Thoracic Aortic Catastrophes
Towards the Endovascular Solution

Frederik Hendrik Willem Jonker

Thoracic Aortic Catastrophes: Towards the Endovascular Solution
Frederik H.W. Jonker, Utrecht University, Faculty of Medicine, University Medical Center Utrecht, the Netherlands.

Thesis Utrecht University, with a summary in Dutch.

ISBN: 978-94-6108-110-0

Printed by: Gildeprint Drukkerijen - Enschede, the Netherlands
Lay-out: Gildeprint Drukkerijen - Enschede, the Netherlands
Cover design: F.H.W. Jonker, J.E. Aruny, Gildeprint Drukkerijen - Enschede, the Netherlands

Thoracic Aortic Catastrophes
Towards the Endovascular Solution

Catastrofes van de aorta thoracalis: Op weg naar de endovasculaire oplossing
(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Utrecht
op gezag van de rector magnificus, prof.dr. J.C. Stoof,
ingevolge het besluit van het college voor promoties
in het openbaar te verdedigen op

donderdag 16 december 2010 des middags te 2.30

door

Frederik Hendrik Willem Jonker

geboren op 11 augustus 1983 te Utrecht

Promotor: Prof.dr. F.L. Moll
Co-promotor: Dr. B.E. Muhs

Publication of this thesis was financially supported by:
Dit proefschrift werd mede mogelijk gemaakt met financiële steun van:

Medtronic CardioVascular, W.L. Gore & Associates, Bard Benelux n.v. en het Chirurgisch Fonds UMC Utrecht.

Financial support by the Netherlands Heart Foundation for the publication of this thesis is gratefully acknowledged.

CONTENTS

Chapter 1

Introduction

The descending thoracic aorta begins at the aortic isthmus between the origin of the left subclavian artery and the ligamentum arteriosum, at the lower border of the 4th thoracic vertebra, and ends at the aortic hiatus in the diaphragm, at the lower border of the 12th thoracic vertebra.[1] Aortic aneurysms and dissections are the principal diseases of the descending thoracic aorta, and occur most commonly in the sixth and seventh decade of life. These thoracic aortic pathologies are rare, but the incidence is increasing, which is likely the result of the increasing age of the population, the rising prevalence of hypertension, and improved diagnostic modalities.[2-4]

Morbidity and mortality from untreated thoracic aortic aneurysms mainly depend on complications such as aneurysm rupture and aneurysm dissection. The five-years survival of patients with untreated thoracic aortic aneurysm larger than 6 cm is only 20% to 54%,[5-7] which is primarily the result of aneurysm rupture. The risks of aneurysm rupture and dissection increase with increasing aortic diameter, and for thoracic aortic aneurysms larger than 6 cm, the yearly rate of rupture, dissection and/or death is 15%.[6,8] Other aortic emergencies of the descending thoracic aorta include aortobronchial and aortoesophageal fistulas, and traumatic thoracic aortic injury.

Thoracic Aortic Aneurysm Rupture and Dissection

Thoracic aortic aneurysm rupture is an aortic catastrophe, with an estimated incidence of 5.0 per 100,000 people per year.[9] Approximately 30% of all ruptured thoracic aortic aneurysms are localized at the descending thoracic aorta (rDTAA), remaining aneurysms are found at the ascending aorta and aortic arch.[9] The prognosis of patients with ruptured thoracic aortic aneurysms is poor, the overall mortality rate is thought to exceed 90% and only 41% of patients are alive on arrival at the emergency department.[9] Although patients that are alive at admission have a more realistic prognosis, the outcomes remain poor and the overall in-hospital mortality of rDTAA in the United States between 1988 and 2002 was 45%.[10]

Acute aortic dissection is another thoracic aortic catastrophe, with an incidence of 2.9 to 3.5 per 100,000 people per year.[3,11,12] The most commonly used classification system for aortic dissection is the Stanford classification, although the DeBakey classification is still being used as well.[13] Stanford Type A dissections involve the ascending aorta and aortic arch, while Stanford Type B dissection arise from the descending aorta. In the absence of complications, acute type B aortic dissections (ABAD) can be managed with medical treatment only, which is associated with low in-hospital mortality rates, between 0% and 7%.[14-18] However, patients suffering from acute type B dissections associated with complications, such as aortic rupture or malperfusion syndromes, typically have very poor outcomes and require immediate intervention.[15,16,18-21]

Thoracic Aortic Fistulas

Rarely, fistulas arise between the descending thoracic aorta, and the esophagus or lungs.[22-24] The etiology of aortoesophageal fistulas (AEF) and aortobronchial fistulas (ABF) is often related to previous thoracic aortic intervention,[22-24] but fistulas can also be associated with thoracic aortic disease such as aortic aneurysms or dissections. Patients with AEF and ABF typically present with hematemesis or hemoptysis, but the presentation is frequently complicated by hypovolemic shock or infective complications.[22-24] ABF and AEF are lethal if left untreated, and immediate repair of the fistula is required, usually followed by intensive antibiotic treatment. Due to the low incidence of ABF and AEF, only small case series have been reported, and little is known about the optimal management of these aortic emergencies.

Traumatic Thoracic Aortic Injury

Trauma is the leading cause of death among people younger than 45 years in the United States, and traumatic thoracic aortic injury (TTAI) is the second most common cause of death among trauma patients worldwide.[25-27] The majority of traumatic aortic injuries are caused by major blunt trauma such as motor-vehicle accidents, and these aortic injuries are typically localized at the aortic isthmus distal to the left subclavian artery.[28-30] Patients with TTAI usually have multiple associated injuries, and typically suffer from substantial blood loss or hypovolemic shock. Approximately 80% to 90% of patients with traumatic thoracic aortic injury expire at the scene of the accident.[31,32] Patients that are admitted alive usually are more stable and this is associated with a better prognosis,[33,34] however, mortality and morbidity remain high due to complications related to the aortic injury and associated injuries.

Management of the Descending Thoracic Aortic Catastrophes

Immediate intervention is typically indicated for patients suffering acute thoracic aortic disease. Open surgical repair has been the traditional treatment of descending thoracic aortic catastrophes since the early fifties.[31,34-36] Surgical repair of thoracic aortic pathologies typically occurs through a left posterolateral thoracotomy, followed by resection of the aortic defect and interposition of the descending aorta using an aortic graft. However, open surgery of acute thoracic aortic disease is a very invasive treatment for patients that are already in a critical condition, resulting in high mortality rates. In addition, surviving patients often suffer from devastating complications including stroke and permanent paraplegia.[10,37]

In the early nineties, Juan Parodi and coworkers introduced endovascular aortic repair for the management of abdominal aortic aneurysm (AAA).[38] Michael Dake and colleagues from Stanford University soon applied thoracic endovascular aortic repair (TEVAR) for the treatment of descending thoracic aortic aneurysms.[39,40] TEVAR is less invasive than open surgery, avoiding thoracotomy and aortic cross-clamping, and is associated with less blood loss and shorter operating times compared with open surgery.[41]

Thoracic aortic disease is less common than abdominal aortic aneurysmal disease,[3,42,43] and the current literature describing the outcomes of endovascular repair of thoracic aortic catastrophes is limited. It remains therefore unclear if an endovascular approach for the management of rDTAA, complicated ABAD, TTAI, ABF and AEF is associated with reduced morbidity and mortality rates. Furthermore, factors that affect the outcomes after TEVAR for thoracic aortic emergencies are currently unknown as well.

Endograft-related complications

Although the early outcomes of endovascular repair of abdominal and thoracic aortic pathologies are encouraging, the endovascular approach is associated with endograft-related complications such as endoleak, endograft migration and collapse.[44-51] Endoleak is diagnosed in 5% to 40% of patients treated with TEVAR,[51-55] and the majority consist of type 1 endoleaks,[51,53-55] which require immediate re-intervention.

Adequate endograft sizing is thought to be essential for minimizing risks of these complications after endovascular repair of abdominal and thoracic aortic disease, and satisfying long-term results.[56,57] Most endograft manufacturers recommend that endografts are oversized between 10% to 20% during TEVAR for a proper fixation and seal. Extreme oversizing could theoretically lead to infolding and collapse of the endograft,[58] while relative undersizing may result in an incomplete seal and inadequate fixation, and subsequent type 1 endoleaks or endograft migration.

Endograft sizing in Patients with Thoracic Aortic Catastrophes

Thoracic aortic catastrophes are often associated with considerable blood loss, or even hypovolemic shock. Although peripheral vasoconstriction is a well known physiologic response to hypovolemic shock, in order to maintain adequate perfusion of vital organs such as the brain and heart, it is currently unknown how the aorta responds to hypovolemia.[59-61] Temporary changes in the aortic diameter during blood loss could lead to incorrect aortic measurements on pre-operative CTA, inadequate endograft sizing and increased risks of endograft-related complications after TEVAR for thoracic aortic emergencies. A better understanding of the aortic physiology during hypovolemic shock could therefore help improve long-term outcomes of TEVAR.

Outline of the Thesis

The trends and outcomes of open treatment and endovascular repair of traumatic aortic injuries will be investigated in **Chapter 2** using the administrative database of the New York State. Pooled outcomes of open repair and endovascular repair of ruptured thoracic aortic aneurysms will be compared in a meta-analysis of the literature in **Chapter 3**. The mortality, stroke and paraplegia rates after open surgery and endovascular repair of ruptured thoracic aortic aneurysms will be further investigated in a multi-center study in **Chapter 4**. Long-term outcomes after

TEVAR for ruptured thoracic aortic aneurysms as well as predictors of 30-day mortality will be explored in **Chapter 5**, while predictors of procedure-related stroke will be discussed in **Chapter 6**. The importance of refractory pain and hypertension in uncomplicated acute type B aortic dissection will be discussed in **Chapter 7**. The impact of age on the management and outcomes of complicated acute type B aortic dissections will be investigated in **Chapter 8**. Endovascular management of aortobronchial and aortoesophageal fistulas will be evaluated in **Chapter 9**, while published outcomes of TEVAR for these fistulas will be analyzed in **Chapter 10**. The changes in aortic diameter in trauma patients admitted with hemodynamic instability will be explored in **Chapter 11**. The exact impact of blood loss and hypovolemic shock on the aortic diameter will be further investigated in an experimental porcine model in **Chapter 12**. The causes and timing of endograft collapse after endovascular management of thoracic aortic disease will be explored in **Chapter 13**, using a systematic review and meta-analysis of the literature. The summary of this thesis can be found in **Chapter 14**, and the summary in Dutch in **Chapter 15**.

REFERENCES

1. Gray H. The Descending Aorta. In: Anatomy of the Human Body. Philadelphia: Lea & Febiger; 1918.
2. Ince H, Nienaber CA. Etiology, pathogenesis and management of thoracic aortic aneurysm. Nat Clin Pract Cardiovasc Med 2007; 4:418-427.
3. Olsson C, Thelin S, Stahle E et al. Thoracic aortic aneurysm and dissection: increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002. Circulation 2006; 114:2611-2618.
4. Elefteriades JA, Farkas EA. Thoracic aortic aneurysm clinically pertinent controversies and uncertainties. J Am Coll Cardiol 2010; 55:841-857.
5. Bickerstaff LK, Pairolero PC, Hollier LH et al. Thoracic aortic aneurysms: a population-based study. Surgery 1982; 92:1103-1108.
6. Davies RR, Goldstein LJ, Coady MA et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. Ann Thorac Surg 2002; 73:17-27.
7. Coady MA, Rizzo JA, Hammond GL et al. Surgical intervention criteria for thoracic aortic aneurysms: a study of growth rates and complications. Ann Thorac Surg 1999; 67:1922-1926.
8. Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. Ann Thorac Surg 2002; 74:S1877-S1880.
9. Johansson G, Markstrom U, Swedenborg J. Ruptured thoracic aortic aneurysms: a study of incidence and mortality rates. J Vasc Surg 1995; 21:985-988.
10. Schermerhorn ML, Giles KA, Hamdan AD et al. Population-based outcomes of open descending thoracic aortic aneurysm repair. J Vasc Surg 2008; 48:821-827.
11. Clouse WD, Hallett JW, Jr., Schaff HV et al. Acute aortic dissection: population-based incidence compared with degenerative aortic aneurysm rupture. Mayo Clin Proc 2004; 79:176-180.
12. Meszaros I, Morocz J, Szlavi J et al. Epidemiology and clinicopathology of aortic dissection. Chest 2000; 117:1271-1278.
13. Erbel R, Alfonso F, Boileau C et al. Diagnosis and management of aortic dissection. Eur Heart J 2001; 22:1642-1681.
14. Nienaber CA, Rousseau H, Eggebrecht H et al. Randomized comparison of strategies for type B aortic dissection: the INvestigation of STEnt Grafts in Aortic Dissection (INSTEAD) trial. Circulation 2009; 120:2519-2528.
15. Golledge J, Eagle KA. Acute aortic dissection. Lancet 2008; 372:55-66.
16. Estrera AL, Miller CC, Goodrick J et al. Update on outcomes of acute type B aortic dissection. Ann Thorac Surg 2007; 83:S842-S845.
17. Tang DG, Dake MD. TEVAR for acute uncomplicated aortic dissection: immediate repair versus medical therapy. Semin Vasc Surg 2009; 22:145-151.

18. Elefteriades JA, Lovoulos CJ, Coady MA et al. Management of descending aortic dissection. Ann Thorac Surg 1999; 67:2002-2005.
19. Trimarchi S, Nienaber CA, Rampoldi V et al. Role and results of surgery in acute type B aortic dissection: insights from the International Registry of Acute Aortic Dissection (IRAD). Circulation 2006; 114:I357-I364.
20. Lansman SL, Hagl C, Fink D et al. Acute type B aortic dissection: surgical therapy. Ann Thorac Surg 2002; 74:S1833-S1835.
21. Umana JP, Lai DT, Mitchell RS et al. Is medical therapy still the optimal treatment strategy for patients with acute type B aortic dissections? J Thorac Cardiovasc Surg 2002; 124:896-910.
22. Hollander JE, Quick G. Aortoesophageal fistula: a comprehensive review of the literature. Am J Med 1991; 91:279-287.
23. Carter R, Mulder GA, Snyder EN, Jr. et al. Aortoesophageal fistula. Am J Surg 1978; 136:26-30.
24. Piciche M, De PR, Fabbri A et al. Postoperative aortic fistulas into the airways: etiology, pathogenesis, presentation, diagnosis, and management. Ann Thorac Surg 2003; 75:1998-2006.
25. WISQARS Leading Causes of Death Reports, 1999-2007. National Center for Injury Prevention and Control September 2010; Available from: http://webappa.cdc.gov/sasweb/ncipc/leadcaus10.html.
26. Schumacher H, Bockler D, von Tengg-Kobligk H et al. Acute traumatic aortic tear: open versus stent-graft repair. Semin Vasc Surg 2006; 19:48-59.
27. Fabian TC, Davis KA, Gavant ML et al. Prospective study of blunt aortic injury: helical CT is diagnostic and antihypertensive therapy reduces rupture. Ann Surg 1998; 227:666-676.
28. Feczko JD, Lynch L, Pless JE et al. An autopsy case review of 142 nonpenetrating (blunt) injuries of the aorta. J Trauma 1992; 33:846-849.
29. Demetriades D, Velmahos GC, Scalea TM et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008; 64:561-570.
30. Riesenman PJ, Farber MA, Rich PB et al. Outcomes of surgical and endovascular treatment of acute traumatic thoracic aortic injury. J Vasc Surg 2007; 46:934-940.
31. Parmley LF, Mattingly TW, Manion WC et al. Nonpenetrating traumatic injury of the aorta. Circulation 1958; 17:1086-1101.
32. Dosios TJ, Salemis N, Angouras D et al. Blunt and penetrating trauma of the thoracic aorta and aortic arch branches: an autopsy study. J Trauma 2000; 49:696-703.
33. Lee RB, Stahlman GC, Sharp KW. Treatment priorities in patients with traumatic rupture of the thoracic aorta. Am Surg 1992; 58:37-43.
34. Mattox KL, Wall MJ, Jr. Historical review of blunt injury to the thoracic aorta. Chest Surg Clin N Am 2000; 10:167-82, x.
35. Lam CR, Ram HH. Resection of the descending thoracic aorta for aneurysm; a report of the use of a homograft in a case and an experimental study. Ann Surg 1951; 134:743-752.

36. Cooley DA, De Bakey ME. Surgical considerations of intrathoracic aneurysms of the aorta and great vessels. Ann Surg 1952; 135:660-680.
37. Crawford ES, Hess KR, Cohen ES et al. Ruptured aneurysm of the descending thoracic and thoracoabdominal aorta. Analysis according to size and treatment. Ann Surg 1991; 213:417-425.
38. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. Ann Vasc Surg 1991; 5:491-499.
39. Dake MD, Miller DC, Semba CP et al. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. N Engl J Med 1994; 331:1729-1734.
40. Mitchell RS, Dake MD, Sembra CP et al. Endovascular stent-graft repair of thoracic aortic aneurysms. J Thorac Cardiovasc Surg 1996; 111:1054-1062.
41. Nienaber CA, Fattori R, Lund G et al. Nonsurgical reconstruction of thoracic aortic dissection by stent-graft placement. N Engl J Med 1999; 340:1539-1545.
42. Melton LJ, III, Bickerstaff LK, Hollier LH et al. Changing incidence of abdominal aortic aneurysms: a population-based study. Am J Epidemiol 1984; 120:379-386.
43. Wilmink AB, Quick CR. Epidemiology and potential for prevention of abdominal aortic aneurysm. Br J Surg 1998; 85:155-162.
44. Corriere MA, Feurer ID, Becker SY et al. Endoleak following endovascular abdominal aortic aneurysm repair: implications for duration of screening. Ann Surg 2004; 239:800-805.
45. Jones JE, Atkins MD, Brewster DC et al. Persistent type 2 endoleak after endovascular repair of abdominal aortic aneurysm is associated with adverse late outcomes. J Vasc Surg 2007; 46:1-8.
46. Zarins CK, Bloch DA, Crabtree T et al. Stent graft migration after endovascular aneurysm repair: importance of proximal fixation. J Vasc Surg 2003; 38:1264-1272.
47. Hobo R, Buth J. Secondary interventions following endovascular abdominal aortic aneurysm repair using current endografts. A EUROSTAR report. J Vasc Surg 2006; 43:896-902.
48. Leurs LJ, Harris PL, Buth J. Secondary interventions after elective endovascular repair of degenerative thoracic aortic aneurysms: results of the European collaborators registry (EUROSTAR). J Vasc Interv Radiol 2007; 18:491-495.
49. Svensson LG, Kouchoukos NT, Miller DC et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. Ann Thorac Surg 2008; 85:S1-41.
50. Sze DY, Mitchell RS, Miller DC et al. Infolding and collapse of thoracic endoprostheses: manifestations and treatment options. J Thorac Cardiovasc Surg 2009; 138:324-333.
51. Preventza O, Wheatley GH, III, Ramaiah VG et al. Management of endoleaks associated with endovascular treatment of descending thoracic aortic diseases. J Vasc Surg 2008; 48:69-73.
52. Morales JP, Greenberg RK, Lu Q et al. Endoleaks following endovascular repair of thoracic aortic aneurysm: etiology and outcomes. J Endovasc Ther 2008; 15:631-638.
53. Parmer SS, Carpenter JP, Stavropoulos SW et al. Endoleaks after endovascular repair of thoracic aortic aneurysms. J Vasc Surg 2006; 44:447-452.

54. Stavropoulos SW, Carpenter JP. Postoperative imaging surveillance and endoleak management after endovascular repair of thoracic aortic aneurysms. J Vasc Surg 2006; 43 Suppl A:89A-93A.
55. Ueda T, Fleischmann D, Dake MD et al. Incomplete endograft apposition to the aortic arch: bird-beak configuration increases risk of endoleak formation after thoracic endovascular aortic repair. Radiology 2010; 255:645-652.
56. van PJ, Schlosser FJ, Muhs BE et al. Oversizing of aortic stent grafts for abdominal aneurysm repair: a systematic review of the benefits and risks. Eur J Vasc Endovasc Surg 2009; 38:42-53.
57. Sternbergh WC, III, Money SR, Greenberg RK et al. Influence of endograft oversizing on device migration, endoleak, aneurysm shrinkage, and aortic neck dilation: results from the Zenith Multicenter Trial. J Vasc Surg 2004; 39:20-26.
58. Canaud L, Alric P, Laurent M et al. Proximal fixation of thoracic stent-grafts as a function of oversizing and increasing aortic arch angulation in human cadaveric aortas. J Endovasc Ther 2008; 15:326-334.
59. Wiggers HC, Ingraham RC. Vasoconstriction and the development of irreversible hemorrhagic shock. Am J Physiol 1948; 153:511-520.
60. Cohn JN, Luria MH. Studies in clinical shock and hypotension. IV. Variations in reflex vasoconstriction and cardiac stimulation. Circulation 1966; 34:823-832.
61. Peitzman AB, Billiar TR, Harbrecht BG et al. Hemorrhagic shock. Curr Probl Surg 1995; 32:925-1002.

Chapter 2

Trends and Outcomes of Endovascular and Open Treatment for Traumatic Thoracic Aortic Injury

Journal of Vascular Surgery 2010;51:565-71

Frederik H.W. Jonker,[1] MD
Jeannine K. Giacovelli,[2] MD
Bart E. Muhs,[1] MD, PhD
Julie Ann Sosa,[1] MA, MD
Jeffrey E. Indes,[1] MD

[1] Section of Vascular Surgery and Interventional Radiology, Yale University School of Medicine, New Haven, Connecticut, USA
[2] Department of Surgery, Mount Sinai School of Medicine, New York, New York, USA

ABSTRACT

Objective:
Traumatic thoracic aortic injury (TTAI) is associated with high mortality rates. Data supporting thoracic endovascular aortic repair (TEVAR) to reduce mortality and morbidity for TTAI is limited to small series and meta-analyses. In this study, we evaluated the trends and outcomes of open surgery and TEVAR for TTAI in New York State.

Methods:
All cases of TTAI in New York State between 2000 and 2007 were extracted from the New York Statewide Planning and Research Cooperative System (SPARCS) database. A diagnosis by International Classification of Diseases, 9th Revision coding of TTAI was required for inclusion.

Results:
We identified 328 patients with TTAI who underwent surgical repair in New York State between 2000 and 2007; mean age of the cohort was 39.3 years ±18 years; 80% were male. Open repair of TTAI was performed in 79.6% and 20.4% underwent TEVAR. Open repair was performed for all cases of TTAI until the introduction of TEVAR in 2005; TEVAR exceeded the use of open repair for TTAI in 2006 and 2007. Additional major injuries were present in 71.7% in the open repair group vs. 91.0% of the TEVAR group (p=0.001). The overall in-hospital mortality rate for the eight year period was significantly increased after open repair of TTAI compared to TEVAR: 17% vs. 6%, (OR 3.19, 95% CI: 1.11 - 9.23, p=0.024). After controlling for the significant covariates, TEVAR independently reduced the risk of death following surgical intervention for TTAI compared to the open procedure (OR 3.8, 95% CI: 1.28 - 10.99, p=0.010). Respiratory complications were the most common postoperative morbidity, and were significantly increased after open repair: 38% vs. 24% (OR 1.95, 95% CI: 1.05 - 3.60, p=0.032). There were no significant differences in cardiac complications, acute renal failure (ARF), paraplegia or stroke. Endoleak and distal embolization each occurred in 9% of patients after TEVAR.

Conclusions:
There has been a shift towards endovascular management of patients with TTAI. This change in surgical strategy has been associated with less post-operative mortality and fewer pulmonary complications in patients suffering from TTAI. TEVAR is associated with significant device-related complications.

INTRODUCTION

Traumatic thoracic aortic injury (TTAI) is the second most common cause of death in trauma patients, accounting for about 8.000 deaths per year in the United States.[1,2] TTAI is typically caused by blunt trauma and occurs in approximately 0.3% of all trauma admissions and in 1.2% of all motor-vehicle accidents.[3,4] Up to 90% of patients with TTAI will die at the scene of an accident.[5,6] A considerable number of patients expires after admission as well, although the in-hospital mortality of patients with TTAI has decreased significantly over time.[7,8] Reasons for improved outcome of TTAI are increased use of passengers restraints, development of trauma centers, institution of β-blockers, improvement in mechanical circulatory support, and introduction of novel surgical procedures and technologies, such as endovascular repair.[4,7]

Open surgical repair with thoracotomy and interposition of an aortic graft has been the traditional method of treating TTAI. In-hospital mortality of open surgery for TTAI is about 20%.[9,10] In addition, there is significant morbidity such as paraplegia in up to 15% of patients.[11] Recently, thoracic endovascular aortic repair (TEVAR) has been established as a safe and feasible technique for treatment of thoracic aortic pathologies.[12,13] TEVAR allows quick exclusion of the aortic lesion and is less invasive than open surgery, which is particularly desirable in patients with TTAI and multiple associated injuries. TEVAR appears to lower mortality and morbidity rates in patients with TTAI.[9-11] Nevertheless, TEVAR is still associated with a number of considerable complications such as endoleak, graft fracture and graft migration, necessitating life-long surveillance.

Due to the low incidence of TTAI, the current literature consists mainly of case series with limited numbers. For the present study, we evaluated all cases of TTAI in New York State from 2000 to 2007 treated with open surgery and TEVAR and the impact of endovascular repair on the in-hospital outcomes of TTAI was investigated.

METHODS

Discharge data for patients who were admitted with TTAI between 2000 and 2007 were extracted from the New York State Statewide Planning And Research Cooperative System (SPARCS) database. Legislatively mandated in the 1970s, this system has been collecting hospital discharge data for more than 30 years (http://www.health.state.ny.us/statistics/sparcs/index.htm). The New York Department of Health maintains the database, which includes 225 hospitals in the State of New York (the third largest state by population in the United States). The database contains individual demographic and clinical information of every patient discharged from an acute-care nonfederal hospital, which must be submitted by the hospital within 60 days after the month of the patient's discharge. Since the introduction of SPARCS, this dataset has been used to support many research projects.

We extracted all patients with TTAI from the SPARCS database on the base of diagnosis codes. All patients with the diagnosis code 901.0 (injury to the thoracic aorta) were included. Those with the ICD-9 codes pertaining to ruptured and non-ruptured thoracic aneurysms (441.1, 441.2) and aortic dissection (441.0) were excluded. The type of surgical repair performed was identified with ICD-9 procedure codes. Patients treated with open surgery had the ICD-9 procedure codes 38.45 (resection of thoracic aorta with replacement) or 38.55 (ligation of thoracic aorta). Patients who received TEVAR were identified with the ICD-9 procedure code 39.73 (endovascular implantation of graft in the thoracic aorta).

The following baseline characteristics were extracted for all patients in open repair and TEVAR groups: age, gender, year of diagnosis, co-morbid diseases, including diabetes mellitus (DM), hypertension, chronic obstructive pulmonary disease (COPD), peripheral vascular disease (PVD), chronic renal insufficiency (CRI), cerebrovascular disease (CVD), hyperlipidemia, and associated injuries including cerebral injury (intracranial hemorrhage, subarachnoid hemorrhage, subdural hemorrhage, extradural hemorrhage), lung injury, cardiac injury, liver injury, spleen injury and pelvic fracture. Additionally, the admission type (emergency, urgent or elective) was determined for all patients. Data regarding the year of each surgical procedure for TTAI were used to demonstrate the trend in operative management.

The following outcomes were compared between patients treated with open surgery and TEVAR: in-hospital mortality, in-hospital complications, including cardiac complications, pulmonary complications, paraplegia, stroke, acute renal failure (ARF), bleeding, infection, mesenteric ischemia, urinary complications, distal embolization and endoleak. The mean length of stay and the disposition after discharge (home, acute care, nursing home, home services, rehabilitation) were compared between both treatment groups.

Statistical analysis

All data were analyzed with SAS system software (SAS Institute, Cary, NC). The Cochran-Armitage trend test was used to investigate the trend in aortic interventions. Categorical variables were compared between patients that were treated with open surgery and TEVAR, using univariate analysis and the chi-square test. Fisher's exact test was used if the expected count was less than 5. Continuous variables with a normal distribution were compared between the open surgery group and the TEVAR group using Students t-test. Outcome results are expressed as both *p* values and 95% confidence intervals (95% CI). *P* values ≤0.050 were considered significant in our univariate analysis, and significant variables were evaluated using simple regression analysis.

Variables obtained using simple logistic regression analysis, with a level of significance ≤0.25, were included in a multiple logistic regression analysis. This multivariable regression model examined the dichotomous outcome (dead/alive), and associated risk factors. Only variables with *P* value ≤0.05 were included in the final model. Independent variables that were significantly correlated with both the outcome: death, and the predictor of interest: type of surgery (TEVAR

vs. open) were stratified and examined individually. Clinical reasoning determined the choice for inclusion between independent variables that significantly correlated with each other.

RESULTS

Incidence of TTAI and trends in operative management

In total, 659 patients admitted with traumatic thoracic aortic injury (TTAI) in New York State between 2000 and 2007 were identified. The annual incidence of TTAI increased slightly over the study period, the mean annual incidence during this period was 82.4 patients (figure 1). Overall, 49.8% (n=328) underwent surgical repair, and this subset of patients was the object of our analysis. The balance of patients underwent conservative therapy or expired before surgical intervention could be performed. The majority of patients received open surgical repair (n=261, 79.6%); remaining patients underwent TEVAR (n=67, 20.4%). Four additional patients underwent both an endovascular and an open surgical procedure and were excluded from further analysis. Open repair was performed for all cases of TTAI until 2005, when endovascular repair was introduced in New York State (Figure 2). TEVAR rapidly became the preferred technique for TTAI by 2006. With the advent of TEVAR in 2005, the proportion of admitted TTAI patients that underwent an aortic intervention significantly increased (figure 3, Cochran-Armitage trend test: p=0.043).

Baseline characteristics

Mean patient age of the TEVAR cohort was 41.6 years and 38.7 years in the open cohort; 79.6% were male. There were no significant differences in the mean age, gender or rates of pre-admission co morbidities between the open repair and TEVAR groups (table 1). Additional injuries to a major organ system were identified in 76% (n=248) of TTAIs. Overall, 91.0% (n=61) of patients in the TEVAR group vs. 71.7% (n=187) of the open repair group had any of these injuries (p=0.001). Admitted patients treated with TEVAR suffered more frequently from cerebral injury (22.4% vs. 8.8%, p=0.002), lung injury (79.1% vs. 53.6%, p<0.001), spleen injury (40.3% vs. 16.1%, p<0.001) and pelvic fracture (38.8% vs. 23.4%, p=0.011) compared with patients treated with open repair (table 1). Admissions in the open repair of TTAI were more frequently coded as emergent than admissions in the TEVAR group; 90.8% (n=237) vs. 80.6% (n=54), p=0.019 (table 1).

Table 1. Admission characteristics

	Open repair (n=261) N or mean (% or ±SD)		TEVAR (n=67) N or mean (% or ±SD)		p value
Age (y)	38.7	(18.0)	41.6	(17.9)	0.242
Male gender	202	(79.8)	59	(78.7)	0.825
Patient history					
DM	10	(3.8)	3	(4.5)	0.809
Hypertension	39	(14.8)	11	(16.4)	0.764
COPD	12	(4.6)	6	(9.0)	0.162
CAD	4	(1.5)	2	(3.0)	0.429
PVD	2	(0.8)	0	0	0.472
CRI	4	(1.5)	0	0	0.308
CVD	4	(1.5)	2	(3.0)	0.429
Hyperlipidemia	4	(1.5)	0	0	0.308
Associated injuries					
Cerebral injury	23	(8.8)	15	(22.4)	0.002
Lung injury	140	(53.6)	53	(79.1)	<0.001
Cardiac injury	9	(3.5)	2	(3.0)	0.298
Liver injury	59	(22.6)	9	(13.4)	0.098
Spleen injury	42	(16.1)	27	(40.3)	<0.001
Pelvic fracture	61	(23.4)	26	(38.8)	0.011
Any of above	187	(71.7)	61	(91.0)	0.001
Admission type					
Emergent	237	(90.8)	54	(80.6)	0.019
Urgent	21	(8.1)	10	(14.9)	0.086
Elective	3	(1.2)	3	(4.5)	0.070

DM diabetes mellitus, *COPD* chronic obstructive pulmonary disease, *CAD* coronary artery disease, *PVD* peripheral vascular disease, *CRI* chronic renal insufficiency, *CVD* cerebrovascular disease, *SD* standard deviation

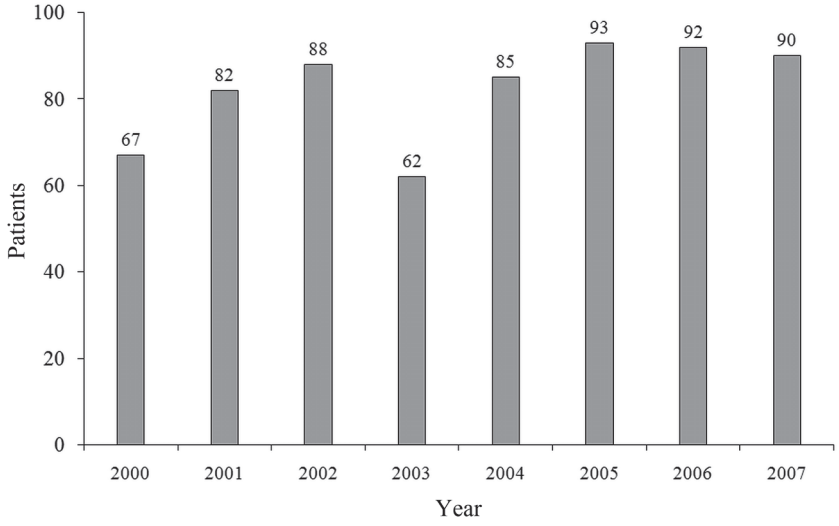

Figure 1. Annual rate of admitted patients with TTAI in New York State

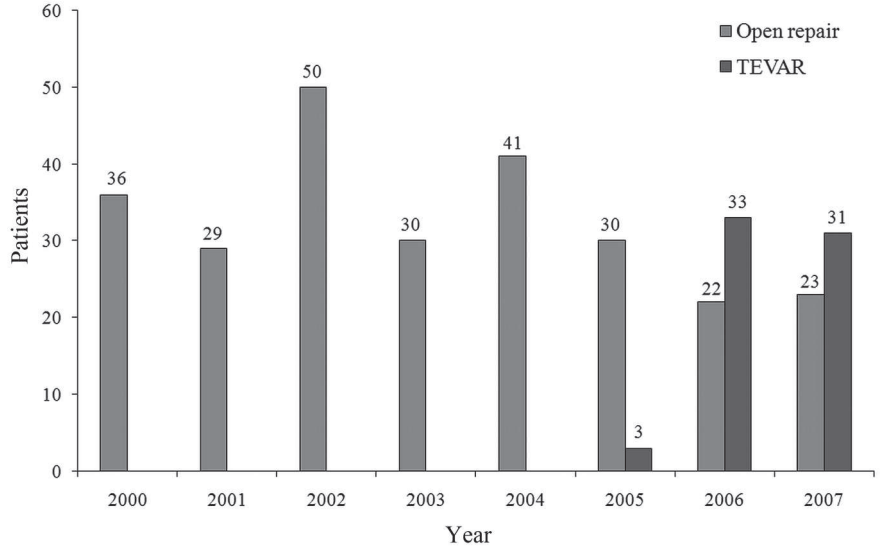

Figure 2. Aortic interventions for TTAI in New York State

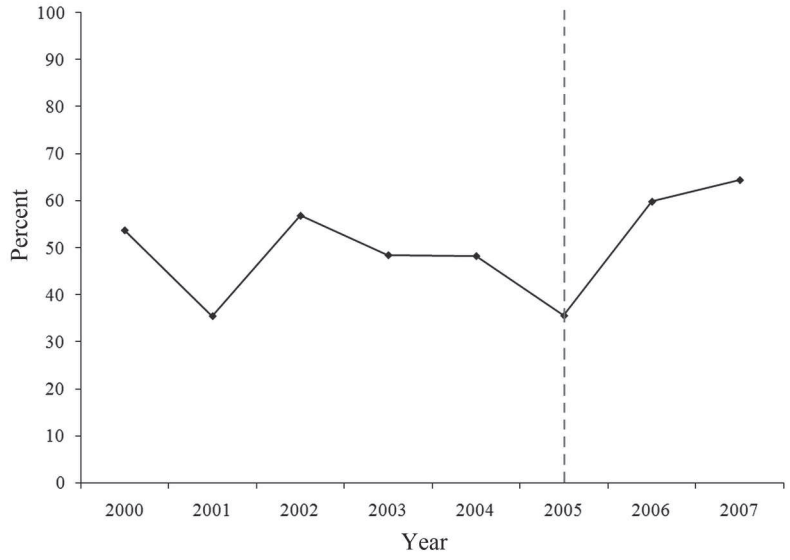

Figure 3. Trend in proportion of patients with TTAI receiving aortic intervention
With the advent of TEVAR in 2005, the proportion of admitted TTAI patients that underwent an aortic intervention significantly increased (Cochran-Armitage trend test: p=0.043).

Patient outcomes

Overall, the in-hospital mortality was 14.6% (n=48) among patients that underwent intervention for TTAI, compared with 24.8% (n=81) in the TTAI patients that did not receive intervention (p=0.001). In our univariate analysis, an increased in-hospital mortality rate for the eight year period was significantly associated with open repair of TTAI compared to TEVAR: 16.9% (n=44) vs. 6.0% (n=4), OR 3.19 (95% CI 1.11 – 9.23, p=0.024).

Of all deaths, 90% (n=43) occurred in patient admitted with an additional injury to a major organ system and 10% (n=5) in patients without additional injuries. In our analysis stratified by the presence of an additional injury, controlling for this likely confounder, 91% (n=39) of the deaths occurred in the open group and 9% (n=4) in the TEVAR group. The in-hospital mortality for the cohort with additional major injuries was 20.9% (39/187) for patients treated with open repair vs. 6.6% (4/61) for patients treated with TEVAR (p=0.010). We did not identify a significant difference in the rates of death comparing open surgery to TEVAR in the population admitted without additional injury.

Emergent admission designation within the SPARCS database was significantly correlated with the presence of an additional injury to a major organ system, and was therefore not included in our regression models. Age, gender and co morbidities were not significant predictors of death in regression analysis. Type of surgery however, was a significant predictor of death after controlling for the presence of additional injury. The patient cohort admitted with additional

injuries was 3.8 times (95% CI: 1.28 - 10.99) as likely to die if they underwent an open procedure compared to TEVAR.

Respiratory complications were the most common post-operative morbidity, and were significantly associated with open repair of TTAI compared with TEVAR: 37.9% (n=99) vs. 23.9% (n=16), OR 1.95 (95% CI: 1.05 – 3.60, p=0.032). Rates of postoperative bleeding were similar after both open repair and TEVAR: 24.5% (n=64) vs. 17.9% (n=12), p=0.253. There were no significant differences in cardiac complications, acute renal failure (ARF), stroke or paraplegia between both groups (table 2). Endoleak and distal embolization occurred each in 9.0% (n=6) after TEVAR (p<0.001).

Table 2. In-hospital outcomes of open repair and TEVAR for TTAI

	Open repair (n=261)		TEVAR (n=67)				
	N	(%)	N	(%)	OR	95% CI	p value
Mortality	44	(16.9)	4	(6.0)	3.19	1.11 - 9.23	0.024
Complications							
Cardiac	14	(5.4)	2	(2,9)	1.84	0.41 - 8.31	0.420
Stroke	6	(2.3)	2	(2.9)	0.76	0.15 - 3.88	0.745
Pulmonary	99	(37.9)	16	(23.9)	1.95	1.05 - 3.60	0.032
Paraplegia	2	(0.8)	0	(0)	1.01	0.99 - 1.02	0.472
ARF	5	(1.9)	2	(3.0)	0.63	0.12 - 3.35	0.589
Bleeding	64	(24.5)	12	(17.9)	1.49	0.75 - 2.95	0.253
Infection	7	(2.7)	2	(3.0)	0.90	0.18 - 4.41	0.892
Mesenteric	2	(0.8)	0	(0)	1.01	0.99 - 1.02	0.472
Urinary	4	(1.5)	0	(0)	1.02	1.00 - 1.03	0.308
Distal embolization	0	(0)	6	(9.0)	-	-	< 0.001
Endoleak	0	(0)	6	(9.0)	-	-	< 0.001

OR Odds ratio, *CI* confidence interval, *ARF* acute renal failure

Mean hospital length of stay was slightly increased after open repair compared with TEVAR, 22.9 days vs. 19.3 days (p=0.085). Most patients were discharged home after repair of TTAI: 29.1% (n=76) of the open repair group and 32.8% (n=22) of the TEVAR group (not significant). Patients who received open repair went more frequently to acute care facilities after discharge, while patients treated with TEVAR were more often discharged to a rehabilitation center or a nursing home (table 3).

Table 3. Discharge characteristics after open repair and TEVAR for TTAI

	Open repair (n=261) N or mean	(% or ±SD)	TEVAR (n=67) N or mean	(% or ±SD)	p value
LOS	22.9	(±20)	19.3	(±14)	0.085
Discharge destination					
Home	76	(29.1)	22	(32.8)	0.553
Acute care facility	73	(28.0)	6	(9.0)	0.001
Nursing home	10	(3.8)	7	(10.5)	0.029
Home services	22	(8.4)	10	(14.9)	0.110
Rehabilitation center	28	(10.7)	16	(23.9)	0.005

LOS length of stay, *SD* standard deviation

DISCUSSION

About eighty patients with traumatic thoracic aortic injury are admitted to hospitals in New York State every year. Recently, there has been a major shift away from open surgery to endovascular management of these patients. This trend has been associated with decreased mortality and postoperative pulmonary complications.

The diagnosis and management of TTAI have undergone several major changes in the last decades. The rapid advancement of computed tomography availability, with its less invasive nature and its sensitivity and specificity, has resulted in its almost complete replacement of aortography for the diagnosis of TTAI.[8] There also have been several developments in treatment strategies. The majority of patients with TTAI still die at the scene of the accident, but for those patients who live to be admitted to hospital, there has been a shift from early to delayed definitive repair.[8] The optimal timing for definitive repair of TTAI is not known, traditionally early repair was preferred in all patients. Generally, patients with TTAI are categorized as "unstable", in whom survival is extremely low, and "stable".[14,15] Clearly, immediate intervention is indicated in unstable patients, delay to evaluation and the operating room are risk factors for mortality.[16] The timing of surgical repair has changed in stable patients with TTAI. In selected cases with major associated injuries, delayed definitive repair has been associated with reduced mortality.[17-19] Antihypertensive therapy with β-blockers can eliminate in-hospital free rupture in these patients, resulting in a further decrease of in-hospital mortality.[1,15,20]

The introduction of TEVAR for the treatment of thoracic aortic pathologies,[12,13] has further changed the management of TTAI. TEVAR allows prompt exclusion of the aortic injury and does not require thoracotomy or aortic clamping, which are undesirable in unstable patients with multiple associated injuries. Blood loss is reduced and systemic heparinization and perioperative lung ventilation are less often necessary. In many centers, endovascular treatment has become the procedure of choice for TTAI, even in young patients.[8,9] We demonstrated a similar

phenomenon in New York State. TEVAR appeared to be preferred in particular for patients with multiple associated injuries (table 1). Furthermore, the proportion of admitted TTAI patients that received an aortic intervention appeared to increase since 2005 when TEVAR became widely available in New York State (figure 3).

In our evaluation, the in-hospital mortality after TEVAR was 6% vs. 17% after open surgery for TTAI, which was a statistically significant difference. After controlling for the significant covariates, TEVAR independently reduces the risk of death following surgical intervention for TTAI compared to the open procedure. Our findings are similar to a recent meta-analysis by Tang et al, which demonstrated a 30-day mortality of 7.6% and 15.2% after TEVAR and open surgery, respectively.[21] Other meta-analyses and large series have shown results comparable to the in-hospital mortality in New York State.[9-11,22-24] The only large evaluation that did not support the superiority of TEVAR for TTAI, was the study of Arthurs et al, that found a 30-day mortality of 19% and 18% after open repair and TEVAR, respectively.[3] However, in their nation-wide analysis of patients with blunt TTAI, they evaluated the results of open and endovascular repairs between 2000 and 2005. Therefore, the endovascular devices utilized in their evaluation represent the initial experience with custom-made devices or off-label use of aortic cuffs.[3] This may explain the increased mortality after TEVAR in their analysis compared with our results and the literature.

In addition, pulmonary complications were significantly reduced with TEVAR. An increased incidence of pneumonia after open repair of TTAI compared with TEVAR has been described previously;[11] particularly in patients with associated major extra-thoracic injuries.[9] Paraplegia is probably the most devastating complication of thoracic aortic interventions, and its incidence is increased after open surgery. Paraplegia occurs in approximately 5.6% to 7% of patients after open surgery, compared to less than 1% after TEVAR.[21,23,24] Demetriades et al demonstrated that procedure-related paraplegia after open surgery for TTAI has significantly decreased from 8.7% to 2.9% during the last decade.[8] This improved outcome could be the result of better resuscitation and a more controlled environment during delayed repair of TTAI.[8,19] Furthermore, shorter aortic cross clamp time and adjuncts for distal aortic perfusion during open TTAI repair, might have contributed to the observed decrease in the incidence of paraplegia,[25,26] although some question the benefits of these such bypass techniques in this patient group.[9,16,27] In our evaluation, permanent paraplegia occurred in less than 1% after open repair and not at all after TEVAR. The reported rate of postoperative stroke, another neurological complication, is decreased after TEVAR compared with open surgery for TTAI as well.[21] Our data did not confirm this finding.

Although the initial results of endovascular treatment for TTAI are encouraging, there continues to be concern about device-related complications. Endoleak and distal embolization were each identified in 9% in the patients undergoing TEVAR. Since TTAI typically occurs at the aortic isthmus, coverage of the left subclavian artery is required in up to 66% of patients for adequate proximal seal.[11,28] Coverage of the left subclavian artery may lead to brachial ischemia, and without revascularization, it may be a risk factor for paraplegia and stroke.[29,30] Furthermore,

thrombosis of the subclavian and brachial arteries, iliac rupture, stent-graft migration, fracture and collapse have all been reported.[24] Unfortunately, limitations in coding prevent us from evaluating these specific complications in the SPARCS data-set.

The experience with TEVAR for TTAI is still very limited and long-term outcomes of TEVAR for TTAI are unknown to date. Therefore, life-long surveillance is indicated after TEVAR. Computed tomography with angiography is the preferred imaging method for surveillance after endovascular treatment, but this would result in a considerable radiation exposure among young trauma patients overtime. The mean age of patients that received TEVAR for TTAI was 39 years in our evaluation, which is considerably younger than patients undergoing endovascular treatment for aortic aneurysms.

For the present study, we investigated the outcomes of a large cohort of patients that received surgical repair for TTAI. Still, there are several potential limitations of our analysis. First, patients in the present study were not randomized by repair type. Since this was an observational study, the open repair and TEVAR groups were not completely identical. TEVAR patients had more additional major injuries while admissions in the open repair of TTAI were more frequently coded as emergent (table 1). These factors may affect the outcomes; therefore, multivariable regression analysis was performed, which confirmed that TEVAR was independently associated with improved in-hospital mortality.

Management of complications such as endoleak after TEVAR could not be extracted from SPARCS, and long-term patient outcomes were not available as well, while these are essential, particularly in patients that received TEVAR. Another limitation is that the ICD-9 procedure code for endovascular repair was initiated in 2005. Although the utilization of thoracic stent-grafts for the treatment of thoracic aortic disease in the United States was approved by the FDA in 2005 as well, some TTAI patients in New York State may have received TEVAR before 2005. It's difficult to determine how these TEVAR patients were coded. If some of these TEVAR patients were included in the open repair group, the in-hospital mortality of the open repair group may be underestimated, since TEVAR appeared to reduce the in-hospital mortality in our analysis.

Furthermore, although the data were prospectively collected in the SPARCS database, there may be a variation in reporting precision and coding errors. Data extracted from administrative databases like SPARCS usually provide reliable information, but co-morbid diseases may be underreported.[31,32] The influence of this potentially confounding factor is thought to be small, since there were no substantial differences in co-morbidity between the open surgery group and the TEVAR group and the prevalence of pre-existing co-morbidities is thought to be relatively low in trauma patients. Moreover, our findings regarding the mortality rates in both repair groups are supported by previous reports.[9-11,21-24]

CONCLUSION

Management of traumatic thoracic aortic injury has undergone major changes recently. In many centers in New York State, endovascular treatment has become the procedure of choice, in particular in case of additional major injuries. This trend is associated with decreased in-hospital mortality and postoperative pulmonary complications in patients suffering from TTAI. However, TEVAR is also associated with significant device-related complications.

REFERENCES

1. Fabian TC, Davis KA, Gavant ML et al. Prospective study of blunt aortic injury: helical CT is diagnostic and antihypertensive therapy reduces rupture. Ann Surg 1998; 227:666-676.
2. Schumacher H, Bockler D, von Tengg-Kobligk H et al. Acute traumatic aortic tear: open versus stent-graft repair. Semin Vasc Surg 2006; 19:48-59.
3. Arthurs ZM, Starnes BW, Sohn VY et al. Functional and survival outcomes in traumatic blunt thoracic aortic injuries: An analysis of the National Trauma Databank. J Vasc Surg 2009; 49:988-994.
4. Michetti CP, Hanna R, Crandall JR et al. Contemporary analysis of thoracic aortic injury: importance of screening based on crash characteristics. J Trauma 2007; 63:18-24.
5. Parmley LF, Mattingly TW, Manion WC et al. Nonpenetrating traumatic injury of the aorta. Circulation 1958; 17:1086-1101.
6. Dosios TJ, Salemis N, Angouras D et al. Blunt and penetrating trauma of the thoracic aorta and aortic arch branches: an autopsy study. J Trauma 2000; 49:696-703.
7. Cook J, Salerno C, Krishnadasan B et al. The effect of changing presentation and management on the outcome of blunt rupture of the thoracic aorta. J Thorac Cardiovasc Surg 2006; 131:594-600.
8. Demetriades D, Velmahos GC, Scalea TM et al. Diagnosis and treatment of blunt thoracic aortic injuries: changing perspectives. J Trauma 2008; 64:1415-1418.
9. Demetriades D, Velmahos GC, Scalea TM et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008; 64:561-570.
10. Riesenman PJ, Farber MA, Rich PB et al. Outcomes of surgical and endovascular treatment of acute traumatic thoracic aortic injury. J Vasc Surg 2007; 46:934-940.
11. Chung J, Owen R, Turnbull R et al. Endovascular repair in traumatic thoracic aortic injuries: comparison with open surgical repair. J Vasc Interv Radiol 2008; 19:479-486.
12. Dake MD, Miller DC, Semba CP et al. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. N Engl J Med 1994; 331:1729-1734.
13. Nienaber CA, Fattori R, Lund G et al. Nonsurgical reconstruction of thoracic aortic dissection by stent-graft placement. N Engl J Med 1999; 340:1539-1545.
14. Lee RB, Stahlman GC, Sharp KW. Treatment priorities in patients with traumatic rupture of the thoracic aorta. Am Surg 1992; 58:37-43.
15. Mattox KL, Wall MJ, Jr. Historical review of blunt injury to the thoracic aorta. Chest Surg Clin N Am 2000; 10:167-82, x.
16. Whitson BA, Nath DS, Knudtson JR et al. Is distal aortic perfusion in traumatic thoracic aortic injuries necessary to avoid paraplegic postoperative outcomes? J Trauma 2008; 64:115-120.

17. Nagy K, Fabian T, Rodman G et al. Guidelines for the diagnosis and management of blunt aortic injury: an EAST Practice Management Guidelines Work Group. J Trauma 2000; 48:1128-1143.
18. Maggisano R, Nathens A, Alexandrova NA et al. Traumatic rupture of the thoracic aorta: should one always operate immediately? Ann Vasc Surg 1995; 9:44-52.
19. Hemmila MR, Arbabi S, Rowe SA et al. Delayed repair for blunt thoracic aortic injury: is it really equivalent to early repair? J Trauma 2004; 56:13-23.
20. Holmes JH, Bloch RD, Hall RA et al. Natural history of traumatic rupture of the thoracic aorta managed nonoperatively: a longitudinal analysis. Ann Thorac Surg 2002; 73:1149-1154.
21. Tang GL, Tehrani HY, Usman A et al. Reduced mortality, paraplegia, and stroke with stent graft repair of blunt aortic transections: a modern meta-analysis. J Vasc Surg 2008; 47:671-675.
22. Buz S, Zipfel B, Mulahasanovic S et al. Conventional surgical repair and endovascular treatment of acute traumatic aortic rupture. Eur J Cardiothorac Surg 2008; 33:143-149.
23. Xenos ES, Abedi NN, Davenport DL et al. Meta-analysis of endovascular vs open repair for traumatic descending thoracic aortic rupture. J Vasc Surg 2008; 48:1343-1351.
24. Hoffer EK, Forauer AR, Silas AM et al. Endovascular stent-graft or open surgical repair for blunt thoracic aortic trauma: systematic review. J Vasc Interv Radiol 2008; 19:1153-1164.
25. Jahromi AS, Kazemi K, Safar HA et al. Traumatic rupture of the thoracic aorta: cohort study and systematic review. J Vasc Surg 2001; 34:1029-1034.
26. Fabian TC, Richardson JD, Croce MA et al. Prospective study of blunt aortic injury: Multicenter Trial of the American Association for the Surgery of Trauma. J Trauma 1997; 42:374-380.
27. Mattox KL. Red River anthology. J Trauma 1997; 42:353-368.
28. Day CP, Buckenham TM. Endovascular repair of the thoracic aorta: predictors of 30-day mortality in patients on the New Zealand Thoracic Aortic Stent Database (NZ TAS). Eur J Vasc Endovasc Surg 2009; 37:160-165.
29. Buth J, Harris PL, Hobo R et al. Neurologic complications associated with endovascular repair of thoracic aortic pathology: Incidence and risk factors. a study from the European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair (EUROSTAR) registry. J Vasc Surg 2007; 46:1103-1110.
30. Fattori R, Nienaber CA, Rousseau H et al. Results of endovascular repair of the thoracic aorta with the Talent Thoracic stent graft: the Talent Thoracic Retrospective Registry. J Thorac Cardiovasc Surg 2006; 132:332-339.
31. Humphries KH, Rankin JM, Carere RG et al. Co-morbidity data in outcomes research: are clinical data derived from administrative databases a reliable alternative to chart review? J Clin Epidemiol 2000; 53:343-349.
32. Powell H, Lim LL, Heller RF. Accuracy of administrative data to assess comorbidity in patients with heart disease. an Australian perspective. J Clin Epidemiol 2001; 54:687-693.

Chapter 3

Meta-analysis of Open versus Endovascular Repair for Ruptured Descending Thoracic Aortic Aneurysm

Journal of Vascular Surgery 2010;51:1026-1032

Frederik H.W. Jonker,[1] MD,
Santi Trimarchi,[2] MD,
Hence J.M. Verhagen,[3] MD, PhD,
Frans L. Moll,[4] MD, PhD,
Bauer E. Sumpio,[1] MD, PhD,
Bart E. Muhs,[1] MD, PhD.

[1] Section of Vascular Surgery and Interventional Radiology, Yale University School of Medicine, New Haven, CT
[2] Section of Vascular Surgery, IRCCS Policlinico San Donato, Milan, Italy
[3] Section of Vascular Surgery, Erasmus University Medical Center, Rotterdam, the Netherlands
[4] Section of Vascular Surgery, University Medical Center Utrecht, the Netherlands

ABSTRACT

Introduction:
Ruptured descending thoracic aortic aneurysm (rDTAA) is associated with high mortality rates. Data supporting thoracic endovascular aortic repair (TEVAR) to reduce mortality compared with open repair is limited to small series. We investigated the contemporary outcomes of open and endovascular repair in the literature.

Methods:
The authors systematically reviewed all studies describing the outcomes of rDTAA treated with either open repair or TEVAR since 1995 using MEDLINE, Cochrane Library CENTRAL, and Embase databases. Case reports, or studies published before 1995 were excluded. All articles were critically appraised for relevance, validity and availability of data regarding treatment outcomes. All data were systematically pooled and meta-analyses were performed to investigate 30-day mortality, myocardial infarction, stroke and paraplegia rates after both repair types.

Results:
Original data of 224 patients with rDTAA treated with either TEVAR (n=143, 64%) or open repair (n=81, 36%) were identified. Mean age of the cohort was 70 ±5.6 years and 70% were male. The 30-day mortality was significantly lower in patients treated with TEVAR for rDTAA compared to patients treated with open repair: 19% vs. 33% (OR 2.15, p=0.016). The 30-day occurrence rates of myocardial infarction (11.1% vs. 3.5%, OR 3.70, p< 0.05), stroke (10.2% vs. 4.1%, OR 2.67, p=0.117) and paraplegia (5.5% vs. 3.1%, OR 1.83, p=0.405) were increased after open repair compared with TEVAR, but for stroke and paraplegia this failed to reach statistical significance. In the TEVAR group, five additional patients died of aneurysm-related causes after 30 days during a median follow-up of 17 ±10 months, follow-up data after open repair was insufficient. The estimated aneurysm-related survival at 3 years after TEVAR was 70.6%.

Conclusion:
Endovascular repair of rDTAA is associated with a significantly lower 30-day mortality compared with open surgical repair. TEVAR was associated with a considerable number of aneurysm-related deaths during follow-up.

INTRODUCTION

The annual incidence of ruptured aneurysm of the thoracic aorta is around 5 per 100,000, which makes it less common than ruptured abdominal aortic aneurysms.[1,2] Approximately 30% of all ruptured thoracic aortic aneurysms are localized at the descending thoracic aorta, remaining ruptured aneurysms are found at the ascending aorta and arch.[1] Overall mortality rates of ruptured thoracic aortic aneurysms of up to 97% have been reported and a minority of patients survive transport to the emergency department.[1]

The traditional treatment of intact and ruptured aneurysms of the descending thoracic aorta has been open surgical resection of the aneurysm and replacement with an interposition graft, which was first performed by Lam and Aram in 1951.[3] Open surgical repair of descending thoracic aortic aneurysms allows inspection of the ruptured aneurysm and possible aortic branches. However, this approach requires thoracotomy, aortic cross clamping, and in some cases cardiopulmonary bypass. Successful endovascular management of a ruptured descending thoracic aortic aneurysm (rDTAA) was first reported by Semba et al in 1997.[4] Thoracic endovascular aortic repair (TEVAR) is less invasive than open repair and may result in quick exclusion of the aneurysm without thoracotomy or aortic clamping.

Recent non-randomized trials have demonstrated 30-day mortality rates of 1.9% to 2.1% after elective endovascular repair of thoracic aortic aneurysms compared with 5.7% to 11.7% after elective open repair.[5-7] In addition, endovascular repair has been associated with improved operative mortality rates for ruptured abdominal aortic aneurysms[8,9] and traumatic thoracic aortic ruptures.[10,11] However, the exact role of TEVAR for the management of rDTAA still has to be better defined, as a result of the low incidence of rDTAA. The purpose of the present study was to perform a meta-analysis evaluating the outcomes of endovascular vs. open repair for the management of rDTAA.

METHODS

Literature search

Medline, Embase and Cochrane Library CENTRAL were searched until June 29th, 2009. The following search string was used for Medline: ("rupture"[tiab] OR "ruptured"[tiab] OR "ruptures"[tiab] OR emergen*[tiab] OR "acute"[tiab] OR perforat*[tiab]) AND ("thoracic"[title] OR "descending"[title]) AND ("aorta"[title] OR "aortic"[title]) AND ("aneurysm"[tiab] OR "aneurysms"[tiab] OR "aneurysmatic"[tiab]) This resulted in 846 articles. A similar search string was used for Embase, resulting in 1390 articles. The Cochrane library CENTRAL database was browsed manually and did not reveal any relevant articles. After removal of duplicate articles, 1743 articles remained. No language or publication date restrictions were applied.

Selection of articles

All titles and abstracts were read by two independent investigators (FHJ and BEM). Inclusion criteria were: (1) articles describing patients with rDTAA treated with TEVAR or open repair, (2) the following patient outcomes were described: 30-day mortality (required), and 30-day complications including stroke, paraplegia and myocardial infarction (preferably). Aneurysm rupture was defined as fresh blood outside the aortic wall on imaging or during surgery. Exclusion criteria included: (1) articles published before 1995, to guarantee that the report represents contemporary practice, (2) case reports (3) thoracic aortic pathologies other than rDTAA, such as ruptured thoraco-abdominal aneurysms, aneurysms of the ascending aorta or arch, penetrating aortic ulcers, (4) no clear description of outcomes of TEVAR or open repair, and (5) no original data presented in the article.

Studies that evaluated other thoracic aortic pathologies besides rDTAA were excluded, unless treatment outcome variables were described separately for the different pathologies. In this manner, many studies had to be excluded for analysis. Other articles written by identical authors and/or institutions were studied in detail and excluded if necessary to prevent inclusions of duplicate cases. Reports from administrative databases were not included, because administrative data is thought to be less reliable and may be published before in other included reports. In total, 28 relevant articles were identified and included in our final selection.[4,12-38]

Data extraction

Two independent investigators analyzed the identified articles (FHJ and BEM). The following characteristics were extracted: age and gender of patients; co-morbidities: aneurysm characteristics such as diameter, contained or free rupture, associated dissection; presence of hypovolemic shock at admission; time interval between diagnosis and aneurysm repair; repair type; consideration for preferred repair type; cerebrospinal fluid drainage; anesthesia type; endograft details including brand, diameter, length and number of stent-grafts used; successful aneurysm exclusion; 30-day mortality; mortality after 30 days; time interval between aneurysm repair and death; cause of death; permanent paraplegia; stroke; myocardial infarction (MI); endograft-related complications, including endoleak, graft migration and fracture; need for vascular re-intervention within 30 days; length of stay in days, and length of follow-up in months. All extracted information was subsequently systematically entered in one database. Totally, original data regarding 224 patients with rDTAA treated with open repair or TEVAR were identified. Availability of the studied variables in the evaluated reports is depicted in table 1.

Statistical analysis

Statistical analyses were performed by FHJ, using SPSS 15.0 software and Comprehensive Meta-analysis V2 software. In all cases, missing data were not defaulted to negative, and denominators reflect only cases reported. Levene's test for equality of variances was used to assess the variance

of the 30-day mortality, paraplegia, stroke and MI rates among the evaluated studies. Equal variances were confirmed for all evaluated outcome variables. Contingency tables with chi-square test were used to compare categorical outcome variables, such as 30-day mortality, paraplegia, stroke and MI occurrence rates, between patients treated with open repair and TEVAR. Continuous variables were compared between both repair groups using Student's t-test. The estimated aneurysm-related survival during follow-up was demonstrated using Kaplan-Meier life table analysis. Differences were considered statistically significant if the *P* value was less than .05.

