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ORIGINAL ARTICLE

Minimally Invasive Versus Conventional Aortic Root Replacement – A Systematic Review and Meta-Analysis☆

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Background Mini-sternotomy has been proven superior to full sternotomy in aortic valve replacement by providing better perioperative outcomes. We investigated whether such technique provides better outcomes in patients undergoing aortic root surgery.

Methods A comprehensive electronic literature search was undertaken among the four major databases (PubMed, Ovid, Scopus and EMBASE) to identify all published studies up to June 2018. The search terms used related to mini-sternotomy versus full sternotomy, aortic root, valve sparing, Bentall procedure. Only articles that compared mini against full sternotomy were considered in this analysis. After excluding articles based on title or abstract, the full text articles selected had reference lists searched for any potential further articles to be included in this review.

Results A total of 2,765 patients were analysed from across eight comparative studies that were included in the quantitative analysis of the parameters of interest that fulfilled the criteria for meta-analysis. Mini-sternotomy aortic root replacement was associated with significantly shorter cardiopulmonary bypass time ($p = 0.009$), lower rate of blood transfusion ($p = 0.01$). additionally, they had lower operative mortality ($p = 0.02$), and shorter stay at intensive care and at hospital ($p = 0.0009$, $p = 0.03$ respectively). However, there was no difference between mini-sternotomy and conventional aortic root replacement in terms of aortic cross-clamp time ($p = 0.28$), total operation time ($p = 0.31$), re-exploration rate for bleeding ($p = 0.28$), stroke rate ($p = 0.90$), wound infection rate ($p = 0.96$), and length of mechanical ventilation ($p = 0.10$).

Conclusion Mini-sternotomy is a safe, feasible alternative option to full sternotomy in aortic root repair. However, the significant heterogeneity in data points to the need for a larger, well-designed trial to support the currently limited literature evidences.

Keywords Aortic surgery • Mini access • Aortic root replacement • Mini-sternotomy

Introduction

Less invasive aortic operations have witnessed a significant expansion in recent years. Instead of full sternotomy, mini-sternotomy typically consists of an upper sternotomy to the third or fourth intercostal space, extending to the right or left intercostal space. Proponents of such approaches advocate their use quoting their potential in reducing postoperative

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pain, postoperative blood transfusions, intensive care and total hospital stay, costs, and improving cosmesis (Figure 1) [1–5]. Achieving such benefits should not, however, come at the expense of surgical completeness, safety, mortality and morbidity. Although current published literature on the use of minimally invasive techniques in treating primary aortic and mitral valve disease is widespread, evidence supporting their use in surgery for aortic root disease is limited and less established [6,7]. Through a systematic review and meta-analysis of all available comparative studies, we aim to evaluate outcomes of patients undergoing aortic root surgery via a minimal access incision (minimally invasive aortic root replacement, MIARR) compared with those undergoing surgery through conventional full sternotomy (conventional aortic root replacement, CARR).

Methods

Search Strategy

An electronic English language literature search was performed following the PRISMA guidelines [8]. There were no geographic or language restrictions imposed. The search strategy adopted was in accordance with the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines [9]. The four major electronic databases (PubMed, Ovid, Scopus and EMBASE) were interrogated and systematically searched from inception to June 2018. Additional studies were obtained through 'hand searching' of university publications and bibliographies of review and original papers.

A number of medical subject headings (MeSH) and free-text terms were combined with Boolean operators optimising search sensitivity. The search terms used were words relating to the incision or access choice (''sternotomy'', ''full sternotomy'', ''mini-sternotomy'', ''partial sternotomy'', or ''J sternotomy''), the surgical site (''aortic root''), or the operation performed (''Bentall'', ''valve sparing'', ''root repair'', or ''root replacement''). After excluding articles based on title or abstract, full text articles selected had reference lists searched for any potential further articles to be included in this review.

