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ORIGINAL ARTICLE

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The Ross procedure versus prosthetic and homograft aortic valve replacement: a systematic review and meta-analysis

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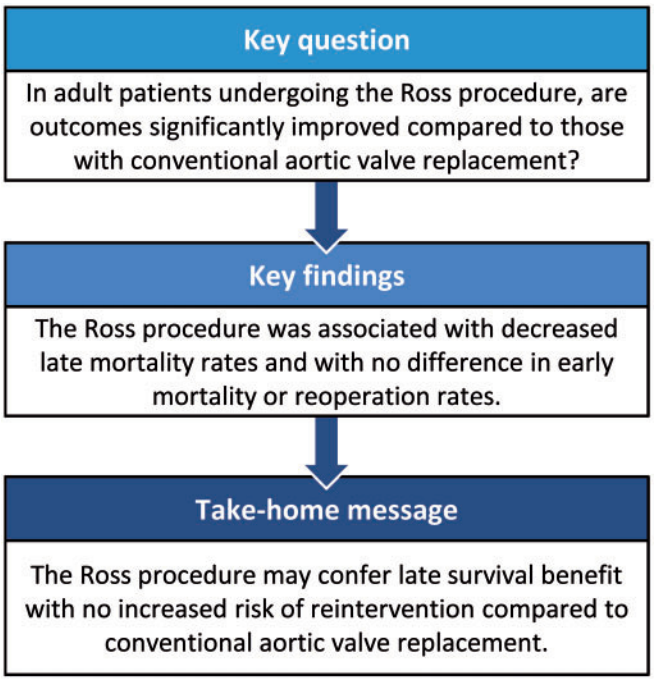

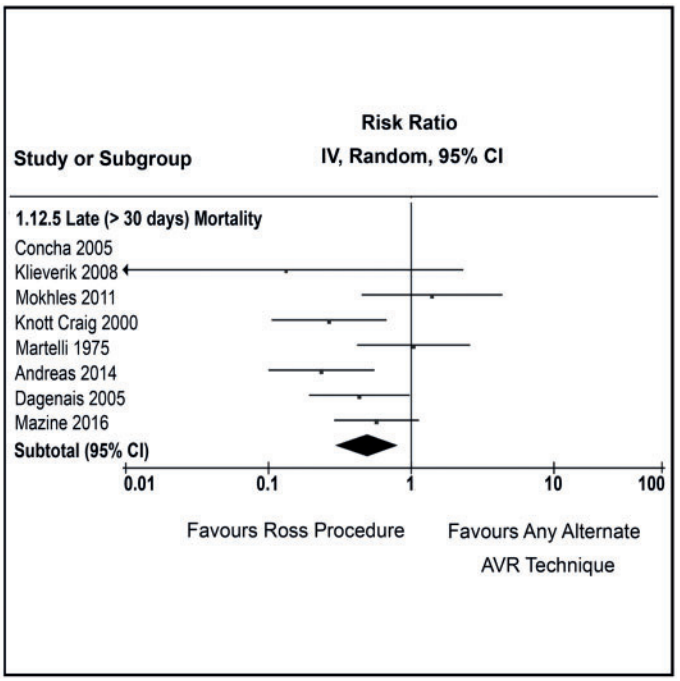

Abstract

OBJECTIVES: Young adults undergoing aortic valve replacement (AVR) have decreased life expectancy compared to matched controls. The Ross procedure aims to improve valve lifespan while avoiding anticoagulation. We prepared a systematic review and meta-analysis to assess the Ross procedure compared to conventional AVR.

METHODS: We searched MEDLINE, EMBASE and Cochrane CENTRAL for studies evaluating the Ross procedure versus any conventional AVR in adult patients. We performed screening, full-text assessment, risk of bias evaluation and data collection independently and in duplicate. We evaluated the risk of bias with the ROBINS-I and Cochrane tools and quality of evidence with the GRADE framework. We pooled data using the random- and fixed-effects models.

