Open versus endovascular thoracic aneurysm repairs In Australia

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Open versus Endovascular Thoracic Aneurysm Repairs In Australia

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Abstract

Objectives: Thoracic aortic aneurysms (TAAs) affect 10 per 100,000 people, and are responsible for significant mortality. Open surgical repair carries substantial risks of both morbidity and mortality. Endovascular TAA repair is a relatively new technology, with numerous proposed benefits over open repair. However, data is yet to demonstrate whether endovascular TAA repairs outperform open repair. We sought to observe trends and outcomes of TAA repairs over the previous decade in order to identify the optimal method of management of thoracic and thoracoabdominal aneurysm repairs, as well as predictors of poor outcome.

Methods: We conducted a retrospective analysis of all patients presenting for management of thoracic and/or aortic (ruptured and non-ruptured) from 2003-2013, at two tertiary-level, acute care hospitals in Sydney, Australia.

Results: 179 patients presented with thoracic or thoracoabdominal aneurysms, 127 of whom were treated surgically, and five of whom presented with aneurysmal rupture. The 52 patients managed non-operatively were more likely to be older, and more likely to be female. Of the patients managed surgically, 69 had ascending aneurysms, 27 had arch aneurysms, and 31 descending TAAs. Thirty-one patients underwent repair of descending TAAs, 12 open and 19 endovascular. Patients undergoing endovascular repair of descending TAAs were significantly older than those undergoing open repair. Operative duration was significantly shorter for endovascular than open repair of arch and descending aneurysms.
There were no differences in morbidity or mortality, duration of hospitalisation, or transfusion requirement between the groups.

Patients over 75 years of age with arch aneurysms were more likely to develop an endoleak or return to theatre than those under 75. Similarly, patients over 75 years undergoing descending aneurysm repair were twice as likely to have an endovascular repair, required more blood transfused, and have a longer ICU and total hospital stay. Otherwise, there were no predictors for poor outcome post-TAA repairs. There was a trend for increasing endovascular repair of descending aneurysms, but no change in morbidity or mortality over time.

**Conclusion:** Overall mortality was low during the study period, but morbidity after open or endovascular thoracic or thoracoabdominal aneurysm repair remains substantial. Apart from reducing surgical duration, endovascular repair demonstrated no additional benefits over open TAA repair. Patients over the age of seventy-five were more likely to suffer adverse events than those under seventy-five. However, the current study demonstrated that either open or endovascular TAA repair can be performed with low morbidity and mortality, even in elderly patients.
Publications and Presentations

The findings of this thesis were published in the *Annals of Vascular Surgery*, Volume 31, p30-38, 2016. This manuscript is included (page 55 of this thesis).

The findings were also presented at the *Royal Australasian College of Surgeons Annual Scientific Congress* on the 9th of May 2014, at the Marina Bay Sands in Singapore (see page 73).
Declaration of Authorship

This thesis is my own work, and contains no material that has been accepted for the award of any degree or diploma at any other institution.

To the best of my knowledge, the thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

Dr Timothy Shiraev
Statement of Contribution by Others

Dr Raffi Qasabian oversaw conception of the research question and design of the study, and assisted in preparation of the manuscript for publication.

Dr Zelda Doyle oversaw conception of the research question and design of the study, supervised statistical analysis, and assisted in preparation of the manuscript before publication.

Dr Timothy Shiraev

Dr Raffi Qasabian

Dr Zelda Doyle
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Mr Daniel Tardo and Mrs Gemille Ninic assisted in data collection.

Cook Medical® kindly provided funding for this research [Ref AI130801R] (See Appendices 3-4).
Abbreviations

AAA: Abdominal aortic aneurysm

ASA: American Society of Anaesthesiologists

CFA: Common femoral artery

CSF: Cerebrospinal fluid

ICU: Intensive care unit

RPAH: Royal Prince Alfred Hospital

SCI: Spinal cord ischemia

TAA: thoracic aortic aneurysm
Introduction

Background

The thoracic aorta is usually 2.5-3cm in diameter depending on sex and body habitus\(^1\). An aneurysm is defined as a greater than fifty percent dilatation of an endothelium-lined vascular structure, thus the thoracic aorta is aneurysmal once it reaches 4.5cm. Thoracic aortic aneurysms (TAAs) include aneurysms involving the ascending aorta (from the aortic annulus to the brachiocephalic trunk), the aortic arch (brachiocephalic trunk to the left subclavian), and the descending aorta (including thoracoabdominal aneurysms, extending from proximal to the left subclavian artery to as far as the infra-renal aorta; see Figure A)\(^2\).

Ascending aneurysms account for fifty percent of TAAs, the arch ten percent, and forty percent involve the descending aorta (of which one quarter extend distal to the diaphragm)\(^3\). TAAs are three to seven times less common than abdominal aortic aneurysms (AAA)\(^4\) but still carry a significant burden of disease, with an incidence of 10 per 100,000 people\(^1\). TAAs affect males twice as frequently as females, with the mean age of TAA repair being 67 years\(^5\).
Factors commonly predisposing to thoracic aneurysm development include hypertension, smoking and chronic obstructive pulmonary disease\textsuperscript{1}. As such, eighty percent of TAAs are defined as being of ‘degenerative’ aetiology, with the relationship of degenerative aneurysms and atherosclerosis discussed below\textsuperscript{6}. In fifteen to twenty percent of TAAs, genetic syndromes predispose to thoracic aortic aneurysms\textsuperscript{7,8}. These syndromes include Marfan’s, Loeys-Dietz, and Ehlers-Danlos syndromes, and predispose to aneurysmal change due firstly to chronic aortic dissection, and secondary to dilatation of the wall of the false lumen\textsuperscript{6}. Inflammatory vasculitides, such as giant cell arteritis, Takayasu arteritis and Rheumatoid arthritis, are responsible for two percent of TAAs\textsuperscript{6,9}. Infective aetiologies are even less common, with pathogens including Salmonella and Staphylococcal species, with syphilitic and tuberculous aneurysms less common still\textsuperscript{6,9}.  

\textit{Figure A – Crawford Classification of thoracoabdominal aneurysms. From Azizzedeh et al\textsuperscript{4}}
Histopathological changes occurring in the wall of aneurysmal thoracic aortic tissue, triggered by the aforementioned predisposing factors, culminate in medial degeneration (previously called cystic medial necrosis\textsuperscript{6,10}). This is characterised by fragmentation of elastic tissue, loss of smooth muscle cells, and accumulation of ground substance within the medial layer of the aortic wall\textsuperscript{10}. While more common in elderly patients, medial degeneration is accelerated by hypertension and atherosclerosis\textsuperscript{6}. Pathogenesis of medial degeneration involves over-expression and over-activation of proteinases (namely the matrix metalloproteinase family, especially matrix metalloproteinase 9\textsuperscript{11}), as well as alterations in transforming growth factor beta (TGF-\textbeta) function\textsuperscript{12} and infiltration by activated T cells and macrophages\textsuperscript{10}, resulting in degradation of the extracellular matrix, and aneurysmal expansion. Aneurysms are described as being either fusiform (a uniform dilatation of the entire aortic circumference, which is more common), or saccular (a localised dilatation of one part of the aortic wall). Saccular aneurysms require more vigilant follow up, as they are more likely to require repair than fusiform aneurysms\textsuperscript{13}.

Ninety-five percent of thoracic aortic aneurysms are asymptomatic\textsuperscript{14}, with the remaining five percent presenting with non-specific symptoms including chest, back, abdominal or flank pain, or symptoms from local compression of the recurrent laryngeal nerve, trachea, or oesophagus\textsuperscript{6}. Symptomatic patients are more likely to have an aneurysm diameter of greater than 5 centimetres\textsuperscript{6}. There is little to be found on clinical examination, and computed tomography or magnetic-resonance angiography are investigations of choice\textsuperscript{1}. Medical therapy includes smoking cessation and beta-blockade to reduce shear stress, with debate currently regarding the efficacy of statins and angiotensin-converting-enzyme
inhibitors for reduction in oxidative stress\textsuperscript{15}. Without surgical intervention, the two-year mortality rate is as high as forty-seven percent in patients unfit for surgery\textsuperscript{16}, due to rupture and rapid exsanguination.
Surgical Management of Thoracic and Thoracoabdominal Aneurysms

Surgical management of thoracic aortic aneurysms was first described in 1955\textsuperscript{17}, in which Etheredge used a homograft (a vascular conduit from the same patient) to replace the resected aneurysm. Current guidelines from the American College of Cardiology Task Force recommend repair of ascending aortic aneurysms only when maximal external diameter reaches 5.0cm, arch repairs at 5.5cm, descending repairs at 5.5cm, or a rapid rate of annual expansion on surveillance\textsuperscript{1}.

Open repair of thoracoabdominal aneurysms involves positioning the patient in the lateral decubitus position with left side up, and exposure is obtained via an incision in the fourth to eighth intercostal space extended to the midline, with the laparotomy continued inferiorly. The retroperitoneum is then accessed, and the diaphragm divided. Cardiopulmonary bypass may be required, dependent on proximal extent of aorta involved, and induced hypothermia may be considered. After systemic heparinisation, the aorta is cross-clamped, with the level of proximal clamp dependent on extent of the aneurysm. The proximal aorta is anastamosed to the proximal graft, followed by reimplantation of visceral and renal vessels. Intercostal artery reimplantation may be performed, dependent on pre-operative imaging, or changes in motor-evoked potentials in the lower limbs during the operative period. After the distal anastamosis is completed and the wound closed, the patient is monitored in the intensive care unit\textsuperscript{6}. 
Although vast improvements in operative technique and peri-operative care (namely anaesthetic and intensive care) have been made since 1955, morbidity and mortality remains high\textsuperscript{18}. A 2006 study showed 19\% perioperative mortality, and a one-year mortality of thirty-one percent\textsuperscript{18}. A recent multi-centre study in France demonstrated that hybrid procedures (open vascular reimplantation simultaneously with endograft repair) are associated with a post-operative mortality of 34\%, due to the invasive nature of the procedure and poor patient selection\textsuperscript{19}. Substantial morbidity in TAA repairs is also common. Arterial supply of the spinal cord is partly via radicular arteries, which arise from the intercostal and lumbar branches of the aorta. Interruption of this arterial supply (due to insertion of stent-grafts during either open or endovascular TAA repair) risks spinal cord ischemia (SCI) and subsequent paraplegia, a complication which occurs in between five and twenty-one percent of TAA repairs\textsuperscript{20}. Visceral ischemia is also a common phenomenon, with post-operative renal failure occurring in up to eight percent of patients\textsuperscript{21}. Cardiorespiratory complications are also commonly experienced (such as acute coronary syndromes and lower respiratory tract infections)\textsuperscript{22,23}. As a result, TAA repair remains a high-risk endeavour, with further improvements in technique and patient selection needed.
Endovascular Repair of Thoracoabdominal Aneurysms

The first endovascular intervention for the treatment of vascular pathologies was described by Seldinger in 1953\textsuperscript{24}, and further developed by Dotter in 1963\textsuperscript{25}. It is now accepted as the optimal method of management for many vascular diseases, including AAA, peripheral vascular disease and chronic gastrointestinal ischemia\textsuperscript{26-29}. The benefits of endovascular interventions include their minimally invasive nature which results in reduced blood loss and a lower risk of infection, reduced procedure time and transfusion requirement, reduced duration of mechanical ventilation, low operative morbidity and mortality, reduced cost, reduced intensive care unit stay, and faster time to mobilisation and discharge from hospital\textsuperscript{27,30-32}. In addition to these general advantages, proposed benefits of endovascular repair specific to TAA include avoidance of the physiological insults of aortic cross-clamping and thoracic or thoracoabdominal incisions in these often frail patients\textsuperscript{20}. Additionally, ability to utilise local anaesthesia in up to 53\% of patients\textsuperscript{33} allows avoidance of cardiorespiratory morbidity and mortality associated with general anaesthesia, as well as reduced hospital stay\textsuperscript{34}. However, endovascular interventions have their own limitations. Endovascular repair can be precluded by poor femoral access (see below), tortuous or occluded iliac vessels preventing placement of the device into the thoracic aorta, or contraindications to iodinated contrast media (including renal failure and anaphylaxis). Further, at least two centimetres of healthy aorta is required as a landing zone (the space needed to anchor the proximal and distal ends of the graft, without covering branches of the aorta), which may be absent in extensive aneurysms.
To undertake an endovascular repair of a TAA, the chosen common femoral artery (CFA) is accessed either percutaneously via Seldinger technique or via femoral cutdown, and a guidewire placed into the ascending aorta. A marking pigtail catheter is likewise inserted via the contralateral CFA. Angiography is used to confirm landing zones, and the covered stent-graft is deployed over the guidewire. Fenestrated endografts are an increasingly used technology, which allow separate stents to be deployed through holes in the endograft to the renal and mesenteric arteries to maintain perfusion to these organs if their position precludes a sufficient landing zone (and would otherwise have been covered by the stent). While these are generally custom made, *in situ* fenestration is increasingly being performed after graft deployment, with cutting balloons and radiofrequency puncture. Closure is percutaneously via a closure device, or oversewing the arteriotomy in the CFA.
Open Versus Endovascular Thoracoabdominal Aneurysm Repair

When comparing open and endovascular thoracoabdominal aneurysm repairs in terms of major endpoints such as mortality, data is conflicted. The largest study to date was conducted by Greenberg et al on 724 patient records and demonstrated no difference in mortality either at one month or one year\(^5\), findings echoed by a Swiss study which saw no difference at one, 12, 24 or 36 months\(^37\). Similarly, a study of US Medicare data between 1998 and 2007 demonstrated that while in the short term patients undergoing endovascular repair were less likely to die (6.1 vs 7.1\%, \(p = 0.07\)), this is lost by two years\(^38\). Several smaller studies agree, finding that a mild perioperative survival benefit is quickly lost, and remains absent at up to 10 years\(^39\)\textsuperscript{\textendash}\textsuperscript{43}. Overall, evidence suggests no difference in long term mortality between endovascular and open TAA repairs. The benefits of either technique in minimising spinal cord ischemia also has not been definitely proven, with only one study of 84 patients demonstrating a reduced risk of SCI\(^5\)\textsuperscript{,39\textendash}41\textsuperscript{,44\textendash}45.