Study Selection and Data Extraction

Inclusion criteria included comparative studies in which the patients underwent aortic root replacement via either a minimal access (MIARR) or a conventional full sternotomy incision (CARR). Studies were excluded based on topic relevance (studies including procedures other than aortic root repair/replacement were exclude), study type (non-comparative and animal studies were excluded), unreported outcomes (studies not reporting any relevant clinical outcomes

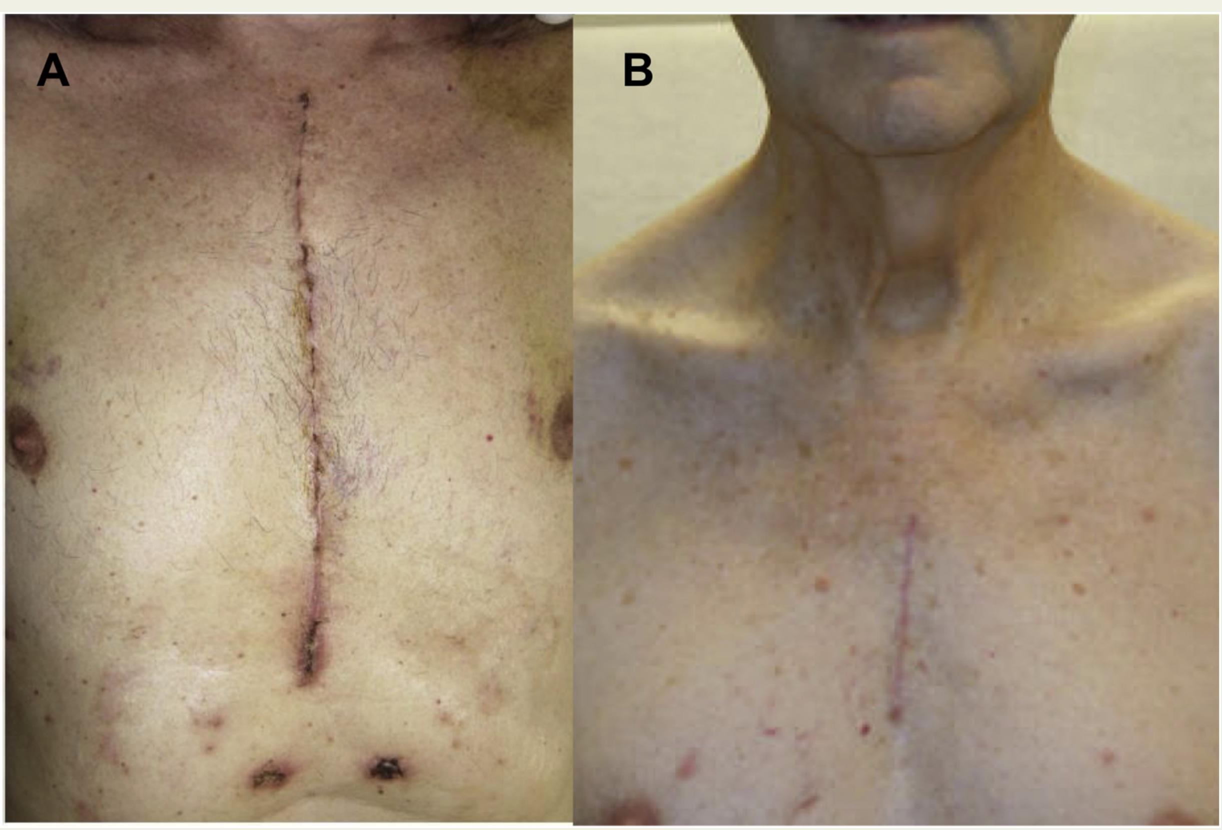

Figure 1 Postoperative scar of full sternotomy (A) and mini-sternotomy (B).

including infection, bleeding, requirement for blood transfusion, ventilation times, hospital stay, neurological complications, renal failure and mortality rate were excluded), patient population (studies including patients aged less than 18 years were excluded) and publication type (reviews, case reports, letters and editorials were excluded). A second check was performed through reference check of all the final list articles to check for any relevant study to be added into the analysis.

Data was extracted from full text articles, figures, and tables. Two independent investigators (AH, AA) performed all aspects of the search strategy, abstract examination, and review of full text articles. There were no major discrepancies. Minor discrepancies were resolved by consensus and arbitration by a third independent reviewer (MB). Assessment for bias for included studies was performed in accordance with latest Cochrane statement.

From each study the following were extracted: the number of cases reported and the potential confounders, their incidence of infection, bleeding, blood transfusion, renal failure, neurological complications and death, and their length of intensive care and in-hospital stay.

