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Pre-morbid function, co-morbidity and frailty predicts outcomes following ruptured abdominal aortic aneurysm (rAAA) repair

Authors: Srinivasan A, Ambler GK, Hayes PD, Chowdhury M, Ashcroft S, Boyle JR, Coughlin PA.

Cambridge Vascular Unit, Cambridge University Hospitals NHS Foundation trust

Correspondence:

Mr. Patrick Coughlin

Cambridge Vascular Unit

Cambridge University Hospitals NHS Foundation Trust

Hills Road

Cambridge

CB2 0QQ

Fax: 01223 216015

Telephone: 01223 245151

Email: patrick.coughlin@addenbrookes.nhs.uk

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Abstract

Objective: Strategies for improving outcomes for patients with rAAA are becoming more evident. The aging population, however, continues to make the decision to intervene often difficult, especially given that traditional risk models do not reflect issues of aging / frailty. This study aimed to integrate measures of function alongside co-morbidity and frailty specific factors to determine outcome.

Methods: Patients treated for a rAAA between January 2006 and April 2014 were assessed. Demographics, mortality and requirement for care following discharge were recorded, as well as a variety of measures of function (physical, social and psychological) and comorbidity. The primary outcome was one-year mortality. Outcome models were generated using multivariate logistic regression and were compared to models of vascular frailty and AAA related outcome.

Results: 184 patients were treated, 108 (59%) underwent an open surgical repair. The overall 30-day and one-year mortality was 21.5% and 31.4% respectively with an overall median hospital LOS of 13 days (IQR 6-27 days). An optimal logistic regression model for 12 month mortality used Katz score, Charlson score, number of admission medicines, visual impairment, hearing impairment, haemoglobin level and statin use as predictors, achieving an area under the ROC curve (AUC) of 0.84.

Conclusions: This novel rAAA model incorporating function and comorbidity offers good predictive power for mortality. It is quick to calculate and may ultimately become helpful for both, patient counselling/selection and comparative audit at a time when outcome in patients with rAAA increasingly come under the spotlight.

Introduction

Although rates of ruptured abdominal aortic aneurysm (rAAA) are felt to be decreasing it still remains a common vascular surgery emergency with an incidence of approximately 13.5 per 100,000 population[1]. Associated short-term mortality rates still remain high with rAAA accounting for around 6000 deaths in the UK per year.[2-3] Survivors often require long hospital stays and such post-operative care is resource intensive.[4-5]

Outcomes following rAAA are increasingly being scrutinised and there is some evidence to suggest that the United Kingdom has a significantly higher in hospital mortality rate following rAAA when compared to the USA. This is in part due to a lower proportion of patients offered intervention in the UK allied to a lower use of endovascular repair.[6]

Patients with a rAAA are often elderly, with significant concomitant co-morbidity and the acuity of the clinical situation means that life-defining decisions need to be made in an extremely short period of time. Although AAA screening is now being rolled out in the UK, it will be a generation until the effects of such an intervention will be seen with regard to a reduction in rAAA rates. As such, the increasing age of the population as a whole means that such clinical decision making with regard to rAAA will continue to tax the vascular surgeon.

There are a number of scoring tools available that have been shown to predict postoperative mortality with variable rates of accuracy.[7-8] The majority of such tools focus predominantly upon a combination of markers of haemodynamic stability alongside factors that reflect poor cardiorespiratory reserve. The only real factor that reflects the concept of pre-morbid physical function is age, which does not accurately reflect patient frailty [9]. As such, given the increasing age of the population that we serve, there is a need to identify age / frailty related factors that may identify patients that have a poor outcome following surgery for a rAAA.

The aims of this study were to identify frailty characteristics in a cohort of patients undergoing repair of a rAAA, and determine which of these characteristics were predictors of adverse short and mid-term outcomes. Such predictors were then compared with previously validated scoring tools that were both AAA and frailty specific[10,11].

Methods

Patients

Consecutive patients undergoing intervention for a rAAA admitted to a large UK tertiary referral vascular surgical centre during the period 1st January 2006 to 30th April 2014 were screened for inclusion in the study. Data was collated from both hospital electronic and paper medical records. As in previous work patients aged less than 65 years were excluded from the analysis [10]. This age was chosen pragmatically in order to focus attention on a subset of patients who were more likely to suffer a degree of frailty. Data was collected on patient demographics, surgical method (EVAR or open repair), in-hospital complications, length of stay (LOS), short and mid term mortality rates, discharge location, care requirement at discharge and frailty specific characteristics as used in previous studies (Table I)[9]. The hospital electronic records system is linked to the United Kingdom Office for National Statistics for collection of mortality data.