RESULTS: Thirteen observational studies and 2 randomized controlled trials (RCTs) were identified ($n = 5346$). No observational study was rated as having low risk of bias. The Ross procedure was associated with decreased late mortality in observational and RCT data [mean length of follow-up 2.6 years, relative risk (RR) 0.56, 95% confidence interval (CI) 0.38–0.84, I^2 = 58%, very low quality]. The RCT estimate of effect was similar (mean length of follow-up 8.8 years, RR 0.33, 95% CI 0.11–0.96, I^2 = 66%, very low quality). No difference was observed in mortality <30 days after surgery. All-site reintervention was similar between groups in cohorts and significantly reduced by the Ross procedure in RCTs (RR 1.41, 95% CI 0.89–2.24, I^2 = 55%, very low quality and RR 0.41, 95% CI 0.22–0.78, I^2 = 68%, high quality, respectively).

CONCLUSIONS: Observational data, with residual confounding, and RCT data suggest a late survival benefit with the Ross procedure with no increased risk of reintervention when compared to conventional AVR. Considering the quality of available evidence and limited follow-up, additional high-quality randomized studies are required to strengthen these findings.

Systematic review PROSPERO registration: CRD42016052512.

Keywords: Aortic valve replacement • The Ross procedure • Pulmonary autograft • Homograft valve replacement • Mechanical valve replacement • Bioprosthetic valve replacement

INTRODUCTION

Aortic valve replacement (AVR) improves survival and quality of life in patients with severe aortic valve disease [1, 2], but mortality after successful surgery remains higher than expected compared to the general population [1]. Life-threatening valve-related complications are thromboembolism, bleeding due to anticoagulation, structural degeneration necessitating reoperation and prosthetic valve endocarditis [2, 3].

The Ross procedure replaces a patient's diseased aortic valve with their own pulmonary valve (pulmonary autograft) and implants a pulmonary homograft in the pulmonary position [4, 5]. The autograft is touted as a living, dynamic structure providing superior haemodynamics, lower risk of thromboembolism (with no long-term anticoagulation requirements) and lower risk of endocarditis. Studies have reported lower incidences of thromboembolism, bleeding or valve-related events with the Ross procedure [6, 7]. The pulmonary homograft, implanted into the low-pressure pulmonary circulation, may be less vulnerable to structural degeneration.

Critics argue that the procedure increases operative risk and converts a single-valve disease into 2-valve disease with the potential for homograft dysfunction requiring reintervention [8]. These concerns have limited enthusiasm for the Ross procedure in adults [9, 10]. However, mechanical AVR is performed more commonly, and these patients have a life expectancy of 20 years shorter than that of age- and gender-matched controls without aortic valve disease [1]. Bioprosthetic AVR in young adults has been associated with a comparable survival deficit with the age-matched general population [11]. We postulate that the Ross procedure provides improved long-term outcomes. The previous meta-analysis comparing the Ross procedure to conventional AVR conducted in 2009, including 12 adult-patient series ($n = 1749$) [12], merits an update since the publication of several large important studies on the Ross procedure and conventional AVR [6, 10].

Research question

In adult patients undergoing the Ross procedure for correction of any aortic valve pathology, are patient outcomes significantly improved from those observed following conventional AVR?

MATERIALS AND METHODS

Eligibility criteria

Types of studies. Randomized trials and observational studies that compared adult patients (16 years of age and older) undergoing the Ross procedure versus conventional AVR were included. We excluded small observational studies ($n < 50$) to minimize the potential for significant bias from differential procedural expertise in centres performing and reporting on low volumes of patients. We also excluded reports from subsets of patients within a consecutive cohort. In studies with both paediatric and adult patients, studies where paediatric patients accounted for <20% of the total population were included. We placed no language constraints.

Interventions. The intervention of interest was the Ross procedure [4] with no limitation on the surgical implantation technique used and concomitant procedures performed at the time of surgery.

Comparators. The comparators included conventional AVR with any standard valve substitute: stented bioprosthesis, stentless bioprosthesis, mechanical valve and homograft.

Outcomes. Studies had to report on at least 1 outcome of interest. These outcomes were selected based on consensus by a

panel of experts, and they were defined as per VARC guidelines [13] when possible or the study definitions otherwise:

- Mortality
  - Early (≤30 days postoperatively);
  - Late (>30 days postoperatively).
- Reintervention to:
  - Aortic valve or ascending aorta;
  - Pulmonary valve or right ventricular outflow tract;
  - Aortic or pulmonary valve, ascending aorta or right ventricular outflow tract (all-site reintervention).
- Stroke
- Clinically significant bleeding
- Thromboembolism: composite of peripheral embolism, stroke, transient ischaemic attack, pulmonary embolism and valve thrombosis
- Health-related quality of life

Search strategy

We searched CENTRAL, MEDLINE and EMBASE from inception to November 2016 (Supplementary Material, File A).