Endovascular approaches have generally been shown to decrease the incidence of renal\(^39\)\textsuperscript{,41\textendash}42 and respiratory failure\(^39\), the duration of ICU\(^41\)\textsuperscript{,42\textendash}45 and hospital stays\(^39\)\textsuperscript{,45}, and rates of reoperation\(^5\)\textsuperscript{,42}. There is however evidence for an increased incidence of endoleaks\(^39\), peripheral vascular complications\(^39\), and increased cost\(^41\)\textsuperscript{,42} with endovascular interventions. Interestingly, patients who underwent endovascular TAA repair reported being significantly more depressed, and scored lower than a healthy cohort on subjective physical and mental domain scores, while the open repair group scored within the normal range\(^37\).
The difficulty with comparative studies is the fact that sicker and older patients are more likely to receive endovascular TAA repair\textsuperscript{5,37,40,41}, thus skewing outcomes. A large meta-regression by Cheng et al (which included traumatic aneurysm repairs) demonstrated that age did not impact outcomes when considering mortality, cerebrovascular accidents and paraplegia\textsuperscript{46}. The 5,888 patients in this study demonstrated endovascular TAA repair to be superior in perioperative mortality, paraplegia, cardiac and respiratory complications, renal dysfunction, and need for transfusion. However, there were no differences in rates of stroke, acute coronary syndromes or mortality beyond 12 months when comparing the two techniques.

While the number of open TAA repair has remained stable in the United States, the incidence of endovascular TAA repairs has increased from zero to thirty-three percent\textsuperscript{43}. This can be attributed to the increasing acceptability of endovascular approaches, as well as the aging population making minimally invasive techniques more attractive, especially in high risk patients\textsuperscript{33}. However, neither open nor endovascular TAA repair has been shown to be the optimal method of management of this condition, which continues to carry significant morbidity and mortality.
Rationale for the Study

To date, few studies have directly compared the benefits of endovascular and open TAA repair\(^5,37,39-42,44\). While some studies are prospective, there are at the time of writing no randomised controlled trials\(^47\). Only two studies have examined data later than 2007, and there are no studies with data more recent than 2010, despite the rapid change in endovascular technology over the last decade. These studies also tend to examine data from single centres, with small sample sizes. The current body of knowledge is limited in that the control group of one of the notable prospective trials\(^39\) has a large part of their open surgical cohort comprised of historical controls, a factor likely to impact both patient selection and cause confounding of other factors. No studies to date have been performed in Australia, and the relative prevalence of endovascular TAA repairs in Australia is unknown. Further, some of the published studies group thoracic and thoracoabdominal aneurysms together\(^41\), limiting the application of these results to TAA repairs specifically. This study will be one of the largest studies of its kind to date internationally, one of the first studies assessing patients across more than one centre, and be the first undertaken in an Australian setting.

Thoracic aortic aneurysms are responsible for a significant mortality if left untreated, and surgical repair itself can comprise a substantial burden of morbidity and mortality. Equipoise remains in the question of open versus endovascular management of thoracic and thoracoabdominal aneurysms, and ascertaining the optimal management of this pathology is essential. A study is required that examines patients from more than one local
clinical centre, using data that is recent, with contemporaneous open and endovascular groups. Such a study should also examine arch and descending aneurysms separately.
Aim of the Study

This study was proposed to compare morbidity, mortality, clinical outcomes and trends over time of open and endovascular repair of thoracic aortic aneurysms in Australia. The findings will compare the clinical outcomes of open and endovascular TAA repairs in two large hospitals. We also seek to assess the impact of age on outcomes. The study will illustrate the clinical feasibility of the two techniques, demonstrating the optimal method of management of TAAs, as well as illustrating improvements in management of this condition over time, and providing direction for future service planning in Australia.
Hypothesis

Our primary hypothesis is that endovascular thoracic and thoracoabdominal aneurysm repair will outperform open repair in regards to mortality. Secondary hypotheses are that endovascular repair would similarly demonstrate superiority regarding complication rate, duration of hospital stay and transfusion requirement over open repair. Additionally, we hypothesised that mortality has decreased over time in all patients undergoing surgical intervention.
Limitations

Potential limitations of this study include its retrospective nature, and the potential of complications of either open or endovascular techniques to be remedied at other institutions (namely after discharge), thus being missed by the data collection methods of the current study. These include (but are not limited to) endoleaks, wound infection and dehiscence, other infective complications and thromboembolic complications. Further, due to the short duration of follow-up, the not insignificant risk of endoleak after endovascular repair will not be captured, and therefore this ‘Achilles heel’ of endovascular aneurysm was not considered in the current study.

As patients not suitable for a large open operation are often selected for endovascular repair, it is possible that patients that undergo endovascular repair will possess more surgical risk factors as previously described, which may interfere with outcome analysis. Further, as there are anatomical contraindications to endovascular repair (both patient and aneurysm morphology), clinicians will select patients for one or other procedure, so selection bias cannot be excluded. In addition, the small numbers, and significant heterogeneity between cases mean that careful consideration must be given when extrapolating these results.

Lastly, comparisons between surgeons and hospitals were not undertaken. While these are potential sources of variability, this study aimed to compare the two surgical techniques, rather than compare outcomes between institutions.
Study Design

Study Questions

The aim of the current study was to compare morbidity, mortality, clinical outcomes and trends over time of open and endovascular repair of thoracic aortic aneurysms in Australia.

The three specific research questions were:

1) Is there a significant difference in in-hospital mortality between open and endovascular thoracic aortic aneurysm repairs?

2) Are there significant differences in complication rates and use of hospital resources between the two procedures?

3) Have mortality rates of patients undergoing TAA repair decreased over the previous decade?
Patient Selection & Data Collection

In order to investigate these hypotheses, a study comparing these two techniques was designed. A retrospective analysis of patient records was conducted at two acute-care hospitals located in Sydney, Australia. Royal Prince Alfred Hospital and St George Hospital are both tertiary level hospitals in metropolitan Sydney with twenty-four hour cardiothoracic and vascular surgery services, with 911 and 547 beds respectively.

To observe patterns over the preceding decade, all patients who presented with thoracic aortic aneurysms (ruptured and un-ruptured) between January 2003 and January 2013 (inclusive) were included. This was achieved by using International Classification of Diseases 10 classifications I71.1 (thoracic aortic aneurysm, ruptured), I71.2 (thoracic aortic aneurysm, without mention of rupture), I71.5 (thoracoabdominal aneurysm, ruptured) and I71.6 (thoracoabdominal aortic aneurysm, without mention of rupture) were used to identify patients who presented with thoracic aortic aneurysms (including descending aneurysms of Crawford Class 0-III).

Various demographic, surgical and clinical variables were collected. Independent variables were collected in order to firstly observe the demographics of the study population, and secondly to control for confounders. They included age, sex, year of intervention, aneurysm type (including Crawford class for descending aneurysms) and size, co-morbidities, American Society of Anaesthesiologists (ASA) score, presence of rupture, use of local or general anaesthetic, open or endovascular intervention, type and brand of graft, use of cardiopulmonary bypass, and use of cerebrospinal fluid (CSF) drainage. Outcome variables (used
to compare groups) included duration of surgical procedure, number of units of blood transfused, in-hospital complications, post-operative paraplegia (as described below), in-hospital mortality, presence of endoleaks, rates of return to theatre (within 24 hours) and re-operation (after the first 24 hours), acute kidney injury (defined as an increase in serum creatinine greater than fifty percent⁴⁹) and acute kidney failure (defined as a tripling of serum creatinine⁴⁹), time to first mobilisation, and duration of hospital and ICU (including coronary care unit) stay.
Paraplegia and paraparesis were defined as follows:

<table>
<thead>
<tr>
<th>Category and Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paraplegia</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>Nil Movement</td>
</tr>
<tr>
<td>1</td>
<td>Minimal motion</td>
</tr>
<tr>
<td>2</td>
<td>Motion, but not against resistance/gravity</td>
</tr>
<tr>
<td>Paraparesis</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Motion against resistance/gravity only</td>
</tr>
<tr>
<td>4</td>
<td>Able to mobilise with assistance</td>
</tr>
</tbody>
</table>

**Table 1 - Scoring system for paraplegia/paraparesis post TAA repair. Modified from Greenberg et al 2008**

Patients were divided into two age groups (over and under the age of seventy-five years) to compare outcomes between younger and more elderly patients. Seventy-five years was chosen as this has been previously found to be the median age of a high risk TAA-repair population. Cook Medical® provided a research scholarship for two research assistants (medical students) who, after ethics approval was gained, were taught to interpret the medical records, and enter data into a de-identified spread-sheet. They were not told the source of the funding until after the data were collected, in order to reduce the risk of bias.
Statistical Analysis

Mann-Whitney U tests were used to assess differences between the medians of groups for continuous variables with skewed distributions, while T-tests were used to compare means. Categorical variables were compared using Pearson Chi-squared Tests. Binomial tests were used to compare observed frequencies. Linear regression was used to assess the relationship between independent and outcome variables, and changes in rates of repair, and morbidity and mortality over time. A p value of 0.05 was considered to be statistically significant. All analyses were performed using SPSS 22 (IBM, New York, New York, United States).
Ethics Approval

Ethics approval was sought and gained from the Human Research Ethics Committees at the University of Notre Dame Australia, with multi-centre ethics approval from the Sydney Local Health District Ethics Review Committee (RPAH Zone). Site-specific ethics approval was gained from the Royal Prince Alfred and St George Hospitals separately.
Manuscript Accepted for Publication in Annals of Vascular Surgery

The manuscript below was accepted for publication in the *Annals of Vascular Surgery* on the 5/08/2015, and published in February 2016, Vol 31, p 30-38. This journal was selected as it is one of the leading international vascular surgery journals.
Endovascular Repair of Arch and Descending Thoracic Aneurysms: a Retrospective Comparison

Thoracic Aneurysm Repairs in Australia

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Abstract

Thoracic aortic aneurysms (TAAs) contribute significant mortality if left untreated, but surgical repair has historically carried substantial risks. We sought to observe trends and outcomes of thoracic aortic repairs, so conducted a retrospective review of all patients who presented for management of TAAs from 2003 to 2013 at two hospitals in Sydney, Australia. 179 patients presented with TAAs over the study period, including 5 ruptures. 52 were treated non-operatively, with 127 surgically repaired. Operative duration was significantly shorter in endovascular than open repair of arch (193 ± 108 vs 396 ± 98 minutes, p = 0.0001) and descending aneurysms (242 ± 116 vs 422.5 ± 161 minutes, p = 0.003). There were no differences in mortality or complication rates (including paraplegia), duration of hospital or ICU stay, or transfusion requirements between endovascular and open TAA repairs. Apart from reduced surgical duration, this study revealed no benefits of endovascular over open TAA repair. Overall morbidity and mortality was low, even in elderly patients.

Key words: thoracic aneurysm repair, open, endovascular, mortality

Abstract: 162 words

Main Body: 3,649 words
Introduction

Thoracic aortic aneurysms (TAAs) include aneurysms involving the ascending aorta (from the aortic annulus to the brachiocephalic trunk), the aortic arch (the brachiocephalic trunk to the left subclavian), and the descending aorta (including thoracoabdominal aneurysms, extending from the left subclavian artery to the infra-renal aorta\textsuperscript{1}). Ascending aneurysms account for sixty percent of TAAs, the arch ten percent, and the descending aorta thirty percent (of which one quarter extend distal to the diaphragm\textsuperscript{2}). TAAs have an incidence of 10 per 100,000\textsuperscript{3}, and if untreated carry a significant burden of disease, with a five-year survival of fifty-four percent\textsuperscript{4}, and up to a forty-seven percent two year mortality in high risk patients\textsuperscript{5}.

