The Fate of Patients Referred to a Specialist Vascular Unit with Large Infra-renal Abdominal Aortic Aneurysms over a Two-year Period


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KEYWORDS
Abdominal aortic aneurysm; Natural history; Turndown; Risk stratification

Abstract  Introduction: The basic premise in managing patients with abdominal aortic aneurysms (AAA) must be to reduce overall mortality from the disease. Operative mortality is widely reported, but data on patients deemed unsuitable for repair are scarce. The purpose of the present study was to report the fate of patients referred with AAA, to define the proportion deemed unsuitable for surgery and to investigate the reasons for conservative treatment.

Methods: All patients who were referred to a regional vascular centre with large (>5.5 cm) infra-renal AAA between 1st January 2008 and 31st December 2009 were included. Patients were classified into two groups; those managed non-operatively, or those offered elective repair. Survival was reported by Kaplan–Meier analysis. Multivariate analysis investigated factors leading to non-operative management.

Results: 251 patients with a mean (s.d.) age of 75(8) years were assessed. Thirty-two (13%) patients were deemed unsuitable for repair, mostly because of medical co-morbidity (16/32). 219/251 (87%) patients underwent repair (25/251 (10%) open repair 194/251 (77%) EVAR) with 1/219 (0.5%) 30-day mortality. AAA repair was associated with significantly greater survival (p < 0.001, log-rank test) at 2 years. In multivariate analysis Glasgow Aneurysm Score, female gender and respiratory disease were significant predictors of the decision to treat patients conservatively (p < 0.001).

Conclusion: Most patients were suitable for surgical intervention with low perioperative mortality. Data on “turndown” rates should be routinely reported to quantify the denominator for operative success.

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Introduction

The decision to repair an abdominal aortic aneurysm (AAA) entails integration of the risk of rupture, the perioperative risk of aneurysm repair, the patient’s life expectancy and their preference regarding treatment. As the aim of AAA repair is to prolong life through the prevention of rupture, surgery should only be performed if the risk of rupture outweighs the risk of surgery, in patients whose life expectancy is long enough to result in long-term benefit.1,2 Lowering operative risk, without increasing the proportion of patients denied surgery, maximises the population benefit of elective AAA repair, and careful patient selection is therefore of paramount importance.3,4

Relatively little is known regarding the natural history of large AAA in patients deemed unsuitable for repair,5 although the EVAR-2 trial demonstrated no short-term benefit of EVAR compared to no intervention in patients unfit for open repair.6 No studies have compared the incidence of factors affecting operative risk or life expectancy between patients undergoing repair of large aneurysms (>5.5 cm) and those managed non-operatively by an institution during the same time period.

There are surprisingly few studies that report the proportion of patients with large aneurysms deemed unsuitable for surgical intervention, even though these data are required to place perioperative mortality in context when quantifying performance. The extent of selection bias affecting many reports therefore remains difficult to quantify, as outcomes for managing patients with AAA should encompass the entire cohort of patients not just those undergoing operative repair. The primary aim of this study was to define the proportion of patients with large AAA managed non-operatively in a tertiary vascular unit over a 2-year period, and to report their survival in comparison to the cohort of patients undergoing operative repair during the same period. A secondary aim of the study was to examine the incidence of factors known to affect operative risk and life expectancy and investigate their impact on the decision to manage patients non-operatively.

Methods

A retrospective review of a prospectively maintained database was undertaken of all patients assessed for repair of an infra-renal AAA between 1/1/2008 and 31/12/2009. Inclusion criteria comprised all patients with infra-renal AAA referred for elective assessment, including patients managed non-operatively. Exclusion criteria comprised patients with ruptured or urgent AAA, aortic dissection, suprarenal or thoracoabdominal aneurysms.

Patients were classified into two groups: those deemed unsuitable for repair, or those offered elective surgery (endovascular or open). In both groups, demographic and clinical data were collected concerning operative risk and co-morbidity. These data included patient demographics, co-morbidity, pre-operative investigations, maximum aneurysm diameter and pre-operative Glasgow Aneurysm Score (GAS).7 The Glasgow Aneurysm Score is a perioperative risk score for aneurysm repair which has been validated in open surgery, and this was calculated using its published definition: risk score = (age in years) + (17 for shock) + (7 for myocardial disease) + (10 for cerebrovascular disease) + (14 for renal disease). The reasons for deeming patients unsuitable for repair were classified according to medical co-morbidity, adverse aneurysm morphology or patient refusal. Co-morbidity was divided into one or more organ systems (cardiovascular, respiratory, renal and cerebrovascular).

