ratio	95% CI's
Age	1.038	1.016-1.061
Sex		
Male	Ref	
Female	1.486	1.017-2.170
Pulmonary State		
No dyspnea	Ref	
Dyspnea	0.821	0.484-1.392
Severe dyspnea	3.300	1.718-6.340
Presenting symptoms		
Ocular symptoms	Ref	
Cortical symptoms	2.130	1.068-4.246
Vertebrobasilar or other symptoms	2.113	0.448-9.966
Perioperative shunting		
No shunting	Ref	
Shunting	2.484	1.664-3.707
Unknown	1.708	0.910-3.207

Eliminated variables: heart rate, potassium, hospital volume, hemoglobin, creatinine, anesthesia, systolic blood pressure, sodium, surgical procedure, cardiac state, time to intervention, neurologic monitoring, preoperative ECG.

patient, treatment and hospital related factors used in this analyses that were proven not to be predictive for major stroke/death are shown at the bottom of table 6.

DISCUSSION

The DACI has been successfully implemented in the Netherlands and covers all Dutch centers, which allows evaluation of quality of care in CEA nationally and between hospitals. In the Netherlands, CEA is performed with an overall low mortality and (major) stroke/death rate and a reasonable guideline adherence, considering time-to- intervention. Whereas time-to-intervention showed significant variation between hospitals, outcome indicators as mortality and (major) stroke/death are not very distinctive due to low overall event rates and no hospitals with a significantly higher event rate. The lack of hospitals with worse outcomes in these indicators hampers a national hospital comparison in the era with a minimum volume of 20 CEA per year per hospital. However, 9 hospitals with a significantly lower major stroke/death rate than the national mean could be identified, from which others possibly could learn. Additionally, predictors for major stroke/death after CEA in symptomatic patients could be identified with the use of DACI data.

Clinical audits are increasingly appreciated as a tool for quality improvement in surgical care and have proven to be effective.[10] A clinical audit provides insight in the process of care and patient outcomes and enables comparison with other healthcare providers, so that areas for

improvement can be identified and targeted improvements can be started. Moreover, with a nationwide audit, volume standards and national guideline adherence can be monitored. For carotid artery interventions, several national audits have been successfully initiated in recent years.[11-13] Additionally, some countries are collaborating in VASCUNET, a subcommittee of the European Society of Vascular Surgery, which makes it possible to compare practice between countries.[5] The percentage of asymptomatic patients undergoing CEA in other European countries varies from <1% to 53%.[5,11] In the DACI 93% of patients had a symptomatic stenosis and 75% of these patients was treated <2 weeks after their first consultation in the hospital, with a variation of 40%-93% between hospitals. Our national guideline aims to treat at least 80% of symptomatic patients <2 weeks after first consultation, consequently this leaves room for improvement. A score of 100% may not be realistic, as patient delay can always occur. Besides the Scandinavian countries, in which 82.5% of patients are treated <2 weeks, most countries are dealing with logistic obstacles to treat symptomatic patients within this term.[11,14] As we know that the risk of a recurrent stroke is the greatest in the first days after the index-event, ideally symptomatic patients should be treated even sooner.[15] Therefore, time-to-intervention will remain a topic of attention and possibly the allowed timeframe will be shortened in the future. The stroke/death rate in the DACI is comparable with outcomes in other audits, with stroke/death rates varying between 0,9%–4.6%.[5,12,14,16-18] It should be noted that national audits often use the outcome measure any stroke/death while the landmark trials also used major stroke/death.[19,20] We believe it is important to make a distinction in the severity of a postoperative stroke and that major stroke/death is a more uniform measure.
CNI and postoperative wound hemorrhage, measured 30 days/in-hospital, were respectively 2.8% and 4.1%. The reported frequencies of CNI vary widely in other studies, as the study design, method of diagnosing the injury and whether or not the patient was assessed by a neurologist also varies per study. This last point is also applicable to the DACI, which entails the risk of underreporting of stroke and/or CNI. However, it has been shown that the majority of CNI will resolve over the first few months and permanent CNI is rare.[21,22]

Additionally, this study shows a hospital comparison of outcomes after CEA in symptomatic patients. With our national minimum threshold of 20 CEA per year per hospital, the majority of hospitals have outcomes comparable with the national mean and there are no hospitals performing worse. In order to improve quality of care, one should look for 'best practice hospitals' or variation between hospitals. An outcome measure like mortality, with a low event rate, shows little variation between hospitals. Some hospitals had no mortality, but this was often not significantly better than the mean. With the outcome measure any stroke/death and major stroke/death, more variation was observed and respectively five and nine hospitals with a significantly lower (major) stroke/death rate could be observed. However, most hospitals perform within the CI's. When comparing those 9 hospitals with a significant lower major stroke/death rate than the national mean with the other hospitals, some differences in practice

were seen. Those 9 hospitals mostly had lower volumes, however this is relative and therefore the minimum volume of 20 seems to be sufficient. Patients were more often referred, general anesthesia was more often performed and in almost all patients intraoperative neurologic monitoring was used. Furthermore, perioperative shunting was less often used in these 9 hospitals, which appeared to be predictive for major stroke/death. Noteworthy, is that previous studies showed contradictory results about the association between perioperative shunting and (major) stroke/death.[23,24] Further research is needed to confirm this association. Patient and disease related factors as female sex, increasing age, severe dyspnea and cortical symptoms as presenting symptoms were predictive for major stroke/death in symptomatic patients, which was partly confirmed in a previous study.[25] Whereas another study showed that cardiac disease was also predictive for (major) stroke/death. Additionally, Smoking, diabetes and the emergency of the surgery were proven to be predictive for (major) stroke/death, but these variables were not included in our model.[17,26,27]

Although some differences in outcomes were observed, no hospitals with significantly worse practice could be identified. This may be caused by the low event rate. In the future, other ways to identify the possible existing variation in quality of care of CEA between hospitals need to be explored. A possible solution, that was recently tested for aortic aneurysm surgery, could be the development of a composite measure, Textbook Outcome, combining process and outcome measures by which a more complete picture of care can be provided.[28]

In its current form, the DACI has several limitations. Since the DACI is an audit for carotid interventions, it does not contain information on patients that did NOT receive surgical treatment. Therefore, the audit does not provide information on intervention-rate and neurologic outcome of all patients with a symptomatic stenosis. With a future link between data from the DACI and data from the Dutch Acute Stroke Audit, this will be possible. With this link, the timeframe between first event and intervention can also be provided, which is more important from a patient perspective. Secondly, the severity of the presenting stroke was not captured in all symptomatic patients, which is important if you want to compare hospitals as fair as possible on patient outcomes. This will be altered in the next update of the web-survey. The data is self-reported so it is possible that the reported mortality and complications are slightly underestimated. A continuously repeated independent data verification will be carried out to minimize this possible discrepancy. Additionally, standardizing postoperative care and follow-up could improve quality of care and could contribute to data quality. Lastly, the DACI only provides information on 30-days/in-hospital outcomes, while the long-term complications and re-interventions are just as important. A future possible link with declaration data from health care insurers might be able to provide this information.

Next to the comparison of results between hospitals on a national level, one could also learn from the comparison of practice and outcomes between different countries.

Describing the initiation and first results of our nationwide audit for carotid interventions could be helpful for other countries and may be an incentive for them to establish a similar audit or can encourage the harmonization of existing national audits. A future international collaboration, in which practice and outcomes can be compared and in which one could learn from each other, can contribute to further quality improvements on a wider scale.

CONCLUSION

In the Netherlands CEA is performed with an overall low mortality and (major) stroke/death rate and a reasonable time-to-intervention. Whereas time-to-intervention showed significant variation between hospitals, outcome indicators as mortality and (major) stroke/death are not very distinctive due to low overall event rates and no hospitals with a significantly higher event rate. Hospital comparison and the identification of 'best practices' is hampered by this lack of variation between hospitals in current outcome indicators. However, data from the DACI can be used for national population studies, as the identification of predictors for major stroke/death in symptomatic patients.

ACKNOWLEDGEMENTS

The authors would like to thank all surgeons, registrars, physician assistants and administrative nurses that registered all the patients in the DACI, as well as the Dutch Audit for Carotid Interventions group. The authors would like to thank Vanessa Leijdekkers for her critical review of the manuscript.

REFERENCES

1. Rothwell PM, Eliasziw M, Gutnikov SA, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *Lancet.* 2003;361(9352):107-116.
2. Writing G, Naylor AR, Ricco JB, et al. Management of Atherosclerotic Carotid and Vertebral Artery Disease: 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg.* 2017.
3. Carotid Stenting Trialists C, Bonati LH, Dobson J, et al. Short-term outcome after stenting versus endarterectomy for symptomatic carotid stenosis: a preplanned meta-analysis of individual patient data. *Lancet.* 2010;376(9746):1062-1073.
4. Bonati LH, Dobson J, Featherstone RL, et al. Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial. *Lancet.* 2015;385(9967):529-538.
5. Vikatmaa P, Mitchell D, Jensen LP, et al. Variation in clinical practice in carotid surgery in nine countries 2005-2010. Lessons from VASCUNET and recommendations for the future of national clinical audit. *Eur J Vasc Endovasc Surg.* 2012;44(1):11-17.
6. http://www.dica.nl/. Accessed 2018.
7. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. *Stroke.* 2007;38(3):1091-1096.
8. Ferguson GG, Eliasziw M, Barr HW, et al. The North American Symptomatic Carotid Endarterectomy Trial : surgical results in 1415 patients. *Stroke.* 1999;30(9):1751-1758.
9. Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. *Br J Surg.* 1991;78(3):355-360.
10. Ivers N, Jamtvedt G, Flottorp S, et al. Audit and feedback: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev.* 2012(6):CD000259.
11. Rudarakanchana N, Halliday AW, Kamugasha D, et al. Current practice of carotid endarterectomy in the UK. *Br J Surg.* 2012;99(2):209-216.
12. Bennett KM, Scarborough JE, Shortell CK. Predictors of 30-day postoperative stroke or death after carotid endarterectomy using the 2012 carotid endarterectomy-targeted American College of Surgeons National Surgical Quality Improvement Program database. *J Vasc Surg.* 2015;61(1):103-111.
13. Troeng T, Bergqvist D, Norrving B, Ahari A. Complications after carotid endarterectomy are related to surgical errors in less than one-fifth of cases. Swedvasc—The Swedish Vascular Registry and The Quality Committee for Carotid Artery Surgery. *Eur J Vasc Endovasc Surg.* 1999;18(1):59-64.
14. Swedvasc. http://www.ucr.uu.se/swedvasc/arsrapporter?task=document.viewdoc&id=173.
15. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ, Carotid Endarterectomy Trialists C. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet.* 2004;363(9413):915-924.
16. NVR-VSQIP. https://www.vsqip.org.uk/reports/2016-annual-report/.
17. Nejim B, Obeid T, Arhuidese I, et al. Predictors of perioperative outcomes after carotid revascularization. *J Surg Res.* 2016;204(2):267-273.
18. Kallmayer MA, Tsantilas P, Knappich C, et al. Patient characteristics and outcomes of carotid endarterectomy and carotid artery stenting: analysis of the German mandatory national quality assurance registry–2003 to 2014. *J Cardiovasc Surg (Torino).* 2015;56(6):827-836.
19. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet.* 1998;351(9113):1379-1387.
20. Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med.* 1998;339(20):1415-1425.