We reviewed Clinicaltrials.gov, ISRCTN Register and WHO ICTRP for relevant unpublished studies. We also reviewed the references of the included studies and prior systematic reviews and consulted subject-matter experts for other potentially relevant studies. We also reviewed conference proceedings for the last 2 years.

Selection process

In duplicate, independent reviewers assessed the eligibility of each study. First, reviewers assessed studies for eligibility based on title and abstract, and any reference retained by either reviewer was included for a full-text review. Reviewers then assessed full articles for inclusion. Incongruences in assessment were resolved through discussion and consensus or a third-party opinion.

Data collection

Reviewers extracted data independently and in duplicate using pre-piloted forms. Outcome data not available in the study report were requested from authors. In the absence of response after 2 contact attempts, the data were deemed unavailable.

Assessment of risk of bias

Randomized controlled trials. The risk of bias was assessed by 2 independent reviewers using the Cochrane Collaboration tool [14].

Observational studies. We used the ROBINS-I [15] risk of bias tool for observational studies.

Data analyses and assessment of heterogeneity

We assessed outcomes based on clinical and methodological heterogeneity to determine whether pooling was appropriate. Data were analysed and pooled separately for randomized controlled trials (RCTs) and observational studies.

We pooled the observational studies that utilized the DerSimonian–Laird method [16]. For randomized trials, we used a fixed-effects model, as only 2 studies were identified, with significant disparity in the size and length of follow-up, making meta-analysis using random effects prone to bias from small trial effects. Point estimates are presented as relative risk (RR) for dichotomous outcomes and mean difference for continuous outcomes. We used the χ^2 test for homogeneity and the I^2 statistic for heterogeneity. In order to explain significant heterogeneity (I^2>50%), we performed subgroup analyses. Publication bias was assessed by visual analysis of funnel plots. RevMan 5.3 [17] was used to conduct these analyses.

Subgroups

We defined the following subgroup analyses *a priori* to explore possible heterogeneity:

1. Aortic stenosis versus insufficiency;
2. Younger (mean ≤40 years) versus older (mean >40 years) patients.

We added a subgroup analysis *a posteriori*:

1. Homograft versus mechanical valve versus bioprosthesis.

Confidence in effect estimates

Confidence in pooled effect estimates was evaluated separately for RCTs and observational studies using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [18].

RESULTS

Our search strategy identified 4195 studies for screening, 672 were reviewed in full-text, and 15 were included for final analysis (Fig. 1). Trial registries and conference proceeding reviews identified no additional relevant studies. These studies (Table 1) included 5346 patients from 13 observational studies and 2 RCTs (one reported at multiple time points) with significant variability in the length of follow-up ranging from index hospital discharge to 14.2 years. Six studies compared the Ross procedure to aortic homograft, 8 studies to mechanical valve and 3 studies to bioprosthetic valves. One study compared the Ross procedure with conventional AVR, which was not further defined [10]. One RCT compared the Ross procedure to homograft AVR [6] and the other to mechanical AVR [19].

One RCT was considered as 'high risk of bias' [19] due to inadequate allocation concealment and selective reporting, and the other was considered as 'unclear risk of bias' [6] due to unclear randomization of sequence generation methods and possible patient follow-up attrition (Fig. 2, Supplementary Material, File B). Four observational cohorts were rated as 'moderate risk of bias' based on the Cochrane ROBINS-I tool [3, 20–22], with all other cohorts judged at either 'serious' or 'critical' risk of bias (Fig. 3, Supplementary Material, File B). Uncontrolled confounding factors, cointerventions and selective reporting were concerns across the observational studies.

