Calculating when elective abdominal aortic aneurysm repair improves survival for individual patients: development of the Aneurysm Repair Decision Aid and economic evaluation

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Scientific summary

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Background

Abdominal aortic aneurysm (AAA) is found in 5–8% of men > 65 years. Rupture is responsible for around 7000 deaths per year in the UK. Each year approximately 4000 patients undergo AAA repair in the UK with the aim of preventing premature death due to AAA rupture. Most patients undergoing elective AAA repair are asymptomatic and, as a consequence of the recently implemented NHS AAA Screening Programme, an increasing number are likely to be detected.

The current indication for elective repair is when the aneurysm reaches 5.5 cm in men and 5.0 cm in women. This indication is based on data from randomised controlled trials demonstrating that AAA surveillance is a safe alternative to early repair in patients with AAA in the size range 4.0–5.4 cm. These conclusions were drawn from a population of all patients aged 60–76 years with AAAs over a wide size range, but they do not necessarily apply to individual patients. For example, the indication for elective AAA repair is unlikely to be the same for a fit and healthy patient aged 65 years and an unfit and immobile patient with comorbidities aged 80 years.

Objective

The objective was to develop an Aneurysm Repair Decision Aid (ARDA) to synthesise and simulate several complex processes and decisions in the management of AAA. This is the first stage in demonstrating that it is feasible to construct and run such a complex model to support surgeon and patient decision-making. The aim of the ARDA is to identify the optimal timing of surgery for each individual patient, to maximise survival and facilitate cost-effective use of resources and optimal clinical care.

Methods

This study combines evidence synthesis with original research. A number of separate algorithms were developed to calculate aneurysm growth rate and risk of rupture, risk of perioperative mortality, and life expectancy and survival. These separate algorithms were then combined into the overall ARDA algorithm to provide patients and surgeons with information that may be helpful in making a decision on the optimal time for AAA repair.

Information on risk factors that influence AAA growth and risk of rupture was developed within the National Institute for Health Research Health Technology Assessment-funded RESCAN project. The RESCAN team obtained individual patient data on 15,475 patients under surveillance for AAAs < 5.5 cm in 18 published studies. Although the number of patients with AAAs that rupture in this size range is small, RESCAN is also the best source of information on which to estimate risk of rupture. A random-effects model was used to assess between-patient variability in AAA size and growth rate. Rupture rates were analysed using joint proportional hazards regression to incorporate predicted AAA diameter as a covariate that changed with time. Predictions for AAAs with diameter > 5.5 cm were extrapolated from pooled data across all studies using random-effects meta-analysis. Rupture risk was calculated by Cox proportional hazards regression adjusted for AAA diameter. For AAA diameters outside the range included in the RESCAN project, information on AAA growth and risk of rupture was taken from previously published studies.

Risk of perioperative mortality

Vascular Governance North West (VGNW) data were used to calculate, for each individual patient, the risk of 30-day mortality following endovascular aneurysm repair (EVAR) and elective open surgical repair using a multiple logistic regression model, incorporating patient-specific risk factors. To assess the performance of this model it was validated along with a number of other published models for perioperative mortality (the Glasgow Aneurysm Score, the Vascular Biochemical and Haematological Outcome Model, the Vascular Physiological and Operative Severity Score for enUmeration of Mortality and the Medicare model) in the National Vascular Database (NVD). Subsequently, the NVD was used to develop the British Aneurysm Repair (BAR) score to predict in-hospital mortality following elective AAA repair. Prospectively collected data on all elective AAA repairs were extracted for analysis and a multiple regression model was fitted using the backwards elimination Akaike information criterion. The performance of the BAR score in separate EVAR and open AAA repair subgroups was assessed and both models were validated using contemporary VGNW data. The area under the receiver operating characteristic curve and various measures of calibration were used to assess model performance.