All patients (operated and unsuitable) were medically managed with an antiplatelet agent, a statin and an anti-hypertensive agent as per Society for Vascular Surgery guidelines on AAA management.8 Perioperative mortality was defined as in-hospital death or that within 30-days of the procedure. Outcomes following EVAR were recorded as per the SVS standard reporting criteria,9 including analysis of long-term mortality from a central database.

Assessing suitability for aneurysm repair

Unit policy was to consider elective repair of all morphologically suitable aneurysms >5.5 cm in diameter, with an endovascular approach as the first line therapy. The unit participates in the UK National Abdominal Aortic Aneurysm Screening Programme (NAAASP),10 although none of the patients reported were identified from screening. Specific physiological criteria with strict cut-offs for surgery were not used to define patients’ fitness for surgery. A combination of individual patient, physiological and aneurysm morphological criteria were assessed in the round.

All patients underwent an electrocardiogram, routine phlebotomy, transthoracic echocardiography and pulmonary function tests. Where indicated, further cardiac investigations were undertaken including dobutamine stress echocardiogram, percutaneous coronary intervention or coronary artery bypass. Patients were assessed on their ability to climb two flights of stairs and 0.625 mm-cut spiral computed tomography (CT) scans were used to assess aneurysm morphology. Each case was discussed in a combined vascular multidisciplinary team meeting and was seen by a consultant vascular anaesthetist prior to operative repair. All patients underwent pre-operative optimisation of medical co-morbidity through referral to specialist physicians where necessary. Details of this practice, which has been shown to improve outcome, have been published previously.11 The final decision to undergo AAA repair was taken by a consultant vascular surgeon in consultation with the patient. Clearly, some patients deemed unsuitable for aneurysm repair at an aortic diameter of 5.5 cm, were reassessed if their aneurysm expanded, as the concept of unsuitability remained relative rather than absolute. The present study reports the result of the final decision taken for each patient.

Statistical analysis

All patients managed non-operatively were identified and the decision to advise against elective aneurysm repair at that particular aortic diameter, was the primary outcome measure. The secondary outcome measure assessed was mortality. Statistical analyses were designed to determine which factors affected the decision to advise against
Discussion

Over a two-year period in which 251 patients with infra-renal AAA were assessed, 13% were deemed unsuitable for surgery at their current aortic diameter. The most common reason for non-operative management was medical co-morbidity, followed by hostile aneurysm morphology and the patient’s own choice to refuse surgery. This result is consistent with the few modern studies of aneurysm repair that have published the proportion of patients who are refused surgery, which is reported as a wide range of 8–35% of those presenting to individual units following systematic literature review (Table 2).

Comparison of results from different centres would be greatly facilitated by the mandatory publication of turn-down rates, which may be of great importance in interpreting the outcomes of aortic surgery. Heterogeneity in turn-down rates might contribute to the difference in mortality from AAA repair seen across international data-sets; for example in figures across Europe collected for the Vascunet database.12 The present study was conducted at a tertiary centre with endovascular expertise, which constrains the applicability of these results. The wider impact of turn-down rates on outcomes may be studied in the future through collection of these data using national audit tools, such as the UK National Vascular Database13 and the UK NAAASP.10

Univariate analysis of decision to advise conservative treatment

A number of factors were identified in univariate analysis as being associated with the decision to recommend against elective aneurysm surgery. These were increasing age, female gender, lower estimated glomerular filtration rate (eGFR), chronic renal disease, low forced expiratory volume in 1 s (FEV₁), chronic respiratory disease, previous cerebrovascular disease, hypertension, smoking status, reduced left ventricular shortening fraction, ischaemic heart disease and higher Glasgow Aneurysm Score (GAS) (Table 1). There was no significant difference in the rate of diabetes or hyperlipidaemia between patients managed non-operatively and patients who underwent AAA repair.