The mean length of follow-up for observational studies was 2.6 years. Excluding the 2 observational studies that reported

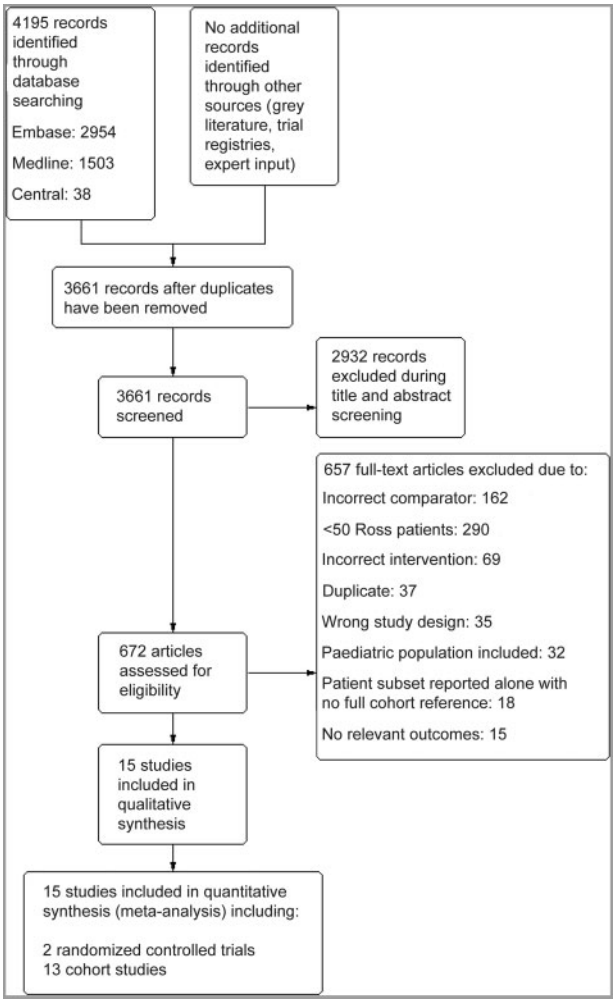

Figure 1: PRISMA flow diagram detailing the progression of article screening over the course of the review.

only outcomes occurring within 30 days, the mean length of follow-up was 4.7 years, and the mean length of follow-up in RCTs was 8.8 years.

Outcomes of the Ross procedure versus conventional aortic valve replacement

A summary of the results of comparisons of the Ross procedure versus any conventional AVR is reported in Table 2, and forest plots are presented in Supplementary Material, File C.

Mortality

Ten observational studies ($n = 2502$) and 2 RCTs ($n = 256$) reported on mortality after >30 days of follow-up. Observational studies and randomized trials showed lower mortality in patients undergoing the Ross procedure compared to any conventional AVR [RR 0.56, 95% confidence interval (CI) 0.38–0.84, I^2 = 58% and RR 0.33, 95% CI 0.11–0.96, I^2 = 66%, respectively]. There was no significant difference in the rate of early mortality between groups in RCTs or observational studies (Table 2) (Supplementary Material, File C). The observational studies showed a decrease in mortality occurring after 30 days from operation (RR 0.49, 95% CI 0.30–0.81, I^2 = 48%). The randomized data were directionally consistent but did not reach statistical significance ($P = 0.09$).

Reintervention

Eleven observational studies ($n = 4585$) and 2 RCTs ($n = 252$) reported on the rate of reintervention on the operated site. Observational studies showed no significant difference between the Ross procedure and conventional AVR; however, randomized trials showed a significant reduction in the risk of reoperation following the Ross procedure (RR 1.41, 95% CI 0.89–2.24, I^2 = 50% and RR 0.41, 95% CI 0.22–0.78, I^2 = 68%, respectively) (Supplementary Material, File C). When assessing only aortic valve reoperation, neither observational nor randomized data showed a significant difference in reoperation rates.

Thromboembolism

The composite 'any thromboembolism' was rarely reported. Therefore, we elected to meta-analyse components separately. Ischaemic stroke at the latest follow-up was reported in 7 cohort studies ($n = 1822$) and 2 RCTs ($n = 252$). Observational studies demonstrated a significantly lower risk of ischaemic stroke following the Ross procedure compared to conventional AVR, while RCTs did not show a significant difference but were directionally consistent with observational results (observational studies: RR 0.24, 95% CI 0.10–0.58, I^2 = 0% and RCTs: RR 0.69, 95% CI 0.11–4.31, I^2 = 21%). Transient ischaemic attack was reported in 6 observational studies ($n = 1515$) and was significantly lower with the Ross procedure (RR 0.21, 95% CI 0.08–0.54, I^2 = 0%). Between-group differences for all other components (valve thrombosis, peripheral embolism and pulmonary embolism) were not significantly different.