Methodological Quality Assessment of Included Studies

Qualitative assessment of included studies was performed using the Newcastle-Ottawa scale (NOS; Table 1) [10]. The NOS was devised specifically for the quality of non-randomised studies included in the meta-analyses. This scale assesses bias of each study using a star-based rating system, with a maximum score of 9 indicating lowest risk of bias, and a minimum of 0 indicating highest risk. Scores ≥7 represent the lack of substantial bias. Quality of included studies was rated by two reviewers (JC, CW). There were no major discrepancies. Minor discrepancies were resolved by consensus and arbitration by a third independent reviewer (AH).

Statistical Analysis

This meta-analysis was performed in line with recommendations from Quality of Reporting of Meta-analyses (QUOROM) and Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines [9,11]. Clinical outcomes were assessed using standard and cumulative meta-analysis techniques, with risk ratios (RR) or weighted mean differences (WMD) used as summary statistics for raw data extracted from each included study. Both fixed- and random-effects models were tested. χ^2 Tests were used to study heterogeneity and the I^2 statistic was used to estimate the proportion of total variation across studies, owing to heterogeneity rather than chance. A cut-off threshold of 50% was chosen and values exceeding this were considered to signify substantial heterogeneity. All p values were two-sided. Statistical analyses were performed using Review Manager v.5.2.1 (Cochrane Collaboration, Oxford, UK). If there was substantial heterogeneity, the possible clinical and methodological reasons for this were explored qualitatively.

Table 1 Newcastle-Ottawa Scale (NOS).

Author	Selection				Comparability	Outcomes		
	Representation of patients receiving open surgery and endovascular treatment	Selection of patients receiving open surgery and endovascular treatment	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Study controls for patient age = * Study controls for preoperative cardiac function and cardiovascular co-morbidities = *	Assessment of outcomes	Follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts
Sun et al. [12]	*	*	*	*	*	*	*	*
Shrestha et al. [13]	*	*	*	*		*	*	*
Mikus et al. [14]	*	*	*	*	*	*	*	*
Levack et al. [15]	*	*	*	*	**	*	*	*
Wachter et al. [16]	*	*	*	*	**	*	*	*
Tabata et al. [17]	*	*	*	*	**	*	*	*
Hilleband et al. [18]	*	*	*	*	*	*	*	*
Monsefi et al. [19]	*	*	*	*	*	*	*	*

Results

Included Studies and Preoperative Characteristics

The initial electronic database search yielded 1,737 articles, of which 70 articles were retrieved for assessment in full-text. After detailed evaluation of these articles and assessment according to inclusion criteria, only eight comparative studies satisfied our selection criteria and were included in the qualitative and quantitative meta-analysis [12–19], as shown in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) chart (Figure 2).

Study and Patient Characteristics

All included studies are summarised in Table 2 [12–19]. There were no randomised controlled trials comparing the two access techniques. The eight eligible comparative studies included a total of 2,765 patients. A total of 974 patients underwent MIARR and 1,791 underwent CARR. Perioperative data from included studies are summarised in Table 3. There was no difference in mean age (60.0 ± 13.2 years in MIARR versus 55.5 ± 15.8 years in CARR, $p = 0.29$). However, the data was significantly heterogeneous ($I^2 = 0.78$, $p < 0.0001$). The prevalence of bicuspid aortic valve was only defined in four studies (421 patients), with a significantly higher prevalence amongst patients undergoing MIARR (45.0% in MIARR versus 31.7% in CARR, $p = 0.03$). There was no significant heterogeneity for this variable ($I^2 = 0.59$, $p = 0.06$).

Surgical Technique

Conventional full sternotomy incision surgery was performed through a median sternotomy and cardiopulmonary bypass was instituted by direct aortic and right atrial cannulation. In contrast, in MIARR, the sternum is divided down the third or fourth intercostal space and then angled horizontally to the right at this level (J technique). Authors of two studies, however, divided the sternum to the left instead [12,19]. Of the studies that reported numbers of specific procedures done, 273 patients underwent the Bentall procedure using either mechanical or biological prostheses, 778 underwent the David procedure (reimplantation), 41 underwent the Yacoub procedure (remodelling), 102 underwent resuspension, and 587 underwent repair with a valved conduit. Cardiopulmonary bypass arterial cannulae were placed in the distal ascending aorta or distal aortic arch, and venous cannulae in the right atrium. Vacuum assisted CPB was used in several studies. Right subclavian artery cannulation was performed in some studies particularly in small patients [15]. Some studies also utilised vents placed into the left atrium via the upper right pulmonary vein after fibrillating the heart [13] and in others left ventricular vents were explicitly avoided [15]. Ventricular epicardial pacing wires were placed prior to weaning from CPB. Only two studies mentioned the use of hypothermia [13,17], and only Tabata et al. mentioned the use of antegrade cerebral perfusion (however, this was limited to cases where circulatory arrest time exceeded more than 30 minutes) [17].