Table 1. Availability of data in the evaluated reports

Variable	All patients (n=224)		TEVAR (n=143)		Open repair (n=81)	
	N	(%)	N	(%)	N	(%)
Age	143	(64)	111	(78)	32	(40)
Gender	93	(42)	72	(50)	21	(26)
Contained rupture	191	(85)	135	(94)	56	(69)
Consideration for repair type	224	(100)	143	(100)	81	(100)
Repair within 24 hours	177	(79)	131	(92)	46	(57)
Anesthesia type	177	(79)	96	(67)	81	(100)
CP Bypass	45	(56)	-	-	45	(56)
Endograft brand	94/143	(66)	94	(66)	-	-
Endograft diameter	38/143	(27)	38	(27)	-	-
Endograft length	21/143	(15)	21	(15)	-	-
30-day mortality	224	(100)	143	(100)	81	(100)
Mortality during follow-up	116/170	(68)	107/116	(91)	9/54	(17)
Days to in-hospital death	30/54	(56)	20/27	(74)	10/27	(37)
Days to follow-up death	5/5	(100)	5/5	(100)	-	-
Cause of in-hospital death	42/54	(78)	24/27	(89)	18/27	(67)
Cause of follow-up death	5/5	(100)	5/5	(100)	-	-
Paraplegia	203	(91)	130	(91)	73	(90)
Stroke	182	(81)	123	(86)	59	(73)
Myocardial infarction	187	(84)	142	(99)	45	(56)
Vascular re-intervention	165	(74)	121	(85)	44	(54)
Endoleak	90/143	(63)	90/143	(63)	-	-
Endograft-related complications	84/143	(59)	84/143	(59)	-	-
Length of follow-up	116/170	(68)	107/116	(91)	9/54	(17)

RESULTS

Baseline characteristics

In total, 28 articles describing 224 patients with rDTAA were identified, including 143 patients (63.8%) treated with TEVAR, and 81 patients (36.2%) treated with open repair. Mean age of patients with rDTAA was 70.0 ±5.6 years, and 69.9% (65/139) of the cohort were male (table 2). Ruptured aneurysms treated with TEVAR tended to be more frequently contained rather than a

free rupture, 75 of 135 (55.6%) vs. 24 of 56 (42.9%), p=0.110. However, these data were only available for 85% of patients (table 1).

Aneurysm repair was performed within 24 hours in 147 of177 patients (83.1%). Considerations for offering open repair were: institution's standard treatment in 42 patients (51.9%), no endovascular repair available in 28 patients (34.6%, in particular before 1999), or unsuitable anatomy for endovascular repair in the remaining 11 patients (13.6%). TEVAR was preferred over open repair because of: emergency in 82 patients (57.3%), co-morbidities in 53 patients (37.1%), and TEVAR was simply the institution's standard treatment for all descending thoracic aortic pathologies in the remaining 8 patients (5.6%).

Table 2. Baseline characteristics of patients with rDTAA

	Open repair (n=81) N (% or ±SD)		TEVAR (n=143) N (% or SD)		p value
Age	70.2	(±1.9)	70.0	(±6.5)	0.831
Male gender	14	(66.7)	51	(70.8)	0.714
Contained rupture	24	(42.9)	75	(55.6)	0.110
Consideration for repair type					<0.001
Institution's standard treatment	42	(51.9)	8	(5.6)	
Emergency treatment	0	(0)	82	(57.3)	
Extensive co-morbidities	0	(0)	53	(37.1)	
Anatomy	11	(13.6)	0	(0)	
Only available treatment	28	(34.6)	0	(0)	
Repair within 24hours	41	(89.1)	106	(80.9)	0.201
General anesthesia	81	(100)	92	(95.8)	0.063
CP bypass	27	(60)			
Endograft brand					
Medtronic Talent®			46	(32.2)	
Gore Excluder®			21	(14.7)	
Gore TAG®			12	(8.4)	
Handmade or other			15	(10.5)	
Unclear			49	(34.3)	

CP cardiopulmonary, *SD* standard deviation

Early mortality

The 30-day mortality was significantly lower in patients treated with TEVAR for rDTAA compared to patients treated with open repair: 27 out of 143 patients (18.9%) vs. 27 out of 81 patients (33.3%), OR 2.15 (95%CI: 1.15-4.01, p=0.016). Data regarding the cause of 30-day mortality were available in 42 of 54 deaths (78%, table 1). Most frequent causes of 30-day mortality after open repair were exsanguination, cardiac complications or stroke, which were each responsible for 5 of 18 deaths (27.7%, figure 1). Besides these causes of death, multi-organ failure (MOF) and infectious complications were common death causes in the TEVAR group.

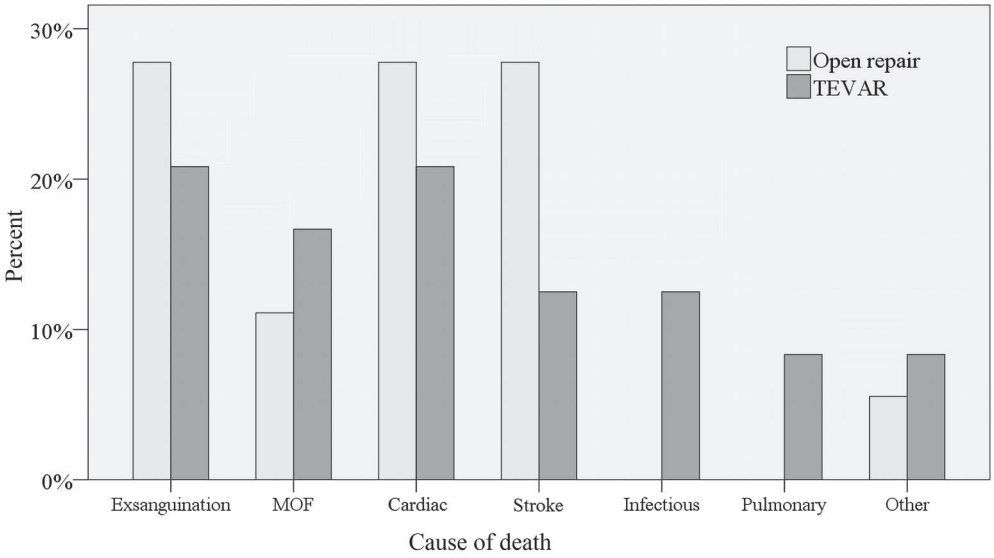

Figure 1. Causes of 30-day mortality
Other causes of death included iatrogenic dissection with abdominal mal perfusion after TEVAR (n=1), superior mesentery artery infarction after TEVAR (n=1), and acute renal failure after open repair of rDTAA

Early complications

Myocardial infarction was reported in 5 of 45 patients (11.1%) after open repair and in 5 of 142 patients (3.5%) after TEVAR (OR 3.5, p=0.047, table 3). Stroke occurred in 6 of 59 patients (10.2%) in the open repair group vs. 5 of 123 patients (4.1%) in the TEVAR group (OR 2.67, p=0.117). In most cases, these complications resulted in death. Permanent paraplegia was reported in 4 of 73 (5.5%) after open repair and in 4 of 130 (3.1%) after TEVAR (OR 1.83, p=0.405).

Vascular reinterventions within 30 days were described in 11 of 121 patients (9.1%) after TEVAR vs. 1 of 44 patients (2.3%) after open repair (OR 0.23, p=0.169). Interventions after TEVAR included repair of a lacerated common iliac artery, external iliac artery or femoral artery in five patients, conversion to open repair because of proximal endoleak in two cases, additional TEVAR because of type 1 endoleak twice, and carotid-carotid bypass once because of overstenting of the left carotid artery. Re-exploration for bleeding after open repair of rDTAA was reported once. Endoleak was reported in 10 of 90 patients (11.1%) at some point during follow-up after TEVAR, which included type I endoleak in nine cases and type II endoleak in one case. Endograft migration was reported once.

Table 3. Thirty-day outcomes of open repair and TEVAR for rDTAA

	Open repair (n=81)		TEVAR (n=143)		OR	95% CI	p value
	N	(%)	N	(%)			
30-day mortality	27	(33.3)	27	(18.9)	2.15	1.15 - 4.01	0.016
Myocardial infarction	5	(11.1)	5	(3.5)	3.70	1.02 - 13.4	0.047
Stroke	6	(10.2)	5	(4.1)	2.67	0.78 - 9.14	0.117
Permanent paraplegia	4	(5.5)	4	(3.1)	1.83	0.44 - 7.53	0.405
Vascular re-intervention	1	(2.3)	11	(9.1)	0.23	0.03 -1.86	0.169

Mortality during follow-up

Reliable data regarding mortality during follow-up were available for 107 of the 116 TEVAR patients (92%) that were alive after 30 days, and for only 9 of 52 patients (17%) in the open repair group. Median follow-up was 17 ±10 months for the TEVAR group and 36 ±13 months for the open repair group. In the TEVAR group, five patients died of aneurysm-related causes after 30-days; the median time interval until death was 139 days (range 87 to 1080 days). Exsanguination due to rupture of the stented aneurysm or the adjacent aortic segment was the cause of death in four patients. Untreated type 1 endoleak caused the rupture in two cases, perforation of the aortic wall by the bare portion of the stent-graft occurred once, and an infected stent-graft led to aortic rupture in the last patient. The fifth aneurysm-related death during follow-up after TEVAR was the result of sepsis due to an aortobronchial fistula. The estimated aneurysm-related survival for patients treated with TEVAR was 70.6% after 3 years (figure 2). No aneurysm-related mortality was reported in the open repair group during follow-up.

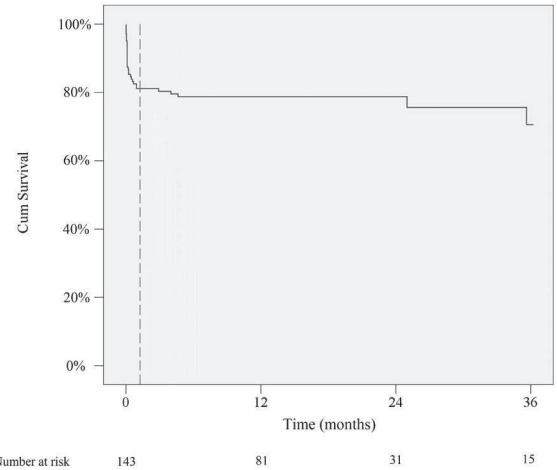

Figure 2. Aneurysm-related survival in patients treated with TEVAR for rDTAA
The estimated aneurysm-related survival at 3 years after TEVAR was 70.6%. The dashed line indicates 30 days after the endovascular procedure. Survival estimates were not performed for patients treated with open repair, since the follow-up data was not available for 83% of patients.

DISCUSSION

In this review of the available literature, thoracic endovascular aortic repair (TEVAR) of ruptured descending thoracic aortic aneurysms (rDTAA) was associated with a significantly lower 30-day mortality rate compared with open repair.

The five-year survival rate of patients with untreated thoracic aortic aneurysms (TAA) is only 20% to 54%,[39,40] which is primarily the result of aneurysm rupture. Risk factors for rupture of thoracic aortic aneurysms are increasing age, female gender, COPD, and, most importantly, increasing aneurysm diameter.[40-43] For TAA greater than 6 cm in diameter, risks of dissection, rupture or death are about 15% per year.[40,42] Since these risks substantially exceed the risk of surgical resection of TAA, elective intervention is generally recommended in aneurysms larger than 6 cm.[42,44-46] Among patients with ruptured thoracic aortic aneurysms, the overall mortality approaches 100%, and just a minority of the patients will be admitted alive to the emergency department.[1] Although the patients that make it to the hospital are thought to have a more realistic outcome, a large part of this group will not survive the operation either.[47]

The traditional treatment of rDTAA has been open surgical resection of the aneurysm and replacement with an interposition graft. Since the introduction of endovascular techniques for the management of abdominal and thoracic aortic disease, this less invasive technique has shown to improve the operative mortality rates of both elective and emergency interventions compared with open surgical repair.[5-11,48] For rDTAA, significant benefits of endovascular repair have not yet been reported, which likely is the result of the relatively low incidence of this disease. Additionally, studies often combine results of rDTAA, traumatic aortic injuries, penetrating aortic ulcers and type B dissections, while these are completely different pathologies.

In this evaluation, the 30-day mortality of open repair of rDTAA was 33%, compared with 19% after TEVAR. Open repair of rDTAA is a more invasive procedure than TEVAR, and patients treated with open repair appeared to suffer more frequently from myocardial infarction, stroke and paraplegia during or shortly after the operation. Myocardial infarction and stroke were important causes of death after open repair. TEVAR does not require thoracotomy, aortic clamping or cardiovascular bypass, and offers prompt exclusion of the ruptured aneurysm which minimizes additional blood loss. These advantageous characteristics of endovascular management of rDTAA appear to result in superior short term outcomes compared to open repair of rDTAA, and TEVAR may therefore be the treatment of first choice in patients with rDTAA.

The cause of concern with endovascular repair of aortic disease remains its durability and the development of endograft-related complications.[49] Endoleak was present in at least 11% after TEVAR, and during a median follow-up of 17 months, 5 of the 107 TEVAR patients with available follow-up data had died of endograft-related complications and the estimated aneurysm-relate survival at 3 years was 71%. Rupture of the stented aneurysm or the adjacent aorta was the main cause of death in these patients, and was caused by type 1 endoleak, perforation of the

aortic wall by the bare portion of the stent-graft, or an infected stent-graft. Risks of endograft-related complications may be increased after emergency procedures. In the emergency setting, physicians can only use those endografts that are available on the shelf stock, and urgent situations may not allow optimal endograft sizing and deployment. Furthermore, hypovolemic shock may result in an decreased aortic diameter, which may contribute to inadequate endograft sizing as well.[50] Therefore, continued surveillance using computed tomography angiography (CTA) after TEVAR, and further improvement of endovascular techniques and endografts design is required.[21,49]

Meta-analyses such as the present study have several limitations, the most important disadvantage is that the data is limited to information provided by the original articles. This can result in incomplete data, such as the follow-up data that was unavailable for the majority of the patients treated with open repair. Furthermore, ruptured aneurysms treated with TEVAR tended to be more frequently contained rather than a free rupture. Blood loss may be more extensive in case of free rupture which could result in hemodynamic instability and poorer outcomes. However, data regarding this variable were missing in 15% as well. In addition, some complications or even deaths may have been underreported in the evaluated studies. Articles in which the description of the outcome variables was unclear were therefore excluded from the meta-analysis. The present study does represent the largest evaluation of patients with rDTAA treated with TEVAR and open repair, and it may offer the best evidence that is currently available regarding the management of this life-threatening disease.

CONCLUSION

Endovascular repair of rDTAA is associated with a significantly lower 30-day mortality compared with open surgical repair in the literature. Furthermore, complications like myocardial infarction, stroke and paraplegia appear to be lower after endovascular repair of rDTAA. However, endovascular repair was associated with a considerable number of aneurysm-related deaths during follow-up, mainly caused by late rupture after TEVAR. Continued surveillance after TEVAR, and further improvement of the design of endografts is required to decrease the endograft-related complications and deaths during follow-up.

REFERENCES

1. Johansson G, Markstrom U, Swedenborg J. Ruptured thoracic aortic aneurysms: a study of incidence and mortality rates. J Vasc Surg 1995; 21:985-988.
2. Acosta S, Ogren M, Bengtsson H et al. Increasing incidence of ruptured abdominal aortic aneurysm: a population-based study. J Vasc Surg 2006; 44:237-243.
3. Lam CR, Ram HH. Resection of the descending thoracic aorta for aneurysm; a report of the use of a homograft in a case and an experimental study. Ann Surg 1951; 134:743-752.
4. Semba CP, Kato N, Kee ST et al. Acute rupture of the descending thoracic aorta: repair with use of endovascular stent-grafts. J Vasc Interv Radiol 1997; 8:337-342.
5. Matsumura JS, Cambria RP, Dake MD et al. International controlled clinical trial of thoracic endovascular aneurysm repair with the Zenith TX2 endovascular graft: 1-year results. J Vasc Surg 2008; 47:247-257.
6. Fairman RM, Criado F, Farber M et al. Pivotal results of the Medtronic Vascular Talent Thoracic Stent Graft System: the VALOR trial. J Vasc Surg 2008; 48:546-554.
7. Bavaria JE, Appoo JJ, Makaroun MS et al. Endovascular stent grafting versus open surgical repair of descending thoracic aortic aneurysms in low-risk patients: a multicenter comparative trial. J Thorac Cardiovasc Surg 2007; 133:369-377.
8. Egorova N, Giacovelli J, Greco G et al. National outcomes for the treatment of ruptured abdominal aortic aneurysm: comparison of open versus endovascular repairs. J Vasc Surg 2008; 48:1092-100, 1100.
9. McPhee J, Eslami MH, Arous EJ et al. 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; 49:817-826.
10. Demetriades D, Velmahos GC, Scalea TM et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008; 64:561-570.
11. Xenos ES, Abedi NN, Davenport DL et al. Meta-analysis of endovascular vs open repair for traumatic descending thoracic aortic rupture. J Vasc Surg 2008; 48:1343-1351.
12. Hyhlik-Durr A, Geisbusch P, von Tengg-Kobligk H et al. Intentional overstenting of the celiac trunk during thoracic endovascular aortic repair: preoperative role of multislice CT angiography. J Endovasc Ther 2009; 16:48-54.
13. Attia C, Farhat F, Boussel L et al. Endovascular repair of lesions involving the descending thoracic aorta. Mid-term morphological changes. Interact Cardiovasc Thorac Surg 2008; 7:595-599.
14. Minatoya K, Ogino H, Matsuda H et al. Replacement of the descending aorta: recent outcomes of open surgery performed with partial cardiopulmonary bypass. J Thorac Cardiovasc Surg 2008; 136:431-435.

15. Bos WT, Verhoeven EL, Zeebregts CJ et al. Emergency endovascular stent grafting for thoracic aortic pathology. Vascular 2007; 15:12-17.
16. Amabile P, Rollet G, Vidal V et al. Emergency treatment of acute rupture of the descending thoracic aorta using endovascular stent-grafts. Ann Vasc Surg 2006; 20:723-730.
17. Delis KT, Gloviczki P, Bjarnason H et al. Endovascular repair of ruptured saccular aneurysms of the descending thoracic aorta. J Vasc Interv Radiol 2006; 17:1527-1533.
18. Kaya A, Heijmen RH, Overtoom TT et al. Thoracic stent grafting for acute aortic pathology. Ann Thorac Surg 2006; 82:560-565.
19. Wheatley GH, III, Gurbuz AT, Rodriguez-Lopez JA et al. Midterm outcome in 158 consecutive Gore TAG thoracic endoprostheses: single center experience. Ann Thorac Surg 2006; 81:1570-1577.
20. Farber MA, Criado FJ. Endovascular repair of nontraumatic ruptured thoracic aortic pathologies. Ann Vasc Surg 2005; 19:167-171.
21. Doss M, Wood JP, Balzer J et al. Emergency endovascular interventions for acute thoracic aortic rupture: four-year follow-up. J Thorac Cardiovasc Surg 2005; 129:645-651.
22. Morishita K, Kurimoto Y, Kawaharada N et al. Descending thoracic aortic rupture: role of endovascular stent-grafting. Ann Thorac Surg 2004; 78:1630-1634.
23. Bortone AS, De CE, D'Agostino D et al. Endovascular treatment of thoracic aortic disease: four years of experience. Circulation 2004; 110:II262-II267.
24. Melnitchouk S, Pfammatter T, Kadner A et al. Emergency stent-graft placement for hemorrhage control in acute thoracic aortic rupture. Eur J Cardiothorac Surg 2004; 25:1032-1038.
25. Ishida M, Kato N, Hirano T et al. Endovascular stent-graft treatment for thoracic aortic aneurysms: short- to midterm results. J Vasc Interv Radiol 2004; 15:361-367.
26. Iannelli G, Piscione F, Di TL et al. Thoracic aortic emergencies: impact of endovascular surgery. Ann Thorac Surg 2004; 77:591-596.
27. Van H, I, Vermassen F, Durieux C et al. Endovascular repair of aortic rupture. Eur J Vasc Endovasc Surg 2003; 26:311-316.
28. Krohg-Sorensen K, Hafsahl G, Fosse E et al. Acceptable short-term results after endovascular repair of diseases of the thoracic aorta in high risk patients. Eur J Cardiothorac Surg 2003; 24:379-387.
29. Sunder-Plassmann L, Scharrer-Pamler R, Liewald F et al. Endovascular exclusion of thoracic aortic aneurysms: mid-term results of elective treatment and in contained rupture. J Card Surg 2003; 18:367-374.
30. Lepore V, Lonn L, Delle M et al. Endograft therapy for diseases of the descending thoracic aorta: results in 43 high-risk patients. J Endovasc Ther 2002; 9:829-837.
31. Girardi LN, Krieger KH, Altorki NK et al. Ruptured descending and thoracoabdominal aortic aneurysms. Ann Thorac Surg 2002; 74:1066-1070.

32. Morgan R, Loosemore T, Belli AM. Endovascular repair of contained rupture of the thoracic aorta. Cardiovasc Intervent Radiol 2002; 25:291-294.
33. Czermak BV, Waldenberger P, Perkmann R et al. Placement of endovascular stent-grafts for emergency treatment of acute disease of the descending thoracic aorta. AJR Am J Roentgenol 2002; 179:337-345.
34. Alric P, Marty-Ane CH. Endovascular treatment of ruptured thoracic aortic aneurysms. J Thorac Cardiovasc Surg 2002; 124:180-182.
35. Estrera AL, Rubenstein FS, Miller CC, III et al. Descending thoracic aortic aneurysm: surgical approach and treatment using the adjuncts cerebrospinal fluid drainage and distal aortic perfusion. Ann Thorac Surg 2001; 72:481-486.
36. Pokela R, Satta J, Juvonen T et al. Surgical and long-term outcome of graft replacement of aneurysms of the descending thoracic aorta. Analysis of 28 consecutive cases. Scand Cardiovasc J 1997; 31:141-145.
37. Hayashi J, Eguchi S, Yasuda K et al. Operation for nondissecting aneurysm in the descending thoracic aorta. Ann Thorac Surg 1997; 63:93-97.
38. Verdant A, Cossette R, Page A et al. Aneurysms of the descending thoracic aorta: three hundred sixty-six consecutive cases resected without paraplegia. J Vasc Surg 1995; 21:385-390.
39. Bickerstaff LK, Pairolero PC, Hollier LH et al. Thoracic aortic aneurysms: a population-based study. Surgery 1982; 92:1103-1108.
40. Davies RR, Goldstein LJ, Coady MA et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. Ann Thorac Surg 2002; 73:17-27.
41. Clouse WD, Hallett JW, Jr., Schaff HV et al. Improved prognosis of thoracic aortic aneurysms: a population-based study. JAMA 1998; 280:1926-1929.
42. Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. Ann Thorac Surg 2002; 74:S1877-S1880.
43. Juvonen T, Ergin MA, Galla JD et al. Prospective study of the natural history of thoracic aortic aneurysms. Ann Thorac Surg 1997; 63:1533-1545.
44. Coady MA, Rizzo JA, Hammond GL et al. Surgical intervention criteria for thoracic aortic aneurysms: a study of growth rates and complications. Ann Thorac Surg 1999; 67:1922-1926.
45. Masuda Y, Takanashi K, Takasu J et al. Expansion rate of thoracic aortic aneurysms and influencing factors. Chest 1992; 102:461-466.
46. Lobato AC, Puech-Leao P. Predictive factors for rupture of thoracoabdominal aortic aneurysm. J Vasc Surg 1998; 27:446-453.
47. Schermerhorn ML, Giles KA, Hamdan AD et al. Population-based outcomes of open descending thoracic aortic aneurysm repair. J Vasc Surg 2008; 48:821-827.
48. Walsh SR, Tang TY, Sadat U et al. Endovascular stenting versus open surgery for thoracic aortic disease: systematic review and meta-analysis of perioperative results. J Vasc Surg 2008; 47:1094-1098.

49. Svensson LG, Kouchoukos NT, Miller DC et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. Ann Thorac Surg 2008; 85:S1-41.
50. van Prehn J, van Herwaarden JA, Muhs BE et al. Difficulties with endograft sizing in a patient with traumatic rupture of the thoracic aorta: the possible influence of hypovolemic shock. J Vasc Surg 2008; 47:1333-1336.

Chapter 4

Open Surgery versus Endovascular Repair of Ruptured Thoracic Aortic Aneurysms

Submitted

Frederik H.W. Jonker,[1] MD,
Hence J.M. Verhagen,[2] MD, PhD,
Peter H. Lin,[3] MD,
Robin H. Heijmen,[4] MD, PhD,
Santi Trimarchi,[5] MD,
W. Anthony Lee,[6] MD,
Frans L. Moll,[7] MD, PhD,
Husam Atamneh,[3] MD,
Vincenzo Rampoldi,[5] MD,
Bart E. Muhs,[1] MD, PhD.

[1] Section of Vascular Surgery and Interventional Radiology, Yale University School of Medicine, New Haven, CT, and VA Connecticut Healthcare System, West Haven, Connecticut, USA
[2] Section of Vascular Surgery, Erasmus University Medical Center, Rotterdam, the Netherlands
[3] Section of Vascular Surgery, Baylor College of Medicine, Houston, Texas, USA,
[4] Section of Cardiothoracic Surgery St. Antonius Hospital, Nieuwegein, the Netherlands
[5] Section of Vascular Surgery, Policlinico San Donato, I.R.C.C.S., University of Milano, Italy
[6] Christine E. Lynn Heart and Vascular Institute , Boca Raton, Florida, USA
[7] Section of Vascular Surgery, University Medical Center Utrecht, the Netherlands.

ABSTRACT

Background

Ruptured descending thoracic aortic aneurysm (rDTAA) is a cardiovascular catastrophe, associated with high morbidity and mortality, which can be managed either by open surgery or thoracic endovascular aortic repair (TEVAR). The purpose of this study is to retrospectively compare the mortality, stroke, and paraplegia rates after open surgery and TEVAR for the management of rDTAA.

Methods

Patients with rDTAA treated with TEVAR or open surgery between 1995 and 2010 at seven institutions were identified and included for analysis. The outcomes between both treatment groups were compared; the primary endpoint of the study was a composite endpoint of death, permanent paraplegia and/or stroke within 30 days after the intervention. Multivariate logistic regression analysis was used to identify risk factors for the primary endpoint.

Results

A total of 161 patients with rDTAA were included, of which 92 were treated with TEVAR and 69 with open surgery. The composite outcome of death, stroke or permanent paraplegia occurred in 36.2% of the open repair group, compared with 21.7% of the TEVAR group (OR 0.49, 95% CI 0.24-0.97, p=0.044). The 30-day mortality was 24.6% after open surgery compared with 17.4% after TEVAR (OR 0.64, 95% CI 0.30-1.39, p=0.260). Risk factors for the composite endpoint of death, permanent paraplegia and/or stroke in multivariate analysis were increasing age (OR 1.04, 95% CI 1.01-1.08, p=0.036) and hypovolemic shock (OR 2.47, 95% CI 1.09-5.60, p=0.030), while TEVAR was associated with a significantly lower risk of the composite endpoint (OR 0.44, 95% CI 0.20-0.95, p=0.039). The aneurysm-related survival of patients treated with open repair was 64.3% at 4 years, compared with 75.2% for patients treated with TEVAR (p=0.191).

Conclusions

Endovascular repair of rDTAA is associated with a lower risk of a composite of death, stroke and paraplegia, compared with traditional open surgery. In rDTAA patients, endovascular management appears the preferred treatment when this method is feasible.

INTRODUCTION

Thoracic aortic aneurysm rupture is a cardiovascular catastrophe with an estimated incidence of 5.0 per 100,000 people per year.[1, 2] The yearly rate of aortic rupture, dissection and/or death for aneurysms larger than 6 cm is around 15%,[3-5] and only a small fraction of all patients with ruptured thoracic aortic aneurysms is admitted alive to the emergency department.[1] The prognosis of patients with ruptured thoracic aortic aneurysms that make it to the hospital and undergo intervention is thought to be more realistic, however, mortality and morbidity rates in this sub group remain substantial.[6-8]

The traditional treatment for ruptured descending thoracic aortic aneurysms (rDTAA), which account for approximately 30% of all ruptured aneurysms of the thoracic aorta,[1] has been for decades open surgical resection followed by interposition of a Dacron graft.[6, 7] Open surgical repair of rDTAA is associated with high mortality rates, and a considerable number of surviving patients suffer from disabling complications such as permanent paraplegia or stroke.[6-9] Thoracic endovascular aortic repair (TEVAR) recently offers a less invasive alternative for the management of descending thoracic aortic pathologies.[10-12] Although TEVAR is increasingly being used for the management of acute thoracic aortic disease,[13-16] it remains unclear if endovascular repair reduces the mortality and morbidity of rDTAA, due to the low incidence of this emergency. The purpose of this multicenter study is to compare the mortality, stroke, and paraplegia rates between patients with rDTAA treated with open surgery and TEVAR.

METHODS

Study population

The following referral centers participated in this project: Yale New Haven Hospital (New Haven, Connecticut), Baylor College of Medicine (Houston, Texas), Christine E. Lynn Heart and Vascular Institute (Boca Raton, Florida), Policlinico San Donato IRCCS (San Donato Milanese, Italy), St. Antonius Hospital (Nieuwegein, the Netherlands), Erasmus University Medical Center (Rotterdam, the Netherlands) and the University Medical Center Utrecht (Utrecht, the Netherlands). The study was approved by the institutional review committee at all participating institutions. Patients with rDTAA treated with TEVAR or open surgery between 1995 and 2010 were identified and included for analysis. Ruptured aneurysm was defined as any disruption of the aneurysmal aortic wall with an extravascular collection of blood. The anatomic extent of the aneurysm was located between the left subclavian artery and the celiac axis in all cases.

Surgical Techniques

At present, the participating hospitals have established a protocol for admitted patients with rDTAA in which endovascular repair has become the preferred treatment. All endovascular procedures were performed in the operating room under general anesthesia by vascular and/or cardiothoracic surgeons. The following endovascular devices were used: Gore TAG® (Gore Medical, Flagstaff, AZ), Medtronic Talent® (Santa Rosa, CA), or Medtronic Valiant® (Santa Rosa, CA). The endograft diameter was oversized compared with the native aortic landing zone diameter by 10% to 20% as recommended by the manufacturer. To ensure an adequate landing zone, overstenting of the left subclavian and/or celiac artery was required in some cases. Routine revascularization of the left subclavian artery was not performed, this depended on the preference of the surgeon, the vertebrobasilar circulation, and the condition of the patient. Contra-indications for TEVAR have changed over the years and may differ between the different participating institutions and physicians. Current contra-indications typically include no proximal or distal aortic neck, or an aortic diameter that is too wide for commercially available thoracic endografts.

Open surgical procedures were typically performed by cardiothoracic surgeons through a posterolateral thoracotomy in the 4th to 6th intercostal space using extracorporeal perfusion support, with a simple clamp technique or hypothermic circulatory arrest (HCA). Indications for HCA included the need to extend the resection into the distal aortic arch or the entire descending thoracic aorta, or if the aortic pathology precluded the use of aortic cross clamping. Reimplantation of intercostal arteries depended on surgeon's preference. Prophylactic CSF drainage during open surgery or TEVAR was only performed if the patient was stable enough, and was thought to have an increased risk for spinal cord ischemia.

Endpoints and Statistical Analysis

The primary endpoint of the study was a composite endpoint of death, permanent paraplegia and/or stroke within 30 days after the intervention. We defined stroke as a new central neurologic deficit within 30 days after the aortic intervention, confirmed as an ischemic or hemorrhagic lesion on computed tomography or magnetic resonance imaging of the brain. The individual components of the primary endpoint were analyzed as secondary endpoints. Secondary endpoints also included other complications, aortic re-intervention within 30 days, hospital length of stay, and aneurysms-related survival during follow-up. Categorical variables were investigated using the chi-square test or the Fisher's exact test, continuous variables using the Student's t-test or Mann-Whitney U test. Multivariate logistic regression analysis was used to investigate independent effects of baseline and operating characteristics on the primary composite endpoint, and 30-day mortality. Variables with a P value <0.2 in univariate analysis were integrated in the multivariate regression model. Kaplan Meier survival analysis was used to investigate the aneurysm-related survival during follow-up after TEVAR and open surgical repair. Aneurysm-related death was defined as death within 30 days, or death after 30 days due

to complications related to the aneurysm and/or intervention. Statistical analysis was performed using SPSS 15.0 software, a *P* value < 0.05 was considered statistically significant.

RESULTS

Overall, 161 patients with rDTAA between 1995 and 2009 were identified, of which 57.1% (n=92) underwent TEVAR and 42.9% (n=69) open surgical repair. Prior to 2000, all admitted patients underwent open surgery (figure 1), compared with 57.4% of patients between 2000 and 2004, and 10% of patients admitted from 2005 (p<0.001). After the first endovascular repair of rDTAA in 2001, the utilization of TEVAR for rDTAA rapidly increased (figure 1).

The mean age of patients treated with TEVAR was 69.4 years, compared with 64.8 years for patients treated with open surgery (p=0.016, table 1). There were no significant differences in gender or pre-existing co-morbidities between the TEVAR and open repair groups. The mean aneurysm diameter of patients that received TEVAR was significantly smaller than those receiving open surgery (55.5 mm vs. 69.5 mm, p<0.001, table 1). Aneurysm repair was performed within 24 hours in 89.4% of the open repair group, and in 85.4% of the TEVAR group (p=0.49). Coverage of the left subclavian artery was needed in 35.9% after TEVAR and coverage of the celiac artery in 5.4%. Left carotid-subclavian bypass was performed in three of the patients in which the left subclavian artery was covered. Cerebrospinal fluid drainage was performed in similar rates in both treatment groups during the intervention (15.9% vs. 18.7%, p=0.65).

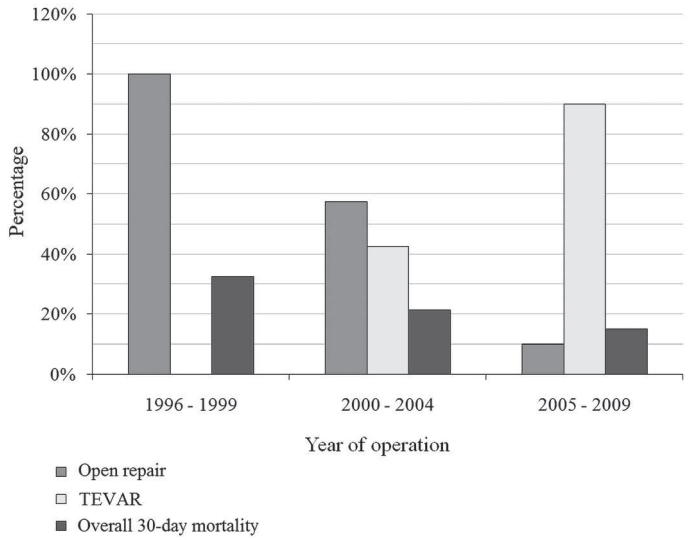

Figure 1. Trends in management and 30-day mortality of ruptured DTAA
The 30-day mortality of rDTAA decreased over the years from 32.4% before 2000, to 21.4% between 2000 and 2004, and 15.0% between 2005 and 2009 (p=0.109).

Table 1. Baseline characteristics

	Open repair (n=69) N	(%)	TEVAR (n=92) N	(%)	p value
Age (y)	64.8	(±12.8)	69.4	(±11.4)	0.016
Male gender	51	(73.9)	62	(67.4)	0.37
Co-morbidities					
Hypertension	42	(60.9)	48	(55.8)	0.53
Diabetes mellitus	15	(21.7)	13	(15.3)	0.30
CAD	29	(42.0)	38	(45.8)	0.64
COPD	21	(30.4)	22	(25.0)	0.45
CRI	12	(17.4)	13	(15.9)	0.80
Carotid disease	8	(11.6)	13	(15.7)	0.47
Hyperlipidemia	20	(29.0)	23	(27.7)	0.86
Prior aortic repair	23	(33.3)	21	(22.8)	0.15
Presentation					
Thoracic pain	47	(75.8)	62	(67.4)	0.26
Hemothorax	36	(52.2)	39	(43.8)	0.29
Hypovolemic shock	18	(26.1)	21	(23.1)	0.66
Aneurysm diameter (mm)	69.5	(±17.4)	55.5	(±20.4)	<0.001
Associated dissection	10	(14.5)	13	(14.3)	0.97
Associated fistula	9	(13.0)	12	(13.2)	0.98

CAD coronary artery disease, *COPD* chronic obstructive pulmonary disease, *CRI* chronic renal insufficiency, *Prior aortic repair* consisted of 29 prior abdominal aortic interventions and 16 prior thoracic aortic interventions; one patient had undergone both a prior abdominal and thoracic aortic intervention.

Early Outcomes

Overall, the 30-day mortality of rDTAA decreased over the years from 32.4% before 2000, to 21.4% between 2000 and 2004, and 15.0% between 2005 and 2009 (p=0.109, figure 1). Among the patients treated with open repair, the 30-day mortality was 24.6% (n=17), compared with 17.4% (n=16) among patients treated with TEVAR (OR 0.64, 95% CI 0.30-1.39, p=0.260). The composite outcome of death, stroke or permanent paraplegia occurred in 36.2% (n=25) of the open repair group, compared with 21.7% (n=20) of the TEVAR group (OR 0.49, 95% CI 0.24-0.97, p=0.044). Permanent paraplegia occurred in 8.7% after open surgery, compared with 2.2% after TEVAR (p=0.059, table 2). The death, stroke and/or paraplegia rates did not differ significantly between the participating institutions.

Postoperative pulmonary complications (31.9% vs. 17.4%, p=0.032) and acute renal failure (24.6% vs. 8.7%, p=0.006) were significantly increased in patients treated with open surgery compared to TEVAR (table 2). Endoleak was diagnosed in 17.4% within the first 30 days after TEVAR (type 1A in 7 patients, type 1B in 3 patients, type 2 in 5 patients and type 3 once). The median hospital length of stay for surviving patients was 22 days (interquartile range 26 days) in the open repair group, compared with 8 days (interquartile range 10 days) in the TEVAR group (p<0.001).

Table 2. Early outcomes

	Open repair (n=69)		TEVAR (n=92)		p value
	N	(%)	N	(%)	
Death, Stroke or Permanent Paraplegia	25	(36.2)	20	(21.7)	0.044
Death	17	(24.6)	16	(17.4)	0.26
Stroke	7	(10.1)	7	(7.6)	0.39
Permanent paraplegia	6	(8.7)	2	(2.2)	0.059
Paraplegia / paraparesis	10	(14.5)	7	(7.6)	0.16
Other complications					
Cardiac complications	9	(13.0)	5	(5.4)	0.090
Pulmonary complications	22	(31.9)	16	(17.4)	0.032
Acute renal failure	16	(24.6)	8	(8.7)	0.006
Visceral ischemia	2	(2.9)	0	(0)	0.18
Aortic re-intervention	2	(2.9)	7	(7.6)	0.30
Median length of stay (days)	22	(26)	8	(10)	<0.001

The median hospital length of stay is shown with the interquartile range, and was calculated for patients that were discharged alive. Among the 7 patients that suffered of stroke after open surgery, 6 had an anterior circulation stroke and one patient had a stroke of the posterior circulation. Among the 7 patients that developed a stroke after TEVAR, 4 had an anterior circulation stroke while 3 patients had a posterior circulation stroke.

Multivariate analysis of endpoints

Independent risk factors for the primary endpoint of death, stroke or permanent paraplegia in multivariate analysis were increasing age (OR 1.04, 95% CI 1.01-1.08, p=0.036) and hypovolemic shock (OR 2.47, 95% CI 1.09-5.60, p=0.030), while TEVAR was associated with a significantly lower risk of the composite endpoint (OR 0.44, 95% CI 0.20-0.95, p=0.039). The risk of death, stroke and/or permanent paraplegia tended to increase after prior aortic repair (OR 2.15, 95% CI 0.95-4.86, p=0.065) (table 3). Independent predictors of 30-day mortality were hypovolemic shock at admission (OR 2.63, 95% CI 1.03-6.70, p=0.044) and a prior aortic repair (OR 2.65, 95% CI 1.08-6.47, p=0.033) (table 4).

Table 3. Independent predictors of death, stroke or permanent paraplegia

Variable	Odds ratio	95% CI	p value
Age	1.04	1.01 – 1.08	0.036
Female gender	0.91	0.40 – 2.08	0.83
Prior aortic repair	2.15	0.95 – 4.86	0.065
Hemothorax	1.29	0.58 – 2.89	0.53
Hypovolemic shock	2.47	1.09 – 5.60	0.030
TEVAR	0.44	0.20 – 0.95	0.039

CI, confidence interval

Table 4. Independent predictors of 30-day mortality

Variable	Odds ratio	95% CI	p value
Age	1.01	0.97 – 1.05	0.58
Female gender	0.94	0.36 – 2.44	0.89
Diabetes mellitus	1.48	0.52 – 4.23	0.47
Prior aortic repair	2.65	1.08 – 6.47	0.033
Hemothorax	2.03	0.81 – 5.07	0.13
Hypovolemic shock	2.63	1.03 – 6.70	0.044
TEVAR	0.78	0.29 – 2.13	0.40

CI, confidence interval

Aneurysm-related survival during follow-up

The median length of follow-up of patients that were alive at 30-days was 34.5 months in the open repair group and 13.5 months in the TEVAR group. After the first 30 days, 7 additional patients in the open repair group died of complications related to the aneurysm and/or intervention, and 5 patients in the TEVAR group. Causes of death in the open repair group were poor general condition and/or congestive heart failure related to surgical intervention (n=3), multi-organ failure (n=2), sepsis (n=1), and unable to be disconnected from the respirator (n=1). Causes of death in the TEVAR group were an infected endograft and/or sepsis (n=3), aortic rupture (n=1) and a poor general condition (n=1). The aneurysm-related survival of patients treated with open repair was 64.3% at 4 years, compared with 75.2% for patients treated with TEVAR (p=0.191, figure 2).

Re-interventions during follow-up

In the TEVAR group, aortic re-interventions were required in 11 patients during follow-up, because of type 1 endoleak in 8 patients, an aortoesophageal fistula in one patient, and aneurismal dilatation of the thoracic aorta without endoleak in two patients. Aortic re-interventions after TEVAR consisted of deployment of an additional endograft in 9 patients, coiling in one patient, and surgical resection of a type III thoracoabdominal aortic aneurysm once. In addition, a thorax drain was placed in 22 patients, an esophagostomy was performed in three patients, and one patient required a thoracotomy to release trapped lung tissue and evacuate a clotted hemothorax.

In the open surgery group, aortic re-interventions were required in 3 patients during follow-up, which consisted of repair of the distal anastomosis because of leakage in two patients and evacuation of an abscess around the aortic graft in one patient. Other re-interventions included a tracheostomy because of respiratory insufficiency (n=10), a pneumonectomy (n=1), necrotectomy and debridement (n=1), and a laparotomy because of visceral ischemia (n=1).

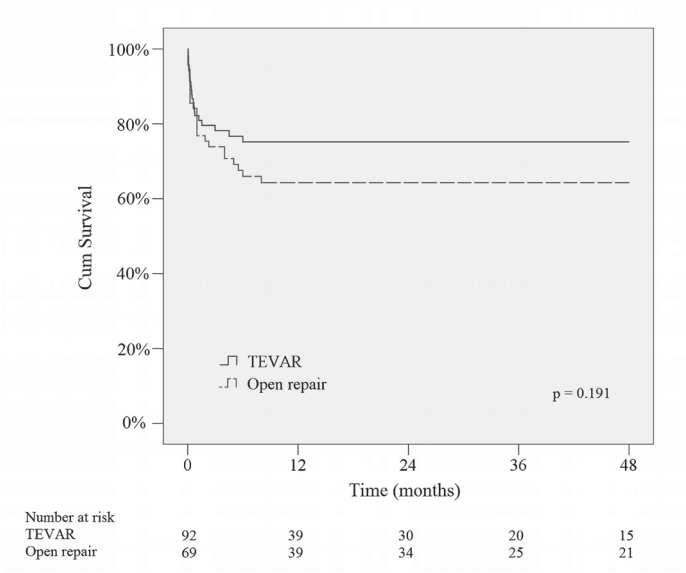

Figure 2. Aneurysm-related survival during follow-up after open repair and TEVAR
The aneurysm-related survival of patients treated with open repair was 64.3% at 4 years, compared with 75.2% for patients treated with TEVAR (p=0.191).

DISCUSSION

TEVAR has revolutionized the management of thoracic aortic disease. Advantages of a minimally invasive endovascular approach are the avoiding of thoracotomy and aortic cross-clamping, reduced operating times and minimal additional blood loss, which are particularly important in rDTAA patients in critical condition. TEVAR is emerging as the preferred treatment for patients with rDTAA at our institutions, although there is currently no strong evidence that an endovascular approach improves survival compared with traditional open surgery.

In the present multi-center analysis, we observed a trend towards reduced 30-day mortality for patients treated with TEVAR (17.4% vs. 24.6%), in accordance with previous reports of experienced centers, in which early mortality rates typically range between 11.4% to 18.9% after TEVAR,[16-18] compared with 22.2% to 33.3% after surgical repair.[9, 18-21] In the United States between 1988 and 2003, the overall in-hospital mortality after open surgical repair of rDTAA was 45%,[6] and the "real world" mortality rate after intervention for rDTAA may therefore be underestimated in the literature. The lower mortality rate after open repair in our evaluation compared to this population-based study,[6] may be related to the fact that the participating institutions in our study were tertiary referral centers, and mortality rates of rDTAA may be reduced in referral and/or large-volume hospitals.[22, 23] Furthermore, referred rDTAA patients that survived transport and received a surgical intervention may have been relatively more stable, which may have contributed to improved outcomes as well.

Improved survival after an endovascular approach compared with open surgery has been observed as well for other thoracic aortic catastrophes including traumatic aortic injuries or complicated type B aortic dissections.[13, 15, 24, 25] Although mortality is a very important outcome measure, the quality of life of surviving patients is also essential when determining the preferred treatment. In descending thoracic aortic interventions, the most feared nonfatal complication is postoperative paraplegia due to interruption of the blood supply to the spinal cord. In this study, the incidence of the composite primary endpoint of death, stroke or paraplegia was significantly reduced after TEVAR, and we observed a trend towards a lower incidence of permanent paraplegia in this group. Previous studies have shown a reduced paraplegia rate after TEVAR for non-ruptured DTAA compared with open surgery.[26, 27] Theoretic explanations for reduced risks of paraplegia after an endovascular approach are no aortic cross clamping during TEVAR, fewer periods of peri operative hypotension due to blood loss or hemodynamic shifts, and slow thrombosis of the aneurysm sac compared with acute occlusion of critical vessels during surgical repair.[27]

Hypovolemic shock at admission was an independent predictor of both 30-day mortality as the composite endpoint of death, stroke and paraplegia. Hypovolemic shock is a strong predictor of death in most acute aortic syndromes,[16, 28-30] and hypovolemia may also lead to inadequate perfusion of the spinal cord and brain, resulting in increased risks of neurologic deficits. Aneurysm rupture, long cross-clamp duration, and intra operative hypotension have been previously correlated with increased risks of spinal cord ischemia and stroke during open thoracic aortic surgery.[8, 31] Several reports have suggested a similar relation between emergency procedures, blood loss or peri operative hypotension, and the occurrence of spinal cord ischemia after TEVAR.[32-35] Prior aortic repair was associated with an increased risk of 30-day mortality as well. Patients that have undergone prior aortic repair may have had a long history of atherosclerotic disease, and a poor general condition, resulting in increased risks of postoperative mortality and morbidity. In addition, open or endovascular repair of rDTAA may be more difficult in a previously reconstructed aorta.

Although TEVAR was associated with improved outcomes, a cause for concern is the occurrence of endograft-related complications.[36, 37] Endoleak was diagnosed in 17% within the first 30 days, and aortic re-interventions were required in about 8% of all patients during the first month. Furthermore, several patients expired due to infected endografts and/or aortic rupture during follow-up after TEVAR. These findings underline the need for close radiologic surveillance during follow-up after endovascular repair of rDTAA, which may be initiated already before discharge of the patient. Nevertheless, in the open repair group a considerable number of patients died as well after the first 30 days, due to multi organ failure or a poor general condition.

An important limitation of the present study was the retrospective observational study design. However, due to the rarity of this condition and its emergent nature, it will be very difficult to ever realize a large randomized study comparing the outcomes of TEVAR versus open surgery of rDTAA. Moreover, because of the superior results of TEVAR for the management of acute thoracic aortic disease in multiple observational studies, including the present evaluation, conducting such a randomized study may be not ethical. Due to the non-randomized observational study design, baseline differences existed between the treatment groups, including an older mean age and a smaller aneurysm diameter in the TEVAR group. The older age of the TEVAR patients may be explained by the increasing life-expectancy of the population, and surgical interventions may have been refused to very elderly patients with rDTAA prior to the endovascular era. There may be several theoretical explanations for the smaller mean aneurysm diameter in the TEVAR group. The proportion of patients with aneurysms > 5.5 cm undergoing elective thoracic aortic repair has increased over the years, due to increased detection rates of thoracic aortic aneurysms, and improved treatment modalities and outcomes.[38, 39] This may have resulted in a lower occurrence of rupture of very large aneurysms, and therefore a relative increase in the occurrence of aortic rupture of aneurysms smaller than 5.5 cm. In addition, very large aneurysms may be more often unsuitable for an endovascular approach, due to inadequate landing zones. In a recent comparative analysis of Patel and colleagues, patients treated with TEVAR for thoracic aortic rupture were significantly older and had a smaller mean aortic diameter as well, when compared to patients treated with open surgery.[16] Another limitation of the study is that most open surgical interventions were performed before 2000, while all endovascular procedures were performed after 2000 in our evaluation, and the outcomes of open surgery for rDTAA may have improved slightly over the years. However, due to the low incidence of rDTAA and the increasing utilization of TEVAR, it is very difficult to obtain a considerable number of rDTAA patients treated with open surgery in more recent years.

CONCLUSIONS

There has been a shift towards endovascular management of patients with rDTAA at our institutions. We observed a lower rate of the composite endpoint of death, stroke and paraplegia, for the rDTAA patients treated with TEVAR compared with traditional open surgery. Furthermore, there was a trend towards lower risks of permanent paraplegia and improved aneurysm-related survival after TEVAR. In rDTAA patients, endovascular management appears the preferred treatment when this method is feasible.

ACKNOWLEDGEMENTS

We would like to thank Michelle Streukens for the data collection.

REFERENCES

1. Johansson G, Markstrom U, Swedenborg J. Ruptured thoracic aortic aneurysms: a study of incidence and mortality rates. J Vasc Surg 1995; 21:985-988.
2. Bickerstaff LK, Pairolero PC, Hollier LH et al. Thoracic aortic aneurysms: a population-based study. Surgery 1982; 92:1103-1108.
3. Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. Ann Thorac Surg 2002; 74:S1877-S1880.
4. Davies RR, Goldstein LJ, Coady MA et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. Ann Thorac Surg 2002; 73:17-27.
5. Coady MA, Rizzo JA, Hammond GL et al. Surgical intervention criteria for thoracic aortic aneurysms: a study of growth rates and complications. Ann Thorac Surg 1999; 67:1922-1926.
6. Schermerhorn ML, Giles KA, Hamdan AD et al. Population-based outcomes of open descending thoracic aortic aneurysm repair. J Vasc Surg 2008; 48:821-827.
7. Achneck HE, Rizzo JA, Tranquilli M et al. Safety of thoracic aortic surgery in the present era. Ann Thorac Surg 2007; 84:1180-1185.
8. Cambria RP, Clouse WD, Davison JK et al. Thoracoabdominal aneurysm repair: results with 337 operations performed over a 15-year interval. Ann Surg 2002; 236:471-479.
9. Minatoya K, Ogino H, Matsuda H et al. Replacement of the descending aorta: recent outcomes of open surgery performed with partial cardiopulmonary bypass. J Thorac Cardiovasc Surg 2008; 136:431-435.
10. Dake MD, Miller DC, Semba CP et al. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. N Engl J Med 1994; 331:1729-1734.
11. Semba CP, Kato N, Kee ST et al. Acute rupture of the descending thoracic aorta: repair with use of endovascular stent-grafts. J Vasc Interv Radiol 1997; 8:337-342.
12. Conrad MF, Cambria RP. Contemporary management of descending thoracic and thoracoabdominal aortic aneurysms: endovascular versus open. Circulation 2008; 117:841-852.
13. Jonker FH, Giacovelli JK, Muhs BE et al. Trends and outcomes of endovascular and open treatment for traumatic thoracic aortic injury. J Vasc Surg 2010; 51:565-571.
14. Demetriades D, Velmahos GC, Scalea TM et al. Diagnosis and treatment of blunt thoracic aortic injuries: changing perspectives. J Trauma 2008; 64:1415-1418.
15. Fattori R, Tsai TT, Myrmel T et al. Complicated acute type B dissection: is surgery still the best option?: a report from the International Registry of Acute Aortic Dissection. JACC Cardiovasc Interv 2008; 1:395-402.
16. Patel HJ, Williams DM, Upchurch GR, Jr. et al. A 15-year comparative analysis of open and endovascular repair for the ruptured descending thoracic aorta. J Vasc Surg 2009.
17. Cambria RP, Crawford RS, Cho JS et al. A multicenter clinical trial of endovascular stent graft repair of acute catastrophes of the descending thoracic aorta. J Vasc Surg 2009; 50:1255-1264.

18. Jonker FH, Trimarchi S, Verhagen HJ et al. Meta-analysis of open versus endovascular repair for ruptured descending thoracic aortic aneurysm. J Vasc Surg 2010; 51:1026-32, 1032.
19. Barbato JE, Kim JY, Zenati M et al. Contemporary results of open repair of ruptured descending thoracic and thoracoabdominal aortic aneurysms. J Vasc Surg 2007; 45:667-676.
20. Girardi LN, Krieger KH, Altorki NK et al. Ruptured descending and thoracoabdominal aortic aneurysms. Ann Thorac Surg 2002; 74:1066-1070.
21. Estrera AL, Rubenstein FS, Miller CC, III et al. Descending thoracic aortic aneurysm: surgical approach and treatment using the adjuncts cerebrospinal fluid drainage and distal aortic perfusion. Ann Thorac Surg 2001; 72:481-486.
22. Birkmeyer JD, Siewers AE, Finlayson EV et al. Hospital volume and surgical mortality in the United States. N Engl J Med 2002; 346:1128-1137.
23. Cowan JA, Jr., Dimick JB, Henke PK et al. Surgical treatment of intact thoracoabdominal aortic aneurysms in the United States: hospital and surgeon volume-related outcomes. J Vasc Surg 2003; 37:1169-1174.
24. Demetriades D, Velmahos GC, Scalea TM et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008; 64:561-570.
25. Visser JJ, Williams M, Kievit J et al. Prediction of 30-day mortality after endovascular repair or open surgery in patients with ruptured abdominal aortic aneurysms. J Vasc Surg 2009; 49:1093-1099.
26. Cheng D, Martin J, Shennib H et al. Endovascular aortic repair versus open surgical repair for descending thoracic aortic disease a systematic review and meta-analysis of comparative studies. J Am Coll Cardiol 2010; 55:986-1001.
27. Bavaria JE, Appoo JJ, Makaroun MS et al. Endovascular stent grafting versus open surgical repair of descending thoracic aortic aneurysms in low-risk patients: a multicenter comparative trial. J Thorac Cardiovasc Surg 2007; 133:369-377.
28. Suzuki T, Mehta RH, Ince H et al. Clinical profiles and outcomes of acute type B aortic dissection in the current era: lessons from the International Registry of Aortic Dissection (IRAD). Circulation 2003; 108 Suppl 1:II312-II317.
29. Rampoldi V, Trimarchi S, Eagle KA et al. Simple risk models to predict surgical mortality in acute type A aortic dissection: the International Registry of Acute Aortic Dissection score. Ann Thorac Surg 2007; 83:55-61.
30. Arthurs ZM, Starnes BW, Sohn VY et al. Functional and survival outcomes in traumatic blunt thoracic aortic injuries: An analysis of the National Trauma Databank. J Vasc Surg 2009; 49:988-994.
31. Goldstein LJ, Davies RR, Rizzo JA et al. Stroke in surgery of the thoracic aorta: incidence, impact, etiology, and prevention. J Thorac Cardiovasc Surg 2001; 122:935-945.

32. Feezor RJ, Martin TD, Hess PJ, Jr. et al. Extent of aortic coverage and incidence of spinal cord ischemia after thoracic endovascular aneurysm repair. Ann Thorac Surg 2008; 86:1809-1814.
33. Martin DJ, Martin TD, Hess PJ et al. Spinal cord ischemia after TEVAR in patients with abdominal aortic aneurysms. J Vasc Surg 2009; 49:302-306.
34. Chiesa R, Melissano G, Marrocco-Trischitta MM et al. Spinal cord ischemia after elective stent-graft repair of the thoracic aorta. J Vasc Surg 2005; 42:11-17.
35. Feezor RJ, Lee WA. Strategies for detection and prevention of spinal cord ischemia during TEVAR. Semin Vasc Surg 2009; 22:187-192.
36. Svensson LG, Kouchoukos NT, Miller DC et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. Ann Thorac Surg 2008; 85:S1-41.
37. Leurs LJ, Harris PL, Buth J. Secondary interventions after elective endovascular repair of degenerative thoracic aortic aneurysms: results of the European collaborators registry (EUROSTAR). J Vasc Interv Radiol 2007; 18:491-495.
38. Elefteriades JA, Farkas EA. Thoracic aortic aneurysm clinically pertinent controversies and uncertainties. J Am Coll Cardiol 2010; 55:841-857.
39. Clouse WD, Hallett JW, Jr., Schaff HV et al. Improved prognosis of thoracic aortic aneurysms: a population-based study. JAMA 1998; 280:1926-1929.

Chapter 5

Outcomes of Endovascular Repair of Ruptured Descending Thoracic Aortic Aneurysms

Circulation 2010;121:2718-23

Frederik H.W. Jonker,[1] MD
Hence J.M. Verhagen,[2] MD, PhD
Peter H. Lin,[3] MD
Robin H. Heijmen,[4] MD, PhD
Santi Trimarchi,[5] MD
W. Anthony Lee,[6] MD
Frans L. Moll,[7] MD, PhD
Husam Athamneh,[3] MD
Bart E. Muhs,[1] MD, PhD

[1] Section of Vascular Surgery and Interventional Radiology, Yale University School of Medicine, New Haven, Connecticut, and VA Connecticut Healthcare System, West Haven, Connecticut, USA
[2] Section of Vascular Surgery, Erasmus University Medical Center, Rotterdam, the Netherlands
[3] Section of Vascular Surgery, Baylor College of Medicine, Houston, Texas, USA
[4] Section of Cardiothoracic Surgery, St. Antonius Hospital, Nieuwegein, the Netherlands
[5] Section of Vascular Surgery, Policlinico San Donato IRRCS, Milan, Italy
[6] Section of Vascular Surgery, University of Florida, Gainesville, Florida, USA
[7] Section of Vascular Surgery, University Medical Center Utrecht, the Netherlands

ABSTRACT

Background:
Thoracic endovascular aortic repair (TEVAR) offers a less invasive approach for the treatment of ruptured descending thoracic aortic aneurysms (rDTAA). Due to the low incidence of this life-threatening condition, little is known about the outcomes of endovascular repair of rDTAA and the factors that affect these outcomes.

Methods and results:
We retrospectively investigated the outcomes of 87 patients that underwent TEVAR for rDTAA at 7 referral centers between 2002 and 2009. The mean age was 69.8 ±12 years and 69.0% were male. Hypovolemic shock was present in 21.8% of patients, and 40.2% were hemodynamically unstable. The 30-day mortality was 18.4%, and hypovolemic shock (OR 4.75, 95% CI 1.37-16.5, p=0.014) and hemothorax at admission (OR 6.65, 95% CI 1.64-27.1, p=0.008) were associated with increased 30-day mortality after adjusting for age. Stroke and paraplegia occurred each in 8.0%, and endoleak was diagnosed in 18.4% of patients within the first 30 days after TEVAR. Four additional patients expired due to procedure-related complications during a median follow-up of 13 months, the estimated aneurysm-related mortality at 4 years was 25.4%.

Conclusion:
Endovascular repair of ruptured descending thoracic aortic aneurysm is associated with encouraging results. The endovascular approach was associated with considerable rates of neurologic complications and procedure-related complications such as endoleak.

INTRODUCTION

Ruptured thoracic aortic aneurysm is rare and the reported annual incidence is only 5 per 100,000.[1] Increasing age, female gender, and increasing aortic diameter have been associated with increased risk of thoracic aortic aneurysm rupture.[1-4] Ruptured thoracic aortic aneurysm is a life-threatening condition, and the overall mortality rate is thought to exceed 90%.[1] The traditional treatment of ruptured aneurysms of the descending thoracic aorta (rDTAA), which account for about 30% of all ruptured thoracic aortic aneurysms,[1] has been open surgical resection of the aneurysm and replacement with an interposition graft. More recently, thoracic endovascular aortic repair (TEVAR) has offered a less invasive alternative for the treatment of rDTAA.[5] Although endovascular management has been shown to improve the survival of patients with ruptured abdominal aortic aneurysm,[6,7] which is more common than rDTAA,[1,8] the outcomes of endovascular repair of rDTAA remain unclear. The current literature is limited to small series of rDTAA managed with endovascular repair, and these studies often combined the results of rDTAA, traumatic aortic injuries, penetrating aortic ulcers and acute type B aortic dissections,[9-15] while these are completely different pathologies.

In the present study, we evaluated the in-hospital and follow-up results of patients with rDTAA managed with endovascular repair at 7 referral centers in the United States and Europe. The influence of patient and procedural characteristics on outcomes after endovascular repair was investigated.

METHODS

Study population

We identified all patients that were treated with endovascular repair for ruptured aneurysms of the descending thoracic aorta at seven referral centers in the United States and Europe between January 2002 and July 2009. The following institutions participated in this project: Yale New Haven Hospital (New Haven, Connecticut), Baylor College of Medicine, (Houston, Texas), University of Florida (Gainesville, Florida), Policlinico San Donato IRRCS (San Donato Milanese, Italy), St. Antonius Hospital (Nieuwegein, the Netherlands), Erasmus University Medical Center (Rotterdam, the Netherlands) and the University Medical Center Utrecht (Utrecht, the Netherlands). The study was approved by the institutional review committee at all participating institutions.

All participating institutions have established a protocol for admitted patients with ruptured descending thoracic aortic aneurysm, in which endovascular repair is the preferred treatment. Contra-indications for TEVAR include no proximal or distal aortic neck, or an aortic diameter that is too wide for commercially available thoracic endografts. Tortuous, calcified or small iliac

arteries do typically not preclude for TEVAR since an iliac conduit can be used for vascular access in these patients. If a patient with rDTAA is unsuitable for an endovascular approach, open surgery is offered, or treatment is refused.

For the present study, ruptured aneurysm was defined as any disruption of the aneurysmal aortic wall with an extravascular collection of blood and/or mediastinal hematoma, hemothorax, or esophageal penetration as documented by preoperative computed tomography angiography (CTA), or transesophageal echocardiography (TEE). Contained rupture was defined as descending thoracic aortic aneurysm with only a contained mediastinal hematoma. Ruptured dissected aneurysms were included only if the aneurysm diameter was larger than 50mm. Patients that were treated with aortic arch replacement besides endovascular repair (e.g. elephant trunk technique) were excluded.

Surgical technique

All endovascular procedures were performed in the operating room under general anesthesia by vascular and/or cardiothoracic surgeons. Preoperative imaging usually consisted of CTA of the chest and abdomen. Intravascular ultrasound (IVUS) and intraoperative TEE were occasionally used to augment the other imaging modalities.

The endograft diameter was oversized compared with the native aortic landing zone diameter by 10% to 20% as recommended by the manufacturer. The endograft was advanced into the desired position and carefully deployed after verification of the correct position using contrast angiography. Proximal and distal landing zones of 20 mm of normal aorta were required to minimize risks on endoleak or endograft migration, coverage of the subclavian and/or celiac artery was required in some cases to ensure an adequate landing zone. Final endograft position and endoleaks were assessed using contrast angiography. All patients were observed at the intensive care unit (ICU) for at least 24 hours postoperatively. Routine CTA of the chest and abdomen was obtained in all patients before discharge.

Statistical Analysis

Data are shown as frequencies and percentages, and mean $\pm$ standard deviation or as a median and interquartile range. Predictors of 30-day mortality were explored using logistic regression analysis. Multivariable regression analysis was not performed since the study population and the expected number of events were thought to be too small for this analysis. Instead, we adjusted for age in our bivariate regression analysis of predictors of 30-day mortality, since increasing age is an important risk factor for mortality. To correct for multiple comparisons, statistical significance was defined as a P value < 0.02. Time of freedom from aneurysm related death and/or thoracic aortic re-intervention was demonstrated using Kaplan-Meier survival curves. Aneurysm-related death was defined as death within 30 days, or death after 30 days due to complications related to the aneurysm and/or endovascular procedure. Statistical analysis was performed using SPSS 15.0 software.