Haemorrhagic stroke

Only 1 observational study [7] ($n = 416$) observed haemorrhagic stroke events. In this study, the risk was not significantly different between the Ross procedure and mechanical valve replacement (RR 0.20, 95% CI 0.01–4.14).

Major bleeding

Study-defined major bleeding was reported in 4 cohort studies ($n = 1279$) showing significantly less major bleeding with the Ross procedure (RR 0.13, 95% CI 0.04–0.46, I^2 = 10%). One RCT reported on major bleeding and found no significant difference between the Ross procedure and homograft AVR.

Health-related quality of life

Health-related quality of life was reported in 1 RCT ($n = 212$) using the SF36 tool. These results showed a significant improvement in 2 questionnaire domains associated with the Ross procedure as compared to homograft AVR: the physical functioning [absolute score – Ross: 51.0 (IQR 45.9–56.1) vs homograft: 48.5 (38.3–56.1) $P = 0.041$] and general health domains [absolute score – Ross: 51.9 (43.1–55.4) vs homograft: 48.0 (35.8–52.9) $P = 0.019$].

Table 1: Summary and characteristics of the included studies

Study ID	*n*	Design	Setting	Population	Intervention/comparator	Mean length of follow-up (years)
Randomized controlled trials						
Doss *et al.* [19]	40	RCT	Single centre	<55 years old	Intervention: Ross Comparator: Mechanical	1
El-Hamamsy *et al.* [6]	216	RCT	Single centre	<69 years old	Intervention: Ross Comparator: Homograft	10.2
Andreas 2014	332	Prospective	Single centre	18–50 years old	Intervention: Ross Comparator: Mechanical	8.9
Bouhout *et al.* [24]	140	Prospective—Propensity matched	Single centre	<65 years old	Intervention: Ross Comparator: Mechanical	0.08
Concha 2005	125	Prospective	Single centre	20–50 years old	Intervention: Ross Comparator: Mechanical	2.54
Dagenais 2005	332	Retrospective	Single centre	45–65 years old	Intervention Ross Comparator 1: Freestyle Comparator 2: Homograft Comparator 3: Mechanical	4.7
Klieverik 2008	169	Prospective	Single centre	16–55 years old	Intervention: Ross Comparator: Homograft	10.1
Knott-Craig 2000	238	Retrospective	Single centre	>16 years old	Intervention: Ross Comparator: Homograft	3
Martelli 1975	259	Retrospective	Single centre	10–77 years old	Intervention: Ross Comparator 1: Homograft Comparator 2: Bioprosthesis	'up to 6 years'
Mastrobuoni 2014	180	Retrospective—Propensity matched	Single centre	Mean 51 years old	Intervention: Ross Comparator: Mechanical	Not specified
Mazine *et al.* [7]	416	Retrospective—Propensity matched	Single centre	16–63 years old	Intervention: Ross Comparator: Mechanical	14.2
Mokhles *et al.* [20]	506	Retrospective—Propensity matched	German Dutch Ross Registry and ESCAT trial patients	18–60 years old	Intervention: Ross Comparator: Mechanical	5.6
Reece *et al.* [10]	2188	Retrospective—Propensity matched	STS ACSD	Median 43 years old	Intervention: Ross Comparator: 'Conventional AVR'	Not specified
Sharabiani	1501	Retrospective—Propensity matched	National congenital heart disease audit—UK	Mean 25 years old	Intervention: Ross Comparator 1: Mechanical Comparator 2: Bioprosthesis	5.5
Choudhary *et al.* [22]	189	Retrospective	Single centre	1–68 years old	Intervention: Ross Comparator: Homograft	2

Full article references are available in Supplementary Material, File B.

AVR: aortic valve replacement; ESCAT: early self-controlled anticoagulation trial; RCT: randomized controlled trial; STS ACSD: Society of Thoracic Surgeons Adult Cardiac Surgery Database.