The Addenbrookes Vascular Frailty Score [10]

The AVFS is a scoring tool composed of 6 easily measured factors that have been shown to predict mortality at 12 months in an unselected cohort of patients with vascular disease, as well as care requirement at discharge and length of hospital stay. A modified AVFS was used in this study substituting Waterlow score with a surrogate nutrition score (supplementary table 1).

The AAA Score[11]

Frailty based models were compared against the published AAA SCORE model, which was developed from data from the United Kingdom National Vascular Database and used multiple imputation methodology together with stepwise model selection to generate preoperative and perioperative models of in-hospital mortality after AAA repair. The database used to develop and test the score comprised of roughly 2/3 elective and 1/3 emergency patients undergoing AAA repair (supplementary table 2).

The primary outcome measure was one-year mortality. Secondary outcomes included requirement for care following discharge and length of hospital stay during the index admission. Data were collected as part of routine service evaluation and no patient identifiable data are presented, so it was not deemed necessary to seek ethical approval or retrospective consent for the study.

Statistical analysis

The effect of frailty characteristics on mortality, requirement for care following discharge (defined as receiving care visits but remaining able to live in their own home or transfer to a local hospital for further rehabilitation / discharge to a care facility) and prolonged length of stay (defined as length of stay greater than the median value) were assessed using both univariate and multivariate regression analyses. Univariate testing for mortality used the log-rank test, while associations with requirement for care following discharge and prolonged length of stay were tested using Fisher's exact test for binary predictors and the Mann-Whitney U-test for integer or continuous predictors. P-values were corrected for multiple testing using the Bonferroni-Holm method[12]. Logistic regression modelling with stepwise variable selection using Akaike's information criterion[13] was used to develop optimal models for 12-month mortality, requirement for care following discharge and prolonged length of stay. The models were then fine-tuned by removing parameters with Wald P-value > .1. Performance of these models was then compared to the AVFS and the AAA SCORE using DeLong's method for comparison of receiver operating characteristic (ROC) curves[14]. Values were considered significant if $P < .05$. As the data set was relatively modest, missing data was handled using the complete case analysis approach during model generation, as it was felt that model based approaches would add little. All cases where it was possible to calculate a score or model were used for ROC curve analysis.

Analysis was performed using the R statistical software version 3.1.1 (The R Foundation for Statistical Computing, http://www.r-project.org/foundation)[15] together with the ‘survival’[16] and ‘pROC’[17] packages.

Results

A total of 205 patients were treated for rAAA during the study period, of whom 21 were aged under 65 at time of presentation, leaving 184 patients to be included in the analysis (median age 77 yrs; 85% male – Figure 1). During the same period 50 patients were turned down for treatment of their rAAA. The overall median age of this cohort was 85 years and 35 were men. Due to the palliated nature of such patients a lot of the required data for the study was not available to allow for further comparisons of patient groups. Out of the 184 treated patients, 108 (59%) underwent an open surgical repair. The overall 30-day and one-year mortality was 21.5% and 31.4% respectively with an overall median hospital LOS of 13 days (IQR 6-27 days). Forty-six patients (25%) died during the index admission. Of the remaining 138, ninety were discharged home with no additional social care package, 27 required care visits but remained able to live in their own home, and 21 were either transferred to a local hospital for further rehabilitation or were discharged to a care facility. Data was missing for some of the key frailty characteristics for 22 patients (16 of whom survived to discharge), so these patients were excluded from the model generation phase of the multivariate analysis. All patients with data available for individual variables were used in the univariate analysis and for ROC curve analysis.