RESULTS

Patient and Operating Characteristics

Eighty-seven patients underwent TEVAR for rDTAA, the mean age was 69.8 ±12 years and 69.0% were male. The mean aneurysm diameter was 54.3 ±20 mm. Hypovolemic shock was present in 21.8% of patients, and 40.2% were hemodynamically unstable (table 1). A contained rupture was diagnosed in 36.8%, and hemothorax was present in 41.4% of patients (table 1).

Endovascular repair was performed within 24 hours in 85.1% (table 2). All patients that were treated after 24 hours had a contained rupture and were hemodynamically stable. These patients were monitored closely at the ICU while the endovascular procedure was planned. The common femoral artery was used for vascular access in 89.7%. Femoral access was not possible in 10.3% because of severe occlusive disease of the iliac arteries, and an iliac conduit (n=8) or the distal abdominal aorta (n=1) was used for vascular access in these patients. The mean graft diameter was 37.5 ±3.7 mm and the total graft length was 115.6 ± 114 mm. Coverage of the left subclavian artery was required for an adequate landing zone in 37.9% and overstenting of the celiac artery was performed in 5.7% (table 2).

Early outcomes

The ruptured aneurysm was successfully excluded during TEVAR in 95.4%. The 30-day mortality was 18.4% (n=16), the median time interval between TEVAR and 30-day death was 11 days (interquartile range 14; limits 1 to 29 days). Multi-organ failure (MOF) and cardiac complications were together responsible for 50.0% (n=8) of the deaths within the first month.

The most common post-operative morbidities were respiratory complications which occurred in 18.4% (n=16) of patients (table 3). Peri-procedural stroke occurred in 8.0% (n=7), including 4 patients (4.6%) that died of stroke. The incidence of postoperative paraplegia was 8.0% (n=7). One of these patients had received cerebrospinal fluid (CSF) drainage during TEVAR. After diagnosis of paraplegia, CSF drainage was started immediately in all patients, for a median duration of 3 days (limits 1 to 4 days). Two patients (2.3%) suffered from permanent paraplegia, while 5 patients (5.7%) had transient paraplegia which resolved during follow-up.

Endoleak was diagnosed on the completion angiogram and/or computed tomography in 18.4% (n=16) within the first 30 days after TEVAR, and consisted of type 1 in 10 patients, type 2 in 5 patients and type 3 once. Type 1 endoleak was detected in 2 additional patients after 30 days.

Table 1. Demographics, Patient history and Presentation

	N or mean	(% or ±SD)
Demographics		
Age (y)	69.8	(±12)
Male gender	60	(69.0)
Patient History		
Hypertension	45	(51.7)
Diabetes Mellitus	9	(10.3)
Hyperlipidemia	22	(25.3)
CAD	37	(42.5)
CABG	14	(16.1)
COPD	22	(25.3)
CRI	12	(13.8)
Prior abdominal aortic intervention	11	(12.6)
Prior thoracic aortic intervention	9	(10.3)
Presentation		
Aneurysm diameter (mm)	54.3	(±20)
Thoracic pain	68	(78.1)
Dyspnea	21	(24.1)
Hemoptysis / hematemesis	12	(13.8)
Hemodynamic instability	35	(40.2)
Hypovolemic shock	19	(21.8)
Hemothorax	36	(41.4)
Contained rupture	32	(36.8)
Associated dissection	10	(11.5)
Associated fistula	10	(11.5)

CAD coronary artery disease, *CABG* coronary artery bypass grafting, *COPD* chronic obstructive pulmonary disease, *CRI* chronic renal insufficiency, *associated fistula*, these patients were admitted with rDTAA and an aortoesophageal or aortobronchial fistula, *SD* standard deviation

Table 2. Operating characteristics

	N	(%)
TEVAR within 24 hours	74	(85.1)
Vascular access		
CFA	78	(89.7)
CIA	8	(9.2)
Abdominal Aorta	1	(1.2)
Graft brand		
Gore TAG®	37	(42.5)
Medtronic Talent®	18	(20.7)
Medtronic Valiant®	17	(19.5)
Different	15	(17.2)
Mean graft diameter (mm)	37.5	(±3.7)
Total graft length (mm)	150.6	(±114)
Number of stents	2.4	(±1.1)
Coverage LSA	33	(37.9)
Coverage CA	5	(5.7)
CSF drainage during TEVAR	17	(19.5)
Additional surgery		
Thorax drainage	21	(24.1)
Esophagectomy	3	(3.4)

CFA common femoral artery, *CIA* common iliac artery, *LSA* left subclavian artery, *CA* celiac artery, *CSF* cerebrospinal fluid.

Table 3. Thirty-day outcomes

	N	(%)
Successful deployment	83	(95.4)
30-day mortality	16	(18.4)
Paraplegia	7	(8.0)
Stroke	7	(8.0)
Cardiac complications	5	(5.7)
Pulmonary complications	16	(18.4)
ARF	8	(9.2)
Bleeding	10	(11.5)
Endoleak	16	(18.4)

Paraplegia was permanent in two patients and transient in five patients

Predictors of 30-day mortality

After adjusting for age, which was a risk factor for 30-day mortality (OR 1.11, p=0.024), the following variables were significant predictors of 30-day mortality (p<0.02): hypovolemic shock (OR 4.75, 95% CI 1.37-16.5, p=0.014) and hemothorax at admission (OR 6.65, 95% CI 1.64-27.1, p=0.008) (table 4). There was a trend towards higher 30-day mortality among hemodynamically instable patients (OR 3.99, 95% CI 1.07-14.9, p=0.039), and patients that had underwent a prior aortic intervention (OR 3.32, 95% CI 0.92-11.99, p=0.067), while more recent endovascular procedures tended to be associated with reduced 30-day mortality (OR 0.74, 95% CI 0.54-1.01, p=0.059).

Table 4. Logistic regression analysis of predictors for 30-day mortality, adjusted for age

Variable	OR	95% CI	P value
Female gender	1.09	0.32 - 3.76	0.89
Hypertension	0.38	0.11 - 1.32	0.13
Diabetes mellitus	3.48	0.68 - 17.8	0.13
Hyperlipidemia	0.46	0.10 - 2.12	0.32
CAD	1.68	0.46 - 6.13	0.43
COPD	1.42	0.38 - 5.26	0.60
CRI	2.27	0.53 - 9.67	0.27
Prior aortic intervention	3.32	0.92 - 11.99	0.067
Aneurysm diameter	1.01	0.98 - 1.04	0.46
Hemodynamic instability	3.99	1.07 - 14.9	0.039
Hypovolemic shock	4.75	1.37 - 16.5	0.014
Hemothorax	6.65	1.64 - 27.1	0.008
Contained rupture	0.66	0.18 - 2.44	0.53
Associated dissection	2.77	0.56 - 13.6	0.21
Associated fistula	1.20	0.21 - 6.80	0.83
Coverage LSA	0.77	0.21 – 2.84	0.70
CSF drainage during TEVAR	0.96	0.23 - 4.12	0.96
Year of procedure	0.74	0.54 - 1.01	0.059

The logistic regression results were adjusted for age, which was a significant risk factor for 30-day mortality (OR 1.11, p=0.024), *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease, *CRI* chronic renal insufficiency, *LSA* left subclavian artery, *CSF* cerebrospinal fluid, *OR* odds ratio, *CI* confidence interval.

Follow-up outcomes

The median follow-up of patients that were alive at 30 days was 13 months (interquartile range 33; limits 1 to 72 months). Four additional patients expired after the first month due to complications related to the ruptured aneurysm and/or endovascular procedure. The first patient died after 46 days due to heart failure and a poor general condition that she had developed after TEVAR. The second patient died of sepsis due to a persistent aortoesophageal fistula at

3 months after TEVAR for rDTAA with aortoesophageal fistula. The last two patients were re-admitted with an infected endograft and died of sepsis at 4.5 and 6 months after the initial endovascular procedure. CTA imaging demonstrated that the infection was due to a new aortoesophageal fistula in the latter patient, the cause of sepsis was unclear in the other case. The estimated aneurysm-related mortality at 4 years was 25.4% (figure 1). For patients admitted with and without hemothorax, the aneurysm-related mortality at 3 years was 43.9% and 12.2%, respectively (p=0.001, figure 2). Twelve patients died during follow-up of causes unrelated to the ruptured aneurysm and/or endovascular procedure, including myocardial infarction (n=5), stroke (n=2), sepsis after resection of a sarcoma (n=1), and unknown (n=4).

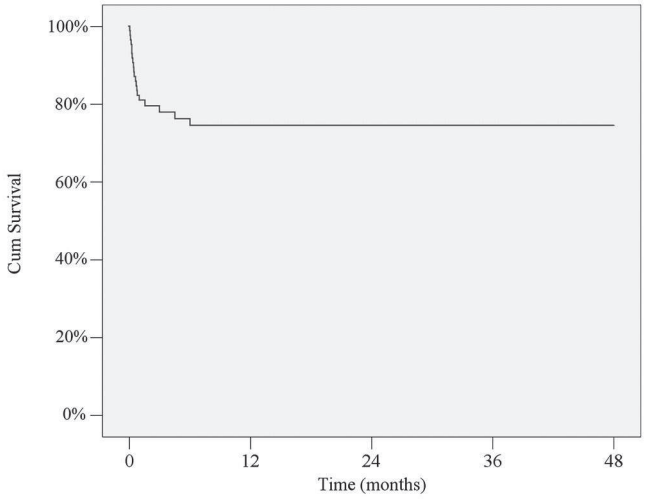

Figure 1. Aneurysm-related survival after endovascular repair of rDTAA
Four additional patients expired after the first month due to complications related to the ruptured aneurysm and/or endovascular procedure. The estimated aneurysm-related mortality at 4 years was 25.4%. The number of patients lost to follow-up (FU) includes all patients that expired after 30-days due to unrelated causes, those that underwent TEVAR recently and have a FU < 48 months, and those that were lost to follow-up.

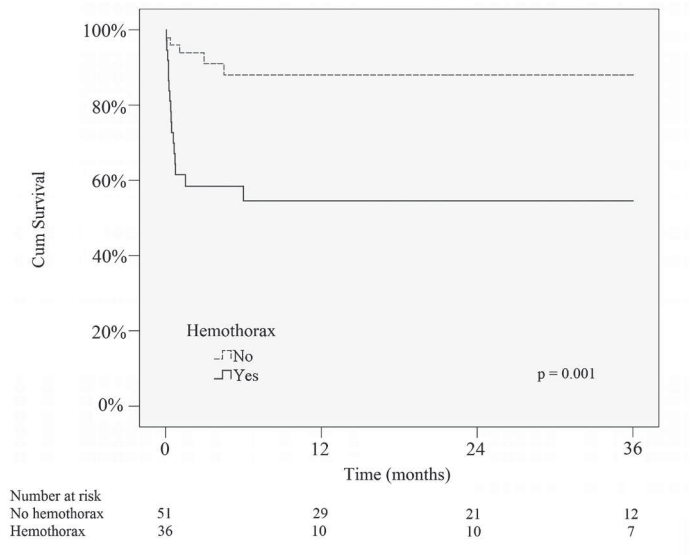

Figure 2. Aneurysm-related survival for patients admitted with and without hemothorax
The aneurysm-related mortality for patients admitted with and without hemothorax at 3 years was 43.9% and 12.2%, respectively (log-rank test: p=0.001).

Thoracic aortic re-interventions were required in 11 patients. Median time interval between initial TEVAR and the re-intervention was 17 days (interquartile range 148 days; limits 1 day to 4 years). Aortic re-intervention was indicated because of type 1 endoleak in 8 patients, an aortoesophageal fistula in one patient and aneurysmal dilatation of the thoracic aorta without detectable endoleak in two patients. The re-intervention consisted of deployment of an additional thoracic endograft in 9 patients, coiling in one patient and open resection of a type III thoraco-abdominal aortic aneurysm once. Freedom from aneurysm-related death and aortic re-intervention at 4 years was 54.9% (figure 3).

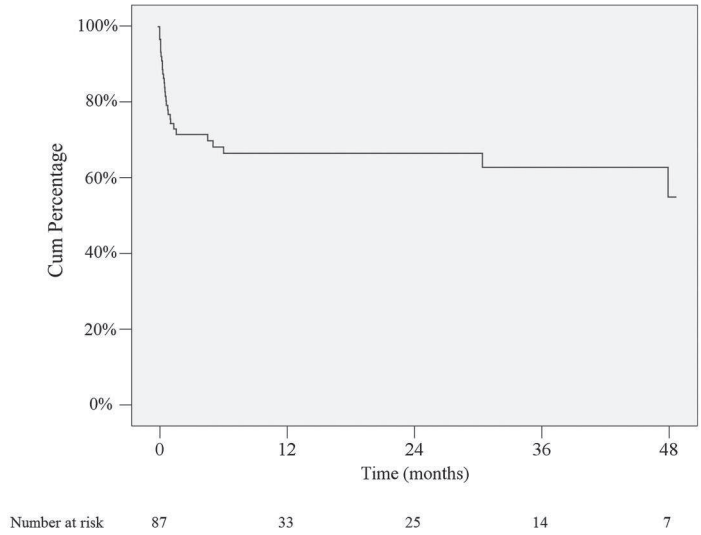

Figure 3. Freedom from aneurysm-related death or thoracic aortic re-intervention
Freedom from aneurysm-related death and aortic re-intervention at 4 years was 54.9%.
Thoracic aortic re-interventions include all re-interventions that were required for complications related to the aneurysm and/or initial endovascular procedure such as endoleak, aneurysmal dilatation and development of aortic fistulas.

DISCUSSION

Thoracic endovascular aortic repair has changed the management of elective and emergency thoracic aortic intervention. TEVAR has shown to improve the operative mortality rates of intact descending thoracic aortic aneurysm,[16] complicated type B aortic dissections[17] and traumatic thoracic aortic injuries.[18,19] For ruptured descending thoracic aortic aneurysms, which is less common than these pathologies, endovascular management has become the treatment of choice at many institutions, although evidence supporting the superiority of TEVAR is lacking. We evaluated the outcomes of endovascular repair of rDTAA in a multicenter analysis, and attempted to investigate factors that affect these results.

The vast majority of patients that suffer from rDTAA will expire before they reach the hospital.[1] Although the patients that make it to the emergency department are thought to have a much better prognosis, a large part of this group will not survive the hospitalization as well. Traditional surgical repair of rDTAA is still associated with high mortality rates, despite improved treatment strategies and peri-operative care. Specialized centers have reported mortality rates between 25% and 30% after open repair of rDTAA,[20-23] but this number may be even underestimated and many

institutions will not operate on these patients. In a population-based analysis, Schermerhorn and colleagues found an in-hospital mortality rate of 45% after open repair of rDTAA.[24]

Endovascular repair allows quick exclusion of rDTAA without cardiovascular bypass, aortic clamping, or thoracotomy. In this evaluation, the 30-day mortality after TEVAR was 18.4% and endovascular repair therefore appears to lower the 30-day mortality rate considerably compared with results of conventional open surgical repair in the literature. Studies describing outcomes of endovascular repair of rDTAA are scarce, available series have reported early mortality rates between 10% and 21% after TEVAR for different acute thoracic aortic pathologies.[9-15] A recent comparative study of Patel and colleagues showed a 30-day mortality of 11.4% after TEVAR compared with 26.5% after open repair of ruptured thoracic aortic dissections and aneurysms.[9] These results suggest a paradigm shift, with TEVAR emerging as the therapy of choice for rDTAA.

Logistic regression analysis showed several risk factors for 30-day mortality after adjusting for age. Hypovolemic shock typically results in poor outcomes, and patients with such admission characteristics had increased 30-day mortality in our evaluation as well. Hemothorax at presentation was a strong predictor of mortality as well, which was more surprising. Hemothorax is a marker for excessive blood loss, and blood in the pleural space may result in respiratory insufficiency and infection in this already critically-ill subset of patients. Prompt drainage of the hemothorax, closely monitoring of the vital functions and respiratory support if needed, may therefore be crucial in these patients.

Endovascular repair of rDTAA was associated with considerable rates of stroke and permanent or temporary paraplegia, which occurred each in 8% of patients. For endovascular repair of intact descending thoracic aortic aneurysms, incidence rates of paraplegia and stroke usually range between 1.3% to 6.6% and 2.5% to 5%, respectively.[25-29] Risks of neurologic complications may be increased after endovascular repair of rDTAA, since the emergency setting often does not allow optimal spinal cord protection, and the hypovolemic state of patients may contribute to insufficient cerebral and spinal cord perfusion. However, only 2.3% of patients suffered from permanent paraplegia, and the incidence of paraplegia and stroke after conventional surgical treatment of rDTAA may be as high as 12.5% and 25%, which further supports the endovascular approach of rDTAA.[20,21]

A reason for concern regarding the endovascular management of rDTAA is the occurrence of endograft-related complications during follow-up. Four patients died after 30 days of complications related to the endovascular procedure, including three patients that died of sepsis due to an infected endograft and/or development of aortoesophageal fistula. Aortoesophageal fistulas are associated with high mortality rates, and definitive esophageal repair is required after endovascular management of an aortoesophageal fistula, to prevent recurrent infections.[30,31] However, two of three patients that died of an infected endograft with sepsis, did not have an aortoesophageal fistula at the initial admission. Risk of infective complications may be increased after emergency TEVAR, since urgent situations may not allow optimal sterility and planning of

the procedure. Continued surveillance using computed tomography (CTA) and a high suspicion for these infective complications is therefore required after endovascular repair of acute thoracic aortic disease.

Another important observation in this evaluation was the high rate of endoleak, which was detected in 18.4% of patients within the first month. The majority of the endoleaks consisted of type 1 endoleak, which is generally associated with adverse outcomes.[32-35] Although some endoleaks resolved spontaneously, aortic re-intervention was required in 8 patients with endoleak and the estimated freedom from aneurysm-related death or intervention was only 54.9% at 4 years. Further improvement of endovascular techniques and endografts design is required to reduce the occurrence of endoleak and the need for re-intervention after TEVAR for rDTAA.[12,36]

Limitations

The multicenter design of this study allowed us to investigate the largest available series of patients treated with endovascular repair of rDTAA, a rare but highly lethal disease. However, several considerations are important when interpreting the results of the present study. First, the sample size of 87 patients may be relatively small for investigating risk factors of 30-day mortality after endovascular repair of rDTAA. Therefore we have not performed multivariable regression analysis, but we did adjust for age in the bivariate regression analysis of 30-day mortality. Though these analyses showed several significant predictors, unknown confounders may have affected the results. In addition, data were collected retrospectively and subject to incomplete or missing reporting of events. Furthermore, the seven centres that participated were tertiary referral sites that have significant expertise and experience in the endovascular management of patients with thoracic aortic pathologies, thus limiting the applicability to centres that lack such capability.

CONCLUSION

Endovascular repair of ruptured descending thoracic aortic aneurysm is associated with encouraging results, and a preferential endovascular approach for the management of this emergency seems appropriate. However, endovascular repair of ruptured descending thoracic aortic aneurysms was still associated with considerable rates of neurologic complications and procedure-related complications such as endoleak. Continued surveillance after successful endovascular management is required, and further improvements of current endovascular devices are needed to reduce the endograft-related complications and deaths during follow-up.

ACKNOWLEDGEMENTS

We would like to thank Michelle Streukens for the data collection.

REFERENCES

1. Johansson G, Markstrom U, Swedenborg J. Ruptured thoracic aortic aneurysms: a study of incidence and mortality rates. J Vasc Surg 1995; 21:985-988.
2. Clouse WD, Hallett JW, Jr., Schaff HV et al. Improved prognosis of thoracic aortic aneurysms: a population-based study. JAMA 1998; 280:1926-1929.
3. Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. Ann Thorac Surg 2002; 74:S1877-S1880.
4. Davies RR, Goldstein LJ, Coady MA et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. Ann Thorac Surg 2002; 73:17-27.
5. Semba CP, Kato N, Kee ST et al. Acute rupture of the descending thoracic aorta: repair with use of endovascular stent-grafts. J Vasc Interv Radiol 1997; 8:337-342.
6. Egorova N, Giacovelli J, Greco G et al. National outcomes for the treatment of ruptured abdominal aortic aneurysm: comparison of open versus endovascular repairs. J Vasc Surg 2008; 48:1092-100, 1100.
7. McPhee J, Eslami MH, Arous EJ et al. 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; 49:817-826.
8. Acosta S, Ogren M, Bengtsson H et al. Increasing incidence of ruptured abdominal aortic aneurysm: a population-based study. J Vasc Surg 2006; 44:237-243.
9. Patel HJ, Williams DM, Upchurch GR, Jr. et al. A 15-year comparative analysis of open and endovascular repair for the ruptured descending thoracic aorta. J Vasc Surg 2009.
10. Kaya A, Heijmen RH, Overtoom TT et al. Thoracic stent grafting for acute aortic pathology. Ann Thorac Surg 2006; 82:560-565.
11. Eggebrecht H, Schmermund A, Herold U et al. Endovascular stent-graft placement for acute and contained rupture of the descending thoracic aorta. Catheter Cardiovasc Interv 2005; 66:474-482.
12. Doss M, Wood JP, Balzer J et al. Emergency endovascular interventions for acute thoracic aortic rupture: four-year follow-up. J Thorac Cardiovasc Surg 2005; 129:645-651.
13. Scheinert D, Krankenberg H, Schmidt A et al. Endoluminal stent-graft placement for acute rupture of the descending thoracic aorta. Eur Heart J 2004; 25:694-700.
14. Morishita K, Kurimoto Y, Kawaharada N et al. Descending thoracic aortic rupture: role of endovascular stent-grafting. Ann Thorac Surg 2004; 78:1630-1634.
15. Amabile P, Rollet G, Vidal V et al. Emergency treatment of acute rupture of the descending thoracic aorta using endovascular stent-grafts. Ann Vasc Surg 2006; 20:723-730.
16. Walsh SR, Tang TY, Sadat U et al. Endovascular stenting versus open surgery for thoracic aortic disease: systematic review and meta-analysis of perioperative results. J Vasc Surg 2008; 47:1094-1098.

17. Fattori R, Tsai TT, Myrmel T et al. Complicated acute type B dissection: is surgery still the best option?: a report from the International Registry of Acute Aortic Dissection. JACC Cardiovasc Interv 2008; 1:395-402.
18. Demetriades D, Velmahos GC, Scalea TM et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008; 64:561-570.
19. Xenos ES, Abedi NN, Davenport DL et al. Meta-analysis of endovascular vs open repair for traumatic descending thoracic aortic rupture. J Vasc Surg 2008; 48:1343-1351.
20. Minatoya K, Ogino H, Matsuda H et al. Replacement of the descending aorta: recent outcomes of open surgery performed with partial cardiopulmonary bypass. J Thorac Cardiovasc Surg 2008; 136:431-435.
21. Barbato JE, Kim JY, Zenati M et al. Contemporary results of open repair of ruptured descending thoracic and thoracoabdominal aortic aneurysms. J Vasc Surg 2007; 45:667-676.
22. Estrera AL, Rubenstein FS, Miller CC, III et al. Descending thoracic aortic aneurysm: surgical approach and treatment using the adjuncts cerebrospinal fluid drainage and distal aortic perfusion. Ann Thorac Surg 2001; 72:481-486.
23. Girardi LN, Krieger KH, Altorki NK et al. Ruptured descending and thoracoabdominal aortic aneurysms. Ann Thorac Surg 2002; 74:1066-1070.
24. Schermerhorn ML, Giles KA, Hamdan AD et al. Population-based outcomes of open descending thoracic aortic aneurysm repair. J Vasc Surg 2008; 48:821-827.
25. Bavaria JE, Appoo JJ, Makaroun MS et al. Endovascular stent grafting versus open surgical repair of descending thoracic aortic aneurysms in low-risk patients: a multicenter comparative trial. J Thorac Cardiovasc Surg 2007; 133:369-377.
26. Cheung AT, Pochettino A, McGarvey ML et al. Strategies to manage paraplegia risk after endovascular stent repair of descending thoracic aortic aneurysms. Ann Thorac Surg 2005; 80:1280-1288.
27. Ellozy SH, Carroccio A, Minor M et al. Challenges of endovascular tube graft repair of thoracic aortic aneurysm: midterm follow-up and lessons learned. J Vasc Surg 2003; 38:676-683.
28. Makaroun MS, Dillavou ED, Kee ST et al. Endovascular treatment of thoracic aortic aneurysms: results of the phase II multicenter trial of the GORE TAG thoracic endoprosthesis. J Vasc Surg 2005; 41:1-9.
29. Matsumura JS, Cambria RP, Dake MD et al. International controlled clinical trial of thoracic endovascular aneurysm repair with the Zenith TX2 endovascular graft: 1-year results. J Vasc Surg 2008; 47:247-257.
30. Jonker FH, Schlosser FJ, Moll FL et al. Outcomes of thoracic endovascular aortic repair for aortobronchial and aortoesophageal fistulas. J Endovasc Ther 2009; 16:428-440.
31. Jonker FH, Heijmen R, Trimarchi S et al. Acute management of aortobronchial and aortoesophageal fistulas using thoracic endovascular aortic repair. J Vasc Surg 2009; 50:999-1004.

32. Morales JP, Greenberg RK, Lu Q et al. Endoleaks following endovascular repair of thoracic aortic aneurysm: etiology and outcomes. J Endovasc Ther 2008; 15:631-638.
33. Preventza O, Wheatley GH, III, Ramaiah VG et al. Management of endoleaks associated with endovascular treatment of descending thoracic aortic diseases. J Vasc Surg 2008; 48:69-73.
34. Parmer SS, Carpenter JP, Stavropoulos SW et al. Endoleaks after endovascular repair of thoracic aortic aneurysms. J Vasc Surg 2006; 44:447-452.
35. Leurs LJ, Harris PL, Buth J. Secondary interventions after elective endovascular repair of degenerative thoracic aortic aneurysms: results of the European collaborators registry (EUROSTAR). J Vasc Interv Radiol 2007; 18:491-495.
36. Svensson LG, Kouchoukos NT, Miller DC et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. Ann Thorac Surg 2008; 85:S1-41.

Chapter 6

Endovascular Repair of Ruptured Thoracic Aortic Aneurysms: Predictors of Procedure-Related Stroke

Annals of Vascular Surgery (in press)

Frederik H.W. Jonker,[1] MD,
Hence J.M. Verhagen,[2] MD, PhD,
Robin H. Heijmen,[3] MD, PhD,
Peter H. Lin,[4] MD,
Santi Trimarchi,[5] MD,
W. Anthony Lee,[6] MD,
Frans L. Moll,[7] MD, PhD,
Husam Athamneh,[4] MD,
Bart E. Muhs,[1] MD, PhD.

[1] Section of Vascular Surgery and Interventional Radiology, Yale University School of Medicine, New Haven, Connecticut, USA
[2] Section of Vascular Surgery, Erasmus University Medical Center, Rotterdam, the Netherlands
[3] Section of Cardiothoracic Surgery, St. Antonius Hospital, Nieuwegein, the Netherlands
[4] Section of Vascular Surgery, Baylor College of Medicine, Houston, Texas, USA
[5] Section of Vascular Surgery, Policlinico San Donato IRRCS, Milan, Italy,
[6] Section of Vascular Surgery, University of Florida, Gainesville, Florida, USA
[7] Section of Vascular Surgery, University Medical Center Utrecht, the Netherlands

ABSTRACT

Objective:
Thoracic endovascular aortic repair (TEVAR) is a valuable tool in the treatment of ruptured descending thoracic aneurysm (rDTAA). A major complication of this procedure is stroke. We investigated the incidence and risk factors for stroke following TEVAR for rDTAA.

Methods:
We retrospectively evaluated the outcomes of all patients that were treated with TEVAR for rDTAA at seven institutions between 2002 and 2009. Ninety-two patients were identified, with a mean age of 69.4 ±11 years and 67% were male. Multivariable logistic regression analysis was used to investigate risk factors for stroke, including demographics, co-morbidities, aneurysm and procedural details.

Results:
The 30-day mortality was 17.4% (n=16), and 7.6% (n=7) suffered from procedure-related stroke. Four out of seven patients with stroke (57.1%) expired within 30 days compared with 14.1% (n=12) of the patients without stroke (OR 8.11, p=0.004). Increasing age was associated with an increased risk of stroke (OR 1.38, 95%CI 1.08 - 1.76, p=0.010), while more recent procedures were associated with a reduced risk of stroke (OR 0.52, 95%CI 0.28 - 0.97, p=0.039) in multivariable regression analysis. The aneurysm-related survival at 1 year after TEVAR was 42.9% for patients that suffered from stroke, and 77.6% for those without stroke (p=0.006).

Conclusions:
Endovascular repair of rDTAA is associated with a considerable risk of stroke, and stroke is an important cause of 30-day mortality in this patient group. Particularly older patients are at risk for developing stroke after endovascular repair of rDTAA. The risk of stroke decreased significantly over time in this evaluation.

INTRODUCTION

Ruptured thoracic aortic aneurysm is a rare but life-threatening condition, requiring immediate intervention.[1,2] Open surgical repair of the aneurysm has been the traditional treatment, however, this approach is associated with high mortality and morbidity, especially neurologic complications.[1-5] Procedure-related stroke is a devastating complication, and its incidence after acute thoracic aortic surgery may be as high as 15% to 25%.[5-7] Thoracic endovascular aortic repair (TEVAR) is a minimally invasive technique that results in quick exclusion of the aortic lesion, which are desirable characteristics when managing acute thoracic aortic pathologies. TEVAR appears to improve the outcomes of elective and emergent thoracic aortic repair,[8-14] and the endovascular approach is emerging as the preferred method for the management of ruptured descending thoracic aortic aneurysm (rDTAA).[11] Though TEVAR does not require thoracic aortic clamping, emboli caused by manipulation of the endovascular device in the diseased aortic arch may result in stroke.[15] The incidence of stroke may be increased during endovascular repair of rDTAA, since urgent situations may not allow optimal endovascular management and hypovolemia may attribute to inadequate cerebral perfusion.

Due to the low incidence of rDTAA, the exact significance of procedure-related stroke during endovascular repair of rDTAA remains unclear. For this study, we investigated the incidence and risk factors of stroke among patients treated with TEVAR for rDTAA at seven institutions in the United States and Europe.

METHODS

Patient selection

We retrospectively evaluated the outcomes of all patients treated with TEVAR for ruptured aneurysms of the descending thoracic aorta at seven referral centers in the United States and Europe between January 2001 and July 2009. The following institutions participated in this project: Yale New Haven Hospital (New Haven, Connecticut), Baylor College of Medicine, (Houston, Texas), University of Florida (Gainesville, Florida), Policlinico San Donato IRRCS (San Donato Milanese, Italy), St. Antonius Hospital (Nieuwegein, the Netherlands), Erasmus University Medical Center (Rotterdam, the Netherlands) and the University Medical Center Utrecht (Utrecht, the Netherlands).

Endovascular repair has become the preferred approach for the treatment of ruptured descending thoracic aortic aneurysms at all participating institutions. For the present study, ruptured aneurysm was defined as any disruption of the aneurysmal aortic wall with extravascular collection of blood as documented by preoperative imaging. Ruptured dissected aneurysms were included only if the aneurysm diameter was larger than 50mm. Stroke wad defined as a new

central neurologic deficit within 30 days after TEVAR, confirmed as an ischemic or hemorrhagic lesion on computed tomography (CT) or magnetic resonance (MR) imaging of the brain. The study was approved by the institutional review committee at all participating institutions.

Surgical technique

All endovascular procedures were performed in the operating room under general anesthesia by vascular and/or cardiothoracic surgeons. The following endovascular devices were used: Gore TAG® (Gore Medical, Flagstaff, AZ), Medtronic Talent® (Santa Rosa, CA), or Medtronic Valiant® (Santa Rosa, CA). The endograft diameter was oversized compared with the native aortic landing zone diameter by 10% to 20% as recommended by the manufacturer. Proximal and distal landing zones of 20 mm of normal aorta were required to minimize risks on endoleak or endograft migration, coverage of the subclavian artery was required in some cases to ensure an adequate proximal landing zone. Prophylactic CSF drainage was only performed if the patient was stable enough, and had risk factors for spinal cord ischemia such as previous abdominal aortic intervention or extensive aortic coverage.

Statistical Analysis

Data are shown as frequencies and percentages, and mean ± standard deviation or as a median and interquartile range. Categorical variables were investigated using the chi-square test and Fisher's exact test when the expected cell count was less than 5; the age of the patients with stroke and without stroke was compared using the Student's t-test. Predictors of procedure-related stroke were explored using univariate logistic regression analysis. Variables with a *P* value <0.02 in univariate analysis were integrated in a multivariable regression model to investigate independent predictors of stroke. Kaplan-Meier life table analysis was used to demonstrate aneurysm-related survival of patients with and without stroke. Statistical analysis was performed using SPSS 15.0 software, a *P* value < 0.05 was considered statistically significant.

RESULTS

Patient and Procedural Characteristics

We identified 92 patients that underwent TEVAR for rDTAA between 2001 and 2009. The utilization of TEVAR for rDTAA increased over time, especially from 2004 (figure 1). The mean age was 69.4 ±12 years, 67% were male and the mean aneurysm diameter was 55 ±20 mm. Pre-existing hypertension was present in 52%, coronary artery disease in 41%, and 14% of patients had a history of unilateral or bilateral carotid disease (table 1). TEVAR was performed within 24 hours in 85%. Coverage of the left subclavian artery (LSA) was required in 36% for an adequate proximal landing zone. Cerebrospinal fluid (CSF) drainage was performed in 19% of patients during the endovascular procedures.

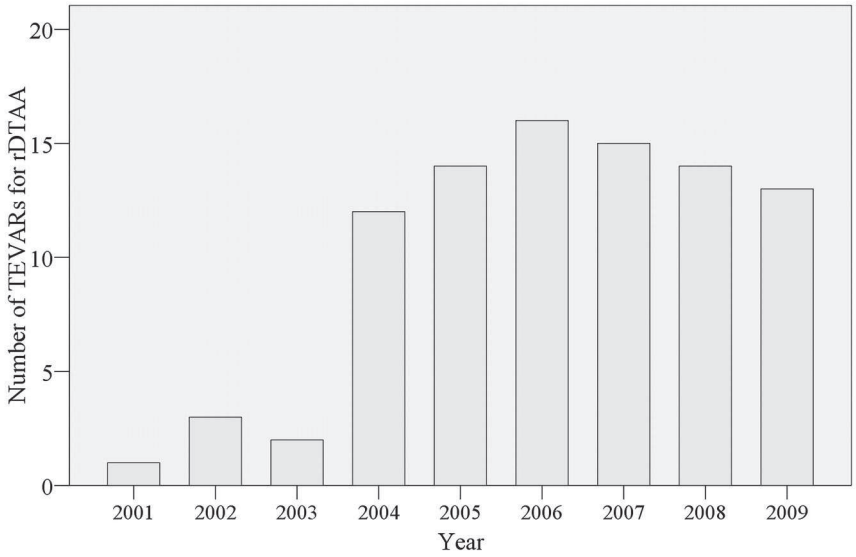

Figure 1. Distribution of TEVAR cases by year

Table 1. Demographics, Patient history, Presentation and Procedural Details

	N or mean	(% or ±SD)
Demographics		
Age (y)	69.4	(±11)
Male gender	62	(67.4)
Patient History		
Hypertension	48	(52.2)
Diabetes Mellitus	13	(15.3)
Hyperlipidemia	23	(25.0)
CAD	38	(41.3)
COPD	22	(23.9)
Carotid disease	13	(14.1)
Prior aortic intervention	21	(22.8)
Presentation		
Aneurysm diameter (mm)	55.5	(±20)
Hypovolemic shock	21	(22.8)
Contained rupture	32	(34.8)
Associated dissection	13	(14.1)
Procedural details		
Endograft diameter	37.4	(±3.7)
Total endograft length	150.6	(±114)
Number of stents	2.4	(±1.1)
Coverage LSA	33	(35.9)
CSF drainage during TEVAR	17	(18.5)

CAD coronary artery disease, *COPD* chronic obstructive pulmonary disease, *LSA* left subclavian artery, *CSF* cerebrospinal fluid drainage, *SD* standard deviation

Procedure-Related Stroke

The 30-day mortality was 17.4% (n=16), procedure-related stroke occurred in 7.6% (n=7) of all patients, and temporary or permanent paraplegia in 7.6% (n=7) as well (table 2). Patients suffering from stroke were older than those that did not develop stroke, 79.7 years vs. 68.6 years (p=0.012). Four out of seven patients that developed stroke were female, and the stroke rate was 13.3% in women compared with 4.8% in men (p=0.150). Among the 13 patients with a ruptured dissected aneurysm, 2 patients suffered from stroke (15.4%), compared with 5 out of 79 patients without associated dissection (6.3%, p=0.257). Procedure-related stroke occurred in 12.1% (n=4) of the endovascular procedures before 2006, compared with 5.1% (n=3) in the cases performed from 2006 (p=0.222).

Ischemic stroke was present in 6 out of 7 patients, and hemorrhagic stroke occurred once. Four out of seven patients with stroke (57.1%) expired within 30 days compared with 14.1% (n=12) of the patients without stroke (OR 8.11, p=0.004). Out of the three stroke patients that were alive at 30 days, two patients had permanent neurologic deficit, while the neurologic symptoms completely resolved in the last patient.

Table 2. Early Outcomes

	N	(%)
30-day mortality	16	(17.4)
Stroke	7	(7.6)
Paraplegia / paraparesis	7	(7.6)
Cardiac complications	5	(5.4)
Pulmonary complications	16	(17.4)
ARF	8	(8.7)
Bleeding	10	(10.9)
Endoleak	16	(17.4)

ARF acute renal failure, Paraplegia was permanent in two patients and transient in five patients.

Risk factors of Procedure-Related Stroke

The variables that significantly affected the risk of stroke in univariate logistic regression analysis (table 3) were increasing age (OR 1.28, p=0.007) and the year of TEVAR (OR 0.65, p=0.045). There was a trend towards higher risks of stroke among females (OR 3.03, p=0.166), or among patients with CAD (OR 3.26, p=0.174). After integrating these variables in a multivariable regression model (table 4), increasing age (OR 1.38, 95%CI 1.08 - 1.76, p=0.010) was still a risk factor for stroke, while more recent procedures were associated with a reduced risk of stroke (OR 0.52, 95%CI 0.28 - 0.97, p=0.039).

A history of carotid disease (p=0.917), hypovolemic shock (p=0.571) or coverage of the LSA (p=0.750), did not appear to affect the occurrence rate of procedure-related stroke after TEVAR for rDTAA (table 3).

Table 3. Univariate Analysis of Risk Factors for Stroke

Variable	OR	95%CI	p value
Age	1.28	1.07 - 1.53	0.007
Female gender	3.03	0.63 - 14.5	0.166
Hypertension	1.06	0.22 - 5.05	0.941
Diabetes mellitus	1.12	0.12 - 10.3	0.922
Hyperlipidemia	2.10	0.43 - 10.2	0.358
CAD	3.26	0.59 - 17.9	0.174
COPD	0.48	0.05 - 4.19	0.504
Carotid disease	0.89	0.10 - 8.06	0.917
Prior aortic intervention	1.70	0.30 - 9.57	0.547
Aneurysm diameter	0.98	0.94 - 1.03	0.428
Hypovolemic shock	0.53	0.06 - 4.65	0.571
Contained rupture	1.39	0.30 - 6.67	0.644
Associated dissection	2.65	0.46 - 15.4	0.276
Total endograft length	1.01	0.99 - 1.02	0.610
Number of stents	1.45	0.81 - 2.58	0.209
Endograft brand	1.28	0.71 - 2.30	0.417
Coverage LSA	0.76	0.14 - 4.15	0.750
CSF drainage during TEVAR	1.84	0.33 - 10.4	0.490
Year of TEVAR	0.65	0.43 - 0.99	0.045
Hospital volume	1.01	0.58 - 1.74	0.978

The variable *Hospital volume* had an ordinal scale, from high volume towards low volume. *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease, *LSA* left subclavian artery, *CSF* cerebrospinal fluid drainage, *OR* Odds ratio, *CI* confidence interval

Follow-up outcomes

The median follow-up of patients that were alive at 30 days was 13 months (interquartile range 33; range 1 to 72 months). Four patients expired after the first month due to complications related to the ruptured aneurysm and/or endovascular procedure, including an infected endograft with sepsis (n=3) and congestive heart failure (n=1). None of the three patients with stroke that were alive at 30 days, died of aneurysm-related causes during follow-up, and the aneurysm-related survival at 1 year after TEVAR was 42.9% for patients that suffered from stroke, and 77.6% for patients without stroke (p=0.006, figure 2).

Table 4. Multivariate Regression Analysis of Risk Factors for Stroke

Variable	OR	95%CI	p value
Age	1.38	1.08 - 1.76	0.010
Female gender	2.70	0.34 - 21.4	0.348
CAD	8.89	0.67 - 118.3	0.080
Year of TEVAR	0.52	0.28 - 0.97	0.039

CAD coronary artery disease, *OR* Odds ratio, *CI* confidence interval

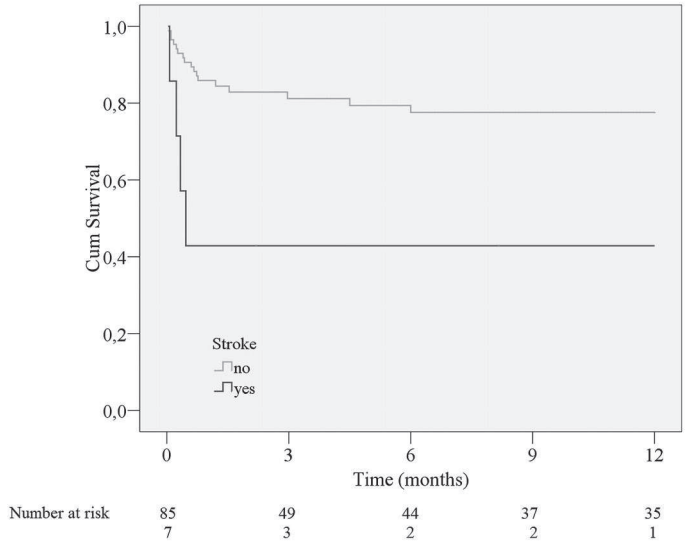

Figure 2. Aneurysm-related survival for patients with and without stroke
The aneurysm-related survival at 1 year after TEVAR was 42.9% for patients that suffered from stroke, and 77.6% for patients without stroke (p=0.006).

DISCUSSION

Procedure-related stroke is a devastating complication of endovascular repair of thoracic aortic pathologies. The most common mechanism of stroke during or after TEVAR is thought to be cerebral embolization of atherosclerotic plaque during manipulation of catheters, guide wire, or endografts in the diseased aortic arch. Other potential etiologies for procedure-related stroke include air emboli, or pre-existing cervical carotid disease and vertebral-basilar disease. All patients in our evaluation appeared to have embolic or ischemic stroke, except for one patient who developed a hemorrhagic stroke. Due to the low incidence of ruptured thoracic aortic aneurysms, the exact risk of stroke after endovascular repair of this emergency is relatively unclear. After evaluating the outcomes of TEVAR for rDTAA at seven referral centers, we found an overall occurrence rate of 7.6%, and this incidence may be even underestimated since there may have been asymptomatic and/or undiagnosed strokes.

The stroke rate after endovascular repair of rDTAA appears to be slightly increased compared with occurrence rates after elective TEVAR, which typically range between 2.5% and 5.8%.[8-10,15-18] There are several theoretic explanations for this inferior result after endovascular repair of rDTAA. Urgent situations may not allow optimal pre-operative planning and screening of classic risk factors for stroke, such as atherosclerotic disease of the arch and supra-aortic arteries.

During emergency endovascular procedures, physicians may be less cautious as well compared with elective interventions, because the main goal is to exclude the ruptured aneurysm as soon as possible to save the patient. Hypovolemia due to blood loss may contribute to insufficient cerebral perfusion as well.

We identified several factors that appeared to affect the risk of stroke. Advanced age was associated with an increased occurrence of stroke, and patients suffering from stroke were on average 11 years older than those that did not develop stroke. Elderly patients may have more extensive atherosclerotic disease in the arch and/or carotids, resulting in higher risk of cerebral embolization during manipulation with endovascular instruments. The EUROSTAR investigators also found that patients with stroke after TEVAR for various aortic pathologies were significantly older than the remaining patients, and age was a borderline significant predictor of stroke in their multivariable regression analysis.[17] Independent predictors of procedure-related stroke in the EUROSTAR registry were duration of the procedure ≥ 2 hours, and female gender.[17] We observed a trend towards a higher stroke rate among female patients as well, which was 13.3% compared with 4.8% in men. The higher incidence in women may be attributed to smaller peripheral arteries in women, and more advanced atherosclerosis.[17] Generally, male gender is a risk factor for the development of atherosclerosis, however, outcomes of cardiovascular disease are typically inferior in women.[19-23]

Though we observed a high overall stroke rate, this adverse effect appeared to be lower in the more recent endovascular procedures. In the early Stanford experience, the occurrence rate of stroke after elective TEVAR was 7%,[24,25] probably secondary to the use of older, large stiff sheath and dilator delivery systems, which required excessive manipulation.[26] Results using newer devices are notable for a marked reduction in risks of stroke and death compared with the first-generation systems.[26] The increasing utilization of TEVAR for the management of rDTAA (figure 1) and subsequent improved operator experience may have contributed to the lower stroke rates over time as well.

Coverage of the left subclavian artery did not did not appear to affect the occurrence rate of stroke after endovascular management of rDTAA, in contrast to the findings of the Talent Thoracic Retrospective Registry.[18] We did not observe an increased stroke risk in case of a history of carotid disease as well, while this was a risk factor after TEVAR in the evaluation of Gutsche and colleagues.[16] However, some of the rDTAA patients that developed stroke after TEVAR may have had undiagnosed carotid disease. Furthermore, the incidence of stroke was not increased among patients with hypovolemic shock at admission, while hypovolemia may theoretically attribute to inadequate cerebral perfusion. Perhaps the patients that were admitted in hypovolemic shock may have been more adequately resuscitated at the moment of the endovascular procedure. In addition, a large number of the patients with hypovolemic shock expired shortly after TEVAR, and some of these patients may have suffered from undiagnosed stroke as well.

Though the endovascular repair of rDTAA was associated with considerable rates of post-operative neurologic complications, the incidence of stroke after emergent open thoracic aortic surgery may be considerably higher, up to 25% in some reports.[5-7] Specialized centers have reported 30-day mortality rates between 25% to 30% after open repair of rDTAA,[3-5,27] but Schermerhorn and colleagues recently found an in-hospital mortality of 45% in their population-based analysis,[2] which may be a more realistic outcome. The 30-day mortality in our evaluation was 17.4%, substantially lower than the reported results of open repair. Therefore, endovascular repair is emerging as the preferred treatment for patients with rDTAA, even though large comparative studies are missing in the literature.

Although this evaluation currently represents the largest available series of patients with rDTAA treated with endovascular repair, several limitation need to be acknowledged. The sample size of 92 patients may be relatively small for multivariable regression analysis, and a larger cohort may have revealed additional risk factors for stroke. In addition, data were collected retrospectively and subject to incomplete or missing reporting of events. Unfortunately, our database did not contain anatomical and radiologic data regarding the arch anatomy, or exact aneurysm location and extent. The risk of stroke may have been increased after endovascular repair of more proximal aneurysms, as suggested by Gutsche et al.[16] Data regarding the length of procedure, which may have affected the risk of stroke,[17] were unavailable as well. Furthermore, the seven centers that participated were tertiary referral sites that have significant expertise and experience in the endovascular management of patients with thoracic aortic pathologies, and the stroke rate after endovascular repair of rDTAA may therefore differ in centers that lack such capability.

CONCLUSION

Endovascular repair of rDTAA is associated with a considerable risk of stroke, and stroke is an important cause of 30-day mortality in this patient group. Particularly older patients are at risk for developing stroke after endovascular repair of rDTAA. The risks of stroke decreased significantly over time in this evaluation. The reported mortality rates and stroke rates after open repair of rDTAA are considerably higher than our results, and a preferential endovascular approach for the management of this emergency appears appropriate.

ACKNOWLEDGEMENTS

We would like to thank Michelle Streukens for the data collection.

REFERENCES

1. Johansson G, Markstrom U, Swedenborg J. Ruptured thoracic aortic aneurysms: a study of incidence and mortality rates. J Vasc Surg 1995; 21:985-988.
2. Schermerhorn ML, Giles KA, Hamdan AD et al. Population-based outcomes of open descending thoracic aortic aneurysm repair. J Vasc Surg 2008; 48:821-827.
3. Barbato JE, Kim JY, Zenati M et al. Contemporary results of open repair of ruptured descending thoracic and thoracoabdominal aortic aneurysms. J Vasc Surg 2007; 45:667-676.
4. Girardi LN, Krieger KH, Altorki NK et al. Ruptured descending and thoracoabdominal aortic aneurysms. Ann Thorac Surg 2002; 74:1066-1070.
5. Minatoya K, Ogino H, Matsuda H et al. Replacement of the descending aorta: recent outcomes of open surgery performed with partial cardiopulmonary bypass. J Thorac Cardiovasc Surg 2008; 136:431-435.
6. Goldstein LJ, Davies RR, Rizzo JA et al. Stroke in surgery of the thoracic aorta: incidence, impact, etiology, and prevention. J Thorac Cardiovasc Surg 2001; 122:935-945.
7. Kawachi Y, Nakashima A, Toshima Y et al. Stroke in thoracic aortic surgery: outcome and risk factors. Asian Cardiovasc Thorac Ann 2003; 11:52-57.
8. Bavaria JE, Appoo JJ, Makaroun MS et al. Endovascular stent grafting versus open surgical repair of descending thoracic aortic aneurysms in low-risk patients: a multicenter comparative trial. J Thorac Cardiovasc Surg 2007; 133:369-377.
9. Makaroun MS, Dillavou ED, Kee ST et al. Endovascular treatment of thoracic aortic aneurysms: results of the phase II multicenter trial of the GORE TAG thoracic endoprosthesis. J Vasc Surg 2005; 41:1-9.
10. Matsumura JS, Cambria RP, Dake MD et al. International controlled clinical trial of thoracic endovascular aneurysm repair with the Zenith TX2 endovascular graft: 1-year results. J Vasc Surg 2008; 47:247-257.
11. Patel HJ, Williams DM, Upchurch GR, Jr. et al. A 15-year comparative analysis of open and endovascular repair for the ruptured descending thoracic aorta. J Vasc Surg 2009.
12. Fattori R, Tsai TT, Myrmel T et al. Complicated acute type B dissection: is surgery still the best option?: a report from the International Registry of Acute Aortic Dissection. JACC Cardiovasc Interv 2008; 1:395-402.
13. Demetriades D, Velmahos GC, Scalea TM et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008; 64:561-570.
14. Jonker FH, Giacovelli JK, Muhs BE et al. Trends and outcomes of endovascular and open treatment for traumatic thoracic aortic injury. J Vasc Surg 2009.
15. Sullivan TM, Sundt TM, III. Complications of thoracic aortic endografts: spinal cord ischemia and stroke. J Vasc Surg 2006; 43 Suppl A:85A-88A.

16. Gutsche JT, Cheung AT, McGarvey ML et al. Risk factors for perioperative stroke after thoracic endovascular aortic repair. Ann Thorac Surg 2007; 84:1195-1200.
17. Buth J, Harris PL, Hobo R et al. Neurologic complications associated with endovascular repair of thoracic aortic pathology: Incidence and risk factors. a study from the European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair (EUROSTAR) registry. J Vasc Surg 2007; 46:1103-1110.
18. Fattori R, Nienaber CA, Rousseau H et al. Results of endovascular repair of the thoracic aorta with the Talent Thoracic stent graft: the Talent Thoracic Retrospective Registry. J Thorac Cardiovasc Surg 2006; 132:332-339.
19. Malenka DJ, O'Connor GT, Quinton H et al. Differences in outcomes between women and men associated with percutaneous transluminal coronary angioplasty. A regional prospective study of 13,061 procedures. Northern New England Cardiovascular Disease Study Group. Circulation 1996; 94:II99-104.
20. Mikhail GW. Coronary heart disease in women. BMJ 2005; 331:467-468.
21. Bairey MN, Bonow RO, Sopko G et al. Women's Ischemic Syndrome Evaluation: current status and future research directions: report of the National Heart, Lung and Blood Institute workshop: October 2-4, 2002: executive summary. Circulation 2004; 109:805-807.
22. Norman PE, Powell JT. Abdominal aortic aneurysm: the prognosis in women is worse than in men. Circulation 2007; 115:2865-2869.
23. Katz DJ, Stanley JC, Zelenock GB. Gender differences in abdominal aortic aneurysm prevalence, treatment, and outcome. J Vasc Surg 1997; 25:561-568.
24. Dake MD, Miller DC, Mitchell RS et al. The "first generation" of endovascular stent-grafts for patients with aneurysms of the descending thoracic aorta. J Thorac Cardiovasc Surg 1998; 116:689-703.
25. Demers P, Miller DC, Mitchell RS et al. Midterm results of endovascular repair of descending thoracic aortic aneurysms with first-generation stent grafts. J Thorac Cardiovasc Surg 2004; 127:664-673.
26. Svensson LG, Kouchoukos NT, Miller DC et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. Ann Thorac Surg 2008; 85:S1-41.
27. Estrera AL, Rubenstein FS, Miller CC, III et al. Descending thoracic aortic aneurysm: surgical approach and treatment using the adjuncts cerebrospinal fluid drainage and distal aortic perfusion. Ann Thorac Surg 2001; 72:481-486.

Chapter 7

Importance of Refractory Pain and Hypertension in Acute Type B Aortic Dissection: Insights from the International Registry of Acute Aortic Dissection

Circulation 2010;122:1283-9

Santi Trimarchi, MD
Kim A. Eagle, MD
Christoph A. Nienaber, MD
Reed E. Pyeritz, MD
Frederik H.W. Jonker, MD
Toru Suzuki, MD
Patrick T. O'Gara, MD
Stuart J. Hutchison, MD
Vincenzo Rampoldi, MD
Viviana Grassi, MD
Eduardo Bossone, MD
Bart E. Muhs, MD, PhD
Arturo Evangelista, MD
Thomas T. Tsai, MD
Jim B. Froehlich, MD
Jeanna V. Cooper, MS
Dan Montgomery, MS
Gabriel Meinhardt, MD
Truls Myrmel, MD
Gilbert R. Upchurch, MD
Thoralf M. Sundt, MD
Eric M. Isselbacher, MD

On behalf of the International Registry of Acute Aortic Dissection (IRAD) investigators

ABSTRACT

Background

In patients with acute type B aortic dissection (ABAD), presence of recurrent or refractory pain and/or refractory hypertension on medical therapy is sometimes used as an indication for invasive treatment. The International Registry of Acute Aortic Dissection (IRAD) was used to investigate the impact of refractory pain and/or refractory hypertension on the outcomes of ABAD.

Methods and results

365 patients affected by uncomplicated ABAD, enrolled in the IRAD from 1996-2004, were categorized according to risk profile in two groups. Patients with recurrent and/or refractory pain or refractory hypertension (group I, n=69), and patients not presenting clinical complications at presentation (group II, n=296) were compared. "High risk" patients with classic complications were excluded from this analysis.

The overall in-hospital mortality was 6.5 %, and was increased in group I compared to group II, 17.4 % vs. 4.0%, p=0.0003. The in-hospital mortality after medical management was significantly increased in group I compared with group II (35.6% vs. 1.5%, p=0.0003). Mortality rates after surgical (20% vs. 28%, p=0.74), or endovascular management (3.7% vs. 9.1%, p=0.50), did not differ significantly between group I and group II, respectively. A multivariable logistic regression model confirmed that recurrent and/or refractory pain or refractory hypertension was a predictor of in-hospital mortality (OR 3.31, 95% CI 1.04-10.45, p=0.041).

Conclusions

Recurrent pain and/or refractory hypertension appeared as clinical signs associated with increased in-hospital mortality, particularly when managed medically. These observations suggest that aortic intervention, such as via an endovascular approach, may be indicated in this intermediate risk group.

INTRODUCTION

Acute type B aortic dissection (ABAD) is associated with various clinical complications which affect in-hospital outcomes. Currently, surgical or endovascular approaches are often advocated for complications of ABAD, including shock, major organ malperfusion, limb ischemia, periaortic bleeding, and rapidly expanding false lumen.[1-8] Such complications are associated with in-hospital mortality rates between 20% and 30% after surgery[1,7,9-11] and 10% to 20% after endovascular management.[7,12-18] However, some clinical conditions, such as recurrent/refractory pain or refractory hypertension, may be signs of extending dissection or impending rupture but have not resulted in any hemodynamic alteration or organ ischemia. The optimal approach for these patients, either medical, endovascular stenting, or surgery, is still debated.[19] Thoracic endovascular aortic repair (TEVAR) is frequently adopted, but the actual evidence to support this practice for ABAD patients with recurrent pain and/or hypertension is limited.

In order to better define the importance of refractory pain and/or refractory hypertension in ABAD, and the optimal approach for these patients, we performed a comprehensive analysis of patients presenting ABAD with only pain or refractory hypertension, but no other complications, enrolled in the International Registry of Acute Aortic Dissection (IRAD). In-hospital outcomes of medical, endovascular or surgical management were compared between ABAD patients presenting with and without pain and/or refractory hypertension.

METHODS

Patient selection

Patients presenting ABAD enrolled in the IRAD between January 1996 and December 2004 were investigated. IRAD is an ongoing multi-national multi-center registry that includes enrolled patients with acute aortic dissection at 24 large referral centers (IRAD centers; online supplemental material). The rationale and methods used in IRAD have previously been described.[20] Acute type B aortic dissection was defined as any acute aortic dissection involving the descending aorta without any entry tear in the ascending aorta and/or in the aortic arch, presenting within 14 days of symptom onset. Intramural hematoma (IMH) was defined as presence of a regionally thickened aortic wall in the absence of evidence of a double lumen and/or intimal flap regardless of imaging modality.[11] For this analysis, both classic dissection and acute IMH were included in the study cohort.

Patients were categorized according to risk profile in two groups. Patients with recurrent/refractory pain or refractory hypertension but no other clinical complications, were defined as intermediate risk patients (group I). Patients without any clinical complications at presentation were categorized as low risk or uncomplicated (group II). “High risk” patients with one or

more of the following complications: shock, periaortic hematoma, spinal cord ischemia, pre-op mesenteric ischemia/infarction, acute renal failure, limb ischemia were excluded from this analysis (n=191). In-hospital outcomes according to presence and type of complication (low risk vs. intermediate risk) and method of treatment were analyzed.

Data collection

Data were collected using a standardized data form of 290 clinical variables including patient demographics, history, clinical presentation, physical findings, imaging studies, management, in-hospital mortality and adverse events. Completed data forms were forwarded to the coordinating center at the University of Michigan. Data forms were reviewed for internal validity and completeness of data, and were then entered into an Access database. For this analysis, 365 ABAD patients were analyzed, of which 69 met our criteria as intermediate risk.

Statistical Analysis

Data are shown as frequencies and percentages, and mean ± standard deviation or as a median if appropriate. Categorical variables were compared between ABAD patients presenting with and without refractory pain and/or refractory hypertension using the chi-square test and Fisher's exact test when appropriate. A multiple logistic regression model was fitted adjusting for the known predictors of in-hospital mortality for ABAD.[8] A *P* value < 0.05 was considered significant. SAS 8.1 software (Cary, NC) was used for all analyses. The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

RESULTS

Patient population

Between 1996 to 2004, 69 patients (18.9%) with ABAD presenting with refractory pain and/or hypertension but no other significant clinical complication were identified (group I). During the same period, 296 patients (81.1%) with uncomplicated ABAD were observed (group II). The mean age was 63.5 ±14 years, and 32.6% (n=119) were females. There were no significant differences between groups in demographics or patient's history (table 1), except for pre-existing hypertension (89.7% vs. 72.7%, p=0.003) and Marfan syndrome (7.3% vs. 2.1%, p= 0.03) which were more frequently present in group I.

In group I (intermediate risk group), patients presented more frequently with an abrupt onset of pain, migrating pain, and radiating pain (table 1). Patients in group I underwent a higher number of diagnostic imaging tests (2.34 vs. 1.99; p=0.02), including aortography and magnetic resonance imaging (MRI). Complete thrombosis of the false lumen was more frequently detected in group II (GI 1.8% vs. GII 15.9%; p=0.005), while patients in Group I tended to have more frequently partial false lumen thrombosis. A trend for involvement of arch vessels and abdominal

vessels was observed in patients with pain and/or hypertension (table 1). In addition, in group I, a larger mean aortic diameter (4.75 cm vs. 4.32 cm; p=0.08), as well as a higher incidence of descending thoracic aorta > 6 cm (16.4% vs. 6.7%; p=0.02) were detected (table 2). Patients in group II were more likely to have a normal chest X-ray (CXR), while widened mediastinum was more often seen in group I.

Table 1. Demographics, history of patients and clinical presentation

Variable	Overall N (%)	Group I Intermediate N (%)	Group II Uncomplicated N (%)	p value
No Patients	365 (100)	69(18.9)	296 (81.1)	
Demographics				
Age-mean (years, ± SD),	63.5 (±13.8)	63.5 (±15.0)	64.3 (±13.1)	0.71
Age ≥ 70 years	145 (39.7)	28 (40.6)	117 (39.5)	0.87
Gender female	119 (32.6)	19 (27.5)	100 (33.8)	0.31
Transferred from other hospital	238 (67.6)	50 (74.6)	188 (66.0)	0.17
Etiology and patients' history				
Marfan syndrome	11 (2.1)	5 (7.3)	6 (2.1)	0.03
Hypertension	274 (75.9)	61 (89.7)	213 (72.7)	0.003
Atherosclerosis	118 (33.4)	22 (33.3)	96 (33.4)	0.98
Bicuspid aortic valve	4 (1.7)	0 (0.0)	4 (2.1)	0.08
Iatrogenic dissection	12 (3.5)	0 (0.0)	12 (4.3)	0.41
Prior aortic dissection	29 (8.1)	7 (10.3)	22 (7.6)	0.47
Prior aortic aneurysm	72 (20.1)	13 (19.1)	59 (20.3)	0.82
Diabetes	17 (4.8)	3 (4.4)	14 (4.9)	0.86
Prior cardiac surgery	69 (19.8)	13 (19.7)	56 (19.9)	0.96
Clinical presentations and signs				
Abrupt onset of pain	294 (83.3)	59 (92.2)	235 (81.3)	0.03
Migrating pain	68 (20.0)	22 (35.5)	46 (16.6)	0.0008
Radiating pain	127 (36.8)	32 (51.6)	95 (33.6)	0.007
Time interval until diagnosis (h)	11.4	19.7	10.5	0.23

Time interval until diagnosis refers to the median time interval from onset of symptoms until the diagnosis in hours. *SD* standard deviation.

In-Hospital Management and Outcomes

In total, 75.9% of patients were managed medically, 13.7% underwent surgery, and 6.5% of patients were treated with endovascular methods. Patients in group I were more frequently managed with surgery (36.2% vs. 8.4%, p<0.001) or endovascular methods (39.1% vs. 3.7%, p<0.001) than patients in group II (table 3). Medical management was more often offered to patients in group II compared to group I (87.8% vs. 24.6%, p<0.001). In group I, the median time interval between onset of symptoms and any invasive treatment was longer compared to the low risk group (240 vs. 100 hours, p=0.005), as well as for the interval between diagnosis and any invasive treatment (236 vs. 72 hours, p=0.004, table 3).