21. Hye RJ, Mackey A, Hill MD, et al. Incidence, outcomes, and effect on quality of life of cranial nerve injury in the Carotid Revascularization Endarterectomy versus Stenting Trial. *J Vasc Surg.* 2015;61(5):1208-1214.
22. de Borst GJ. Cranial nerve palsy should not be included within a primary composite endpoint in carotid surgery trials. *Eur J Vasc Endovasc Surg.* 2014;47(6):583-584.
23. Aburahma AF, Mousa AY, Stone PA. Shunting during carotid endarterectomy. *J Vasc Surg.* 2011;54(5):1502-1510.
24. Bennett KM, Scarborough JE, Cox MW, Shortell CK. The impact of intraoperative shunting on early neurologic outcomes after carotid endarterectomy. *J Vasc Surg.* 2015;61(1):96-102.
25. Goodney PP, Likosky DS, Cronenwett JL, Vascular Study Group of Northern New E. Factors associated with stroke or death after carotid endarterectomy in Northern New England. *J Vasc Surg.* 2008;48(5):1139-1145.
26. Kuhan G, Gardiner ED, Abidia AF, et al. Risk modelling study for carotid endarterectomy. *Br J Surg.* 2001;88(12):1590-1594.
27. Kragsterman B, Logason K, Ahari A, Troeng T, Parsson H, Bergqvist D. Risk factors for complications after carotid endarterectomy—a population-based study. *Eur J Vasc Endovasc Surg.* 2004;28(1):98-103.
28. Karthaus EG, Lijftogt N, Busweiler LAD, et al. Textbook Outcome: A Composite Measure for Quality of Elective Aneurysm Surgery. *Ann Surg.* 2017.

CHAPTER 9

Quality indicator 'time to carotid endarterectomy'

E.G. Karthaus, A.J.A. Meershoek, L.J. Kappelle, G.J. de Borst

Medisch Contact 2018

Bij patiënten met een recente *transient ischaemic attack* (TIA) of een niet-invaliderend herseninfarct, veroorzaakt door een hooggradige stenose in de ipsilaterale arteria carotis, kan chirurgische verwijdering van deze stenose – door middel van een carotisendarteriëctomie (CEA) – het risico op een recidief herseninfarct verlagen. Deze aanbeveling is gebaseerd op twee gerandomiseerde studies, uitgevoerd in de periode 1981-1996.[1 2] De combinatie van doorgemaakte neurologische symptomen en de ernst van de stenose waren destijds de belangrijkste factoren om een CEA te laten verrichten.

Factor tijd

In de afgelopen jaren is daar de factor tijd aan toegevoegd, waarbij tijd bij voorkeur gedefinieerd is als het tijdsverloop tussen de eerste neurologische symptomen (het zogenaamde indexevent) en revascularisatie. De conclusie van een post-hoc-meta-analyse van bovenstaande trials was dat revascularisatie binnen veertien dagen na het indexevent effectiever is, wat betreft preventie van nieuwe herseninfarcten, dan een latere ingreep.[3 4] Het aantal patiënten dat geopereerd moet worden om één herseninfarct in de komende vijf jaar te voorkomen (NNT) is 5 voor patiënten die binnen veertien dagen gerandomiseerd werden en 125 voor patiënten die na twaalf weken gerandomiseerd werden, wat betekent dat de operatie na twaalf weken niet meer zinvol is. Dit komt door een zeer hoog natuurlijk risico op een recidief herseninfarct in de eerste dagen na het indexevent, terwijl dit risico in de weken daarna geleidelijk afneemt en een plateau bereikt.

Op basis van de post-hoc-meta-analyse was het advies om revascularisatie bij voorkeur binnen twee weken na het indexevent uit te voeren.[5] Men moet zich hierbij realiseren dat dit geen geplande primaire analyse was en dat het getal van veertien dagen geen uitkomst van een vooraf vastgestelde calculatie was, maar destijds als willekeurige afkapwaarde is vastgesteld. Om het in perspectief te plaatsen: had men destijds met tijdsblokken van tien of twintig dagen gewerkt, dan spraken wij nu over een afkapwaarde van respectievelijk tien of twintig dagen. In 'real time' betreft het een glijdende schaal waarbinnen snelle interventie effectiever is. De afkapwaarde van veertien dagen is hierbij dus geen scheidslijn voor goede of slechte kwaliteit van zorg.

Semispoedoperatie

De adviezen zijn inmiddels verwerkt in internationale richtlijnen met de aanbeveling om patiënten binnen de termijn van veertien dagen na de eerste neurologische symptomen te opereren. Dat betekent dat de ingreep als een semispoedoperatie moet worden beschouwd.[6 7] Een kanttekening bij de grenswaarde van veertien dagen is de manier waarop deze tot stand is gekomen. De tijd tot interventie werd in de genoemde trials gemeten vanaf randomisatie tot aan interventie, in plaats van vanaf het indexevent tot aan interventie. Deze nuance is belangrijk, aangezien de patiënt het hoogste risico op een recidief infarct heeft gedurende de dagen direct volgend op het indexevent. Daarnaast hanteerden andere trials verschillende definities van timing. Het indexevent werd gedefinieerd als het eerste moment van symptomen,

maar ook als het moment van de meest recente symptomen. Deze verschillen in definities hebben natuurlijk grote invloed op de daadwerkelijke duur tot revascularisatie.[7]

Risicoafweging

Het gevaar van het vaststellen van een grenswaarde is dat deze een eigen leven gaat leiden en een absolute afkapwaarde gaat vormen waarbinnen interventie zinvol is en waarbuiten deze niet meer zinvol zou zijn. De winst van interventie wordt echter altijd bepaald door de verhouding tussen het operatierisico en het risico op een recidief herseninfarct. Binnen de eerdergenoemde studies was het operatierisico (risico op een beroerte en/of overlijden binnen dertig dagen), rond de 6 procent. Maar in de afgelopen decennia is dit risico in Nederland gedaald naar een percentage tot onder de 4 procent.[8] Bovendien weten we tegenwoordig dat ook andere factoren het risico op een recidief herseninfarct verhogen: het mannelijk geslacht, een hogere leeftijd, een irregulair aspect van de plaque en een presentatie met corticale symptomen.[4] Juist bij deze groep patiënten kan een interventie waarschijnlijk ook in de periode na veertien dagen nog winst opleveren in het voorkomen van een nieuw ernstiger herseninfarct, mits het operatierisico acceptabel is.

Uiteraard geldt: hoe sneller de interventie, hoe beter. Het is echter niet wenselijk om een interventie buiten kantoortijden te verrichten. Ook achten wij het niet zinvol om drie maanden na het indexevent nog een interventie te verrichten.

Kwaliteitsregistratie

Sinds juni 2013 registreren de ziekenhuizen in Nederland alle patiënten die een carotisinterventie ondergaan in een nationale kwaliteitsregistratie, de Dutch Audit for Carotid Interventions (DACI).[8] Deze registratie brengt proces en uitkomsten van carotischirurgie landelijk, maar ook per individueel ziekenhuis, in kaart. Vanuit verschillende belanghebbende partijen is er daarbij veel aandacht voor de kwaliteitsindicator 'tijd tot interventie'. Deze indicator geeft per ziekenhuis het percentage patiënten met een symptomatische carotisstenose weer die binnen de termijn van veertien dagen geopereerd zijn, gemeten vanaf het eerste consult in het ziekenhuis. Jaarlijks worden er in Nederland ongeveer 2200 patiënten met een symptomatisch carotisstenose geopereerd.[8] De norm is dat 90 procent van de patiënten binnen veertien dagen behandeld moet zijn. In de jaren 2014 tot en met 2016 varieerde dit percentage tussen de 70 en 79 procent.[8]

Op dit moment valt dus één op de vijf patiënten buiten de gestelde norm, waarbij benadrukt moet worden dat de tijd pas wordt gemeten vanaf het eerste consult in het ziekenhuis. Deze kwaliteitsindicator zal de komende jaren worden aangepast naar medische relevantie en uitgaan van de tijd tussen de eerste neurologisch symptomen en de uiteindelijke interventie. De tijd tussen de eerste symptomen en het eerste ziekenhuisconsult bedroeg de afgelopen jaren gemiddeld zeven dagen.[7] Met deze extra vertraging zal het percentage patiënten dat buiten de tweewekenperiode wordt behandeld naar verwachting rond de 50 procent uitkomen en

bij handhaven van bestaande logistiek binnen en buiten het ziekenhuis zal één op de twee patiënten derhalve niet volgens de geldende richtlijnen behandeld worden.

Starre focus

De focus op het percentage patiënten dat binnen veertien dagen na het eerste consult in het ziekenhuis een CEA ondergaat, stimuleert artsen om de multidisciplinaire samenwerking te verbeteren en hun zorgpaden efficiënt in te richten. Dat is een uitstekende stimulans en gunstig voor het totale cohort aan symptomatische patiënten die een CEA moeten ondergaan om een maximaal aantal herseninfarcten te voorkomen.

Het beoordelen van ziekenhuizen op een percentage van interventies binnen de termijn van veertien dagen heeft echter ook nadelen. Een starre focus op deze termijn zou ervoor kunnen zorgen dat er bij patiënten met een indicatie voor interventie, bij wie de ingreep buiten de grens van veertien dagen dreigt te vallen, wordt afgezien van CEA. In onze optiek mag het nooit zo zijn dat patiënten geen adequate zorg krijgen omdat ziekenhuizen en behandelaars een 'slechte' score dreigen te behalen op een kwaliteitsindicator. Hoewel deze kwaliteitsindicator de interne processen in het ziekenhuis kan verbeteren, biedt hij de individuele patiënt dus niet altijd de optimale zorg. Het is wenselijk om patiënten met een symptomatische hooggradige carotis stenose zo snel mogelijk en bij voorkeur binnen 14 dagen na de eerste symptomen te behandelen. Echter, op basis van patiëntkarakteristieken en een aantoonbaar laag operatierisico is CEA ook na de termijn van 14 dagen effectief in het voorkomen van een herseninfarct.

