Endovascular aortic repair versus open surgical repair for descending thoracic aortic disease: a systematic review and meta-analysis of comparative studies

CRD summary
This review concluded that thoracic endovascular aortic repair (TEVAR) for descending thoracic aortic disease significantly reduced mortality at 30 days, paraplegia, renal insufficiency, transfusions, re-operation for bleeding, overall complications, pneumonia and length of stay versus open surgery. The effect on longer term mortality was not significant. The uncertain quality of included studies made the reliability of the conclusions unclear.

Authors' objectives
To compare the safety and effectiveness of thoracic endovascular aortic repair (TEVAR) versus open surgical repair for descending thoracic aortic disease.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and INAHTA were searched from 1990 to March 2009 for publications in any language; search terms were reported. Surgical meeting abstracts (2006 to 2009) and FDA devices database were searched. MEDLINE was additionally searched tangentially for related articles. Individual searches were performed using the commercial names of individual stents. The bibliography of each retrieved article and recent overview articles were handsearched. Authors of clinical studies and experts were contacted in order to access unpublished studies.

Study selection
All studies that compared TEVAR versus open surgical repair for descending thoracic aortic disease that included at least 10 adult patients were eligible for inclusion. Primary outcomes were morbidity, mortality and resource-related outcomes. Eligible studies had to report at least one relevant outcome. Definitions of individual clinical outcomes were provided.

Eligible aortic pathologies were: thoracic aortic aneurysm, dissection, rupture, trauma, penetrating aortic ulcer and intramural haemorrhage, whether chronic or acute and emergent or elective. Studies of coarctation, Marfan syndrome, hybrid procedures, Type A aneurysm and combined thoracic and abdominal disease were excluded. Most studies used a mixture of two or more stents. Studies were conducted in USA, Canada, Australia, Europe and Asia between 1981 and 2007. Most studies were of trauma patients; others were mixed pathology, aneurysm, dissection and rupture. Mean age of patients was 54 years for TEVAR patients and 51 years for open surgery patients. There were more male than female patients. Some patients had comorbidities, which were similar across treatment groups.

Two independent reviewers performed the selection. Disagreements were resolved by consensus with a third reviewer as adjudicator.

Assessment of study quality
No formal quality assessment was performed. Some relevant criteria were assessed: study design, type of control (overlapping, concomitant or historic), use of consecutive enrolment and loss to follow-up.

Relevant data was extracted by the lead reviewer and checked by at least one other reviewer.

Data extraction
Data were extracted using standard forms by the lead reviewer and checked by at least one of four other reviewers. Any disagreements were resolved by consensus with international authors at designated consensus meetings. The most recent data were extracted when data were available from studies after different follow-up times (unless older results were more comprehensive). The number of events for each outcome was extracted in order to calculate odds ratios (OR) and
95% confidence intervals (CI) or mean differences with 95% CI for continuous data.

**Methods of synthesis**

Odds ratios and weighted mean differences (WMD) were pooled using a random-effects model, since heterogeneity was expected. Heterogeneity was determined using the I² test (I² >50% indicated significant heterogeneity). Subanalyses were performed using a mixed-effects analysis by study design, aortic pathology and type of stent. Potential confounding was evaluated by comparison of the baseline patient and study design characteristics in the two intervention groups. Meta-regressions were then performed to measure the impact of these baseline characteristics on the effect size for death, stroke or paraplegia and for the year of patient enrolment. Since some patient overlap was found for different studies, data was aggregated by study type (single centre, multicentre trial and registries) and results were combined only when the degree of overlap was likely to be low. Intention-to-treat data were used where possible.

Sensitivity analyses were performed based on study quality. These compared prospective versus retrospective studies, consecutive versus non-consecutive patient recruitment and historic versus concomitant control groups; only studies with similar follow-up between TEVAR and open surgery groups were used. Publication bias was assessed using Egger's test and visually from funnel plots.

**Results of the review**

Forty-three studies were identified (n=5,888, range 10 to 1,788): four multicentre observational trials (n=973, range 125 to 384) and 39 single-centre studies. The single-centre trials included three registries (n=3,060, range 242 to 1,788) with concomitant controls. The remaining 36 studies were cohort studies or case series with concurrent (14 concomitant and 10 overlapping studies) or historical (12 studies) control groups. Characteristics of TEVAR and open surgical repair patients were similar except that TEVAR patients were significantly older than the open repair patients (p=0.001).