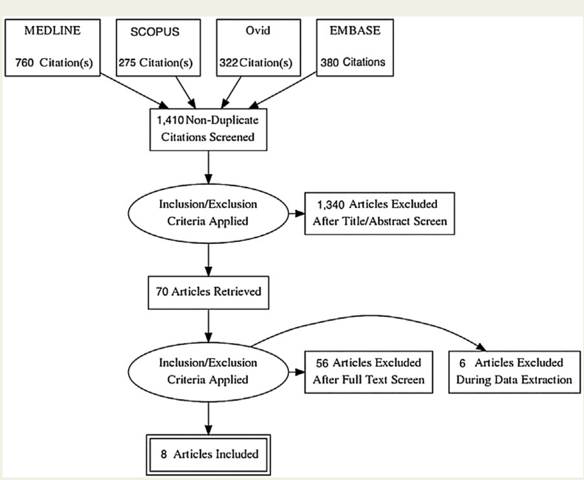

Figure 2 PRISMA flowchart.

Cardiopulmonary Bypass, Aortic Cross-Clamp (ACx) and Operative Times

Cardiopulmonary bypass times were reported in all included studies (2,765 patients), aortic cross-clamp (ACx) in seven studies (2,469 patients), and total operative times in four studies (319 patients). Mean CPB times were shorter in the MIARR (101.7 ± 33.5 mins in MIARR vs 109.6 ± 52.9 mins in CARR, $p = 0.009$; Figure 3A). There was no statistically significant difference in the mean ACx times (76.1 ± 24.7 mins in MIARR vs 78.0 ± 31.5 mins in CARR, $p = 0.28$; Figure 3B) and total operation time (252.8 ± 56.3 mins in MIARR vs 249.7 ± 54.1 mins in CARR, $p = 0.31$). The latter analysis was, however, based on a much small denominator pool and hence the risk of a type II error was larger. Moreover, data of CBP, cross-clamp and operative times were significantly heterogeneous ($I^2 = 0.61$ [$p = 0.01$], 0.85 [$p < 0.00001$] and 0.86 [$p < 0.0001$], respectively).

Conversion to Full Sternotomy

Of the eight included studies, three mentioned specifically the incidence of conversion [13,15,19]. Spanning a total of 684 patients undergoing MIARR, only 11 (1.61%) patients required conversion to full sternotomy. Reasons for conversion included inadequate exposure (n = 5), postoperative bleeding (n = 3), bleeding not amenable to repair via a limited incision (n = 2), or coronary dissection after cardioplegia (n = 1).

Perioperative Mortality

There were only 28 operative mortalities reported in all eight comparative studies. Overall, the rate of operative mortality was significantly lower in the MIARR group compared with the CARR group (0.411% in MIARR vs 1.34% in CARR, $p = 0.02$; Figure 4). There was no significant heterogeneity in the data ($I^2 = 0.00$, $p = 1.00$). Only two studies reported the

Table 2 **Study characteristics of the articles included in the systematic reviews and meta-analysis.**