REFERENTIES

1. Barnett HJ, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med 1998; 339 (20): 1415-25.
2. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). Lancet 1998; 351 (9113): 1379-87.
3. Rothwell PM, Eliasziw M, Gutnikov SA, Fox AJ, Taylor DW, Mayberg MR, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. Lancet 2003; 361 (9352): 107-16.
4. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ, Carotid Endarterectomy Trialists C. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. Lancet 2004; 363 (9413): 915-24.
5. Coull AJ, Lovett JK, Rothwell PM, Oxford Vascular S. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: implications for public education and organisation of services. BMJ 2004; 328 (7435): 326.
6. Writing G, Naylor AR, Ricco JB, de Borst GJ, Debus S, de Haro J, et al. Management of Atherosclerotic Carotid and Vertebral Artery Disease: 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg. 2017.
7. den Hartog AG, Moll FL, van der Worp HB, Hoff RG, Kappelle LJ, de Borst GJ. Delay to carotid endarterectomy in patients with symptomatic carotid artery stenosis. Eur J Vasc Endovasc Surg. 2014;47(3):233-9
8. http://www.dica.nl/.

CHAPTER 10

Summary, general discussion & future perspectives

SUMMARY

Dutch Surgical Aneurysm Audit

Clinical audits are used to measure and improve quality of health care and are embedded in the current Dutch care landscape.[1] Besides serving as a tool for physicians to improve their care, a clinical audit also provides information to other stakeholders (e.g. patients, administrators and health insurers) in a time where transparency about practice and outcome is essential.

Since 2013, all patients undergoing abdominal aortic aneurysm (AAA) surgery in the Netherlands are required to be registered in the Dutch Surgical Aneurysm Audit (DSAA).[2] From these patients, information about indication, process and outcomes of care is collected and subsequently be used to calculate quality indicators. At the start of the DSAA, around 3500 patients were registered by 61 hospitals each year. Since the expansion of the DSAA in 2016, with patients undergoing thoracic aortic surgery and AAA revision surgery, this annual number has now reached around 4000 patients. Due to the merging of hospitals and centralization of complex care, currently 59 hospitals are performing AAA surgery in the Netherlands.

Initially, the stakeholders had the need to be able to monitor postoperative mortality and to be able to make a fair comparison between hospitals on this outcome measure. However, due to the low event rate of postoperative mortality in elective AAA surgery, little variation between hospitals was observed, and this did not provide any leads for quality improvement. As a result hereof additional quality measures for AAA surgery were investigated concerning the indication, treatment and outcome measures. As DSAA has full national coverage it is real world data and therefore the data is also suitable for analyses of epidemiological issues.

From the first analyzes of the DSAA we have learned that elective AAA surgery is frequently performed on patients with a smaller aortic diameter than in which surgery is recommended in the guideline (males ≥55mm and females ≥50mm).[3] As early intervention has proven to be not beneficial and can lead to unnecessary adverse outcomes for patients, this required further investigation.[4,5] In **chapter 2** we showed that guideline deviation regarding the aneurysm diameter for elective repair is present in 17% of patients and happens more frequently in males, young patients, patients without co-morbidities, patients treated with endovascular aneurysm repair (EVAR) and in lower hospital volumes. There is a wide variation (2-40%) in guideline deviation regarding the treatment of small aneurysms between Dutch vascular surgical units (VSU, i.e. hospitals). Subsequently, when the variation in guideline deviation was evaluated over time, VSUs that rarely deviate from the guideline could be identified, as well as VSUs that structurally did. In order to get more insight into reasons to deviate from the guideline, an online questionnaire was distributed among all Dutch VSU. These questionnaires showed that there is agreement among Dutch VSUs on acceptable reasons to perform elective surgery on patients with a small aortic aneurysm, such as saccular shape

of the aneurysm and a large iliac component. However, the extent to which the indications mentioned in the questionnaire occur in actual practice (DSAA data) varied. Lastly, when we asked VSUs to estimate their own percentage of guideline deviations regarding aortic diameters, their estimations were in 75% not concordant with their actual practice and lower than as registered in the DSAA. From these results, we concluded that VSUs are not always aware of their own practice. By integrating the percentage guideline deviation regarding aneurysm diameter into the feedback system of the audit since 2018, VSUs can now easily monitor their own practice which may help to decrease unbeneficial elective surgery and the variation in practice.

Although a saccular shape of the aneurysm was reported by Dutch VSUs to be an acceptable reason for early surgical intervention as the asymmetrical shape of a saccular aneurysm might predispose them to rupture, we found little scientific evidence to support this. Based on case reports and case series of which the largest included 78 saccular shaped abdominal aortic aneurysms (SaAAA), current European and American guidelines suggest that early surgical treatment of SaAAAs is recommended but no threshold for intervention is provided.[6-8] As aneurysm shape was registered in the DSAA since 2016, we were able to compare clinical presentation, treatment and outcome between the relatively rare SaAAAs and more common fusiform shaped AAAs (FuAAA) in the Dutch population as is addressed in **chapter 3.** SaAAA was registered in 6.1% (6.5% elective, 4.8% acute) of all patient in the DSAA. Patient characteristics between SaAAA and FuAAA were comparable, except acute SaAAA patients were more often female compared to acute FuAAA patients. In line with the prevailing belief that SaAAA are more likely to rupture, elective patients with a SaAAA were operated at smaller diameters than elective FuAAA patients and the majority of elective SaAAA patients were undergoing surgery with a diameter <55mm. More striking was the finding that acute SaAAA patients were significantly more often presented with smaller diameters than acute FuAAA patients. This difference resulted in a relative risk (RR) on an acute presentation of >3 in SaAAAs with diameters <55mm compared to FuAAAs of the same size and >15 in SaAAAs with diameter <45mm. These findings support the current idea that SaAAA should be electively treated at smaller aortic diameters than FuAAAs. The exact diameter threshold for elective repair of SaAAA is difficult to determine, but a threshold of ≥45mm seems acceptable. In both the elective and acute setting, SaAAA and FuAAA had similar surgical treatments and no differences were found in postoperative outcomes.

Chapter 4 describes the current practice of elective open surgical repair (OSR) for AAA in the Netherlands with a focus on the hospital volume in which these procedures are performed. With EVAR being standard care in the elective setting, the use of OSR has decreased and is performed in only 22% of patients undergoing elective AAA repair in the Netherlands, containing a selected group of patients with most likely more difficult aneurysms.[9] In contrast to elective EVAR in which postoperative mortality decreased to <1%, postoperative mortality after elective OSR remained unchanged at 5%. With the aim

to improve postoperative outcomes after elective OSR, patient characteristics associated with postoperative mortality in the DSAA and the association between hospital volume and postoperative mortality were evaluated. Female sex, increasing age, pulmonary co-morbidities, preoperative hemoglobin and preoperative creatinine levels have shown to be independently associated with postoperative mortality after elective OSR in the Dutch population. Despite the fact that OSR is decreasingly performed, no distinction is made between EVAR and OSR within the current Dutch volume standard of 20 elective AAA procedures per hospital per year.[10] Because of this, elective OSR is performed in 59 hospitals in the Netherlands, in which the total elective OSR volume (during a period of 6 years) varied from 1 to 141. Between hospitals the adjusted postoperative mortality ranged from 0-16%. Due to the low mean annual volumes, no hospitals with a significantly higher postoperative mortality could be identified. Additionally, annual hospital volume of elective OSR was not associated with postoperative mortality after elective OSR in the current Dutch population. Based on these findings we could not substantiate a volume standard for elective OSR.

Previous studies comparing postoperative mortality between EVAR and OSR in patients with a ruptured AAA (RAAA) have shown conflicting results. Whereas observational studies suggested a survival benefit after EVAR, no randomized controlled trial studies have confirmed this.[11-16] Both study designs have their drawbacks. As the benefit of EVAR in the elective setting is clear, it is expected that this benefit of EVAR should also apply in the acute setting, but this had not yet been demonstrated. In **chapter 5** the difference in in postoperative mortality between EVAR and OSR in RAAA patients was evaluated with three different statistical techniques, using DSAA data.
Of all RAAA patients undergoing acute surgery in the Netherlands, 62% was treated with OSR and 38% with EVAR. Patients were treated in 61 hospitals, and percentage of treatment with EVAR varied from 0-100%. The crude postoperative mortality after OSR was 34.9% and 22.6% after EVAR. With standard linear regression analysis and propensity score (PS) analysis adjusting for observed confounders a significant 30 days/in-hospital survival benefit of 12.3% and 13.2% respectively, could been demonstrated for RAAA patients undergoing EVAR, compared to RAAA patients undergoing OSR. Using instrumental variable (IV) analysis (pseudo-randomization) to adjust for observed and unobserved confounders, a postoperative survival benefit (statistical non-significant) of approximately 8.9% was seen in EVAR patients. Additionally, hospitals were divided in two groups based on the percentage of EVAR in RAAA patients, with the median as cutoff point. Patients operated in hospitals with a high percentage of EVAR (38-100%EVAR) in RAAA patients had a 2.0% lower crude postoperative mortality compared to patients operated in hospitals with a low percentage of EVAR (0-37%EVAR) in RAAA patients.

In the search for more distinctive outcome measures in elective AAA surgery, several composite measures have been explored. In **chapter 6** Textbook Outcome (TO), a composite measure

including all desired outcomes, is described for elective AAA surgery and tested on DSAA data. The scientific committee of the DSAA decided that TO is achieved if no intraoperative complications, no postoperative surgical complications, no re-intervention, no prolonged hospital stay (LOS) (EVAR ≤ 4 days, OSR ≤ 10 days), no readmission within 30 days after discharge and/or no postoperative mortality within 30 days after surgery or at discharge did occur. Due to the difference in type of surgery, different definitions for LOS were used between EVAR and OSR. TO was realized in 71% of EVAR patients and 53% of OSR patients. The main reasons why TO was not achieved were a prolonged LOS in both surgical procedures, re-admissions after discharge for EVAR patients and postoperative complications for OSR patients. With TO a greater inter-hospital variation was observed compared to single outcome indicators, especially in OSR. Variation remained mostly within the confidence intervals making it difficult to identify 'best practices'. However, by using TO individual hospitals can see where they can improve to achieve desired outcomes. TO is therefore initially particularly suitable as an instrument for internal quality improvement and not for hospital comparison. Since 2019 TO is included in the DSAA feedback system for hospitals.

While the focus in clinical auditing is often on immediate visible postoperative outcomes, it is also important to consider the more long-term outcomes when measuring quality of care. Besides long term mortality, secondary aortic related reinterventions is an important measure. Previous studies have already shown that with the increasing use of EVAR, the number of aorta-related re-interventions has also increased.[17-19] Since the expansion of the DSAA in 2016, all secondary aortic reinterventions (SARs) performed in the Netherlands were also registered in the audit, making it possible to generate long-term outcomes by linking data. Because this data has only recently been added, it is not yet possible to make statements about the incidence of re-interventions, but with the first analyses of this data we were able to provide insight into the scope of the problem in **chapter 7**. In two years of time, 691 patients underwent a SAR in the Netherlands, which counts for almost 10% of all AAA procedures annually performed. The most frequent indication for SARs were endoleaks. The majority of SARs was performed in an elective setting and more than half with an endovascular procedure. Postoperative mortality of SARs was comparable with results after primary AAA repair, in all urgency settings.