Subgroup analyses

We conducted subgroup analyses (Table 3) to explore potential sources of heterogeneity for the 2 outcomes with an I^2 >50%: mortality and reintervention. We limited these analyses to observational studies.

When stratifying by conventional AVR valve type (homograft versus Ross, mechanical valve versus Ross and bioprosthesis versus Ross), we found a significant mortality benefit that favoured the Ross procedure when compared to mechanical valves, and no significant difference was observed when compared to bioprosthesis or homograft. The relative risk of operated-site reintervention stratified by a comparator suggested no significant difference for homograft or bioprosthesis but significantly increased the risk of reoperation with the Ross procedure when compared to mechanical AVR. We found no significant interaction between patient age and treatment. Due to the absence of reporting specifically on preoperative aortic stenosis or insufficiency, we were unable to perform this subgroup analysis.

Publication bias

Interpretation was limited by the small number of studies for inclusion in the funnel plots ($n < 10$), but we noted no suggestion of significant publication bias on funnel plot inspection.

Quality of evidence

We evaluated the quality of evidence for each outcome based on the GRADE framework. For observational studies, we downgraded all outcomes. The main domains decreasing the confidence in the point estimates were inconsistency for unexplained heterogeneity and risk of bias. For RCTs, we downgraded the

quality of evidence for mortality and reintervention due to imprecision and inconsistency (Supplementary Material, File D).

DISCUSSION

This meta-analysis suggests that the Ross procedure significantly reduces mortality at the latest follow-up with no significant difference in early mortality when compared to conventional AVR. Further, the data suggest no increased risk of reoperation to either the pulmonary or aortic valve and a significantly lower risk of ischaemic stroke, transient ischaemic attack and major bleeding. However, confidence in the results is decreased because the data are of very low quality. The risk of bias was significant throughout the literature reviewed, and statistical reporting practices did not allow correction for confounding. In subgroup analyses, the mortality benefit was only significant when comparing the Ross procedure with mechanical AVR, but the findings for reoperation were consistent in all subgroups.

Our findings are not consistent with the conclusions of a study by Reece *et al.* [10]. This group concluded that an increased early mortality associated with the Ross procedure should preclude its use given the existence of less morbid alternatives. Based on our results, the current body of evidence does not suggest an increase in early mortality with the Ross procedure. Reece *et al.* leveraged a national US database that likely includes a number of operators who are either new to the technique or who do not perform it regularly: the average number of the Ross procedures performed was 5 cases/year/centre. A recent large propensity-matched series from centres of high Ross volume demonstrates a similar benefit compared to mechanical AVR, and it corroborates this conclusion [23]. The experience of the surgeons performing the Ross procedure must be taken into consideration when defining the utility of this procedure [24], and it may explain the absence of increased mortality with the Ross procedure in an expertise-based trial [6].

We did not demonstrate an increase in operated-valve reintervention with the Ross procedure, but the mean length of follow-up was only 2.9 years. Longer-term data are needed as between-group differences may appear with longer follow-up. The short durability of left-sided bioprostheses in young patients [2, 25] would likely lead to a greater risk of reinterventions in the conventional AVR group. The potential of a more durable bioprosthetic substitute has become increasingly promising as percutaneous intervention strategies for both aortic and pulmonary reoperation emerge. These strategies may significantly reduce the morbidity associated with reintervention [26, 27].

The risk of lifelong anticoagulation must be strongly considered in active young patients who require AVR. Our results suggest a significant increase in major bleeding in the conventional AVR group. Based on the most recent systematic review on mechanical prostheses in young patients [25], the choice of mechanical prostheses likely drives this finding. The importance of bleeding events is sometimes minimized, but a strong association between major bleeding and mortality has been established [28]. The mortality benefit at 2.9-year follow-up with the Ross procedure may be related to the significantly lower bleeding risk, and this is supported by the subgroup analysis that showed significantly lower mortality only when compared to mechanical AVR.

