Improving the management of ruptured abdominal aortic aneurysms: a prospective study of 558 cases: Analysis plan

The IMPROVE trial is the largest, contemporary (2009-2013), prospective study of the management of patients with ruptured abdominal aortic aneurysm (rAAA). The previous largest prospective study of rAAA management reported on 473 patients entered between 1998 and 2011 [Mayer D et al Ann Surg 2012].

The primary outcome of the IMPROVE trial, 30-day mortality, and associated costs are reported separately. Here we select from this large cohort of patients (n=613), those with ruptured or symptomatic abdominal aortic aneurysm (n=558) for separate analyses, designed to provide insight into improving future patient care. These analyses will include:

1 Analyses within randomised group.

>   A 30-day mortality and costs for patients randomised in hours and out of hours

>   *Hypothesis: out of hours team skills may be lower than in hours, where procedures may take place without any consultant present.*

>   In-hours to be defined as 8am-4pm Monday – Friday. The overall 30-day mortality percentages will be presented by in/out of hours randomisation time with 95% confidence intervals calculated by large-sample methods. Logistic regression with a Wald test will be used to assess the statistical significance of in hours and out of hours randomisation on the effectiveness of the EVAR strategy by including an interaction term. Incremental cost (95% CI) will also be reported by subgroup, using a linear regression (assuming Normality) with an interaction term. As this is an additional subgroup analysis not specified in the original analysis plan, results are hypothesis generating only and need to be interpreted with caution.

>   Data to be adjusted for Hardman Index, age,gender and maximum aneurysm diameter.

2 Analyses of total cohort of rAAA patients for 30-day (in hospital) mortality and length of stay.

>   A By primary presentation versus secondary (hospital transfer patients)

>   *Hypothesis: secondary presentation patients have better Hardman scores and outcomes than primary patients, by survival of the fittest they have survived transfer. The current Urgent and Emergency Care Review aims for patients to arrive directly at the specialist Vascular Centre, so it is important to assess (a) whether the primary and secondary patients have different demographics (age, gender, Hardman Index, lowest blood pressure) and (b) whether outcomes are different in the two groups either because selected (younger, fitter) patients are transferred .*

>   A summary of 30-day mortality rates with 95% confidence intervals will be shown by primary vs. secondary presentation. Confidence intervals will be calculated using large-sample statistics.

>   B By lowest pre-operative blood pressure, fluids administered (pre and/or intraoperative).

Hypotheses: Lowest blood pressure is not associated with 30-day survival because overadminstration of fluid and/or blood products is associated with higher mortality.

The correlation between lowest pre-operative blood pressure and amount of IV fluids administered will be investigated through the use of a scatter plot, with an R^2 – statistic reported. Intraoperative fluids (blood, platelets, plasma) will also be reported for individuals undergoing an operation and their correlation with lowest pre-operative blood pressure plotted.

A summary of 30-day mortality rates with 95% confidence intervals will be shown by both quartiles of lowest pre-operative blood pressure and quartiles of IV fluids administered. Confidence intervals will be calculated using large-sample statisticsC By time from randomisation to operating theatre, length of operative procedure, type of anaesthesia

Hypotheses: For patients with ruptured aneurysm, delays and lengthy procedures adversely influence survival and general anaesthesia relaxes abdominal muscle tone, which results in disruption of temporary blood tamponade, rapid blood loss from the aorta and hence higher mortality.

A summary of 30-day mortality rates with 95% confidence intervals will be shown by quartiles of length of time from randomisation to operating theatre (rAAA patients only) by quartiles of length of operative procedure (including those that die in theatre) and by type of anaesthesia.

D By centre rate of randomisation

Hypothesis: centres treating large numbers of ruptures/time have more practiced and skilled teams with improved patient survival rates and shorter lengths of hospital stay.

A summary of 30-day mortality rates with 95% confidence intervals will be shown by quartiles of rate of randomisation.

All above analyses (A-D) adjusted for Hardman index, age, gender and aneurysm diameter.

<u>3 Other descriptive information</u>.

A Diagnostic accuracy, differential diagnoses, when ECG is essential

Item 1A of particular interest to UK clinicians; all other items of wider interest.