Although vast improvements have been made since the first surgical repair of a TAA in 1955\textsuperscript{6}, perioperative mortality remains as high as nineteen percent, with one-year mortality of up to thirty-one percent\textsuperscript{7}. Further, a recent study demonstrated mortality to be as high as thirty-four percent in the post-operative period post hybrid TAA repair (open vascular reimplantation simultaneously with endograft repair)\textsuperscript{8}. Substantial morbidity is also common. Interruption of spinal arterial supply runs the risk of spinal cord ischemia (SCI) and subsequent paraplegia, while renal ischemia risks acute kidney injury and failure. Each of these complications can occur in up to eight percent of TAA repairs\textsuperscript{9-11}. Cardiorespiratory complications are also commonly experienced\textsuperscript{12,13}. As a result, TAA repair remains a high-risk endeavour.
Endovascular repair is accepted as the optimal method of management for many vascular diseases\textsuperscript{14-17}. Reported benefits include reduced blood loss and infection risk, reduced procedure time and transfusion requirement, reduced duration of mechanical ventilation, low operative morbidity and mortality, reduced cost, reduced intensive care unit stay, and faster time to mobilisation and discharge from hospital\textsuperscript{17-20}. In addition to these general advantages, proposed benefits of endovascular repair specific to TAAs include avoidance of the physiological insults of aortic cross-clamping and thoracic or thoracoabdominal incisions\textsuperscript{11}. Ability to utilise local anaesthesia in up to fifty-three percent of patients\textsuperscript{21} allows avoidance of cardiorespiratory morbidity and mortality associated with general anaesthesia, as well as reduced hospital stay.

To date, apart from the landmark study by Greenberg et al\textsuperscript{9}, the studies that have directly compared the benefits of endovascular and open TAA repair\textsuperscript{22-27} are generally from single centres, have small sample sizes, and only two have examined data more recently than 2007. Many studies group thoracic and thoracoabdominal aneurysms, limiting the application of these results. Thus, we sought to observe clinical outcomes of open and endovascular TAA repairs in two Australian tertiary-referral hospitals over the previous decade, examining ascending, arch, and descending aneurysms separately. We hypothesised that morbidity and mortality has decreased over the last decade, and that endovascular outperformed open TAA repair.
Materials & Methods

A retrospective analysis of patient records was conducted at the Royal Prince Alfred and St George Hospitals, which are tertiary level acute-care hospitals in Sydney, Australia. International Classification of Diseases 10 classifications I71.1 (thoracic aortic aneurysm, ruptured), I71.2 (thoracic aortic aneurysm, without mention of rupture), I71.5 (thoracoabdominal aneurysm, ruptured) and I71.6 (thoracoabdominal aortic aneurysm, without mention of rupture) were used to identify patients who presented with degenerative thoracic aortic aneurysms (including descending aneurysms of Crawford Class 0-III) between January 2003 and January 2013. Clinicopathologic manifestations included acute severe pain, chronic pain, acute rupture, and incidental findings. All treating surgeons were consultants, with 10 cardiothoracic and 11 vascular surgeons between the two hospitals. All vascular surgeons were skilled at both endovascular and open procedures. Due to the timeframe, the surgical teams and multidisciplinary teams varied across the study period.

Demographic, surgical and clinical variables were collected. Independent variables included age, sex, year of intervention, aneurysm type (defined as above, with descending aneurysms classified as per 2010 Society for Vascular Surgery Reporting Standards\(^{28}\) and size, co-morbidities, American Society of Anesthesiologists (ASA) score, presence of rupture, use of local or general anaesthetic, open or endovascular intervention, type and brand of graft, use of cardio-pulmonary bypass, and use of cerebrospinal fluid (CSF) drainage. Patients undergoing ascending aortic repair plus hemi-arch replacement were included in the ascending group, and not in the arch group. Patients with disease extending across multiple
areas of the aorta were excluded to prevent confounding. Patients who had undergone previous open debranching were considered as part of the endovascular group, as only an endovascular procedure was performed, and the open procedure was not performed during that admission. Patients undergoing hybrid repair were included in the endovascular group. Outcome variables included duration of surgical procedure, number of units of blood transfused, in-hospital complications, post-operative paraplegia (as previously described⁹), in-hospital mortality, presence of endoleaks, rates of return to theatre (within 24 hours) and re-operation (after the first 24 hours), acute kidney injury (defined as an increase in serum creatinine greater than fifty percent³⁹) and acute kidney failure (defined as a tripling of serum creatinine³⁹), time to first mobilisation, and duration of hospital and ICU (including coronary care unit) stay. Patients were also divided into two age groups (over and under the age of seventy-five years) to compare outcomes between younger and more elderly patients (seventy-five years was chosen as this has been previously found to be the median age of a high risk TAA-repair population⁵). Indication for CSF drainage was determined by the operating surgeon, with patients having undergone previous abdominal aortic aneurysm repair requiring pre-operative angiography to investigate spinal cord perfusion.

Mann-Whitney U tests were used to assess differences between the medians of groups for continuous variables with skewed distributions, while t tests were used to compare means. Categorical variables were compared using Pearson Chi-squared Tests. Binomial tests were used to compare observed frequencies. Logistic regression was used to assess the relationship between independent and outcome variables, with Cox Regression to compare mortality rates of endovascular and open repairs, as well as baseline characteristics. A p
value of 0.05 was considered to be statistically significant. All analyses were performed using SPSS 22 (IBM, New York, New York, United States).

Ethics approval was gained from the Human Research Ethics Committees at the University of Notre Dame Australia, with multi-centre ethics approval from the Sydney Local Health District Ethics Review Committee (RPAH Zone). Site specific ethics approval was gained from the Royal Prince Alfred and St George Hospitals separately.
Results

Patients Undergoing Non-Surgical Management

There were fifty-two patients with thoracic aneurysms that were managed without surgery (16 ascending, 24 arch, and 12 descending), due to a combination of surgery being deemed inappropriate due to age and comorbidities making survival unlikely, or patient refusal. Five of these patients presented with aneurysm rupture (1 ascending, 2 arch, and 2 descending). There was no difference in gender (p = 0.488). Of the 8 patients that died in hospital (including all five ruptures), average time to mortality was 3 days, with 4 dying within 24 hours of presentation. The ruptured aneurysms were not offered surgical intervention due to likely futility, based on presentation, age (all but one being over 85 years of age) and comorbidities. When compared to patients undergoing surgical management, patients managed conservatively were markedly older (64.4 ± 13.1 vs 73.9 ± 16.0 years, p <0.001), more likely to be female (31 vs 56%, p = 0.001), had shorter hospital stays (11.6 ± 13.6 vs 6.7 ± 10.2 days, p = 0.023), and were five-times more likely to die in hospital (3.1 vs 15.4%, p = 0.002). There was no change in the non-operative rate over time.
Repair of Ascending Thoracic Aortic Aneurysms

Sixty-nine patients underwent open repair of an ascending TAA, with an average age of 63.0 ± 12.5 years. Mean aneurysm size was 55.4 ± 10.6, with average ASA score 3.2 ± 0.6. 52.2% (36 patients) were smokers, 29.0% (20 patients) had ischemic heart disease, 58.0% (40 patients) had hypertension, and 10.2% (7 patients) had diabetes. Patients were twice as likely to be male (66.7 vs 33.3%, p = 0.008). Average duration of surgery was 350 ± 101 minutes, with mean duration of ICU stay 4.5 ± 6.0 days, and total hospital stay 11.6 ± 16.0 days. 3 patients (4.4%) returned to theatre within 24 hours, and 3 patients (4.4%) underwent re-operation after the first day. An average of 2.9 ± 4.3 units of packed red cells were transfused, and mean time to mobilisation was 3.6 ± 7.5 days. One patient died, secondary to a cardiac arrest while in ICU. Of the 11 patients (15.9%) suffering cardiac complications, 9 patients suffered AF, and 4 suffered ventricular tachycardia (two of which responded to cardioversion, and two required internal cardiac massage). The 6 patients (8.7%) suffering infective complications included three with pneumonia, two with sepsis, and one with a sternotomy infection. Other complications included 3 respiratory (4.4%), 1 renal (1.5%), 2 neurologic (2.9%), 4 haemorrhagic (5.8%), and 2 vaso-occlusive (2.9%). Patients over the age of 75 were no different to those under 75, in terms of baseline or outcome variables.
Arch Repairs

Twenty-seven patients underwent arch aneurysm repair during the study period, twenty open and seven endovascular (with two of the seven being hybrid procedures). There was no difference in baseline characteristics and co-morbidities between these two groups (Table 2). Patients were four times more likely to be male (p = 0.006). Of the endovascular patients, one patient had undergone previous de-branching (left subclavian and carotid), two patients underwent hybrid repair, and the remaining four had their left subclavian covered (after appropriate pre-operative imaging). One patient had her endovascular repair under local anaesthetic, and one open patient required two grafts. All open repairs were performed via sternotomy and received cardiopulmonary bypass (CPB). One endograft patient received CSF drainage, and one endograft patient did not go to ICU post-operatively. Causes for return to theatre in the endovascular group included a groin haematoma, and a broncho-aortic fistula.

Duration of endovascular arch aneurysm repair was half as long as open repair (p = 0.0001), although there were no other differences in outcome between the two groups (Table 2). One patient suffered acute kidney injury (in the open group), one suffered a sternotomy wound infection, and seven of the patients developed atrial fibrillation. There were 2 endoleaks (28.6%), one Type 1a, and one Type 1b.

Patients over the age of 75 had significantly larger arch aneurysms (63.5 ± 8.7 vs 52.1 ± 9.5mm, p = 0.035), were more likely to undergo an unplanned return to theatre (25.0 vs 0.0%, p = 0.015), or develop an endoleak (25.0 vs 4.4% p = 0.048), despite no differences in
other baseline co-morbidities. There was also no difference in mortality nor complications when compared to patients under 75 years of age. Linear regression revealed no significant relationship between surgical duration or aneurysm size and outcome variables. There was no change in the percentage of endovascular arch procedures performed over the duration of the study period (Figure A1 – See Appendix), nor the rate of morbidity and mortality (p > 0.05).
**Descending Repair**

Thirty-one patients underwent repair of descending aortic aneurysms, twelve open and nineteen endovascular. Three had undergone previous abdominal aortic aneurysm repair. There was no difference between rates of males and females undergoing descending repair (p = 0.071). Patients undergoing endografting were significantly older (75.6 ± 7.2 vs 55.9 ± 17.2 years, p = 0.0001), but otherwise were no different regarding baseline characteristics and co-morbidities (Table 3). Three patients had undergone previous vascular debranching (one patient underwent re-implantation of a renal artery, and two patients underwent re-implantation of mesenteric arteries), and four patients underwent hybrid repair (three required re-implantation of the left subclavian artery, one left subclavian and left carotid). Twenty-three patients required only one endograft, seven patients required two, and one patient required four. Four patients received grafts with fenestrations to the renal arteries bilaterally. In the open group, approaches included nine anterolateral thoracotomies, and three posterolateral thoracotomies. Six patients in the open group (50%), and six patients in the endovascular group (32%) underwent CSF drainage, with one open and two endovascular patients having had previous abdominal aortic aneurysm repair.

Descending aneurysm endografting was a significantly shorter procedure, taking less than sixty-percent of the time of open repair (p = 0.003). There were no other differences in peri- and post-operative characteristics between the two groups (Table 3). There were six endoleaks in the endograft group, two Type 1a, one Type 1b, two Type 2, and one Type 3. Of the three endovascular patients requiring return to theatre, one was to exclude ischemic gut, one to treat an endoleak, and one due to groin haematoma. Three patients who
underwent descending aneurysm repair died (11%). There was one death from acute kidney failure, and two from sepsis. Acute renal failure occurred in two patients in the open group (one secondary to intravenous contrast), with acute kidney injury in one endograft patient. Linear regression revealed no significant relationship between aneurysm size nor surgical duration and outcome variables. Further, multivariable analysis with Cox regression revealed there was no difference in hazard of mortality for endovascular over open repair (Hazard Ratio of endovascular versus open repair 1.16, 95% CI 0.67 – 1.82, p = 0.83).

Similarly, there was no relationship between age, aneurysm size, and comorbidities on morbidity (p>0.05). Two endovascular patients suffered paraplegia which resolved, one of whom had previous abdominal aortic aneurysm repair.

Patients over the age of 75 were almost twice as likely to have an endovascular procedure (83.3 vs 47.4%, p = 0.045). They were also more likely to require more blood transfused (5.5 ± 9.7 vs 1.2 ± 1.9 units, p = 0.008), have a longer ICU stay (5.5 ± 9.7 vs 3.5 ± 2.2 days, p = 0.032), non-ICU stay (10.1 ± 6.9 vs 6.1 ± 3.4, p = 0.003) and total hospital stay (14.1 ± 10.0 vs 9.6 ± 4.0 days, p = 0.006).