Multivariate analysis of decision for non-operative management

Single-level multivariate logistic regression demonstrated that higher Glasgow Aneurysm Score (GAS) (OR 1.111, 95% CI 1.058–1.167, p < 0.001) chronic pulmonary disease (OR 10.892, 95% CI 3.621–32.765, p < 0.001) and female gender (OR 11.256, 95% CI 3.960–31.996, p < 0.001) were significant predictors of the decision to advise against elective surgery in multivariate analysis.

Survival analysis in operated patients and patients deemed unsuitable for surgery

In patients managed non-operatively, survival at 1 month, 6 months, 1 year, 18 months and 2 years respectively was 94%, 91%, 52%, 40% and 35% respectively. In patients undergoing AAA repair, survival at these timepoints was 99%, 92%, 90%, 85%, and 85% respectively (Fig. 2). There was a significant survival advantage in the group who underwent AAA repair (p < 0.001, log-rank test).
The present study identified a significantly lower survival in patients deemed unsuitable for surgery, compared to those who underwent operative repair. This finding highlights the high mortality associated with appropriately selected patients with AAA who did not undergo surgery. A limitation of this retrospective observational study was the lack of information regarding cause of death, as few patients underwent autopsy. This limits discussion of whether an appropriate selection of cases was chosen for operative management in local practice, as aneurysm-related mortality in the non-operatively managed cohort remained unquantified.

Operated patients had fewer significant co-morbidities, and numerous factors were significantly associated with non-operative management using univariate analysis. In multivariate analysis, only GAS, female gender and respiratory disease appeared significant. In the present study the most common co-morbidity underlying conservative management was severe chronic obstructive pulmonary disease (COPD), with nine patients being managed conservatively because of end-stage COPD.

Risk scores such as the Glasgow Aneurysm Score (GAS) have proved important in stratifying operative risk and have been validated for the prediction of mortality after open repair. Although a consideration of GAS reflects the greater co-morbidity seen in patients who underwent conservative management, its greater utility in predicting the outcome of aneurysm repair in the endovascular era remains unclear.

**Figure 1**  A flow-chart to illustrate the fate of 251 patients with infra-renal AAA referred to the tertiary vascular unit over a 2-year period. Abbreviations, CVS: Cardiovascular System; RS: Respiratory System; AAA: Abdominal Aortic Aneurysm; EVAR: Endovascular Aneurysm Repair.

<table>
<thead>
<tr>
<th>Table 1 Univariate analysis of factors leading to non-operative management.</th>
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<tbody>
<tr>
<td><strong>Factor</strong></td>
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<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Male gender</td>
</tr>
<tr>
<td>GAS</td>
</tr>
<tr>
<td>eGFR (ml/min)</td>
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<tr>
<td>Renal Disease</td>
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<tr>
<td>Lung Disease</td>
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<td>FEV1 (L)</td>
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<tr>
<td>Cerebrovascular Disease</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Smoking</td>
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<tr>
<td>LV Shortening</td>
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<tr>
<td>Ischaemic Heart Disease</td>
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<tr>
<td>Diabetes</td>
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<td>Hyperlipidaemia</td>
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Abbreviations: GAS, Glasgow Aneurysm Score; eGFR, estimated glomerular filtration rate; FEV1, Forced expiratory volume in 1 s; LV Shortening, Left Ventricular Shortening.
undetermined. A recent study of several risk scores validated for open repair has suggested that none of the available scores predict the outcome of EVAR accurately enough to be recommended for clinical use in individual patients.\textsuperscript{14} Therefore, the prospective role of such scoring systems should remain limited within the complex consideration of whether to offer patients surgery for AAA until risk scores can be validated for EVAR.

The role of female gender was in the decision to offer surgery for AAA was significant in multivariate analysis. This is consistent with the literature concerning gender and operative risk, as several studies have demonstrated poorer

Table 2  Reported turndown rates; studies which state the proportion of all patients referred with abdominal aortic aneurysm but treated non-operatively.