Table 2. Diagnostic imaging studies and findings

Variable	Overall N (%)	Group I Intermediate N (%)	Group II Uncomplicated N (%)	p value
Diagnostic imaging studies				
No. of studies per patient	2.06	2.34	1.99	0.02
Any imaging study				
TEE	229 (70.9)	43 (68.2)	186 (71.5)	0.60
CT	345 (96.1)	65 (95.6)	280 (96.2)	0.80
MRI	85 (27.9)	26 (43.3)	59 (24.1)	0.002
Aortogram	91 (29.7)	26 (41.9)	65 (26.6)	0.01
Diagnostic imaging findings				
Arch vessel involvement	17 (5.6)	6 (10.0)	11 (4.5)	0.09
Abdominal vessel involvement	107 (29.6)	25 (36.2)	82 (28.1)	0.18
Intramural hematoma	40 (11.4)	6 (8.8)	34 (12.0)	0.45
False lumen thrombosis	150 (53.2)	28 (50.0)	122 (54.0)	0.59
Complete thrombosis	37 (13.1)	1 (1.8)	36 (15.9)	0.005
Partial thrombosis	113 (40.1)	27 (48.1)	86 (38.1)	0.16
Mean aortic arch diameter (cm, ±SD)	3.68 (±0.9)	3.62 (±1.0)	3.72 (±0.9)	0.56
Mean desc. aorta diameter (cm, ±SD)	4.41 (±1.3)	4.75 (±1.7)	4.32 (±1.2)	0.08
Descending aorta >6 cm	23 (8.8)	9 (16.4)	14 (6.7)	0.02
Intimal tear desc aorta	111 (39.2)	27 (43.5)	84 (38.0)	0.42
Site origin left subcl	179 (53.4)	30 (44.8)	149 (51.7)	0.30
Site origin desc aorta	87 (26.0)	16 (23.9)	71 (24.6)	0.89
Site origin abdominal	19 (5.7)	3 (4.5)	16 (5.6)	0.72
Chest X Ray				
Normal	76 (22.3)	8 (12.5)	68 (24.5)	0.03
Pleural effusion	46 (14.0)	12 (19.0)	34 (12.8)	0.20
Widened mediastinum	163 (48.5)	44 (67.7)	119 (43.9)	0.006

TEE trans-esophageal echocardiography, *TTE* trans-thoracic echocardiography, *CT* computerized tomography, *MRI* magnetic resonance imaging, *SD* standard deviation.

The overall in-hospital mortality was 6.5 %, but was significantly increased in group I compared to group II, 17.4 % vs. 4.0%, p=0.0003 (table 3, figure 1). Among group I, the in-hospital mortality rate was 35.6% after medical management, 20% after surgical management and 3.7% after endovascular management (p=0.019). The in-hospital mortality after medical management was significantly higher in group I compared with group II (35.6% vs. 1.5%, p=0.0003, figure 2). Among the six patients who expired after medical management in group 1, aortic rupture was the cause of death in four cases. Mortality rates after surgical (20% vs. 28%, p=0.74), or endovascular management (3.7% vs. 9.1%, p=0.50), did not differ significantly between the two groups (table 3).

Table 3. In-hospital management and mortality

Variable	Overall N (%)	Group I Intermediate N (%)	Group II Uncomplicated N (%)	p value
Definitive Management				
Medical Rx	277 (75.9)	17 (24.6)	260 (87.8)	<0.001
Surgery	50 (13.7)	25 (36.2)	25 (8.4)	<0.001
Endovascular	38 (10.4)	27 (39.1)	11 (3.7)	<0.001
Time interval until invasive treatment				
From onset of symptoms (h)	211.5	240.0	99.9	0.005
From diagnosis (h)	168.0	236.2	72.0	0.004
Mortality	24 (6.5)	12 (17.4)	12 (4.0)	0.0003
Medical	10 (3.7)	6 (35.6)	4 (1.5)	0.0003
Surgical	12 (24.0)	5 (20.0)	7 (28.0)	0.74
Endovascular	2 (5.2)	1 (3.7)	1 (9.1)	0.50

Time interval until invasive treatment refers to the median time interval in hours between onset of symptoms or diagnosis until invasive treatment.

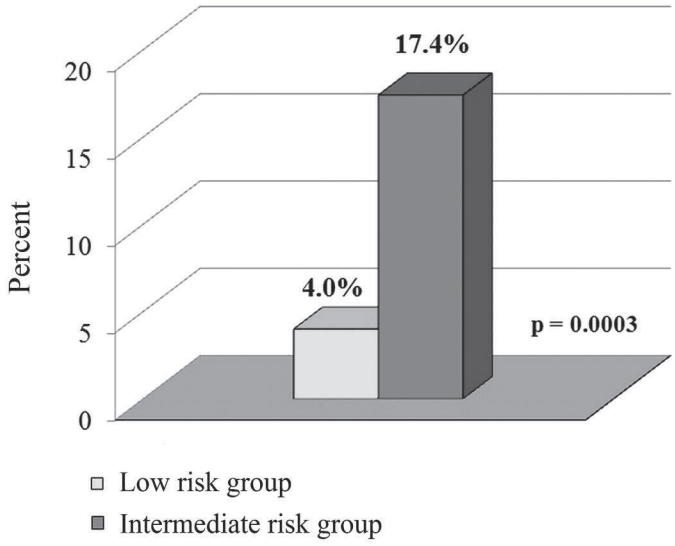

Figure 1. Overall in-hospital mortality rates in the low-risk and intermediate risk groups
The intermediate risk group consists of ABAD patients with recurrent/refractory pain or refractory hypertension but no other clinical complications

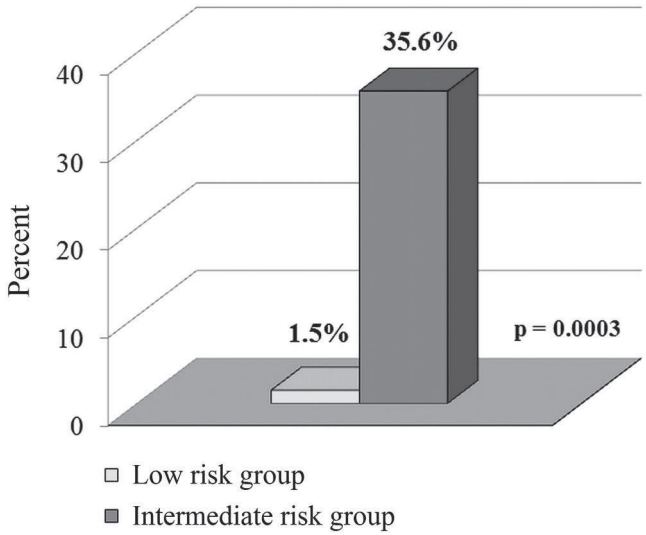

Figure 2. In-hospital mortality rates after medical management
The intermediate risk group consists of ABAD patients with recurrent/refractory pain or refractory hypertension but no other clinical complications

We used the multiple logistic regression model to examine the relationship of refractory pain and/or refractory hypertension, and mortality after adjusting for the effects of known predictors of in-hospital mortality in the overall cohort of 365 ABAD patients. The model suggested that recurrent and/or refractory pain or refractory hypertension (intermediate risk group) was an independent predictor of in-hospital mortality (OR 3.31, 1.04-10.45, p=0.041). In this cohort, age ≥ 70 years (OR 5.11, 95% CI 1.70-15.39, p=0.004) and absence of chest pain at admission (OR 3.49, 95% CI 1.01-12.09, p=0.048) were predictors of death as well (table 4). A plot of the observed vs. the predicted mortality confirmed that these three factors discriminate well in death prediction and that there was little departure from a good fit with the data; Hosmer and Lemeshow Test: Chi-square (5df) = 5.05, p=0.655 (figure 3).

DISCUSSION

Patients presenting with ABAD have traditionally been categorized as uncomplicated, for which medical treatment has been accepted as an adequate mode of therapy with mortality rates between 1% and 6%, and complicated with features such as rupture, spinal cord ischemia, acute renal failure, mesenteric or limb ischemia, all of which typically require surgical or endovascular intervention and even with optimal treatment are associated with mortality rates of 20% to 30% after sugery[1,7,9-11] and 10% to 20% after endovascular management.[7,12-18]

Table 4. Multivariable logistic regression model for predictors of in-hospital mortality[8]

Variable	Odds ratio	95% CI	p value
Age ≥70 years	5.11	1.70 – 15.39	0.004
Female gender	1.04	0.37 – 2.95	0.932
Hypotension	3.27	0.33 – 31.77	0.306
Absence of chest pain	3.49	1.01 – 12.09	0.048
Intermediate risk group	3.31	1.04 – 10.45	0.041
Abdominal vessel involvement	0.78	024 – 2.54	0.684

Hosmer and Lemeshow Test: Chi-square (5df) = 5.05, p=0.655.

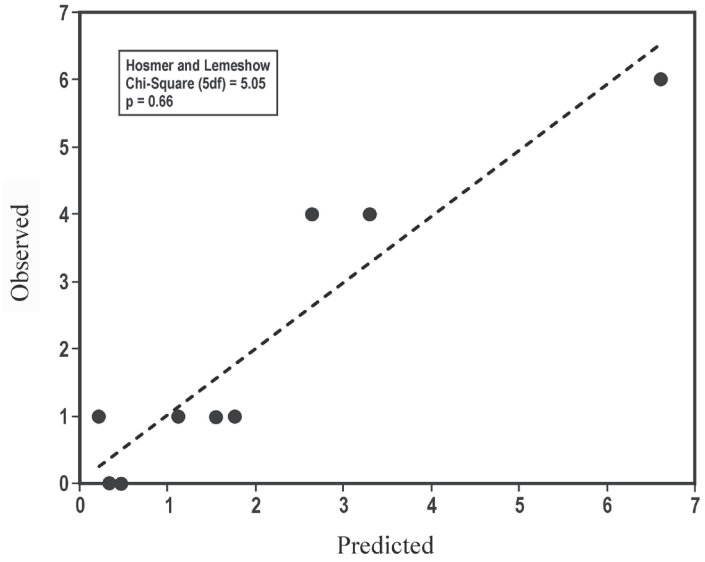

Figure 3. Plot of observed versus predicted deaths using the logistic regression model
Hosmer-Lemeshow Chi-sq (5 df): 5.05, p = 0.655

For those patients in the low risk group, we observed that medical management is associated with excellent in-hospital results (mortality rate 1.5%), appearing as the safest in-hospital therapy in the absence of classic complications, refractory hypertension and/or pain. The significance of ABAD with refractory hypertension and/or refractory or recurrent pain, in the absence of other complications, is currently less well defined. Although some authors have suggested that these signs/symptoms may not result in poorer outcomes and may be treated with medical management and careful monitoring alone,[19] others have argued that refractory pain or hypertension are foreshadowing impending rupture and adverse outcomes, and therefore should be considered for more aggressive intervention.[5,11,21]

The IRAD database offers a unique opportunity to analyze the outcomes in large numbers of this subset of ABAD patients. In the present analysis, we observed an in-hospital mortality of 17% among patients with refractory hypertension and/or pain, which was significantly higher compared to patients without these symptoms (4%, p=0.0003), but consistently lower than the in-hospital mortality of "classic" complicated ABAD.[1,7-11] After adjusting for known risk factors,[8] refractory pain and/or hypertension was an independent predictor for in-hospital mortality. ABAD patients presenting with refractory hypertension and/or pain symptoms, in the absence of other complications, therefore are at intermediate risk for an adverse in-hospital outcome.

We observed several differences in patient's history, presentation and diagnostic imaging findings that may have contributed to the poor outcomes of the patients with refractory hypertension and/or pain which have also been reported by others.[8,9,22] These include a history of Marfan syndrome (p=0.03), a larger descending thoracic aortic diameter (p=0.08), partial thrombosis of the false lumen (p=0.16), abdominal vessel involvement (p=0.18), and a widened mediastinum on CXR (p=0.006). Interestingly, patients in the intermediate risk group also presented more frequently with an abrupt onset of pain (p=0.03), and with migrating pain (p=0.0008), which on univariate analyses were associated with decreased mortality,[8] perhaps because such clinical signs led to an earlier diagnosis and a more prompt therapy.

In the present study, more invasive treatment of ABAD with refractory hypertension and/or pain was associated with improved outcomes, while approximately one third of the patients managed medically expired. In these patients, the most common cause of death was aortic rupture. In the intermediate risk group, the observed differences in mortality between endovascular and medical management could reflect the effectiveness of endovascular methods, although a selection bias may be present and patients treated with medical management may have had more unfavorable characteristics such as a higher age or no chest pain at admission (table 4). Recent reports have suggested that endovascular management of complicated ABAD provides a better survival than medical treatment or open surgery.[7,12-18] Endovascular approaches are increasingly becoming the first line treatment for complicated ABAD cases, and are increasingly used for uncomplicated and chronic dissections as well.[7,14] This report would suggest that this trend may also be beneficial for patients in the intermediate risk group presenting with refractory hypertension and/or pain.

Limitations

Several considerations are important when interpreting the results of the present study. IRAD is an observational study in which participating centers have different approaches to diagnosis and management, creating potential biases in patient selection, which may be minimized in one single center series. Patients were not randomized to a predetermined management strategy, and the results rather reflect a retrospective observation. In the absence of large randomized trials, and given the rapid evolution of endovascular aortic stent graft therapy for acute aortic syndromes,

there remains some uncertainty as to the optimal strategy to manage this subset of patients. For this evaluation, we included patients that presented with ABAD between 1996 and 2004. Endovascular methods and treatment strategies have advanced in recent years, and current results of endovascular management may be improved compared with our results. This may further support an endovascular approach for ABAD patients with recurrent pain and/or hypertension.

CONCLUSION

In ABAD completely uncomplicated patients, medical therapy was associated with excellent in-hospital outcomes. Contrariwise, the presence of recurrent pain and/or refractory hypertension was associated with increased in-hospital mortality, particularly when managed medically. These observations suggest that aortic intervention, such as via an endovascular approach, may be indicated in this intermediate risk group.

REFERENCES

1. Elefteriades JA, Lovoulos CJ, Coady MA et al. Management of descending aortic dissection. Ann Thorac Surg 1999; 67:2002-2005.
2. Glower DD, Fann JI, Speier RH et al. Comparison of medical and surgical therapy for uncomplicated descending aortic dissection. Circulation 1990; 82:IV39-IV46.
3. Masuda Y, Yamada Z, Morooka N et al. Prognosis of patients with medically treated aortic dissections. Circulation 1991; 84:III7-13.
4. Lansman SL, McCullough JN, Nguyen KH et al. Subtypes of acute aortic dissection. Ann Thorac Surg 1999; 67:1975-1978.
5. Lansman SL, Hagl C, Fink D et al. Acute type B aortic dissection: surgical therapy. Ann Thorac Surg 2002; 74:S1833-S1835.
6. Umana JP, Lai DT, Mitchell RS et al. Is medical therapy still the optimal treatment strategy for patients with acute type B aortic dissections? J Thorac Cardiovasc Surg 2002; 124:896-910.
7. Fattori R, Tsai TT, Myrmel T et al. Complicated acute type B dissection: is surgery still the best option?: a report from the International Registry of Acute Aortic Dissection. JACC Cardiovasc Interv 2008; 1:395-402.
8. Suzuki T, Mehta RH, Ince H et al. Clinical profiles and outcomes of acute type B aortic dissection in the current era: lessons from the International Registry of Aortic Dissection (IRAD). Circulation 2003; 108 Suppl 1:II312-II317.
9. Trimarchi S, Nienaber CA, Tsai TT. In Search For Optimal Treatment Of Complicated Acute Type B Aortic Dissections: Insights from The International Registry Of Aortic Dissection (IRAD). Circulation 114[18], 432-433. 2006. Ref Type: Abstract
10. Estrera AL, Miller CC, Goodrick J et al. Update on outcomes of acute type B aortic dissection. Ann Thorac Surg 2007; 83:S842-S845.
11. Trimarchi S, Nienaber CA, Rampoldi V et al. Role and results of surgery in acute type B aortic dissection: insights from the International Registry of Acute Aortic Dissection (IRAD). Circulation 2006; 114:I357-I364.
12. Khoynezhad A, Donayre CE, Omari BO et al. Midterm results of endovascular treatment of complicated acute type B aortic dissection. J Thorac Cardiovasc Surg 2009; 138:625-631.
13. Patel HJ, Williams DM, Meerkov M et al. Long-term results of percutaneous management of malperfusion in acute type B aortic dissection: implications for thoracic aortic endovascular repair. J Thorac Cardiovasc Surg 2009; 138:300-308.
14. Kische S, Ehrlich MP, Nienaber CA et al. Endovascular treatment of acute and chronic aortic dissection: midterm results from the Talent Thoracic Retrospective Registry. J Thorac Cardiovasc Surg 2009; 138:115-124.

15. Feezor RJ, Martin TD, Hess PJ, Jr. et al. Early outcomes after endovascular management of acute, complicated type B aortic dissection. J Vasc Surg 2009; 49:561-566.
16. Verhoye JP, Miller DC, Sze D et al. Complicated acute type B aortic dissection: midterm results of emergency endovascular stent-grafting. J Thorac Cardiovasc Surg 2008; 136:424-430.
17. Schoder M, Czerny M, Cejna M et al. Endovascular repair of acute type B aortic dissection: long-term follow-up of true and false lumen diameter changes. Ann Thorac Surg 2007; 83:1059-1066.
18. Duebener LF, Lorenzen P, Richardt G et al. Emergency endovascular stent-grafting for life-threatening acute type B aortic dissections. Ann Thorac Surg 2004; 78:1261-1266.
19. Januzzi JL, Movsowitz HD, Choi J et al. Significance of recurrent pain in acute type B aortic dissection. Am J Cardiol 2001; 87:930-933.
20. Hagan PG, Nienaber CA, Isselbacher EM et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. JAMA 2000; 283:897-903.
21. Hata M, Sezai A, Niino T et al. Prognosis for patients with type B acute aortic dissection: risk analysis of early death and requirement for elective surgery. Circ J 2007; 71:1279-1282.
22. Tsai TT, Evangelista A, Nienaber CA et al. Partial thrombosis of the false lumen in patients with acute type B aortic dissection. N Engl J Med 2007; 357:349-359.

Chapter 8

Age-related Decision Making in Complicated Acute Type B Aortic Dissection: Insights from the International Registry of Acute Aortic Dissection

Submitted

Frederik H.W. Jonker, MD
Santi Trimarchi, MD
Bart E. Muhs, MD, PhD
Vincenzo Rampoldi, MD
Jeanna V Cooper, MS
Daniel G Montgomery, MS
James B Froehlich, MD
Mark D Peterson, MD
Kristian Bartnes, MD
Venu Gourineni, MD
Vijay S. Ramanath, MD
Alan C Braverman, MD
Christoph A Nienaber, MD
Eric M Isselbacher, MD
Kim A. Eagle, MD

On behalf of the IRAD Investigators

ABSTRACT

Introduction

Complicated acute type B aortic dissection (ABAD) generally requires urgent intervention. The purpose of this study was to investigate the impact of increasing age on the management and outcomes of complicated ABAD.

Methods and results

We analyzed the outcomes of 464 patients with complicated ABAD (44.0%) among the 1054 type B patients enrolled in the International Registry of Acute Aortic Dissection (IRAD) between 1996 and 2010. All patients with complicated ABAD were categorized according to age by decade and management type (medical, surgical or endovascular treatment), and outcomes were subsequently investigated in the different age groups. The mean age for patients treated with surgery was 60.5 years, compared with 62.1 years in the endovascular group, and 66.8 years in the medical management group ($p<0.001$). The utilization of surgery progressively decreased with patient age, while the rate of medical management significantly increased with age ($p<0.001$). The in-hospital mortality rates for complicated patients ≤ 70 years vs. > 70 years were 7.7% vs. 35.7% for endovascular treatment ($p=0.012$), 13.5% vs. 32.8% for surgical treatment ($p=0.001$), and 14.6% vs. 26.6% for medical treatment ($p=0.036$). Predictors of mortality in multivariate regression analysis were: age > 70 years (OR 6.6, 95% CI 1.9-22.8), hypotension/shock (OR 10.0, 95% CI 2.8-36.3), lack of chest/back pain (OR 4.4, 95% CI 1.1-18.1), and pre-operative limb ischemia (OR 5.4, 95% CI 1.4-20.9).

Conclusions

In complicated ABAD, age has a dramatic impact on the treatment modality chosen, given that less invasive management is more frequently offered to older patients. Age affects the outcome of complicated ABAD as well, since the mortality rates significantly increased with age, irrespective of the management type.

INTRODUCTION

Acute type B aortic dissection (ABAD) is a cardiovascular emergency with considerable mortality and morbidity.[1-4] In the absence of complications, ABAD is typically managed with medical treatment only, which is associated with low in-hospital mortality rates, between 0% and 8%.[3-5] ABAD associated with complications, such as aortic rupture, malperfusion of the lower limbs, acute renal failure, or visceral ischemia, is associated with much poorer outcomes, and mortality rates usually ranging between 10% to 30%.[3-8] Invasive treatment, either surgery or endovascular, is indicated in patients with complicated ABAD.[3-8]

Elderly patients typically have more pre-existing co-morbidities, and advanced age is a well known risk factor for mortality after thoracic aortic intervention, including surgery for acute type A and B aortic dissections.[5,9,10] The age of a patient should always be taken into account, when selecting treatment modality, and for elderly patients with complicated ABAD, medical management may serve as an alternative to invasive treatment. Due to the relatively low incidence of ABAD, the exact impact of age on the management and outcomes of complicated ABAD remains unclear. The International Registry of Acute Aortic Dissection (IRAD) represents the largest cohort of patients with acute aortic dissection, and therefore offers a unique opportunity to study this cardiovascular emergency. In this study, we used the IRAD Registry to investigate the outcomes of complicated ABAD after medical, surgical and endovascular treatment in different age groups, in order to gain insight regarding effectiveness of current treatment strategies for patients with complicated ABAD.

METHODS

Patient selection

IRAD is an ongoing multi-center registry that includes patients with acute aortic dissection at 24 large referral centers, which rationale and methods have previously been described.[11] In this study, ABAD was defined as any acute aortic dissection involving the descending aorta without any entry tear in the ascending aorta, presenting within 14 days of symptom onset.

For the present study, we included all patients with complicated ABAD enrolled in the IRAD between January 1996 and February 2010. Complicated ABAD was defined as one or more of the following complications: shock, periaortic hematoma, spinal cord ischemia, pre-operative mesenteric ischemia/infarction, acute renal failure, limb ischemia, recurrent hypertension, recurrent and/or refractory pain. Patients with uncomplicated aortic dissection or traumatic aortic dissection were excluded, as well as those patients for which data regarding age was unavailable.

All patients with complicated ABAD were categorized according to patient age by decade, and management type (medical, surgical or endovascular treatment). The management and outcomes were subsequently investigated in the different age groups. The study was approved by the institutional review committee at all participating IRAD institutions.

Data collection and Analysis

Data were collected using a standardized data form of 290 clinical variables including patient demographics, history, clinical presentation, physical findings, imaging studies, management, and in-hospital mortality. Completed data forms were forwarded to the coordinating center at the University of Michigan. Data forms were reviewed for internal validity and completeness of data, and were then entered into an Access database.

Summary statistics were presented as frequencies and percentages, mean ± standard deviation, or as a median and interquartile range. Missing data were not defaulted to negative and denominators reflect only actual reported cases. Nominal variables were compared between patients ≤70 years and >70 years, and between medical, surgical and endovascular groups, using the Chi-square test or two-sided Fisher exact test. The mean age of patients treated with medical, surgical and endovascular treatment, was compared using the ANOVA test.

Multivariate logistic regression analysis was performed to investigate independent predictors of in-hospital mortality among patients with complicated ABAD. Variables suggestive of an unadjusted association to in-hospital mortality ($p<0.20$) were integrated in a multivariable regression model to calculate independent effects on mortality. SPSS 17.0 was utilized for the analyses, and a P value < 0.05 was considered significant.

RESULTS

Demographics, Medical History and Presentation

Complicated ABAD was present in 44.0% (n=464) of the 1054 type B patients in IRAD. The mean age of complicated ABAD patients was 63.3 ±14.2 years (figure 1), 35.8% (n=166) of patients were older than 70 years and 64.2% (n=298) were ≤ 70 years. The mean age of patients undergoing surgery was 60.5 years compared with 62.1 years for patients treated with endovascular management and 66.8 years for patients with medical management ($p<0.001$). The younger cohort consisted of more male patients (72.1% vs. 60.2%, p=0.001).

The elderly patients with complicated ABAD had more frequently a history of hypertension (88.9% vs. 80.2%, p=0.011), diabetes mellitus (15.3% vs. 5.8%, p=0.001), atherosclerosis (60.4% vs. 21.7%, $p<0.001$), and prior aortic aneurysm (29.6% vs. 14.4%, $p<0.001$). Marfan's Syndrome was diagnosed in 7.2% of patients with complicated ABAD ≤ 70 years (table 1), compared with none of the patients ≥ 70 years ($p<0.001$).

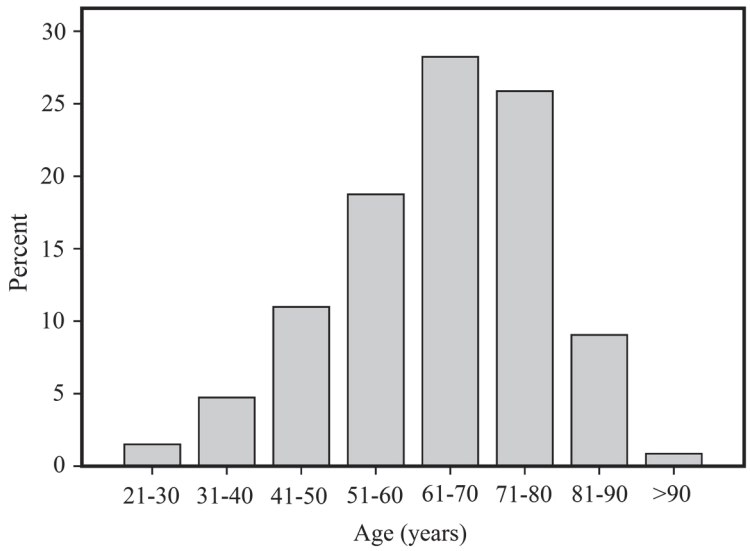

Figure 1. Age of patients with complicated ABAD in IRAD
The mean age of complicated ABAD patients was 63.3 ±14.2 years (figure 1), 35.8% (n=166) of patients were older than 70 years and 64.2% (n=298) were ≤ 70 years.

Table 1. Demographics and Patient History

Variable	Age ≤70 (n=298) N (%)	Age >70 (n=166) N (%)	p value
Demographics			
Male gender	215 (72.1)	100 (60.2)	0.001
Etiology and History			
Hypertension	231 (80.2)	144 (88.9)	0.011
Diabetes	16 (5.8)	24 (15.3)	0.001
Atherosclerosis	60 (21.7)	96 (60.4)	<0.001
Marfan's syndrome	21 (7.2)	0 (0)	<0.001
Prior aortic aneurysm	41 (14.4)	47 (29.6)	<0.001
Prior aortic dissection	43 (15.7)	25 (15.8)	0.972
Prior cardiac surgery	52 (18.7)	38 (26.0)	0.080
Cardiac catheterization	22 (9.6)	18 (14.8)	0.148
Iatrogenic dissection	5 (1.8)	4 (2.5)	0.644

Presentation and Signs

An abrupt onset of pain was present in 92.3% of the elderly patients, compared with 86.9% of the younger cohort (p=0.085). Patients ≤ 70 years presented more frequently with visceral ischemia (15.7% vs. 6.3%, p=0.002), limb ischemia (25.7% vs. 5.7%, p<0.001) and pulse deficits (26.9% vs. 13.4%, p<0.001). Recurrent hypertension was more common in the younger

patients as well (11.3% vs. 2.8%, p=0.001). There were no differences in acute renal failure, spinal cord ischemia, shock, or refractory and/or recurrent pain between ABAD patients ≤ and > 70 years (table 2).

Pleural effusion was observed on chest X-rays in 28.9% of the patients above 70 years, compared with 18.7% of the patients ≤ 70 years (p=0.025). Periaortic hematoma, suggesting aortic rupture, was more frequently shown by additional imaging in the elderly cohort (41.0% vs. 22.5%, p<0.001), while abdominal vessel involvement was less common (23.5% vs. 48.1%, p<0.001). The mean diameter of the descending thoracic aorta was larger in patients above 70 years (5.1 cm vs. 4.4 cm, p=0.016).

Table 2. Presentation, Signs and Imaging Results

Variable	Age ≤70 (n=298) N (%)	Age >70 (n=166) N (%)	p value
Clinical Presentation and Signs			
Abrupt onset of pain	238 (86.9)	144 (92.3)	0.085
Lack of chest/back pain	33 (11.8)	18 (11.0)	0.803
Shock at presentation	7 (2.5)	5 (3.1)	0.771
Spinal cord ischemia	5 (1.8)	2 (1.3)	0.612
Limb ischemia	71 (25.7)	9 (5.7)	<0.001
Visceral ischemia	44 (15.7)	10 (6.3)	0.002
Acute renal failure	83 (30.3)	45 (28.3)	0.512
Any pulse deficit	68 (26.9)	18 (13.4)	0.001
Recurrent pain	55 (23.1)	27 (18.8)	0.223
Refractory pain	25 (11.0)	13 (9.0)	0.548
Recurrent hypertension	28 (11.3)	4 (2.8)	0.001
Diagnostic imaging results			
Chest X-ray			
Pleural effusion	45 (18.7)	43 (28.9)	0.025
Mediastinal widening	116 (49.2)	83 (56.5)	0.164
Additional imaging findings			
Diameter descending aorta (cm)	4.4 (±1.2)	5.1 (±2.8)	0.016
Peri-aortic hematoma	64 (22.5)	68 (41.0)	<0.001
Abdominal vessel involvement	136 (48.1)	38 (23.5)	<0.001

Management

Invasive treatment was offered to 57.5% of the complicated cohort, and consisted of surgery in 46.1% and endovascular treatment in 11.4% of all patients. The remaining 42.5% of the complicated cohort received medical treatment alone (table 3). The number of patients undergoing surgery decreased with increasing age, while the proportion of patients that received medical treatment alone increased with increasing age (table 4, figure 2). Surgery was offered to 52.3% of all patients ≤ 70 years, and to only 34.9% of patients older than 70 years (p<0.001). Among the patients ≤ 70 years, medical treatment was offered to 34.6% of patients, while 56.6%

of the elderly cohort was treated medically (p<0.001). The number of patients undergoing endovascular management slightly decreased with increasing age of the ABAD patients (figure 2): an endovascular approach was offered to 13.1% of the patients ≤ 70 years, compared with 8.4% of the elderly patients (p=0.131).

Table 3. In-hospital management and Mortality of ABAD

	Overall N (%)	Age ≤70 (n=298) N (%)	Age >70 (n=166) N (%)	p value
Definitive management				
Medical	197 (42.5)	103 (34.6)	94 (56.6)	<0.001
Surgery	214 (46.1)	156 (52.3)	58 (34.9)	<0.001
Endovascular	53 (11.4)	39 (13.1)	14 (8.4)	0.131
In-hospital mortality	88 (19.0)	39 (13.1)	49 (29.5)	<0.001
Medical	40 (20.3)	15 (14.6)	25 (26.6)	0.036
Surgery	40 (18.7)	21 (13.5)	19 (32.8)	0.001
Endovascular	8 (15.1)	3 (7.7)	5 (35.7)	0.012

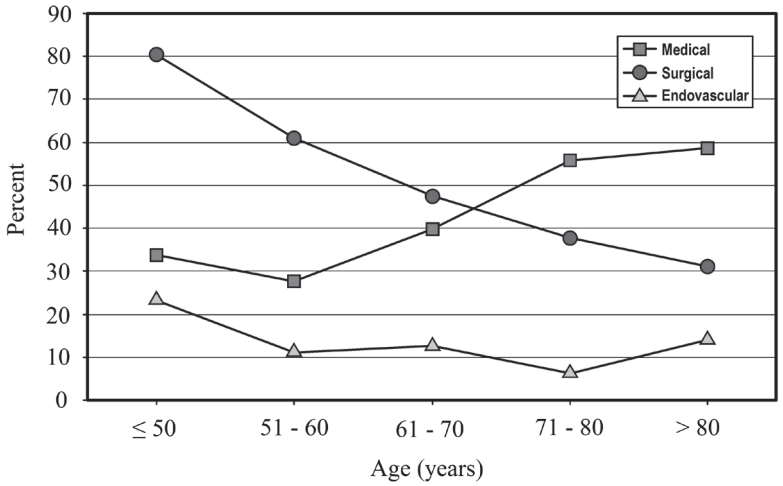

Figure 2. Management of complicated ABAD in different age groups
The mean age for patients treated with surgery was 60.5 years, compared with 62.1 years in the endovascular group, and 66.8 years in the medical management group (p<0.001).

Table 4. Management and Outcomes in different age groups

Age group (years)	≤ 50 (n=80)	> 50 - 60 (n=87)	> 60 - 70 (n=131)	> 70 - 80 (n=120)	> 80 (n=46)
Management					
Medical	27 (33.8)	24 (27.6)	52 (39.7)	67 (55.8)	27 (58.7)
Surgery	41 (51.3)	53 (60.9)	62 (47.3)	45 (37.5)	13 (28.3)
Endovascular	12 (15.0)	10 (11.5)	17 (13.0)	8 (6.7)	6 (13.0)
Mortality	10 (12.5)	11 (12.6)	18 (13.7)	27 (22.5)	22 (47.8)
Medical	4 (14.8)	3 (12.5)	8 (15.4)	12 (17.9)	13 (48.1)
Surgery	5 (12.2)	8 (15.1)	8 (12.9)	13 (28.8)	6 (46.2)
Endovascular	1 (8.3)	0 (0)	2 (11.8)	2 (25.0)	3 (50.0)

Outcomes

The overall in-hospital mortality of complicated ABAD in IRAD was 19.0%. The mortality rate after endovascular treatment of complicated ABAD was 15.1%, and the mortality rates after surgical and medical treatment were 18.7% and 20.3% (table 3), respectively (p=0.675). The overall in-hospital mortality rate was 13.1% among patients ≤ 70 years, compared with 29.5% among patients older than 70 years (p<0.001). For patients ≤ 70 years, there was a trend towards lower mortality after endovascular treatment (table 4, figure 3), while for patients older than 70, the mortality was slightly lower after medical management (table 3, 4). The in-hospital mortality significantly increased with increasing age after medical, surgical and endovascular treatment (table 3). In particular after the seventh decade, the mortality considerably increased, approaching 50% after medical, surgical and endovascular treatment for ABAD patients > 80 years (table 4, figure 3).

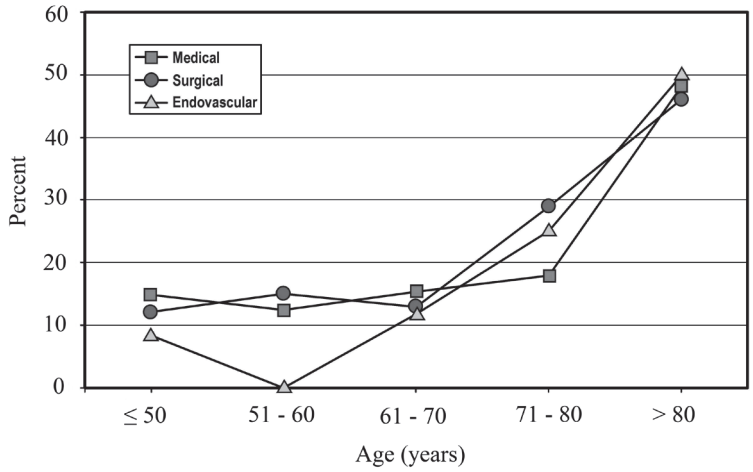

Figure 3. In-hospital mortality of complicated ABAD in different age groups
The overall in-hospital mortality rate after endovascular treatment was 15.1%, and the mortality rates after surgical and medical treatment were 18.7% and 20.3%, respectively (p=0.675)

Predictors of in-hospital mortality

Multivariate logistic regression analysis showed that age > 70 years was a strong predictor of mortality among patients with complicated ABAD (OR 6.6, 95% CI 1.9-22.8) (table 5). Other independent predictors of mortality were hypotension/shock at admission (OR 10.0, 95% CI 2.8-36.3), lack of chest/back pain at presentation (OR 4.4, 95% CI 1.1-18.1), and pre-operative limb ischemia (OR 5.4, 95% CI 1.4-20.9).

Table 5. Independent predictors of in-hospital mortality

Variable	Odds ratio	95%CI	p value
Age >70	6.62	1.92 – 22.82	0.003
Female gender	0.84	0.22 – 3.24	0.798
Branch vessel involvement	1.09	0.32 – 3.77	0.888
Lack of chest/back pain	4.37	1.06 – 18.07	0.042
Refractory pain/hypertension	1.79	0.54 – 5.98	0.343
Hypotension / shock	10.01	2.75 – 36.31	<0.001
Visceral ischemia pre-op	2.41	0.54 – 10.81	0.252
Limb ischemia pre-op	5.40	1.40 – 20.88	0.014
Acute renal failure pre-op	0.47	0.10 – 2.12	0.324

DISCUSSION

Our analysis shows that increasing patient age has a dramatic impact on the management and outcomes of complicated ABAD. The rate of surgical repair progressively decreased with age, while the rate of medical management significantly increased with age. There was a non significant trend towards lower mortality after endovascular treatment, but patients older than 70 years had a significantly increased mortality rate, irrespective of the management type.

Although patients with uncomplicated ABAD have a favorable prognosis, outcomes of complicated ABAD are generally poor, and improvements in current treatment strategies for these patients are needed. The proportion of patients with complicated ABAD was 44% in IRAD, similar to previous studies in which 30% to 47% of all ABAD patients had complications at presentation.[3,5,6,8,12,13] Invasive treatment, either surgical or endovascular management, is generally indicated in patients with complicated ABAD,[3-6,8] in order to treat these complications and prevent further decline of the patient's condition.

Acute aortic syndromes are typically associated with significant morbidity and mortality, and the risks of surgery are dramatically increased in elderly patients. Advanced age is an important predictor of death after intervention for ruptured abdominal aortic aneurysms,[14-17] ruptured thoracic aortic aneurysms,[8,18,19] traumatic thoracic aortic injuries,[20] and acute type A and B aortic dissections.[5,9,10,19,21] This IRAD report confirms that age > 70 years is a strong and independent

risk factor for mortality (OR 6.6) among patients with complicated ABAD. Mortality rates increased significantly with increasing age, irrespective of surgical, endovascular or medical treatment. Elderly patients more frequently have extensive pre-existing co-morbidities, such as hypertension, atherosclerosis, and diabetes (table 1), which results in an increased risk of an adverse outcome. In the current study, elderly patients had higher rates of aortic aneurysms, a measure of advanced atherosclerosis, associated with increased cardiovascular mortality.[22,23] Moreover, periaortic hematoma, suggestive of aortic rupture, was more common in elderly patients as well, and this sign is a strong predictor of mortality.[24] Another factor that may have contributed to adverse outcomes in the elderly patients, is the fact that this cohort consisted of relatively more female patients, and women with cardiovascular disease have been shown to have inferior outcomes compared with men.[25-29]

Because of the increased risks of thoracic aortic surgery in elderly patients, physicians appeared to offer invasive treatment less frequently to complicated ABAD patients. It is also plausible that some patients with advanced age refused invasive therapy. The rate of surgical repair progressively decreased with age, while the rate of medical management significantly increased with age. Endovascular treatment, which was not yet available in the early years of the IRAD, was offered in similar rates in the different age categories. On average, the descending aortic diameters were larger in patients > 70 years, which may correlate with a higher frequency of unsuitable landing zones for an endograft in these elderly patients. Generally, the utilization of endovascular management of thoracic aortic emergencies is becoming more widespread due to its less invasiveness compared with surgery, which is especially desirable in elderly patients with extensive co-morbidities.

In IRAD, the overall in-hospital mortality of complicated ABAD was 19%, which is comparable to the results of other evaluations which typically report mortality rates between 10% and 30% for complicated ABAD.[3,6,8,12,13] We observed a non significant trend towards lower mortality after endovascular treatment (15.1%), compared with surgery (18.7%) or medical treatment (20.3%). Recent reports have suggested that endovascular management of complicated ABAD is associated with lower mortality rates, often between 10% and 20%, compared with a more invasive surgical approach.[6,30-35] However, randomized controlled trials comparing the outcomes of surgery and endovascular treatment of complicated ABAD have not been performed to date.

In the present evaluation of all complicated ABAD patients in IRAD, the largest complicated ABAD cohort ever studied, we did not observe a statistically significant improvement in survival after endovascular management. This may be the result of the relatively small number of endovascular repairs in IRAD, non-superiority of this approach and/or the fact that IRAD is a non-randomized observational database, in which potential benefit of treatment is hidden by selection bias. Patients with complicated ABAD that were offered endovascular treatment were significantly older than those treated with surgery, and endovascular management may have

served as a last option in some patients in critical condition, which were thought to be unfit for open surgery.

Although invasive treatment is typically recommended for complicated ABAD, 42% of all patients with complicated ABAD in IRAD received medical treatment only. Why this high percentage of patients did not undergo an intervention remains unclear. Surprisingly, the outcomes of medical management of complicated ABAD were acceptable, and the mortality rate after medical treatment was slightly lower compared with mortality rates after surgical or endovascular treatment among patients older than 70 years. Therefore, medical treatment may be a reasonable alternative in the management of complicated ABAD among patients above 70 years. However, due to the observational characteristics of IRAD, the patients treated with medical management may have had less catastrophic complications, such as recurrent pain and/or hypertension, than those who presented with aortic rupture or ischemic complications which were managed with invasive treatment.

The findings of the present study should be viewed in the light of its limitations. Given the observational nature of the registry, patients were not randomized to a predetermined management strategy, and therefore a selection bias could have been present. In the absence of large randomized trials, there remains uncertainty as to the optimal strategy to manage patients with complicated ABAD. Furthermore, use of in-hospital mortality as an endpoint is necessary and important to patients; however it is not sufficient for a full evaluation of the outcomes of patients with complicated ABAD. In particular, long-term survival and quality of life are critical to deciding which the "best" strategy is for an individual patient presenting with aortic dissection.

CONCLUSIONS

This study demonstrates that increasing age has a dramatic impact on the management and outcomes of complicated ABAD. The rate of surgical repair progressively decreased with age, while the rate of medical management significantly increased with age, which may serve as an alternative to invasive treatment in elderly patients. Among patients younger than 70 years, a non-significant trend towards lower mortality after endovascular repair was observed, but the mortality rate of complicated ABAD significantly increased with age, irrespective of the management type.

REFERENCES

1. Anagnostopoulos CE, Prabhakar MJ, Kittle CF. Aortic dissections and dissecting aneurysms. Am J Cardiol 1972; 30:263-273.
2. Wheat MW, Jr. Acute dissecting aneurysms of the aorta: diagnosis and treatment--1979. Am Heart J 1980; 99:373-387.
3. Elefteriades JA, Lovoulos CJ, Coady MA et al. Management of descending aortic dissection. Ann Thorac Surg 1999; 67:2002-2005.
4. Golledge J, Eagle KA. Acute aortic dissection. Lancet 2008; 372:55-66.
5. Trimarchi S, Nienaber CA, Rampoldi V et al. Role and results of surgery in acute type B aortic dissection: insights from the International Registry of Acute Aortic Dissection (IRAD). Circulation 2006; 114:I357-I364.
6. Fattori R, Tsai TT, Myrmel T et al. Complicated acute type B dissection: is surgery still the best option?: a report from the International Registry of Acute Aortic Dissection. JACC Cardiovasc Interv 2008; 1:395-402.
7. Fann JI, Sarris GE, Mitchell RS et al. Treatment of patients with aortic dissection presenting with peripheral vascular complications. Ann Surg 1990; 212:705-713.
8. Eggebrecht H, Lonn L, Herold U et al. Endovascular stent-graft placement for complications of acute type B aortic dissection. Curr Opin Cardiol 2005; 20:477-483.
9. Trimarchi S, Eagle KA, Nienaber CA et al. Role of age in acute type A aortic dissection outcome: Report from the International Registry of Acute Aortic Dissection (IRAD). J Thorac Cardiovasc Surg 2010.
10. Ehrlich MP, Ergin MA, McCullough JN et al. Results of immediate surgical treatment of all acute type A dissections. Circulation 2000; 102:III248-III252.
11. Hagan PG, Nienaber CA, Isselbacher EM et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. JAMA 2000; 283:897-903.
12. Umana JP, Lai DT, Mitchell RS et al. Is medical therapy still the optimal treatment strategy for patients with acute type B aortic dissections? J Thorac Cardiovasc Surg 2002; 124:896-910.
13. Estrera AL, Miller CC, Goodrick J et al. Update on outcomes of acute type B aortic dissection. Ann Thorac Surg 2007; 83:S842-S845.
14. McPhee J, Eslami MH, Arous EJ et al. 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; 49:817-826.
15. Egorova N, Giacovelli J, Greco G et al. National outcomes for the treatment of ruptured abdominal aortic aneurysm: comparison of open versus endovascular repairs. J Vasc Surg 2008; 48:1092-100, 1100.
16. Giles KA, Hamdan AD, Pomposelli FB et al. Population-based outcomes following endovascular and open repair of ruptured abdominal aortic aneurysms. J Endovasc Ther 2009; 16:554-564.

17. Wanhainen A, Bylund N, Bjorck M. Outcome after abdominal aortic aneurysm repair in Sweden 1994-2005. Br J Surg 2008; 95:564-570.
18. Schermerhorn ML, Giles KA, Hamdan AD et al. Population-based outcomes of open descending thoracic aortic aneurysm repair. J Vasc Surg 2008; 48:821-827.
19. Olsson C, Thelin S, Stahle E et al. Thoracic aortic aneurysm and dissection: increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002. Circulation 2006; 114:2611-2618.
20. Arthurs ZM, Starnes BW, Sohn VY et al. Functional and survival outcomes in traumatic blunt thoracic aortic injuries: An analysis of the National Trauma Databank. J Vasc Surg 2009; 49:988-994.
21. Mehta RH, O'Gara PT, Bossone E et al. Acute type A aortic dissection in the elderly: clinical characteristics, management, and outcomes in the current era. J Am Coll Cardiol 2002; 40:685-692.
22. Newman AB, Arnold AM, Burke GL et al. Cardiovascular disease and mortality in older adults with small abdominal aortic aneurysms detected by ultrasonography: the cardiovascular health study. Ann Intern Med 2001; 134:182-190.
23. Freiberg MS, Arnold AM, Newman AB et al. Abdominal aortic aneurysms, increasing infrarenal aortic diameter, and risk of total mortality and incident cardiovascular disease events: 10-year follow-up data from the Cardiovascular Health Study. Circulation 2008; 117:1010-1017.
24. Mukherjee D, Evangelista A, Nienaber CA et al. Implications of periaortic hematoma in patients with acute aortic dissection (from the International Registry of Acute Aortic Dissection). Am J Cardiol 2005; 96:1734-1738.
25. Nienaber CA, Fattori R, Mehta RH et al. Gender-related differences in acute aortic dissection. Circulation 2004; 109:3014-3021.
26. Mikhail GW. Coronary revascularisation in women. Heart 2006; 92 Suppl 3:iii19-iii23.
27. Malenka DJ, O'Connor GT, Quinton H et al. Differences in outcomes between women and men associated with percutaneous transluminal coronary angioplasty. A regional prospective study of 13,061 procedures. Northern New England Cardiovascular Disease Study Group. Circulation 1996; 94:II99-104.
28. Norman PE, Powell JT. Abdominal aortic aneurysm: the prognosis in women is worse than in men. Circulation 2007; 115:2865-2869.
29. Schlosser FJ, Vaartjes I, van der Heijden GJ et al. Mortality after elective abdominal aortic aneurysm repair. Ann Surg 2010; 251:158-164.
30. Khoynezhad A, Donayre CE, Omari BO et al. Midterm results of endovascular treatment of complicated acute type B aortic dissection. J Thorac Cardiovasc Surg 2009; 138:625-631.
31. Patel HJ, Williams DM, Meerkov M et al. Long-term results of percutaneous management of malperfusion in acute type B aortic dissection: implications for thoracic aortic endovascular repair. J Thorac Cardiovasc Surg 2009; 138:300-308.

32. Kische S, Ehrlich MP, Nienaber CA et al. Endovascular treatment of acute and chronic aortic dissection: midterm results from the Talent Thoracic Retrospective Registry. J Thorac Cardiovasc Surg 2009; 138:115-124.
33. Feezor RJ, Martin TD, Hess PJ, Jr. et al. Early outcomes after endovascular management of acute, complicated type B aortic dissection. J Vasc Surg 2009; 49:561-566.
34. Verhoye JP, Miller DC, Sze D et al. Complicated acute type B aortic dissection: midterm results of emergency endovascular stent-grafting. J Thorac Cardiovasc Surg 2008; 136:424-430.
35. Duebener LF, Lorenzen P, Richardt G et al. Emergency endovascular stent-grafting for life-threatening acute type B aortic dissections. Ann Thorac Surg 2004; 78:1261-1266.

Chapter 9

Acute Management of Aortobronchial and Aortoesophageal Fistulas using Thoracic Endovascular Aortic Repair

Journal of Vascular Surgery 2009;50:999-1004

Frederik H.W. Jonker,[1] MD
Robin Heijmen,[2] MD, PhD
Santi Trimarchi,[3] MD
Hence J.M. Verhagen,[4] MD, PhD
Frans L. Moll,[5] MD, PhD
Bart E. Muhs,[1] MD, PhD

[1] Section of Vascular Surgery and Interventional Radiology, Yale University School of Medicine, New Haven, Connecticut, USA
[2] Section of Cardiothoracic Surgery, St. Antonius Hospital, Nieuwegein, The Netherlands
[3] Section of Vascular Surgery, Policlinico San Donato IRCCS, Milan, Italy
[4] Section of Vascular Surgery, Erasmus University Medical Center, Rotterdam, the Netherlands
[5] Section of Vascular Surgery, University Medical Center Utrecht, the Netherlands

ABSTRACT

Introduction

Aortobronchial fistula (ABF) and aortoesophageal fistula (AEF) are rare but lethal if untreated. Open thoracic surgery is associated with high operative mortality and morbidity. In this case series we sought to investigate outcomes of thoracic endovascular aortic repair (TEVAR) for emergency cases of ABF and AEF.

Methods

We retrospectively reviewed all patients with AEF and ABF treated with TEVAR in three European teaching hospitals between 2000 and January 2009. Eleven patients were identified including 6 patients with ABF, 4 patients with AEF and one patient with a combined ABF and AEF. In-hospital outcomes and follow-up after TEVAR were evaluated.

Results

Median age was 63 years (interquartile range 31); 8 were male. Ten patients presented with hemoptysis or hematemesis; 4 developed hemorrhagic shock. All patients underwent immediate TEVAR, and three AEF patients required additional esophageal surgery. Five patients died (45%), including three patients with AEF, one patient with ABF and one patient with a combined ABF and AEF, after a median duration of 22 days (interquartile range 51 days). The patient with AEF that survived had received early esophageal reconstruction. Causes of death were: sepsis (n=2), ARDS (n=1), thoracic infections (n=1) and aortic rupture (n=1). Median follow-up of surviving patients was 45 months (interquartile range 45 months). Six additional vascular interventions were performed in three survivors.

Conclusion

TEVAR does prevent immediate exsanguination in patients admitted with AEF and ABF but after initial deployment of the endograft and control of the hemodynamic status, most patients, in particular those with AEF, are at risk for infectious complications. Early esophageal repair after TEVAR appears to improve the survival in case of AEF. Therefore, TEVAR may serve as bridge to surgery in emergency cases of AEF with subsequent definitive open operative repair of the esophageal defect as soon as possible. In patients with ABF, additional open surgery may not be necessary after the endovascular procedure.

INTRODUCTION

Fistulas between the thoracic aorta and the esophagus or lungs are rare. Aortobronchial fistula (ABF) and aortoesophageal fistula (ABF) usually arise in thoracic aortic disease such as aneurysms or after previous thoracic aortic surgery.[1-5] ABF has been reported in patients with pulmonary diseases like tuberculosis (TBC), intrapulmonary Aspergillus abcess, after bronchial stenting or previous lobectomy.[6-8] AEF has been associated with esophageal carcinoma, ingestion of foreign bodies and even iatrogenic esophageal perforation or Barrett's esophagus.[9-12] Both ABF and AEF often present with acute hemoptysis or hematemesis.

Due to the excessive bleeding, ABF and AEF are lethal if untreated, however, open thoracic aortic repair of ABF and AEF is associated with high mortality and morbidity in this critically-ill population as well.[1-5,13] Thoracic endovascular aortic repair (TEVAR) has shown to be an effective method for treatment of thoracic aortic disease.[14-16] TEVAR is less invasive than open thoracic aortic surgery and is associated with decreased operative duration. Since the introduction of TEVAR, several cases of successful endovascular management of ABF and AEF have been reported.[6,7,9-11,17] However, it is unclear if these promising reports were exceptional cases. Furthermore, several reported cases were performed in subacute settings instead of emergencies, and long-term outcomes are often missing. If patients with ABF or AEF are treated with TEVAR alone, the esophageal or bronchial defect is not repaired. Lung tissue and the esophagus are non sterile cavities in which risks of graft-infections after endovascular treatment for fistulas are likely to be permanently increased, which are crucial when considering long-term outcomes. In this series, we evaluated the in-hospital and follow-up outcomes of emergency cases of ABF and AEF treated with TEVAR, to assess the applicability of endovascular therapy for these rare entities.

METHODS

We retrospectively reviewed all patients with AEF and ABF treated with TEVAR in Policlinico S. Donato I.R.C.C.S., Milan, Italy, the University Medical Center Utrecht and the St. Antonius Hospital, Nieuwegein, both located in the Netherlands. Approval of the human ethics committee was obtained in all institutions. Between 2000 and January 2009, 11 cases treated with TEVAR were identified, including 6 patients with ABF, 4 patients with AEF and one patient with a combined ABF and AEF.

The median age of patients was 63 years (range 30 years to 77 years; interquartile range 31 years); 8 were male (73%). Causes of the fistula were: previous open thoracic aortic surgery with implantation of a Dacron prosthesis (n=4), thoracic aortic aneurysm (TAA) (n=3), previous TEVAR (n=2), ingestion of a chicken bone (n=1) and infection of a Dacron graft of the thoracic aorta since two months, which was treated by intravenous antibiotic therapy (n=1). All patients

showed an acute presentation of symptoms. Ten patients suffered from progressive hemoptysis and/or hematemesis; 4 patients developed hemorrhagic shock due to excessive bleeding. Hemorrhagic shock was present in three out of four patients with AEF. The Classification of Hemorrhage from the American College of Surgeons[18] was used to assess if patients were in hemorrhagic shock on admission. Patients with blood loss ≥1500ml, a pulse rate ≥ 120 beats/min, respiratory rate ≥30 / minute, and a decreased blood pressure, were classified as admitted in hemorrhagic shock (hemorrhage class III or class IV).

In two other patients, bacteremia was diagnosed by blood cultures. One of these suffered from an infected Dacron prosthesis of the thoracic aorta which was treated with Ceftriaxon 2g/day. After 2 months the patient developed massive hemoptysis and bronchoscopy revealed ABF which was treated by TEVAR. The other patient was admitted with acute hemoptysis, thoracic pain, dyspnea and fever. CTA diagnosed ABF which was treated with TEVAR. Blood cultures turned out positive and the patient received Augmentin 4dd1200 mg during 3 months. In both patients, there was no evidence of septic shock when TEVAR was offered and no vasopressors were needed. Cause and presentation of the fistula for the 11 patients are depicted in table 1.

Table 1. Patient characteristics

Gender / age		Fistula type	Medical history	Fistula cause	Symptoms	Shock/ infection
1.	M / 46	ABF	Bentall procedure + CABG in 2001, aortic arch replacement in 2002	Previous aortic surgery	HMP, TP, DP, F	N / Y
2.	F / 63	ABF	Bentall procedure in 1996, aortic graft for TAA in 2003	Previous aortic surgery	HMP, TP	Y / N
3.	M / 30	ABF	Repair of aortic coarctation in 1977	TAA (64mm)	HMP, DP	N / N
4.	M / 60	ABF	Aortic graft for type A aortic dissection in 2003, aortic graft for TAA + PTCA + CVA in 2004	Previous aortic surgery	HMP, TP	N / N
5.	M /77	ABF	COPD, CAD, CRI, HT	Ruptured TAA	HMP, TP, DP	N / N
6.	M / 68	ABF	Type B dissection in 1985, aortic graft for TAA in March 2008, aortic graft infection in August 2008	Aortic graft infection*	HMP	N / Y
7.	M / 65	AEF	TEVAR for TAA in 2007, HT	Previous TEVAR	TP	N / N
8.	F / 40	AEF	Aortic graft for type A aortic dissection in 2007, 2x open repair of AEF in 2007	Previous aortic surgery	HMT	Y / N
9.	F / 71	AEF	COPD, HT	Ruptured TAA (65mm)	HMT, TP, DP	Y / N
10.	M / 31	AEF		Ingestion chicken bone	HMT, TP, dysphagia	Y / N
11.	M / 75	ABF + AEF	TEVAR for TAA 3 months ago, COPD, CRI, HT	Previous TEVAR	HMP, HMT, TP, DP	N / N

ABF aortobronchial fistula, *AEF* aortoesophageal fistula, *TP* thoracic pain, *HMP* hemoptysis, *HMT* hematemesis, *DP* dyspnea, *F* fever, *COPD* chronic obstructive pulmonary disease, *CAD* coronary artery disease, *CRI* chronic renal insufficiency, *HT* hypertension, *TAA* thoracic aortic aneurysm

Ten fistulas were diagnosed using computed tomography angiography (CTA); diagnosis was made using bronchoscopy in one patient with ABF. TEVAR was preferred over open thoracic aortic surgery at these institutions because of emergency. Operations were performed under general anesthesia. The endovascular device was inserted through the common femoral artery in all cases; the angiographic catheter was positioned into the thoracic aorta via a guide wire from the right brachial artery in three cases. Patients were treated with the following endografts: Gore TAG™ (n=4), Medtronic Talent™ (n=3), Medtronic Valiant™ (n=3) and Gore Thoracic Excluder™ (n=1). Details regarding diameter, total length and number of endografts used during the initial endovascular procedure are depicted in table 2. All patients received perioperative antibiotics intravenously. Surviving patients received oral antibiotics after discharge; duration of antibiotic therapy ranged from 4 weeks to 3 months.

The following outcomes were investigated: successful exclusion of the fistula during initial TEVAR, complications, additional open surgery, vascular re-interventions, mortality, hospital length of stay and long-term follow up. Mortality after TEVAR was compared between ABF and AEF using the Fisher's exact test; the survival after TEVAR was demonstrated using Kaplan Meier life table analysis (SPSS version 15.0).

Table 2. Procedural characteristics

	Vascular Access	Graft details	Number of grafts	PLZ / coverage LSCA	Additional thoracic surgery	Additional antibiotic therapy
1.	CFA+BA	Excluder, 34x200	1	2 / Y	-	Augmentin 4dd1200mg, 3 months
2.	CFA	TAG, 28x150	1	4 / N	-	Amoxicillin 3dd500mg, 10 weeks
3.	CFA+BA	Talent, 32x150	2	2 / Y	-	Augmentin 3dd 625mg, until death
4.	CFA	Talent, 38x100	1	2 / Y	-	Cefuroxim 2dd 500mg, 3 months
5.	CFA	TAG, 37x200	1	3 / N	-	Not applicable
6.	CFA	Valiant, 36x110	1	2 / Y	-	Ceftriaxon 2g/d IV*
7.	CFA+BA	Valiant, 42x150	1	3 / N	Esophageal exclusion, drainage aneurysm sac and mediastinum after 17 days.	Metronidazol / cefuroxim, 4 weeks
8.	CFA	Valiant, 30x150	1	3 / N	-	No applicable
9.	CFA	TAG, 27x150	1	4 / N	Esophageal exclusion after 18 days	No applicable
10.	CFA	TAG, 28x100	1	2 / Y	Neck exploration after 1 day, esophagectomy and gastric tube after 4 days.	Augmentin 3dd 625mg, 3 months
11.	CFA	Talent, 42x110	1	2 / Y	-	No applicable

All patients received perioperative intravenous (IV) antibiotics; surviving patients were prescribed oral antibiotics. *PLZ:* proximal landing zone, *LSCA* left subclavian artery, *CFA* common femoral artery, *BA* brachial artery.
* This patient already received antibiotic therapy prior to TEVAR because of infected Dacron prosthesis of the thoracic aorta.

RESULTS

Complete exclusion of the fistula was successfully achieved during initial TEVAR in 9 cases (82%). In the remaining 2 patients, a second endograft was successfully placed in one patient after 2 days because of considerable type 1 endoleak, the last patient died after 2 days due to aortic rupture, which was probably caused by endoleak type 1. The left subclavian artery was covered during the endovascular procedures in 6 patients (54%). Median hospital length of stay was 15 days (range 2 days to 89 days; interquartile range 15 days).

Additional thoracic surgery

Additional open thoracic surgery was performed in three patients with AEF. A 31-years old male (patient 10) suffered from AEF after ingestion of a chicken bone 8 days earlier. He required neck exploration one day after TEVAR to evacuate a large amount of blood and clot which had caused respiratory insufficiency. A few days later, abdominal esophagectomy with gastric tube reconstruction was performed. Another patient, a 71-years old female in which the AEF was caused by a ruptured TAA received bipolar esophageal exclusion including cervical esophagostomy and jejunostomy 18 days after TEVAR (patient 9). The last patient which received additional open surgery was a 65-years old male in which AEF was caused by previous TEVAR (patient 7). He had undergone successful TEVAR for AEF but one week after discharge he was readmitted with mediastinitis which was treated by drainage of the mediastinum and aneurysm sac, followed by esophageal exclusion and jejunostomy.

Mortality

Four patients died during hospitalization and one patient died shortly after readmission (45%). The median time interval until death was 22 days (range 2 to 89 days; interquartile range 51 days). Figure 1 depicts the survival after TEVAR for ABF and AEF; no patients died during the initial endovascular procedure. Two out of 4 patients which were admitted with hypovolemic shock eventually expired after 7 and 89 due to infectious complications (patients 8 and 9). Death occurred in 3 patients with AEF, one patient with ABF and one patient with combined ABF and AEF, Fisher's exact test: p=0.133.

The patient with the combined ABF and AEF died from delayed aortic rupture 2 days after TEVAR (patient 11). A 40-years old female was admitted with hypovolemic shock after recurrent AEF, and showed recurrent hemoptysis after TEVAR, followed by development of mediastinitis and sepsis. She died one week after TEVAR (patient 8). Another patient which had developed ABF after a ruptured TAA, showed type 1 endoleak after 2 days, requiring placement of an additional endograft (patient 5). After the re-intervention, the patient developed renal failure and ARDS which resulted in death 22 days after initial TEVAR. The 65-years old male who was re-admitted with mediastinitis died 36 days after endovascular exclusion of AEF, due to sepsis. The last patient who died was the 71-years old female which had received bipolar esophageal exclusion for AEF. She suffered from aortic rupture at the proximal endograft neck which was treated with placement of a second endograft. The patient developed respiratory failure due to severe thoracic infections, resulting in death after an ICU stay of almost 3 months. The patient with AEF that received early esophageal repair a few days after TEVAR was the only patient with AEF that did not expire (patient 10).