When linking data, approximately a quarter of SAR patients was previously registered in the DSAA for their primary AAA repair (2013-2017), which implies that the remaining three quarters had their primary AAA repair before the start of the audit (<2013) and therefore information on their primary AAA repair is lacking.

In the subgroup of SARs with linked data, the vast majority of SARs followed after primary DSAA registered EVAR procedures (169/181). When looking at the stent types used in their primary AAA repair, an overrepresentation of endovascular aneurysm sealing system grafts was seen. Only half of the primary EVAR procedures could again be treated with an endovascular procedure during SAR. Furthermore, one-fifth of patients with a primary elective AAA procedure underwent an acute symptomatic or ruptured SAR. With more

years of auditing, the proportion of SARs that can be linked to their primary intervention will increase and eventually be complete, making it possible to provide a national incidence of SAR and to evaluate SAR-rates between surgical techniques. Additionally, by evaluating SAR rates between stent types the audit can serve as a tool to detect stent related problems.

Dutch Audit for Carotid Interventions

Since June 2013, all patient undergoing carotid artery interventions in the Netherlands are registered in the Dutch Audit for Carotid interventions (DACI).[20] In **chapter 8** it is shown that the DACI could be successfully implemented in the Netherlands with nationwide coverage of all hospitals, allowing the evaluation of quality of carotid endarterectomy (CEA) care nationally and between hospitals. From its start, approximately 2500 patients are registered in the DACI by 52 hospitals annually. After the first years of auditing we concluded that CEA is performed with an overall low mortality and (major) stroke/death rate. Additionally, there was a reasonable guideline adherence regarding the indicator time-to-intervention, with 75% of symptomatic patients undergoing surgery within 2 weeks after first hospital consultation. Whereas time-to-intervention showed significant variation between hospitals, outcome indicators as mortality and (major) stroke/death are not very distinctive due to low overall event rates and no hospitals with a significantly higher event rate. The lack variation in these indicators hampers a national hospital comparison in the era with a minimum volume of 20 CEA per year per hospital. However, 9 hospitals with a significantly lower major stroke/death rate than the national mean could be identified, from which others possibly could learn. Additionally, with the use of DACI data, the following predictors for major stroke/death after CEA in symptomatic patients could be identified: age, female gender, severe respiratory diseases, presenting with cortical symptoms.

In **chapter 9** it is explained how the quality indicator time-to-intervention was established and how it should be interpreted. The guideline to treat patients with a symptomatic carotid stenosis within 2 weeks after the first hospital visit is based on a post-hoc meta-analysis of two randomized trials, performed in 1981-1996.[21-24] In this post-hoc meta-analysis, 14 days was chosen as cut-off values, in which revascularization within this term appeared to be more effective in preventing a recurrence of transient ischemic attack (TIA) or ischemic stroke than outside this term and in which revascularization after 12 weeks was not considered useful. It should be noted that 14 days is a chosen number rather than an outcome of a calculation and that in practice it is a sliding scale in which earlier intervention is more effective in preventing a recurrent stroke. Establishing a quality indicator as time-to-intervention stimulates physicians to improve multidisciplinary collaboration and to organize their care pathways more effectively. Such an external stimulus is beneficial for the total cohort of symptomatic patients undergoing CEA, in order to prevent the maximum number of strokes. However, care should be taken that this quality indicator is not seen as a dividing line within which intervention is effective and beyond which is not.

An important nuance to be made is that the aforementioned studies measured the time interval from the moment of first symptoms or last symptoms until surgery. Though, the quality indicator start measuring from first hospital consultation. As previous research has shown that there is an average pre-hospital (patient related) delay of 7 days, it is chosen to only measure the interval in which hospitals can influence when defining the quality indicator.[25] Hospital factors associated with delay in time to intervention were found: age, prior CEA, presenting with ocular symptoms and an indirect referral.[26]

GENERAL DISCUSSION AND FUTURE PERSPECTIVES

Development/improvement of the audit and indicators

New quality indicators have emerged as a result of developments in vascular surgical care and new insights, among others based on information from the audits. More years of registration in the DSAA and DACI will have to show whether the introduction of new indicators has also contributed to the improvement of processes of care and eventually the outcomes of care. Feedback about processes of care will likely lead to improvements more easily, since it generally clearly indicates where to act on. This is in contrast to most single outcome indicators, which often requires further research to discover why hospitals score poorly on the relevant outcome. Although awareness of your outcomes alone can contribute to improve performance, it is especially important that hospitals are given clear tools to be able to improve, such as in Textbook outcome and Failure to Rescue.[27-29]

Since the expansion of the DSAA in 2016, SAR procedures and interventions of the thoracic aorta have also been registered. Additionally, since then a distinction between infra, juxta and suprarenal aneurysms of the abdominal aorta was made within the DSAA. With time, more insight into these subgroups will become available. As discussed in chapter 7, it will be possible in due course to determine the incidence of SAR procedures per surgical technique and in addition, the audit can serve as a tool to detect problems with stent grafts.[30]

Thoracic aortic procedures often overlap with abdominal aortic procedures, not only because they merge anatomically but also because the experience of one procedure contributes to the experience of the other. In endovascular procedures, it is also important to be able to distinguish between procedures in which branches of the aorta are individually stented or not, as these are technically more difficult procedures with a higher risk of perioperative complications.

Currently, no volume standards have been set for the performance of branched aortic interventions. In the first years of registration of the thoraco-abdominal and supra-renal aneurysms we found that some hospitals perform these procedures frequently and some only sporadically.[9] The results of branched aortic interventions and the volume in which they are performed will be a point of attention in the coming years.

Collaboration with other medical specialties / audits

As certain procedures on the thoracic aorta are also performed by cardiothoracic surgeons, contact has been sought with the Dutch Association of Cardiothoracic Surgeons.[31] The cardiothoracic surgeons register all their procedures in their own quality registry 'Dutch Heart Registration'(NHR).[32] By organizing the DSAA and the NHR in such a way that aortic procedures are registered similarly, these data files could be combined in the future in order to obtain a complete overview of the procedures performed per hospital. It is debatable whether these numbers could be added together with regard to a volume standard. Vascular surgeons and cardiothoracic surgeons often function as two separate departments, which makes it

questionable whether these procedures can be seen as a shared experience. Nevertheless, it is first of all important to make these data transparent.
The scientific committee of the DACI has looked into a possible collaboration with the 'Dutch Acute Stroke Audit' (DASA), as patients with a symptomatic carotid stenosis are also registered in the DASA because of their neurological presentation. An important and still unanswered question is the number of patients with symptomatic carotid stenosis who will have a recurrent stroke while waiting for carotid endarterectomy, preventing them from undergoing surgery. Originally, all patients with a transient ischemic attack or ischemic cerebrovascular accident (CVA) were registered in the DASA. However, because of the enormous registration burden due to the case load, it was decided to focus the audit on ischemic CVAs. As a result, a large part of the DACI patients is no longer included in the DASA, leaving this question unanswered.

Merging of different data sources

DICA is investigating whether data from individual audits, including the DSAA and DACI, could be linked to existing databases, such as electronic patient records (EPR) and Vektis. When patient data needed for the audits could be directly and easily extracted from the EPRs, they no longer need to be registered manually. This would greatly contribute to reducing the registration burden.
Vektis has a database in which the financial data of health insurers in the Netherlands is collected.[33] As a result it has information about comorbidities and the date of death for every patient in the Netherlands. Such a link would provide insight into the long-term survival of all patients undergoing aortic and carotid surgery in the Netherlands. This would be extremely meaningful information for efficiency purposes. An obstacle to this link is the new privacy legislation whereby certain personally identifying data may not be registered or used in a quality registry. It is still a question of finding a way in which this data can be reliably linked and in which the privacy of patients is safeguarded.

International collaboration

In 1997, an international collaboration was initiated under the name VASCUNET for clinical and administrative vascular registries in Europe and Australia with the aim of improving the quality, safety and effectiveness of vascular healthcare.[34] There are now 27 countries, including the Netherlands, affiliated with VASCUNET, which can all provide data for certain research projects. By bundling data and thus increasing the patient population, certain epidemiological issues, such as conditions or complications with a low event rate, can be better investigated. Comparing results between countries remains difficult. This is mainly due to the differences in the national organization of quality measurement. The way in which the Dutch health care and its quality monitoring is organized, ensures that all patients undergoing aortic or carotid surgery respectively are registered in the DSAA and DACI. This full national coverage makes our quality registers unique. For the other participating countries, it is not always certain

whether all patients are registered in the national country, or it is actually known that only a selection of hospitals participate in the registration. This hampers a fair comparison of results between countries.

Volume standards and centralization of care

An ongoing discussion is the hospital volume in which certain procedures should be performed. Two conflicting interests intersect: on the one hand, good accessibility of care is desirable in which patients can receive certain care as close to home as possible, and on the other hand, it is important that the team providing the care do this often enough to be able to deliver good quality of care. With the current volume standards of 20 elective AAA procedures and 20 CEAs, there are approximately 60 hospitals across the country that perform these procedures. As described in chapter 4, there is no separate volume standard for elective OSR within AAA surgery, which means that hospitals can perform this procedure once a year. Comparable examples are the treatment complex branched abdominal and thoracic aneurysms and ruptured AAAs. When complex low-volume care is performed in too many hospitals, it is difficult to monitor the quality of care.

A low number of procedures per hospital results in wide confidence intervals in which outliers are difficult to detect. In addition, when the total volume is low a single "event" (for example, mortality or a complication) more or less strongly influences the hospital outcome which makes is difficult to achieve constant outcomes over several years.

In the search for new volume standards, we encounter the same statistical limitations.

As showed in chapter 4, we were unable to demonstrate associations between volume and postoperative mortality in elective OSR. It may be possible that this association is actually not there or that with the current distribution of elective OSR procedures divided over 59 hospitals in the Netherlands, several of which perform only a few procedures per year, we were unable to demonstrate an association. If no decision can be made on the basis of the available data, a consensus should be sought on the basis of reasonableness. We have to ask ourselves how often a surgical procedure must be carried out in order to be able to deliver sufficient quality as a team. Does a procedure have to be performed at least once or twice a month, or even once a week? Regardless of the number, new volume standards will bring about a shift in care with fewer hospitals (and therefore fewer surgeons) performing these procedures and most patients will have to travel further of have to be transported to receive this care.

Focus of the audits

Clinical auditing is a labor-intensive process in which doctors spend a lot of time registering patients instead of providing patient care. Reducing the registration burden is therefore placed high on the agenda. In the DSAA, more than half of the patients registered annually are elective EVAR procedures. In this group, low mortality and postoperative complications have been seen since the start of the audit, which did not change over time and in which no outliers are seen.

In addition to the search for more distinctive outcome indicators, one could also decide to focus the audit on certain areas of attention, where more monitoring is desirable or where potential improvements can be achieved, such as in OSR, complex aneurysms and ruptured AAAs. It is debatable that, in addition to the focus areas, the elective EVAR group would no longer be registered or that only a limited set of variables in these patients would be collected. In the latter case, the continuity of the dataset is preserved and thus also retains a signaling function.