The Ross procedure is thought to be of greatest benefit to younger patients because it provides a durable valve substitute, which does not require lifelong anticoagulation and, thus, improves quality of life. However, none of the studies included in our review reported on health-related quality of life. Although studies focusing on this question report a benefit of the Ross procedure over conventional AVR [29], these studies did not meet

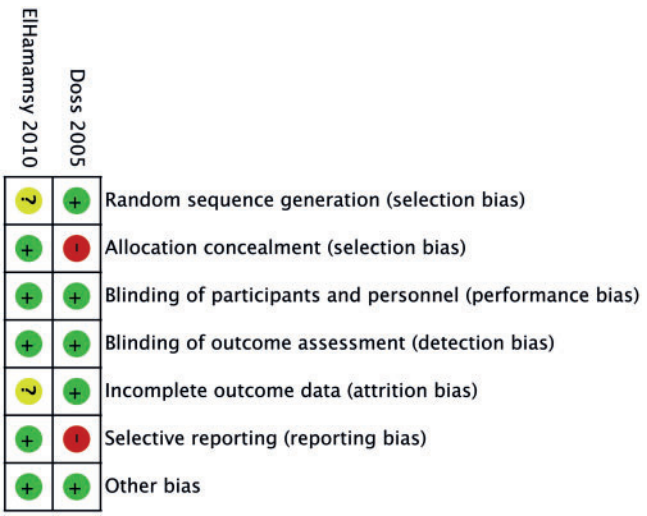

Figure 2: Risk of bias for randomized controlled trials. Green circles indicate low risk of bias, yellow circles indicate unclear risk of bias, and red circles indicate high risk of bias.

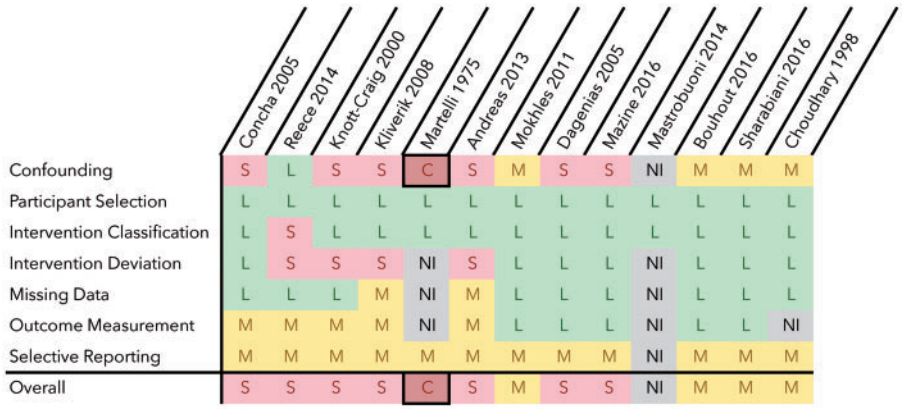

Figure 3: Risk of bias for observational studies. C: critical; L: low risk of bias; M: moderate; NI: non-sufficient information; S: serious.

Table 2: Summary of meta-analysis: results by outcome, time point and study design