There was a significant increase in the percentage of endovascular descending aneurysm repairs over time (R2 = 0.453, β = 0.673, p = 0.033; Figure 1), but there was no change in rates of morbidity and mortality (p > 0.05).
Discussion

While the total number of TAA repairs has increased in the United States over the last 2 decades, the rate of open repair has remained constant\textsuperscript{30}. Endovascular repair rates now account for 31 percent of all repairs, and are likely to continue to rise\textsuperscript{30}. In the current study, we found a similar trend for increasing endovascular repairs of descending aneurysms in Australia. This is likely due to the perceived high mortality rates of open repair\textsuperscript{31}, the increasing acceptability of endovascular approaches, and the aging population making minimally invasive techniques more attractive. While one study demonstrated no difference\textsuperscript{32}, it has been suggested that descending endovascular TAA repairs are less costly in the short term (despite the considerable expense of the endograft itself\textsuperscript{25, 33, 34}). It is therefore possible that the increasing pressure to minimise health spending may be contributing to the increasing number of endovascular repairs, although there is evidence that endografting may become more expensive in the long term, due to surgeon follow up and CT surveillance\textsuperscript{25}. However, new developments in endovascular technology, and potential decreases in endograft costs\textsuperscript{34} make endografting a viable option in an increasing proportion of patients. In fact, the most recent analysis of endovascular and open TAA repairs suggested that endovascular repair is more cost effective, notably as intervention rates post-operatively were less than expected\textsuperscript{35}. This suggests that with time, endovascular repair is indeed becoming the more financially viable option. The decrease in percentage of endovascular repairs between 2004 and 2006 is likely an artefact, due to the small total number of descending TAA repairs (two and three repairs in 2005 and 2006 respectively).
At the institutions examined in this study, we saw extremely low peri-operative mortality rates in patients undergoing thoracic aortic aneurysm repairs. Three percent of patients undergoing surgical management died during the study period, likely due to both improving technique, as well as careful patient selection (for example, non-operative patients were seen to be on average ten years older). However, patients over the age of 75 years were noted not to have a higher mortality rate, suggesting perhaps that endovascular repairs of descending TAAs may be appropriate in elderly patients, ones that may have been denied an operation previously – although it may be careful selection of patients in the current study that resulted in such outcomes. Interestingly, there was no difference in mortality rates nor complication rates between endovascular and open TAA repairs. In the current literature, data is conflicted regarding survival benefits and complication rates between open and endovascular approaches. The largest study to date from Greenberg et al demonstrated no difference in mortality either at one month or one year, findings echoed by a Swiss study which saw no difference at one, twelve, twenty-four or thirty-six months. Similarly, a study of US Medicare data between 1998 and 2007 demonstrated that while in the short term there may be a borderline mortality benefit from endovascular repair (6.1 vs 7.1%, p = 0.07), this is lost by two years. Several smaller studies concur, finding that a mild perioperative survival benefit is quickly lost, and remains absent at up to ten years. Overall, current evidence suggests no difference in long-term mortality between endovascular and open TAA repairs, with the mortality rate of the current study similar to that previously seen.
The comparative benefits of either open or endovascular techniques in minimising spinal cord ischemia also have not been seen, with only one study demonstrating a reduced risk of SCI in endovascular TAA repairs\textsuperscript{22}. In the current study, only two patients suffered paraplegia post-operatively, both of whom had undergone endografting of their descending aorta. The observed paraplegia rate of 8% post endografting is similar to the 3-7% seen in recent studies\textsuperscript{9, 22, 23, 25, 26, 37}. This is interesting given that the use of spinal drains in our study institutions (at 50 and 32%) is much lower than previously observed, with up to 66 and 79% of patients undergoing prophylactic CSF drainage for open and endovascular repairs respectively\textsuperscript{25}. Although a recent Cochrane analysis suggested that data is limited and needs further study\textsuperscript{38}, the largest and most recent randomised controlled trial\textsuperscript{39} found CSF drainage is effective in preventing SCI. As such, further randomised controlled trials into the efficacy of CSF drainage in preventing spinal cord ischemia are required.

No difference was seen in complication rate, when comparing open and endovascular thoracoabdominal aneurysm repair. Although not statistically significant, patients undergoing endovascular descending TAA repair were seen to suffer more paraplegic and infectious complications, but the numbers of patients suffering these complications being small makes this difficult to interpret. While not demonstrated in this study, endovascular approaches have generally been shown to decrease the incidence of renal failure\textsuperscript{22, 25, 27}, respiratory failure\textsuperscript{22}, duration of ICU\textsuperscript{25, 27, 37} and hospital stays\textsuperscript{22, 37}, and rates of reoperation\textsuperscript{9, 27}. However, with endovascular interventions there is the added risk of endoleaks\textsuperscript{22} and peripheral vascular complications\textsuperscript{22}, with evidence for increased cost\textsuperscript{25, 27}. Interestingly, patients who underwent endovascular TAA repair reported being significantly more
depressed, and scored lower than a healthy cohort on subjective physical and mental domain scores, while the open repair group scored within the normal range\textsuperscript{24}.

The difficulty with such studies is that sicker and more elderly patients are more likely to receive endovascular TAA repair\textsuperscript{9, 23-25}, thus skewing outcomes. In fact, the current study demonstrated that patients undergoing endovascular repair were on average five and twenty years older for arch and descending aneurysm repairs respectively. However, a large meta-analysis (which included repairs of aortic trauma, dissections, ulcers and intra-mural haemorrhage) by Cheng et al and included 5,888 patients demonstrated that age did not impact outcomes when considering mortality, cerebrovascular accidents and paraplegia\textsuperscript{40}. Similarly, we found that although patients over the age of seventy-five years were more likely to undergo endovascular interventions, there was no difference in peri-operative mortality, likely due to appropriate patient selection, and pre-operative planning and assessment. However, these patients were more likely to return to theatre within 24 hours, suffer endoleaks, have a higher transfusion requirement, and have a longer hospital and ICU stay, despite no differences in baseline comorbidities. While patients over 75 years had larger arch aneurysms than those under 75, size of aneurysm was found not to correlate with peri- and post-operative outcome. These findings suggest that while surgical repair of TAAs in elderly patients is likely to carry a low burden of mortality, these patients are at increased risk of post-operative complications.
The key limitations of this study are its retrospective nature, and its small sample sizes. Sample size is notably an issue for endovascular treatment of arch and descending aneurysms, notably as ICU stay appears to be (non-significantly) greater for endovascular than open repairs. Additionally, as the endovascular group includes patients who underwent hybrid procedures, their duration of stay and complication rate were not likely to differ from open repairs. As such, a more accurate comparison of endovascular and open repairs would contrast open and pure endovascular repairs, with no open procedures. Due to the relative rarity of thoracic aneurysms, sample sizes remain small, and studies are universally retrospective. As a result, it is difficult to make conclusive decisions regarding optimal surgical management from such studies. In fact, a 2009 Cochrane review has called for randomised controlled trials on TAA repairs to definitively address the endovascular versus open query41.

In conclusion, surgical repair of thoracic aortic aneurysms in carefully selected patients in Australia is associated with minimal mortality, but considerable morbidity. Apart from a reduced surgical duration, the present study revealed no benefits of endovascular over open TAA repair, with economic factors possibly driving the increasing proportion of descending endografts seen. Overall, endovascular repair continues to perform well, especially in high-risk and elderly patients, and should be considered intervention of choice in suitable patients. Elderly patients are at increased risk of complications, but appropriate patient selection and preoperative planning make TAA repair a valid option in increasingly elderly and frail patients.
Declaration of Conflicting Interests

The authors declare that there is no conflict of interest.

Funding Acknowledgement

Cook Medical provided a research scholarship for the two research assistants, who were not told the source of the funding until after the data was collected in order to reduce risk of bias. Funding was also used for administrative costs (eg, retrieving medical records from storage).
References


Tables

Table 1 – Characteristics for all thoracic aneurysm patients, with comparisons between those who underwent conservative and surgical management. Results are presented as means with standard deviations. Categorical variables are expressed as raw number, with percentage of the total in brackets. *p > 0.05

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
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<th>Surgical</th>
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<tr>
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<td>52</td>
<td>127</td>
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<tr>
<td>Age (years)</td>
<td>67.2 ± 14.6</td>
<td>73.9 ± 16.0</td>
<td>64.4 ± 13.1</td>
<td>&lt;0.001*</td>
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<td>Male Gender (%)</td>
<td>111 (62.0%)</td>
<td>23 (44%)</td>
<td>88 (69.3%)</td>
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<tr>
<td>Aneurysm Type</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>Ascending (%)</td>
<td>93 (52.0%)</td>
<td>24 (46.2%)</td>
<td>69 (54.3%)</td>
<td>0.542</td>
</tr>
<tr>
<td>Arch (%)</td>
<td>43 (24.0%)</td>
<td>16 (30.8%)</td>
<td>27 (21.3%)</td>
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<td>Descending (%)</td>
<td>41 (22.9%)</td>
<td>10 (19.2%)</td>
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<td>2 (3.8%)</td>
<td>0 (0.0%)</td>
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<td>Aneurysm size (mm)</td>
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<td>60.2 ± 15.5</td>
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<td>Smoking status (%)</td>
<td>87 (48.6%)</td>
<td>15 (28.9%)</td>
<td>72 (56.6%)</td>
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<td>Ischemic heart disease (%)</td>
<td>60 (33.5%)</td>
<td>20 (38.4%)</td>
<td>40 (31.5%)</td>
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<td>Hypertension (%)</td>
<td>123 (68.7%)</td>
<td>39 (75.0%)</td>
<td>83 (65.4%)</td>
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<td>Diabetes (%)</td>
<td>22 (12.3%)</td>
<td>7 (13.5%)</td>
<td>15 (11.8%)</td>
<td>1.000</td>
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<td>In-hospital Mortality (n)</td>
<td>12 (6.7%)</td>
<td>8 (15.4%)</td>
<td>4 (3.1%)</td>
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<td>Duration of Hospital Stay (Days)</td>
<td>10.2 ± 12.8</td>
<td>6.7 ± 10.2</td>
<td>11.6 ± 13.6</td>
<td>0.023*</td>
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Table 2 – Baseline, peri- and post-operative characteristics for patients undergoing arch aneurysm repair. Results are presented as means with standard deviations. Categorical variables are expressed as raw number, with percentage of the total in brackets. *p < 0.05. €Excluding pneumonia, which has been classified as ‘Infectious’. £Excluding paraplegia/paraparesis.

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<th>Total</th>
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<td>7</td>
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<td><strong>Age (years)</strong></td>
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<td>62.9 ± 11.0</td>
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<td><strong>Male gender (%)</strong></td>
<td>21 (77.8%)</td>
<td>16 (80.0%)</td>
<td>5 (71.4%)</td>
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<td><strong>Aneurysm size (mm)</strong></td>
<td>53.0 ± 10.1</td>
<td>52.7 ± 10.9</td>
<td>58.2 ± 6.4</td>
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<td><strong>Smoking status (%)</strong></td>
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<td><strong>Ischemic heart disease (%)</strong></td>
<td>9 (33.3%)</td>
<td>6 (30.0%)</td>
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<td><strong>Hypertension (%)</strong></td>
<td>22 (81.5%)</td>
<td>15 (75.0%)</td>
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<td><strong>Diabetes (%)</strong></td>
<td>6 (22.2%)</td>
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<td><strong>ASA Score</strong></td>
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<td>3.1 ± 0.5</td>
<td>2.8 ± 0.8</td>
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<td><strong>Duration of Surgery (min)</strong></td>
<td>343 ± 134</td>
<td>396 ± 98</td>
<td>193 ± 108</td>
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<td><strong>Return to theatre within 24hrs (%)</strong></td>
<td>1 (3.7%)</td>
<td>0 (0.0%)</td>
<td>1 (14.3%)</td>
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<td><strong>Re-operation (%)</strong></td>
<td>2 (7.4%)</td>
<td>1 (5.0%)</td>
<td>1 (14.3%)</td>
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<tr>
<td><strong>Complications (%)</strong></td>
<td>18</td>
<td>12</td>
<td>6</td>
<td>0.850</td>
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<tr>
<td><strong>Respiratory €</strong></td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
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<tr>
<td><strong>Renal</strong></td>
<td>1 (3.7%)</td>
<td>1 (5.0%)</td>
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<tr>
<td><strong>Paraplegia/paraparesis</strong></td>
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<td><strong>Cardiac</strong></td>
<td>9 (33.3%)</td>
<td>7</td>
<td>2 (28.6%)</td>
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<td><strong>Infectious</strong></td>
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<td>2</td>
<td>1 (14.3%)</td>
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<td><strong>Neurologic €</strong></td>
<td>1 (3.7%)</td>
<td>0 (0%)</td>
<td>1 (14.3%)</td>
<td>0.607</td>
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<td><strong>Vaso-occlusive</strong></td>
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<td>0 (0%)</td>
<td>0 (0%)</td>
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<td><strong>Haemorrhagic</strong></td>
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<td><strong>Units of Blood Transfused</strong></td>
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### Table 2 continued

<table>
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<th>Endoleaks</th>
<th>Type I (%)</th>
<th>Type II (%)</th>
<th>Duration of ICU Stay (days)</th>
<th>Time to First Mobilisation (days)</th>
<th>Duration of Non-ICU Stay (days)</th>
<th>Total Duration of Hospital Stay (days)</th>
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<tr>
<td></td>
<td>2 (7.4%)</td>
<td>-</td>
<td>4.5 ± 6.9</td>
<td>3.2 ± 8.0</td>
<td>7.2 ± 11.3</td>
<td>11.3 ± 12.3</td>
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<td>Type I (%)</td>
<td></td>
<td>-</td>
<td>3.45 ± 2.11</td>
<td>1.75 ± 1.1</td>
<td>6.25 ± 4.0</td>
<td>9.7 ± 4.6</td>
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<td>Type II (%)</td>
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<td>Time to First Mobilisation (days)</td>
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<td>Total Duration of Hospital Stay (days)</td>
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Table 3 – Baseline, peri- and post-operative characteristics for patients undergoing descending aneurysm repair. Results are presented as means with standard deviations. Categorical variables are expressed as raw number, with percentage of the total in brackets.