Life expectancy and survival

Prospectively collected data on 4070 elective AAA repairs from VGNW were used to analyse risk factors for long-term survival. Survival data were analysed using the Kaplan–Meier method and differences in survival were compared using the log-rank test. Multivariate Cox proportional hazards models were used to identify significant preoperative prognostic indicators of long-term survival. Although our VGNW data were derived entirely from patients surviving AAA repair, the same model was used to calculate underlying survival in patients who had not yet undergone repair; this survival was subsequently influenced by risk of rupture and perioperative mortality due to elective or emergency repair as appropriate.

Developing the Aneurysm Repair Decision Aid

A discrete event simulation (DES) model was developed to simulate the subsequent life events for each individual patient, starting from age and AAA diameter at initial diagnosis. This approach was selected because it allows the incorporation of all of the above algorithms predicting different aspects of the AAA pathway while also displaying the confidence with which the patient and clinician can interpret any output. The expected growth rate, risk of rupture, risk of dying from other causes, expected time to repair at any given AAA diameter and risk of perioperative mortality and subsequent survival are then simulated 100,000 times for each patient and the median survival and mean costs and quality-adjusted life-years (QALYs) an individual patient could expect are estimated.

Economic evaluation

Use was made of the ARDA to simulate the likely costs, QALYs and cost-effectiveness of the decision to repair and to explore the underlying uncertainty associated with the economic data. The comparator was the current guideline to repair when the aneurysm reaches 5.0 cm (women) or 5.5 cm (men) in diameter. The perspective taken was that of the NHS, social care providers and patients. This viewpoint comprises the key components of a societal perspective. The measure of health benefit for the primary analysis was the QALY. The time horizon for the model is lifetime from identification of the AAA to death from any cause. The lifetime impact was discounted at 3.5%.

The population for the model is people with a confirmed AAA smaller than current thresholds for surgery or people who present with an AAA at or above the current thresholds for surgery. As with the clinical effectiveness analysis, this population is characterised by eight vignettes that describe patients eligible for elective surgical repair.

The DES model developed for the clinical effectiveness analysis was used as the basis for the analysis of the relative cost-effectiveness of the new algorithm. The overall model structure and processes were not changed. The cost and utility values associated with events in the model were added to estimate net costs and QALYs for each of the eight patient vignettes.

Cost and utility data for the economic model were identified from a focused systematic review, review of the NHS reference costs data set and a prospective study of patient records held in the VGNW programme. A focused electronic search was conducted in October 2012 (updated April 2014) to identify studies published between January 2004 and April 2014. This was supplemented by a search of published UK data sets and National Institute for Health and Care Excellence technology appraisals. Titles and abstracts were reviewed by two researchers using predefined inclusion and exclusion criteria and data extraction forms. Descriptive statistics were used to summarise the data to populate the model.

Clinical and service use data for a sample of patients ($n = 118$) included in the VGNW database were reviewed between January 2009 and April 2012 to gather and cost service use information about preoperative, perioperative, and postoperative appointments, scans, and procedures clinically associated with the AAA repair. Descriptive statistics summarised cost data to supplement the systematic review.

For the primary analysis, the model estimated the incremental cost-effectiveness ratio associated with intervening at the aneurysm size identified by the ARDA as maximising QALYs gained. Sensitivity analyses explored data uncertainty and the impact of key assumptions and design choices. A probabilistic sensitivity analysis was conducted for the primary analysis and each of the sensitivity analyses. A cost-effectiveness acceptability analysis estimated the probability that an algorithm to maximise QALYs gained was cost-effective compared with the current guidelines.

Results

Predicting perioperative mortality

The VGNW model included the following risk factors: age, female sex, diabetes, raised serum creatinine level, respiratory disease, antiplatelet medication and open surgery. The area under the curve (AUC) was 0.70 on validation with acceptable calibration. On external validation using the NVD, the VGNW model demonstrated good discrimination with an AUC of 0.71 and acceptable calibration. The BAR model developed on the NVD included the following risk factors: open repair, age, female sex, serum creatinine over 120 µmol/l, cardiac disease, abnormal electrocardiogram (ECG), previous aortic surgery or stent, abnormal white cell count, abnormal serum sodium, AAA diameter and American Society of Anesthesiologists grade. The AUC (bias-corrected) was 0.77 with good calibration. On external validation using VGNW data, the BAR score demonstrated overall excellent discrimination (AUC 0.83) with retained discriminatory ability in procedural subgroups and good calibration.