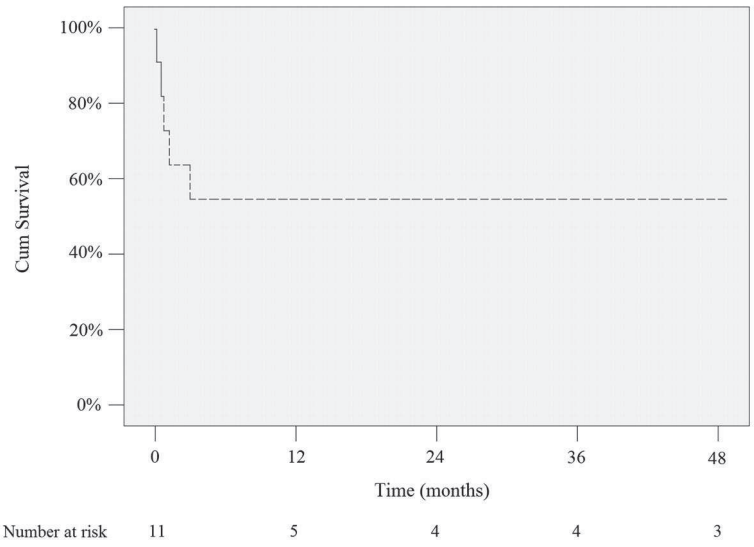

Figure 1. Long-term survival after TEVAR for ABF and AEF
No deaths occurred after 3 months. Median follow-up of surviving patients was 45 months (range 3 months to 61 months; interquartile range 45 months)

Follow-up

Median follow-up of surviving patients was 45 months (range 3 months to 61 months; interquartile range 45 months). Six additional vascular interventions were performed in three survivors during this period. A left sided-carotid subclavian bypass was performed prior to TEVAR to extend the proximal landing zone in a 68-years old male with ABF after an infected aortic graft prior to TEVAR. Postoperatively the patient suffered from Horner's syndrome due to damage of the sympathic nerve fibers (patient 6).

The patient with AEF after ingestion of a chicken bone needed a repeat TEVAR one day after the initial procedure. The manipulation during the open surgical procedure resulted in severe bleeding which necessitated deploying of a longer endograft inside the first one. Nine months after discharge, he presented with thrombosis of both popliteal arteries which was treated with embolectomy. CTA showed infolding of the second endograft and a giant Palmaz stent was placed in the second endograft with resolution of the complication.

The third survivor which required re-interventions was a 30-years old male (patient 3), which had developed TAA with concomitant ABF after open repair of an aortic coarctation. During TEVAR the ABF was excluded but coverage of the left subclavian artery was necessary in order to have a safe proximal landing zone. Endovascular ballooning was performed 3 days after the first endovascular procedure because of type 1 endoleak, with immediate good result. After discharge, the patient suffered from brachial claudication which was treated successfully with transposition

of the left subclavian artery. The other 3 survivors did not require re-intervention although one suffered from mild brachial claudication due to coverage of the left subclavian artery during initial TEVAR. Outcomes of TEVAR are depicted in table 3.

Table 3. Outcomes of 11 patients undergoing TEVAR for ABF and AEF

	Successful TEVAR	LOS (days)	Complications	Additional vascular intervention	Fistula-related death	Length of follow-up
1.	Y	7	-	-	-	49 months
2.	Y	15	-	-	-	41 months
3.	Y	22	Endoleak type 1, brachial claudication	Endovascular ballooning after 3 days, transposition LSCA after 6 months	-	61 months
4.	Y	8	Brachial claudication	-	-	54 months
5.	N	22	Endoleak type 1, renal failure, ARDS	TEVAR after 2 days	ARDS	22 days
6.	Y	60*	Horner syndrome	Left sided-carotid subclavian bypass prior to TEVAR	-	3 months
7.	Y	7	Mediastinitis	-	Sepsis	36 days
8.	Y	7	Recurrence hemoptysis, mediastinitis	-	Sepsis	7 days
9.	Y	89	Aortic rupture at proximal endograft neck, thoracic infections	TEVAR after 40 days	Thoracic infections	89 days
10.	Y	19	Bleeding after 24 hours, infolding of inner endograft	TEVAR after 1 day, embolectomy and insertion giant Palmaz stent after 9 months	-	15 months
11.	N	2	Aortic rupture	-	Aortic rupture	2 days

Successful TEVAR was defined as complete exclusion of the fistula during initial TEVAR. *LOS* hospital length of stay in days, *LSCA* left subclavian artery. * This patient was already hospitalized for 2 months because of an infected Dacron prosthesis of the thoracic aorta; he was discharged 14 days after TEVAR.

DISCUSSION

In this case series, TEVAR prevented immediate exsanguination caused by ABF or AEF; no patients died during the initial endovascular procedure. However, 5 out of 11 patients with ABF or AEF died of complications between 2 days and 3 months after the initial endovascular procedure (figure 1).

Aortobronchial and aortoesophageal fistulas are scarce and usually arise in thoracic aortic disease or after previous thoracic aortic repair. ABF and AEF regularly present with excessive bleeding; repair of the fistula is the only curative treatment.[1-5] Adequate management of ABF or AEF consists of control of hemorrhage, repair of the bronchial or esophageal defect, control of infectious complications and maintenance of sufficient distal perfusion. Traditional surgical

repair of ABF usually occurs by a posterolateral thoracotomy, followed by resection of the involved aortic area of the fistula and replacement of this part by a prosthetic graft. Bronchial or lung surgical repair may consist of primary closure or partial resection of lung tissue. The bronchial segment of the fistula has been treated conservatively in cases in which the exclusion of the aortic side of the fistula was considered adequate. In the literature, in-hospital mortality of open surgery for ABF ranges from 15% to 24%.[1,2] The most frequently used approach for open AEF repair is a left thoracotomy, followed by aortic replacement with a prosthetic or cryopreserved homograft, or an extra-anatomic bypass in case of severe mediastinal sepsis.[5,19] Open thoracic surgery for AEF is, however, associated with a high operative mortality, which is usually caused by exsanguination of the patient. [3-5] Precise mortality rates of classic surgery are missing in the literature, due to the rare occurrence of AEF.

TEVAR is less invasive than open thoracic surgery and allows prompt exclusion of thoracic aortic fistulas and control of hemorrhage. No patients died of exsanguination during TEVAR in our series. However, the follow-up outcomes after TEVAR were poor. Many patients in our evaluation developed infectious complications or recurrent bleeding within the first 3 months after the initial endovascular procedure, which reasonably leaded to death in 5 cases (45%). Endovascular treatment of ABF or AEF alone, does not allow debridement of the potentially contaminated thoracic cavity. Additionally, the fistula is not repaired and a connection between the lungs or esophagus with the endograft, the thoracic aorta and the thoracic cavity is maintained. This results in continued exposure to contaminated contents of the esophagus or lungs and high risks of serious infections. Therefore, additional surgical repair of the fistula, which may include debridement of the thoracic cavity, supported by broad-spectrum antibiotic therapy for at least several months, most likely will improve outcomes after successful endovascular treatment.

In the literature, numerous cases of endovascular management of ABF[6-8,20-22] and AEF[9-11,23-25] have been reported, some with a fatal outcome.[22-24] Antibiotic therapy was frequently prescribed,[6,8,10,11,20,22,24,25] additional open surgical repair was performed in several cases,[6,9,11,25] and sometimes no additional therapy was offered.[21,23] Since case reports often represent exceptional single cases, it is difficult to draw valid conclusions regarding the applicability of endovascular management of ABF and AEF on the basis of these reports. Larger cases series of TEVAR for ABF demonstrated a mortality between 0% to 25% at 3 years after the endovascular procedure.[17,26] Our results are inconsistent with these reports. We have several hypotheses for the inferior outcome in our series. A possible explanation for the different outcome, is the indication for TEVAR. In the Bockler et al and Wheatley et al series, endovascular management was preferred in patients with ABF because of co-morbid diseases and previous thoracotomy.[17,26] In our series, TEVAR was indicated because of emergency treatment in all patients. This difference could have affected our results.

Another substantial difference with these previous series is that we also evaluated outcomes of 4 patients with AEF and one patient with combined ABF and AEF, besides 6 patients with

ABF. Deaths in our series included the patient with combined ABF and AEF and 3 out of 4 patients with AEF; only one of 6 patients with ABF expired. It appears that patients with AEF have a worse outcome after TEVAR compared to patients with ABF, although strong conclusions cannot be made due to the small sample size of this series.

Differences in outcomes after TEVAR between ABF and AEF have not been described previously in the literature. In this series, 3 out of 4 patients with AEF were admitted with hemorrhagic shock (table 1), while only one of 6 patients with ABF suffered from shock. Hemorrhagic shock is generally accepted as a risk factor for mortality and the association of AEF and shock may have led to poorer outcomes in this series. Two of three patients with AEF and shock expired; death was, however, caused by infectious complications instead of exsanguination. ABF and AEF are often associated with infections due to the presence of open air and esophageal contents in the chest. Exposure to esophageal contents is possibly more virulent than exposure to the open air as well, resulting in increased risks of infective complications after TEVAR for AEF compared to ABF.

Although no additional thoracic surgical procedures were performed in case of ABF, three out of four patients with AEF received additional esophageal surgical repair. In one case within a few days after TEVAR and the remaining two patients underwent delayed repair after more than 2 weeks (table 2). The patient in which esophageal surgery was performed a few days after the initial endovascular procedure, was the only patient with AEF which did not expire; remaining patients died of infectious complications (table 3). This finding suggests a more aggressive surgical approach of AEF, shortly after initial stabilization by TEVAR.

Topel et al recently published promising results of a combined approach for management of AEF. They used TEVAR as a bridging procedure in the acute setting, which was followed by in situ repair with cryopreserved homografts and long-term antibiotic therapy.[19] This combined approach could be a valuable option for emergency cases of AEF, and, possibly, a more aggressive surgical strategy after initial TEVAR could have prevented some lethal complications in our series.

CONCLUSION

Emergency endovascular repair of ABF and AEF is associated with poor results. Patients with AEF treated with TEVAR appear to have an inferior outcome compared to patients with ABF. TEVAR does prevent immediate exsanguination in patients admitted with AEF and ABF but after initial deployment of the endograft and control of the hemodynamic status, most patients, in particular those with AEF, are at risk for infectious complications. Early esophageal repair appears to improve the survival in case of AEF. Therefore, TEVAR may serve as bridge to surgery in emergency cases of AEF with subsequent definitive open operative repair of the esophageal defect as soon as possible. In patients with ABF, additional open surgery may not be necessary after the endovascular procedure.

REFERENCES

1. Piciche M, De PR, Fabbri A et al. Postoperative aortic fistulas into the airways: etiology, pathogenesis, presentation, diagnosis, and management. Ann Thorac Surg 2003; 75:1998-2006.
2. MacIntosh EL, Parrott JC, Unruh HW. Fistulas between the aorta and tracheobronchial tree. Ann Thorac Surg 1991; 51:515-519.
3. Carter R, Mulder GA, Snyder EN, Jr. et al. Aortoesophageal fistula. Am J Surg 1978; 136:26-30.
4. Hollander JE, Quick G. Aortoesophageal fistula: a comprehensive review of the literature. Am J Med 1991; 91:279-287.
5. Prokakis C, Koletsis E, Apostolakis E et al. Aortoesophageal fistulas due to thoracic aorta aneurysm: surgical versus endovascular repair. Is there a role for combined aortic management? Med Sci Monit 2008; 14:RA48-RA54.
6. Islam S, Williams DM, Teitelbaum DH. Aortobronchial fistula from invasive Aspergillus infection of the lung: an endovascular approach to repair. J Pediatr Surg 2005; 40:e19-e22.
7. Alric P, Berthet JP, Branchereau P et al. Endovascular repair for acute rupture of the descending thoracic aorta. J Endovasc Ther 2002; 9 Suppl 2:II51-II59.
8. Yoo JH, Lee CT, Shim YS et al. Aortobronchial fistula presenting as recurrent hemoptysis and successfully treated with an endovascular stent graft. Respiration 2001; 68:537-539.
9. Ikeda Y, Morita N, Kurihara H et al. A primary aortoesophageal fistula due to esophageal carcinoma successfully treated with endoluminal aortic stent grafting. J Thorac Cardiovasc Surg 2006; 131:486-487.
10. Chan YC, Ting AC, Law S et al. Secondary infection of a pre-existing thoracic aortic aneurysm by iatrogenic oesophageal perforation with aorta-oesophageal fistula formation. Eur J Cardiothorac Surg 2009; 35:365-367.
11. Zamora CA, Sugimoto K, Tsuji Y et al. Stent-grafting of an infected aortoesophageal fistula following ingestion of a fish bone. J Endovasc Ther 2005; 12:522-523.
12. Guillem P, Porte H, Techer E et al. Aortoesophageal fistula of uncommon origin: perforation of a Barrett's ulcer. Dis Esophagus 2003; 16:259-260.
13. Eggebrecht H, Baumgart D, Radecke K et al. Aortoesophageal fistula secondary to stent-graft repair of the thoracic aorta. J Endovasc Ther 2004; 11:161-167.
14. Dake MD, Miller DC, Semba CP et al. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. N Engl J Med 1994; 331:1729-1734.
15. Mitchell RS, Miller DC, Dake MD. Stent-graft repair of thoracic aortic aneurysms. Semin Vasc Surg 1997; 10:257-271.
16. Nienaber CA, Fattori R, Lund G et al. Nonsurgical reconstruction of thoracic aortic dissection by stent-graft placement. N Engl J Med 1999; 340:1539-1545.
17. Wheatley GH, III, Nunez A, Preventza O et al. Have we gone too far? Endovascular stent-graft repair of aortobronchial fistulas. J Thorac Cardiovasc Surg 2007; 133:1277-1285.

18. Committee on Trauma, American College of Surgeons. Advanced Trauma Life Support Manual. Chicago: 1997.
19. Topel I, Stehr A, Steinbauer MG et al. Surgical strategy in aortoesophageal fistulae: endovascular stentgrafts and in situ repair of the aorta with cryopreserved homografts. Ann Surg 2007; 246:853-859.
20. Kokotsakis J, Misthos P, Athanasiou T et al. Endovascular stenting for primary aortobronchial fistula in association with massive hemoptysis. Tex Heart Inst J 2007; 34:369-372.
21. Sachithanandan A, McCafferty I, Riley P et al. Emergency endovascular stent graft repair of aorto-bronchial fistulas postcoarctation repair. J Card Surg 2007; 22:524-526.
22. Karmy-Jones R, Lee CA, Nicholls SC et al. Management of aortobronchial fistula with an aortic stent-graft. Chest 1999; 116:255-257.
23. Xia M, Guo JZ, Zhan Q et al. Aortoesophageal fistula caused by descending aortic pseudoaneurysm: one case report. Chin Med J (Engl) 2007; 120:2149-2150.
24. Gonzalez-Fajardo JA, Gutierrez V, Martin-Pedrosa M et al. Endovascular repair in the presence of aortic infection. Ann Vasc Surg 2005; 19:94-98.
25. Taylor BJ, Stewart D, West P et al. Endovascular repair of a secondary aortoesophageal fistula: a case report and review of the literature. Ann Vasc Surg 2007; 21:167-171.
26. Bockler D, Schumacher H, Schwarzbach M et al. Endoluminal stent-graft repair of aortobronchial fistulas: bridging or definitive long-term solution? J Endovasc Ther 2004; 11:41-48.

Chapter 10

Outcomes of Thoracic Endovascular Aortic Repair for Aortobronchial and Aortoesophageal Fistulas

Journal of Endovascular Therapy 2009;16:428-40

Frederik H.W. Jonker,[1] MD,
Felix J.V. Schlösser,[1] MD, PhD
Frans L. Moll,[2] MD, PhD
Joost A. van Herwaarden,2 MD, PhD
Jeffrey E. Indes,[1] MD
Hence J.M. Verhagen,[3] MD, PhD
Bart E. Muhs,[1] MD, PhD

[1] Section of Vascular Surgery and Interventional Radiology, Yale University School of Medicine, New Haven, Connecticut, USA
[2] Section of Vascular Surgery, University Medical Center Utrecht, Utrecht, the Netherlands
[3] Section of Vascular Surgery, Erasmus University Medical Center, Rotterdam, the Netherlands

ABSTRACT

Purpose

To analyze the outcomes of thoracic endovascular aortic repair (TEVAR) for aortobronchial fistula (ABF) and aortoesophageal fistula (AEF).

Methods

The authors reviewed all published cases of ABF and AEF treated with TEVAR indexed in the MEDLINE, Cochrane Library CENTRAL, and EMBASE databases. After removal of duplicates, 850 articles were scrutinized for relevance and validity. Exclusion criteria included: (1) no clear description of the organs involved with the fistula, (2) no description of outcomes after TEVAR for ABF or AEF, or (3) no original data presented in the article. In this manner, 66 relevant articles were identified that included original data on 114 patients (76 men; mean age 63±1.5 years) with ABF (n=71) or AEF (n=43). Meta-analyses were performed to investigate outcomes of TEVAR for ABF and AEF.

Results

Patients with AEF presented more frequently with hypovolemic shock [14 (33%) versus 19 (13%), p=0.012] and systemic infection [15 (36%) versus 6 (9%), p<0.001] compared to patients with ABF. In-hospital mortality was 3% (n=2) after TEVAR for ABF and 19% (n=8) after TEVAR for AEF (p=0.004). Additional thoracic surgery in the first 30 days after TEVAR was performed in 3% (n=2) of ABF patients and in 37% (n=16) of AEF patients (p<0.001); 12 AEF patients who had received esophageal surgery in the first month after TEVAR showed lower fistula-related mortality during 6 months of follow-up compared to patients who did not receive additional esophageal surgery (p=0.018).

Conclusion

TEVAR is associated with superior outcomes in patients with ABF. Endovascular management of AEF is associated with poor results and should not be considered definitive treatment. TEVAR could serve as a bridge to surgery for emergency cases of AEF only, with definitive open surgical correction of the fistula undertaken as soon as possible.

INTRODUCTION

The thoracic aorta is located in the posterior mediastinal cavity, where it is closely surrounded by thoracic organs. Rarely, fistulas arise between the thoracic aorta and the esophagus (aortoesophageal fistula, ABF) or lungs (aortobronchial fistula, ABF), typically due to thoracic aortic disease or previous thoracic aortic surgery. ABF and AEF present commonly with hemoptysis and hematemesis and are usually lethal if left untreated; open thoracic aortic repair of thoracic fistulas is associated with high mortality and morbidity in this critically-ill population. [1-6] Recently, thoracic endovascular aortic repair (TEVAR) has shown success in exclusion of thoracic aortic aneurysms (TAA) and other thoracic aortic pathologies.[7-9] TEVAR is less invasive than open thoracic aortic surgery and is associated with shorter operating times. However, both lung tissue and the esophagus are non-sterile cavities that are contaminated by micro-organisms, which present a continuing risk of infection. Hence, these fistulas are relative contraindications to endovascular management of thoracic aortic pathologies. Nonetheless, TEVAR could be valuable in preventing exsanguination in emergencies or in fistulas patients with significant co-morbidities. Because TEVAR is a relatively new technique and ABF and AEF have relatively low incidences, outcomes of TEVAR for thoracic aortic fistulas are lacking; the current literature is limited to case reports and small case series.

In this study, we reviewed all evidence in the literature regarding mortality and complications after endovascular management of patients with ABF and AEF. Clinical differences between patients with ABF and those with AEF treated with TEVAR were investigated as well.

METHODS

Literature search

Medline, EMBASE, and Cochrane Library CENTRAL were searched until January 29, 2009. The following search string was used for Medline: ((“aorta”[Title/Abstract] OR “aortic”[Title/Abstract] OR “aortal”[Title/Abstract] OR “aorta, thoracic”[MeSH Terms] OR “aorta, abdominal”[MeSH Terms] OR “aorta”[MeSH Terms]) AND (bronch*[Title/Abstract] OR esophag*[Title/Abstract] OR oesophag*[Title/Abstract] OR trachea*[Title/Abstract])) AND (fistul*[Title/Abstract] OR “Fistula”[MeSH Terms]) OR (“aortoesophageal”[Title/Abstract] OR “aorta-esophageal”[Title/Abstract] OR “aorto-tracheal”[Title/Abstract] OR “aortobronchial”[Title/Abstract] OR “aorto-bronchial”[Title/Abstract]), which resulted in 671 articles. No language or publication date restrictions were applied. A similar search string was used for EMBASE, identifying 413 articles. The Cochrane library CENTRAL database was browsed manually and did not reveal any relevant articles. After removal of duplicates, 850 articles remained.

Selection of articles

All titles and abstracts were read by 2 independent investigators (F.H.J and F.J.S). Articles were included if they contained data on patients who had undergone TEVAR for ABF or AEF. Exclusion criteria included: (1) no clear description of the organs involved with fistula, (2) no description of outcomes after TEVAR for ABF or AEF, and (3) no original data presented. Other articles written by identical authors and/or institutions were studied in detail and excluded if necessary to prevent duplication of cases. All extracted information was entered into a database. In this manner, 66 relevant articles were identified for the analysis.

Data extraction

Two independent investigators (F.H.J and F.J.S) scrutinized the identified articles to extract the following characteristics: age and gender; cause of fistula; presence and/or history of TAA; previous aortic intervention and indications; time interval between previous aortic intervention and presentation of fistula in months; comorbidity and ASA classification; symptoms of the fistula; acute presentation, defined by presentation within 3 days after development of symptoms, or acute progression of symptoms; presence of hypovolemic shock at admission; presence of infection at admission; diagnostic studies performed; results of diagnostic studies; contraindications for open repair; time interval between diagnosis and TEVAR in months; type of anesthesia; endovascular access site; graft characteristics, including graft length, diameter, and model; proximal landing zone; technical success of TEVAR, defined by successful exclusion of the fistula during the initial endovascular procedure; treatment with antibiotic drugs and duration of this treatment; in-hospital and long-term follow-up outcomes, including graft-related complications (endoleak, stent-graft migration, or stent fracture); non-graft-related complications (sepsis and/or mediastinitis, pneumonia, myocardial infarction, paraplegia, renal failure, and iliac rupture), open and endovascular re-interventions, time interval until re-intervention, and mortality; fistula-related mortality, defined by death during hospitalization for TEVAR and death caused by fistula- or graft-related complications; cause of death; and length of follow-up in months, defined by the time period between the initial TEVAR and subsequent death or the most recent follow-up visit.

Patient Population

Totally original data were obtained regarding 114 patients (76 men; mean age 63 ±1.5 years, range 11–88), of whom 71 had ABF (48 men; mean age 64.0±1.8 years, range 11–88) and 43 presented with AEF (28 men; mean age 62.0±2.5 years, range 20–87).[10-75] The availability of individual data in these cases of ABF and AEF is depicted in table 1, while figure 1 represents the distribution of TEVAR cases for ABF and AEF by publication date of the article that described the case. Demographics and data on presentation, symptoms, and diagnosis are given in table 2.

Table 1. Availability of individual data

Variable	N	(%)	Variable	N	(%)
Age	94	(83)	Graft brand	93	(82)
Gender	104	(91)	LSCA covered	89	(78)
Fistula type	114	(100)	Success TEVAR	114	(100)
Fistula cause	106	(93)	Removal of TEVAR	114	(100)
Time between thoracic aortic surgery and fistula presentation	39/47	(82)	Hospital length of stay	70	(62)
			Length of follow-up	114	(100)
Acute presentation	114	(100)	Fistula-related death	114	(100)
Hypovolemic shock	107	(94)	Exact cause of death	21/21	(100)
Systemic infection	107	(94)	Time until death	21/21	(100)
Hemoptysis	104	(91)	Complications	110	(96)
Hematemesis	104	(91)	Graft-related complications	110	(96)
Thoracic pain	91	(80)	Additional thoracic surgery	114	(100)
Dyspnea	91	(80)	Additional surgery within 30 days	114	(100)
Dysphagia	91	(80)	Time until additional surgery	23/23	(100)
Melena	91	(80)	Aortic re-interventions	114	(100)
Diagnosis	98	(85)	Re-intervention within 30 days	114	(100)
Time between diagnosis and TEVAR	96	(84)	Indication re-interventions	23/23	(100)
Indication TEVAR	114	(100)	Time interval until re-intervention	23/23	(100)
General anesthesia	98	(86)	Antibiotics after discharge	104	(91)
Vascular access	98	(86)	Length antibiotic therapy	104	(91)

LSCA left subclavian artery

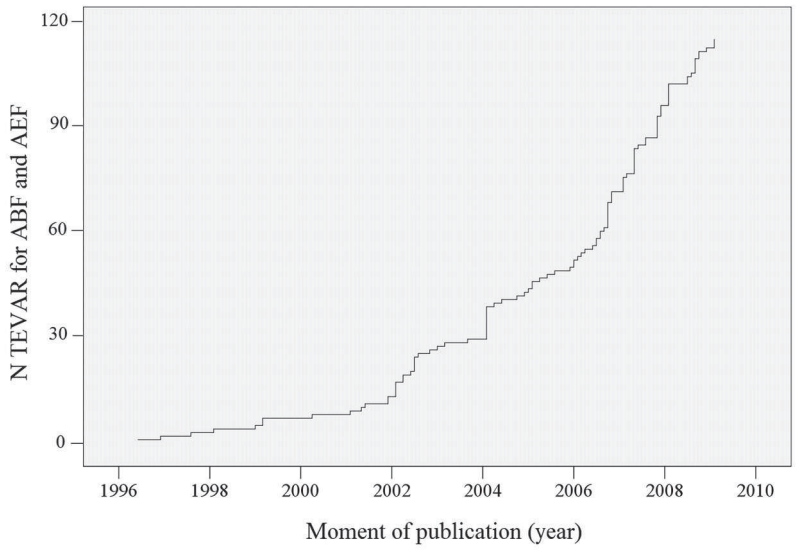

Figure 1. Number of patients undergoing TEVAR for ABF and AEF by publication date

Statistical analysis

Contingency tables with the chi-square test or Student *t* test were used to compare in-hospital outcomes of patients with ABF versus patients with AEF. Univariate and multivariate logistic regression analyses were performed to study the associations between patient and procedural characteristics and in-hospital mortality. Kaplan-Meier life-table analysis was used to compare fistula-related death after TEVAR between patients with ABF and those with AEF. Variables were examined only if the percentage of missing data was <15%. Statistical analyses were performed with SPSS software (version 15.0; SPSS, Chicago, IL, USA); P <0.05 was considered significant.

RESULTS

AORTOBRONCHIAL FISTULAS

Presentation and diagnosis

The most common cause of ABF development (figure 2) was previous thoracic aortic repair (36, 51%), including 32 open surgical procedures and 4 TEVARs. The interval between previous thoracic aortic repair and the presentation of the ABF and AEF is depicted in figure 3. Most patients presented with hemoptysis (59, 91%); 5 (8%) had dyspnea (table 2). The majority of patients (64, 65%) showed an acute presentation (symptoms or acute progression in <3 days); hypovolemic shock was present in 9 (13%) and systemic infection (bacteremia, mycotic aneurysms, mediastinitis or severe thoracic infections) in 6 (9%). An 11-year-old patient suffered from an intrapulmonary *Aspergillus* abscess secondary to acute myeloid leukemia, which caused an aortobronchial fistula.[45] Most patients underwent several imaging studies before the ABF was diagnosed; diagnosis was often based on clinical suspicion and findings of additional imaging. Practically all patients underwent computed tomographic angiography (CTA), which confirmed the diagnosis in 34 (48%). Angiography and bronchoscopy initially diagnosed the ABF in 12 (17%) and 5 (7%), respectively.

Operative characteristics

TEVAR was preferred over open thoracic aortic surgery in 42 (59%) patients because of comorbid conditions and in 29 (41%) patients because of required emergency treatment (table 3). General anesthesia was used for 60 (85%) cases; the endovascular device was inserted through the common femoral artery in 51 (72%) patients. Complete exclusion of the fistula during the initial TEVAR procedure was successfully achieved in nearly all (64, 90%) patients. Coverage of the left subclavian artery (LSA) was required to create a sufficient proximal landing zone in 6 (8%) cases. Two patients required additional thoracic surgery within 30 days (lung lobectomy and thoracotomy for hematothorax, respectively). Antibiotic therapy was prescribed in 30 (42%) patients for >2 weeks.

Table 2. Demographics and presentation

Variable	ABF (N = 71) N or mean (% or ±SEM)		AEF (N = 43) N or mean (% or ±SEM)	
Age (y)	64	(±1.8)	62	(±2.5)
Male gender	48	(69)	28	(68)
Presentation				
Hemoptysis	59	(91)	0	(0)
Hematemesis	0	(0)	33	(77)
Thoracic pain	1	(2)	9	(21)
Dyspnea	5	(8)	1	(2)
Dysphagia	0	(0)	6	(15)
Acute presentation	46	(65)	41	(95)
Hypovolemic shock	9	(13)	14	(33)
Systemic infection [a]	6	(9)	15	(36)
Diagnosis				
CTA	34	(48)	23	(53)
Angiography	12	(17)	8	(19)
Esophagoscopy			5	(12)
Bronchoscopy	5	(7)		
Other [c]	8	(13)	3	(7)
Missing	12	(17)	4	(11)
TEVAR within 24 hours after diagnosis	46	(65)	35	(81)

ABF aortobronchial fistula, *AEF* aortoesophageal fistula, *CTA* computed tomographic angiography, *Including bacteremia, mycotic aneurysms, mediastinitis, and severe thoracic infections.

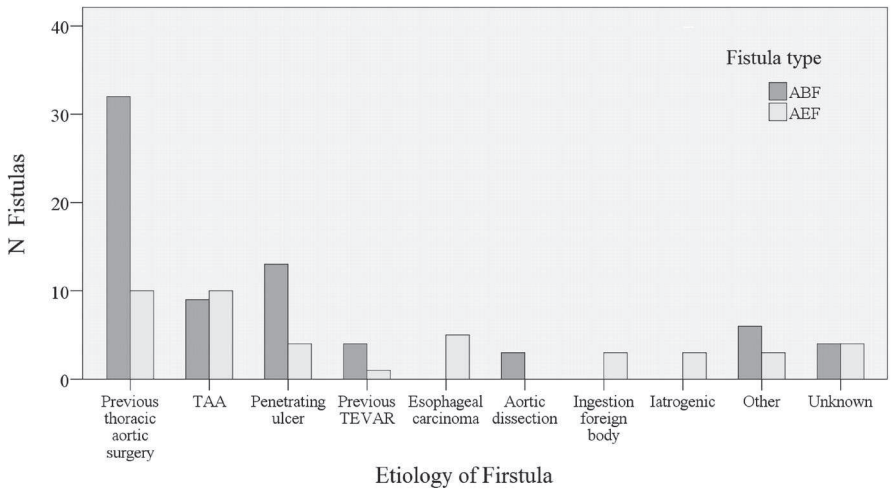

Figure 2. Etiology of aortobronchial and aortoesophageal fistulas
Other causes of fistula development include Barret's esophagus, ingestion of hydrochloric acid with suicidal intent, intrapulmonary *Aspergillus* abscess, pulmonary tuberculosis, previous lobectomy, previous esophagectomy, trauma, severe chronic obstructive pulmonary disease with bronchial stents, and resection of an intimal sarcoma of the descending aorta.

Table 3. Operative characteristics

Variable	Aortobronchial fistulas N = 71	(%)	Aortoesophageal fistulas N = 43	(%)
Indication TEVAR				
Emergency	29	(41)	27	(63)
Co-morbid conditions	42	(59)	16	(37)
General anesthesia	60	(85)	36	(84)
Vascular access				
Common femoral artery	51	(72)	31	(72)
Common iliac artery	11	(15)	1	(2)
Distal abdominal aorta	2	(3)	0	(0)
Brachial artery	2	(3)	0	(0)
Missing	5	(7)	11	(26)
Graft brand				
Medtronic Talent™	27	(38)	12	(28)
Gore Excluder™	11	(15)	2	(5)
Gore TAG™	9	(13)	1	(2)
Cook Zenith™	5	(7)	9	(21)
Other	11	(15)	6	(14)
Missing	4	(6)	12	(28)
LSCA covered	6	(8)	6	(14)
Antibiotic therapy (>2 weeks)	30	(42)	27	(63)
< 3 months	23	(32)	13	(30)
3 - 6 months	0	(0)	2	(5)
≥ 6 months	7	(10)	12	(28)

ABF aortobronchial fistula, *AEF* aortoesophageal fistula, *LSCA* left subclavian artery.
*In 5 AEF cases, the endograft was replaced by an aortic graft <3 weeks after TEVAR.

Outcomes

Median hospital length of stay was 5 days (mean 10, range 2–30); median follow-up was 22 months (mean 23, range 0.1–108). Two (3%) ABF patients died in-hospital after TEVAR owing to sepsis and respiratory failure, respectively (table 4). Seven (10%) patients experienced in-hospital complications and 11 (16%) had evidence of endoleak.

Over a median 125 days (mean 184; range 2–750) after TEVAR, 5 patients died of fistula-related causes (3 cases of sepsis and 2 delayed ruptures; figure 4). During follow-up, 18 thoracic aortic re-interventions were performed in 16 patients, most frequently a repeat TEVAR (n=13). Two patients underwent open thoracic aortic surgery. Transposition of the LSA was performed in 3 cases. Indications for re-interventions were endoleak (n=7), recurrent fistula and/or hemoptysis (n=7), brachial claudication after coverage of the LSA (n=3), and delayed rupture (n=1). Median time until aortic re-intervention was 1.4 months (mean 11.6; range 1 day to 108 months).

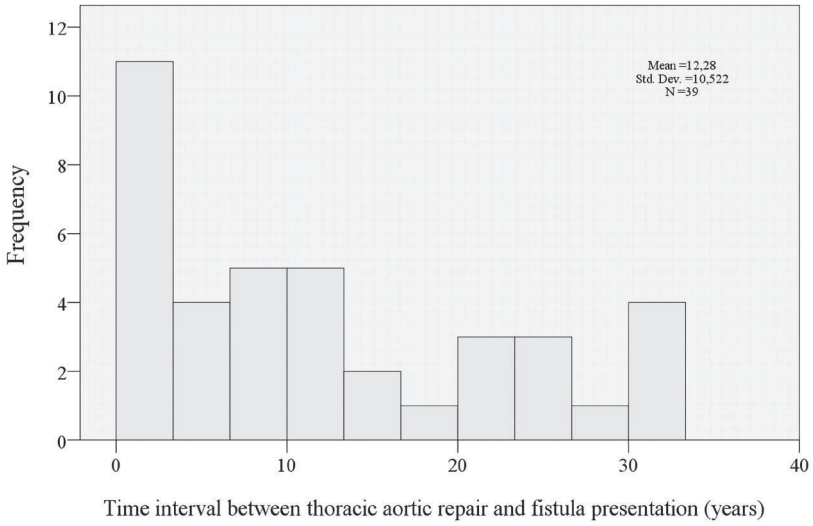

Figure 3. Time interval between previous thoracic aortic surgery or TEVAR and fistula presentation
Previous thoracic aortic surgery caused the development of the fistula in 42 cases of ABF and AEF; previous TEVAR was the cause in 5 cases. The exact time between these procedures and subsequent fistula presentation was not described in 8 cases.

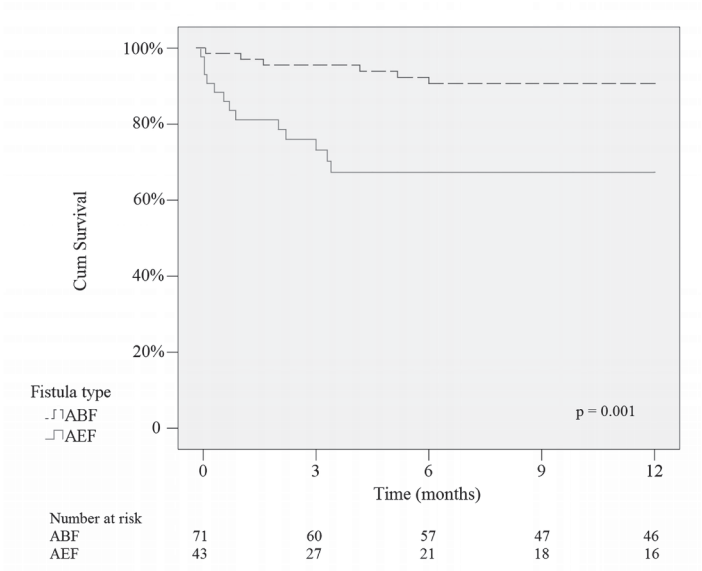

Figure 4. Fistula-related mortality during the first year after TEVAR for ABF and AEF

AORTESOPHAGEAL FISTULAS

Presentation and diagnosis

TAAs and previous open thoracic aortic surgery caused AEF in 10 (23%) patients (Fig. 2). The interval between previous thoracic aortic repair and presentation of the AEF is presented in figure 3. Most patients presented with hematemesis (33, 77%) and thoracic pain (9, 21%). Dysphagia was described in 6 (15%). The majority of patients (41, 95%) showed an acute presentation, accompanied by hypovolemic shock in 14 (33%) and systemic infection in 15 (36%). CTA was performed in most patients. AEF was initially diagnosed by CTA in 23 (53%) patients, while angiography and esophagoscopy were most important for diagnosing the fistula in 9 (19%) and 5 (12%) patients, respectively.

Table 4. Outcomes of TEVAR

Variable	Aortobronchial fistulas N = 71	(%)	Aortoesophageal fistulas N = 43	(%)
Technical success TEVAR	64	(90)	39	(91)
In-hospital death	2	(3)	8	(19)
In-hospital complications*	7	(10)	6	(14)
Sepsis and/or mediastinitis	1	(1)	2	(5)
Pulmonary complications	2	(3)	1	(2)
Renal failure	1	(1)	2	(5)
Paraplegia	0	(0)	1	(2)
Myocardial infarction	1	(1)	0	(0)
Iliac artery rupture	2	(3)	0	(0)
Endoleak †	11	(16)	2	(5)
Additional thoracic surgery < 30d	2	(3)	16	(37)
Additional thoracic surgery >30 d	1		3	
Esophageal surgery	0		15	
Mediastinal drainage	1		4	
Enterostomy	0		5	
Coloplasty	0		4	
Intercostal muscle flap	0		2	
Lobectomy	2		0	
Aortic re-intervention < 30 d	6	(9)	5	(12)
Aortic re-interventions > 30 d	10		3	
2nd TEVAR	13		2	
Open thoracic aortic surgery ‡	2		6	
Transposition of left SCA	3		0	

ABF aortobronchial fistula, A*EF* aortoesophageal fistula. Percentages for events occurring after discharge are not given because length of follow-up varied, which resulted in incomplete data.
*Does not include patients who expired during hospitalization. †9 type I and 4 type II.
‡Including replacement for an aortic graft (n=5) and drainage of the aneurysm sac in 2 cases.

Operative characteristics

TEVAR was preferred over open thoracic aortic surgery in 27 (67%) emergent cases and in 16 (33%) patients with comorbid conditions (table 3). General anesthesia was used for 36 (84%) procedures, during which the endovascular device was inserted through the common femoral artery in 31 (72%).

Complete exclusion of the fistula during the initial TEVAR procedure was successfully achieved in 39 (91%) patients. Coverage of the LSA was required for a sufficient proximal landing zone in 6 (14%). The thoracic endograft was replaced by an aortic graft in 5 (12%) AEF patients within 3 weeks after the endovascular procedure; 4 of these patients received a cryopreserved homograft.[74] Additional thoracic surgery was performed in 16 (37%) patients within 30 days, most commonly esophageal surgery (n=12). Antibiotic therapy was prescribed in 27 (63%) patients for >2 weeks.

Outcomes

Median hospital length of stay was 19 days (mean 23; range 0–77); median follow-up was 5 months (mean 10; range 0–80). Eight (19%) patients died in-hospital after TEVAR for AEF due to exsanguination (n=4), sepsis (n=3), or pulmonary arrest (n=1). Six additional patients died at a median 21 days (mean 38; range 0–102) due to fistula-related disease (4 cases of sepsis and 2 exsanguinations after delayed aortic rupture; figure 4). All patients dying in-hospital after TEVAR for ABF and AEF had an acute presentation. Univariate logistic regression analysis showed that hypovolemic shock (p=0.040) and previous aortic surgery (p=0.023) increased the risk of in-hospital mortality after TEVAR for AEF (table 5). However, multivariate logistic regression analysis revealed no significant associations.

AEF patients who had undergone esophageal surgery within 30 days after TEVAR had a significantly lower mortality (p=0.018) during 6 months of follow-up compared to patients who did not undergo esophageal reconstruction in the first 30 days (figure 5). A comparison of patients with and without open surgical esophageal reconstruction revealed no significant differences between the 2 groups with regard to the available patient and procedural variables, including history of thoracic aortic intervention before TEVAR, presence of hypovolemic shock at presentation, or the presence of systemic infection after TEVAR.

In-hospital complications and endoleak occurred in 6 (14%) and 2 (5%) patients, respectively (table 4). Thoracic aortic re-interventions were performed in 8 patients at a median interval of 3 weeks (mean 5 months; range 2 weeks to 18 months). In addition to the 5 endograft replacements, 2 patients underwent repeat TEVAR for recurrent bleeding and 1 patient had the aneurysm sac debrided during esophageal surgery.

Table 5. Preoperative variables affecting in-hospital mortality after TEVAR for AEF

Variable	OR	95% CI	p value
Age	1.03	0.97 - 1.09	0.400
Male gender	0.29	0.05 - 1.58	0.154
Previous aortic surgery	7.47	1.27 - 44.0	0.023
TAA	1.88	0.36 - 9.65	0.452
Hematemesis	-	-	0.999
Thoracic pain	1.49	0.24 - 9.36	0.673
Dysphagia	2.80	0.40 - 19.6	0.300
Hypovolemic shock	6.67	1.09 - 40.7	0.040
Systemic infection	1.31	0.25 - 6.88	0.748

Univariate logistic regression analysis of variables that were present in >10% of patients with aortoesophageal fistula (AEF). Age, gender, and variables with p<0.2 were integrated in a multivariate logistic regression model to calculate independent effects on in-hospital mortality, which did not show any significant risk factors. *OR* odds ratio, *CI* confidence interval, *TAA* thoracic aortic aneurysm.

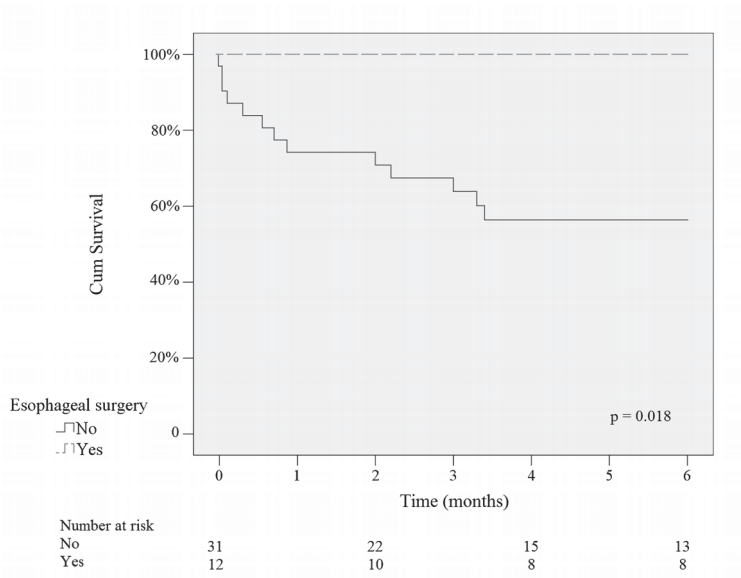

Figure 5. Survival of AEF patients with and without additional esophageal surgery within 30 days after TEVAR

CLINICAL DIFFERENCES BETWEEN ABF AND AEF

Patients with AEF had different presentations than patients with ABF (table 2). AEF patients more frequently had an acute presentation (95% versus 65% for ABF, p<0.001), with higher incidences of hypovolemic shock (33% versus 13%, p=0.012) and systemic infection (36% versus 9%, p<0.001) than patients with ABF. Patients with AEF more frequently underwent emergent

TEVAR (63%) compared to ABF patients (41%, p=0.023). After the endovascular procedures, additional thoracic surgery within 30 days was more frequently performed in AEF patients (37% versus 3%, p<0.001). Antibiotic therapy for >2 weeks was prescribed more frequently for AEF patients (63% versus 42%, p=0.013).

In-hospital mortality (table 4) was higher after TEVAR for AEF (19%) compared to AEF (3%; p=0.004). Kaplan-Meier life-table analysis showed that fistula-related death was increased during the first year after TEVAR for AEF compared to ABF (p=0.001; figure 4). Overall in-hospital complications and aortic re-interventions performed within 30 days after TEVAR did not differ significantly between ABF and AEF patients (table 4). However, replacement of the thoracic endograft was done only in AEF patients (5, 12%), while all endografts were left in situ in ABF patients during hospitalization (p=0.003).

DISCUSSION

Thoracic aortic fistulas are often caused by previous thoracic aortic surgery and usually present with excessive bleeding. Our analysis demonstrated that TEVAR for ABF is associated with acceptable results and low (3%) in-hospital mortality. Patients with AEF, however, showed a more acute presentation, with hypovolemic shock or systemic infection, and had a relatively high in-hospital mortality rate (~20%) after TEVAR.

The largest previously published study of thoracic aortic fistulas undergoing TEVAR described 8 patients with ABF.[51] In our current review, the outcomes of 114 patients who underwent TEVAR for ABF and AEF were analyzed, thus representing the largest number of patients undergoing TEVAR for these thoracic aortic lesions. Although the unique approach of this study allowed us to present in-hospital and follow-up outcomes of TEVAR for ABF and AEF, the study design had several limitations. Data were obtained from case reports and case series. Case reports regularly present exceptional cases, making these findings not necessarily applicable to the actual population. The influence of this publication bias may, however, be relatively small in this study because every AEF or ABF is a rare disorder and may offer sufficient new information for publication. Furthermore, physicians may be inclined to publish successful cases of TEVAR for ABF and AEF rather than unsuccessful cases. Another disadvantage is that our data were limited to information provided by the original articles. These disadvantages are important to consider when interpreting the presented results.

Thoracic aortic fistulas often arise after pseudoaneurysm formation secondary to aortic interventions, and several pathophysiological differences have been described between ABF and AEF. Although both types of fistulas connect the thoracic aorta with unsterile cavities, the first exposes the circulation to the open air and the latter to esophageal contents, which results in different presentations, symptom severity, and prognosis. Therefore, ABF and AEF require different management.

Aortobronchial fistulas affect the left lung more frequently than the right, which can be explained by the shorter distance from the descending thoracic aorta. Fistulas between the ascending aorta and the right lung are rare.[2] Although patients with ABF showed a less acute presentation than patients with AEF, ABF is lethal if left untreated, so urgent management is frequently indicated.[2] During open surgical repair of ABF, the thoracic aorta is most frequently approached by a posterolateral thoracotomy, followed by resection of the involved aortic area of the fistula and replacement of this segment by a prosthetic graft. In the literature, in-hospital mortality of open surgery for ABF ranges from 15% to 24%.[2,6] The first successful case of TEVAR for ABF was performed in 1993 by Campagna et al.[72] In the current manuscript, the in-hospital mortality of TEVAR for ABF treatment was only 3%. Hence, endovascular management appears to show superior perioperative results compared to open thoracic surgery, although several fistula-related deaths occurred during follow-up after TEVAR.

Although aortoenteric fistulas are most commonly located in the duodenum, they have been reported in all different portions of the gastrointestinal tract, from esophagus to rectum.[4] Aortoesophageal fistulas allow high-pressure aortic blood to enter the esophagus and unsterile esophageal contents to enter the aorta or the mediastinal cavity.[4] In 1914, Chiari first described the clinical triad of AEF: mid-thoracic pain, sentinel hemorrhage, eventually followed by exsanguination.[76] In our evaluation, AEF was often associated with shock and systemic infection. Therefore, immediate repair was often indicated after diagnosis of AEF.

The main goals in the management of AEF is to control hemorrhage and to prevent microbial contamination of the mediastinum.[5] Open surgery allows repair of the involved aortic and esophageal components of the fistula, as well as drainage of the infected mediastinum. Open thoracic surgery will, therefore, be offered to most patients with AEF who are in relatively good physical condition. The most frequently used approach for AEF repair is a left thoracotomy, followed by aortic replacement with a prosthetic or cryopreserved homograft, or an extra-anatomical bypass in case of severe mediastinal sepsis.[5,74] Open thoracic surgery is, however, associated with high mortality rates as a result of its invasiveness, particularly in patients who are in poor condition or are suffering from hemorrhagic shock. Precise mortality rates of open surgery for AEF are missing in the literature due to the rarity of AEF.

TEVAR is less invasive than open thoracic surgery and allows prompt exclusion of the AEF, preventing exsanguination. In this evaluation, the in-hospital mortality of TEVAR for AEF was 18%, which is considerably higher than in patients who underwent TEVAR for ABF, but mortality of open thoracic surgery for AEF is thought to be even higher.[1,4,5] Unfortunately, additional thoracic surgery and/or aortic re-interventions were often required after TEVAR, and numerous fistula-related deaths occurred after discharge due to sepsis and recurrent bleeding. Additional esophageal surgery within the first month after TEVAR for AEF was associated with lower mortality during the first half year after TEVAR in our analysis. This finding might be partially explained by the fact that some patients who received only TEVAR died before esophageal

surgery could be performed. However, several deaths occurred up to 3 months after TEVAR and may hypothetically have been prevented by earlier open surgical re-intervention after TEVAR (figure 5). These patients who did not undergo additional esophageal surgery continued to be exposed to esophageal contents, resulting in ongoing risks on graft infection, mediastinitis, and sepsis. Therefore, more aggressive surgical management supported by intensive antibiotic therapy may potentially be justified after TEVAR for AEF. TEVAR could serve as a bridge to surgery in emergency AEF cases, with definitive open operative repair undertaken as soon as possible after optimizing the condition of the patient. Topel and colleagues recently demonstrated promising results with this combined approach for AEF, using primary endovascular repair followed by replacement of the endograft with a cryopreserved homograft.[74]

CONCLUSION

TEVAR is associated with superior outcomes in patients with ABF. Endovascular management of AEF is associated with relatively high in-hospital and long-term mortality and should not be considered definitive surgery. TEVAR could serve as a bridge to surgery for emergency cases of AEF only, with definitive open surgical repair undertaken as soon as possible.

REFERENCES

1. Carter R, Mulder GA, Snyder EN, Jr. et al. Aortoesophageal fistula. Am J Surg 1978; 136:26-30.
2. Piciche M, De PR, Fabbri A et al. Postoperative aortic fistulas into the airways: etiology, pathogenesis, presentation, diagnosis, and management. Ann Thorac Surg 2003; 75:1998-2006.
3. Eggebrecht H, Baumgart D, Radecke K et al. Aortoesophageal fistula secondary to stent-graft repair of the thoracic aorta. J Endovasc Ther 2004; 11:161-167.
4. Hollander JE, Quick G. Aortoesophageal fistula: a comprehensive review of the literature. Am J Med 1991; 91:279-287.
5. Prokakis C, Koletsis E, Apostolakis E et al. Aortoesophageal fistulas due to thoracic aorta aneurysm: surgical versus endovascular repair. Is there a role for combined aortic management? Med Sci Monit 2008; 14:RA48-RA54.
6. MacIntosh EL, Parrott JC, Unruh HW. Fistulas between the aorta and tracheobronchial tree. Ann Thorac Surg 1991; 51:515-519.
7. Dake MD, Miller DC, Semba CP et al. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. N Engl J Med 1994; 331:1729-1734.
8. Mitchell RS, Miller DC, Dake MD. Stent-graft repair of thoracic aortic aneurysms. Semin Vasc Surg 1997; 10:257-271.
9. Nienaber CA, Fattori R, Lund G et al. Nonsurgical reconstruction of thoracic aortic dissection by stent-graft placement. N Engl J Med 1999; 340:1539-1545.
10. Lew WK, Rowe VL, Cunningham MJ et al. Endovascular management of mycotic aortic aneurysms and associated aortoaerodigestive fistulas. Ann Vasc Surg 2009; 23:81-89.
11. Pitton MB, Herber S, Schmiedt W et al. Long-term follow-up after endovascular treatment of acute aortic emergencies. Cardiovasc Intervent Radiol 2008; 31:23-35.
12. Kpodonu J, Rodriguez-Lopez JA, Ramaiah VG et al. Endoluminal graft therapy for the treatment of an aorto-bronchial fistula: mid-term follow-up. J Card Surg 2008; 23:530-532.
13. Kenny D, Margey R, Turner MS et al. Self-expanding and balloon expandable covered stents in the treatment of aortic coarctation with or without aneurysm formation. Catheter Cardiovasc Interv 2008; 72:65-71.
14. Zuber-Jerger I, Hempel U, Rockmann F et al. Temporary stent placement in 2 cases of aortoesophageal fistula. Gastrointest Endosc 2008; 68:599-602.
15. Civilini E, Bertoglio L, Melissano G et al. Aortic and esophageal endografting for secondary aortoenteric fistula. Eur J Vasc Endovasc Surg 2008; 36:297-299.
16. Akaraviputh T, Sriprayoon T, Prachayakul V et al. Endoscopic diagnosis of secondary aortoesophageal fistula. Endoscopy 2008; 40 Suppl 2:E90.
17. Seet E, Beevee S, Cheng A et al. The Sengstaken-Blakemore tube: uses and abuses. Singapore Med J 2008; 49:e195-e197.

18. Saratzis N, Melas N, Saratzis A et al. Minimally invasive endovascular intervention in emergent and urgent thoracic aortic pathologies: single center experience. Hellenic J Cardiol 2008; 49:312-319.
19. Chan YC, Ting AC, Law S et al. Secondary infection of a pre-existing thoracic aortic aneurysm by iatrogenic oesophageal perforation with aorta-oesophageal fistula formation. Eur J Cardiothorac Surg 2008.
20. Sachithanandan A, McCafferty I, Riley P et al. Emergency endovascular stent graft repair of aorto-bronchial fistulas postcoarctation repair. J Card Surg 2007; 22:524-526.
21. Wheatley GH, III, Nunez A, Preventza O et al. Have we gone too far? Endovascular stent-graft repair of aortobronchial fistulas. J Thorac Cardiovasc Surg 2007; 133:1277-1285.
22. Vallbohmer D, Holscher AH, Brunkwall J et al. Management of a traumatic aortoesophageal fistula in a patient with a right-sided aortic arch. J Thorac Cardiovasc Surg 2007; 134:1375-1376.
23. Min X, Guo J, Zhan Q et al. Aortoesophageal fistula caused by descending aortic pseudoaneurysm: one case report. Chinese Medical Journal 2007; 120:2149-2150.
24. Kokotsakis J, Misthos P, Athanasiou T et al. Endovascular stenting for primary aortobronchial fistula in association with massive hemoptysis. Tex Heart Inst J 2007; 34:369-372.
25. Taylor BJ, Stewart D, West P et al. Endovascular repair of a secondary aortoesophageal fistula: a case report and review of the literature. Ann Vasc Surg 2007; 21:167-171.
26. Takahashi Y, Sasaki Y, Shibata T et al. Homemade endovascular treatment of postoperative aortobronchial fistulas. Jpn J Thorac Cardiovasc Surg 2006; 54:301-303.
27. Baril DT, Carroccio A, Ellozy SH et al. Evolving strategies for the treatment of aortoenteric fistulas. J Vasc Surg 2006; 44:250-257.
28. Amabile P, Rollet G, Vidal V et al. Emergency treatment of acute rupture of the descending thoracic aorta using endovascular stent-grafts. Ann Vasc Surg 2006; 20:723-730.
29. Iyer VS, Mackenzie KS, Tse LW et al. Early outcomes after elective and emergent endovascular repair of the thoracic aorta. J Vasc Surg 2006; 43:677-683.
30. Quintana AL, Aguilar EM, Heredero AF et al. Aortobronchial fistula after aortic coartactation. J Thorac Cardiovasc Surg 2006; 131:240-243.
31. Ikeda Y, Morita N, Kurihara H et al. A primary aortoesophageal fistula due to esophageal carcinoma successfully treated with endoluminal aortic stent grafting. J Thorac Cardiovasc Surg 2006; 131:486-487.
32. Marcheix B, Lamarche Y, Perrault P et al. Endovascular management of pseudo-aneurysms after previous surgical repair of congenital aortic coarctation. Eur J Cardiothorac Surg 2007; 31:1004-1007.
33. Ting AC, Cheng SW, Ho P et al. Endovascular stent graft repair for infected thoracic aortic pseudoaneurysms--a durable option? J Vasc Surg 2006; 44:701-705.
34. Metz R, Kimmings AN, Verhagen HJ et al. Aortoesophageal fistula successfully treated by endovascular stent-graft. Ann Thorac Surg 2006; 82:1117-1119.

35. Pirrelli S, Bozzani A, Arici V et al. Endovascular treatment of acute haemoptysis secondary to aortobronchial fistula. Eur J Vasc Endovasc Surg 2006; 32:366-368.
36. Marone EM, Baccari P, Brioschi C et al. Surgical and endovascular treatment of secondary aortoesophageal fistula. J Thorac Cardiovasc Surg 2006; 131:1409-1410.
37. Zamora CA, Sugimoto K, Tsuji Y et al. Stent-grafting of an infected aortoesophageal fistula following ingestion of a fish bone. J Endovasc Ther 2005; 12:522-523.
38. Kaw LL, Jr., Owens EL, Kansal N. Endovascular repair of an aortopulmonary fistula via the axillary artery. Ann Vasc Surg 2005; 19:487-491.
39. Bos WT, Verhoeven EL, Zeebregts CJ et al. Emergency endovascular stent grafting for thoracic aortic pathology. Vascular 2007; 15:12-17.
40. Assink J, Vierhout BP, Snellen JP et al. Emergency endovascular repair of an aortoesophageal fistula caused by a foreign body. J Endovasc Ther 2005; 12:129-133.
41. Dagenais F, Normand JP, Turcotte R et al. Changing trends in management of thoracic aortic disease: where do we stand with thoracic endovascular stent grafts? Can J Cardiol 2005; 21:173-178.
42. Munneke G, Loosemore T, Smith J et al. Pseudoaneurysm after aortic coarctation repair presenting with an aortobronchial fistula successfully treated with an aortic stent graft. Clin Radiol 2006; 61:104-108.
43. Gonzalez-Fajardo JA, Gutierrez V, Martin-Pedrosa M et al. Endovascular repair in the presence of aortic infection. Ann Vasc Surg 2005; 19:94-98.
44. bdul-Ghani A, Pisipati S, McWilliams R et al. Aorto-bronchial fistula following aortic and bronchial stenting of a thoracic aneurysm. Eur J Cardiothorac Surg 2006; 29:419-421.
45. Islam S, Williams DM, Teitelbaum DH. Aortobronchial fistula from invasive Aspergillus infection of the lung: an endovascular approach to repair. J Pediatr Surg 2005; 40:e19-e22.
46. Bonavina L, Lupattelli T, Bona D et al. Bronchoesophageal fistula after endovascular repair of ruptured aneurysm of the descending thoracic aorta. J Vasc Surg 2005; 41:712-714.
47. Smaroff GG, Keenan R.J., Birdas T, Ju B. Aortobronchial fistula resulting from bronchial stents treated with endovascular stent grafting. American College of Chest Physicians. Cardiovascular I . 2004. Ref Type: Conference Proceeding
48. Martin M, Steele S, Mullenix P et al. Endoscopic diagnosis of a clinically silent aortoesophageal fistula: case report and review of the literature. Ann Vasc Surg 2004; 18:352-356.
49. Nishibe T, Koizumi J, Kudo F et al. Successful endovascular stent-graft treatment for an aortoesophageal fistula caused by a descending thoracic aortic aneurysm: report of a case. Surg Today 2004; 34:529-531.
50. Numan F, Arbatli H, Yagan N et al. Endovascular treatment of an aortobronchial fistula. Cardiovasc Intervent Radiol 2004; 27:71-73.
51. Bockler D, Schumacher H, Schwarzbach M et al. Endoluminal stent-graft repair of aortobronchial fistulas: bridging or definitive long-term solution? J Endovasc Ther 2004; 11:41-48.

52. Ramaiah V, Rodriguez-Lopez J, Diethrich EB. Endografting of the thoracic aorta. J Card Surg 2003; 18:444-454.
53. Leobon B, Roux D, Mugniot A et al. Endovascular treatment of thoracic aortic fistulas. Ann Thorac Surg 2002; 74:247-249.
54. Guillem P, Porte H, Techer E et al. Aortoesophageal fistula of uncommon origin: perforation of a Barrett's ulcer. Dis Esophagus 2003; 16:259-260.
55. Orend KH, Scharrer-Pamler R, Kapfer X et al. Endovascular treatment in diseases of the descending thoracic aorta: 6-year results of a single center. J Vasc Surg 2003; 37:91-99.
56. Alric P, Berthet JP, Branchereau P et al. Endovascular repair for acute rupture of the descending thoracic aorta. J Endovasc Ther 2002; 9 Suppl 2:II51-II59.
57. Oppenheimer R, Brotherton L. Aortobronchial fistula: a rare etiology for hemoptysis. Ear Nose Throat J 2002; 81:257-259.
58. Haulon S, Koussa M, Beregi JP et al. Stent-graft repair of the thoracic aorta: short-term results. Ann Vasc Surg 2002; 16:700-707.
59. Van Doorn RC, Reekers J, de Mol BA et al. Aortoesophageal fistula secondary to mycotic thoracic aortic aneurysm: endovascular repair and transhiatal esophagectomy. J Endovasc Ther 2002; 9:212-217.
60. D'Ancona G, Dagenais F, Bauset R. Endoluminal stenting of the aorta as treatment of aortoesophageal fistula due to primary aortic disease. Tex Heart Inst J 2002; 29:216-217.
61. Thompson CS, Ramaiah VG, Rodriquez-Lopez JA et al. Endoluminal stent graft repair of aortobronchial fistulas. J Vasc Surg 2002; 35:387-391.
62. Bond SE, McGuinness CL, Reidy JF et al. Repair of secondary aortoesophageal fistula by endoluminal stent-grafting. J Endovasc Ther 2001; 8:597-601.
63. Burks JA, Jr., Faries PL, Gravereaux EC et al. Endovascular repair of bleeding aortoenteric fistulas: a 5-year experience. J Vasc Surg 2001; 34:1055-1059.
64. Yoo JH, Lee CT, Shim YS et al. Aortobronchial fistula presenting as recurrent hemoptysis and successfully treated with an endovascular stent graft. Respiration 2001; 68:537-539.
65. Caiati JM, Marin ML, Flores RM et al. Endovascular management of an aortobronchial fistula arising after resection of a primary aortic sarcoma: a case report. Vasc Surg 2001; 35:73-79.
66. Kramer S, Pamler R, Seifarth H et al. Endovascular grafting of traumatic aortic aneurysms in contaminated fields. J Endovasc Ther 2001; 8:262-267.
67. Kato N, Tadanori H, Tanaka K et al. Aortoesophageal fistula-relief of massive hematemesis with an endovascular stent-graft. Eur J Radiol 2000; 34:63-66.
68. Miyata T, Ohara N, Shigematsu H et al. Endovascular stent graft repair of aortopulmonary fistula. J Vasc Surg 1999; 29:557-560.
69. Karmy-Jones R, Lee CA, Nicholls SC et al. Management of aortobronchial fistula with an aortic stent-graft. Chest 1999; 116:255-257.