*p <0.05. €Excluding pneumonia, which has been classified as ‘Infectious’. £Excluding paraplegia/paraparesis.

<table>
<thead>
<tr>
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<th>Total</th>
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<td>Aneurysm size (mm)</td>
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<td>Hypertension (%)</td>
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<td>0 (%)</td>
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</tr>
<tr>
<td>III (%)</td>
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<td>Duration of Surgery (min)</td>
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<td>Return to theatre within 24hrs (%)</td>
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<td>Re-operation (%)</td>
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<tr>
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<td>0 (0%)</td>
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<td>Haemorrhagic (%)</td>
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<td>3 (15.8%)</td>
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<td>Type II</td>
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<td>2 (10.5%)</td>
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<td>Type III</td>
<td>1 (3.2%)</td>
<td>-</td>
<td>1 (5.3%)</td>
<td>-</td>
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<td><strong>Duration of ICU Stay (days)</strong></td>
<td>4.3 ± 6.2</td>
<td>3.9 ± 3.0</td>
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<td><strong>Time to First Mobilisation (days)</strong></td>
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<td><strong>Duration of Non-ICU stay (days)</strong></td>
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<td><strong>Duration of Hospital Stay (days)</strong></td>
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<td>12.7 ± 6.9</td>
<td>11.5 ± 8.6</td>
<td>0.389</td>
</tr>
</tbody>
</table>
Figure

Figure 1 – Percentage of patients undergoing endovascular descending aneurysm repair per year over the study period. $R^2 = 0.453$, $\beta = 0.673$, $p = 0.033$
Open versus Endovascular Repair of Arch and Descending Thoracic Aneurysms: A Retrospective Comparison

Timothy P. Shiraev,1,2 Raffi Qasabian,1 Daniel Tardo,2 Gemlle Ninic,2 and Zelda Doyle,2
Campdenw and Darlinghurst, New South Wales, Australia

Background: Thoracic aortic aneurysms (TAA)s contribute significant mortality if left untreated, but surgical repair has historically carried substantial risks.

Methods: We sought to observe trends and outcomes of open and endovascular thoracic endovascular aneurysm repair thoracic aortic repairs, so conducted a retrospective review of all patients who presented for management of TAA from 2003 to 2013 at 2 hospitals in Sydney, Australia.

Results: A total of 179 patients presented with TAA over the study period, including 5 ruptures. Fifty-two were treated nonoperatively, with 127 surgically repaired. Operative duration was significantly shorter in endovascular than open repair of arch (193 ± 108 vs. 386 ± 98 min, P = 0.0001) and descending aneurysms (242 ± 116 vs 422.5 ± 161 min, P = 0.003). There were no differences in mortality or complication rates (including paraplegia), duration of hospital or intensive care unit stay, or transfusion requirements between endovascular and open TAA repairs.

Conclusions: Apart from reduced surgical duration, this study revealed no benefits of endovascular over open TAA repair. Overall morbidity and mortality were low, even in elderly patients.

INTRODUCTION

Thoracic aortic aneurysms (TAA)s include aneurysms involving the ascending aorta (from the aortic annulus to the brachiocephalic trunk), the aortic arch (the brachiocephalic trunk to the left subclavian), and the descending aorta (including thoracoabdominal aneurysms, extending from the left subclavian artery to the infrarenal aorta1). Ascending aneurysms account for 60% of TAA, the arch 10%, and the descending aorta 30% (of which one-quarter extend distal to the diaphragm). TAA have an incidence of 10 per 100,000,3 and if untreated carry a significant burden of disease, with a 5-year survival of 54%,4 and up to a 47% 2-year mortality in high-risk patients (interestingly, 53% of these deaths are not aneurysm related).5

Although vast improvements have been made since the first surgical repair of a TAA in 1955,6 perioperative mortality remains as high as 19%, with 1-year mortality of up to 31%.7 Furthermore, a recent study demonstrated mortality to be as high as 34% in the postoperative period after hybrid TAA repair (open vascular reimplantation simultaneously with endograft repair).8 Substantial
morbidity is also common. Interruption of spinal arterial supply runs the risk of spinal cord ischemia (SCI) and subsequent paraplegia, whereas renal ischemia risks acute kidney injury and failure. Each of these complications can occur in up to 8% of TAA repairs.\textsuperscript{9–11} Cardiorespiratory complications are also commonly experienced.\textsuperscript{12,13} As a result, TAA repair remains a high-risk endeavor.

Endovascular repair is accepted as the optimal method of management for many vascular diseases.\textsuperscript{14–17} Reported benefits include reduced blood loss and infection risk, reduced procedure time and transfusion requirement, reduced duration of mechanical ventilation, low operative morbidity and mortality, reduced cost, reduced intensive care unit (ICU) stay, and faster time to mobilization and discharge from hospital.\textsuperscript{17–20} In addition to these general advantages, proposed benefits of endovascular repair specific to TAA's thoracic endovascular aneurysm repair (TEVAR) include avoidance of the physiological insults of aortic cross-clamping and thoracic or thoracoabdominal incisions.\textsuperscript{21} Ability to use local anesthesia in up to 54% of patients\textsuperscript{22} allows avoidance of cardiorespiratory morbidity and mortality associated with general anesthesia, as well as reduced hospital stay.

To date, apart from the landmark study by Greenberg et al.\textsuperscript{9} the studies that have directly compared the benefits of TEVAR and open TAA repair\textsuperscript{22–27} are generally from single centers, have small sample sizes, and only 2 have examined data more recently than 2007. Many studies group thoracic and thoracoabdominal aneurysms, limiting the application of these results. Thus, we sought to observe clinical outcomes of open and endovascular TAA repairs in 2 Australian tertiary-referral hospitals over the previous decade, examining ascending, arch, and descending aneurysms separately. We hypothesized that morbidity and mortality has decreased over the last decade, and that TEVAR outperformed open TAA repair.

**MATERIALS AND METHODS**

A retrospective analysis of patient records was conducted at the Royal Prince Alfred and St George Hospitals, which are tertiary level acute-care hospitals in Sydney, Australia. \textit{International Classification of Diseases 10 classifications} I71.1 (TAA, ruptured), I71.2 (TAA, without mention of rupture), I71.5 (thoracoabdominal aneurysm, ruptured), and I71.6 (thoracoabdominal aortic aneurysm, without mention of rupture) were used to identify patients who presented with degenerative TAA's (including descending aneurysms of Crawford class 0–III\textsuperscript{28}) between January 2003 and January 2013. Clinico-pathologic manifestations included acute severe pain, chronic pain, acute rupture, and incidental findings. All treating surgeons were consultants, with 10 cardiothoracic and 11 vascular surgeons between the 2 hospitals. All vascular surgeons were skilled at both endovascular and open procedures. Because of the time frame, the surgical teams and multidisciplinary teams varied across the study period. Various demographic, surgical, and clinical variables were collected from patient records by research assistants who deidentified the data before they were seen by the principal investigators. Cook Medical\textsuperscript{29} provided a research scholarship for the 2 research assistants, who were not told the source of the funding until after the data were collected, reducing risk of bias. Independent variables included age, sex, year of intervention, aneurysm type (defined as above, with descending aneurysms classified as per 2010 Society for Vascular Surgery Reporting Standards\textsuperscript{30}), and size, comorbidities, American Society of Anesthesiologists (ASA) score, the presence of rupture, use of local or general anesthetic, open or endovascular intervention, type and brand of graft, use of cardiopulmonary bypass, and use of cerebrospinal fluid (CSF) drainage. Patients undergoing ascending aortic repair plus hemiarch replacement were included in the ascending group, and not in the arch group. Patients with disease extending across multiple areas of the aorta were excluded to prevent confounding. Patients who had undergone previous open debranching were considered as part of the endovascular group, as only an endovascular procedure was performed, and the open procedure was not performed during that admission. Patients undergoing hybrid repair were included in the endovascular group. Outcome variables included duration of surgical procedure, number of units of blood transfused, in-hospital complications, postoperative paraplegia (as previously described\textsuperscript{31}), in-hospital mortality, presence of endoleaks, rates of return to theater (within 24 hr) and reoperation (after the first 24 hr), acute kidney injury (defined as an increase in serum creatinine greater than 50%)\textsuperscript{32} and acute kidney failure (defined as a tripling of serum creatinine\textsuperscript{33}), time to first mobilizations, and duration of hospital and ICU (including coronary care unit) stay. Patients were also divided into 2 age groups (over and under the age of 75 years) to compare outcomes between younger and more elderly patients (75 years was chosen as this has been previously found to be the median age of a high-risk TAA-repair population\textsuperscript{34}).
Indication for CSF drainage was determined by the operating surgeon, with patients having undergone previous abdominal aortic aneurysm repair requiring preoperative angiography to investigate spinal cord perfusion.

Mann–Whitney U tests were used to assess differences between the medians of groups for continuous variables with skewed distributions, whereas t tests were used to compare means. Categorical variables were compared using Pearson chi-squared tests. Binomial tests were used to compare observed frequencies. Logistic regression was used to assess the relationship between independent and outcome variables, with Cox regression to compare mortality rates of endovascular and open repairs, as well as baseline characteristics. A P value of 0.05 was considered to be statistically significant. All analyses were performed using SPSS 22 (IBM, New York, NY).

Ethics approval was gained from the Human Research Ethics Committees at the University of Notre Dame Australia, with multicenter ethics approval from the Sydney Local Health District Ethics Review Committee (RPAH zone). Site specific ethics approval was gained from the Royal Prince Alfred and St George Hospitals separately.

RESULTS

Patients Undergoing Nonsurgical Management

There were 52 patients with thoracic aneurysms that were managed without surgery (16 ascending, 24 arches, and 12 descending), because of a combination of surgery being deemed inappropriate due to age and comorbidities making survival unlikely, or patient refusal. Five of these patients presented with aneurysm rupture (1 ascending, 2 arches, and 2 descending). There was no difference in gender (P = 0.488). Of the 8 patients that died in hospital (including all 5 ruptures), average time to mortality was 3 days, with 4 dying within 24 hr of presentation. The ruptured aneurysms were not offered surgical intervention due to likely futility, based on presentation, age (all but one being over 85 years of age) and comorbidities. When compared with patients undergoing surgical management (Table 1), patients managed conservatively were markedly older (64.4 ± 13.1 vs. 73.9 ± 16.0 years, P < 0.001), more likely to be female (31 vs. 56%, P = 0.001), had shorter hospital stays (11.6 ± 13.6 vs. 6.7 ± 10.2 days, P = 0.023), and were 5 times more likely to die in hospital (31 vs. 15.4%, P = 0.002). There was no change in the nonoperative rate over time.

Repair of Ascending TAs

Sixty-nine patients underwent open repair of an ascending TAA, with an average age of 63.0 ± 12.5 years. Mean aneurysm size was 55.4 ± 10.6, with average ASA score 3.2 ± 0.6. Overall 52.2% (36 patients) were smokers, 29.0% (20 patients) had ischemic heart disease, 58.0% (40 patients) had hypertension, and 10.2% (7 patients) had diabetes. Patients were twice as likely to be male (66.7 vs. 33.3%, P = 0.008). Average duration of surgery was 350 ± 101 min, with mean duration of ICU stay 4.5 ± 6.0 days, and total hospital stay 11.6 ± 16.0 days. Three patients (4.4%) returned to theater within 24 hr, and 3 patients (4.4%) underwent reoperation after the first day. An average of 2.9 ± 4.3 units of packed red cells was transfused, and mean time to mobilization was 3.6 ± 7.5 days. One patient died, secondary to a cardiac arrest while in ICU. Of the 11 patients (15.9%) suffering cardiac complications, 9 patients suffered AF, and 4 suffered ventricular tachycardia (two of which responded to cardioversion and 2 required internal cardiac massage). The 6 patients (8.7%) suffering infective complications included 3 with pneumonia, 2 with sepsis, and 1 with a sternotomy infection. Other complications included 3 respiratory (4.4%), 1 renal (1.5%), 2 neurologic (2.9%), 4 hemorrhagic (5.8%), and 2 vaso-occlusive (2.9%). Patients over the age of 75 were no different to those under 75, in terms of baseline or outcome variables.