Mortality

Univariate analysis revealed that after correction for multiple testing, overall mortality was significantly higher ($P<.05$) in patients with a Charlson score greater than 1, in patients who were relatively anaemic on admission (haemoglobin less than 102 g/L), and in those patients who were taking more than five medications on admission. An optimal logistic regression model for 12 month mortality used Katz score, Charlson score, number of admission medicines, visual impairment, hearing impairment, haemoglobin level and statin use as predictors, achieving an area under the ROC curve (AUC) of 0.84. A simplified score, which we refer to henceforth as the Ruptured Aneurysm Frailty Score (RAFS – Table 2) using 2 points each for functional independence (Katz score=6) or anaemia (haemoglobin less than 102 g/L) and 1 point each for Charlson score greater than 1, polypharmacy (greater than 5 medications on admissions), visual impairment, absence of hearing impairment, and not being on a statin preoperatively achieved an AUC of 0.81 (Figure 2). Both of these performed better than either the published AAA SCORE model (AUC=0.65) or the generic Addenbrookes Vascular Frailty Score (AUC=0.66); P<.01 for all comparisons. Furthermore, increasing RAFS score equated to increased mortality (Figure 3).

Length of stay

Univariate analysis revealed that after correction for multiple testing, there were no significant predictors of prolonged length of stay (defined as length of stay longer than the median value). An optimal logistic regression model for prolonged length of stay used living alone, memory problems, open surgical repair, evidence of malnutrition, haemoglobin level and serum albumin on admission as predictors, achieving an AUC of 0.70. None of the risk scores developed for prediction of mortality (the AAA SCORE, AVFS, or the RAFS presented above) were good predictors of prolonged length of stay (AUC 0.55, 0.51 and 0.54 respectively).

Requirement for care following discharge

Univariate analysis revealed that after correction for multiple testing, care was required following discharge significantly more frequently (P<.05) in patients who were older and in those patients who were taking more medications on admission. An optimal logistic regression model for requirement for care following discharge used living alone, number of admission medicines, haemoglobin level and serum albumin on admission as predictors, achieving an area under the ROC curve (AUC) of 0.74. The AVFS performed similarly (AUC=0.70), but neither the AAA SCORE, nor the RAFS presented above were good predictors of requirement for care following discharge (AUC=0.60 for both scores, $P<.05$ showing significant inferiority of these to both the full model and the AVFS).

Discussion

This study is the first study to specifically examine the effect of frailty specific factors on outcome in patients undergoing an intervention for a ruptured abdominal aortic aneurysm. We have identified a number of factors that combined are able to accurately predict one year mortality and as such have developed the Ruptured Aneurysm Frailty Score (RAFS). This score outperforms other frailty and AAA specific scoring systems. Frailty is an increasingly relevant concept in surgery as a whole and specifically in vascular surgery due to the patient demographics, and our previous study identified frailty specific factors that predicted poor outcome across a group of patients with a range of vascular conditions[10]. What we were not able to determine from that study was the effect of frailty specific factors in specific higher risk vascular interventions of which treatment for a rAAA is perhaps the most relevant.

The RAFS incorporates a number of frailty specific characteristics, co-morbidity (Charlson score, polypharmacy, anaemia), physical function (Katz score) and geriatric syndrome (hearing and visual impairment) and as such reflects the multifaceted nature of frailty. Although we have not determined the time taken to measure the RAFS we feel that this is an easily collated score especially given the increasing use of computerised medical records allied to the fact that there is usually a family member with the patient at the time of presentation.

The relevance of statin prescription to the score may reflect those patients with a prior diagnosis of atherosclerotic disease (coronary, cerebral or peripheral). Anaemia in itself is a recognised factor for poor long-term prognosis in vascular surgery patients but in this study may also reflect the size of the rupture and potentially reflect the degree of haemodynamic instability[18-19]. The Hardman score (1 point for either age >76 years, loss of consciousness after presentation, hemoglobin <90 g/L, serum creatinine >190 μ mol/L or electrocardiographic (ECG) signs of ischemia) is a well-validated scoring tool to determine outcome in patients with a ruptured AAA [20-21]. One variable in the Hardman index is a haemoglobin level < 90 g/L which has been shown in a previous meta-analysis to be an independent predictor for outcome [22].

The fact that the introduction of AAA screening programmes will take some time to yield true benefit allied to the increasing age of the population means that the assessment and prediction of mortality of the older patient with a rAAA has current relevance. Frailty, defined by some as a multi-dimensional vulnerability due to age-associated decline in physiological reserve, is a recognised cause of poor outcomes in both elective and emergent surgery and is recognised to be a significant issue in vascular surgery[23-26].