70. Semba CP, Sakai T, Slonim SM et al. Mycotic aneurysms of the thoracic aorta: repair with use of endovascular stent-grafts. J Vasc Interv Radiol 1998; 9:33-40.
71. Oliva VL, Bui BT, Leclerc G et al. Aortoesophageal fistula: repair with transluminal placement of a thoracic aortic stent-graft. J Vasc Interv Radiol 1997; 8:35-38.
72. Campagna AC, Wehner JH, Kirsch CM et al. Endovascular stenting of an aortopulmonary fistula presenting with hemoptysis. A case report. J Cardiovasc Surg (Torino) 1996; 37:643-646.
73. Chuter TA, Ivancev K, Lindblad B et al. Endovascular stent-graft exclusion of an aortobronchial fistula. J Vasc Interv Radiol 1996; 7:357-359.
74. Topel I, Stehr A, Steinbauer MG et al. Surgical strategy in aortoesophageal fistulae: endovascular stentgrafts and in situ repair of the aorta with cryopreserved homografts. Ann Surg 2007; 246:853-859.
75. Mok VW, Ting AC, Law S et al. Combined endovascular stent grafting and endoscopic injection of fibrin sealant for aortoenteric fistula complicating esophagectomy. J Vasc Surg 2004; 40:1234-1237.
76. Chiari H. Ueber Premdkorperverletzung des Oesophagus mit Aortenperforation. Ber Klin Wochenschr 1914; 51

Chapter 11

Aortic Endograft Sizing in Trauma Patients with Hemodynamic Instability

Journal of Vascular Surgery 2010;52:39-44

Frederik H.W. Jonker,[1] MD
Hence JM Verhagen,[2] MD, PhD
Hamid Mojibian,[3] MD
Kimberly A. Davis,[4] MD
Frans L. Moll,[5] MD, PhD
Bart E. Muhs,[1] MD, PhD.

[1] Sections of Vascular Surgery and Interventional Radiology, Yale University School of Medicine, New Haven, Connecticut, USA
[2] Section of Vascular Surgery, Erasmus University Medical Center, Rotterdam, the Netherlands
[3] Section of Interventional Radiology, Yale University School of Medicine, New Haven, Connecticut, USA
4 Section of Trauma, Surgical Critical Care and Surgical Emergencies, Yale University School of Medicine, New Haven, Connecticut, USA
5 Section of Vascular Surgery, University Medical Center Utrecht, the Netherlands

ABSTRACT

Objectives

To investigate changes in aortic diameter in hemodynamically unstable trauma patients, and the implications for sizing of thoracic aortic endovascular repair (TEVAR) in patients with traumatic thoracic aortic injury (TTAI).

Methods

We retrospectively evaluated all trauma patients that were admitted with hemodynamic instability (mean arterial pressure < 95mmHg, and a pulse ≥100 beats/minute) and underwent computed tomography (CT) of the thorax and abdomen both at admission and at another moment (control CT scan), at the Yale New Haven Hospital between 2002 and 2009. The CT examinations were reviewed in a blinded fashion and the aortic diameter was measured at 6 different levels by a cardiovascular radiologist. Differences in aortic diameter between the initial CTs obtained in the trauma bay and the control CTs were compared using the paired Student's t-test.

Results

Forty-three patients were identified, including 32 males. Mean age was 37±16 years, mean injury severity score was 26±15, the mean pulse and blood pressure were 122 beats/min and 103/63mmHg, respectively. Overall, the mean aortic diameter was significantly larger at the control CT examinations compared with the initial CT examinations while hemodynamically unstable, at all evaluated levels. Among patients with a pulse ≥ 130/min, the mean increase in aortic diameter was most consistent at the level of the mid descending thoracic aorta (DTA, +12.6%, p=0.003) and at the level of the infrarenal aorta (+12.6%, p=0.004).

Conclusion

The aortic diameter decreases dramatically in trauma patients with hemodynamic instability. This decrease in aortic diameter could theoretically lead to inaccurate aortic measurements and undersizing of the endograft in hemodynamically unstable TTAI patients requiring TEVAR. Further research is needed to better predict the actual aortic diameters in individual hemodynamically unstable patients requiring endovascular aortic repair.

INTRODUCTION

Traumatic thoracic aortic injury (TTAI) is the second most common cause of death in trauma patients, accounting for about 8.000 deaths per year in the United States.[1,2] Thoracic endovascular aortic repair (TEVAR) has recently offered a less invasive method for the management of TTAI. Large series and meta-analyses have shown that endovascular repair of TTAI significantly reduces the in-hospital mortality and morbidity compared with conventional open surgical repair,[3-7] and that a major shift has occurred in favour of endovascular management of TTAI.[3,8,9] A substantial part of admitted patients with TTAI have multiple injuries with associated hemodynamic instability or hypovolemic shock, a leading cause of death in trauma patients worldwide.[10]

Hemodynamic forces may result in significant conformation changes of the thoracic aorta.[11] However, currently it remains unclear how the aorta reacts to hemodynamic instability or hypovolemic shock. A decrease in the aortic diameter of 30% has been described in an anecdotal case report of a hypovolemic patient with TTAI.[12] Pre-operative computed tomography angiography (CTA) is typically used for endograft sizing in patients requiring TEVAR, and considerably decreased aortic diameters in patients undergoing CTA could result in inaccurate aortic measurements and undersizing of the endograft.

In the present study, potential aortic changes were investigated in trauma patients that were admitted with hemodynamic instability, in order to better understand the dynamic morphology of the aorta, and to optimize endograft sizing in TTAI patients.

METHODS

Study population

A retrospective trauma registry inquiry (Clinical Data Management, Denver, Co) identified all trauma patients that were admitted with hemodynamic instability at the emergency department of an ACS verified and state designated level I trauma center, between July 1st 2002 and July 1st 2009. The study was approved by the institutional review committee of the Yale University School of Medicine. Admission demographics and recorded vital signs were used to select the patients suffering from hemodynamic instability following traumatic injuries. Inclusion criteria were: 1) multiple traumatic injuries, 2) a mean arterial pressure ≤ 95 mmHg and pulse ≥ 100 beats/min, 3) computed tomography (CT) examinations of the thorax and abdomen were performed both at admission and at another moment when the patients was thought to be hemodynamically stable (control CT scan). Exclusion criteria were: 1) patients younger than 18 years, 2) incomplete data sets, and 3) a time interval between both CT examinations of more than 12 months.

Data collection

All CT examinations were performed on either a General Electric (Milwaukee, WI) 4-slice or 64-slice Volume Computed Tomography System. The CT studies were non-gated, and were reviewed in a blinded fashion by a cardiovascular radiologist with 5 years of experience. Axial CT images were used to measure the aortic diameter at 6 different levels including the ascending aorta at the level of the pulmonary artery, the mid aortic arch, the proximal descending thoracic aorta (DTA) at the level of the termination of the aortic arch, the mid DTA, the distal DTA 1 cm above the celiac axis, and the infrarenal abdominal aorta. If the aorta was angulated, multiplanar reformations were used to measure the proper aortic diameter perpendicular to the long axis of the aorta. Subsequently, the maximum and minimum diameters of the inferior vena cava (IVC) were measured at the level of mid infrarenal IVC halfway between the most superior renal vein and the convergence of the common iliac veins.

Statistical analysis

The diameter measurements of aorta and IVC were compared in all patients between the CTs at admission, and the control CTs. The paired Student's t-test was used to investigate potential diameter differences in the overall cohort, and among patients with a pulse above 130 / minute. SPSS software version 15.0 was used for all statistical analyses, a *P* Value < 0.05 was considered statistically significant.

RESULTS

Admission characteristics

Forty-three patients were selected for evaluation. The median time interval between the measurement of the vital signs and the CT examination was 30 minutes (interquartile range 26 minutes; range 0 to 97 minutes), and the median time interval between the CT examination at admission to the emergency department while hemodynamically unstable, and the control CT examination was 11 days (interquartile range 28 days, range 1.5 days to 351 days). The mean age was 37.2 ±16 years (range 18 to 90 years), and 74% were male (table 1). Mean pulse was 121.6 ±18 beats/min (range 100 to 170), and 27.9% (n=12) had a pulse ≥ 130/min. The mean arterial pressure (MAP) of the cohort was 77.3 mmHg (range 54.3 to 94 mmHg), the mean respiratory rate was 21.9 (range 12 to 35), and 16.3% (n=7) were already intubated and mechanically ventilated when the first vital signs were recorded at the emergency department.

Table 1. Admission characteristics

	N or mean	(% or ±SD)
Age	37.2	(±16)
Male gender	32	(74)
Trauma		
Motor vehicle crash	28	(65)
Gunshot / stab wounds	7	(16)
Fall	8	(19)
Injury Severity Score	25.7	(±16)
Vital signs		
Pulse	121.6	(±18)
Systolic pressure	103.4	(±16)
Diastolic pressure	63.3	(±12)
MAP	77.3	(±12)
Respiratory rate	21.9	(±6.1)
Hematocryt	35.5	(±7.5)

MAP mean arterial pressure, *SD* standard deviation

Changes in aortic diameter

Overall, the mean aortic diameter was significantly larger at the control CT examinations compared with the CT examinations at admission while hemodynamically unstable, at all evaluated levels (table 2). The overall mean increase in aortic diameter varied from 3.3% ($p=0.012$) at the level of the ascending aorta, to 11.2% ($p<0.001$) at the level of the infrarenal aorta (table 2). The increase in aortic diameter varied considerably among individual patients as well, and in some cases however, no increase in aortic diameter, or even a smaller aortic diameter was observed on the control CT examination (table 2). The correlation between the MAP of the trauma patients while hemodynamically unstable, and the increase in aortic diameter at the level of the mid DTA on the control CT is depicted in figure 1.

The mean increase in aortic diameter at the different levels appeared to be larger among patients admitted with a pulse ≥ 130 (table 3, figure 2). In this subgroup, the mean increase in aortic diameter was most consistent at the level of the mid DTA (+12.6%, $p=0.003$) and at the level of the infrarenal aorta (+12.6%, $p=0.004$). At the remaining levels, the mean increase in aortic diameter failed to reach statistical significance (table 3), most likely due to the small sample size (n=12).

Table 2. Mean diameter changes of the aorta and IVC (N=43)

Level	HD unstable (mm)	Control (mm)	Diff (mm)	Diff (%)	Range (%)	p value
Aorta						
Ascending	27.4	28.3	0.9	3.3	-10.8 - 19.8	0.012
Arch	22.2	23.6	1.4	6.3	-7.5 - 26.1	0.011
Proximal DTA	21.9	23.1	1.2	5.5	-6.7 - 38.8	0.010
Mid DTA	19.2	21.1	1.8	9.4	-8.0 - 40.0	<0.001
Distal DTA	18.1	19.4	1.3	7.2	-7.9 - 54.3	<0.001
Infrarenal	14.3	15.9	1.6	11.2	-5.9 - 44.9	<0.001
Inferior vena cava						
Max diameter	19.9	21.6	1.7	8.5	-8.3 - 49.1	0.002
Min diameter	11.6	15.8	4.2	36.2	-12.8 - 203.1	<0.001

IVC inferior vena cava, *DTA* descending thoracic aorta, *HD* unstable hemodynamically unstable, Diff difference in mm

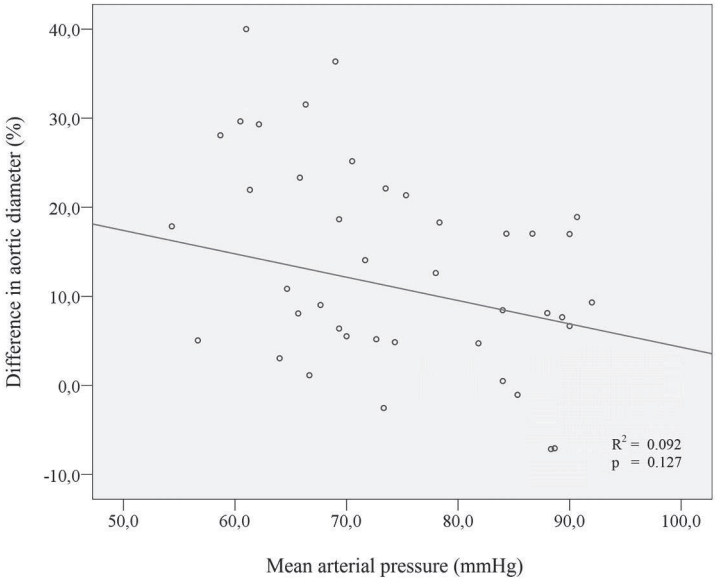

Figure 1. MAP of trauma patients while hemodynamically unstable, and increase in aortic diameter at the level of the mid DTA on the control CT
MAP mean arterial pressure, *DTA*: descending thoracic aorta.

Table 3. Mean diameter changes of the aorta and IVC in patients with a pulse ≥ 130/min (N=12)

Level	HD unstable (mm)	Control (mm)	Diff (mm)	Diff (%)	Range (%)	p value
Aorta						
Ascending	26.2	27.3	1.1	4.2	-1.3 - 17.6	0.184
Arch	21.1	22.8	1.7	8.1	-7.5 - 16.3	0.382
Proximal DTA	20.3	22.9	2.6	12.8	-3.2 - 38.8	0.068
Mid DTA	18.3	20.6	2.3	12.6	6.7 - 36.4	0.003
Distal DTA	18.2	19.4	1.2	6.6	-7.3 - 25.7	0.133
Infrarenal	14.3	16.1	1.8	12.6	3.0 - 33.9	0.004
Inferior vena cava						
Max diameter	19.3	22.2	2.9	15.0	-6.4 - 48.7	0.028
Min diameter	11.5	16.1	4.6	40.0	-12.8 - 170.0	0.016

IVC inferior vena cava, *DTA* descending thoracic aorta, *HD* unstable hemodynamically unstable, Diff difference in mm

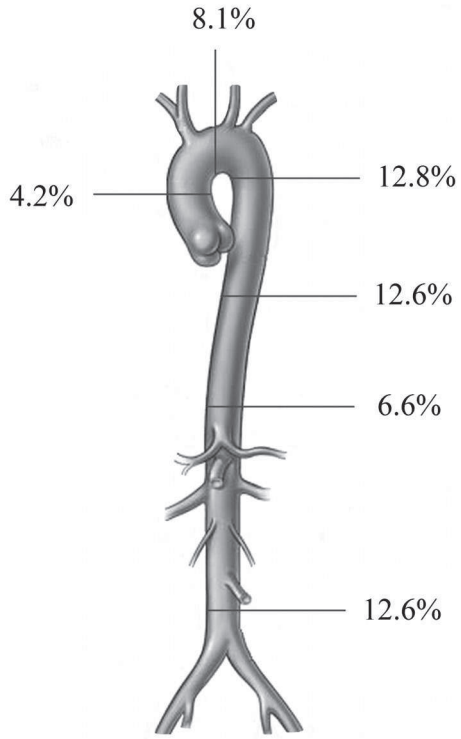

Figure 2. Mean difference in aortic diameter in patients with a pulse ≥ 130/min
The mean increase in aortic diameter on the control CT was most consistent at the level of the mid descending thoracic aorta (p=0.003) and at the level of the infrarenal aorta (p=0.004), the mean increase in aortic diameter failed to reach statistical significance at the remaining levels.

Conformational changes of the IVC

Overall, the maximum and minimum IVC diameters were 8.5% (p=0.002) and 36.2% (p<0.001) larger on the control CT examination compared with the CT at admission while hemodynamically unstable. Since the increase in minimum IVC diameter was substantially larger than the increase in the maximum IVC diameter, it appears that the shape of the IVC changed as well, from an elliptic shape to a more round shape on the control CTs. The change in IVC measurements varied considerably among individual patients, and in some cases no increase or even a decrease in the minimum and/or maximum diameter of the IVC was observed on the control CT examination (table 2).

The mean increase in IVC diameters appeared to be larger among patients admitted with a pulse ≥ 130 (table 3). In this group, the maximum and minimum IVC diameters increased with 15.0% (p=0.028) and 40.0% (p=0.016), respectively.

DISCUSSION

Endovascular repair has shown to reduce the in-hospital mortality and morbidity of TTAI compared with conventional open surgical repair,[3-7] and a major shift has recently occurred from open surgery towards endovascular management of TTAI.[3,8,9] However, endovascular management of TTAI is still plagued by considerable endoleak rates, typically ranging between 2.8% to 14.3%.[3-6,13-15] The majority of these endoleaks are proximal type 1 endoleaks, which often require re-intervention or even explantation of the endograft.[4,14,15]

Several factors may attribute to the relatively high occurrence of endoleak in this patient group. Blunt TTAI is typically located at the aortic isthmus distal to the left subclavian artery.[4,16-18] Endografts may conform poorly to the inner curvature of the aortic arch, which may result in increased risks of endograft-related complications such as endoleak. The emergency nature may also contribute to high endoleak rates. For emergency TEVAR, physicians can only use those endografts that are available as stock. In addition, urgent situations may not allow optimal endograft sizing and deployment, which may increase risks of endoleak.

The results of this study suggest another factor that may lead to inadequate endograft sizing, namely the influence of hemodynamic instability on the aortic diameter. A considerable percentage of patients with TTAI are admitted with hemodynamic instability and/or in hypovolemic shock as a result of associated injuries. We observed that the aortic diameter was significantly smaller, from the ascending thoracic aorta to the infrarenal aorta, on the CT examination of hemodynamically unstable trauma patients, compared with the control CT. In some cases, the aortic diameter was up to 40% larger on the control CT examination compared with the CT examination while hemodynamically unstable at admission. A theoretic explanation for this observation may be that substantial blood loss led to a shortage in circulating blood volume, which subsequently may

have resulted in decreased pressure on the aortic wall, causing the aorta to collapse. However, reliable data regarding the circulating blood volume or the resuscitation status of the trauma patients were not available for this evaluation, so we cannot confirm this hypothesis. Van Prehn et al have previously described a hypovolemic patient with TTAI that successfully underwent TEVAR, but the post-operative CTA showed an increase in aortic diameter of 30%.[12] Except for this case report, no studies have previously investigated the influence of hemodynamic instability or hypovolemic shock on the aortic diameter to our knowledge, and the present patient series therefore represents the first study that has demonstrated significantly decreased aortic diameters in hemodynamically unstable trauma patients.

These findings may have implications for the endovascular management of acute thoracic aortic disease. Pre-operative CTA is typically used for aortic measurements and endograft sizing in patients requiring TEVAR. However, considerably decreased aortic diameters in a hemodynamically unstable TTAI patient undergoing CTA likely result in inaccurate aortic measurements and undersizing of the endograft. Theoretically, an inadequate proximal seal of the endograft may lead to increased risks of type 1 endoleaks, although there is currently no evidence available that undersizing during TEVAR is associated with type 1 endoleak. Most endograft manufacturers recommend oversizing by 10% to 20%. In trauma patients admitted with a pulse ≥ 130/minute, we found that the actual DTA diameter was on average about 13% larger than measured on the CT at admission. If similar aortic changes would occur in admitted TTAI patients with comparable vital signs, a physician could consider to increase the percentage of oversizing of the endograft when performing TEVAR on a hemodynamically unstable TTAI patient. However, excessive oversizing may increase risks of enfolding or collapse of the endograft,[19-21] a serious and potentially lethal complication, and further studies are therefore needed to confirm our findings, before such a recommendation can be made.

If the observed decrease in aortic diameter is related to a shortage of circulating volume, then an alternative to excessive oversizing of the endograft may be delaying the endovascular procedure until adequate resuscitation has been achieved. Recently, there has been a trend towards delayed repair of TTAI in more stable patients, which appears to improve survival.[2,22-26] Institution of antihypertensive medication can reduce the risk of aortic rupture in these patients, resulting in a further decrease of in-hospital mortality.[2,26-28] Delayed repair may allow complete resuscitation, and additional CTA imaging can provide more reliable data regarding the actual aortic measurements for endograft sizing in these patients. However, this strategy is only possible in selected TTAI patients, and delaying TEVAR could be fatal in some hemodynamically unstable patients. Moreover, this approach would result in additional radiation exposure and treatment costs.

In this evaluation, the increase in aortic diameter on the control CT was not consistent in all patients, and in some cases no increase in aortic diameter, or even a slightly smaller aortic diameter was seen on the control CT examination. There are several theoretic explanations for

the inconsistent findings. The few patients in which no decreased aortic diameters were seen on the initial CT at the trauma bay, may have been hemodynamically unstable due to other causes than blood loss, or may have been more stable during CT examination due to fluid resuscitation. The exact vital signs and adequacy of resuscitation of the patient at the moment of the CT examination are difficult to determine retrospectively, which is an important weakness of the present study. There may have been inaccurate aortic measurements in some patients, or the aorta may have been measured at a slightly different level on the second CT scan by the single observer. Additionally, the aorta exhibits significant pulsation with each heart cycle,[11,29,30] and the aortic diameter is typically larger in systole than in diastole, which may have contributed to the relatively wide range of the increase in aortic diameter among individual patients.

A considerable percentage of patients with ruptured abdominal aortic aneurysms[31-33] and ruptured thoracic aortic aneurysms[34,35] are admitted with hemodynamic instability and/or hypovolemic shock, which could result in aortic diameter changes in these patients as well. However, potential aortic changes may be less spectacular in hemodynamically unstable patients with ruptured aortic aneurysms than in TTAI patients, since patients with aortic aneurysms typically are much older and the aorta may be more stiff and calcified.

We observed even more remarkable increases of the diameters of the inferior vena cava, used as a marker for adequacy of resuscitation. In particular the minimum diameter decreased dramatically on the CT examination while hemodynamically unstable, which suggests that the inferior vena cava changed shape as well during hemodynamic instability, from an approximately round shape to a more elliptic shape. Decreasing diameters of the IVC during hemodynamic instability and/or hypovolemic shock has been described before,[36-39] and some have opted that the IVC diameter is more sensitive than the blood pressure alone for identifying a hypovolemic state in trauma patients.[36]

Limitations

The findings of the present study should be viewed within its limitations. The median time interval between CT and the recorded vital signs was 30 minutes, and due to the retrospective design of the study, the exact vital signs and adequacy of resuscitation of the patient at the moment of the CT examination are difficult to determine. Consequently, the increase in aortic diameter may be even underestimated. Additionally, the cardiovascular circulation is a complex balance. Many factors may affect the aortic diameter, including anti hypertensive medication, hormones, pre-existing co-morbidities such as atherosclerosis, diabetes mellitus and others which may have confounded our results. Therefore, we could only conclude that aortic changes occur in hemodynamically unstable trauma patients, but we could not derive a model from our data to predict actual aortic diameters in admitted trauma patients. Additional research, preferably a prospective multi-center study is needed. ECG-gated CT would be most suitable for such a study, since this imaging modality considers the normal aortic dynamics. However, since most

trauma patients will not undergo two ECG-gated CT examinations of the thorax and abdomen, it may be very difficult to realize such a study, and an experimental animal study may be more practical.

CONCLUSION

We observed that trauma patients that are admitted with hemodynamic instability have a significantly smaller aortic diameter on the CT at admission compared with a control CT examination. The decrease in aortic diameter was observed in the entire aorta, from the ascending thoracic aorta to the infrarenal abdominal aorta. This decrease in aortic diameter could theoretically lead to inaccurate aortic diameter measurements and undersizing of the endograft in hemodynamically unstable TTAI patients requiring TEVAR. Further research is needed to better predict the actual aortic diameters in individual hemodynamically unstable patients requiring endovascular aortic repair.

ACKNOWLEDGEMENTS

The authors greatly appreciate the support of Mr. Calvin Norway and the registrars of the Trauma Registry of Yale New Haven Hospital, New Haven, CT, for their assistance in the creation of this manuscript.

REFERENCES

1. Schumacher H, Bockler D, von Tengg-Kobligk H et al. Acute traumatic aortic tear: open versus stent-graft repair. Semin Vasc Surg 2006; 19:48-59.
2. Fabian TC, Davis KA, Gavant ML et al. Prospective study of blunt aortic injury: helical CT is diagnostic and antihypertensive therapy reduces rupture. Ann Surg 1998; 227:666-676.
3. Jonker FH, Giacovelli JK, Muhs BE et al. Trends and outcomes of endovascular and open treatment for traumatic thoracic aortic injury. J Vasc Surg 2010; 51:565-571.
4. Demetriades D, Velmahos GC, Scalea TM et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008; 64:561-570.
5. Tang GL, Tehrani HY, Usman A et al. Reduced mortality, paraplegia, and stroke with stent graft repair of blunt aortic transections: a modern meta-analysis. J Vasc Surg 2008; 47:671-675.
6. Hoffer EK, Forauer AR, Silas AM et al. Endovascular stent-graft or open surgical repair for blunt thoracic aortic trauma: systematic review. J Vasc Interv Radiol 2008; 19:1153-1164.
7. Xenos ES, Abedi NN, Davenport DL et al. Meta-analysis of endovascular vs open repair for traumatic descending thoracic aortic rupture. J Vasc Surg 2008; 48:1343-1351.
8. Demetriades D, Velmahos GC, Scalea TM et al. Diagnosis and treatment of blunt thoracic aortic injuries: changing perspectives. J Trauma 2008; 64:1415-1418.
9. Lebl DR, Dicker RA, Spain DA et al. Dramatic shift in the primary management of traumatic thoracic aortic rupture. Arch Surg 2006; 141:177-180.
10. Angele MK, Schneider CP, Chaudry IH. Bench-to-bedside review: latest results in hemorrhagic shock. Crit Care 2008; 12:218.
11. Muhs BE, Vincken KL, van PJ et al. Dynamic cine-CT angiography for the evaluation of the thoracic aorta; insight in dynamic changes with implications for thoracic endograft treatment. Eur J Vasc Endovasc Surg 2006; 32:532-536.
12. van Prehn J, van Herwaarden JA, Muhs BE et al. Difficulties with endograft sizing in a patient with traumatic rupture of the thoracic aorta: the possible influence of hypovolemic shock. J Vasc Surg 2008; 47:1333-1336.
13. Buz S, Zipfel B, Mulahasanovic S et al. Conventional surgical repair and endovascular treatment of acute traumatic aortic rupture. Eur J Cardiothorac Surg 2008; 33:143-149.
14. Orend KH, Zarbis N, Schelzig H et al. Endovascular treatment (EVT) of acute traumatic lesions of the descending thoracic aorta--7 years' experience. Eur J Vasc Endovasc Surg 2007; 34:666-672.
15. Neschis DG, Moainie S, Flinn WR et al. Endograft repair of traumatic aortic injury-a technique in evolution: a single institution's experience. Ann Surg 2009; 250:377-382.
16. Feczko JD, Lynch L, Pless JE et al. An autopsy case review of 142 nonpenetrating (blunt) injuries of the aorta. J Trauma 1992; 33:846-849.

17. Whitson BA, Nath DS, Knudtson JR et al. Is distal aortic perfusion in traumatic thoracic aortic injuries necessary to avoid paraplegic postoperative outcomes? J Trauma 2008; 64:115-120.
18. Riesenman PJ, Farber MA, Rich PB et al. Outcomes of surgical and endovascular treatment of acute traumatic thoracic aortic injury. J Vasc Surg 2007; 46:934-940.
19. Bandorski D, Bruck M, Gunther HU et al. Endograft Collapse After Endovascular Treatment for Thoracic Aortic Disease. Cardiovasc Intervent Radiol 2010.
20. Canaud L, Alric P, Desgranges P et al. Factors favoring stent-graft collapse after thoracic endovascular aortic repair. J Thorac Cardiovasc Surg 2009.
21. Muhs BE, Balm R, White GH et al. Anatomic factors associated with acute endograft collapse after Gore TAG treatment of thoracic aortic dissection or traumatic rupture. J Vasc Surg 2007; 45:655-661.
22. Demetriades D, Velmahos GC, Scalea TM et al. Blunt traumatic thoracic aortic injuries: early or delayed repair--results of an American Association for the Surgery of Trauma prospective study. J Trauma 2009; 66:967-973.
23. Symbas PN, Sherman AJ, Silver JM et al. Traumatic rupture of the aorta: immediate or delayed repair? Ann Surg 2002; 235:796-802.
24. Hemmila MR, Arbabi S, Rowe SA et al. Delayed repair for blunt thoracic aortic injury: is it really equivalent to early repair? J Trauma 2004; 56:13-23.
25. Holmes JH, Bloch RD, Hall RA et al. Natural history of traumatic rupture of the thoracic aorta managed nonoperatively: a longitudinal analysis. Ann Thorac Surg 2002; 73:1149-1154.
26. Pate JW, Fabian TC, Walker W. Traumatic rupture of the aortic isthmus: an emergency? World J Surg 1995; 19:119-125.
27. Camp PC, Shackford SR. Outcome after blunt traumatic thoracic aortic laceration: identification of a high-risk cohort. Western Trauma Association Multicenter Study Group. J Trauma 1997; 43:413-422.
28. Mattox KL, Wall MJ, Jr. Historical review of blunt injury to the thoracic aorta. Chest Surg Clin N Am 2000; 10:167-82, x.
29. van Prehn J, Vincken KL, Muhs BE et al. Toward endografting of the ascending aorta: insight into dynamics using dynamic cine-CTA. J Endovasc Ther 2007; 14:551-560.
30. van Keulen JW, van PJ, Prokop M et al. Dynamics of the aorta before and after endovascular aneurysm repair: a systematic review. Eur J Vasc Endovasc Surg 2009; 38:586-596.
31. Visser JJ, Williams M, Kievit J et al. Prediction of 30-day mortality after endovascular repair or open surgery in patients with ruptured abdominal aortic aneurysms. J Vasc Surg 2009; 49:1093-1099.
32. Peppelenbosch N, Cuypers PW, Vahl AC et al. Emergency endovascular treatment for ruptured abdominal aortic aneurysm and the risk of spinal cord ischemia. J Vasc Surg 2005; 42:608-614.
33. Korhonen SJ, Ylonen K, Biancari F et al. Glasgow Aneurysm Score as a predictor of immediate outcome after surgery for ruptured abdominal aortic aneurysm. Br J Surg 2004; 91:1449-1452.

34. Girardi LN, Krieger KH, Altorki NK et al. Ruptured descending and thoracoabdominal aortic aneurysms. Ann Thorac Surg 2002; 74:1066-1070.
35. Barbato JE, Kim JY, Zenati M et al. Contemporary results of open repair of ruptured descending thoracic and thoracoabdominal aortic aneurysms. J Vasc Surg 2007; 45:667-676.
36. Yanagawa Y, Sakamoto T, Okada Y. Hypovolemic shock evaluated by sonographic measurement of the inferior vena cava during resuscitation in trauma patients. J Trauma 2007; 63:1245-1248.
37. Yanagawa Y, Nishi K, Sakamoto T et al. Early diagnosis of hypovolemic shock by sonographic measurement of inferior vena cava in trauma patients. J Trauma 2005; 58:825-829.
38. Sefidbakht S, Assadsangabi R, Abbasi HR et al. Sonographic measurement of the inferior vena cava as a predictor of shock in trauma patients. Emerg Radiol 2007; 14:181-185.
39. Jeffrey RB, Jr., Federle MP. The collapsed inferior vena cava: CT evidence of hypovolemia. AJR Am J Roentgenol 1988; 150:431-432.

Chapter 12

The Impact of Hypovolemic Shock on the Aortic Diameter in a Porcine Model

European Journal of Vascular and Endovascular Surgery 2010;40:564-71

Frederik H.W. Jonker,[1] MD,
Hamid Mojibian,[2] MD,
Felix J.V. Schlösser,[1] MD, PhD,
Donald M. Botta,[3] MD,
Jeffrey E. Indes,[1] MD,
Frans L. Moll,[4] MD, PhD,
Bart E. Muhs,[1] MD, PhD

[1] Section of Vascular Surgery and Interventional Radiology, Yale University School of Medicine, New Haven, Connecticut, and VA Connecticut Healthcare System, West Haven, Connecticut, USA
[2] Section of Interventional Radiology, Yale University School of Medicine, New Haven, Connecticut, USA
[3] Section of Cardiothoracic Surgery, Yale University School of Medicine, New Haven, Connecticut, USA
[4] Section of Vascular Surgery, University Medical Center Utrecht, the Netherlands

ABSTRACT

Objectives

To investigate the impact of hypovolemic shock on the aortic diameter in a porcine model, and to determine the implications for the endovascular management of hypovolemic patients with traumatic thoracic aortic injury (TTAI).

Materials and methods

The circulating blood volume of seven Yorkshire pigs was gradually lowered in 10% increments. At 40% volume loss, an endograft was deployed in the descending thoracic aorta, followed by gradual fluid resuscitation. Potential changes in aortic diameter during the experiment were recorded using intravascular ultrasound (IVUS).

Results

The aortic diameter decreased significantly at all evaluated levels during blood loss. The ascending aortic diameter decreased on average with 38% after 40% blood loss (range 24% - 62%, p=0.018), the descending thoracic aorta with 32% (range 18% - 52%, p=0.018), and the abdominal aorta with 28% (range 15% - 39%, p=0.018). The aortic diameters regained their initial size during fluid resuscitation.

Conclusion

The aortic diameter significantly decreases during blood loss in this porcine model. If these changes take place in hypovolemic TTAI patients as well, it may have implications for TEVAR. Increased oversizing of the endograft, or additional CT or IVUS imaging after fluid resuscitation for more adequate aortic measurements, may be needed in TTAI patients with considerable blood loss.

INTRODUCTION

Thoracic endovascular aortic repair (TEVAR) offers an effective treatment for acute thoracic aortic pathologies including traumatic thoracic aortic injury (TTAI).[1-5] Endovascular repair of TTAI is associated with mortality rates between 6.0% to 13.5%, compared with 16.9% to 23.5% after traditional open surgery,[1-5] and the utilization of TEVAR for TTAI has dramatically increased during the last decade.[1,6,7] TEVAR is, however, still plagued by endoleak in 2.8% to 14.3% after endovascular repair of TTAI.[1-4,8-10] The majority of these endoleaks are proximal type 1 endoleaks, and urgent re-intervention is often needed.[2,8,10] Adequate endograft sizing using pre-operative computed tomography angiography (CTA), is thought to be important for minimizing risks of endoleak and other endograft-related complications, and improvement of the long-term outcomes after endovascular repair.[11]

TTAI patients are frequently admitted with significant blood loss or hypovolemic shock. Although peripheral vasoconstriction is a well known response to hypovolemic shock in order to maintain perfusion of the heart and brain,[12-14]the effects of hypovolemia on the aortic dimensions remain currently unclear. In a previous study, we found that trauma patients admitted with hypotension and tachycardia have smaller aortic measurements on the CT at admission compared with a second CT when hemodynamically stable.[15] Such changes of the aortic diameter may be the result of hypovolemia, and could lead to inadequate aortic measurements on pre-operative CTA, and undersizing of the endograft. The purpose of this study is to investigate the exact impact of blood loss on the aortic dimensions in an experimental porcine model.

METHODS

Study Subjects

Seven healthy male Yorkshire pigs with a mean weight of 34.8 ±6.3 kg (table 1) were obtained from the Yale Animal Resources Center (YARC), and housed for at least one week prior to the experiment under controlled conditions. The animals received a standard nonsupplemented diet and water until 12 hours before the study, when the animals were fasted and only had access to water. The experimental protocol was approved and regulated by the Institutional Animal Care & Use Committee (IACUC) of Yale University.

Equipment

Prior to the procedure, the exact weight of the subject was measured and the circulating blood volume was calculated, which is approximately 65 mL/kg for a Yorkshire pig.[16,17] Ketamine (2.2 mg/kg IM), Telazol® (4.4 mg/kg IM), Xylazine (2.2 mg/kg IM) and atropine (0.05 mg/kg IM) were administered by a veterinarian for induction and intubation, and isoflorane/oxygen

1.0%-3.5% was used for maintenance of the anesthesia. The blood pressure and heart rate were constantly recorded during the experiment using an intra arterial line. Other anesthetic monitoring included the respiratory rate, pulse oximetry and body temperature. The aortic dimensions were studied using an s5 Intravascular Ultrasound (IVUS) Imaging System (Volcano Inc Corp, Rancho Cordova, CA) and a Visions® PV8.2F Catheter (Volcano Inc Corp, Rancho Cordova, CA). The surgical procedures were performed by a team of interventional radiologists, vascular and cardiothoracic surgeons, all experienced with IVUS imaging.

Table 1. Subject characteristics

	Mean	(±SD)
Weight (kg)	34.8	(±6.3)
Circulating blood volume[a] (L)	2.28	(±0.41)
Planned blood loss (L)	0.91	(±0.16)
Vitals signs at baseline		
Systolic blood pressure	92.6	(±13.1)
Diastolic blood pressure	48.3	(±11.1)
MAP	64.7	(±7.3)
Heart rate	87.1	(±9.1)
Vital signs after 40% blood loss		
Systolic blood pressure	35.4	(±14.5)
Diastolic blood pressure	23.6	(±10.3)
MAP	29.4	(±11.3)
Heart rate	112.9	(±22.5)

Baseline vital signs were obtained after induction of general anesthesia. *MAP* mean arterial pressure.
[a] The circulating blood volume of a Yorkshire pig is approximately 65 mL/kg. *SD* standard deviation.

Experiment

A midline laparotomy was performed after induction of general anesthesia, and the distal abdominal aorta was cannulated. A small (9Fr) sheath was introduced, followed by a dilator and a 18Fr working sheath. The IVUS catheter was inserted through the sheath for baseline measurements of the aortic diameter, at the level of the ascending thoracic aorta 2 cm distal to the aortic valve, the descending thoracic aorta 2 cm distal to the left subclavian artery, and the infrarenal abdominal aorta just distal to the renal arteries. Aortic diameter measurements were obtained during the cardiac systole. Subsequently, the circulating blood volume was gradually lowered in 10% increments through the sheath using a syringe. The aortic measurements and vital signs were measured at each 10% increment, until the subject had lost 40% of its circulating blood volume.

At 40% volume loss, the descending thoracic aortic measurements at baseline and at 40% blood loss were used to select a stent graft size (AneuRx limb, Medtronic Vascular Inc, Santa

Rosa, CA). The stent graft was deployed in the descending thoracic aorta, and IVUS was used to assess adequate endograft deployment. Afterwards, the animal received controlled fluid resuscitation with normal saline in 10% increments through the sheath using a syringe until complete resuscitation was achieved. At the end of the procedure, the subject was euthanized using Euthasol® (0.22 mg/kg IV), and autopsy with thoracotomy and aortotomy was performed to inspect the aorta and endograft in vivo.

Statistical Analysis

Data are shown as mean ± standard deviation and range. The Wilcoxon test for paired samples was used to compare continuous variables such as the aortic diameter at different moments of the experiment. The true aortic diameters were used for statistical analysis, which represent the luminal diameter on IVUS imaging (intima to intima). The relation between blood loss and/or vital signs, and the descending thoracic aortic diameter was investigated using linear regression analysis of the five data points (0%, 10%, 20%, 30%, and 40% blood loss) of the seven subjects. SPSS software version 15.0 was used for all statistical analyses, a P value < 0.05 was considered statistically significant.

RESULTS

Aortic dimensions during blood loss

The mean duration from measurement of baseline aortic measurements until 40% blood loss, was 32 minutes (range 24 to 38, table 2). The aortic diameter decreased significantly at all three evaluated levels during blood loss (figure 1). At the level of the ascending thoracic aorta, the mean aortic diameter decreased from 17.7 mm to 10.9 mm after 40% blood loss (p=0.018), which represents a mean decrease of 38.2% of its original diameter (range 24.2% - 62.4%, table 2). At the level of the descending thoracic aorta, the diameter decreased on average with 31.6% (range 18.3% - 52.3%), from 14.6 mm to 10.0 mm (p=0.018). The decrease in descending aortic diameter was consistent in all seven subjects, and approximated a linear function (figure 2). For the infrarenal abdominal aorta, the mean decrease in diameter was 27.6% (range 15.4% - 39.3%), from 10.4 mm to 7.5 mm after 40% blood loss (p=0.018).

Table 2. Mean aortic diameter during lowering of the blood volume

Normal		10%	20%	30%	40%	Reduction (%)	Range (%)	p value
Ascending (mm)	17.7	15.2	13.8	12.4	10.9	38.2	24.2 - 61.4	0.018
Descending (mm)	14.6	13.8	11.8	11.2	10.0	31.6	18.3 - 52.3	0.018
Infrarenal (mm)	10.4	9.8	9.4	8.5	7.5	27.6	15.4 - 39.3	0.018
Time (min)	0	12.1	18.3	24.7	32.0	-	24 - 38	-

Reduction (%) refers to the decrease in aortic diameter after 40% blood loss compared with the initial aortic measurements. *Time (min)* refers to the time interval in minutes between measurement of the baseline aortic diameters at the beginning of the experiment, and the aortic measurements at each 10% increment.

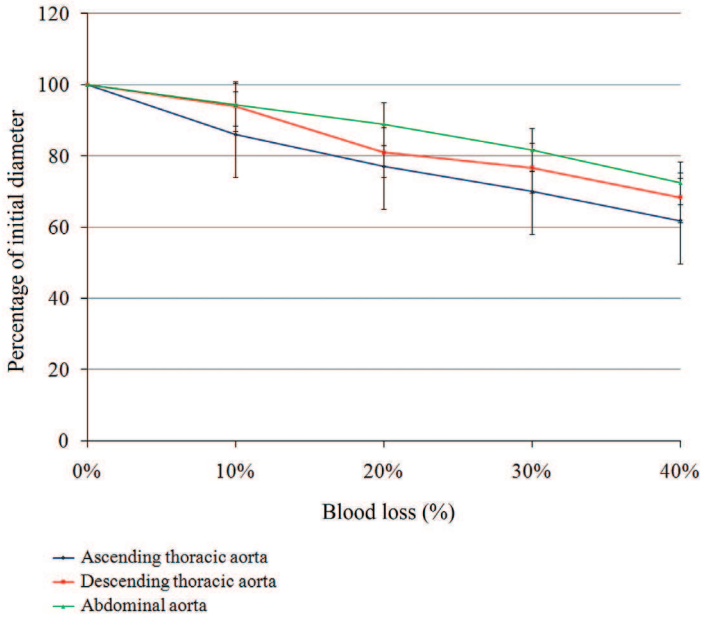

Figure 1. Aortic diameters during lowering of the blood volume
Error bars represent the 95% confidence interval of the mean.

Relation blood loss, vitals, and descending thoracic aortic diameter

Linear regression analysis was used to explore the relation between blood loss and/or vitals, and the descending thoracic aortic diameter. The degree of blood loss was strongly associated with a decrease of the aortic diameter: regression coefficient (RC): -1.18, 95% CI: -1.70 - -0.67 (table 3). This suggests that in our subjects, the descending thoracic aortic diameter decreases with 1.18 mm or 8.1%, every time the animal loses 10% of its blood volume. There was also a significant relation between the systolic pressure (RC 0.07, 95% CI 0.04-0.10), diastolic pressure (RC 0.15, 95% CI 0.09-0.19), or mean arterial pressure (RC 0.10, 95% CI 0.05 - 0.15) and the diameter of the descending aorta (table 3).

Table 3. Effects of blood loss and vital signs on the descending thoracic aortic diameter in linear regression analysis

	RC	95% CI	p value
Blood loss [a]	-1.18	-1.70 - -0.67	<0.001
Systolic blood pressure	0.07	0.04 - 0.10	<0.001
Diastolic blood pressure	0.15	0.09 - 0.19	<0.001
Mean arterial pressure	0.10	0.05 - 0.15	<0.001
Heart rate	-0.03	-0.08 - 0.03	0.339
Respiratory rate	0.01	-0.09 - 0.11	0.886

Univariate linear regression was used to investigate effects on the descending thoracic aortic diameter. Multivariate regression analysis was not performed because there is a strong correlation between blood loss, blood pressure and heart rate.
[a] The variable blood loss had an ordinal scale, either 0%, 10%, 20%, 30% or 40%. RC: regression coefficient, CI: confidence interval.

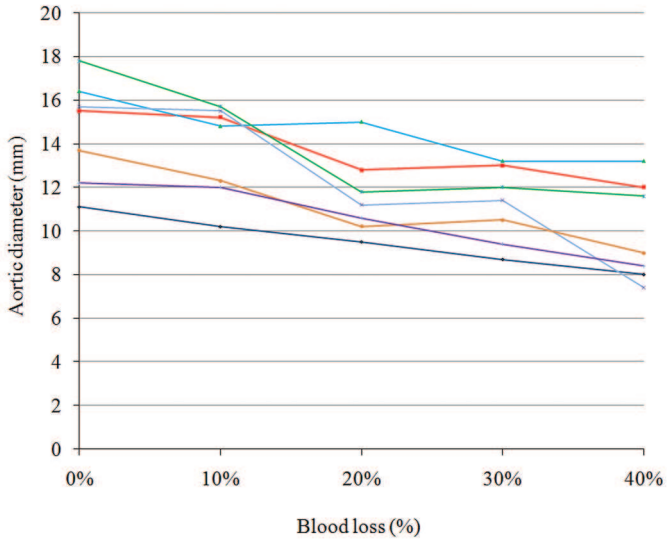

Figure 2. Descending thoracic aortic diameter in all subjects during blood loss
The lines represent the individual descending thoracic aortic diameter of the seven subjects during lowering of the blood volume.

Stent graft deployment

After lowering the blood volume with 40%, a stent graft was successfully deployed in the descending thoracic aorta in all subjects, and IVUS did not show any endoleaks or stent graft enfolding. The mean diameter and length of the stent grafts were 14.5 ±1.8 mm (range 12 - 16), and 108.0 ±13 mm (range 85 - 185). The stent grafts were oversized by 47% ±24% (range 25% - 80%) compared with descending thoracic aortic diameter obtained after 40% blood loss.

Aortic dimensions during stent graft deployment and fluid resuscitation

The mean duration from stenting until complete fluid resuscitation was 12.8 minutes (table 4). The mean diameters of the ascending aorta, the stented descending aorta, and the abdominal aorta increased after stenting (table 4). During fluid resuscitation, the diameter of the ascending and abdominal aorta further increased and approximately regained their original size (97.1% and 99.0%, respectively, figure 3). The lumen of the stented descending thoracic aorta further increased during resuscitation as well (11.7 mm to 12.5 mm, p=0.023), which may suggest that the stent graft further unfolded during fluid resuscitation (table 4).

Type 1 endoleak was detected using IVUS imaging in two of the seven subjects during resuscitation (29%). In these cases, the diameter of the descending thoracic aorta had decreased with 27.9% and 52.3%, and the stent graft was oversized by 50% and 62%, respectively. In the first case, the endoleak was observed after 30% resuscitation, and in the second subject, a large endoleak was seen after 20% fluid resuscitation, and the leakage further increased during continued resuscitation (figure 4).

Table 4. Aortic diameters during stent deployment and fluid resuscitation

	Before stenting	After stenting	+20%	Complete resuscitation	Original diameter (%)	Range (%)	p value
Blood loss	40%	40%	20%	0%	0%	0%	
Ascending (mm)	10.9	12.9	14.8	17.2	97.1	91.9 - 113.5	0.018
Descending (mm) [a]	10.0	11.7	11.8	12.5	85.6	68.5 - 94.6	0.018
Infrarenal (mm)	7.5	9.0	9.4	10.3	99.0	85.8 - 125.1	0.018
Time (min)	32.0	41.7	48.7	54.5	-	53 - 60	-

[a] The stent graft was deployed after 40% blood loss in the descending thoracic aorta, and from that moment the diameter measured by IVUS actually represents the stent lumen.
Time (min) refers to the time interval in minutes from measurement of the baseline aortic diameters at the beginning of the experiment.

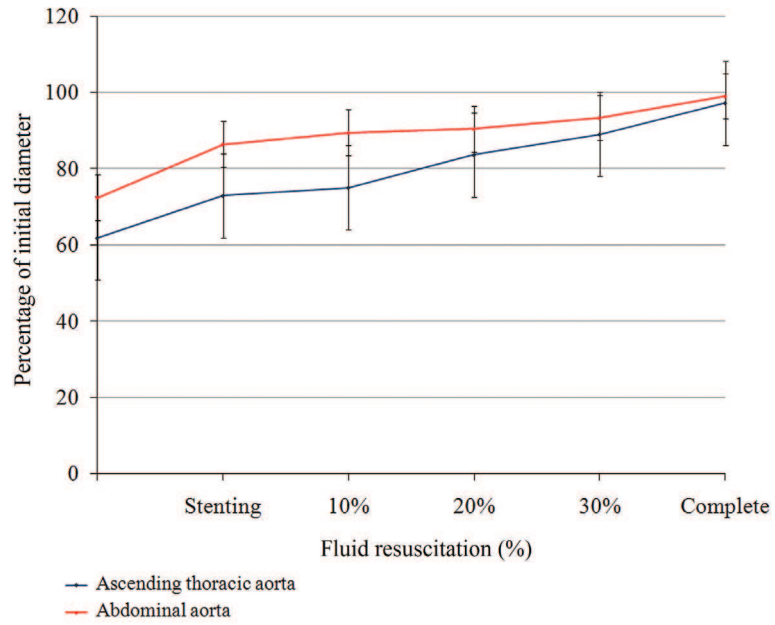

Figure 3. Increase of the ascending and abdominal aortic diameter during resuscitation
The descending thoracic aorta was not included in this figure because the stent graft was deployed in the descending thoracic aorta, and from that moment the diameter measured by IVUS actually represents the stent lumen. Error bars represent the 95% confidence interval of the mean.

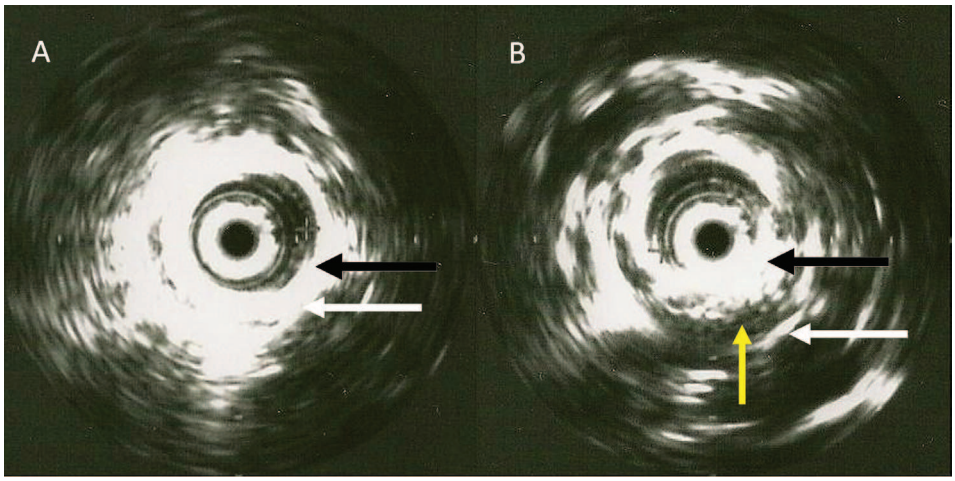

Figure 4. IVUS images of a type 1 endoleak after complete resuscitation

A. In this subject, the descending thoracic aortic diameter decreased from 15.5 mm to 7.4 mm (52.3%) after 40% blood loss, and a 12 mm stent graft was deployed (62% oversizing). Black arrow: stent graft; white arrow: aortic wall.
B. The same subject after complete fluid resuscitation. A large endoleak (yellow arrow) is visible between the stent graft (black arrow) and the aortic wall (white arrow). The leakage was already detected after 20% fluid resuscitation, and further increased during continued resuscitation.

Autopsy

The subjects were euthanized after complete fluid resuscitation was achieved in all subjects and final vital signs and aortic diameters were obtained. Subsequently, autopsy with thoracotomy and aortotomy was performed to inspect the aorta and endograft. No abnormalities were found during autopsy, and all stent grafts were adequately deployed in the descending thoracic aorta and no stent enfolding was observed (figure 5).

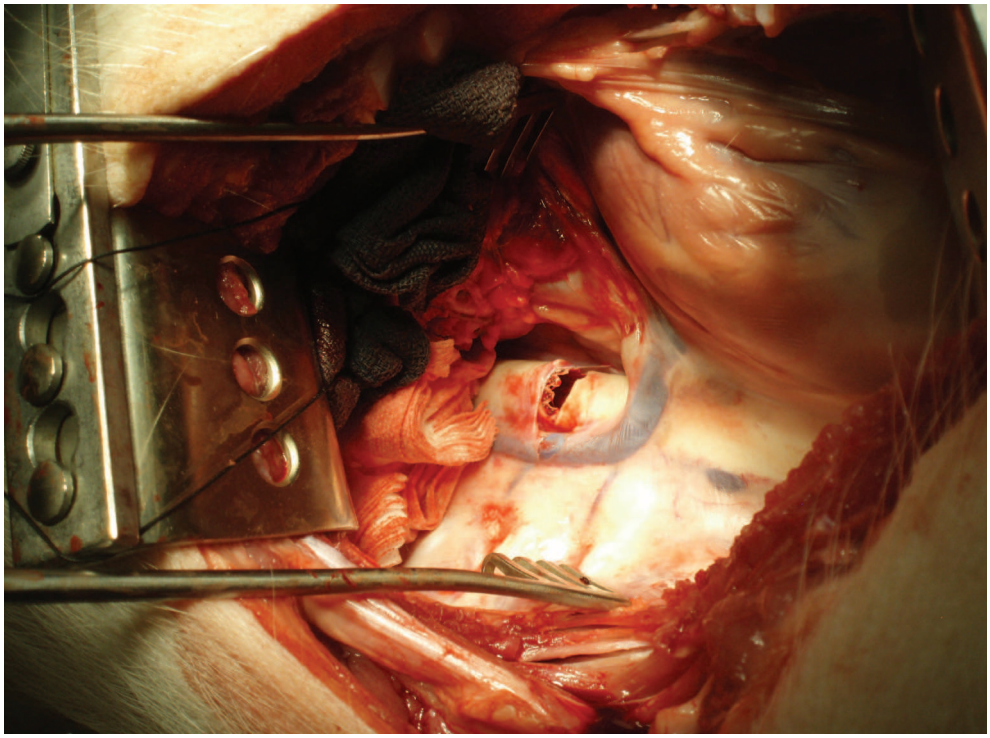

Figure 5. Descending thoracic aorta and proximal stent graft at autopsy
No abnormalities were found during autopsy, the stent grafts were adequately deployed in the descending thoracic aorta, and no stent enfolding was observed.

DISCUSSION

In this porcine model, we studied the effects of blood loss and hypovolemic shock on the aortic diameter using IVUS, an accurate imaging method to investigate the aortic morphology.[18] This revealed that the aortic diameter dramatically decreases during blood loss and hypovolemic shock. The decrease in diameter already occurred after 10% blood loss at all evaluated levels, and the aortic dimensions continued to decrease with decreasing blood volume. The explanation

for these striking observations could be that the shortage in circulating blood volume results in decreased pressure on the aortic wall, causing the aorta to collapse. Endogenous production of vasoconstrictors during hypovolemia may perhaps contribute to the reduction in aortic diameter as well.

Because of the many anatomical and functional similarities with regard to the cardiovascular system between swine and human,[16,17] we expect that hypovolemia could also affect the human aortic dimensions. In a previous study, we observed that the descending thoracic aortic diameter was on average about 13% smaller on CTs of trauma patients admitted with a heart rate ≥ 130 per minute and a mean arterial pressure < 95mmHg, compared with a second CT scan while the patients were hemodynamically stable.[15] Due to the retrospective design of the study, the exact blood loss was difficult to determine in these trauma patients.[15] Taking the observations in the trauma patients and the porcine model into account, we assume that hypovolemia in humans could lead to a decrease in aortic diameter. Since patients with TTAI are often admitted to the emergency department with considerable blood loss or hypovolemic shock, our findings may have implications for the endovascular management of TTAI.

Endograft sizing for TEVAR is usually performed using the pre-operative CTA scan, however, if the diameter of the descending thoracic aorta is considerably smaller at admission due to blood loss, physicians may undersize the endograft. This mismatch between the aortic diameter and the endograft could theoretically result in increased risks of endoleak or other endograft related complications such as endograft migration. Most endograft manufacturers recommend that an endograft is oversized by 10% to 20% of the normal aortic diameter during TEVAR for an adequate seal with the aortic wall. In this porcine model, the mean descending aortic diameter was 81% of its original size after lowering the blood volume with 20%. If a similar decrease in aortic diameter would occur in a TTAI patient with 20% blood loss (1L for a patient of 70 kg[19-21]), an endograft may be oversized on average by 42% (115 / 0.81) of the diameter at that moment, to obtain the recommended 15% oversizing of the normal aortic diameter. The required percentage of oversizing would theoretically further increase with increasing blood loss (figure 6).

Naturally, additional research in human subjects is needed, before strong recommendations about oversizing of the endograft can be made. The exact decrease of the descending thoracic aorta in human patients with hypovolemic shock remains unclear at this moment, but physicians could consider to increase the percentage of oversizing of the endograft when performing TEVAR on a hypovolemic patient with TTAI. The aorta of young trauma patients may be substantially smaller than the smallest endograft size currently available. This often necessitates physicians to oversize the endograft by more than 20%, which may be acceptable in hypovolemic TTAI patients based on our findings. Caution is needed, however, because extreme oversizing of the endograft may increase risks of adverse effects, such as endograft collapse.[22-24]

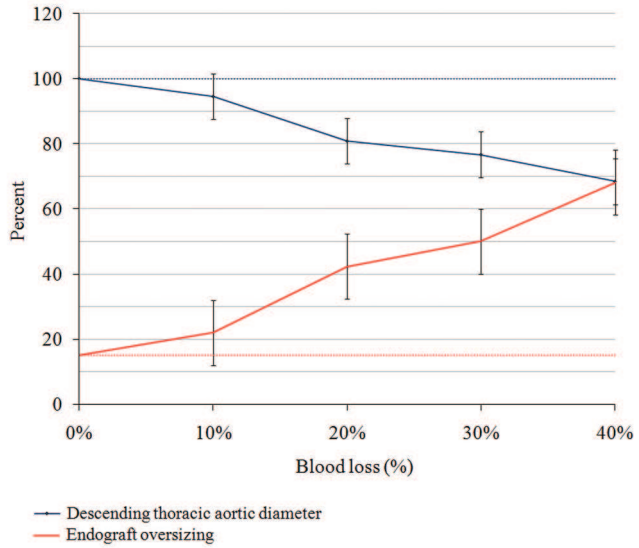

Figure 6. Descending thoracic aortic diameter and theoretic percentage of oversizing of the endograft related to circulating blood volume
The red line represents the theoretic percentage of oversizing of the aortic diameter to obtain a 15% oversizing of the normal aortic diameter, which is recommended by most endograft manufacturers. Error bars represent the 95% confidence interval of the mean.

In the experiments, the aorta approximately regained its original size after complete fluid resuscitation. IVUS demonstrated type 1 endoleak in two subjects when the aortic diameter enlarged during resuscitation, despite excessive oversizing of the stent graft (figure 4), which exemplifies the clinical dilemma of aortic endograft sizing in hypovolemic patients. An alternative to increased oversizing of the stent graft in hypovolemic patients requiring TEVAR, may be delaying the TEVAR procedure until adequate resuscitation has been achieved, followed by additional CTA or IVUS imaging for more accurate aortic measurements. Recent reports have suggested that delaying TEVAR in more stable TTAI patients is associated with improved survival.[25-27] However, the strategy to delay the endovascular procedure could be lethal in some patients in hypovolemic shock. IVUS offers the benefit of real time sizing during the endovascular procedure, when the patient may be better resuscitated than during the CT scan at admission. The aortic measurements on IVUS during endovascular repair may therefore be more reliable, and regular use of IVUS during TEVAR of TTAI may be recommended.

Patients with ruptured aneurysms of the abdominal (rAAA) or thoracic aorta (rTAA) also present with an aortic wall defect and associated hemorrhage,[28-31] which may result in aortic diameter changes in these patients as well. In particular rAAA is more common than TTAI, and diameter changes due to blood loss could have implications for endovascular repair (EVAR) of rAAA. A few studies have analyzed predictors of type 1 endoleaks after EVAR of abdominal aortic

aneurysms, however, these did not investigate the effects of aneurysm rupture or hypovolemia on the incidence of type 1 endoleak.[32,33] TTAI patients typically are much younger than patients with aortic aneurysms, which usually have a history of atherosclerotic disease.[28-31] Aortic compliance decreases with age,[34,35] likely due to a loss of elasticity and increased prevalence of aortic calcification.[36-38] The previously healthy aorta of young trauma patients may therefore be more compliant, and potential aortic changes could be more extreme in TTAI patients presenting with hypovolemic shock, than in patients with ruptured aortic aneurysms.

To our knowledge, the present experimental study is the first study that has investigated the impact of blood loss on the aortic dimensions, which revealed remarkable changes of the aortic diameter during lowering of the volume. Still, several limitations are important when interpreting the results. Obviously, the current observations in Yorkshire pigs cannot directly be extrapolated to human patients with TTAI. Despite many anatomical and functional similarities between swine and human,[16,17] the findings need to be further validated in human subjects, before valid recommendations with regard to increased oversizing can be made. However, it is difficult to investigate the aortic dynamics in human patients with hypovolemic shock, because these patients are in a critical condition and therefore unsuitable for participation in a prospective research study. A different aspect that warrants further research is the impact of shock on the aortic distention througout the cardiac cycle. The aorta is known to expand during the cardiac systole,[39,40] and the degree of expansion may be affected by hypovolemia. The relatively small sample size of seven subjects is a limitation as well, nevertheless, the findings were consistent in all subjects (figure 3) and statistically significant at all evaluated levels (table 2).

CONCLUSIONS

This study demonstrates that the aortic diameter significantly decreases during blood loss in a porcine model. Assuming that these changes in diameter take place as well in humans, this may have implications for the endovascular management of patients with TTAI. Increased oversizing of the endograft, or additional CT or IVUS imaging after fluid resuscitation, may be needed in TTAI patients admitted with considerable blood loss undergoing TEVAR.

REFERENCES

1. Jonker FH, Giacovelli JK, Muhs BE et al. Trends and outcomes of endovascular and open treatment for traumatic thoracic aortic injury. J Vasc Surg 2010; 51:565-571.
2. Demetriades D, Velmahos GC, Scalea TM et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008; 64:561-570.
3. Tang GL, Tehrani HY, Usman A et al. Reduced mortality, paraplegia, and stroke with stent graft repair of blunt aortic transections: a modern meta-analysis. J Vasc Surg 2008; 47:671-675.
4. Hoffer EK, Forauer AR, Silas AM et al. Endovascular stent-graft or open surgical repair for blunt thoracic aortic trauma: systematic review. J Vasc Interv Radiol 2008; 19:1153-1164.
5. Xenos ES, Abedi NN, Davenport DL et al. Meta-analysis of endovascular vs open repair for traumatic descending thoracic aortic rupture. J Vasc Surg 2008; 48:1343-1351.
6. Demetriades D, Velmahos GC, Scalea TM et al. Diagnosis and treatment of blunt thoracic aortic injuries: changing perspectives. J Trauma 2008; 64:1415-1418.
7. Lebl DR, Dicker RA, Spain DA et al. Dramatic shift in the primary management of traumatic thoracic aortic rupture. Arch Surg 2006; 141:177-180.
8. Neschis DG, Moainie S, Flinn WR et al. Endograft repair of traumatic aortic injury-a technique in evolution: a single institution's experience. Ann Surg 2009; 250:377-382.
9. Buz S, Zipfel B, Mulahasanovic S et al. Conventional surgical repair and endovascular treatment of acute traumatic aortic rupture. Eur J Cardiothorac Surg 2008; 33:143-149.
10. Orend KH, Zarbis N, Schelzig H et al. Endovascular treatment (EVT) of acute traumatic lesions of the descending thoracic aorta--7 years' experience. Eur J Vasc Endovasc Surg 2007; 34:666-672.
11. van Prehn J, Schlosser FJ, Muhs BE et al. Oversizing of aortic stent grafts for abdominal aneurysm repair: a systematic review of the benefits and risks. Eur J Vasc Endovasc Surg 2009; 38:42-53.
12. WIGGERS HC, INGRAHAM RC, . Vasoconstriction and the development of irreversible hemorrhagic shock. Am J Physiol 1948; 153:511-520.
13. Cohn JN, Luria MH. Studies in clinical shock and hypotension. IV. Variations in reflex vasoconstriction and cardiac stimulation. Circulation 1966; 34:823-832.
14. Peitzman AB, Billiar TR, Harbrecht BG et al. Hemorrhagic shock. Curr Probl Surg 1995; 32:925-1002.
15. Jonker FH, Verhagen HJ, Mojibian H et al. Aortic endograft sizing in trauma patients with hemodynamic instability. J Vasc Surg 2010.
16. Hannon JP, Bossone CA, Wade CE. Normal physiological values for conscious pigs used in biomedical research. Lab Anim Sci 1990; 40:293-298.
17. Stanton H, Mersmann H. Swine in Cardiovascular Research. Boca Raton, Florida: CRC Press Inc; 1986.