REFERENCES

1. Dutch Institute for Clinical Auditing (DICA). http://www.dica.nl/.
2. Dutch Surgical Aneurysm Audit. https://dica.nl/dsaa/home. Accessed 16.04.2021.
3. DSAA annual report 2014. https://www.dica.nl/jaarrapportage-2014/assets/uploads/DICA-JAAR-OFFLINE-2014.pdf.
4. Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med.* 2002;346(19):1437-1444.
5. Powell JT, Brown LC, Forbes JF, et al. Final 12-year follow-up of surgery versus surveillance in the UK Small Aneurysm Trial. *Br J Surg.* 2007;94(6):702-708.
6. Shang EK, Nathan DP, Boonn WW, et al. A modern experience with saccular aortic aneurysms. *J Vasc Surg.* 2013;57(1):84-88.
7. Wanhainen A, Verzini F, Van Herzeele I, 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.
8. Chaikof EL, Dalman RL, Eskandari MK, 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 e72.
9. DSAA annual report 2017. 2017; http://dica.nl/jaarrapportage-2017/home.
10. Volume standards Dutch Society for Surgery. 2019; https://assets.heelkunde.nl/p/491520/none/Normen 8_1 versie april 2021.pdf.
11. Giles KA, Hamdan AD, Pomposelli FB, Wyers MC, Dahlberg SE, Schermerhorn ML. Population-based outcomes following endovascular and open repair of ruptured abdominal aortic aneurysms. *J Endovasc Ther.* 2009;16(5):554-564.
12. Giles KA, Pomposelli FB, Hamdan AD, Wyers MC, Schermerhorn ML. Comparison of open and endovascular repair of ruptured abdominal aortic aneurysms from the ACS-NSQIP 2005-07. *J Endovasc Ther.* 2009;16(3):365-372.
13. McPhee J, Eslami MH, Arous EJ, Messina LM, Schanzer A. Endovascular treatment of ruptured abdominal aortic aneurysms in the United States (2001-2006): a significant survival benefit over open repair is independently associated with increased institutional volume. *J Vasc Surg.* 2009;49(4):817-826.
14. Investigators IT, Powell JT, Sweeting MJ, et al. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ.* 2014;348:f7661.
15. Reimerink JJ, Hoornweg LL, Vahl AC, et al. Endovascular repair versus open repair of ruptured abdominal aortic aneurysms: a multicenter randomized controlled trial. *Ann Surg.* 2013;258(2):248-256.
16. Desgranges P, Kobeiter H, Katsahian S, et al. Editor's Choice–ECAR (Endovasculaire ou Chirurgie dans les Anevrysmes aorto-iliaques Rompus): A French Randomized Controlled Trial of Endovascular Versus Open Surgical Repair of Ruptured Aorto-iliac Aneurysms. *Eur J Vasc Endovasc Surg.* 2015;50(3):303-310.
17. De Bruin JL, Baas AF, Buth J, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1881-1889.
18. United Kingdom ETI, Greenhalgh RM, Brown LC, et al. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1863-1871.
19. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM, investigators Et. 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. *Lancet.* 2016;388(10058):2366-2374.
20. Dutch Audit for Carotid Interventions. https://dica.nl/daci/home. Accessed 16.04.2021.
21. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet.* 1998;351(9113):1379-1387.
22. Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid

Endarterectomy Trial Collaborators. *N Engl J Med.* 1998;339(20):1415-1425.
23. Rothwell PM, Eliasziw M, Gutnikov SA, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *Lancet.* 2003;361(9352):107-116.
24. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ, Carotid Endarterectomy Trialists C. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet.* 2004;363(9413):915-924.
25. den Hartog AG, Moll FL, van der Worp HB, Hoff RG, Kappelle LJ, de Borst GJ. Delay to carotid endarterectomy in patients with symptomatic carotid artery stenosis. *Eur J Vasc Endovasc Surg.* 2014;47(3):233-239.
26. Kuhrij LS MA, Karthaus EG, Vahl AC, Hamming JF, Nederkoorn PJ, de Borst GJ. Factors Associated with Hospital Dependent Delay to Carotid Endarterectomy in the Dutch Audit for Carotid Interventions. *Eur J Vasc Endovasc Surg.* 2019;58(4):495-501.
27. Karthaus EG, Lijftogt N, Busweiler LAD, et al. Textbook Outcome: A Composite Measure for Quality of Elective Aneurysm Surgery. *Ann Surg.* 2017.
28. Lijftogt N, Karthaus EG, Vahl A, 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):652-661.
29. Kuhrij LS KE, Vahl AC, Willems MCM, Elshof JW, de Borst GJ. A Composite Measure for Quality of Care in Patients with Symptomatic Carotid Stenosis Using Textbook Outcome. *Eur J Vasc Endovasc Surg.* 2020;60(4):502-508.
30. Karthaus EG VA, Elsman BHP, Wouters MWJM, de Borst GJ, Hamming JF. National Numbers of Secondary Aortic Reinterventions after Primary Abdominal Aortic Aneurysm Surgery from the Dutch Surgical Aneurysm Audit. 2020;68:234-244.
31. Nederlandse Vereniging voor Thoraxchirurgie. Nederlandse Vereniging voor Thoraxchirurgie. Accessed 18.04.2021.
32. Nederlandse Hart Registratie. https://nederlandsehartregistratie.nl/. Accessed 18.04.2021.
33. Vektis. https://www.vektis.nl/.
34. VASCUNET. https://vascunet.org/.

CHAPTER 11

Summary in Dutch

SUMMARY IN DUTCH

De Dutch Surgical Aneurysm Audit

Clinical audits worden gebruikt om de kwaliteit van gezondheidszorg te meten en te verbeteren en zijn ingebed in de huidige praktijk[1] Naast dat het als middel kan dienen voor artsen om hun zorg te verbeteren, verschaft een clinical audit ook informatie aan andere belanghebbende partijen (bijvoorbeeld patiënten, bestuurders en zorgverzekeraars), in een tijd waarin transparantie over zorgprocessen en uitkomsten van zorg essentieel zijn. Sinds 2013 worden alle patiënten die in Nederland een chirurgische interventie ondergaan vanwege een aneurysma van de abdominale aorta (AAA), verplicht geregistreerd in de Dutch Surgical Aneurysma Audit (DSAA).[2] Van deze patiënten wordt informatie over de indicatie voor de ingreep, het proces en de uitkomsten van zorg verzameld en vervolgens gebruikt om kwaliteitsindicatoren te berekenen. Bij de start van de DSAA werden jaarlijks ongeveer 3500 patiënten door 61 ziekenhuizen geregistreerd. Sinds de uitbreiding van de DSAA in 2016, waarna ook patiënten die thoracale aortachirurgie en AAA-revisiechirurgie ondergaan werden geïncludeerd, komt dit jaarlijkse aantal nu ongeveer uit op 4000 patiënten. Door de fusie van ziekenhuizen en centralisatie van complexe zorg voeren momenteel 59 ziekenhuizen in Nederland AAA-chirurgie uit.

Aanvankelijk was er vanuit verschillende belanghebbende partijen de wens om de postoperatieve mortaliteit te kunnen monitoren en om aan de hand van deze uitkomstmaat vervolgens een eerlijke vergelijking tussen ziekenhuizen te kunnen maken. Vanwege de lage incidentie van postoperatieve mortaliteit bij electieve AAA-chirurgie, werd er echter weinig variatie tussen ziekenhuizen waargenomen en dit gaf vervolgens geen aanknopingspunten voor kwaliteitsverbetering. Als gevolg hiervan zijn aanvullende kwaliteitsindicatoren onderzocht met betrekking tot de indicatiestelling, de behandeling en de uitkomst van AAA-chirurgie. Doordat alle ziekenhuizen in Nederland deelnemen aan de DSAA is er een volledige landelijke dekking en beschikt de DSAA over 'real world' data. Dit maakt de data ook geschikt voor het analyseren van epidemiologische vraagstukken.

Uit de eerste analyses van de DSAA hebben we geleerd dat electieve AAA-chirurgie vaak wordt uitgevoerd bij patiënten met een kleinere aortadiameter dan waarbij een operatie wordt aanbevolen in de landelijke en Europese richtlijn (mannen ≥55mm en vrouwen ≥50mm).[3] Aangezien vroege interventie geen overlevingsvoordeel blijkt te geven en kan leiden tot onnodige nadelige resultaten voor patiënten, was nader onderzoek nodig.[4,5] In **hoofdstuk 2** lieten we zien dat in 17% van de patiënten die electieve AAA-chirurgie ondergingen er werd afgeweken van de richtlijn met betrekking tot de diameter van het aneurysma waarbij interventie geïndiceerd is. Het afwijken van de richtlijn gebeurt vaker bij mannen, jonge patiënten, patiënten zonder comorbiditeit, patiënten behandeld met endovasculaire aneurysmareparatie (EVAR) en bij lagere ziekenhuisvolumes. Er bestaat een grote variatie (2-

40%) tussen Nederlandse vaatchirurgische eenheden (VSU, ziekenhuizen) in het afwijken van de richtlijn met betrekking tot de behandeling van kleine aneurysmata. Wanneer de variatie in het afwijken van de richtlijn over tijd werd geëvalueerd, konden VSU's worden geïdentificeerd die zelden afwijken van de richtlijn, evenals VSU's die dat structureel doen. Om meer inzicht te krijgen in de redenen om af te wijken van de richtlijn is een online vragenlijst verspreid onder alle Nederlandse VSU's. Uit deze vragenlijsten bleek dat er overeenstemming is onder Nederlandse VSU's over acceptabele redenen om electieve chirurgie uit te voeren bij patiënten met een klein aorta-aneurysma, zoals bijvoorbeeld de sacculaire vorm van het aneurysma en een grote iliacale component. De mate waarin de in de vragenlijst genoemde indicaties in de praktijk voorkomen (DSAA-gegevens) varieerde echter. Ten slotte, toen we de VSU's vroegen om in te schatten in hoeveel patiënten zij afwijken van de richtlijn met betrekking tot aortadiameters, waren hun schattingen voor 75% niet in overeenstemming met hetgeen ze in praktijk uitvoerden en een onderschatting ten op zichtte van hetgeen geregistreerd in de DSAA. Uit deze resultaten concludeerden we dat VSU's zich niet altijd bewust zijn van hun eigen praktijk. Door de het percentage patiënten waarin werd afgeweken van de richtlijn met betrekking tot de diameter van het aneurysma te integreren in het onlinefeedbacksysteem van de audit, kunnen VSU's sinds 2018 eenvoudig hun eigen indicatiestelling monitoren, wat kan helpen om onnodige vroege electieve chirurgie en de variatie in de praktijk te verminderen.