Survival following abdominal aortic aneurysm repair

Median survival was 8.1 years, with 5- and 10-year survival rates of 70.2% and 41% respectively. The model developed for survival following elective AAA repair using VGNW data included the following risk factors for reduced survival: age, female sex, ischaemic heart disease, abnormal serum sodium, serum creatinine > 120 µmol/l, anaemia and abnormal ECG. Statin and platelet-inhibitory therapy were associated with improved survival.

The Aneurysm Repair Decision Aid

Discrete event simulation achieved reproducible and reliable data that included the following summary information that would be useful to patients and vascular surgeons making a decision on whether or not to repair an asymptomatic AAA of any given size: life expectancy; 1-, 5- and 10-year survival; the risk of dying of rupture; perioperative mortality in the event of EVAR or open surgical repair; the probability that a repair would be undertaken in the patient's lifetime; using current indications (AAA 5.0 cm in women and 5.5 cm in men).

In addition, the ARDA produces the following information based on risks associated with repair at some future date: the risk of dying from other causes; the chances of surviving rupture; predicted AAA growth rate at the relevant size; risk of rupture over the next 1 year; 1-, 5- and 10-year postoperative survivals; median age for the AAA to reach any given threshold; time to reach any given threshold.

Overall, the economic model indicates high uncertainty in the mean expected costs or QALYs between the new clinical algorithm and current thresholds for surgery. The net costs of the algorithm ranged between a saving of £405 [95% confidence interval (CI) –£17,655 to £13,576] and a net cost of £2716 (95% CI –£13,650 to £22,552). All the vignettes and aneurysm sizes were associated with a net QALY gain, which ranged between 0.006 (95% CI –7.516 to 7.510) and 0.047 (95% CI –8.962 to 9.055). The net costs and QALYs were characterised by wide 95% CIs, which crossed zero. The probability that the new algorithm was cost-effective was around 50% for all of the primary analyses, with a net benefit that ranged between –£1831 (95% CI –£150,921 to £144,164) and £2338 (95% CI –£5110 to £12,425) for vignettes. Again the 95% CIs are wide and cross zero. The sensitivity analysis to explore the impact of using life-years gained, alternative cost and utility estimates did not change this result. Overall, uncertainty in the data inputs indicate that further work is needed to assess whether or not decisions based on the ARDA are likely to be cost-effective.

Conclusion

The ARDA produces detailed information that may be useful to individual patients and their surgeons when considering whether or not to repair an asymptomatic AAA at each surveillance interval after their AAA reaches 4.0 cm in diameter. As the ARDA calculates cost and QALY data, the cost-effectiveness and underlying uncertainty of each potential decision can also be calculated.

As far as the authors are aware this is the first time that DES methodology has been applied in an attempt to facilitate clinical decision-making. The work reported here demonstrates that the ARDA has the potential to be adopted into clinical practice, although additional research and development is required before it can be recommended for routine use in the clinic. It is also important to note that the ARDA is not designed to be used to predict when repair should be undertaken in the future; rather, it should be rerun at each surveillance stage to calculate the consequences of advancing age, observed AAA growth and new comorbidities.

The evidence and results of the clinical effectiveness analysis of the DES model suggest that patient-related preoperative factors should certainly be considered when making clinical decisions regarding elective AAA repair. The overall results of the economic evaluation indicate a high level of uncertainty about whether or not the repair decision with and without the ARDA is cost-effective. This is because of data limitations and a range of modelling assumptions.

The ARDA can be utilised as a decision support tool for patients and clinicians. The information provided can facilitate the patient and clinician in making joint and informed decisions on the timing and appropriateness of intervention. The acceptability of the DES algorithm approach to clinicians and patients needs to be formally tested, as does the feasibility of incorporating it into routine practice. Further research is required to address uncertainty about key parameters and validate the model in other settings. It is vital, going forward, that robust information on the risk of reintervention or complications following both open repair and EVAR be incorporated into the algorithm, as this has important quality-of-life and cost implications.

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