There was a significant reduction for TEVAR versus open repair for all-cause mortality at 30 days (OR 0.44, 95% CI 0.33 to 0.59; 37 studies), paraplegia or paraparesis (OR 0.42, 95% CI 0.28 to 0.63; 26 studies), cardiac complications (OR 0.37, 95% CI 0.20 to 0.66), neurological complications (OR 0.37, 95% CI 0.23 to 0.59), respiratory complications (OR 0.25, 95% CI 0.18 to 0.33), overall complications (OR 0.19, 95% CI 0.10 to 0.36), transfusions (OR 0.01, 95% CI 0.002 to 0.04), re-operation for bleeding (OR 0.26, 95% CI 0.11 to 0.62), renal dysfunction (OR 0.40, 95% CI 0.25 to 0.63) and pneumonia (OR 0.14, 95% CI 0.23 to 0.71). There was evidence of significant statistical heterogeneity for overall complications (I²=63%). There was a significant decrease in length of hospital stay (WMD -7 days, 95% CI -10 to -5 days), total intensive care unit length of stay (WMD -4 days, 95% CI -5 to -3 days) and procedure time (WMD -142 min, 95% CI -200 to -87 min, I²=90%) for TEVAR versus open repair. Other comparisons were not statistically significant.

When the analysis was performed separately for multicentre and single-centre studies, there were few significant changes in the results. However, multicentre studies showed a significant reduction in stroke (OR 0.46, 95% CI 0.25 to 0.85; three studies) and acute myocardial infarction (OR 0.26, 95% CI 0.08 to 0.86) for TEVAR versus open repair and heterogeneity was reduced. The reduction in pneumonia with TEVAR was not significant for multicentre studies with increased heterogeneity (I²=73%) and also not significant for re-operation for bleeding for multicentre studies. The reduction in cardiac complications was not significant for single-centre studies. Separate analysis of the registry data alone gave a significant reduction in overall complications for TEVAR versus open repair, but no significant reduction for all-cause mortality at 30 days, one year or two to three years and for stroke, myocardial infarction and renal dysfunction.

Meta-regression to adjust for age imbalance, study design and pathology did not significantly change the results. There was no evidence of publication bias for mortality or metaregression analysis. Other results were reported.

**Authors' conclusions**

Results from non-randomised studies suggested that TEVAR may reduce early death, paraplegia, renal insufficiency, transfusions, re-operation for bleeding, overall complications (which included cardiac, neurological and respiratory complications), pneumonia and length of hospital stay compared with open surgery without a significant need for re-intervention during mid-term follow-up. Sustained benefits on survival were not proven.
The review addressed a well-defined question in terms of participants, interventions, study design and relevant outcomes. Relevant databases were searched in any language. Unpublished studies were considered. Publication bias was assessed. Study quality was not assessed formally, but some relevant criteria were assessed and data reported and the authors acknowledged limitations with including only non-randomised studies. Efforts were made to reduce error and bias in the review process. There appeared to be an error in the number of studies described, which was 43 not 42 studies. The authors reported that there may have been some overlap of datasets despite efforts to avoid this. Relevant study details were reported, but no specific details of study design, length of follow-up and loss to follow-up were given. Statistical heterogeneity was assessed and there was evidence for heterogeneity with some outcomes. The statistical method used for the meta-analyses seemed appropriate. Relevant sensitivity analyses and meta-regressions were performed. The authors acknowledged issues with some open surgery procedures having longer follow-up than TEVAR. The uncertain quality of included studies made the reliability of the conclusions unclear.

Implications of the review for practice and research

Practice: The authors stated that the review showed reduced risk of paraplegia/paraparesis in patients who received TEVAR. This had important implications for the long-term functionality of quality of life for patients who underwent thoracic aortic repair.

Research: The authors identified a need for high-quality randomised controlled trials with adequate power and complete follow-up to confirm these results and address longer term survival, stroke, need for re-intervention, quality of life, patient functionality and cost effectiveness of TEVAR.

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