18. Arko FR, Murphy EH, Davis CM, III et al. Dynamic geometry and wall thickness of the aortic neck of abdominal aortic aneurysms with intravascular ultrasonography. J Vasc Surg 2007; 46:891-896.
19. Cameron J, Skofronick J, Grant R. Physics of the Body. Madison, WI: Medical Physics Publishing; 1999.
20. Gutierrez G, Reines HD, Wulf-Gutierrez ME. Clinical review: hemorrhagic shock. Crit Care 2004; 8:373-381.
21. American College of Surgeons Committee on Trauma. Advanced trauma life support program for doctors. Chicago: 2004.
22. Bandorski D, Bruck M, Gunther HU et al. Endograft Collapse After Endovascular Treatment for Thoracic Aortic Disease. Cardiovasc Intervent Radiol 2010.
23. Canaud L, Alric P, Desgranges P et al. Factors favoring stent-graft collapse after thoracic endovascular aortic repair. J Thorac Cardiovasc Surg 2009.
24. Muhs BE, Balm R, White GH et al. Anatomic factors associated with acute endograft collapse after Gore TAG treatment of thoracic aortic dissection or traumatic rupture. J Vasc Surg 2007; 45:655-661.
25. Demetriades D, Velmahos GC, Scalea TM et al. Blunt traumatic thoracic aortic injuries: early or delayed repair--results of an American Association for the Surgery of Trauma prospective study. J Trauma 2009; 66:967-973.
26. Symbas PN, Sherman AJ, Silver JM et al. Traumatic rupture of the aorta: immediate or delayed repair? Ann Surg 2002; 235:796-802.
27. Hemmila MR, Arbabi S, Rowe SA et al. Delayed repair for blunt thoracic aortic injury: is it really equivalent to early repair? J Trauma 2004; 56:13-23.
28. Veith FJ, Lachat M, Mayer D et al. Collected world and single center experience with endovascular treatment of ruptured abdominal aortic aneurysms. Ann Surg 2009; 250:818-824.
29. Karkos CD, Harkin DW, Giannakou A et al. Mortality after endovascular repair of ruptured abdominal aortic aneurysms: a systematic review and meta-analysis. Arch Surg 2009; 144:770-778.
30. Patel HJ, Williams DM, Upchurch GR, Jr. et al. A comparative analysis of open and endovascular repair for the ruptured descending thoracic aorta. J Vasc Surg 2009; 50:1265-1270.
31. Jonker FH, Trimarchi S, Verhagen HJ et al. Meta-analysis of open versus endovascular repair for ruptured descending thoracic aortic aneurysm. J Vasc Surg 2010; 51:1026-1032.
32. Sampaio SM, Panneton JM, Mozes GI et al. Proximal type I endoleak after endovascular abdominal aortic aneurysm repair: predictive factors. Ann Vasc Surg 2004; 18:621-628.
33. Albertini J, Kalliafas S, Travis S et al. Anatomical risk factors for proximal perigraft endoleak and graft migration following endovascular repair of abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 2000; 19:308-312.

34. Mohiaddin RH, Underwood SR, Bogren HG et al. Regional aortic compliance studied by magnetic resonance imaging: the effects of age, training, and coronary artery disease. Br Heart J 1989; 62:90-96.
35. Sonesson B, Hansen F, Stale H et al. Compliance and diameter in the human abdominal aorta--the influence of age and sex. Eur J Vasc Surg 1993; 7:690-697.
36. Mohiaddin RH, Schoser K, Amanuma M et al. MR imaging of age-related dimensional changes of thoracic aorta. J Comput Assist Tomogr 1990; 14:748-752.
37. Bazan HA, Pradhan S, Mojibian H et al. Increased aortic arch calcification in patients older than 75 years: implications for carotid artery stenting in elderly patients. J Vasc Surg 2007; 46:841-845.
38. Takeda S, Watanabe H, Matsuzawa T. Age-related change in calcifications in the thoracic aorta: a study with computed tomography. Tohoku J Exp Med 1986; 149:73-78.
39. Muhs BE, Vincken KL, van PJ et al. Dynamic cine-CT angiography for the evaluation of the thoracic aorta; insight in dynamic changes with implications for thoracic endograft treatment. Eur J Vasc Endovasc Surg 2006; 32:532-536.
40. Lu TL, Rizzo E, Marques-Vidal PM et al. Variability of ascending aorta diameter measurements as assessed with electrocardiography-gated multidetector computerized tomography and computer assisted diagnosis software. Interact Cardiovasc Thorac Surg 2010; 10:217-221.

Chapter 13

Endograft Collapse after Thoracic Endovascular Aortic Repair

Journal of Endovascular Therapy 2010 (in press)

Frederik H.W. Jonker,[1] MD
Felix J.V. Schlosser,[1] MD, PhD
Arnar Geirsson,[2] MD
Bauer E. Sumpio,[1] MD, PhD
Frans L. Moll,[3] MD, PhD
Bart E. Muhs,[1] MD, PhD

[1] Section of Vascular Surgery and Interventional Radiology, Yale University School of Medicine, New Haven, Connecticut, USA
[2] Section of Cardiothoracic Surgery, Yale University School of Medicine, New Haven, Connecticut, USA,
[3] Section of Vascular Surgery, University Medical Center Utrecht, the Netherlands.

ABSTRACT

Purpose

To provide insight into the causes, timing, and optimal management of endograft collapse after thoracic endovascular aortic repair (TEVAR).

Methods

A comprehensive review was conducted of all published cases of endograft collapse after TEVAR identified using Medline, Cochrane Library Central, and EMBASE. In total, 32 articles describing 60 patients (45 men; mean age 40.6 ±17.2 years, range 17–78) with endograft collapse were included. All data were extracted from the articles and systematically entered into a database for meta-analysis.

Results

In the 60 cases of endograft collapse, TEVAR had most commonly been applied to repair traumatic thoracic aortic injuries (39, 65%), followed by acute and chronic type B aortic dissections (9, 15%). The median time interval between TEVAR and diagnosis of endograft collapse was 15 days (range 1 day to 79 months). On average, the collapsed endografts were oversized by 26.7%±12.0% (range 8.3%–60.0%). Excessive oversizing was reported as the primary cause of endograft collapse in 20%, and a small radius of curvature of the aortic arch was responsible for 48% of the cases. The 30-day mortality was 8.3%, and the freedom from procedure-related death at 3 years after diagnosis of stent-graft collapse was 83.1% for asymptomatic patients compared with 72.7% for patients who had symptoms at diagnosis (p=0.029).

Conclusion

Endograft collapse typically occurs shortly after TEVAR, most frequently after endovascular repair of traumatic aortic injury. A high level of suspicion for endograft collapse in the first month after TEVAR, as well as further improvement of current endovascular devices, may be required to improve the long-term outcomes of patients after TEVAR.

INTRODUCTION

Thoracic endovascular aortic repair (TEVAR) has changed the management of descending thoracic aortic disease. For aortic emergencies in particular, such as traumatic thoracic aortic injuries or complicated acute type B aortic dissections, TEVAR appears to substantially decrease the operative mortality rates compared with open surgery.[1-6]

The utilization of TEVAR has dramatically increased in the last decade.[2,7-9] Despite the encouraging early results of TEVAR, the procedure is also associated with endograft-related complications during follow-up.[10,11] Endograft collapse, which is probably one of the most serious sequelae, can lead to acute aortic occlusion and multiorgan failure due to malperfusion.[12]

To improve the long-term prognosis of TEVAR patients, more insight into the causes, timing and optimal management of endograft collapse after TEVAR is necessary. The purpose of this study was to investigate the possible causes, presentation, treatment, and outcomes of this complication by means of a review of the available data regarding endograft collapse after TEVAR.

METHODS

Literature Search

Medline, EMBASE, and Cochrane Library Central databases were searched until February 9, 2010. The following search string was used for Medline: (collapse[tiab] OR collapsed[tiab] OR collapses[tiab] OR infolding[tiab] OR infolded[tiab] OR kinking[tiab]) AND (aorta[tiab] OR aortic[tiab] OR aortas[tiab]) AND (endovascular[tiab] OR percutaneous[tiab] OR transluminal[tiab] OR stent[tiab] OR stents[tiab] OR endograft[tiab] OR endografts[tiab] OR stent-graft[tiab] OR stent-grafts[tiab] OR graft[tiab] OR grafts[tiab] OR TEVAR[tiab]). Using a similar search string for EMBASE, a total of 384 articles were identified in the 2 databases. The Cochrane database was browsed manually and did not reveal any relevant articles.

Selection of Articles

All titles and abstracts were read by 2 independent investigators (F.H.J. and F.J.S.). Articles were selected if the report included patients who had developed endograft collapse after TEVAR. Exclusion criteria were: (1) endograft collapse after endovascular abdominal aortic repair, (2) no clear description of patient outcomes, and (3) no original data presented in the article. Articles written by identical authors and/or institutions were studied in detail and excluded if necessary to prevent duplication. In this manner, 32 relevant articles describing 60 patients (45 men; mean age 40.6 ±17.2 years, range 17–78) with thoracic endograft collapse were eligible for analysis.[1,12-42]

Data Extraction

Two independent investigators analyzed the identified articles (F.H.J. and F.J.S.) to extract the following data: demographics, incidence, initial procedures, endograft details, percentage of oversizing for patients with and without endograft collapse, time interval until endograft collapse, cause and symptoms of collapse, treatment details, time interval until treatment, early mortality and complications, and follow-up complications. Subsequently, all extracted data were systematically entered into a database. Availability of individual variables in the evaluated cases of endograft collapse is depicted in table 1.

Table 1. Availability of individual data

Variable	N	(%)	Variable	N	(%)
Age	47/60	(78)	Cause of collapse	52/60	(87)
Gender	51/60	(85)	Time interval until diagnosis	52/60	(87)
Aortic pathology	60/60	(100)	Location collapse	55/60	(92)
Aortic diameter	44/60	(73)	Symptoms	56/60	(93)
Endograft type	60/60	(100)	Treatment type	60/60	(100)
Endograft diameter	45/60	(75)	Mortality	60/60	(100)
Endograft length	39/60	(65)	Complications	60/60	(100)
Number of stents	47/60	(78)	Time interval until death	8/8	(100)
Oversizing collapsed endograft	45/60	(75)	Cause of death	8/8	(100)

Statistical Analysis

Summary statistics were presented as frequencies and percentages, mean ± standard deviation, or as a median and interquartile range (IQR). Missing data were not defaulted to negative, and denominators reflect only actual reported cases. Categorical variables were investigated using the chi-square test or the Fisher exact test when the expected cell count was <5. Continuous variables with an approximately normal distribution were investigated using the Student *t* test; nonparametric continuous variables were explored using the Mann-Whitney U test. Kaplan-Meier life-table analysis was used to demonstrate the overall freedom from procedure-related death during follow-up and to compare the survival rates between symptomatic and asymptomatic patients. Procedure-related death was defined as all fatalities within 30 days of diagnosis of the endograft collapse, as well as deaths after 30 days due to complications related to the endograft collapse or other endograft-related complications. $P < 0.05$ was considered statistically significant. Statistical analyses were performed with SPSS software (version 15.0; SPSS, Chicago, IL, USA).

RESULTS

Initial Procedures and Devices

In the 60 cases of endograft collapse examined, TEVAR was most commonly applied to repair traumatic thoracic aortic injuries (39, 65%), followed by acute and chronic type B aortic dissections (9, 15%). Patients with endograft collapse after TEVAR for traumatic aortic injuries were significantly younger than those with collapse after TEVAR for different aortic pathologies (33.1 versus 50.7 years, p<0.001).

The Gore TAG endograft was most frequently used during the initial TEVAR, accounting for 77% (n=46) of all published endograft collapses. Cook Zenith endografts were used in 10% (n=6) of the original procedures, and the remaining 13% were performed using various commercial or handmade devices (table 2). On average, the collapsed endografts were oversized by 26.7%±12.0% (range 8.3%–60.0%, median 23.8%). Oversizing ≥20% was present in 67% (n=30) of TEVARs (figure 1), and the endograft was oversized ≥40% in 16% (n=7) of the cohort. There was no significant difference in oversizing between traumatic lesions and non-traumatic lesions (27.1% versus 25.9%, p=0.765). The mean percentage of oversizing for patients without endograft collapse was available in 6 reports describing 150 control patients.[13,14,21,22,35,37] The weighted mean percentage of oversizing in these patients was 16.8%±4.2%, which was significantly smaller than the mean percentage of oversizing in the patients with endograft collapse (26.7%, p<0.001).

Table 2. Demographics, Aortic Pathology and Initial Procedure

	N or Mean	(% or ±SD)
Age (y)	40.6	(±17)
Male gender	45	(88.2)
Aortic pathology requiring TEVAR		
Traumatic aortic injury	39	(65.0)
Thoracic aortic aneurysm	7	(11.7)
Acute type B dissection	5	(8.3)
Chronic type B dissection	4	(6.7)
Aortic coarctation	2	(3.3)
Aortoesophageal fistula	2	(3.3)
Intramural hematoma	1	(1.7)
Aortic diameter (mm)	22.6	(±3.4)
Endograft type		
Gore TAG	46	(76.7)
Cook Zenith	6	(10.0)
Other	8	(13.3)
Endograft diameter	28.6	(±3.9)
Endograft length	127.1	(±33.8)
Number of stents	1.2	(±0.5)
Oversizing (%)	26.7	(±12.0)

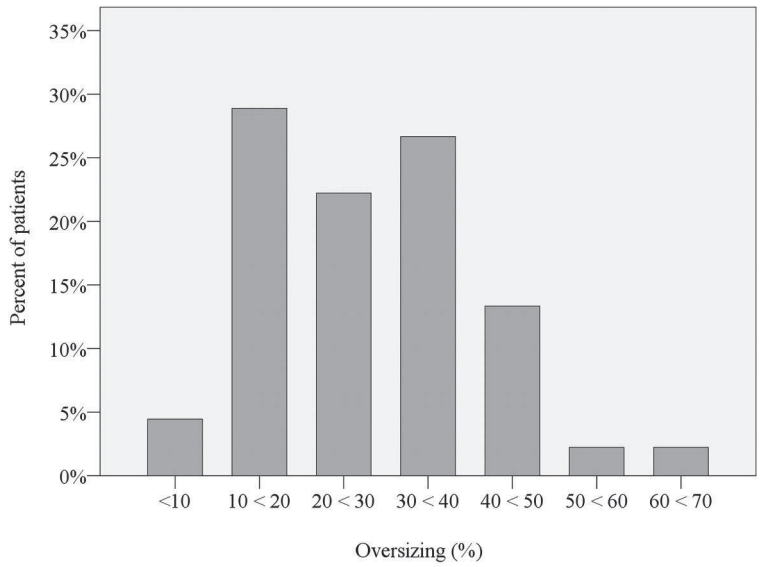

Figure 1. Percentage of oversizing of the endograft during the initial procedure
In aortic dissections, the normal aortic diameter was used to calculate the percentage of oversizing, and not the aortic diameter of the narrowed lumen.

Timing and Presentation of Endograft Collapse

The median time interval between TEVAR and diagnosis of endograft collapse was 15 days (IQR 78, absolute range 1 day to 79 months). Among all cases of endograft collapse, 65% (n=34) was diagnosed within the first month after TEVAR, and 75% (n=39) within the first 3 months (figure 2). The endograft collapse was asymptomatic in 59% (n=33), while 41% (n=23) of patients had symptoms related to the collapse at the moment of diagnosis. The most common finding was no or weak femoral pulses, which was present in 20% (n=11) of all patients. Other frequent symptoms of collapse were thoracic pain and acute renal failure, which each occurred in 13% (n=7) of the cohort (table 3).

Possible Causes of Endograft Collapse

Excessive oversizing was reported as the primary cause of endograft collapse in 20% (n=12). A small radius of curvature of the aortic arch, resulting in inadequate apposition of the proximal endograft to the aortic wall ("bird-beak"), was given as the main cause of endograft collapse in 48% (n=29) of the cases (figure 3). Maldeployment of the endograft and/or endograft failure was responsible for 10% (n=6), and the collapse was thought to be caused by progression of aortic disease in 7% (n=4).

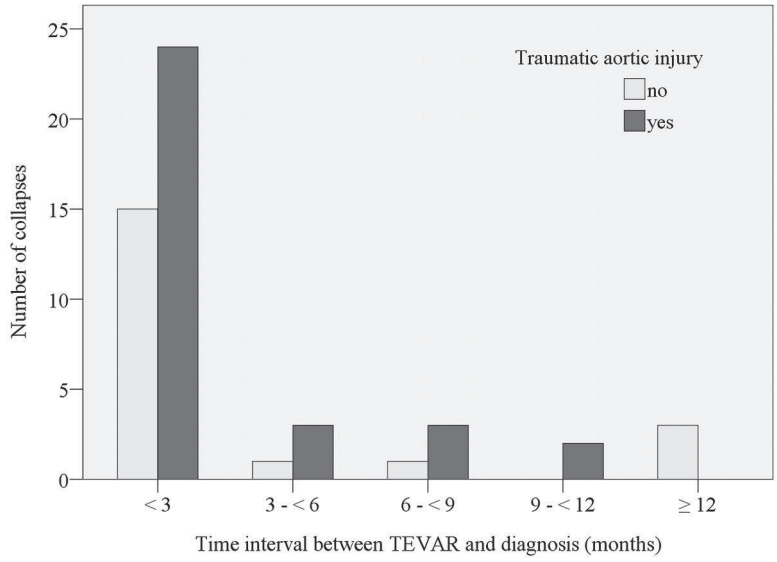

Figure 2. Time interval between TEVAR and diagnosis of Endograft Collapse
The median time interval between TEVAR and diagnosis of endograft collapse was 15 days (range 1 day to 79 months).

Table 3. Collapse Characteristics and Presentation

	N	(%)
Location collapse		
Proximal endograft	36	(65.5)
Distal endograft	9	(16.4)
Entire endograft	10	(18.2)
Presentation		
Asymptomatic	33	(58.9)
Symptoms and signs	23	(41.1)
No / weak femoral pulses	11	(19.6)
Acute renal failure	7	(12.5)
Thoracic pain	7	(12.5)
Abdominal pain	4	(7.1)
Hypertension / pressure gradient	7	(12.5)
Other	6	(10.7)

Other symptoms include dyspnea (n=3), limb pain or paresthesia (n=2), and ventricular fibrillation (n=1)

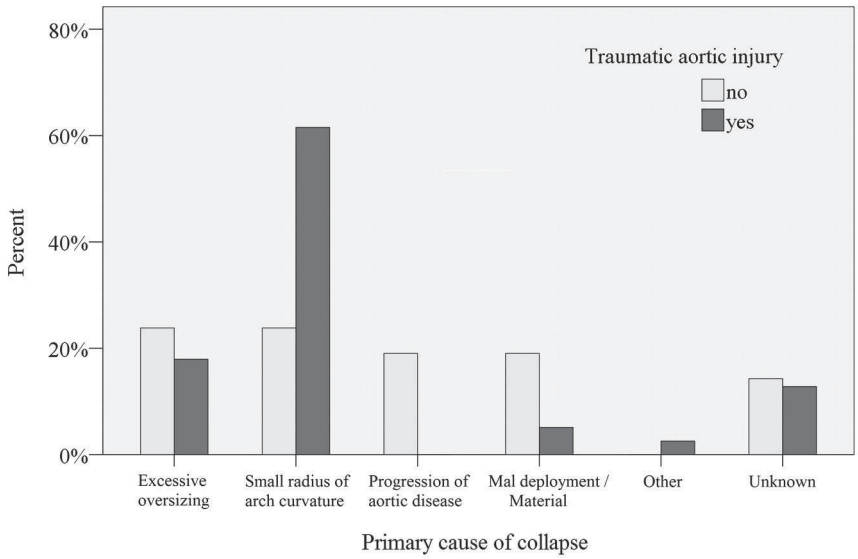

Figure 3. Causes of Endograft Collapse after TEVAR
The primary cause of collapse describes the reported mechanism that was thought to be the most important reason for collapse of the endograft. Percentages were calculated for traumatic and non-traumatic lesions separately. *Other* includes a patient that suffered from endograft collapse after cardio pulmonary resuscitation.

Management

After diagnosis of the endograft collapse, 87% (n=52) of patients were offered an intervention (table 4). Endovascular methods were used in 68% (n=41) of all patients, primarily deployment of an additional endograft (n=36, 60%). Other endovascular methods included dilatation of the endograft (n=3) or embolization of the left subclavian artery (n=2) to achieve complete thrombosis of the aneurysm sac or false lumen. A surgical intervention was offered to 18% (n=11) of the cohort; this typically consisted of surgical explantation of the endograft (n=9, 15%).

Eight (13%) patients did not undergo an intervention because of patient refusal, physician preference for conservative management, or death before an intervention could be offered.

Early Outcomes

Five (8.3%) patients died within 30 days of the diagnosis of endograft collapse owing to multiorgan failure (n=2), cerebral hemorrhage (n=1), cardiac arrest (n=1), and aortic rupture (n=1). All deaths were directly related to thoracic aortic occlusion due to the endograft collapse, except for the patient who died of cerebral hemorrhage 7 days after diagnosis and treatment of the collapsed endograft (50 days after TEVAR for trauma). The 30-day mortality among symptomatic patients was 21.7% (n=5), while no asymptomatic patients died in the first month (p=0.009). Among

patients who received an intervention, the 30-day mortality was 3.8% (1 death each in the surgical and endovascular groups), while 3 (38%) of the 11 patients without treatment expired (p=0.014). An additional 15% of the cohort (n=9) developed complications and/or required a second reintervention (table 4). Seven patients required in total nine reinterventions which included deployment of an additional endograft (n=5), bowel resection (n=2), embolization (n=1) and resection of an aortoesophageal fistula (n=1).

Table 4. Treatment and Outcomes of Endograft Collapse

	N	(%)
Management		
Surgical	11	(18.3)
Surgical explantation	9	(15.0)
Axillo-bifem bypass	2	(3.3)
Endovascular	41	(68.3)
Ballooning alone	3	(5.0)
Additional stent	36	(60.0)
Embolization of LSA	2	(3.3)
No intervention	8	(13.3)
Outcomes		
30-day mortality	5	(8.3)
Complications	9	(15.0)
Renal failure	2	(3.3)
Paraplegia	2	(3.3)
Bowel necrosis	2	(3.3)
Re-intervention	7	(13.5)

LSA, left subclavian artery. *Complications* do not include patients that expired. The number of patients that underwent intervention (n=52) was used as the denominator for calculating the percentage of re-interventions needed, instead of the overall number of patients (n=60). *Re-interventions* consisted of 6 endovascular procedures, including deployment of additional second stents (n=5) and embolization (n=1). One patient required esophagectomy because of an aortoesophageal fistula.

Follow-up Outcomes

The median follow-up after diagnosis of endograft collapse was 6.0 months (IQR 14, absolute range 1–54 months). During follow-up, 3 additional deaths related to the collapsed endograft were reported; the estimated freedom from procedure-related death at 3 years was 77.5% (figure 4). One patient expired due to progression of a partial collapse resulting in multiorgan failure 3 months after diagnosis. Another patient died 3.5 months after diagnosis due to sepsis after explantation of an infected endograft. The third patient suffered a cardiac arrest after explantation of the endograft at 31 months after the diagnosis. The estimated freedom from procedure-related death at 3 years was 83.1% for asymptomatic patients compared with 72.7% for patients who had symptoms at diagnosis of endograft collapse (p=0.029, figure 5).

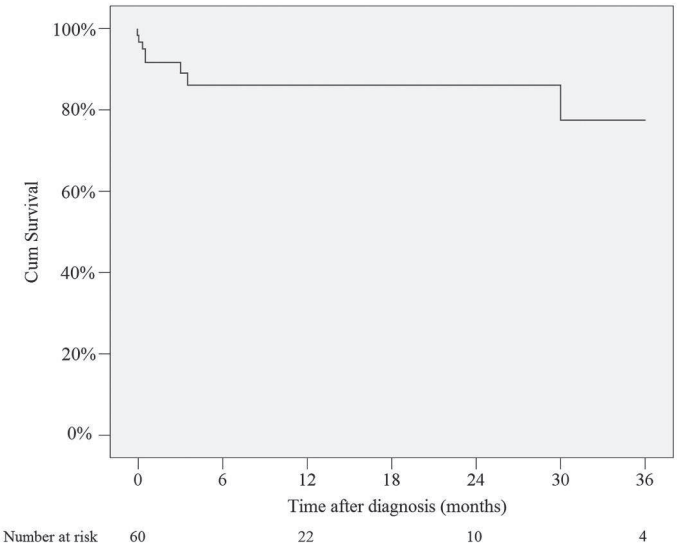

Figure 4. Survival after diagnosis of endograft collapse
The procedure-related survival at 3 years after diagnosis of endograft collapse was 77.5%

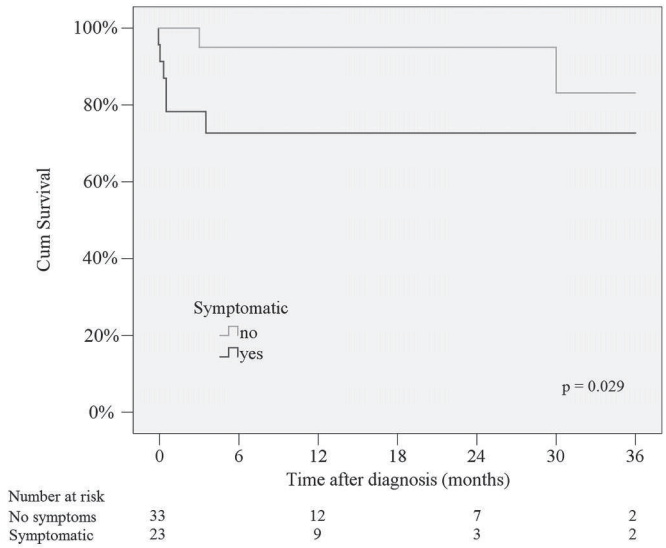

Figure 5. Survival for patients with and without symptoms at diagnosis
At 3 years, the procedure-related survival was 83.1% for asymptomatic patients with endograft collapse, compared with 72.7% for patients that were symptomatic at diagnosis of endograft collapse (p=0.029). Data regarding symptoms at diagnosis were unavailable for four patients (6.7%).

DISCUSSION

TEVAR is emerging as the preferred technique for elective or emergent treatment of descending thoracic aortic disease. However, the endovascular approach has been plagued by endograft-related complications such as endograft collapse.[10,11] Due to increasing popularity of TEVAR for the management of thoracic aortic disease, the number of patients developing endograft collapse may increase in the coming years.

The majority of the reported cases were diagnosed within the first month after TEVAR, most frequently after endovascular repair of traumatic injury, so a high level of suspicion for this complication may be needed in this particular patient group. Although nearly two thirds of the published endograft collapses occurred after endovascular repair of aortic injuries, large series suggest that only 6% to 11% of all TEVAR cases are performed for acute traumatic lesions.[43-46] The relatively high rate of endograft collapse in trauma patients may have several explanations. Trauma patients are typically young and may have relatively small aortas, which often necessitate excessive stent-graft oversizing. This mismatch between the endograft and aortic diameter may lead to incomplete deployment and infolding of the endograft,[47,48] increasing the risk of endograft collapse.

However, endograft oversizing <20% was present in about one third of all cases, so extreme oversizing cannot be the only explanation for the occurrence of endograft collapse after TEVAR. The aortic anatomy may be crucial as well in the development of this complication. Young patients, especially, often have a small radius to the curve of the aortic arch, which appeared to be the most common cause of endograft collapse in trauma patients. The pathogenesis of endograft collapse appears to be multifactorial, and other factors, including the aortic pulsatility and blood flow velocities, may impact the risk of this complication in individual patients as well.[15,49]

The vast majority of published endograft collapses in this analysis occurred after the use of the Gore TAG prosthesis. Caution is needed when interpreting this observation because the TAG stent-graft was the first thoracic endograft approved for market in the United States, and it is a popular device in other countries as well. In the beginning of 2009, over 33,500 Gore TAG devices had been sold,[50] so this device may therefore be the most used device since the introduction of TEVAR. On the other hand, the relatively weak radial force of the TAG endograft[22] could make this device more prone to collapse, but this cannot be concluded based on the presented data.

Canaud and colleagues previously investigated the proximal fixation of commercially available thoracic endografts as a function of oversizing and increasing aortic arch angulation.[47] During dynamic tests in human cadaveric aortas, they found that the Medtronic Valiant endograft remained apposed to the aortic wall at each increment of neck angulation and degree of oversizing, while they observed a lack of device-wall apposition for the Gore TAG, Cook Zenith, and Bolton Medical Relay endografts during dynamic testing. Increasing the oversizing

of these endografts negatively impacted device-wall apposition; however, no endograft collapse was seen during their experiments.[47]

Most patients with endograft collapse did not have symptoms related to the endograft failure; in these patients, the abnormality was detected during standard follow-up imaging, supporting the importance of continued surveillance after TEVAR. Patients who had symptoms at diagnosis likely had a more severe aortic occlusion than asymptomatic patients; common signs were decreased femoral pulses or acute renal failure due to malperfusion. Although these symptoms often led to a quick diagnosis, there was an increased mortality among symptomatic patients.
After diagnosis of the collapse, the majority of patients underwent a reintervention, typically by re-stenting of the collapsed endograft. The few patients who did not receive an endovascular or surgical intervention had a significantly higher mortality rate, which may support an invasive approach for the management of endograft collapse. A minimally invasive endovascular reintervention may be preferred for the management of most cases. Re-expansion of an endograft with dilation only may lead to early recurrence of the collapse,[13,15,31] so deployment of an additional endograft may be a more definitive solution. However, in a completely collapsed endograft with acute aortic occlusion, surgical explantation of the device may be the only adequate treatment. Decision making may be more difficult in patients without symptoms, and although endovascular stenting may prevent further progression of the collapse and future complications, spontaneous re-expansion has been reported as well after conservative management.[17,23]

As always, prevention is better than cure, and measures should be taken to reduce the occurrence rate of endograft collapse. Because the utilization of TEVAR for the management of thoracic aortic disease is expected to further increase, improvements in current endovascular devices may be necessary to limit the number of cases of endograft collapse. Perhaps a different endograft type is needed for trauma patients, with specific collapse-resistant characteristics such as increased radial strength. Such endografts should also adjust better to an aortic arch with a small curvature radius, preventing the endograft from assuming the "bird-beak" configuration. In addition, smaller endograft sizes should be available for physicians at any time to avoid excessive oversizing in emergency cases involving small aortas.

Because endograft collapse after TEVAR is a relatively rare event, the collection of original data from a large number of patients with endograft collapse is very difficult. The largest group of patients with endograft collapse after TEVAR to date that has been reported consisted of 7 cases collected from 5 centers.[12] The most important disadvantage of a meta-analysis is that the data are limited to information provided in the original articles, which can result in inadequate or incomplete information. For example, data regarding the exact radius of the aortic arch, which was often reported as the main cause of endograft collapse, was available only for a minority of the cases. Furthermore, the exact degree of occlusion or compression was often unclear, which is likely related to patient symptoms and subsequent outcome. Current risks of endograft collapse may be reduced due to better operator experience and the use of newer endografts compared with

the first-generation devices. However, such data were typically unavailable as well; moreover, the number of patients was thought to be too small to stratify according to the year of the procedure. Even with these limitations, we believe that the present summary of the published data about endograft collapse provides more insights into the possible causes, presentation, management, and outcome of this serious complication of TEVAR.

CONCLUSION

Endograft collapse typically occurs shortly after TEVAR, most frequently after endovascular repair of traumatic aortic injuries. The causes of endograft collapse may often be multifactorial, and a small radius of curvature in the aortic arch and excessive oversizing are present in most cases. Endograft collapse is associated with considerable mortality and morbidity, especially if patients are symptomatic at diagnosis. A high level of suspicion for endograft collapse in the first month after TEVAR and further improvement of current endovascular devices may be required to improve the long-term outcomes of TEVAR patients.

REFERENCES

1. Demetriades D, Velmahos GC, Scalea TM et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008; 64:561-570.
2. Jonker FH, Giacovelli JK, Muhs BE et al. Trends and outcomes of endovascular and open treatment for traumatic thoracic aortic injury. J Vasc Surg 2010; 51:565-571.
3. Tang GL, Tehrani HY, Usman A et al. Reduced mortality, paraplegia, and stroke with stent graft repair of blunt aortic transections: a modern meta-analysis. J Vasc Surg 2008; 47:671-675.
4. Xenos ES, Abedi NN, Davenport DL et al. Meta-analysis of endovascular vs open repair for traumatic descending thoracic aortic rupture. J Vasc Surg 2008; 48:1343-1351.
5. Hoffer EK, Forauer AR, Silas AM et al. Endovascular stent-graft or open surgical repair for blunt thoracic aortic trauma: systematic review. J Vasc Interv Radiol 2008; 19:1153-1164.
6. Fattori R, Tsai TT, Myrmel T et al. Complicated acute type B dissection: is surgery still the best option?: a report from the International Registry of Acute Aortic Dissection. JACC Cardiovasc Interv 2008; 1:395-402.
7. Demetriades D, Velmahos GC, Scalea TM et al. Diagnosis and treatment of blunt thoracic aortic injuries: changing perspectives. J Trauma 2008; 64:1415-1418.
8. Cook J, Salerno C, Krishnadasan B et al. The effect of changing presentation and management on the outcome of blunt rupture of the thoracic aorta. J Thorac Cardiovasc Surg 2006; 131:594-600.
9. Golledge J, Eagle KA. Acute aortic dissection. Lancet 2008; 372:55-66.
10. Leurs LJ, Harris PL, Buth J. Secondary interventions after elective endovascular repair of degenerative thoracic aortic aneurysms: results of the European collaborators registry (EUROSTAR). J Vasc Interv Radiol 2007; 18:491-495.
11. Svensson LG, Kouchoukos NT, Miller DC et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. Ann Thorac Surg 2008; 85:S1-41.
12. Hinchliffe RJ, Krasznai A, Schultzekool L et al. Observations on the failure of stent-grafts in the aortic arch. Eur J Vasc Endovasc Surg 2007; 34:451-456.
13. Bandorski D, Bruck M, Gunther HU et al. Endograft Collapse After Endovascular Treatment for Thoracic Aortic Disease. Cardiovasc Intervent Radiol 2010.
14. Neschis DG, Moainie S, Flinn WR et al. Endograft repair of traumatic aortic injury-a technique in evolution: a single institution's experience. Ann Surg 2009; 250:377-382.
15. Sze DY, Mitchell RS, Miller DC et al. Infolding and collapse of thoracic endoprostheses: manifestations and treatment options. J Thorac Cardiovasc Surg 2009; 138:324-333.
16. Rajani RR, Dente CJ, Ball CG et al. Collapse of a thoracic aortic stent graft after cardiopulmonary resuscitation. Am Surg 2009; 75:626-627.

17. Ponton A, Garcia I, Arnaiz E et al. Spontaneous re-expansion of a collapsed thoracic endoprosthesis: case report. J Vasc Surg 2008; 48:1585-1588.
18. Megalopoulos A, Soulountsi V, Vasiliadis K et al. Early endograft collapse following endovascular treatment of a traumatic thoracic aortic disruption: a case report. Minerva Chir 2009; 64:431-436.
19. Lazar HL, Varma PK, Shapira OM et al. Endograft collapse after thoracic stent-graft repair for traumatic rupture. Ann Thorac Surg 2009; 87:1582-1583.
20. Kotelis D, Lopez-Benitez R, Tengg-Kobligk H et al. Endovascular repair of stent graft collapse by stent-protected angioplasty using a femoral-brachial guidewire. J Vasc Surg 2008; 48:1609-1612.
21. Fernandez V, Mestres G, Maeso J et al. Endovascular Treatment of Traumatic Thoracic Aortic Injuries: Short- and Medium-term Follow-up. Ann Vasc Surg 2010; 24:160-166.
22. Feezor RJ, Hess PJ, Jr., Martin TD et al. Endovascular treatment of traumatic thoracic aortic injuries. J Am Coll Surg 2009; 208:510-516.
23. Costanza M, Sivia P, Amankwah K et al. Compression and spontaneous re-expansion of a thoracic endograft placed for acute, traumatic injury of the proximal thoracic aorta. J Vasc Surg 2009; 49:771-773.
24. Canaud L, Alric P, Desgranges P et al. Factors favoring stent-graft collapse after thoracic endovascular aortic repair. J Thorac Cardiovasc Surg 2009.
25. Annamalai G, Cook R, Martin M. Endograft collapse following endovascular repair of traumatic aortic injury. Diagn Interv Radiol 2009.
26. Xu SD, Yang BZ, Fan ZM et al. Complications of open stent-graft in treatment of aortic dissection. Interact Cardiovasc Thorac Surg 2009; 8:114-116.
27. Leung DA, Davis I, Katlaps G et al. Treatment of infolding related to the gore TAG thoracic endoprosthesis. J Vasc Interv Radiol 2008; 19:600-605.
28. Palma JH, Guilhen JS, Gaia DF et al. Early complication after hybrid thoracic aortic aneurysm repair. Interact Cardiovasc Thorac Surg 2008; 7:441-443.
29. van Herwaarden JA, Jahrome AK, van Hillegersberg R et al. Endoluminal Repair of an Aortoesophageal Fistula. Endovascular Today 2007;65-67.
30. Rodd CD, Desigan S, Hamady MS et al. Salvage options after stent collapse in the thoracic aorta. J Vasc Surg 2007; 46:780-785.
31. Orend KH, Zarbis N, Schelzig H et al. Endovascular treatment (EVT) of acute traumatic lesions of the descending thoracic aorta--7 years' experience. Eur J Vasc Endovasc Surg 2007; 34:666-672.
32. Muhs BE, Balm R, White GH et al. Anatomic factors associated with acute endograft collapse after Gore TAG treatment of thoracic aortic dissection or traumatic rupture. J Vasc Surg 2007; 45:655-661.
33. Go MR, Barbato JE, Dillavou ED et al. Thoracic endovascular aortic repair for traumatic aortic transection. J Vasc Surg 2007; 46:928-933.

34. Arslan B, Turba UC, Matsumoto AH. Thoracic Aortic Endograft Collapse after Endovascular Treatment of a Traumatic Pseudoaneurysm. Seminars in Interventional Radiology 2007; 24:279-287.
35. Tehrani HY, Peterson BG, Katariya K et al. Endovascular repair of thoracic aortic tears. Ann Thorac Surg 2006; 82:873-877.
36. Steinbauer MG, Stehr A, Pfister K et al. Endovascular repair of proximal endograft collapse after treatment for thoracic aortic disease. J Vasc Surg 2006; 43:609-612.
37. Hoornweg LL, Dinkelman MK, Goslings JC et al. Endovascular management of traumatic ruptures of the thoracic aorta: a retrospective multicenter analysis of 28 cases in The Netherlands. J Vasc Surg 2006; 43:1096-1102.
38. Agnoletti G, Bonnet D, Sidi D. Secondary collapse of a Palmaz stent implanted for native aortic coarctation. Heart 2005; 91:506.
39. Melissano G, Tshomba Y, Civilini E et al. Disappointing results with a new commercially available thoracic endograft. J Vasc Surg 2004; 39:124-130.
40. Surlan M, Pavcnik D, Gabrijelcic T et al. Late complications and shape changes of the endografts after gigantic thoracic aortic aneurysm repair over a 7-year follow-up. Thorac Cardiovasc Surg 2002; 50:104-108.
41. Cambria RP, Brewster DC, Lauterbach SR et al. Evolving experience with thoracic aortic stent graft repair. J Vasc Surg 2002; 35:1129-1136.
42. Taylor PR, Gaines PA, McGuinness CL et al. Thoracic aortic stent grafts--early experience from two centres using commercially available devices. Eur J Vasc Endovasc Surg 2001; 22:70-76.
43. Buth J, Harris PL, Hobo R et al. Neurologic complications associated with endovascular repair of thoracic aortic pathology: Incidence and risk factors. a study from the European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair (EUROSTAR) registry. J Vasc Surg 2007; 46:1103-1110.
44. Fattori R, Nienaber CA, Rousseau H et al. Results of endovascular repair of the thoracic aorta with the Talent Thoracic stent graft: the Talent Thoracic Retrospective Registry. J Thorac Cardiovasc Surg 2006; 132:332-339.
45. Leurs LJ, Bell R, Degrieck Y et al. Endovascular treatment of thoracic aortic diseases: combined experience from the EUROSTAR and United Kingdom Thoracic Endograft registries. J Vasc Surg 2004; 40:670-679.
46. Feezor RJ, Martin TD, Hess PJ, Jr. et al. Extent of aortic coverage and incidence of spinal cord ischemia after thoracic endovascular aneurysm repair. Ann Thorac Surg 2008; 86:1809-1814.
47. Canaud L, Alric P, Laurent M et al. Proximal fixation of thoracic stent-grafts as a function of oversizing and increasing aortic arch angulation in human cadaveric aortas. J Endovasc Ther 2008; 15:326-334.
48. Schurink GW, Aarts NJ, van Baalen JM et al. Stent attachment site-related endoleakage after stent graft treatment: An in vitro study of the effects of graft size, stent type, and atherosclerotic wall changes. J Vasc Surg 1999; 30:658-667.

49. Muhs BE, Vincken KL, van PJ et al. Dynamic cine-CT angiography for the evaluation of the thoracic aorta; insight in dynamic changes with implications for thoracic endograft treatment. Eur J Vasc Endovasc Surg 2006; 32:532-536.
50. Gore TAG Thoracic Endoprosthesis. Annual Clinical Update. April 2010. 2010. Ref Type: Report

Chapter 14

Summary and General Discussion

Descending thoracic aortic catastrophes include a variety of acute pathologies of the descending thoracic aorta, which are all associated with high morbidity and mortality, requiring immediate intervention. For this thesis, we explored the management and outcomes of several thoracic aortic catastrophes, including traumatic thoracic aortic injury, ruptured descending thoracic aortic aneurysm, acute type B aortic dissection, and aortobronchial and aortoesophageal fistulas. Open surgical repair has been the traditional treatment of these thoracic aortic catastrophes since the early fifties.[1-4] Thoracic endovascular aortic repair (TEVAR) recently offers a less invasive alternative for the management of elective and acute thoracic aortic disease.[5-7] Although the use of TEVAR has increased, few studies have compared the outcomes of both treatment modalities for the management of thoracic aortic catastrophes, perhaps due to the low incidence of these emergencies.

This thesis also studied the impact of hypovolemia on the aortic dimensions, and the potential implications for the endovascular management of acute thoracic aortic disease. Thoracic aortic catastrophes are often associated with considerable blood loss and hypovolemic shock.[8-10] Although peripheral vasoconstriction is a well known physiologic response to hypovolemic shock, in order to maintain adequate perfusion of the heart and brain, it is currently unknown how the aorta responds to hypovolemia.

PART 1. MANAGEMENT OF THORACIC AORTIC CATASTROPHES

Traumatic Thoracic Aortic Injury

Traumatic thoracic aortic injury (TTAI) is the second most common cause of death in trauma patients worldwide.[11,12] The trends and outcomes of open and endovascular treatment of TTAI were investigated using the New York Statewide Planning and Research Cooperative System (SPARCS) database in **Chapter 2**. Our analysis revealed that a major shift has occurred towards endovascular management of TTAI during the last decade. Although patients treated with TEVAR had more major additional injuries, the overall in-hospital mortality rate was significantly lower after endovascular repair compared with open surgery. After adjusting for major additional injuries, the difference in survival between both treatment groups was even larger [OR 3.8, 95%CI 1.3-11.0]. Hence, the minimally invasive characteristics of TEVAR appear especially beneficial for patients with serious associated injuries, which cannot tolerate thoracotomy or aortic cross-clamping. Recent meta-analyses and a large evaluation of the American Association for the Surgery of Trauma (AAST) supported our findings, showing mortality rates between 7.2% to 8.4% after TEVAR and 15.2% to 23.5% after open surgery,[13-16] which seem to justify an endovascular approach for the management of TTAI.

A remaining cause for concern is the occurrence of endograft-related complications such as endoleak, which was diagnosed in 9% of the patients in the state of New York. Other evaluations

have reported endoleak rates between 5% to 15% after TEVAR for TTAI,[13,14,16-18] and the majority consist of proximal type 1 endoleaks which usually require re-intervention.[13,17,18]

Ruptured Descending Thoracic Aortic Aneurysm

Ruptured descending thoracic aortic aneurysm (rDTAA) is another aortic catastrophe associated with high morbidity and mortality.[19,20] In **Chapter 3**, we compared the pooled outcomes of open surgery and TEVAR for rDTAA in a meta-analysis of the contemporary literature. The overall 30-day mortality was 19% after TEVAR for rDTAA, which was significantly lower compared with the pooled mortality rate after open surgery, which was 33% [OR 2.2, 95% CI 1.2-4.0]. To further investigate the outcomes after both treatments for rDTAA, a multi-center evaluation was performed which is discussed in **Chapter 4**. The primary endpoint of the study was of a composite endpoint of death, stroke and permanent paraplegia after TEVAR and open surgery. After adjusting for significant risk factors including advanced age and hypovolemic shock, we found that TEVAR was associated with a reduced risk of this composite endpoint [OR 0.49, 95% CI 0.24-0.97]. Furthermore, there was a trend towards lower 30-day mortality after TEVAR, 17.4% vs. 24.6%, respectively. TEVAR therefore appears to be the preferred treatment for rDTAA. However, all participating hospitals were large referral centers and outcomes are generally superior in high-volume hospitals with experienced surgeons.[21,22] Therefore, our data may underestimate the mortality rates after open and endovascular repair of rDTAA.

In **Chapter 5**, predictors of 30-day mortality and long-term outcomes after TEVAR were explored. Advanced age [OR 1.11], hypovolemic shock [OR 4.75] and hemothorax [OR 6.65] appeared risk factors for 30-day mortality after TEVAR. While advanced age[20,23-26] and hypovolemic shock[26-28] are well known predictors of a poor prognosis among patients with acute thoracic aortic disease, the strong association between hemothorax and 30-day mortality was more surprising. Hemothorax is a sign of substantial blood loss, and could increase risks of respiratory insufficiency and infections. Again, the endograft-related complications after TEVAR were concerning, endoleak was diagnosed in 18% within the first month, and the freedom from aneurysm-related death and aortic re-intervention at 4 years was only 54.9%.

Endovascular management of rDTAA was also associated with a considerable risk of peri-procedural stroke, which occurred in 7.6% of all patients. Predictors of peri-procedural stroke after endovascular repair of rDTAA were analyzed in **Chapter 6**. This analysis showed that advanced age was an independent risk factor for stroke after TEVAR [OR 1.4, 95% CI 1.1-1.8]. Elderly patients may have more extensive atherosclerotic disease in the aortic arch and carotid arteries, resulting in higher risk of cerebral embolization during manipulation with instrumentarium. More recent endovascular procedures were associated with a lower risk of stroke [OR 0.52, 95% CI 0.28-0.97], which may be related to improvements in operator experience and endograft design.[29,30]

Acute Type B Aortic Dissection

The optimal management of patients presenting acute type B aortic dissection (ABAD) was investigated using data from the International Registry of Acute Aortic Dissection (IRAD), which contains the largest cohort of ABAD patients. ABAD in the absence of complications can generally be managed with medical therapy. In **Chapter 7**, we found that patients with uncomplicated ABAD with recurrent pain and/or refractory hypertension had substantially increased in-hospital mortality [OR 3.3, 95% CI 1.04-10.5], particularly when managed medically. Recurrent pain and/or refractory hypertension may be signs of extending dissection or pending aortic rupture, and ABAD patients with these signs may be at intermediate risk for an adverse outcome. These observations suggest that a more invasive treatment, such as via endovascular approach, is indicated in this intermediate risk group.

An intervention is generally indicated if ABAD is associated with complications, such as acute renal failure, visceral ischemia, limb ischemia, paraplegia, or aortic rupture. The impact of age on the management and outcomes of complicated ABAD in IRAD were evaluated in **Chapter 8**. The utilization of surgery for complicated ABAD progressively decreased with patient age, while the rate of definitive medical management significantly increased with age, most likely because advanced age is a risk factor for mortality and morbidity after thoracic aortic intervention.[20,23-26] The mortality rates significantly increased with age, irrespective of the management type. For patients younger than 70 years, there was a non-significant trend towards lower mortality after endovascular treatment, while medical management was associated with a slightly lower mortality rate for the elderly cohort. Recent reports have suggested that endovascular management of complicated ABAD is associated with lower mortality rates, often between 10% and 20%, compared with 20% to 30% after a more invasive surgical approach.[31-37] However, these reports were not stratified according to the age of patients. Based on these studies and the IRAD data, TEVAR may be the preferred treatment for patients with complicated ABAD, especially for those younger than 70 years.

Thoracic Aortic Fistulas

Aortobronchial (ABF) and aortoesophageal (AEF) fistulas are extremely rare entities, with a very poor prognosis.[38-41] Patients often present with hemoptysis and hematemesis, respectively, which will eventually lead to exsanguination if left untreated. Both lung tissue and the esophagus are non-sterile cavities that are contaminated by micro-organisms, which present a continuing risk of infection. Hence, these fistulas are relative contraindications to deployment of an endograft. In **Chapter 9**, we evaluated the outcomes of all patients with ABF and AEF treated with TEVAR. Overall, we identified only 11 cases of endovascular management of ABF and AEF at the participating institutions. Although no perioperative deaths occurred, five of the 11 patients expired due to infective complications within the first months after TEVAR, and especially endovascular management of AEF appeared to be associated with a low survival rate.

To further investigate if TEVAR may serve as a definite solution for thoracic aortic fistulas, we analyzed all published cases of endovascular management of ABF and AEF in **Chapter 10**. The in-hospital mortality rate after TEVAR for ABF (3%) was significantly lower than for those treated with TEVAR for AEF (19%), and at 6 months after TEVAR, ABF patients still had a significantly better survival rate. For patients with ABF, TEVAR appeared as a definite treatment, associated with lower mortality compared with traditional results of open surgery, which ranges between 15% and 24% in the literature.[38,39] After TEVAR for AEF, however, additional esophageal surgery was often needed to treat the fistula. Patients that did not undergo esophageal repair after TEVAR had a significantly increased mortality rate during follow-up, primarily due to infective complications from the persistent connection with the esophagus. In AEF patients, TEVAR may therefore serve as a bridge to surgery, with definite surgical repair of the fistula and/or esophageal reconstruction undertaken as soon as possible to prevent infection of the endograft.

PART 2. IMPROVING THE DURABILITY OF TEVAR

Our studies suggest that TEVAR improves the prognosis of most thoracic aortic catastrophes. Randomized studies have shown that the survival advantage for patients treated with endovascular aortic repair (EVAR) for non-ruptured abdominal aortic aneurysms (AAA) compared with open surgery did not sustain during follow-up.[42-44] For most thoracic aortic catastrophes, however, we do not expect that the early advantages of TEVAR will diminish completely over time, because of the substantial differences in mortality and morbidity after both treatments. The endovascular treatment of these acute pathologies is still associated with considerable endograft-related complications, such as endoleak in 5% to 30%[13,14,16-18,28,45,46] and endograft collapse in 0% to 10%.[17,47-49] To further improve the long-term outcomes of patients with thoracic aortic catastrophes, reduction of the incidence of endograft failure is needed. Adequate endograft sizing is thought to be essential for minimizing risks of these complications after endovascular repair of abdominal and thoracic aortic disease, and satisfying long-term results.

The Impact of Hypovolemia on the Aortic Diameter

Hypovolemic shock may affect the aortic dimensions, which could lead to inadequate endograft sizing. The aortic changes in trauma patients admitted with hemodynamic instability were investigated in **Chapter 11**. This study revealed that the aortic diameter was significantly larger at control the CT examinations, compared with the initial CT examinations when patients were hemodynamically unstable. Among those patients admitted with a heart rate ≥ 130, the mean difference at the level of the mid descending thoracic aorta was 12.6%. Possibly, the decreased pressure on the aortic wall due to blood loss, and endogenous production of vasoconstrictors may have caused the decrease in aortic diameter. The increase in aortic diameter on the control CT

was not consistent in all patients, in some patients the difference in aortic diameter was more than 40%, while no difference was found in a few patients. The cardiovascular system is a complex balance, and many variables may affect the aortic compliance and diameter, including the age of patients, circulating blood volume, pre-existing co-morbidities such as diabetes mellitus and atherosclerosis, and use of anti-hypertensive medication.

In **Chapter 12**, we further investigated the impact of blood loss and hypovolemic shock on the aortic diameter in a porcine model. The circulating blood volume of seven Yorkshire pigs was gradually lowered in 10% increments. At 40% blood loss, an endograft was deployed in the descending thoracic aorta, followed by gradual fluid resuscitation. Potential changes in aortic diameter during the experiment were recorded using intravascular ultrasound (IVUS). We observed that the aortic diameter gradually decreased in all subjects, at the level of the ascending, descending and abdominal aorta. The descending thoracic aorta was on average 31.8% smaller after 40% blood loss. The aortic diameters quickly regained their initial size during fluid resuscitation.

These aortic changes could theoretically take place in all patients with considerable blood loss, but we expect that these changes will be most extreme in young TTAI patients. Because aortic compliance decreases with age[50,51] due to a loss of elasticity and increased prevalence of aortic calcification,[52-54]we believe that aortic changes may be less dramatic in patients with ruptured aortic aneurysms who are typically much older than the average trauma patient.

Implications for TEVAR of Thoracic Aortic Catastrophes

Endograft sizing for TEVAR is usually performed using the pre-operative CTA scan, however, if the diameter of the descending thoracic aorta is considerably smaller at admission due to blood loss, physicians may undersize the endograft. This mismatch between the aortic diameter and the endograft could theoretically result in increased risks of endoleak or other endograft related complications such as endograft migration after TEVAR. Physicians performing TEVAR should be aware that changes in aortic diameter due to hypovolemia could take place, and there may be two options to adjust for this phenomenon.

First, because the actual aortic diameter measurements may be larger than observed on pre-operative CTA, physicians could consider to slightly increase the percentage of oversizing of the endograft. Because of the many variables that may affect the aortic dimensions, it is difficult to provide a recommendation with regard to the exact percentage of oversizing needed in hypovolemic patients. Based on the finding that the mid descending thoracic aorta of trauma patients with a pulse > 130/min and a MAP < 95mmHg was on average 12.6% smaller on the CT at admission, physicians could consider to apply on average around 20% to 30% oversizing in TTAI patients with similar vital signs, instead of the standard 10% to 20% oversizing.

An alternative to increasing the percentage of oversizing could be performing additional imaging after fluid resuscitation for more adequate aortic measurements. Several recent studies have suggested that delaying TEVAR for patients with TTAI improves survival,[55-58] and our findings would support this approach. Additional imaging could be performed either using a second CT scan or using IVUS during the endovascular procedure. However, some studies suggest that fluid resuscitation should be limited in patients with hemorrhagic shock due to trauma or ruptured aneurysm, because fluid restriction may limit internal bleeding and its associated loss of platelets and clotting factors.[59-63]

Caution is needed when increasing the percentage of oversizing during TEVAR, because some reports suggest that this may increase risks of endograft collapse, an uncommon but serious complication of TEVAR.[47,49,64] In **Chapter 13**, we analyzed published data of endograft collapse after TEVAR, to provide more insight into the causes and timing of this adverse outcome. The most reported cause of endograft collapse was a small radius of the curvature of the aortic arch, resulting in "bird beaking" of the endograft. Excessive oversizing was also reported as a common cause of collapse, the collapsed endografts were on average oversized by 26.7%, which is outside the instructions-for-use (IFU) criteria of the available thoracic endografts. Interestingly, 65% of all published thoracic endograft collapses had occurred after endovascular repair of TTAI, while only 6% to 11% of all TEVAR cases are performed for this pathology.[65-68] A possible explanation for the increased risks of collapse after TEVAR for TTAI is that young trauma patients may have relatively small aortas, which often necessitates excessive oversizing using the smallest available endograft. In addition, young patients typically have a smaller radius of the curvature of the aortic arch. Therefore, increased oversizing of the endograft may be only appropriate for TTAI patients with hypovolemia, and not for hemodynamically stable patients.

Future Perspectives

This thesis suggests that short-term and mid-term results of endovascular repair of most thoracic aortic pathologies are improved compared with traditional open surgery. Our studies all had an observational design, while a randomized controlled trial (RCT) is generally the ideal study design for comparing two treatment modalities. It will be very difficult to ever realize RCT's evaluating the results of both treatments for the various thoracic aortic catastrophes due to the low incidence of these entities and its emergent nature. Perhaps performing such RCT's, would be unethical as well because current observational data including our studies suggest a considerable survival benefit after TEVAR.

Long-term follow-up data of TEVAR for these pathologies are unavailable at this moment, because this treatment modality has been only available for about a decade. Most patients with thoracic aortic aneurysms and dissections are in their sixties or seventies,[69,70] with a median life-expectancy of less than 10 years. The mean age of trauma patients, however, is around 40 years,[13-16] and these patients will need to live with a thoracic endograft for more than 30 years

on average. This situation underlines the need for data regarding the longer-term outcomes after TEVAR of thoracic aortic catastrophes, especially TTAI.

The main disadvantage of TEVAR at this moment is the risk of endograft-related complications during follow-up.[71,72] Future research should further investigate which patient and procedural characteristics affect the occurrence of endograft failure, in order to lower its incidence. Our studies have shown that hypovolemia affects the aortic dimensions and endograft sizing, and additional studies may help us to better predict the normal aortic diameters in hypovolemic patients requiring TEVAR. Improvements in endograft design could contribute to reduction of endograft-related complications as well.

Currently, only thoracic aortic catastrophes of the descending thoracic aorta can be managed with endovascular treatment, while just 30% of ruptured thoracic aortic aneurysms and 30% to 40% of all aortic dissections are found at this part of the thoracic aorta.[19,69,70] For aortic dissections or ruptured aneurysms originating at the ascending aorta and aortic arch, surgical resection remains the standard management.[69-73] Branched thoracic endografts for the aortic arch and supra-aortic arteries are already being used,[74,75] but deployment of these experimental endografts requires high expertise and is currently associated with considerable operating times, making this promising technique at this moment less suitable for the management of thoracic aortic catastrophes.

Life-long surveillance using CTA is required after TEVAR, and regular CTA examinations will result in substantial radiation exposure and treatment costs over time, in particular for young trauma patients with TTAI treated with TEVAR. Future research should therefore focus on new, more affordable, imaging modalities for surveillance, which avoid the use of contrast agent or radiation. Duplex ultrasound appears to offer a less expensive reliable tool for surveillance after endovascular repair of AAA,[76-78] and similar imaging methods should ideally be developed for surveillance after TEVAR.

The shift towards endovascular management of patients with thoracic aortic catastrophes has resulted in substantially reduced morbidity and mortality rates. A better understanding of the aortic dynamics, as well as advancements in endograft design are likely to result in a reduction of endograft-related complications, and further improvements of the prognosis of patients with acute thoracic aortic disease.

REFERENCES

1. Lam CR, Ram HH. Resection of the descending thoracic aorta for aneurysm; a report of the use of a homograft in a case and an experimental study. Ann Surg 1951; 134:743-752.
2. Cooley DA, De Bakey ME. Surgical considerations of intrathoracic aneurysms of the aorta and great vessels. Ann Surg 1952; 135:660-680.
3. Parmley LF, Mattingly TW, Manion WC et al. Nonpenetrating traumatic injury of the aorta. Circulation 1958; 17:1086-1101.
4. Mattox KL, Wall MJ, Jr. Historical review of blunt injury to the thoracic aorta. Chest Surg Clin N Am 2000; 10:167-82, x.
5. Dake MD, Miller DC, Semba CP et al. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. N Engl J Med 1994; 331:1729-1734.
6. Mitchell RS. Endovascular stent graft repair of thoracic aortic aneurysms. Semin Thorac Cardiovasc Surg 1997; 9:257-268.
7. Semba CP, Kato N, Kee ST et al. Acute rupture of the descending thoracic aorta: repair with use of endovascular stent-grafts. J Vasc Interv Radiol 1997; 8:337-342.
8. Wiggers HC, Ingraham RC. Vasoconstriction and the development of irreversible hemorrhagic shock. Am J Physiol 1948; 153:511-520.
9. Cohn JN, Luria MH. Studies in clinical shock and hypotension. IV. Variations in reflex vasoconstriction and cardiac stimulation. Circulation 1966; 34:823-832.
10. Peitzman AB, Billiar TR, Harbrecht BG et al. Hemorrhagic shock. Curr Probl Surg 1995; 32:925-1002.
11. Schumacher H, Bockler D, von Tengg-Kobligk H et al. Acute traumatic aortic tear: open versus stent-graft repair. Semin Vasc Surg 2006; 19:48-59.
12. Fabian TC, Richardson JD, Croce MA et al. Prospective study of blunt aortic injury: Multicenter Trial of the American Association for the Surgery of Trauma. J Trauma 1997; 42:374-380.
13. Demetriades D, Velmahos GC, Scalea TM et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008; 64:561-570.
14. Tang GL, Tehrani HY, Usman A et al. Reduced mortality, paraplegia, and stroke with stent graft repair of blunt aortic transections: a modern meta-analysis. J Vasc Surg 2008; 47:671-675.
15. Xenos ES, Abedi NN, Davenport DL et al. Meta-analysis of endovascular vs open repair for traumatic descending thoracic aortic rupture. J Vasc Surg 2008; 48:1343-1351.
16. Hoffer EK, Forauer AR, Silas AM et al. Endovascular stent-graft or open surgical repair for blunt thoracic aortic trauma: systematic review. J Vasc Interv Radiol 2008; 19:1153-1164.
17. Neschis DG, Moainie S, Flinn WR et al. Endograft repair of traumatic aortic injury-a technique in evolution: a single institution's experience. Ann Surg 2009; 250:377-382.

18. Orend KH, Zarbis N, Schelzig H et al. Endovascular treatment (EVT) of acute traumatic lesions of the descending thoracic aorta--7 years' experience. Eur J Vasc Endovasc Surg 2007; 34:666-672.
19. Johansson G, Markstrom U, Swedenborg J. Ruptured thoracic aortic aneurysms: a study of incidence and mortality rates. J Vasc Surg 1995; 21:985-988.
20. Schermerhorn ML, Giles KA, Hamdan AD et al. Population-based outcomes of open descending thoracic aortic aneurysm repair. J Vasc Surg 2008; 48:821-827.
21. Birkmeyer JD, Siewers AE, Finlayson EV et al. Hospital volume and surgical mortality in the United States. N Engl J Med 2002; 346:1128-1137.
22. Birkmeyer JD, Stukel TA, Siewers AE et al. Surgeon volume and operative mortality in the United States. N Engl J Med 2003; 349:2117-2127.
23. Mehta RH, O'Gara PT, Bossone E et al. Acute type A aortic dissection in the elderly: clinical characteristics, management, and outcomes in the current era. J Am Coll Cardiol 2002; 40:685-692.
24. Ehrlich M, Fang WC, Grabenwoger M et al. Perioperative risk factors for mortality in patients with acute type A aortic dissection. Circulation 1998; 98:II294-II298.
25. Achneck HE, Rizzo JA, Tranquilli M et al. Safety of thoracic aortic surgery in the present era. Ann Thorac Surg 2007; 84:1180-1185.
26. Rampoldi V, Trimarchi S, Eagle KA et al. Simple risk models to predict surgical mortality in acute type A aortic dissection: the International Registry of Acute Aortic Dissection score. Ann Thorac Surg 2007; 83:55-61.
27. Suzuki T, Mehta RH, Ince H et al. Clinical profiles and outcomes of acute type B aortic dissection in the current era: lessons from the International Registry of Aortic Dissection (IRAD). Circulation 2003; 108 Suppl 1:II312-II317.
28. Patel HJ, Williams DM, Upchurch GR, Jr. et al. A comparative analysis of open and endovascular repair for the ruptured descending thoracic aorta. J Vasc Surg 2009; 50:1265-1270.
29. Dake MD, Miller DC, Mitchell RS et al. The "first generation" of endovascular stent-grafts for patients with aneurysms of the descending thoracic aorta. J Thorac Cardiovasc Surg 1998; 116:689-703.
30. Demers P, Miller DC, Mitchell RS et al. Midterm results of endovascular repair of descending thoracic aortic aneurysms with first-generation stent grafts. J Thorac Cardiovasc Surg 2004; 127:664-673.
31. Fattori R, Tsai TT, Myrmel T et al. Complicated acute type B dissection: is surgery still the best option?: a report from the International Registry of Acute Aortic Dissection. JACC Cardiovasc Interv 2008; 1:395-402.
32. Khoynezhad A, Donayre CE, Omari BO et al. Midterm results of endovascular treatment of complicated acute type B aortic dissection. J Thorac Cardiovasc Surg 2009; 138:625-631.