Outcomes in patients undergoing repair of an AAA have significantly driven changes in the delivery of vascular surgical care, with specific volume outcome relationships being central to such changes [27-8]. More recently, attention has focused upon outcomes in patients presenting with a rAAA. The IMPROVE study showed no difference in 30 day mortality rate with a strategy of endovascular repair versus open repair for patients with suspected ruptured abdominal aortic aneurysm which has been further confirmed by a more recent individual patient meta-analysis combining data reporting 90 day mortality not only from the IMPROVE study but also from similar studies from Holland and France [29-30]. During the study period over 1200 patients were admitted to the 30 clinical recruiting sites with a diagnosis of a rAAA with half of these patients recruited into the study. A major reason for the lack of inclusion of all patients within the study was a lack of 24/7 emergency EVAR service but also may in part reflect issues with associated co-morbidity. Furthermore, such findings may also be related to "turn down rate", which in a seminal paper by Karthikesalingam *et al.* was found to be in excess of 40% within the

UK[6]. This paper assessed a cohort of nearly 35000 patients with a rAAA in England and the USA, finding that the USA had superior results when determining in-hospital mortality, palliation rates, and rEVAR. Reduced mortality was associated with increased use of endovascular repair, increased hospital caseload (volume) for rAAA, high hospital bed capacity, hospitals with teaching status, and admission on a weekday. Centralisation of vascular surgery services in the UK to larger centres may reduce the turn down rate of patients with rAAA, but use of the RAFS may help guide surgeons to identify patients who may benefit from repair but more importantly allow for comparative audit. While we recognise that there may be factors with regard to this study that are specific to the UK healthcare system specifically with regard to the healthcare systems in place it is expected that patient specific factors are likely to be the same when compared to the US population.

Numerous risk prediction tools have been developed for both the assessment of frailty and outcome after intervention for a rAAA. We have used well-validated and statistically robust scores to determine AAA and frailty specific predictors and the fact that the RAFS is superior highlights the unique factors and challenges associated with the presentation of patients with a rAAA.

The study is open to bias by the nature of its design, specifically with regard to the management of patients with a rAAA. The 50 patients who were palliated during the study period were not included in the overall analysis. This is in part related to the primary outcome measures that we have used (mid term mortality) as well as the retrospective analysis we have performed with a lack of required data available within this cohort of patients. On the whole, the only core reasons for palliation within our unit would be the diagnosis of moderate / severe dementia, metastatic malifnancy and home oxygen. Indeed, we provide a 24/7-endovascular service for patients with a rAAA but type of surgery was not a predictor of mortality within our analysis. Furthermore, we were also a major enrolling centre for the UK IMPROVE study[3], which limits the bias towards an EVAR first approach. Finally, our low turn down rate lends weight to the validity of the results although it is likely that those patients who were turned down were the sickest and the frailest as judged clinically and by the "end of the bed test" although a formal "end of the bed test" assessment was not able to be determined due to the retrospective nature of the study. This study does however involve a relatively large cohort, considered both open and endovascular repair, includes patients from a wide geographical area with varied socio-economic status and takes into account the most recent improvements in peri- and post-operative care associated with a large university hospital. However, this dataset needs further validation in multicentre prospective studies.

A further limitation is the presence of a limited amount of missing data, effecting 22 (11.8%) of the cohort, and limiting the multivariate analysis. While this limited the number of patients available during the model generation phase of the analysis, very few data points were missing for any one variable and very few cases (patients) had multiple missing values (19 patients had one missing item, one had 2 and two had 3 missing items). As a result, each of the models and scores shown in the ROC curve analysis used data from the vast majority of patients – for example it was possible to calculate the RAFS for all but 6 of the 184 patients. Therefore we feel that it is unlikely that this small amount of missing data introduced significant bias.

Determining operative risk in patients undergoing emergency aortic surgery is a difficult process, as multiple variables converge to affect overall mortality and outcom[30]. Patient frailty is almost certainly a contributing factor [31].

In conclusion, our study indicates that there are frailty specific factors that predict poorer outcome in patients presenting with a RAAA and as such is further objective evidence on which vascular surgeons are able to base their clinical decisions when assessing patients with a rAAA. It is also likely to aid in comparative audit at a time when surgeon specific outcomes are becoming increasingly relevant.

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