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REVIEW

Aortic Re-operation After Replacement of the Proximal Aorta: A Systematic Review and Meta-Analysis

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WHAT THIS PAPER ADDS

To the best of the authors' knowledge, this is the first meta-analysis to examine risk of recurrent aortic surgery after proximal aortic grafting, as well as to differentiate risk in relation to initial surgical indication (dissection, aneurysm) and presence of Marfan syndrome. Data provide clear evidence that aortic re-operation occurs in a sizable proportion of patients, for which risk is greatest among patients with aortic dissection.

Objective/background: The aim was to estimate risk of aortic re-operation, and re-operative morbidity and mortality, following replacement of the proximal aorta for aneurysm or dissection.

Methods: A meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement and the Meta-Analysis of Observational Studies in Epidemiology guidelines. A comprehensive literature review was performed to identify all articles reporting aortic re-operation after proximal aortic replacement. The proximal aorta was defined as extending to the origin of the brachiocephalic trunk. The incidence rate for aortic re-operation (IRAR) was calculated, and stratified based on presence/absence of connective tissue disorders, as well as initial surgical indication. Pooled in hospital mortality and post-operative complication rates were estimated.

Results: In total, 7821 patients who underwent proximal aortic replacement from 47 studies were included: 8.3% ($n = 649$) had Marfan syndrome (MS). During a weighted mean follow up of 4.7 $\pm$ 0.3 years, 11.5% ($n = 903$) underwent aortic re-operation. Mean weighted time between initial surgery and re-operation was 5.2 $\pm$ 0.2 years. IRAR was 2.4% per person-year (PPY) (confidence interval [CI] 2.1–2.8%). Patients with MFS had a threefold higher IRAR (6.0% PPY, CI 4.1–8.8%) than did patients without a connective tissue disorders (2.3% PPY, CI 1.9–2.7%; $p < .001$). IRAR was 2.5% PPY (CI 2.1–3.0%) after operation for dissection and 1.3% PPY (CI 0.9–2.0%) after operation for aneurysm ($p = .004$ for subgroup differences). IRAR proximal and distal to the left subclavian artery was 1.2% PPY (CI 1.0–1.5%) and 1.3% PPY (CI 1.1–1.6%), respectively. The pooled in hospital mortality and complication rates after re-operation were 14.31% (CI 11.28–17.99%) and 18.08% (CI 10.54–29.25%), respectively. On meta-regression, initial operation for dissection was the only significant predictor of aortic re-operation (beta = .030, $p = .001$).

Conclusion: Aortic re-operation occurs at a mean rate of 2.4% per person-year in the five years after proximal aortic replacement and is strongly associated with initial operation for dissection.

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INTRODUCTION

Prosthetic replacement of the proximal aorta provides life-saving benefits for patients with aortic dissection (AoD), as well as for those with aortic aneurysms (AA). Despite the known benefits of surgery, long-term risks of re-operation remain. Prosthetic grafting entails localised resection of aortic tissue but does not address alterations in aortic tissue

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substrate in non-grafted segments. In addition, grafting alters aortic geometry and entails implantation of prosthetic material with different material properties compared with native aortic tissue. These factors can potentially increase pulse wave energy transmission to distal aortic segments, and thereby contribute to the risk of recurrent AoD or AA. In this context, systematic data regarding residual risk following initial proximal aortic repair are necessary to tailor surveillance and prognostic assessment of at risk cohorts.

Among patients with sporadic AoD, several population based studies have shown that mortality is elevated after aortic replacement,[1–3] and that residual false lumen patency impairs long-term prognosis.[4,5] Among patients with genetically mediated AA, data from the authors' group reported that >50% of AoD occurred in patients with Marfan syndrome (MS) who had previously undergone aortic surgery—supporting the notion that surgical risk persists despite adequate initial repair.[6] Despite this, longitudinal data regarding re-operation following initial aortic surgery have been largely derived from single centre studies of variable size and follow up duration, prohibiting objective cross sectional assessment of the aortic re-intervention risk.