Hoewel een sacculaire vorm van het aneurysma door Nederlandse VSU's werd gerapporteerd als een acceptabele reden voor vroege chirurgische interventie, aangezien de asymmetrische vorm van een sacculair aneurysma het vatbaar zou kunnen maken voor een ruptuur, vonden we weinig wetenschappelijk bewijs om dit te ondersteunen. Op basis van case reports en case series, waarvan de grootste 78 sacculair gevormde abdominale aorta-aneurysmata (SaAAA) omvatte, suggereren de huidige Europese en Amerikaanse richtlijnen dat vroege chirurgische behandeling van SaAAA's wordt aanbevolen, maar er wordt geen drempelwaarde voor interventie gegeven.[6-8] Doordat sinds 2016 de vorm van het aneurysma in de DSAA is geregistreerd, konden we de klinische presentatie, de behandeling en de uitkomsten vergelijken tussen de relatief zeldzame SaAAA's en de meer voorkomende fusiforme AAA's (FuAAA) in de Nederlandse populatie, zoals beschreven in **hoofdstuk 3**. Een SaAAA werd geregistreerd bij 6,1% (6,5% electief, 4,8% acuut) van alle patiënten in de DSAA. Patiëntkenmerken tussen SaAAA en FuAAA waren vergelijkbaar, behalve dat acute SaAAA-patiënten vaker vrouwelijk waren dan acute FuAAA-patiënten. In overeenstemming met de heersende opvatting dat een SaAAA een grotere kans heeft om vroeg te ruptureren, werden electieve patiënten met een SaAAA geopereerd bij kleinere diameters dan electieve FuAAA-patiënten en onderging de meerderheid van de electieve SaAAA-patiënten een operatie bij een diameter <55 mm. Opvallend was de bevinding dat acute SaAAA-patiënten zich significant vaker presenteerden met kleinere diameters dan acute FuAAA-patiënten. Dit verschil resulteerde in een relatief risico (RR) van een acute presentatie van >3 bij SaAAA's met een diameter <55 mm in vergelijking met FuAAA's van dezelfde grootte en van >15 bij SaAAA's met een diameter

<45 mm. Deze bevindingen ondersteunen het huidige idee dat SaAAA electief moet worden behandeld bij kleinere aortadiameters dan FuAAA's. De exacte diameter drempelwaarde voor electieve chirurgie bij SaAAA is moeilijk te bepalen, maar een afkapwaarde van ≥45 mm lijkt acceptabel. In zowel de electieve als de acute setting hadden SaAAA en FuAAA vergelijkbare chirurgische behandelingen en werden er geen verschillen gevonden in de postoperatieve uitkomsten.

Hoofdstuk 4 beschrijft de huidige praktijk van de electieve open chirurgie (OSR) voor AAA in Nederland, met een focus op het ziekenhuisvolume waarin deze procedures worden uitgevoerd. Omdat EVAR in de electieve setting inmiddels standaardzorg is, is het gebruik van OSR afgenomen en wordt dit slechts bij 22% van de patiënten die electieve AAA-chirurgie ondergaan in Nederland uitgevoerd. Het betreft daarom een geselecteerde groep patiënten met hoogstwaarschijnlijk moeilijkere aneurysmata.[9] In tegenstelling tot electieve EVAR waarbij de postoperatieve mortaliteit daalde tot <1%, bleef de postoperatieve mortaliteit na electieve OSR onveranderd op 5%. Met het doel om de postoperatieve uitkomsten na electieve OSR te verbeteren, werd in de DSAA gezocht naar patiëntkenmerken die geassocieerd zijn met postoperatieve mortaliteit. Daarnaast werd de associatie tussen ziekenhuisvolume en postoperatieve mortaliteit geëvalueerd. Vrouwelijk geslacht, toenemende leeftijd, pulmonale comorbiditeiten, preoperatieve hemoglobine- en preoperatieve creatininespiegels blijken onafhankelijk geassocieerd te zijn met postoperatieve mortaliteit na electieve OSR in de Nederlandse populatie.

Ondanks dat OSR steeds minder wordt uitgevoerd, wordt er binnen de huidige Nederlandse volumenorm van 20 electieve AAA-ingrepen per ziekenhuis per jaar, geen onderscheid gemaakt tussen EVAR en OSR.[10] Hierdoor wordt electieve OSR in 59 ziekenhuizen in Nederland uitgevoerd, waarbij het totale electieve OSR-volume (gedurende een periode van 6 jaar) varieerde van 1 tot 141. De gecorrigeerde postoperatieve mortaliteit varieerde tussen ziekenhuizen van 0-16%. Door de lage gemiddelde jaarvolumes konden geen ziekenhuizen worden geïdentificeerd met een significant hogere postoperatieve mortaliteit. Bovendien was het jaarlijkse ziekenhuisvolume van electieve OSR niet geassocieerd met postoperatieve mortaliteit na electieve OSR in de huidige Nederlandse populatie. Op basis van deze bevindingen konden we geen volumenorm voor electieve OSR onderbouwen.

Eerdere studies die de postoperatieve mortaliteit tussen EVAR en OSR vergeleken bij patiënten met een geruptureerd AAA (RAAA) lieten tegenstrijdige resultaten zien. Terwijl observationele studies een overlevingsvoordeel suggereerden na EVAR, hebben de grote randomised controlled trials dit niet kunnen bevestigen.[11-16] Beide studiedesigns hebben hun nadelen. Doordat het voordeel van EVAR in de electieve setting duidelijk bewezen is, werd verwacht dat dit ook zou gelden in de acute setting, maar dit werd vooralsnog nooit aangetoond. In **hoofdstuk 5** werd het verschil in postoperatieve mortaliteit tussen EVAR

en OSR bij RAAA-patiënten geëvalueerd door middel van drie verschillende statistische technieken, gebruikmakend van DSAA-data.

Van alle RAAA-patiënten die een acute operatie ondergingen in Nederland, werd 62% behandeld met OSR en 38% met EVAR. Patiënten werden behandeld in 61 ziekenhuizen en het percentage behandeling met EVAR varieerde van 0-100%. De ongecorrigeerde postoperatieve mortaliteit na OSR was 34,9% en 22,6% na EVAR. Met een standaard lineaire regressieanalyse en propensity score (PS)-analyse, gecorrigeerd voor waargenomen confounders, kon een significant 30 dagen/in-hospital overlevingsvoordeel van respectievelijk 12,3% en 13,2% worden aangetoond voor RAAA-patiënten die EVAR ondergaan, vergeleken met RAAA-patiënten die OSR ondergaan.

Door middel van instrumentele variabele (IV) analyse (pseudo-randomisatie), om te corrigeren voor waargenomen en niet-geobserveerde confounders, werd een postoperatief overlevingsvoordeel (statistisch niet-significant) van ongeveer 8,9% waargenomen bij EVAR-patiënten. Bovendien werden ziekenhuizen verdeeld in twee groepen op basis van het percentage EVAR bij RAAA-patiënten, met de mediaan als afkappunt. Patiënten geopereerd in ziekenhuizen met een hoog percentage EVAR (38-100% EVAR) in RAAA-patiënten hadden een 2,0% lagere ongecorrigeerde postoperatieve mortaliteit vergeleken met patiënten geopereerd in ziekenhuizen met een laag percentage EVAR (0-37% EVAR) in RAAA-patiënten.

In de zoektocht naar meer onderscheidende uitkomstmaten voor electieve AAA-chirurgie zijn verschillende samengestelde kwaliteitsmaten onderzocht. In **hoofdstuk 6** wordt Textbook Outcome (TO), een samengestelde maat die alle gewenste uitkomsten omvat, beschreven voor electieve AAA-chirurgie en getest op DSAA-gegevens. De wetenschappelijke commissie van de DSAA heeft besloten dat TO wordt bereikt als er geen intra-operatieve complicatie, geen postoperatieve chirurgische complicatie, geen re-interventie, geen verlengde ziekenhuisopname (LOS) (EVAR ≤ 4 dagen, OSR ≤ 10 dagen), geen heropname binnen 30 dagen na ontslag en/of geen postoperatieve mortaliteit binnen 30 dagen na operatie of bij ontslag is. Vanwege het verschil in het type operatie werden verschillende definities voor LOS gebruikt tussen EVAR en OSR. TO werd gerealiseerd bij 71% van de EVAR-patiënten en 53% van de OSR-patiënten. De belangrijkste redenen waarom TO niet werd bereikt, waren een verlengde LOS bij beide chirurgische procedures, heropnames na ontslag voor EVAR-patiënten en postoperatieve complicaties voor OSR-patiënten. Bij TO werd een grotere variatie tussen ziekenhuizen waargenomen in vergelijking met enkelvoudige uitkomstindicatoren, met name bij OSR. De variatie bleef grotendeels binnen de betrouwbaarheidsintervallen, waardoor het moeilijk was om 'best practices' te identificeren. Echter door TO te gebruiken, kunnen individuele ziekenhuizen zien waar ze kunnen verbeteren om de gewenste resultaten te bereiken. TO is daarom in eerste instantie vooral geschikt als instrument voor interne kwaliteitsverbetering en

niet voor ziekenhuisvergelijking. TO is sinds 2019 opgenomen in het DSAA-feedbacksysteem voor ziekenhuizen.

Hoewel de focus bij clinical auditing vaak ligt op direct zichtbare postoperatieve resultaten, is het bij het meten van de kwaliteit van zorg ook van belang om de langetermijnresultaten in overweging te nemen. Naast langetermijnoverleving zijn secundaire aorta-gerelateerde re-interventies een belangrijke uitkomstmaat. Eerdere studies hebben al aangetoond dat met het toenemende gebruik van EVAR het aantal aorta gerelateerde re-interventies ook is toegenomen.[17-19] Sinds de uitbreiding van de DSAA in 2016 zijn, naast primaire ingrepen, alle secundaire aorta-re-interventies (SAR's) die werden uitgevoerd in Nederland ook geregistreerd in de audit, waardoor het mogelijk is om langetermijnresultaten te genereren door gegevens van beide ingrepen te koppelen. Omdat deze gegevens pas recentelijk zijn toegevoegd, is het nog niet mogelijk uitspraken te doen over de incidentie van SAR's, maar met de eerste analyses van deze gegevens hebben we in **hoofdstuk 7** inzicht kunnen geven in de omvang van het probleem. In twee jaar tijd ondergingen 691 patiënten in Nederland een SAR; dat is goed voor bijna 10% van alle AAA-ingrepen die jaarlijks worden uitgevoerd. De meest voorkomende indicatie voor SAR's was endoleaks. De meeste SAR's werden uitgevoerd in een electieve setting en meer dan de helft werd uitgevoerd met een endovasculaire procedure. De postoperatieve mortaliteit van SAR's was vergelijkbaar met de resultaten na primaire AAA-chirurgie, in zowel de electieve, acuut symptomatische en geruptureerde setting.