Arch Repairs

Twenty-seven patients underwent arch aneurysm repair during the study period, 20 open and 7 endovascular (with 2 of the 7 being hybrid procedures). There was no difference in baseline characteristics and comorbidities between these 2 groups (Table II). Patients were 4 times more likely to be male (P = 0.006). Of the TEVAR patients, one patient had undergone previous debranching (left subclavian and carotid), 2 patients underwent hybrid repair, and the remaining 4 had their left subclavian covered (after appropriate preoperative imaging). One patient had her endovascular repair under local anesthetic, and 1 open patient required 2 grafts. All open repairs were performed via sternotomy and received cardiopulmonary bypass (CPB). One TEVAR patient received CSF drainage, and 1 TEVAR patient did not go to ICU postoperatively. Causes for return to theater in the endovascular group included a groin hematoma, and a broncho-aortic fistula.

Duration of endovascular arch aneurysm repair was half as long as open repair (P = 0.0001).
Table I. Characteristics for all thoracic aneurysm patients, with comparisons between those who underwent conservative and surgical management

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<th>Conservative</th>
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<th>P value</th>
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<td>52</td>
<td>127</td>
<td></td>
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<tr>
<td>Age (years)</td>
<td>67.2 ± 14.6</td>
<td>73.9 ± 16.0</td>
<td>64.4 ± 13.1</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>111 (62.0)</td>
<td>23 (44)</td>
<td>88 (69.3)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Aneurysm type</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascending (%)</td>
<td>93 (52.0)</td>
<td>24 (46.2)</td>
<td>69 (54.3)</td>
<td>0.542</td>
</tr>
<tr>
<td>Arch (%)</td>
<td>43 (24.0)</td>
<td>16 (30.8)</td>
<td>27 (21.3)</td>
<td>0.072</td>
</tr>
<tr>
<td>Descending (%)</td>
<td>41 (22.9)</td>
<td>10 (19.2)</td>
<td>31 (24.4)</td>
<td>0.618</td>
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<td>Unknown (%)</td>
<td>2 (1.1)</td>
<td>2 (3.8)</td>
<td>0 (0.0)</td>
<td></td>
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<tr>
<td>Aneurysm size (mm)</td>
<td>57.7 ± 14.6</td>
<td>60.2 ± 15.5</td>
<td>56.6 ± 14.1</td>
<td>0.114</td>
</tr>
<tr>
<td>Smoking status (%)</td>
<td>87 (48.6)</td>
<td>15 (28.9)</td>
<td>72 (56.6)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Ischemic heart disease (%)</td>
<td>60 (33.5)</td>
<td>20 (38.4)</td>
<td>40 (31.5)</td>
<td>0.379</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>123 (68.7)</td>
<td>39 (75.0)</td>
<td>83 (65.4)</td>
<td>0.148</td>
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<tr>
<td>Diabetes (%)</td>
<td>22 (12.3)</td>
<td>7 (13.5)</td>
<td>15 (11.8)</td>
<td>1.000</td>
</tr>
<tr>
<td>In-hospital mortality (%)</td>
<td>12 (6.7)</td>
<td>8 (15.4)</td>
<td>4 (3.1)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Duration of hospital Stay (days)</td>
<td>10.2 ± 12.8</td>
<td>6.7 ± 10.2</td>
<td>11.6 ± 13.6</td>
<td>0.023*</td>
</tr>
</tbody>
</table>

*P > 0.05.

Results are presented as means with standard deviations. Categorical variables are expressed as raw number, with percentage of the total in brackets.

although there were no other differences in outcome between the 2 groups (Table II). One patient suffered acute kidney injury (in the open group), 1 suffered a sternotomy wound infection, and 7 of the patients developed atrial fibrillation. There were 2 endoleaks (28.6%), 1 type la, and 1 type lb.

Patients over the age of 75 had significantly larger arch aneurysms (63.5 ± 8.7 vs. 52.1 ± 9.5 mm, P = 0.035), were more likely to undergo an unplanned return to theater (25.0 vs. 0.0%, P = 0.015), or develop an endoleak (25.0 vs. 4.4% P = 0.048), despite no differences in other baseline comorbidities. There was also no difference in mortality nor complications when compared with patients less than 75 years of age. Linear regression revealed no significant relationship between surgical duration or aneurysm size and outcome variables. There was no change in the percentage of endovascular arch procedures performed over the duration of the study period, nor the rate of morbidity and mortality (P > 0.05).

**Descending Repair**

Thirty-one patients underwent repair of descending aortic aneurysms, 12 open and 19 endovascular. Three had undergone previous abdominal aortic aneurysm repair. There was no difference between rates of males and females undergoing descending repair (P = 0.071). Patients undergoing TEVAR were significantly older (75.6 ± 7.2 vs. 55.9 ± 17.2 years, P = 0.0001), but otherwise were no different regarding baseline characteristics and comorbidities (Table III). Three patients had undergone previous vascular debranching (1 patient underwent reimplantation of a renal artery, and 2 patients underwent reimplantation of mesenteric arteries), and 4 patients underwent hybrid repair (3 required reimplantation of the left subclavian artery, 1 left subclavian and left carotid). Twenty-three patients required only one endograft, 7 patients required 2, and 1 patient required 4. Four patients received grafts with fenestrations to the renal arteries bilaterally. In the open group, approaches included 9 anterolateral thoracotomies, and 3 posterolateral thoracotomies. Six patients in the open group (50%) and 6 patients in the TEVAR group (32%) underwent CSF drainage, with 1 open and 2 endovascular patients having had previous abdominal aortic aneurysm repair.

Descending aneurysm endografting was a significantly shorter procedure, taking less than 60% of the time of open repair (P = 0.003). There were no other differences in perioperative and postoperative characteristics between the 2 groups (Table III). There were 6 endoleaks in the TEVAR group, 2 type 1a, 1 type 1b, 2 type 2, and 1 type 3. Of the 3 TEVAR patients requiring return to theater, 1 was to exclude ischemic gut, 1 to treat an endoleak, and 1 due to groin hematoma. Three patients who underwent descending aneurysm repair died (11%). There was one death from acute kidney failure, and 2 from sepsis. Acute renal failure occurred in 2 patients in the open
### Table II. Baseline, perioperative, and postoperative characteristics for patients undergoing arch aneurysm repair

<table>
<thead>
<tr>
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<th>All patients</th>
<th>Open repair</th>
<th>Endovascular repair</th>
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<td>Number (years)</td>
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<td>20</td>
<td>7</td>
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</tr>
<tr>
<td>Male gender (%)</td>
<td>64.1 ± 11.4</td>
<td>62.9 ± 11.0</td>
<td>67.7 ± 12.8</td>
<td>0.363</td>
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<tr>
<td>Aneurysm size (mm)</td>
<td>53.0 ± 10.1</td>
<td>52.7 ± 10.9</td>
<td>58.2 ± 6.4</td>
<td>0.083</td>
</tr>
<tr>
<td>Smoking status (%)</td>
<td>13 (48.2)</td>
<td>9 (45.0)</td>
<td>4 (57.1)</td>
<td>0.580</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>22 (81.5)</td>
<td>15 (75.0)</td>
<td>7 (100)</td>
<td>0.143</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>6 (22.2)</td>
<td>5 (25.0)</td>
<td>1 (14.3)</td>
<td>0.557</td>
</tr>
<tr>
<td>ASA score</td>
<td>3 ± 0.6</td>
<td>3.1 ± 0.5</td>
<td>2.8 ± 0.8</td>
<td>0.413</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>343 ± 134</td>
<td>396 ± 98</td>
<td>193 ± 108</td>
<td>&lt;0.000*</td>
</tr>
<tr>
<td>Return to theater within 24 hr (%)</td>
<td>1 (3.7)</td>
<td>0 (0.0)</td>
<td>1 (14.3)</td>
<td>0.085</td>
</tr>
<tr>
<td>Reoperation (%)</td>
<td>2 (7.4)</td>
<td>1 (5.0)</td>
<td>1 (14.3)</td>
<td>0.419</td>
</tr>
<tr>
<td>In-hospital mortality (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>—</td>
</tr>
<tr>
<td>Complications (%)</td>
<td>18</td>
<td>12</td>
<td>6</td>
<td>0.850</td>
</tr>
<tr>
<td>Respiratory (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>—</td>
</tr>
<tr>
<td>Renal (%)</td>
<td>1 (3.7)</td>
<td>1 (5.0)</td>
<td>0 (0)</td>
<td>0.850</td>
</tr>
<tr>
<td>Paraplegia/paraparesis (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>—</td>
</tr>
<tr>
<td>Cardiac</td>
<td>9 (33.3)</td>
<td>7</td>
<td>2 (28.6%)</td>
<td>0.808</td>
</tr>
<tr>
<td>Infectious</td>
<td>3 (11.1%)</td>
<td>2</td>
<td>1 (14.3%)</td>
<td>0.893</td>
</tr>
<tr>
<td>Neurologic (%)</td>
<td>1 (3.7)</td>
<td>0 (0)</td>
<td>1 (14.3)</td>
<td>0.607</td>
</tr>
<tr>
<td>Vasopressive (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>—</td>
</tr>
<tr>
<td>Hemorrhagic (%)</td>
<td>3 (11.1)</td>
<td>2 (10.0)</td>
<td>2 (28.6)</td>
<td>0.498</td>
</tr>
<tr>
<td>Units of blood transfused</td>
<td>2.88 ± 4.2</td>
<td>3.45 ± 2.1</td>
<td>1.3 ± 2.2</td>
<td>0.162</td>
</tr>
<tr>
<td>Endoleaks</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type I (%)</td>
<td>2 (7.4)</td>
<td>—</td>
<td>2 (28.6)</td>
<td>—</td>
</tr>
<tr>
<td>Type II (%)</td>
<td>0</td>
<td>—</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Duration of ICU stay (days)</td>
<td>4.5 ± 6.9</td>
<td>3.45 ± 2.11</td>
<td>7.4 ± 13.3</td>
<td>0.464</td>
</tr>
<tr>
<td>Time to first Mobilization (days)</td>
<td>3.2 ± 8.0</td>
<td>1.75 ± 1.1</td>
<td>7.3 ± 15.8</td>
<td>0.978</td>
</tr>
<tr>
<td>Duration of non-ICU stay (days)</td>
<td>7.2 ± 11.3</td>
<td>6.25 ± 4.0</td>
<td>8.4 ± 10.5</td>
<td>0.850</td>
</tr>
<tr>
<td>Total duration of hospital stay (days)</td>
<td>11.3 ± 12.3</td>
<td>9.7 ± 4.6</td>
<td>15.9 ± 23.6</td>
<td>0.341</td>
</tr>
</tbody>
</table>

*P < 0.05.
Results are presented as means with standard deviations. Categorical variables are expressed as raw number, with percentage of the total in brackets.

Excluding pneumonia, which has been classified as "Infectious."
Excluding paraplegia and/or paraparesis.

Group (one secondary to intravenous contrast), with acute kidney injury in 1 endograft patient. Linear regression revealed no significant relationship between aneurysm size nor surgical duration and outcome variables. Furthermore, multivariable analysis with Cox regression revealed there was no difference in hazard of mortality for TEVAR over open repair (hazard ratio of endovascular versus open repair 1.16, 95% CI 0.67–1.82, P = 0.83). Similarly, there was no relationship between age, aneurysm size, and comorbidities on morbidity (P > 0.05). Two endovascular patients suffered paraplegia which resolved, one of whom had previous abdominal aortic aneurysm repair. There was no difference in morbidity, mortality, or other outcome variable between hybrid or debranching patients, and other endovascular patients (P > 0.05). Similarly, excluding hybrid or debranching endovascular patients from the analysis did not change outcomes when compared with open repair.

Patients over the age of 75 were almost twice as likely to have an endovascular procedure (83.3 vs. 47.4%, P = 0.045). They were also more likely to require more blood transfused (5.5 ± 9.7 vs. 1.2 ± 1.9 units, P = 0.008), have a longer ICU stay (5.5 ± 9.7 vs. 3.5 ± 2.2 days, P = 0.032), non-ICU stay (10.1 ± 6.9 vs. 6.1 ± 3.4, P = 0.003), and total hospital stay (14.1 ± 10.0 vs. 9.6 ± 4.0 days, P = 0.006).