This meta-analysis was designed to (i) estimate the risk of aortic re-operation after proximal aortic replacement; (ii) determine the temporal and anatomical distribution of the aortic re-intervention; (iii) assess differential post-operative risk factors for aortic re-intervention; and (iv) estimate the risk of the aortic re-intervention.

METHODS

The meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines (Table S1; see Supplementary Material).[7,8]

Search strategy

A medical librarian (M.D.) performed comprehensive searches to identify studies that evaluated re-operation on the aorta following initial operation on the proximal aorta. For study purposes, the proximal aorta was defined as extending to the origin of the brachiocephalic trunk. Full details of the search strategy are provided in Table S2 (see Supplementary Material).

Study selection and inclusion criteria

Database searches were conducted, de-duplicated, and screened by four preliminary reviewers (A.D.F., J.L., G.S., and J.W.W): a fourth independent reviewer (M.G.) confirmed adequacy of studies based on predefined inclusion and exclusion criteria for titles and abstracts. Articles considered for inclusion included studies in which adults (≥18 years old) underwent open or endovascular re-operation on the aorta following initial surgery for AA or AoD on the proximal aorta, as defined above. Studies including patients undergoing initial operation on other aortic segments were excluded. Studies reporting re-operation on the aortic valve were also excluded. The full text of initially screened studies was then retrieved for a second round of eligibility screening. Reference lists of articles selected for inclusion in the study were also searched and additional studies included (i.e., backward snowballing). The full PRISMA flow diagram outlining the study selection process is shown in Fig. S1 (see Supplementary Material). The Newcastle—Ottawa Quality Assessment Scale for Cohort Studies for Critical appraisal of eligible studies was used (Table S3; see Supplementary Material). Studies with scores of six or more were included.[9]

Clinical outcomes/definitions

The primary outcome was the incidence rate of aortic re-operation (IRAR; open or endovascular). Aortic re-operation rates were further stratified based on (i) clinical history of connective tissue disorder; (ii) indication for initial surgery (AA repair or AoD); and (iii) location (proximal vs. distal to the left subclavian artery). The pooled rates of in hospital mortality and morbidity after re-operation were also calculated.

Morbidity was defined as the incidence of at least one of the following: post-operative myocardial infarction, stroke, need for tracheostomy, and renal failure requiring dialysis. Diagnosis and definition of connective tissue disorders were those used in the original papers (see Table 1).

Data extraction and statistical analysis

Extracted variables included the following: study name, publication year, study design, age, surgical procedure, prevalence and type of connective tissue disorders (using definitions applied in source papers), number of initial operations for AA/AoD, number/type of aortic re-operation, in hospital mortality, and morbidity after re-operation.

Measurement data are reported as mean ± SD. For aortic re-operation, IRAR with underlying Poisson process with a constant event rate was used to account for different follow up times of the various studies with the total number of events observed within a treatment group out of the total person-time of follow up for that treatment group calculated from study follow up. Pooled event rates with 95% confidence interval (CI) were calculated for the binary outcomes. Uni- and multivariable meta-regression was used to assess the effect of age, initial operation for aneurysm or dissection, and MS on the incidence and time of aortic re-operation. Subgroup analyses were conducted to compare IRAR in (i) Marfan versus non-connective cohorts; (ii) AoD versus AA cohorts; and (iii) proximal versus distal to the left subclavian artery.

The Cochran Q statistic and the I^2 test were used to assess studies' heterogeneity. For the primary outcome, if heterogeneity was significant ($I^2 > 75\%$), a leave-one-out sensitivity analysis was performed.[10] Funnel plot and Egger's regression test were used to assess for potential publication bias. A random effect model (inverse variance method) was used for the whole analysis. Hypothesis testing for equivalence was set at the two tailed .05 level.

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