<table>
<thead>
<tr>
<th>Author</th>
<th>Study Period</th>
<th>Turndown Rate</th>
<th>Operative Techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Szilagyi 1966\textsuperscript{34}</td>
<td>1944–1965</td>
<td>32% (223/703)</td>
<td>Open</td>
</tr>
<tr>
<td>Bardram 1980\textsuperscript{35}</td>
<td>1970–1979</td>
<td>22% (43/197)</td>
<td>Open</td>
</tr>
<tr>
<td>Perko 1993\textsuperscript{36}</td>
<td>1979–1988</td>
<td>11% (79/735)</td>
<td>Open</td>
</tr>
<tr>
<td>Ruberti 1985\textsuperscript{37}</td>
<td>1965–1983</td>
<td>9% (53/594)</td>
<td>Open</td>
</tr>
<tr>
<td>Campbell 1986\textsuperscript{38}</td>
<td>1979–1984</td>
<td>12% (18/153)</td>
<td>Open</td>
</tr>
<tr>
<td>Woodburn 2001\textsuperscript{39}</td>
<td>1998–1999</td>
<td>35% (35/115)</td>
<td>Open and EVAR</td>
</tr>
<tr>
<td>Heikennen 2002\textsuperscript{40}</td>
<td>1990–1998</td>
<td>18% (35/194)</td>
<td>Open and EVAR</td>
</tr>
<tr>
<td>Tamburaja 2003\textsuperscript{41}</td>
<td>1995–1999</td>
<td>28% (128/457)</td>
<td>Open</td>
</tr>
<tr>
<td>Tanquilut 2002\textsuperscript{42}</td>
<td>1994–2000</td>
<td>8% (19/226)</td>
<td>Open and EVAR</td>
</tr>
</tbody>
</table>
outcomes from both open and endovascular aneurysm repair in female patients. The increased operative risk associated with AAA in female patients should be incorporated into the complex consideration of the decision to operate.15–19

As the goal of elective AAA repair is to prolong life in a population of patients by preventing rupture, the decision to refuse surgery requires a balance of the risk of rupture without operative repair, the risk of death unrelated to rupture, the patient-specific risk of post-operative mortality and their preference.8 The risk of rupture without surgery is dependent on the natural history of aneurysmal disease. There is a consensus that aneurysms larger than 5.5 cm mandate repair in fit candidates,20 so attempts to quantify the probability of rupture of untreated large aneurysms rely on a highly selected group of patients unfit for surgery or refusing surgery, and have produced heterogeneous data.21

In previous studies the majority of patients unfit for surgery died from causes other than rupture, namely cardiorespiratory disease, and few would have benefited from AAA repair.22 Conversely, others have found that AAA rupture was the predominant cause of death in patients with an untreated AAA >5.5 cm, with a median time to rupture of just 9 months in patients with AAA >7 cm.16 The Veterans Affairs Study demonstrated a 9.4% 1-year risk of rupture in unoperated AAA of 5.5–5.9 cm, rising to 32.5% in AAA greater than 7 cm.

Data from the EVAR-2 trial suggested no survival advantage was delivered by EVAR in poor surgical candidates.6 Prospective and randomised natural history studies may underestimate rupture risk as the indication for surgery changes in relation to aneurysm growth. Clearly, many factors other than aneurysm size may contribute to rupture risk, including peak wall stress23 or the high level of optimal medical therapy delivered to conservatively managed patients.6 A recent meta-analysis suggested a rupture rate of 27 per 100 patient years for aneurysms >6 cm diameter, and a randomised trial of surveillance versus intervention remains unlikely for large aneurysms.21

Important limitations of the present descriptive study include the greater prevalence of co-morbidity in patients not offered AAA repair, the lack of information regarding cause of death in those managed conservatively, and the applicability of these results outside tertiary centres. Furthermore, the group of patients managed non-operatively in the present report were heterogeneous; with underlying reasons including medical co-morbidity (without strict cut-off criteria), adverse aneurysm morphology, patient refusal and advanced age relative to the group of patients undergoing AAA repair. This limited comparative analysis with patients offered repair. Greater knowledge of patient preference,24–28 the refinement of physiological scoring systems to predict outcome after open AAA repair29,30 and morphological scoring systems for outcome after EVAR31,32 will add to the data available to surgeons evaluating the decision to treat AAA. With the development of more accurate risk stratification, computer-aided decision modelling may represent a useful adjunct to clinical judgement in high-risk and complex cases.33

Conclusion

In conclusion, few studies have published the rate at which patients have been turned down for AAA repair, yet these data are important in defining institutional performance. Without the publication of turndown rates and the widespread use of a more robust risk scoring system for peri-operative mortality, it is difficult to comprehensively compare outcomes between centres. Future studies of AAA repair should routinely report the proportion of patients turned down for surgery.

Conflict of Interest/Funding

None.

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