There was a significant increase in the percentage of endovascular descending aneurysm repairs over time (R² = 0.453, β = 0.673, P = 0.03; Fig. 1), but there was no change in rates of morbidity and mortality (P > 0.05).
Table III. Baseline, perioperative, and postoperative characteristics for patients undergoing descending aneurysm repair

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>Open repair</th>
<th>Endovascular repair</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (n)</td>
<td>31</td>
<td>12</td>
<td>19</td>
<td>—</td>
</tr>
<tr>
<td>Age (years)</td>
<td>68.0 ± 15.33</td>
<td>55.9 ± 17.2</td>
<td>75.6 ± 7.2</td>
<td>&lt;0.005*</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>21 (67.7)</td>
<td>7 (58.3)</td>
<td>14 (73.7)</td>
<td>0.373</td>
</tr>
<tr>
<td>Aneurysm size (mm)</td>
<td>62.8 ± 22.2</td>
<td>66.3 ± 21.4</td>
<td>59.6 ± 23.3</td>
<td>0.461</td>
</tr>
<tr>
<td>Smoking status (%)</td>
<td>23 (74.2)</td>
<td>8 (66.7)</td>
<td>15 (79.0)</td>
<td>0.447</td>
</tr>
<tr>
<td>Ischemic heart disease (%)</td>
<td>11 (35.5)</td>
<td>3 (25.0)</td>
<td>8 (42.1)</td>
<td>0.332</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>21 (67.7)</td>
<td>7 (58.3)</td>
<td>14 (73.7)</td>
<td>0.373</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>2 (6.5)</td>
<td>0 (0)</td>
<td>2 (10.5)</td>
<td>0.245</td>
</tr>
<tr>
<td>ASA score</td>
<td>3.4 ± 0.7</td>
<td>3.8 ± 0.7</td>
<td>3.3 ± 0.7</td>
<td>0.079</td>
</tr>
<tr>
<td>Crawford classification</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 (%)</td>
<td>6 (19.4)</td>
<td>2 (16.7)</td>
<td>4 (21.1)</td>
<td>0.763</td>
</tr>
<tr>
<td>I (%)</td>
<td>21 (67.7)</td>
<td>9 (75.0)</td>
<td>12 (63.2)</td>
<td>0.492</td>
</tr>
<tr>
<td>II (%)</td>
<td>2 (6.5)</td>
<td>0 (0)</td>
<td>2 (10.5)</td>
<td>0.245</td>
</tr>
<tr>
<td>III (%)</td>
<td>2 (6.5)</td>
<td>1 (8.3)</td>
<td>1 (5.3)</td>
<td>0.735</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>311 ± 160</td>
<td>422.5 ± 161</td>
<td>242 ± 116</td>
<td>0.003*</td>
</tr>
<tr>
<td>Return to theater within 24 hr (%)</td>
<td>4 (12.9)</td>
<td>3 (25)</td>
<td>1 (5.3)</td>
<td>0.110</td>
</tr>
<tr>
<td>Reoperation (%)</td>
<td>4 (12.9)</td>
<td>2 (16.7)</td>
<td>2 (10.5)</td>
<td>0.619</td>
</tr>
<tr>
<td>In-hospital mortality (%)</td>
<td>3 (9.7)</td>
<td>1 (8.3)</td>
<td>2 (10.5)</td>
<td>0.841</td>
</tr>
<tr>
<td>Complications (total)</td>
<td>23</td>
<td>9</td>
<td>14</td>
<td>0.330</td>
</tr>
<tr>
<td>Respiratory* (%)</td>
<td>9 (29.0)</td>
<td>4 (33.3)</td>
<td>5 (26.3)</td>
<td>0.218</td>
</tr>
<tr>
<td>Renal (%)</td>
<td>3 (9.7)</td>
<td>2 (16.7)</td>
<td>1 (5.3)</td>
<td>0.296</td>
</tr>
<tr>
<td>Paraplegia/paraparesis (%)</td>
<td>2 (6.5)</td>
<td>0 (0)</td>
<td>2 (10.5)</td>
<td>0.245</td>
</tr>
<tr>
<td>Cardiac (%)</td>
<td>1 (3.2)</td>
<td>0 (0)</td>
<td>1 (5.3)</td>
<td>0.419</td>
</tr>
<tr>
<td>Infectious (%)</td>
<td>4 (12.9)</td>
<td>0 (0)</td>
<td>4 (21.1)</td>
<td>0.089</td>
</tr>
<tr>
<td>Neurologic* (%)</td>
<td>2 (6.5)</td>
<td>1 (8.3)</td>
<td>1 (5.3)</td>
<td>0.735</td>
</tr>
<tr>
<td>Vasocclusive (%)</td>
<td>0 (0.0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>—</td>
</tr>
<tr>
<td>Hemorrhagic (%)</td>
<td>2 (6.5)</td>
<td>2 (16.7)</td>
<td>0 (0)</td>
<td>0.066</td>
</tr>
<tr>
<td>Units of blood transfused</td>
<td>2.9 ± 5.5</td>
<td>3.9 ± 7.6</td>
<td>2.2 ± 3.7</td>
<td>0.704</td>
</tr>
<tr>
<td>Endoleaks</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type I (%)</td>
<td>3 (9.7)</td>
<td>—</td>
<td>3 (15.8)</td>
<td>—</td>
</tr>
<tr>
<td>Type II (%)</td>
<td>2 (6.5)</td>
<td>—</td>
<td>2 (10.5)</td>
<td>—</td>
</tr>
<tr>
<td>Type III (%)</td>
<td>1 (3.2)</td>
<td>—</td>
<td>1 (5.3)</td>
<td>—</td>
</tr>
<tr>
<td>Duration of ICU stay (days)</td>
<td>4.3 ± 6.2</td>
<td>3.9 ± 3.0</td>
<td>4.5 ± 7.6</td>
<td>0.562</td>
</tr>
<tr>
<td>Time to first Mobilization (days)</td>
<td>2.8 ± 1.9</td>
<td>3.7 ± 2.2</td>
<td>2.4 ± 1.5</td>
<td>0.100</td>
</tr>
<tr>
<td>Duration of non-ICU stay (days)</td>
<td>7.5 ± 5.4</td>
<td>8.8 ± 5.2</td>
<td>6.9 ± 5.5</td>
<td>0.177</td>
</tr>
<tr>
<td>Duration of hospital stay (days)</td>
<td>11.9 ± 7.9</td>
<td>12.7 ± 6.9</td>
<td>11.5 ± 8.6</td>
<td>0.389</td>
</tr>
</tbody>
</table>

* \(P < 0.05\).

Results are presented as means with standard deviations. Categorical variables are expressed as raw number, with percentage of the total in brackets.

*Excluding pneumonia, which has been classified as "Infectious."

*Excluding paraplegia/paraparesis.

DISCUSSION

Although the total number of TAA repairs has increased in the United States over the last 2 decades, the rate of open repair has remained constant.\(^{30}\) Endovascular repair rates now account for 31% of all repairs and are likely to continue to rise.\(^{30}\) In the present study, we found a similar trend for increasing endovascular repairs of descending aneurysms in Australia. This is likely because of the perceived high mortality rates of open repair,\(^{31}\) the increasing acceptability of endovascular approaches, and the aging population making minimally invasive techniques more attractive. Although one study demonstrated no difference,\(^{32}\) it has been suggested that descending endovascular TAA repairs are less costly in the short term (despite the considerable expense of the endograft itself\(^{25,33,34}\)). It is therefore possible that the increasing pressure to minimize health spending may be contributing to the increasing number of
endovascular repairs, although there is evidence that endografting may become more expensive in the long term, due to surgeon follow-up and computed tomography surveillance. However, new developments in endovascular technology, and potential decreases in endograft costs make TEVAR a viable option in an increasing proportion of patients. The decrease in percentage of endovascular repairs between 2004 and 2006 is likely an artefact, because of the small total number of descending TAA repairs (2 and 3 repairs in 2005 and 2006, respectively).

At the institutions examined in this study, we saw extremely low perioperative mortality rates in patients undergoing TAA repairs. Three percent of patients undergoing surgical management died during the study period, likely due to both improving technique, and careful patient selection (e.g., nonoperative patients were seen to be on average 10 years older). However, patients over the age of 75 years were noted not to have a higher mortality rate, suggesting perhaps that endovascular repairs of descending TAA may be appropriate in elderly patients, ones that may have been denied an operation previously—although it may be careful selection of patients in the present study that resulted in such outcomes. Interestingly, there was no difference in mortality rates nor complication rates between endovascular and open TAA repairs. In the current literature, data are conflicted regarding survival benefits and complication rates between open and endovascular approaches. The largest study to date from Greenberg et al. demonstrated no difference in mortality either at 1 month or 1 year, findings echoed by a Swiss study which saw no difference at 1, 12, 24, or 36 months. Similarly, a study of US Medicare data between 1998 and 2007 demonstrated that whereas in the short term there may be a borderline mortality benefit from endovascular repair (6.1 vs. 7.1%, $P = 0.07$), this is lost by 2 years. Several smaller studies concur, finding that a mild perioperative survival benefit is quickly lost, and remains absent at up to 10 years. Overall, current evidence suggests no difference in long-term mortality between endovascular and open TAA repairs.

The comparative benefits of either open or endovascular techniques in minimizing SCI also have not been seen, with only one study demonstrating a reduced risk of SCI in endovascular TAA repairs. In the present study, only two patients suffered paraplegia postoperatively, both of whom had undergone TEVAR of their descending aorta. The observed paraplegia rate of 8% post endografting is similar to the 3–7% seen in recent studies. This is interesting given that the use of spinal drains in our study institutions (at 50% and 32%) is much lower than previously observed, with up to 66% and 79% of patients undergoing prophylactic CSF drainage for open and endovascular repairs, respectively. Although a recent Cochrane analysis suggested that data are limited and need further study, the largest and most recent randomized controlled trial found CSF drainage is effective in preventing SCI.
While not demonstrated in this study, TEVAR has generally been shown to decrease the incidence of renal failure, respiratory failure, duration of ICU and hospital stays, and rates of reoperation. However, with endovascular interventions there is the added risk of endoleaks and peripheral vascular complications, with evidence for increased cost. Interestingly, patients who underwent TEVAR reported being significantly more depressed, and scored lower than a healthy cohort on subjective physical and mental domain scores, whereas the open repair group scored within the normal range. However, it must be noted that endovascular interventions are preferable in suitable patients.

The difficulty with such studies is that sicker and more elderly patients are more likely to receive endovascular TAA repair, thus skewing outcomes. In fact, the present study demonstrated that patients undergoing endovascular repair were on average 5 and 20 years older for arch and descending aneurysm repairs, respectively. However, a large meta-analysis (which included repairs of aortic trauma, dissections, ulcers, and intramural hemorrhage) by Cheng et al. and included 5,888 patients demonstrated that age did not impact outcomes when considering mortality, cerebrovascular accidents and paraplegia. Similarly, we found that although patients over the age of 75 years were more likely to undergo endovascular interventions, there was no difference in perioperative mortality, likely because of appropriate patient selection, and preoperative planning and assessment. However, these patients were more likely to return to theater within 24 hr, suffer endoleaks, have a higher transfusion requirement, and have a longer hospital and ICU stay, despite no differences in baseline comorbidities. Although patients over 75 years had larger arch aneurysms than those under 75, size of aneurysm was found not to correlate with perioperative and postoperative outcome. These findings suggest that whereas surgical repair of TAA in elderly patients is likely to carry a low burden of mortality, these patients are at increased risk of postoperative complications.

Limitations

The key limitations of this study are its retrospective nature and its small sample sizes. Sample size is notably an issue for endovascular treatment of arch and descending aneurysms, notably as ICU stay appears to be (nonsignificantly) greater for endovascular than open repairs. In addition, as the endovascular group includes patients who underwent hybrid procedures, their duration of stay and complication rate were not likely to differ from open repairs. As such, a more accurate comparison of endovascular and open repairs would contrast open and pure endovascular repairs, with no open procedures. Because of the relative rarity of thoracic aneurysms, sample sizes remain small, and studies are universally retrospective. As a result, it is difficult to make conclusive decisions regarding optimal surgical management from such studies. In fact, a 2009 Cochrane review has called for randomized controlled trials on TAA repairs to definitively address the endovascular versus open query.

Conclusions

In conclusion, surgical repair of TAA in carefully selected patients in Australia is associated with minimal mortality but considerable morbidity. Apart from a reduced surgical duration, the present study revealed no benefits of endovascular over open TAA repair, with economic factors possibly driving the increasing proportion of descending endografts seen. Overall, endovascular repair continues to perform well, especially in high-risk and elderly patients, and should be considered intervention of choice in suitable patients. Elderly patients are at increased risk of complications, but appropriate patient selection and preoperative planning make TAA repair a valid option in increasingly elderly and frail patients.

REFERENCES


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Conclusion

Thoracic and thoracoabdominal aneurysms continue to carry a significant burden of disease, and while medical management is appropriate for patients with smaller aneurysms, surgical intervention is indicated for patients with aortic diameters of greater than 5 - 5.5 centimetres. Once the mainstay of definitive treatment, open surgical management has long been associated with significant morbidity and mortality given the extent and location of the pathology. Endovascular repair is accepted as the optimal method of management for many vascular diseases, but clinical equipoise remains in thoracic and thoracoabdominal aneurysm repairs, due to a lack of evidence. It is possible that this is analogous to endovascular versus open repairs of abdominal aortic aneurysms, where the first trials (notably the landmark EVAR-1 trial\textsuperscript{50}), suggested that equipoise persisted, although subsequent studies have demonstrated that endovascular AAA repair is the gold standard, for both ruptured and intact AAAs\textsuperscript{31,51}. As such, it is possible that the relatively young technology of endovascular thoracic aneurysm repair is merely awaiting sufficient evidence before its use can be considered to be either superior or inferior to open repair.

In attempting to contribute to the current body of knowledge, this two-centre study demonstrated that although endovascular repairs markedly reduced surgical duration, no other benefits in morbidity or mortality were seen. This agrees with the current literature suggesting that while there may be a mild short-term benefit (if any), this is quickly lost. Current thinking in abdominal aortic aneurysm repairs is that open repair may be the optimal method of surgical management in young, low risk patients, given the reduced need
for re-intervention in the long term\textsuperscript{52}. Similarly, while endovascular repairs demonstrate some mild short-term benefits such as that seen in the current study, this may be offset by long-term endograft complications such as endoleaks and graft migration, and open surgery may remain the mainstay of treatment in low risk patients. In addition, with open repairs being less costly in the long term, this may be the more viable financial option. However, hybrid and debranching procedures added minimal morbidity and had no impact on mortality, suggesting these are likely to play an increasing role.