Ongeveer een kwart van de SAR-patiënten was eerder geregistreerd in de DSAA voor hun primaire AAA-ingreep (2013-2017), wat inhoudt dat de overige patiënten hun primaire AAA-ingreep hebben gehad vóór de start van de audit (<2013); daardoor ontbreekt informatie over hun primaire AAA-ingreep.

In de subgroep analyse, waarbij data over de SAR gekoppeld werd aan de primaire ingreep, bleek dat de overgrote meerderheid van SAR's volgde na primaire DSAA-geregistreerde EVAR-procedures (169/181). Bij het evalueren van het type stent dat werd gebruikt bij de primaire AAA-ingreep, werd een oververtegenwoordiging van 'endovasculair aneurysm sealing system stent' gezien. Slechts de helft van de primaire EVAR-procedures kon tijdens de SAR opnieuw worden behandeld met een endovasculaire procedure. Bovendien onderging in de subgroep een vijfde van de patiënten met een primaire electieve AAA-procedure vervolgens in een acute setting (acuut symptomatisch of ruptuur) een SAR. Met meer jaren van auditing, zal het aandeel SAR's dat kan worden gekoppeld aan hun primaire interventie toenemen en uiteindelijk volledig zijn, waardoor het mogelijk wordt om een nationale incidentie van SAR te geven en om SAR-percentages tussen chirurgische technieken te evalueren. Bovendien kan de audit, door SAR-percentages tussen verschillende stenttypes te evalueren, dienen als een hulpmiddel om stent-gerelateerde problemen op te sporen.

Dutch Audit for Carotid Interventions

Sinds juni 2013 worden alle patiënten die in Nederland carotischirurgie ondergaan, geregistreerd in de Dutch Audit for Carotid Interventions (DACI).[20] In **hoofdstuk 8** wordt aangetoond dat de DACI met succes in Nederland is geïmplementeerd met een landelijke dekking van alle ziekenhuizen, waardoor de kwaliteit van de zorg voor carotis-endarteriëctomie (CEA) nationaal en tussen ziekenhuizen kan worden geëvalueerd. Vanaf de start van de audit worden jaarlijks ongeveer 2500 patiënten door 52 ziekenhuizen geregistreerd in de DACI. Na de eerste jaren van auditing hebben we geconcludeerd dat CEA wordt uitgevoerd met een algemeen laag sterftecijfer en laag (ernstige) beroerte/sterftecijfer. Bovendien was er een redelijke naleving van de richtlijn met betrekking tot de indicator tijd-tot-interventie, waarbij 75% van de patiënten met een symptomatische carotisstenose een operatie onderging binnen 2 weken na het eerste consult in het ziekenhuis. Waar de procesindicator tijd-tot-interventie significante variatie liet zien tussen ziekenhuizen, zijn uitkomstindicatoren als mortaliteit en (ernstige) beroerte/dood niet erg onderscheidend vanwege de lage algemene event-rates en het ontbreken van ziekenhuizen met een significant hogere event-rate. Het gebrek aan variatie in deze indicatoren bemoeilijkt een landelijke ziekenhuisvergelijking in het tijdperk met een minimumvolume van 20 CEA per jaar per ziekenhuis. Er konden echter 9 ziekenhuizen worden geïdentificeerd met een significant lager aantal beroertes/sterftecijfers dan het landelijk gemiddelde, waarvan andere mogelijk kunnen leren. Bovendien konden met het gebruik van DACI-data de volgende voorspellers voor ernstige beroerte/overlijden na CEA bij patiënten met een symptomatische carotisstenose worden geïdentificeerd: leeftijd, vrouwelijk geslacht, ernstige luchtwegaandoeningen, presentatie met corticale symptomen.

In **hoofdstuk 9** wordt uitgelegd hoe de kwaliteitsindicator tijd-tot-interventie tot stand is gekomen en hoe deze moet worden geïnterpreteerd. De richtlijn, welke adviseert om patiënten met een symptomatische carotisstenose binnen 2 weken na het eerste ziekenhuisbezoek te behandelen, is gebaseerd op een post-hoc meta-analyse van twee gerandomiseerde studies, uitgevoerd in 1981-1996.[21-24] In deze post-hoc meta-analyse werd 14 dagen gekozen als afkapwaarde, waarbij revascularisatie binnen deze termijn effectiever bleek te zijn in het voorkomen van een recidief transient ischaemic attack (TIA) of ischemisch cerebrovasculair accident (CVA) dan buiten deze termijn en waarbij revascularisatie na 12 weken niet zinvol werd geacht. Hierbij moet worden opgemerkt dat 14 dagen een gekozen getal is in plaats van een uitkomst van een berekening en dat het in de praktijk een glijdende schaal is waarbij eerder ingrijpen effectiever is in het voorkomen van een recidief CVA. Het vaststellen van een kwaliteitsindicator als tijd-tot-interventie stimuleert artsen om de multidisciplinaire samenwerking te verbeteren en zorgpaden beter in te richten. Een dergelijke externe prikkel is gunstig voor het totale cohort van symptomatische patiënten die CEA ondergaan, om het aantal beroertes te voorkomen. Er moet echter voor worden gewaakt dat deze kwaliteitsindicator wordt gezien als een scheidslijn waarbinnen interventie effectief is en daarbuiten niet.

Een belangrijke nuancering is dat in de bovengenoemde onderzoeken het tijdsinterval is gemeten vanaf het moment van de eerste of laatste symptomen tot aan de operatie. Echter, de kwaliteitsindicator begint met meten vanaf het eerste consult in het ziekenhuis. Aangezien uit eerder onderzoek is gebleken dat er een gemiddelde pre-ziekenhuis (patiënt-gerelateerde) vertraging is van 7 dagen, is bij het vaststellen van de kwaliteitsindicator gekozen om alleen het interval te meten waarbinnen ziekenhuizen invloed kunnen uitoefenen.[25]

REFERENTIES

1. Dutch Institute for Clinical Auditing (DICA). http://www.dica.nl/.
2. Dutch Surgical Aneurysm Audit. https://dica.nl/dsaa/home. Accessed 16.04.2021.
3. DSAA annual report 2014. https://www.dica.nl/jaarrapportage-2014/assets/uploads/DICA-JAAR-OFFLINE-2014.pdf.
4. Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med.* 2002;346(19):1437-1444.
5. Powell JT, Brown LC, Forbes JF, et al. Final 12-year follow-up of surgery versus surveillance in the UK Small Aneurysm Trial. *Br J Surg.* 2007;94(6):702-708.
6. Shang EK, Nathan DP, Boonn WW, et al. A modern experience with saccular aortic aneurysms. *J Vasc Surg.* 2013;57(1):84-88.
7. Wanhainen A, Verzini F, Van Herzeele I, 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.
8. Chaikof EL, Dalman RL, Eskandari MK, 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 e72.
9. DSAA annual report 2017. 2017; http://dica.nl/jaarrapportage-2017/home.
10. Volume standards Dutch Society for Surgery. 2019; https://assets.heelkunde.nl/p/491520/none/Normen 8_1 versie april 2021.pdf.
11. Giles KA, Hamdan AD, Pomposelli FB, Wyers MC, Dahlberg SE, Schermerhorn ML. Population-based outcomes following endovascular and open repair of ruptured abdominal aortic aneurysms. *J Endovasc Ther.* 2009;16(5):554-564.
12. Giles KA, Pomposelli FB, Hamdan AD, Wyers MC, Schermerhorn ML. Comparison of open and endovascular repair of ruptured abdominal aortic aneurysms from the ACS-NSQIP 2005-07. *J Endovasc Ther.* 2009;16(3):365-372.
13. McPhee J, Eslami MH, Arous EJ, Messina LM, Schanzer A. Endovascular treatment of ruptured abdominal aortic aneurysms in the United States (2001-2006): a significant survival benefit over open repair is independently associated with increased institutional volume. *J Vasc Surg.* 2009;49(4):817-826.
14. Investigators IT, Powell JT, Sweeting MJ, et al. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ.* 2014;348:f7661.
15. Reimerink JJ, Hoornweg LL, Vahl AC, et al. Endovascular repair versus open repair of ruptured abdominal aortic aneurysms: a multicenter randomized controlled trial. *Ann Surg.* 2013;258(2):248-256.
16. Desgranges P, Kobeiter H, Katsahian S, et al. Editor's Choice–ECAR (Endovasculaire ou Chirurgie dans les Anevrysmes aorto-iliaques Rompus): A French Randomized Controlled Trial of Endovascular Versus Open Surgical Repair of Ruptured Aorto-iliac Aneurysms. *Eur J Vasc Endovasc Surg.* 2015;50(3):303-310.
17. De Bruin JL, Baas AF, Buth J, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1881-1889.
18. United Kingdom ETI, Greenhalgh RM, Brown LC, et al. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1863-1871.
19. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM, investigators Et. 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. *Lancet.* 2016;388(10058):2366-2374.
20. Dutch Audit for Carotid Interventions. https://dica.nl/daci/home. Accessed 16.04.2021.
21. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet.* 1998;351(9113):1379-1387.
22. Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid

Endarterectomy Trial Collaborators. *N Engl J Med.* 1998;339(20):1415-1425.

23. Rothwell PM, Eliasziw M, Gutnikov SA, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *Lancet.* 2003;361(9352):107-116.
24. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ, Carotid Endarterectomy Trialists C. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet.* 2004;363(9413):915-924.
25. den Hartog AG, Moll FL, van der Worp HB, Hoff RG, Kappelle LJ, de Borst GJ. Delay to carotid endarterectomy in patients with symptomatic carotid artery stenosis. *Eur J Vasc Endovasc Surg.* 2014;47(3):233-239.

APPENDICES

List of publications
Dankwoord
Curriculum Vitae

List of publications

2022

Alberga AJ, de Bruin JL, Bastos Gonçalves F, **Karthaus EG**, Wilschut JA, van Herwaarden JA, Wever JJ, Verhagen HJM. Nationwide Outcomes of Octogenarians Following Open or Endovascular Management After Ruptured Abdominal Aortic Aneurysms
J Endovasc Ther 2022 Mar 21;15266028221083460 *Ahead of print*

Alberga AJ, **Karthaus EG,** Wilschut JA, de Bruin JL, Akkersdijk GP, Geelkerken BH, Hamming JF, Wever JJ, Verhagen HJM. Treatment Outcome Trends for Non-Ruptured Abdominal Aortic Aneurysms: A Nationwide Prospective Cohort Study
Eur J Vasc Endovasc Surg 2022 Feb;63(2):275-283

2021

Alberga AJ, **Karthaus EG**, van Zwet EW, de Bruin JL, van Herwaarden JA, Wever JJ, Verhagen HJM. Outcomes in Octogenarians and the Effect of Comorbidities After Intact Abdominal Aortic Aneurysm Repair in the Netherlands: A Nationwide Cohort Study
Eur J Vasc Endovasc Surg. 2021 Jun;61(6):920-928

Lijftogt N, Vahl AC, **Karthaus EG**, van der Willik EM, Amadio S, van Zwet EW, Hamming JF. Effects of hospital preference for endovascular repair on postoperative mortality after elective abdominal aortic aneurysm repair: analysis of the Dutch Surgical Aneurysm Audit
BJS Open. 2021 May 7;5(3):zraa065.