Outcomes	Number of studies	Number of participants	Effect estimate RR (95% CI)	*P*-value	I^2 (%)	Quality of evidence
Mortality						
Total mortality at >30 day follow-up—Cohorts	10	2502	0.56 (0.38–0.84)	0.005	58	Very low
Early (<30 days)—Cohorts	12	4830	0.93 (0.47–1.83)	0.83	62	Very low
Late (>30 days)—Cohorts	8	2314	0.49 (0.30–0.81)	0.006	48	Very low
Total mortality at >30 day follow-up—RCTs	2	256	0.33 (0.11–0.96)	0.04	66	Very low
Late (>30 days)—RCTs	2	252	0.39 (0.13–1.16)	0.09	59	Very low
Early (<30 days)—RCTs	2	256	0.33 (0.04–3.15)	0.34		Very low
Reintervention						
All-site reintervention—Cohorts	11	4585	1.41 (0.89–2.24)	0.15	50	Very low
All-site reintervention—RCTs	2	252	0.41 (0.22–0.78)	0.007	68	Very low
Aortic site reintervention—Cohorts	9	2464	1.02 (0.62–1.69)	0.94	44	Very low
Aortic site reintervention—RCTs	2	252	0.13 (0.04–0.38)	0.0002	86	Very low
Bleeding						
Major bleeding—per study protocol—Cohorts	4	1279	0.13 (0.04–0.46)	0.001	10	Moderate
Major bleeding—per study protocol—RCTs	1	212	Not estimatable			High
Haemorrhagic stroke—Cohorts	2	541	0.20 (0.01–4.14)	0.30		Very low
Haemorrhagic stroke—RCTs	1	212	Not estimatable			High
Thromboembolic events						
Pulmonary embolism—Cohorts	4	815	4.00 (0.50–32.17)	0.19	0%	Very low
Valve thrombosis—Cohorts	5	1469	0.87 (0.08–9.40)	0.91	42%	Very low
Valve thrombosis—RCTs	1	212	Not estimatable			
Ischaemic stroke—Cohorts	6	1822	0.24 (0.10–0.58)	0.002	0%	Moderate
Ischaemic stroke—RCTs	2	252	0.69 (0.11–4.31)	0.69	21%	Moderate
TIA—Cohorts	6	1515	0.21 (0.08–0.54)	0.001	0%	Moderate
Peripheral embolism—Cohorts	5	1237	0.63 (0.16–2.54)	0.21	0%	Very low
Peripheral embolism—RCTs	1	212	Not estimatable			
HrQoL						
HrQoL—SF 36 Physical functioning	1	212	Absolute - Ross: 51.0 (IQR 45.9–56.1) vs homograft: 48.5 (38.3–56.1) MD not estimatable	**0.041**		
HrQoL—SF 36 General health	1	212	Absolute - Ross: 51.9 (43.1–55.4) vs homograft: 48.0 (35.8–52.9) MD not estimatable	**0.019**		

CI: confidence interval; HrQoL: health related quality of life; IQR: interquartile range; MD: mean difference; RCT: randomized controlled trial; RR: relative risk; TIA: transient ischaemic attack.

Bold values are statistically significant ($P<0.05$).

Table 3: Subgroup analyses

Outcomes	Number of studies	Number of participants	Effect estimate RR (95% CI)	*P*-value	I^2 (%)	Quality of evidence
Mortality—total at >30 day follow-up						
Homograft valve	5	878	0.58 (0.26–1.29)	0.18	71	Very low
Mechanical valve	6	1462	0.49 (0.36–0.67)	<0.001	35	Very Low
Bioprosthesis	3	640	0.67 (0.12–3.63)	0.64	84	Very low
Mean patient age <40	5	1306	0.47 (0.30–0.73)	<0.001	0	Very low
Mean patient age >40	5	1161	0.43 (0.19–0.94)	0.03	82	Very low
All-site reintervention						
Homograft valve	4	726	0.95 (0.50–1.80)	0.87	41	Very low
Mechanical valve	6	1452	1.66 (1.11–2.49)	0.01	0	Very low
Bioprosthesis	3	640	0.69 (0.25–1.91)	0.47	50	Very low
Mean patient age <40	5	1306	0.47 (0.30–0.73)	<0.001	71	Very low
Mean patient age >40	5	3197	1.40 (0.41–4.83)	0.008	71	Very low

CI: confidence interval; RR: relative risk.

the eligibility criteria of our review as they included <50 Ross patients. Considering the importance of quality of life, future work should address this question.

Strengths and weaknesses

The strengths of our study are that we carefully searched the literature, objectively assessed the risk of bias and the quality of evidence, and excluded small observational studies that are subject to reporting and surgical expertise bias.

Potential limitations are that we included observational studies, which are subject to confounding that we could not correct for, and have limited available follow-up time. We also compared the Ross procedure with a range of control interventions, and we had limited power to perform separate comparisons with mechanical, homograft and bioprosthetic AVR. The literature included in the analysis also spans a long time-period (1975–2016) potentially introducing effect estimate of heterogeneity as a result of changes to standards of care over time (i.e. anticoagulation management post-mechanical AVR); however, our low estimates of heterogeneity do not appear to indicate that this was the case.

CONCLUSION

In non-elderly adults requiring AVR, the Ross procedure may improve the outcomes compared to conventional AVR. Our results suggest a survival benefit with the Ross procedure with no increased risk of reintervention, but the evidence is of very low quality. The surgical community should prioritize the generation of a large, appropriately powered, expertise-based randomized trial to definitively address the risks and benefits of the Ross procedure compared to conventional AVR.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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