A comparatively low mortality rate was observed across all repairs, both open and endovascular, suggesting TAA repair is a relatively safe procedure despite patients being highly comorbid. This is likely due to both improvements in technique and technology, as well as careful patient selection, with conservatively-managed patients over a decade older on average. There is also likely a selection bias which cannot be understated. Planning of a thoracic aneurysm repair, whether open or endovascular, is a complex process, and patients are rarely suitable for both (due to patient comorbidity, or aneurysm morphology). As such, it is difficult to compare open and endovascular TAA repairs head-to-head, as in the clinical setting it is not simply a case of “either-or”. Given the complex nature of the pathology, it is likely that endovascular management will continue to be chosen in patients with amenable aortic anatomy, given the possible reduction in short term risk.
As has been observed in the United States, we demonstrated a trend for increasing endovascular repair of descending TAAs in Australia, although there was no change in morbidity nor mortality over the study period. Further, the rate of paraplegia post endografting was comparable to similar studies despite a low rate of cerebrospinal fluid drainage, demonstrating that the role of CSF drainage in endovascular TAA repairs remains unclear.

Elderly patients were noted to be at increased risk of complications, have a higher transfusion requirement and length of hospital stay than younger patients. However, appropriate patient selection and preoperative planning make both open and endovascular repair a valid option in increasingly elderly patients, with endovascular repair performing well in these high-risk patients.

In order to definitively establish the comparative efficacy of endovascular and open repairs of thoracic aortic aneurysms, large randomised controlled trials are needed. These should be conducted with a method similar to the landmark DREAM trial that compared endovascular and open repair of abdominal aortic aneurysms, and a similar protocol for long term follow up. However, as discussed above, the complex nature of thoracic and thoracoabdominal aneurysms make head-to-head comparisons difficult, as randomisation would have to be carefully considered given aneurysm morphologies. Further, given the relative scarcity of thoracoabdominal aneurysms, it would be difficult to generate significant numbers for such a study.
In summary, this study demonstrated low mortality in both endovascular and open thoracic aneurysm repair, but with considerable morbidity. As there was no difference seen between open and endovascular approaches, either option is suitable in appropriately selected patients. However, further studies are needed to elucidate the optimal management of thoracoabdominal aneurysms.
References


Appendix 1: Statement of Contribution by Co-Author

**Dr Raffi Qasabian:** I hereby state that I oversaw conception of the research question and design of the study, choice of journal for submission, and assisted in preparation of the manuscript for publication.

**Dr Zelda Doyle:** I hereby state that I oversaw conception of the research question and design of the study, supervised statistical analysis, and assisted in preparation of the manuscript before publication.

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Dr Raffi Qasabian

Dr Zelda Doyle
Appendix 2: Presentation to Royal Australian College of Surgeons Annual Scientific Meeting. Marina Bay Sands, Singapore. May 5-9, 2014
Vascular Surgery (cont'd)

9.30am  Use Of Cerebral Oximetry For Intraoperative Monitoring During Carotid Endarterectomy
V506  Jane Cross (Sydney)

9.40am  Carotid Stenting: A Valuable Adjunct To Vascular Surgical Practice
V507  Bernard Bourke (Geofford)

9.50am  Duplex Ultrasound In Vascular Access
John Swinnen (Sydney)

10.00am - 10.30am MORNING TEA - FRIDAY

10.30am - 12noon  PLENARY SESSION: SURGEONS OF THE 21ST CENTURY – PROFESSIONALS, TECHNICIANS OR TRADESMEN?
Level 4, Orchid 4204 - 4206/4304 - 4306
Chair: Michael Grigg (Melbourne)

10.30am  BJSS Lecture – Aspirations
Bruce Keogh (London, UK)

11.00am  ANZLS Lecture – Perspectives
John Harris (Sydney)

11.30am  Reality
Michael Grigg (Melbourne)

12noon - 12.30pm  KEYNOTE LECTURE
Level 4, Melati 4002 – 4003
Chair: Damien Holdaway (Geelong)
Carotid Trials: An Update. The Proposed ECST II Trial
Jonathan Beard (London, UK)

12.30pm - 1.30pm  LUNCH - FRIDAY

1.30pm  RESEARCH PAPERS, “QUICK SHOTS”

1:45pm  Enhancing Remote Ischemic Preconditioning For Protection In Vascular Surgery
V517  Kate Thomas (Dunedin)

1:50pm  *Is The Life Expectancy For Patients Who Are Successfully Treated For A Ruptured AAA The Same As A Matched Population Of Similar Age And Gender?
V512  Nedal Kafis (Sydney)

1:55pm  Muscle Wasting Following The Treadmill Training Of Patients With Intermittent Claudication
V513  Simon Yun (Adelaide)

2:00pm  Outcome Predictors Of Median Arcuate Ligament Syndrome
V514  Kelvin Ho (Brisbane)

2:05pm  One Year’s Experience With The Jetstream™ Pathway Device For Femoro-popliteal Disease
V515  Imran Javed (Suva, Fiji)

2:10pm  Comparison Of Peak Wall Stress In Ruptured, Symptomatic And Intact Abdominal Aortic Aneurysms
V516  Surabhi Khasa (Douglas)

2:15pm  Diagnosis, Incidence And Clinical Implications Of Myocardial Injury In Vascular Surgery
V511  Kate Thomas (Dunedin)

2:20pm  *Ten Years Of Thoracic Aneurysms In Sydney
Timothy Shiraev (Sydney)

2:25pm  *Asynchronous And Partly Anastomotic Aneurysm Development Past Open Abdominal Aortic Aneurysm Repair: Is Current Surveillance Appropriate?
V519  Kalpa Perera (Melbourne)

2:35pm  The Effect Of Anaesthesia On Upper Limb Arteriovenous Fistula Creation: Complications And Follow-Up Protocols
V520  Jason Chuen (Melbourne)
Appendix 3: Application to Cook Medical for Research Funding

**COOK FUNDING REQUEST INTAKE FORM**

Dr Timothy Shiraev, Dr Raffi Qasabian, Dr Zelda Doyle  
The University of Notre Dame, Sydney

I. General Information

Name of Requestor: School of Medicine  
Legal Name of Organization requesting product: The University of Notre Dame, Sydney  
**Address:** 160 Oxford St, Darlinghurst, NSW 2010  
Contact Person: Timothy Shiraev  
Title: Dr  
Phone Number: 0409 805 052  
**Fax:** 9357 7680  
**Email:** timothy.shiraev1@my.nd.edu.au  
**Website:** [www.nd.edu.au/sydney/schools/medicine/](http://www.nd.edu.au/sydney/schools/medicine/)

Is the organization to receive product or funds a bona fide non-profit or registered charity recognized by the applicable governmental tax authority? **Yes No**

Has the organization requested or received funds from Cook before? **Yes No Unsure**

II. Research Grant Information

A. Attachments

The following documentation MUST BE INCLUDED for the application to be considered:

- A study protocol including stated objectives, data analysis, safety, privacy, and a time line for the study  
- A detailed budget indicating how the requested funds/product will be utilized.  
- Credentials of the researcher(s).  
- W-9 Tax Form (U.S. only). N/A
B. Purpose of Request

What are the anticipated start and end dates for the research?

Data collection is to commence upon ethics approval, likely late July 2013, and be completed by late December 2013. Data analysis will begin December 2013, to be completed by January 2014. Construction of the introduction (including background and rationale) and methods section of the manuscript was commenced in February 2013, and writing of the results and discussion section will begin in January 2014, to be completed by March 2014.

How will the research benefit patients and contribute to healthcare, now or in the future?

The findings will compare the clinical outcomes of open and endovascular TAAA repairs in two large hospitals. It will be one of the largest studies of its kind to date internationally, the first multi-centre study, and the first undertaken in an Australian setting. The study will illustrate the clinical and economic feasibility of the two techniques, demonstrating the optimal method of management of TAAAs, as well as illustrating improvements in management of this condition over time, and providing direction for future service planning in Australia.

How will outcomes be measured?

International Classification of Diseases version 10 classification I71.6 (thoracoabdominal aortic aneurysm, without mention of rupture) will be used to identify patients diagnosed with thoracoabdominal aortic aneurysm (Crawford Class I-III), and inclusion and exclusion criteria similar to those used in the DREAM trial on AAAs of 2010 will be applied. Various demographic, surgical and clinical variables will be collected from patient records by research assistants who will de-identify the data before it is seen by the principal investigators. The research assistants are medical students from the University of Notre Dame, and will be paid for their time. Independent variables will include age, sex, year of intervention, Crawford class, co-morbidities, pre-operative creatinine, open or endovascular intervention, type of graft and circulatory adjuncts used, and use of cerebrospinal fluid drainage. Outcome variables will include in-hospital complications, post-operative paraplegia, in-hospital mortality, duration of surgical procedure, contrast dose, radiographic screening time, blood loss, re-operation rates, time to first mobilisation, post-operative creatinine, and duration of hospital stay. In-patient cost will be estimated using the respective costs of the open and endovascular grafts.
What deliverables and milestones will there be? How will progress be reported?

Preliminary analyses will be performed on completion of the data (December 2013), with the final results to be submitted as a manuscript (to the journal *Circulation*) in March 2014.

Does the research involve human subjects?

Yes, but not directly, as data is being collected from paper medical records, and no patients will be contacted.

Does the research involve Cook product(s)? Explain:

Yes. Cook is one of the types of endograft used in repair of thoracoabdominal aortic aneurysms in the study hospitals, and so will be one of the types of graft included in the analysis.

If known, check the relevant therapeutic or diagnostic area:

Aortic Intervention
Critical Care
Endoscopy
Interventional Radiology
Cardiac Lead Management
Surgery
Urology
Peripheral Intervention
Women's Health
C. Product and/or Funding Request

What product(s) are you requesting from Cook? (Include product name, quantity, and global product number, if known). If, at Cook’s sole discretion, an item is unavailable for donation, please list an acceptable substitute:

Nil

Amount of funding requested from Cook (please indicate type of currency):

$3,000 AUD. This includes $1,250 for each of the two students (50 hours of data collection, at $25 AUD per hour) to a total of $2,500, and $500 for the fee of retrieval of medical records from off-site storage at St George Hospital.

Total amount of funding needed to complete the project:

$3,000 AUD.

Are other commercial sponsors being secured for the event?

No

Check Information

Check made payable to: The School of Medicine. University of Notre Dame, Sydney

Mail check to:
160 Oxford St, Darlinghurst, NSW, 2010

Checks cannot be processed without receipt of a signed W-9 Tax Form (U.S. only)

Wire transfer information: N/A

Account Name: Bank Name: N/A

Account Number: Bank Location (U.S. - City/State International - City/Country) N/A

Bank Identifier Code (Swift code): Routing Number (IBAN # or ABA #): N/A
D. Verification
This request for funding was completed by the undersigned, who certifies to the accuracy of the information provided:

**Name:** Edward Waters

**Date:** 9/7/13

**Email address:** edward.waters@nd.edu.au

E. Submission
Please direct the completed form, attachments and any questions to the appropriate Cook Donation Review Team administrator.

Asia Pacific (APAC)

______________________________________________
grantsapac@cookmedical.com
Fax: +61 7 3341 3841
Phone: +61 7 3841 1188
Appendix 4: Approval Letter from Cook Medical for Research Funding

22 August
Ref: A130301R

Dr T Shiraev
University of Notre Dame
School of Medicine
160 Oxford Street
Darlinghurst NSW 2010

Dear Dr Shiraev

At the last meeting of the Cook Donation Review Team (CDRT) your application dated 9/7/13 requesting financial assistance from Cook Medical was reviewed.

Cook Medical is pleased to advise that your request has been approved. The particulars of the funding are as follows:

- Cook Medical agrees to donate funds to the value of AUD$3,000 (GST inclusive) to be used for educational purposes.
- The funding provided must only be used for the purpose as defined on your application.
- The funding is provided as a single payment.
- Any future requests for funding must be submitted through the CDRT.
- Approval of this request for funding does not guarantee future acceptance of similar requests.

So that we may make payment to the designated Education Fund at University of Notre Dame, either by cheque or eft, please forward a Tax Invoice to Cook Medical, to my attention, for the total amount of $3,000.

Please ensure that the Tax Invoice contains the following information:

- ABN
- If registered for GST please indicate the amount of GST included
- If you want Cook to electronically lodge the funds, please advise your EFT details.

Cook Medical wishes to confirm that this payment is not made in return for, or in expectation of, the purchase of our products.

Yours sincerely,

Margaret Howard
Compliance/CDRT Administrator
COOK MEDICAL

Cc
S Kennedy
Appendix 4: Additional Figure

Figure A1 – Percentage of patients undergoing endovascular arch aneurysm repair per year over the study period. $R^2 = 0.19$, $p = 0.89$