33. Trimarchi S, Nienaber CA, Rampoldi V et al. Role and results of surgery in acute type B aortic dissection: insights from the International Registry of Acute Aortic Dissection (IRAD). Circulation 2006; 114:I357-I364.
34. Feezor RJ, Martin TD, Hess PJ, Jr. et al. Early outcomes after endovascular management of acute, complicated type B aortic dissection. J Vasc Surg 2009; 49:561-566.
35. Verhoye JP, Miller DC, Sze D et al. Complicated acute type B aortic dissection: midterm results of emergency endovascular stent-grafting. J Thorac Cardiovasc Surg 2008; 136:424-430.
36. Duebener LF, Lorenzen P, Richardt G et al. Emergency endovascular stent-grafting for life-threatening acute type B aortic dissections. Ann Thorac Surg 2004; 78:1261-1266.
37. Patel HJ, Williams DM, Meerkov M et al. Long-term results of percutaneous management of malperfusion in acute type B aortic dissection: implications for thoracic aortic endovascular repair. J Thorac Cardiovasc Surg 2009; 138:300-308.
38. MacIntosh EL, Parrott JC, Unruh HW. Fistulas between the aorta and tracheobronchial tree. Ann Thorac Surg 1991; 51:515-519.
39. Piciche M, De PR, Fabbri A et al. Postoperative aortic fistulas into the airways: etiology, pathogenesis, presentation, diagnosis, and management. Ann Thorac Surg 2003; 75:1998-2006.
40. Carter R, Mulder GA, Snyder EN, Jr. et al. Aortoesophageal fistula. Am J Surg 1978; 136:26-30.
41. Hollander JE, Quick G. Aortoesophageal fistula: a comprehensive review of the literature. Am J Med 1991; 91:279-287.
42. 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; 362:1881-1889.
43. Greenhalgh RM, Brown LC, Powell JT et al. Endovascular versus open repair of abdominal aortic aneurysm. N Engl J Med 2010; 362:1863-1871.
44. Lederle FA, Freischlag JA, Kyriakides TC et al. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. JAMA 2009; 302:1535-1542.
45. Cambria RP, Crawford RS, Cho JS et al. A multicenter clinical trial of endovascular stent graft repair of acute catastrophes of the descending thoracic aorta. J Vasc Surg 2009; 50:1255-1264.
46. Geisbusch P, Kotelis D, Weber TF et al. Endovascular repair of ruptured thoracic aortic aneurysms is associated with high perioperative mortality and morbidity. J Vasc Surg 2010; 51:299-304.
47. Sze DY, Mitchell RS, Miller DC et al. Infolding and collapse of thoracic endoprostheses: manifestations and treatment options. J Thorac Cardiovasc Surg 2009; 138:324-333.
48. Leung DA, Davis I, Katlaps G et al. Treatment of infolding related to the gore TAG thoracic endoprosthesis. J Vasc Interv Radiol 2008; 19:600-605.
49. Bandorski D, Bruck M, Gunther HU et al. Endograft collapse after endovascular treatment for thoracic aortic disease. Cardiovasc Intervent Radiol 2010; 33:492-497.
50. Mohiaddin RH, Underwood SR, Bogren HG et al. Regional aortic compliance studied by magnetic resonance imaging: the effects of age, training, and coronary artery disease. Br Heart J 1989; 62:90-96.

51. Sonesson B, Hansen F, Stale H et al. Compliance and diameter in the human abdominal aorta--the influence of age and sex. Eur J Vasc Surg 1993; 7:690-697.
52. Mohiaddin RH, Schoser K, Amanuma M et al. MR imaging of age-related dimensional changes of thoracic aorta. J Comput Assist Tomogr 1990; 14:748-752.
53. Bazan HA, Pradhan S, Mojibian H et al. Increased aortic arch calcification in patients older than 75 years: implications for carotid artery stenting in elderly patients. J Vasc Surg 2007; 46:841-845.
54. Takeda S, Watanabe H, Matsuzawa T. Age-related change in calcifications in the thoracic aorta: a study with computed tomography. Tohoku J Exp Med 1986; 149:73-78.
55. Demetriades D, Velmahos GC, Scalea TM et al. Blunt traumatic thoracic aortic injuries: early or delayed repair--results of an American Association for the Surgery of Trauma prospective study. J Trauma 2009; 66:967-973.
56. Symbas PN, Sherman AJ, Silver JM et al. Traumatic rupture of the aorta: immediate or delayed repair? Ann Surg 2002; 235:796-802.
57. Hemmila MR, Arbabi S, Rowe SA et al. Delayed repair for blunt thoracic aortic injury: is it really equivalent to early repair? J Trauma 2004; 56:13-23.
58. Pate JW, Fabian TC, Walker W. Traumatic rupture of the aortic isthmus: an emergency? World J Surg 1995; 19:119-125.
59. Veith FJ, Lachat M, Mayer D et al. Collected world and single center experience with endovascular treatment of ruptured abdominal aortic aneurysms. Ann Surg 2009; 250:818-824.
60. Bickell WH, Wall MJ, Jr., Pepe PE et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. N Engl J Med 1994; 331:1105-1109.
61. Roberts K, Revell M, Youssef H et al. Hypotensive resuscitation in patients with ruptured abdominal aortic aneurysm. Eur J Vasc Endovasc Surg 2006; 31:339-344.
62. van der Vliet J, van Aalst DL, Schultze Kool LJ et al. Hypotensive hemostatis (permissive hypotension) for ruptured abdominal aortic aneurysm: are we really in control? Vascular 2007; 15:197-200.
63. Kwan I, Bunn F, Roberts I. Timing and volume of fluid administration for patients with bleeding. Cochrane Database Syst Rev 2003;CD002245.
64. Muhs BE, Balm R, White GH et al. Anatomic factors associated with acute endograft collapse after Gore TAG treatment of thoracic aortic dissection or traumatic rupture. J Vasc Surg 2007; 45:655-661.
65. Buth J, Harris PL, Hobo R et al. Neurologic complications associated with endovascular repair of thoracic aortic pathology: Incidence and risk factors. a study from the European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair (EUROSTAR) registry. J Vasc Surg 2007; 46:1103-1110.
66. Fattori R, Nienaber CA, Rousseau H et al. Results of endovascular repair of the thoracic aorta with the Talent Thoracic stent graft: the Talent Thoracic Retrospective Registry. J Thorac Cardiovasc Surg 2006; 132:332-339.

67. Leurs LJ, Bell R, Degrieck Y et al. Endovascular treatment of thoracic aortic diseases: combined experience from the EUROSTAR and United Kingdom Thoracic Endograft registries. J Vasc Surg 2004; 40:670-679.
68. Feezor RJ, Martin TD, Hess PJ, Jr. et al. Extent of aortic coverage and incidence of spinal cord ischemia after thoracic endovascular aneurysm repair. Ann Thorac Surg 2008; 86:1809-1814.
69. Ince H, Nienaber CA. Etiology, pathogenesis and management of thoracic aortic aneurysm. Nat Clin Pract Cardiovasc Med 2007; 4:418-427.
70. Hagan PG, Nienaber CA, Isselbacher EM et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. JAMA 2000; 283:897-903.
71. Svensson LG, Kouchoukos NT, Miller DC et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. Ann Thorac Surg 2008; 85:S1-41.
72. Hiratzka LF, Bakris GL, Beckman JA et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with Thoracic Aortic Disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. Circulation 2010; 121:e266-e369.
73. Golledge J, Eagle KA. Acute aortic dissection. Lancet 2008; 372:55-66.
74. Chuter TA, Schneider DB. Endovascular repair of the aortic arch. Perspect Vasc Surg Endovasc Ther 2007; 19:188-192.
75. Schoder M, Lammer J, Czerny M. Endovascular aortic arch repair: hopes and certainties. Eur J Vasc Endovasc Surg 2009; 38:255-261.
76. Schmieder GC, Stout CL, Stokes GK et al. Endoleak after endovascular aneurysm repair: duplex ultrasound imaging is better than computed tomography at determining the need for intervention. J Vasc Surg 2009; 50:1012-1017.
77. Beeman BR, Doctor LM, Doerr K et al. Duplex ultrasound imaging alone is sufficient for midterm endovascular aneurysm repair surveillance: a cost analysis study and prospective comparison with computed tomography scan. J Vasc Surg 2009; 50:1019-1024.
78. Chaer RA, Gushchin A, Rhee R et al. Duplex ultrasound as the sole long-term surveillance method post-endovascular aneurysm repair: a safe alternative for stable aneurysms. J Vasc Surg 2009; 49:845-849.

Chapter 15

Nederlandse Samenvatting

Voor dit proefschrift hebben wij de behandeling en resultaten van diverse acute pathologieën van de aorta thoracalis descendens geëvalueerd, waaronder traumatische aortarupturen, geruptureerde aneurysmata van de thoracale aorta, acute type B aortadissecties, en aortobronchiale en aorto-oesofageale fistulae. Open chirurgie is de traditionele behandeling geweest van deze acute ziektebeelden van de aorta thoracalis descendens sinds het begin van de jaren vijftig.[1-4] Thoracic endovascular aortic repair (TEVAR) biedt sinds enkele jaren een minimaal invasieve behandeling voor pathologieën van de thoracale aorta.[5-7] Alhoewel het gebruik van deze endovasculaire behandeling is toegenomen in de afgelopen jaren, zijn er tot nu toe maar weinig studies geweest die de resultaten van open chirurgie en TEVAR voor de behandeling van deze acute ziektebeelden hebben vergeleken, waarschijnlijk als gevolg van de lage incidentie van deze pathologieën.

Voor dit proefschrift hebben wij ook de invloed van hypovolemische shock op de afmetingen van de aorta bestudeerd, alsmede de mogelijke implicaties voor de endovasculaire behandeling van acute ziektebeelden van de thoracale aorta. Patienten met dergelijke ziektebeelden hebben vaak veel bloed verloren of zijn zelfs in hypovolemische shock.[8-10] Hoewel perifere vasoconstrictie een bekende respons is op hypovolemische shock, om de bloedflow naar het hart en de hersenen te kunnen waarborgen, is het op dit moment onbekend hoe de aorta reageert op hypovolemie.

DEEL 1. ACUTE PATHOLOGIEËN VAN DE THORACALE AORTA

Traumatische Aortarupturen

Traumatische aortaruptuur (TAR) is wereldwijd de op een na meest voorkomende doodsoorzaak na trauma.[11,12] De resultaten van open chirurgie en TEVAR voor de behandeling van traumatische aortarupturen zijn bestudeerd met behulp van de New York Statewide Planning and Research Cooperative System (SPARCS) database in **Hoofdstuk 2**. Onze analyse liet zien dat TEVAR in de afgelopen jaren de meest gebruikte behandeling is geworden voor TAR. Hoewel de patiënten die behandeld waren met TEVAR over het algemeen meer ernstige letsels hadden dan patiënten behandeld met open chirurgie, was de ziekenhuis-mortaliteit significant lager na TEVAR vergeleken met open chirurgie. Het verschil in overleving tussen beide behandelingsopties was zelfs groter nadat de analyse gecorrigeerd was voor geassocieerde letsels [OR 3.8, 95%CI 1.3-11.0]. De minimaal invasieve eigenschappen van TEVAR lijken dus vooral voordelig te zijn voor de behandeling van zwaargewonde patiënten, welke waarschijnlijk geen thoracotomie of aortaklem kunnen verdragen. Andere studies hebben vergelijkbare bevindingen gerapporteerd, met een mortaliteit tussen de 7.2% en 8.4% na een endovasculaire behandeling van TAR, vergeleken met 15.2% tot 23.5% na open chirurgie.[13-16]

Een nadeel van de endovasculaire behandeling van TAR is het optreden van endograft-gerelateerde complicaties zoals endoleak, welke in 9% van de patiënten in de staat New York na TEVAR is gediagnosticeerd. Endoleak wordt typisch in 5% tot 15% van de patienten na een

endovasculaire behandeling van TAR geobserveerd,[13,14,16-18] en vaak betreft dit type 1 endoleaks waarvoor normaliter directe re-interventie geïndiceerd is.[13,17,18]

Geruptureerde Aneurysmata van de Thoracale Aorta

Een geruptureerd aneurysma is een ander acuut ziektebeeld van de aorta thoracalis descendens, welke geassocieerd is met hoge morbiditeit en mortaliteit.[19,20] **Hoofdstuk 3** beschrijft de resultaten van een meta-analyse van alle recent gepubliceerde studies naar de uitkomsten van open chirurgie of TEVAR voor geruptureerde thoracale aneurysmata. De gepoolde 30-dagen mortaliteit na TEVAR was 19%, welke significant lager was dan de gepoolde mortaliteit na open chirurgie welke 33% was [OR 2.2, 95% CI 1.2-4.0]. Om de uitkomsten na beide operaties verder te bestuderen, is er een multi-center studie verricht welke in **Hoofdstuk 4** is beschreven. Het primaire eindpunt van de studie was een gecombineerd eindpunt van overlijden, permanente paraplegie, en/of cerebrovasculair accident (CVA) binnen 30 dagen na de operatie. Dit gecombineerde eindpunt trad op in 22% van de patiënten behandeld met TEVAR, vergeleken met 36% van de patiënten behandeld met open chirurgie. Na correctie voor andere risicofactoren bleek TEVAR het risico op overlijden, permanente paraplegie, en/of CVA significant te verlagen [OR 0.49, 95% CI 0.24-0.97]. TEVAR lijkt daarom de eerste keus behandeling van geruptureerde thoracale aneurysmata. Echter, alle ziekenhuizen die aan de studie meewerkten zijn grote ervaren klinieken, en chirurgische resultaten zijn over het algemeen beter in ziekenhuizen met een groot volume en ervaren chirurgen.[21,22] In ziekenhuizen met minder ervaren chirurgen zou de morbiditeit en mortaliteit na een open of endovasculaire behandeling van deze ziekte een stuk hoger kunnen uitvallen.

Risicofactoren voor 30-dagen mortaliteit en langer-termijn uitkomsten na TEVAR zijn geanalyseerd in **Hoofdstuk 5**. Oudere leeftijd [OR 1.11], hypovolemische shock [OR 4.75], en hematothorax bleken risicofactoren voor 30-dagen mortaliteit. Hoewel oudere leeftijd[20,23-26] en hypovolemische shock[26-28] vaak geassocieerd zijn met een slechte prognose, is de sterke associatie tussen hematothorax en verhoogde mortaliteit meer verassend. Hematothorax is vaak een teken van excessief bloedverlies, en zou kunnen leiden tot respiratoire complicaties. Opnieuw was er een hoge incidentie van endoleak, welke gediagnosticeerd werd in 18% binnen de eerste maand na TEVAR. De endovasculaire behandeling van geruptureerde thoracale aneurysmata was ook geassocieerd met een aanzienlijk risico op CVA, wat in 8% van alle patiënten optrad. Risicofactoren voor CVA na TEVAR zijn geanalyseerd in **Hoofdstuk 6**. Deze analyse liet zien dat oudere leeftijd een onafhankelijke risicofactor was voor CVA na TEVAR [OR 1.4, 95% CI 1.1-1.8]. Oudere patiënten hebben waarschijnlijk vaker uitgebreide atherosclerose van de aortaboog en carotiden, waardoor er vaker cerebrale embolizatie kan optreden tijdens manipulatie met endovasculaire instrumenten. De meer recente endovasculaire procedures waren geassocieerd met een lager risico op CVA [OR 0.52, 95% CI 0.28-0.97], wat kan wijzen op toegenomen ervaring van de operateurs en verbeterde endovasculaire instrumenten.[29,30]

Acute Type B Aortadissectie

De optimale behandeling van patiënten met acute type B aortadissecties (ABAD) zijn bestudeerd met behulp van de International Registry of Acute Aortic Dissection (IRAD). Patienten met ABAD zonder verdere complicaties kunnen over het algemeen behandeld worden met medicamenteuze therapie. In **Hoofdstuk 7** bleek echter dat patiënten met terugkerende pijn of therapieresistente hypertensie een veel hogere mortaliteit hebben [OR 3.3, 95% CI 1.04-10.5], vooral na medicamenteuze therapie. Terugkerende pijn of therapieresistente hypertensie kunnen wijzen op progressie van de dissectie of dreigende aortaruptuur en een meer invasieve behandeling, bijvoorbeeld TEVAR, lijkt geïndiceerd in deze patiëntengroep.

Een interventie is normaal gesproken noodzakelijk indien ABAD is geassocieerd met complicaties zoals acuut nierfalen, darmischemie, ischemie van de onderste extremiteiten, paraplegie of aortaruptuur. De invloed van de leeftijd van de patiënten op de behandeling en uitkomsten van gecompliceerde ABAD zijn bestudeerd in **Hoofdstuk 8**. Het aantal patiënten dat chirurgie onderging nam significant af naarmate de leeftijd van de patiënten toenam, terwijl het gebruik van medicamenteuze behandeling toenam met leeftijd, waarschijnlijk aangezien oudere leeftijd een risicofactor is voor mortaliteit en morbiditeit na thoracale aortachirurgie.[20,23-26]

De mortaliteit van gecompliceerd ABAD nam significant toe, onafhankelijk van de therapie die was aangeboden. Voor patiënten jonger dan 70 jaar was de mortaliteit iets lager na een endovasculaire behandeling, terwijl medicamenteuze behandeling in een iets lagere mortaliteit resulteerde in patiënten ouder dan 70 jaar. Recente studies hebben laten zien dat de endovasculaire behandeling van gecompliceerde ABAD is geassocieerd met een verlaagde mortaliteit, vaak tussen de 10% en 20%, vergeleken met 20% tot 30% na meer invasieve open chirurgie.[31-37] Gebaseerd op deze studies en de IRAD data lijkt TEVAR de beste behandeling voor gecompliceerd ABAD, vooral voor patiënten jonger dan 70 jaar.

Fistulae van de Thoracale Aorta

Aortobronchiale (ABF) en aorto-oesofageale fistulae (AEF) zijn extreem zeldzame ziektebeelden, met een erg slechte prognose.[38-41] Deze patiënten presenteren zich vaak met hemoptysis of hematemesis en patiënten zullen overlijden als de fistula niet behandeld wordt. Zowel longweefsel als de oesofagus zijn niet-steriele holtes, welke gecontamineerd zijn met micro-organismen, welke een voortdurende risico op infectie vormen. Daarom zijn deze fistulae een relatieve contra-indicatie voor het plaatsen van een endograft. In **Hoofdstuk 9** hebben we de resultaten van TEVAR voor ABF en AEF geëvalueerd. Er waren slechts 11 patiënten met ABF en AEF welke een endovasculaire behandeling hadden ondergaan. Hoewel er geen peroperatieve sterfgevallen waren, overleden 5 van de 11 patiënten vanwege infecties gedurende de eerste maanden na TEVAR en vooral de endovasculaire behandeling van AEF leek geassocieerd met een lage overleving. Om te bepalen of TEVAR een definitieve behandeling zou kunnen zijn voor deze fistulae, werden alle gepubliceerde casus over de endovasculaire behandeling van ABF en AEF geanalyseerd in

Hoofdstuk 10. De ziekenhuis-mortaliteit was significant lager na TEVAR voor ABF (3%) vergeleken met TEVAR voor AEF (19%) in de literatuur. Een endovasculaire benadering leek een definitieve oplossing voor patiënten met ABF, met een lagere mortaliteit dan traditionele open chirurgie welke geschat wordt tussen de 15% en 24%.[38,39] Na TEVAR voor AEF, was aanvullende oesofaguschirurgie echter vaak nodig om de fistula te behandelen. De patiënten die geen aanvullende oesofaguschirurgie ondergingen na TEVAR hadden een significant verhoogde mortaliteit, voornamelijk als gevolg van ernstige infecties. Voor patiënten met AEF zou TEVAR daarom kunnen fungeren als een "bridge to surgery", welke zo snel mogelijk gevolgd dient te worden door definitieve chirurgische correctie van de fistula.

DEEL 2. HET VERBETEREN VAN DE DUURZAAMHEID VAN TEVAR

TEVAR lijkt de korter-termijn uitkomsten van de meeste acute ziektes van de aorta thoracalis descendens te verbeteren vergeleken met open chirurgie. Gerandomiseerde studies hebben laten zien dat de 30-dagen mortaliteit en morbiditeit significant lager is na een endovasculaire behandeling van intacte aneurysmata van de abdominale aorta (AAA) vergeleken met open chirurgie, maar dat de langer-termijn overleving na een aantal jaar hetzelfde is.[42-44] Voor de meeste acute pathologieën van de thoracale aorta lijken de korter-termijn uitkomsten na TEVAR echter zo veel beter dan die na open chirurgie, dat het onwaarschijnlijk is dat deze winst na TEVAR op de langer-termijn geheel zal verdwijnen.

Een groot nadeel van de endovasculaire behandeling van de thoracale aorta is het optreden van endograft-gerelateerde complicaties zoals endoleak in 5% tot 30%[13,14,16-18,28,45,46] en collaps van de endograft in 0% to 10% van alle patiënten.[17,47-49] Reductie van deze endograft-gerelateerde complicaties is daarom essentieel om de prognose van patiënten met acute pathologieën van de thoracale aorta verder te verbeteren. Een correcte maat endograft lijkt noodzakelijk voor het minimaliseren van de risico's op endoleak en collaps van de endograft.

De Invloed van Hypovolemie op de Aorta

Hypovolemische shock zou de afmetingen van de aorta kunnen veranderen. Mogelijke veranderingen van de aortadiameter bij traumapatiënten die zich presenteren met hemodynamische instabiliteit zijn onderzocht in **Hoofdstuk 11**. Deze studie liet zien dat de aortadiameter significant groter was op de controle CT scans, vergeleken met de aortadiameter bij opname op het moment dat de patiënten hemodynamisch instabiel waren. Het gemiddelde verschil in diameter op het niveau van de mid aorta thoracalis descendens was 12.6% bij patiënten met een hartslag boven de 130 per minuut. Mogelijke verklaringen voor het afnemen van de aortadiameter zijn een verminderde druk op de aortawand door hypovolemie of endogene productie van vasoconstrictieve hormonen. Het exacte verschil in aortadiameter tussen beide

CT scans varieerde aanzienlijk onder de geïncludeerde patiënten, in sommige patiënten was dit verschil groter dan 40%, terwijl in andere patiënten geen verschil werd gemeten. De cardiovasculaire circulatie is een complex evenwicht en vele variabelen oefenen mogelijk invloed uit op de aortadiameter, waaronder de patiëntenleeftijd, bloedverlies, co-morbiditeiten zoals diabetes mellitus en atherosclerose en het gebruik van antihypertensiva.

In **Hoofdstuk 12** is de exactie invloed van bloedverlies op de afmetingen van de aorta verder onderzocht in een experimentele varkensstudie. Tijdens deze experimenten werd het circulerend bloedvolume van 7 Yorkshire varkens geleidelijk in stappen van 10% verlaagd. Na 40% bloedverlies werd er een endograft geplaatst in de thoracale aorta, gevolgd door geleidelijke vulling van het proefdier. Mogelijke veranderingen van de afmetingen van de aorta werden bestudeerd met behulp van intravasculaire ultrasound (IVUS). We observeerden dat de aortadiameter geleidelijk afnam in alle proefdieren, zowel op het niveau van de aorta ascendens als op het niveau van de aorta descendens en de abdominale aorta. Na vulling namen de aortadiameters snel weer hun oorspronkelijke afmetingen aan.

Deze veranderingen van de aortadiameter zouden theoretisch in elke patiënt met excessief bloedverlies kunnen optreden, maar waarschijnlijk zijn deze veranderingen het meest extreem bij jonge traumapatiënten met TAR. Aangezien bij oudere patienten de prevalentie van atherosclerose hoger is en de elasticiteit van de aorta afneemt,[50-54] kunnen potentiele veranderingen van de aorta minder uitgesproken zijn bij oudere patiënten met geruptureerde aneurysmata.

Implicaties voor TEVAR van Acute Pathologieën

De juiste maat endograft wordt doorgaans bepaald naar aanleiding van de preoperatieve CTA scan. Echter, als de diameter van de thoracale aorta aanzienlijk afgenomen is bij opname als gevolg van bloedverlies, zou dit kunnen leiden tot "undersizing", een te kleine maat endograft. Deze wanverhouding tussen de ware aortadiameter en de endograft kan theoretisch leiden tot een verhoogd risico op endoleak en andere complicaties zoals migratie van de endograft.

Daarom is het belangrijk dat specialisten er rekening mee houden dat de afmetingen van de aorta af kunnen nemen gedurende hypovolemie, er zijn twee opties om voor dit fenomeen te corrigeren. Ten eerste, aangezien de ware aortadiameter groter kan zijn dan de afmetingen op de preoperatieve CTA scan, zouden specialisten kunnen overwegen om het percentage "oversizing" te vergroten, dat wil zeggen een relatief grotere maat endograft te gebruiken. Vanwege de vele variabelen die de ware aortadiameter beinvloeden, is het moeilijk om een aanbeveling te doen met betrekking tot het exacte percentage oversizing dat nodig is. Gezien de bevinding dat de diameter van de mid aorta descendens bij trauma patiënten met een hartslag boven de 130/minuut en een MAP beneden de 95mmHg gemiddeld 12.6% kleiner was bij opname, zou een endograft gemiddeld 20% tot 30% oversized kunnen worden bij TAR patiënten met dezelfde karakteristieken, in plaats van de standaard aanbevolen 10% tot 20% oversizing.

Een alternatief zou kunnen zijn om de beeldvorming te herhalen nadat de patiënt een betere vullingstatus heeft, voor meer betrouwbare metingen van de aorta. Uit een aantal recente studies lijkt dat het uitstellen van TEVAR bij multi-traumapatienten, zodat andere levensbedreigende letsels eerst behandeld kunnen worden, de gemiddelde overleving van patiënten met TAR doet toenemen.[55-58] Deze vertraging van de endovasculaire behandeling van TAR zou theoretisch ook voordelig kunnen zijn voor het bepalen van de correcte maat endograft. Andere studies beweren echter dat men de vochtsuppletie moet beperken bij patiënten met hemorrhagische shock als gevolg van trauma of geruptureerde aneurysmata, aangezien vochtbeperking verdere interne bloedingen en het verlies van bloedplaatjes en stollingsfactoren zou kunnen minimaliseren.[59-63]

Een nadeel van het vergroten van het percentage oversizing, is dat dit theoretisch zou kunnen leiden tot een verhoogd risico op collaps van de endograft, een niet veelvoorkomende maar serieuze complicatie na TEVAR.[47,49,64] In **Hoofdstuk 13** zijn alle gepubliceerde gevallen van collaps van de endograft na TEVAR geanalyseerd, om meer inzichten in deze complicatie te verschaffen. Een kleine straal van de aortaboog, resulterend in "bird beaking" van de endograft was de meest beschreven oorzaak van collaps van de endograft. Een veel te grote maat endograft was ook een vaak beschreven oorzaak en gemiddeld waren de endografts 26.7% te groot voor de aorta, terwijl de meeste producenten van thoracale endografts oversizing van 10% tot 20% adviseren. Verassend genoeg trad 65% van alle gepubliceerde collapsen op na TEVAR voor TAR, terwijl deze aandoening doorgaans in slechts 6% tot 11% de indicatie is voor TEVAR.[65-68] Het risico op collaps lijkt dus hoger na een endovasculaire behandeling van TAR, wat verschillende verklaringen kan hebben. Allereerst zijn traumapatiënten doorgaans jonger en hebben daardoor een relatief kleinere aorta, waardoor de kleinst beschikbare maat endograft al vaak veel te groot is voor de aorta. Daarnaast hebben jonge traumapatiënten ook vaak een aortaboog met een relatief kleine straal. Daarom lijkt het gebruik van een endograft die meer dan 20% groter is dan de aortadiameter alleen verantwoord bij TAR patiënten met hypovolemische shock.

Wat brengt de toekomst?

De korter-termijn uitkomsten van de endovasculaire behandeling van de meeste acute thoracale pathologieën lijken superieur te zijn ten opzichte van open chirurgie in dit proefschrift. Onze studies hadden allemaal een observationeel karakter, terwijl een gerandomiseerde studie over het algemeen de beste methode is om twee therapieën te vergelijken. Het is echter onwaarschijnlijk dat de uitkomsten van deze twee operaties voor acute ziektes van de thoracale aorta ooit vergeleken zullen worden in een gerandomiseerde studie, gezien de extreem lage incidentie van deze aandoeningen. Misschien is het onderhand ook onethisch om dergelijke gerandomiseerde studies uit te voeren aangezien het verschil in mortaliteit aanzienlijk lijkt in observationele studies.

Langer-termijn data na TEVAR voor deze pathologieën zijn op dit moment nog onduidelijk, doordat deze behandeling pas beschikbaar is gekomen in het afgelopen decennium. Patiënten met aneurysmata of dissecties van de thoracale aorta zijn vaak ouder dan 60 jaar,[69,70] met

een de gemiddelde leeftijdsverwachting van minder dan 10 jaar. De gemiddelde leeftijd van traumapatienten is echter rond de 40 jaar[13-16] en deze patiënten zullen met een thoracale endograft moeten leven voor meer dan 30 jaar. Dit benadrukt het belang van onderzoek naar de langer-termijn resultaten van TEVAR voor acute ziektebeelden, met name TAR.

Het belangrijkste nadeel van TEVAR op dit moment blijft het risico op endograft-gerelateerde complicaties gedurende follow-up.[71,72] Toekomstige studies zouden daarom moeten onderzoeken welke patiënt- en operatiekarakteristieken het risico op deze complicaties beinvloeden, om uiteindelijk het optreden te doen verlagen. Onze studies hebben laten zien dat hypovolemie de dimensies van de aorta beïnvloedt, vervolgstudies zouden kunnen worden gebruikt om de normale aortadiameter van hypovolemische patiënten die TEVAR ondergaan beter te voorspellen. Verbeteringen in het ontwerp van de huidige endografts zou ook kunnen bijdragen aan een reductie van endoleak en andere endograft-gerelateerde complicaties.

Op dit moment kan alleen een gedeelte van de acute ziektebeelden van de aorta thoracalis descendens met TEVAR worden behandeld, terwijl slechts 30% van alle geruptureerde thoracale aneurysmata en 30% tot 40% van alle aortadissecties uitgaan van dit gedeelte van de thoracale aorta.[19,69,70] Voor geruptureerde aneurysmata en dissecties uitgaande van de aorta ascendens of proximale arcus aortae blijft open chirurgie daarom nog de standaardbehandeling.[69-73] De zogenaamde "branched endograft", met stents voor de arteriën van de aortaboogvaten, wordt al gebruikt,[74,75] maar het plaatsen van deze experimentele stent neemt veel tijd in beslag en vereist veel expertise. Deze veelbelovende techniek lijkt daarom op dit moment nog ongeschikt voor de behandeling van acute ziektebeelden van de arcus aortae.

Levenslange controle met behulp van CTA scans is op dit moment vereist na TEVAR, wat zal resulteren in toenemende behandelingskosten en stralingsbelasting van de patiënten, vooral na een endovasculaire behandeling van jonge traumapatiënten met TAR. Toekomstig onderzoek zal zich daarom ook moeten richten op het ontwikkelen van nieuwe, betaalbare beeldvormingsmethodes zonder gebruik van straling of contrastmiddel. Duplex lijkt een betrouwbaar middel voor controle van patiënten na een endovasculaire behandeling van abdominale aneurysmata,[76-78] en hopelijk zullen vergelijkbare methodes ook ontwikkeld worden voor controle na TEVAR.

Endovasculaire methodes worden in toenemende mate gebruikt voor de behandeling van acute ziektebeelden van de thoracale aorta, wat lijkt te resulteren in verlaagde mortaliteit en morbiditeit. De toenemende kennis van de dynamische eigenschappen van de aorta en aanpassingen aan de huidige endograft zal waarschijnlijk in de toekomst leiden tot een reductie van de endograft-gerelateerde complicaties en een verdere verbetering van de prognose van patiënten met deze levensbedreigende aandoeningen.

REFERENCES

1. Lam CR, Ram HH. Resection of the descending thoracic aorta for aneurysm; a report of the use of a homograft in a case and an experimental study. Ann Surg 1951; 134:743-752.
2. Cooley DA, De Bakey ME. Surgical considerations of intrathoracic aneurysms of the aorta and great vessels. Ann Surg 1952; 135:660-680.
3. Parmley LF, Mattingly TW, Manion WC et al. Nonpenetrating traumatic injury of the aorta. Circulation 1958; 17:1086-1101.
4. Mattox KL, Wall MJ, Jr. Historical review of blunt injury to the thoracic aorta. Chest Surg Clin N Am 2000; 10:167-82, x.
5. Dake MD, Miller DC, Semba CP et al. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. N Engl J Med 1994; 331:1729-1734.
6. Mitchell RS. Endovascular stent graft repair of thoracic aortic aneurysms. Semin Thorac Cardiovasc Surg 1997; 9:257-268.
7. Semba CP, Kato N, Kee ST et al. Acute rupture of the descending thoracic aorta: repair with use of endovascular stent-grafts. J Vasc Interv Radiol 1997; 8:337-342.
8. Wiggers HC, Ingraham RC. Vasoconstriction and the development of irreversible hemorrhagic shock. Am J Physiol 1948; 153:511-520.
9. Cohn JN, Luria MH. Studies in clinical shock and hypotension. IV. Variations in reflex vasoconstriction and cardiac stimulation. Circulation 1966; 34:823-832.
10. Peitzman AB, Billiar TR, Harbrecht BG et al. Hemorrhagic shock. Curr Probl Surg 1995; 32:925-1002.
11. Schumacher H, Bockler D, von Tengg-Kobligk H et al. Acute traumatic aortic tear: open versus stent-graft repair. Semin Vasc Surg 2006; 19:48-59.
12. Fabian TC, Richardson JD, Croce MA et al. Prospective study of blunt aortic injury: Multicenter Trial of the American Association for the Surgery of Trauma. J Trauma 1997; 42:374-380.
13. Demetriades D, Velmahos GC, Scalea TM et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008; 64:561-570.
14. Tang GL, Tehrani HY, Usman A et al. Reduced mortality, paraplegia, and stroke with stent graft repair of blunt aortic transections: a modern meta-analysis. J Vasc Surg 2008; 47:671-675.
15. Xenos ES, Abedi NN, Davenport DL et al. Meta-analysis of endovascular vs open repair for traumatic descending thoracic aortic rupture. J Vasc Surg 2008; 48:1343-1351.
16. Hoffer EK, Forauer AR, Silas AM et al. Endovascular stent-graft or open surgical repair for blunt thoracic aortic trauma: systematic review. J Vasc Interv Radiol 2008; 19:1153-1164.
17. Neschis DG, Moainie S, Flinn WR et al. Endograft repair of traumatic aortic injury-a technique in evolution: a single institution's experience. Ann Surg 2009; 250:377-382.

18. Orend KH, Zarbis N, Schelzig H et al. Endovascular treatment (EVT) of acute traumatic lesions of the descending thoracic aorta--7 years' experience. Eur J Vasc Endovasc Surg 2007; 34:666-672.
19. Johansson G, Markstrom U, Swedenborg J. Ruptured thoracic aortic aneurysms: a study of incidence and mortality rates. J Vasc Surg 1995; 21:985-988.
20. Schermerhorn ML, Giles KA, Hamdan AD et al. Population-based outcomes of open descending thoracic aortic aneurysm repair. J Vasc Surg 2008; 48:821-827.
21. Birkmeyer JD, Siewers AE, Finlayson EV et al. Hospital volume and surgical mortality in the United States. N Engl J Med 2002; 346:1128-1137.
22. Birkmeyer JD, Stukel TA, Siewers AE et al. Surgeon volume and operative mortality in the United States. N Engl J Med 2003; 349:2117-2127.
23. Mehta RH, O'Gara PT, Bossone E et al. Acute type A aortic dissection in the elderly: clinical characteristics, management, and outcomes in the current era. J Am Coll Cardiol 2002; 40:685-692.
24. Ehrlich M, Fang WC, Grabenwoger M et al. Perioperative risk factors for mortality in patients with acute type A aortic dissection. Circulation 1998; 98:II294-II298.
25. Achneck HE, Rizzo JA, Tranquilli M et al. Safety of thoracic aortic surgery in the present era. Ann Thorac Surg 2007; 84:1180-1185.
26. Rampoldi V, Trimarchi S, Eagle KA et al. Simple risk models to predict surgical mortality in acute type A aortic dissection: the International Registry of Acute Aortic Dissection score. Ann Thorac Surg 2007; 83:55-61.
27. Suzuki T, Mehta RH, Ince H et al. Clinical profiles and outcomes of acute type B aortic dissection in the current era: lessons from the International Registry of Aortic Dissection (IRAD). Circulation 2003; 108 Suppl 1:II312-II317.
28. Patel HJ, Williams DM, Upchurch GR, Jr. et al. A comparative analysis of open and endovascular repair for the ruptured descending thoracic aorta. J Vasc Surg 2009; 50:1265-1270.
29. Dake MD, Miller DC, Mitchell RS et al. The "first generation" of endovascular stent-grafts for patients with aneurysms of the descending thoracic aorta. J Thorac Cardiovasc Surg 1998; 116:689-703.
30. Demers P, Miller DC, Mitchell RS et al. Midterm results of endovascular repair of descending thoracic aortic aneurysms with first-generation stent grafts. J Thorac Cardiovasc Surg 2004; 127:664-673.
31. Fattori R, Tsai TT, Myrmel T et al. Complicated acute type B dissection: is surgery still the best option?: a report from the International Registry of Acute Aortic Dissection. JACC Cardiovasc Interv 2008; 1:395-402.
32. Khoynezhad A, Donayre CE, Omari BO et al. Midterm results of endovascular treatment of complicated acute type B aortic dissection. J Thorac Cardiovasc Surg 2009; 138:625-631.

33. Trimarchi S, Nienaber CA, Rampoldi V et al. Role and results of surgery in acute type B aortic dissection: insights from the International Registry of Acute Aortic Dissection (IRAD). Circulation 2006; 114:I357-I364.
34. Feezor RJ, Martin TD, Hess PJ, Jr. et al. Early outcomes after endovascular management of acute, complicated type B aortic dissection. J Vasc Surg 2009; 49:561-566.
35. Verhoye JP, Miller DC, Sze D et al. Complicated acute type B aortic dissection: midterm results of emergency endovascular stent-grafting. J Thorac Cardiovasc Surg 2008; 136:424-430.
36. Duebener LF, Lorenzen P, Richardt G et al. Emergency endovascular stent-grafting for life-threatening acute type B aortic dissections. Ann Thorac Surg 2004; 78:1261-1266.
37. Patel HJ, Williams DM, Meerkov M et al. Long-term results of percutaneous management of malperfusion in acute type B aortic dissection: implications for thoracic aortic endovascular repair. J Thorac Cardiovasc Surg 2009; 138:300-308.
38. MacIntosh EL, Parrott JC, Unruh HW. Fistulas between the aorta and tracheobronchial tree. Ann Thorac Surg 1991; 51:515-519.
39. Piciche M, De PR, Fabbri A et al. Postoperative aortic fistulas into the airways: etiology, pathogenesis, presentation, diagnosis, and management. Ann Thorac Surg 2003; 75:1998-2006.
40. Carter R, Mulder GA, Snyder EN, Jr. et al. Aortoesophageal fistula. Am J Surg 1978; 136:26-30.
41. Hollander JE, Quick G. Aortoesophageal fistula: a comprehensive review of the literature. Am J Med 1991; 91:279-287.
42. Greenhalgh RM, Brown LC, Powell JT et al. Endovascular versus open repair of abdominal aortic aneurysm. N Engl J Med 2010; 362:1863-1871.
43. 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; 362:1881-1889.
44. Lederle FA, Freischlag JA, Kyriakides TC et al. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. JAMA 2009; 302:1535-1542.
45. Cambria RP, Crawford RS, Cho JS et al. A multicenter clinical trial of endovascular stent graft repair of acute catastrophes of the descending thoracic aorta. J Vasc Surg 2009; 50:1255-1264.
46. Geisbusch P, Kotelis D, Weber TF et al. Endovascular repair of ruptured thoracic aortic aneurysms is associated with high perioperative mortality and morbidity. J Vasc Surg 2010; 51:299-304.
47. Sze DY, Mitchell RS, Miller DC et al. Infolding and collapse of thoracic endoprostheses: manifestations and treatment options. J Thorac Cardiovasc Surg 2009; 138:324-333.
48. Leung DA, Davis I, Katlaps G et al. Treatment of infolding related to the gore TAG thoracic endoprosthesis. J Vasc Interv Radiol 2008; 19:600-605.
49. Bandorski D, Bruck M, Gunther HU et al. Endograft collapse after endovascular treatment for thoracic aortic disease. Cardiovasc Intervent Radiol 2010; 33:492-497.
50. Mohiaddin RH, Underwood SR, Bogren HG et al. Regional aortic compliance studied by magnetic resonance imaging: the effects of age, training, and coronary artery disease. Br Heart J 1989; 62:90-96.

51. Mohiaddin RH, Schoser K, Amanuma M et al. MR imaging of age-related dimensional changes of thoracic aorta. J Comput Assist Tomogr 1990; 14:748-752.
52. Sonesson B, Hansen F, Stale H et al. Compliance and diameter in the human abdominal aorta--the influence of age and sex. Eur J Vasc Surg 1993; 7:690-697.
53. Bazan HA, Pradhan S, Mojibian H et al. Increased aortic arch calcification in patients older than 75 years: implications for carotid artery stenting in elderly patients. J Vasc Surg 2007; 46:841-845.
54. Takeda S, Watanabe H, Matsuzawa T. Age-related change in calcifications in the thoracic aorta: a study with computed tomography. Tohoku J Exp Med 1986; 149:73-78.
55. Demetriades D, Velmahos GC, Scalea TM et al. Blunt traumatic thoracic aortic injuries: early or delayed repair--results of an American Association for the Surgery of Trauma prospective study. J Trauma 2009; 66:967-973.
56. Symbas PN, Sherman AJ, Silver JM et al. Traumatic rupture of the aorta: immediate or delayed repair? Ann Surg 2002; 235:796-802.
57. Hemmila MR, Arbabi S, Rowe SA et al. Delayed repair for blunt thoracic aortic injury: is it really equivalent to early repair? J Trauma 2004; 56:13-23.
58. Pate JW, Fabian TC, Walker W. Traumatic rupture of the aortic isthmus: an emergency? World J Surg 1995; 19:119-125.
59. Veith FJ, Lachat M, Mayer D et al. Collected world and single center experience with endovascular treatment of ruptured abdominal aortic aneurysms. Ann Surg 2009; 250:818-824.
60. Bickell WH, Wall MJ, Jr., Pepe PE et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. N Engl J Med 1994; 331:1105-1109.
61. Roberts K, Revell M, Youssef H et al. Hypotensive resuscitation in patients with ruptured abdominal aortic aneurysm. Eur J Vasc Endovasc Surg 2006; 31:339-344.
62. van der Vliet J, van Aalst DL, Schultze Kool LJ et al. Hypotensive hemostatis (permissive hypotension) for ruptured abdominal aortic aneurysm: are we really in control? Vascular 2007; 15:197-200.
63. Kwan I, Bunn F, Roberts I. Timing and volume of fluid administration for patients with bleeding. Cochrane Database Syst Rev 2003;CD002245.
64. Muhs BE, Balm R, White GH et al. Anatomic factors associated with acute endograft collapse after Gore TAG treatment of thoracic aortic dissection or traumatic rupture. J Vasc Surg 2007; 45:655-661.
65. Buth J, Harris PL, Hobo R et al. Neurologic complications associated with endovascular repair of thoracic aortic pathology: Incidence and risk factors. a study from the European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair (EUROSTAR) registry. J Vasc Surg 2007; 46:1103-1110.
66. Fattori R, Nienaber CA, Rousseau H et al. Results of endovascular repair of the thoracic aorta with the Talent Thoracic stent graft: the Talent Thoracic Retrospective Registry. J Thorac Cardiovasc Surg 2006; 132:332-339.

67. Leurs LJ, Bell R, Degrieck Y et al. Endovascular treatment of thoracic aortic diseases: combined experience from the EUROSTAR and United Kingdom Thoracic Endograft registries. J Vasc Surg 2004; 40:670-679.
68. Feezor RJ, Martin TD, Hess PJ, Jr. et al. Extent of aortic coverage and incidence of spinal cord ischemia after thoracic endovascular aneurysm repair. Ann Thorac Surg 2008; 86:1809-1814.
69. Ince H, Nienaber CA. Etiology, pathogenesis and management of thoracic aortic aneurysm. Nat Clin Pract Cardiovasc Med 2007; 4:418-427.
70. Hagan PG, Nienaber CA, Isselbacher EM et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. JAMA 2000; 283:897-903.
71. Svensson LG, Kouchoukos NT, Miller DC et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. Ann Thorac Surg 2008; 85:S1-41.
72. Hiratzka LF, Bakris GL, Beckman JA et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with Thoracic Aortic Disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. Circulation 2010; 121:e266-e369.
73. Golledge J, Eagle KA. Acute aortic dissection. Lancet 2008; 372:55-66.
74. Chuter TA, Schneider DB. Endovascular repair of the aortic arch. Perspect Vasc Surg Endovasc Ther 2007; 19:188-192.
75. Schoder M, Lammer J, Czerny M. Endovascular aortic arch repair: hopes and certainties. Eur J Vasc Endovasc Surg 2009; 38:255-261.
76. Schmieder GC, Stout CL, Stokes GK et al. Endoleak after endovascular aneurysm repair: duplex ultrasound imaging is better than computed tomography at determining the need for intervention. J Vasc Surg 2009; 50:1012-1017.
77. Beeman BR, Doctor LM, Doerr K et al. Duplex ultrasound imaging alone is sufficient for midterm endovascular aneurysm repair surveillance: a cost analysis study and prospective comparison with computed tomography scan. J Vasc Surg 2009; 50:1019-1024.
78. Chaer RA, Gushchin A, Rhee R et al. Duplex ultrasound as the sole long-term surveillance method post-endovascular aneurysm repair: a safe alternative for stable aneurysms. J Vasc Surg 2009; 49:845-849.

Chapter 16

Review Committee

Acknowledgements

List of publications

Curriculum Vitae

REVIEW COMMITTEE

Prof.dr. I.H.M. Borel Rinkes
Department of Surgery, University Medical Center Utrecht
Utrecht, the Netherlands

Prof.dr. W.P.Th.M. Mali
Department of Radiology, University Medical Center Utrecht
Utrecht, the Netherlands

Prof.dr. P.A.F.M. Doevendans
Department of Cardiology, University Medical Center Utrecht
Utrecht, the Netherlands

Prof.dr. H.J.M. Verhagen
Department of Vascular Surgery, Erasmus University Medical Center
Rotterdam, the Netherlands

ACKNOWLEDGEMENTS

Geachte Prof.dr. F.L. Moll, beste Frans, ik ben u erg dankbaar voor de unieke kans die u mij geboden heeft om aan Yale promotieonderzoek te doen. Aanvankelijk was het een pittige beslissing om voor 2 jaar naar het buitenland te verhuizen, maar achteraf heb ik er geen moment spijt van gehad en zijn deze jaren voorbij gevlogen. Het was een onvergetelijke ervaring en zonder twijfel een belangrijk fundament voor mijn verdere loopbaan en leven. Ondanks uw enorme staat van dienst en overvolle agenda, bent u enorm toegankelijk geweest en heeft u altijd tijd vrijgemaakt om onze onderzoeksprojecten te bespreken en te filosoferen over de volgende stap. U bent een groot voorbeeld voor mij en het was een geweldige eer om onder uw supervisie te mogen promoveren. Ik hoop nog veel van u te mogen leren in de toekomst.

Dear Dr. B.E. Muhs, Dear Bart, thank you very much for offering me the opportunity to do PhD research at the Yale University School of Medicine. It has been a fantastic experience being part of such a distinguished institution and the last years are without a doubt a very important experience for my further career and personal life. We practically had daily contact regarding our research projects, which resulted in a very fruitful collaboration and a good friendship. I admire your efficient way of combining your job as a surgeon, with research activities and your personal life. I truly appreciate the opportunity you gave me to explore the United States on many different occasions, both for scientific purposes as for leisure. I am convinced that we will continue our collaboration and friendship in future.

Dear Dr. S. Trimarchi, Dear Santi, we have had a fantastic and very productive collaboration in the relatively short period that we have known each other (you call it our research company). I am very grateful for the opportunity to visit your institution in Italy on multiple occasions; you are a great host and an even better friend. Coincidentally, we have matching interests both in the medical field as on the soccer field and I will never forget the games that we watched in Giuseppe Meazza. I am hoping to continue our collaboration and friendship. Forza Inter, e grazie mille!

Prof.dr. H.J.M. Verhagen, beste Hence, we hebben een erg prettige en productieve samenwerking gehad gedurende de afgelopen twee jaar. Hartelijk dank voor uw relevante en doeltreffende suggesties met betrekking tot onze vele gezamenlijke onderzoeksprojecten. Ik kon altijd binnen een dag een reactie van u verwachten naar aanleiding van het laatste manuscript, wat ik erg op prijs heb gesteld. Ik vind het erg indrukwekkend en inspirerend wat u op relatief jonge leeftijd al bereikt heeft in de vaatchirurgische wereld en ik hoop dat wij de vruchtbare samenwerking kunnen continueren in de komende jaren.

Prof.dr. B.E. Sumpio, dear Bauer, thank you very much for the opportunity to perform research within your section. It has been an honor and great pleasure to be part of your section, and I am delighted that you will be a member of the reading committee of this thesis. I am hoping that we can continue this wonderful collaboration between Yale and Utrecht for many more years.

Dear members of the reading committee, Prof.dr. I.H.M. Borel Rinkes, Prof.dr. H.J.M. Verhagen, Prof.dr. W.P.Th.M. Mali, Prof.dr. P.A.F.M. Doevendans, Prof.dr B.E. Sumpio, Dr. J.E. Aruny, Dr. J.A. van Herwaarden, Dr. R.H. Heijmen: thank you very much for your time, expertise and critical assessment of this thesis.

Dr. F.J.V. Schlosser, (toekomstig) professor, beste Felix, de afgelopen twee jaar gingen wij bijna dagelijks met elkaar om, hebben we veel mooie tripjes gemaakt en zijn wij goede vrienden geworden. Je bent een grote steun geweest bij mijn aankomst op Yale en gedurende mijn promotieonderzoek. Veel succes met je opleiding op Yale, en living the American Dream!

Dr. J.E. Indes and Dr. D.M. Botta, dear Jeff and Donald, thank you very much for participating in the pig study. The experiments were very interesting, which resulted in an important chapter of this thesis.

Dr. P.H. Lin, Dr. W.A. Lee, Prof.dr. B.E. Sumpio, Dr. R.H. Heijmen, Dr. J.E. Indes, Dr. D.M. Botta, Dr. H. Mojibian, prof. dr. V. Rampoldi, Dr. K.A. Davis, Dr. J.K. Giacovelli Dr. J.A. Sosa, Dr. H. Athamneh, Dr. J.A. van Herwaarden, Dr. A. Geirsson, and other co-authors: thank you very much for participating in our research projects and your excellent edits regarding the manuscripts.

Employees of the Yale Animal Resources Center (YARC), thank you very much for assisting us during the pig experiments, without your help it would have been impossible to realize this study.

Dr. J.E. Aruny, dear John, I am delighted that you will be a member of the reading committee of this thesis. Thank you very much for providing the great images for the cover of the book. I am looking forward to a sailing trip on your beautiful yacht; see you next year in Utrecht again!

Dr. K.A. Eagle, dear Kim, it has been an honor to meet you and to participate in multiple IRAD projects. I am hoping to stay involved in future IRAD projects, and to engage several Dutch institutions into the IRAD.

Dear Jeanna, Dan, Eva and other IRAD-ians, thank you for all your help, support and statistical analyses for the many IRAD projects. Because of your efforts, Santi and I were able to collect an

enormous amount of interesting data during two short visits to the IRAD coordinating center in Ann Arbor.

J.M.A van Veen en S.J. Hora Siccama, beste Cobie en Susan, hartelijk dank voor jullie fantastische ondersteuning voor de promotie en het symposium. Ik vind het altijd erg gezellig om langs te komen bij de Vaat en met jullie bij te kletsen.

Paranimfen, beste Tjeerd en Frits, (toekomstig) collega en teamgenoot, we hebben een mooie tijd gehad in Utrecht, en het was erg gezellig om de laatste jaren met jullie op de Domstreet te wonen. Ik weet zeker dat we nog lang goede vrienden zullen blijven.

Jasper, veel succes het komend jaar op Yale, aan jou nu de taak om de relatie tussen het Utrecht en Yale warm te houden. Geniet ervan!

Onderzoekers van de heelkunde in het UMCU en op Yale: bedankt voor de vele mooie momenten in binnen- en buitenland!

Annick en Conker, ik ben er trots op dat jullie mijn zusje en broertje zijn. Ondanks jullie drukke agenda's zijn jullie mij beiden wezen opzoeken in New Haven en New York, wat supergezellig was.

Lieve papa en mama, bedankt voor alle steun en vertrouwen. Van jongs af aan hebben jullie me veel vrijheid gegeven, maar tegelijkertijd ook voldoende discipline bijgebracht, wat goed van pas is gekomen in Amerika. Ik vind het altijd heerlijk om thuis te komen in Oog en Al en kijk uit naar de safari in Tanzania met de gehele familie.

Dear Michelle, lieve Michi, you have witnessed this thesis from the beginning and you have been an incredible support. We have had a lot of fun during the last two years, but we're just getting started!

LIST OF PUBLICATIONS

Published or accepted manuscripts

Jonker FH, Schlösser FJ, Geirsson A, Sumpio BE, Moll FL, Muhs BE. Endograft Collapse after Thoracic Endovascular Aortic Repair. Journal of Endovascular Therapy 2010 (in press).

Jonker FH, Verhagen HJ, Lin PH, Heijmen RH, Trimarchi S, Lee WA, Moll FL, Athamneh H, Muhs BE. Endovascular Repair of Ruptured Thoracic Aortic Aneurysms: Predictors of Procedure Related Stroke. Annals of Vascular Surgery 2010 (in press).

Jonker FH, Verhagen HJ, Lin PH, Heijmen RH, Lee WA, Trimarchi S, Moll FL, Athamneh H, Muhs BE. Endovascular Treatment of Ruptured Thoracic Aortic Aneurysms in Patients older than 75 years. European Journal of Vascular and Endovascular Surgery 2010 (in press).

Jonker FH, Mojibian H, Schlösser FJ, Botta DM, Indes JE, Moll FL, Muhs BE. The Impact of Hypovolaemic Shock on the Aortic Diameter in a Porcine Model. European Journal of Vascular and Endovascular Surgery 2010;40:564-71.

Jonker FH, Verhagen HJ, Lin PH, Heijmen RH, Trimarchi S, Lee WA, Moll FL, Athamneh H, Muhs BE. Outcomes of endovascular repair of ruptured descending thoracic aortic aneurysms. Circulation 2010;121:2718-23.

Trimarchi S, Eagle KA, Nienaber CA, Pyritz RE, **Jonker FH**, Suzuki T, O'Gara PT, Hutchison SJ, Rampoldi V, Grassi V, Bossone E, Muhs BE, Evangelista A, Tsai TT, Froehlich JB, Cooper JV, Montgomery DG, Meinhardt G, Myrmel T, Upchurch GE, Sundt TM, Isselbacher EM. Importance of Refractory Pain and Hypertension in Acute Type B Aortic Dissection: Insights from the International Registry of Acute Aortic Dissection. Circulation 2010;122:1283-9.

Jonker FH, Aruny J, Moll FL, Muhs BE. Commentary: reduction of type II endoleak using embolization of the aneurysm sac during EVAR. Journal of Endovascular Therapy 2010;17:525-6.

Jonker FH, Verhagen HJ, Mojibian H, Davis KA, Moll FL, Muhs BE. Aortic endograft sizing in trauma patients with hemodynamic instability. Journal of Vascular Surgery 2010;52:39-44.

Trimarchi S, **Jonker FH**, Muhs BE, Grassi V, Righini P, Upchurch GR, Rampoldi V. Long-term out Trends and outcomes of endovascular and open treatment for traumatic thoracic aortic injury.

comes of surgical aortic fenestration for complicated acute type B aortic dissections. Journal of Vascular Surgery 2010;52:261-6.

Jonker FH, Schlosser FJ, Indes JE, Sumpio BE, Botta DM, Moll FL, Muhs BE. Management of type A aortic dissections: a meta-analysis of the literature. Annals of Thoracic Surgery 2010;89:2061-6.

Jonker FH, Trimarchi S, Verhagen HJ, Moll FL, Sumpio BE, Muhs BE. Meta-analysis of open versus endovascular repair for ruptured descending thoracic aortic aneurysm. Journal of Vascular Surgery 2010;51:1026-1032.

Jonker FH, Giacovelli JK, Muhs BE, Sosa JA, Indes JE. Trends and outcomes of endovascular and open treatment for traumatic thoracic aortic injury. Journal of Vascular Surgery 2010;51:565-71.

Jonker FH, Schlösser FJ, Dewan M, Huddle M, Sergi M, Indes JE, Dardik A, Muhs BE. Abdominal aortic aneurysm repair in obese patients: improved outcome after endovascular treatment compared with open surgery. Vascular and Endovascular Surgery 2010;44:105-9.

Indes JE, Shah HJ, **Jonker FH**, Ohki T, Veith FJ, Lipsitz EC. Subintimal angioplasty is superior to SilverHawk atherectomy for the treatment of occlusive lesions of the lower extremities. Journal of Endovascular Therapy 2010;17:243-50.

Jonker FH, Indes JE, Moll FL, Muhs BE. Management of Iatrogenic Injuries of the Supra-aortic Arteries. Journal of Cardiothoracic and Vascular Anesthesia 2010;24:322-9.

Trimarchi S, Eagle KA, Nienaber CA, Rampoldi V, **Jonker FH**, De Vincentiis C, Frigiola A, Menicanti L, Tsai T, Froehlich J, Evangelista A, Montgomery DG, Bossone E, Cooper JV, Li J, G Deeb M, Meinhardt G, Sundt TM, Isselbacher EM; International Registry of Acute Aortic Dissection (IRAD) Investigators. Role of age in acute type A aortic dissection outcome: Report from the International Registry of Acute Aortic Dissection (IRAD). Journal of Thoracic and Cardiovascular Surgery 2010;140:784-9.

Jonker FH, Schlösser FJ, Dewan M, Huddle M, Sergi M, Dardik A, Muhs BE. Patients with abdominal aortic aneurysm and chronic obstructive pulmonary disease have improved outcomes with endovascular aneurysm repair compared with open repair. Vascular 2009;17:316-24.

Jonker FH, Aruny J, Muhs BE. Management of type II endoleaks: preoperative versus postoperative versus expectant management. Seminars in Vascular Surgery 2009;22:165-71.

Jonker FH, Schlösser FJ, Moll FL, van Herwaarden JA, Indes JE, Verhagen HJ, Muhs BE. Outcomes of thoracic endovascular aortic repair for aortobronchial and aortoesophageal fistulas. Journal of Endovascular Therapy 2009;16:428-40.

Jonker FH, Schlösser FJ, Dewan M, Huddle M, Sergi M, Dardik A, Muhs BE. Influence of obesity on in-hospital and midterm outcomes after endovascular repair of abdominal aortic aneurysm. Journal of Endovascular Therapy 2009;16:302-9.

Jonker FH, Heijmen R, Trimarchi S, Verhagen HJ, Moll FL, Muhs BE. Acute management of aortobronchial and aortoesophageal fistulas using thoracic endovascular aortic repair. Journal of Vascular Surgery 2009;50:999-1004.

Jonker FH, Schlösser FJ, Moll FL, Muhs BE. Dissection of the abdominal aorta. Current evidence and implications for treatment strategies: a review and meta-analysis of 92 patients. Journal of Endovascular Therapy 2009;16:71-80.

Submitted manuscripts

Jonker FH, Verhagen HJ, Lin PH, Heijmen RH, Lee WA, Trimarchi S, Moll FL, Athamneh H, Rampoldi V, Muhs BE. Open Surgery versus Endovascular Repair of Ruptured Thoracic Aortic Aneurysms.

Jonker FH, Trimarchi S, Muhs BE, Rampoldi V, Cooper JV, Montgomery DG, Froehlich JB, Peterson MD, Bartnes K, Gourineni V, Ramanath VS, Braverman AC, Nienaber CA, Isselbacher EM, Eagle KA. Age-related Decision Making in Complicated Acute Type B Aortic Dissection: Insights from the International Registry of Acute Aortic Dissection.

Trimarchi S, **Jonker FH**, Isselbacher EM, Froehlich J, Upchurch GR, Muhs BE, Grassi V, Rampoldi V, Cooper JV, Montgomery DG, O'Gara PT, Nienaber CA, Eagle KA. Characterizing Patients with Acute Type B Aortic Dissection in the Absence of Aortic Dilatation.

Trimarchi S, **Jonker FH**, Hutchison S, Isselbacher E, Paper L, Cooper JV, Froehlich JB, Muhs BE, Rampoldi V, Grassi V, Evangelista A, Meinhardt G, Beckman J, Myrmel T, Pyeritz RE, Hirsch AT, Sundt T, Nienaber CA, Eagle KA. Descending Aortic Diameter ≥ 5.5 is not an Accurate Predictor of Acute Type B Aortic Dissection.

CURRICULUM VITAE

Frederik Hendrik Willem Jonker was born on August 11, 1983, in Utrecht, the Netherlands. After graduating from the Christelijk Gymnasium Utrecht, he entered the Utrecht University School of Medicine in 2001. During Medical School, he spent three months in Cape Town, South Africa, for a research fellowship at the Trauma Department of the Tygerberg Hospital. Frederik combined Medical School with playing premier league field hockey in the first men's team of s.v. Kampong. As captain of Kampong, the team became National Champion as well as European Champion indoor hockey. He was also selected for the National Indoor Hockey Team. After completing his medical degree in June 2008, he was invited by prof.dr. Frans L. Moll and Dr. Bart E. Muhs to do PhD research at the section of vascular surgery of the Yale University School of Medicine in New Haven, Connecticut, USA. The main focus of his research was the management of acute thoracic aortic disease, which is presented in this thesis. Frederik also spent two months in Milan, Italy, to collaborate with Dr. Santi Trimarchi, who introduced him to the International Registry of Acute Aortic Dissection (IRAD).
During his research fellowship in the United States, Frederik presented his work at numerous prestigious meetings, including the American Heart Association, the Society for Clinical Vascular Surgery, the Peripheral Vascular Surgery Society, the New England Society for Vascular Surgery, the Eastern Vascular Society, and the Veith Symposium. In 2011, Frederik will start his general surgery residency at the Erasmus University Medical Center in Rotterdam, the Netherlands, under supervision of prof.dr. J.N.M. IJzermans.