2020

Karthaus EG, Lijftogt N, Vahl AC, van der Willik EM, Amadio S, van Zwet EW, Hamming JF. Patients with a Ruptured Abdominal Aortic Aneurysm are better Informed in Hospital with an 'EVAR-preferrence' Strategy: An instrumental Variable Analysis of the DSAA.
Annals of Vascular Surgery 2020 Nov;69:332-344.

Kuhrij LS, **Karthaus EG**, Vahl AC, Willems MCM, Elshof JW, de Borst GJ. A composite measure for quality of care in patients with symptomatic carotid stenosis using Textbook Outcome. Eur J Vasc Endovasc Surg. 2020 Oct;60(4):502-508

Karthaus EG, Vahl AC, Elsman BHP, Wouters MWJM, de Borst GJ, Hamming JF. National Numbers of Secondary Aortic Reinterventions after Primary Abdominal Aortic Surgery from the Dutch Surgical Aneurysm Audit.
Annals of Vascular Surgery: 2020 Apr 24:S0890-5096(20)30353-8

Karthaus EG, Vahl AC, van der Werf LR, Elsman BHP, van Herwaarden JA, Wouters MWJM, Hamming JF. Variation in Surgical Treatment of Abdominal Aortic Aneurysms with Small Aortic Diameters in the Netherlands. Ann Surg. 2020 Apr;271(4):781-789

2019

Karthaus EG, Tong, TML, Vahl A, Hamming JF. Saccular Abdominal Aortic Aneurysms: Patient Characteristics, Clinical Presentation, Treatments and Outcomes in the Netherlands. Ann Surg. 2019 Nov;270(5):852-858

Detering R, **Karthaus EG**, Borstlap WAA, Marijnen CAM, van de Velde CJH, Bemelman WA, Beets GL, Tanis PJ, Aalbers AGJ. Treatment and survival of locally recurrent rectal cancer: a cross-sectional population study 15 years after the Dutch TME trial. Eur J Surg Oncol. 2019 Nov;45(11):2059-2069

Kuhrij LS, Meershoek AJA, **Karthaus EG,** Vahl A, Hamming JF, Nederkorn PJ, de Borst GJ. Factors Associated with Hospital-dependent delay to carotid endarterectomy in the Dutch Audit for Carotid Interventions. Eur J Vasc Endovasc Surg. 2019 Oct;58(4):495-501

Van der Werf LR, Voeten SC, van Loe CMM, **Karthaus EG,** Wouters MWJM, Prins HA. Data verification of national clinical audits in the Netherlands. BJS Open. 2019 Aug 19;3(6):857-864

2018

Karthaus EG, Vahl A, Kuhrij LS, Elsman BHP, Geelkerken RH, Wouters MWJM, Hamming JF, de Borst GJ. The Dutch Audit for Carotid Interventions: Transparency in Quality of Carotid Endarterectomy in Symptomatic Patients in the Netherlands. Eur J Vasc Endovasc Surg: 2018 Oct;56(4):476-485

Karthaus EG, Meershoek AJA, Kappelle LJ, de Borst GJ. Kwaliteitsindicator carotischirurgie benadeelt patient. Medisch Contact 2018 sept 6. Nummer 36, p 30-32

Lijftogt N, **Karthaus EG**, Vahl AC, van Zwet EW, van der Willik EM, Tollenaar RAEM, Hamming JF, Wouters MWJM. Failure to Rescue–A Closer look at Mortality Rates Has No Added Value for Hospital Comparison but is Useful for Team Quality Assessment in Abdominal Aortic Aneurysm Surgery in the Netherlands. Eur J Vasc Endovasc Surg: 2018 Aug 22. pii: S1078-5884(18)30421-0.

Kappelle LJ, **Karthaus EG,** Meershoek AJA, de borst GJ. When is carotid endarterectomy actually indicated for stenosis. Ned Tijdschr Geneeskd. 2018 Jun 1:162

2017

Karthaus EG, Lijftogt N, Busweiler LAD, Elsman BHP, Wouters MWJM, Vahl AC, Hamming JF. Textbook Outcome: A Composite Measure for Quality of Elective Aneurysm Surgery.
Ann Surg. 2017 Nov;266(5):898-904.

Karthaus EG, Zettervall SL, Buck DB, Soden PA, Ultee KHJ, Schermerhorn ML, Weyers M. Clinical Presentation, Management, Follow-up and Outcomes of Isolated Celiac and Superior Mesenteric Artery Dissections. J Vasc Surg 2017 jan;65(1):91-98.

2016

Karthaus EG, Post ICJH, Akkersdijk GJM. Spontaneous aortoenteric fistula involving the sigmoid: A case report and review of literature. Int J Surg Case Rep 2016; 19:97-9

2015

Buck DB, **Karthaus EG**, Soden PA, Ultee KHJ, van Herwaarden JA, Moll FL, Schermerhorn ML. Percutaneous versus Femoral Cutdown Access for Endovascular Aneurysm Repair.
J Vasc Surg 2015 Jul;62(1):16-21

Dankwoord

Dit proefschrift is tot stand gekomen dankzij de hulp en steun van velen, wie ik allemaal zeer dankbaar ben. Een aantal personen wil ik graag nog in het bijzonder bedanken.

Mijn promotor prof. dr. J.F. Hamming. Beste Jaap, ik wil je bedanken dat je me de vrijheid en het vertrouwen gaf om zelf invulling te geven aan dit proefschrift en promotietraject. Het sparren over de verschillende onderzoeksvraagstukken en jouw begeleiding om de boodschap van een artikel scherp te formuleren hebben dit proefschrift gemaakt tot wat het is.

Mijn promotor prof. dr. G.J. de Borst. Beste Gert Jan, ondanks dat het zwaartepunt van dit proefschrift meer op de aneurysma chirurgie kwam te liggen, dacht je bij elk onderzoek mee en heeft jouw oog voor detail onze artikelen verbeterd. Daarnaast wil ik je bedanken dat ik altijd welkom was om bij de Utrechtse artsonderzoekersgroep aan te haken, wat ontzettend gezellig was.

Mijn copromotor dr. A.C. Vahl, Beste Anco, jouw enthousiasme voor de audits en interesse in de toepassing van uitdagende statistische methoden waren aanstekelijk en hebben een belangrijke bijdrage geleverd aan dit proefschrift. De snelheid waarmee jij mijn werk las en van feedback voorzag was geweldig en ontzettend motiverend. Ik had me geen betere copromotor kunnen wensen.

Mijn begeleider bij DICA prof. dr. M.W.J.M. Wouters. Beste Michel, ik bewonder je talent om in de bergen van data de interessante onderwerpen te vinden en om vanuit een originele invalshoek naar kwaliteitsvraagstukken te kijken. Ik heb hier veel van geleerd en vind het altijd fijn om met je samen te werken.

Het bestuur en wetenschappelijke commissie van de DSAA en DACI en alle vaatchirurgen, verpleegkundigen en registratiemedewerkers die de data geregistreerd hebben. Zonder jullie inzet was dit proefschrift er niet geweest.

Alle collega's bij DICA en in het bijzonder Linde, Pauline, Julia, Naomi, Laurien, Robin, Michiel, Leonie, Fieke en Stijn. Ik kijk met veel plezier terug op mijn tijd bij DICA, wat was het gezellig met jullie!

In de periode waarin ik dit proefschrift heb geschreven heb ik veel steun gehad aan mijn lieve vrienden en familie, zonder jullie was deze periode lang niet zo leuk geweest.

Mijn Paranimfen, mijn vriendschap met jullie is me erg dierbaar en ik ben blij dat jullie vandaag naast mij staan. Lieve Joséphine, al leef je vaak aan de andere kant van de wereld, je

bent voor mij altijd dichtbij. Lieve Fleur, bij jou kan ik altijd terecht. Jouw steun en luisterend oor betekenen veel voor me.

Mijn Schwessie, lieve Lot, wat bof ik met jou als mijn zus en de sterke band die wij hebben. Je staat onvoorwaardelijk voor me klaar met raad en daad en schroomt niet om me af en toe een spiegel voor te houden.

Mijn ouders, mijn trouwste supporters die elk artikel van dit proefschrift hebben meegelezen. Ik ben bevoorrecht door het warme nest waar ik samen met Lot heb mogen opgroeien en de onvoorwaardelijke liefde en steun die jullie altijd geven. Lieve Mam, jouw rust en stabiliteit zijn uniek en maken het altijd heerlijk om met jou te zijn. Pap, ik kan met jou alles van het leven bespreken en voel me altijd gehoord en gesteund door mijn ontzettend trotse en lieve vader.

Mijn liefste Meelf, voor je geduld en het vertrouwen in mij dat ik dit proefschrift uiteindelijk nog wel zou afmaken. Ik ben trots op wat we samen hebben en zijn. Jij maakt mij gelukkig.

Tot slot lieve Rutger, wat een feest dat jij er bent!

Curriculum Vitae

Eleonora (Noor) Karthaus was born on the 7th of October 1988 in Deventer. After graduating from the Etty Hillesum Lyceum in Deventer in 2007, she moved to Amsterdam. After studying history for 1 year, she started to study medicine at the Vrije Universiteit of Amsterdam in 2008. During her studies, she worked at BISLIFE in Leiden where she was responsible for the processes of donor screening and co-ordination of retrieval of donor tissue. In 2014, she conducted her scientific research internship at the department of vascular surgery at BIDMC in Boston. She investigated the differences in outcomes between surgical and percutaneous introduction of Endovascular Aneurysm Repair (EVAR), using data from the American National Quality Registry. After receiving her medical degree in 2015, she started her first job as a junior doctor at the department of surgical oncological disciplines at the Antoni van Leeuwenhoek in Amsterdam. In 2016, she enrolled in the combined PhD program at the Dutch Institute of Clinical Auditing and Leiden University, where she was responsible for the daily management of the national vascular surgical clinical audits (Dutch Surgical Aneurysm Audit, Dutch Audit for Carotid Interventions and the Dutch Audit for Peripheral Artery disease). Under the supervision of Prof. dr. J.F. Hamming, Prof. dr. G.J. de Borst and Dr. A.C. Vahl, she investigated various issues regarding the evaluation of quality of care in abdominal aortic aneurysm and carotid artery surgery in the Netherlands, which resulted in this thesis. During this three-year period, she completed the clinical epidemiology course program at the LUMC. In 2019 Noor started working as a junior doctor of the department of surgery in the OLVG in Amsterdam, after which she started as surgical resident in training in the Gelre Hospital Apeldoorn in 2020. Currently, Noor lives with her boyfriend Meelf in Amsterdam and together they have a son Rutger and a dog Sjaak.


EXLIBRIS
E.G. KARTHAUS