Author	Year	Country	Type of study	Total no. of patients	MIARR (n)	CARR (n)	Primary endpoints
Sun et al. [12]	2000	China	Retrospective non-randomised study	29	8	21	Aortic root replacement by a superior ministernotomy provides a safe alternative with sufficient exposure. It also results in reduced trauma, faster recovery and reduction of mediastinal drainage compared to the full sternotomy.
Shrestha et al. [13]	2015	Germany	Prospective study	40	26	14	Valve sparing aortic root replacement with ministernotomy is safe in young patients with isolated aortic root aneurysm and no leaflet calcification, with comparable outcome to operations performed under full sternotomy.
Mikus et al. [14]	2017	Italy	Retrospective non-randomised study	165	53	112	Ministernotomy via a partial J-shaped sternotomy is a safe option for aortic root replacement in a selected group of patients with complex pathologies, including chronic aneurysm from calcified degenerative disease, annuloaortic ectasia and chronic infective endocarditis. Early outcomes are comparable with a slight advantage of minimally invasive approach in operative times, incidence of atrial fibrillation and postoperative ventilation times.
Levack et al. [15]	2017	United states	Retrospective study	1,827	568	1,259	In elective patients with primary and isolated aortic root pathology, ministernotomy via a J incision is associated with a similar risk of complications but shorter ICU and total stay and lower costs, compared to full sternotomy.
Wachter et al. [16]	2016	Germany	Retrospective non-randomised study (matched pair analysis)	192	117	75	Compared to full sternotomy, valve sparing aortic root replacement with minimally invasive upper hemisternotomy is able to demonstrate comparable outcomes in complications for up to 5 years. It is also resulted in shorter ICU stay and mechanical ventilation.
Tabata et al. [17]	2007	United States	Retrospective non-randomised study	158	79	79	Minimal access surgery through upper hemisternotomy is a safe procedure for aortic root operatives with or without valve replacement. It results in shorter length of hospital stay compared to full sternotomy, with comparable operative times, morbidity and mortality.
Hilleband et al. [18]	2016	Germany	Prospective study	58	33	25	Aortic root replacement with valved conduits performed through a partial upper sternotomy is a safe alternative for conventional full sternotomy approach with similar operative times and comparable clinical results.
Monsefi et al. [19]	2017	Germany	Prospective study	296	90	206	The David procedure performed with a reversed J upper hemisternotomy resulted in similar outcomes at midterm follow-up (median 3 years postoperatively) compared to full sternotomy. It is also associated with significantly less need of packed red cell transfusion.

Abbreviations : CARR, conventional aortic root replacement; MIARR, minimally invasive aortic root replacement; ICU, intensive care unit

Table 3 Perioperative characteristics and data.

	MIARR	CARR	P-value
Number of patients (n)	974	1791	
Preoperative data			
Mean age (years)	60.0	55.5	0.29
Male (%)	73.7	77.7	
Mean BMI (kg/m^2)	27.7	27.9	
Bicuspid aortic valve (%)	45.0	31.7	0.03
Mean ejection fraction (%)	58.9	56.2	
Marfan syndrome (%)	6.15	6.35	
Coronary artery disease (%)	7.69	31.5	
COPD (%)	7.08	10.1	
Hypertension (%)	60.3	61.8	
Diabetes (%)	5.18	6.97	
Atrial fibrillation or flutter (%)	3.48	2.28	
Indication for operation			
Aortic regurgitation (%)	66.3	70.0	
Aortic stenosis (%)	45.4	28.7	
Associated aortic aneurysm/aortic root dilatation (%)	27.4	49.5	
Operative data			
Mean operation time (minutes)	252.8	249.7	0.31
Mean cardiopulmonary bypass time (minutes)	101.7	109.6	0.009
Mean aortic cross-clamp time (minutes)	76.1	78.0	0.28
Mean red blood cell transfused (U)	1.92	2.75	0.01
Conversion to full sternotomy (%)	1.53	N/A	
Concomitant procedure			
Aortic leaflet repair (%)	47.4	30.5	
Coronary artery bypass graft (%)	4.31	19.5	
Postoperative data			
Mean length of intensive care unit stay (days)	1.41	2.31	0.0009
Mean length of hospital stay (days)	6.81	7.66	0.03
Mean length of mechanical ventilation (days)	0.559	1.24	0.10
Re-exploration for bleeding (%)	4.62	5.30	0.28
Sternal wound infection (%)	0.335	0.206	0.96
Stroke (%)	0.850	0.799	0.90
Renal failure (%)	2.78	3.36	0.001
Operative mortality (%)	0.411	1.34	0.02

Abbreviations: BMI, body mass index; CARR, conventional aortic root replacement; COPD, chronic obstructive pulmonary disease; MIARR, minimally invasive aortic root replacement; N/A, not applicable.

causes of death for mortalities in their series, with one dying from low cardiac output syndrome, one from neurogenic shock due to generalised cerebral oedema, one from therapy-refractory ventricular fibrillation, and one from heart failure following a postoperative stroke [16,18].

Re-Exploration and Blood Transfusion Rates After Surgery

The incidence of re-exploration for bleeding and blood transfusion was reported by eight (2,765 patients) and four (693 patients) studies, respectively. Although the reported re-explorations rate was lower in those undergoing MIARR, this did not reach statistical significance (4.62% in MIARR vs 5.30% in CARR, p = 0.28; Figure 5). The mean red blood cells transfused were lower after MIARR when compared with CARR (1.92 ± 3.17U in MIARR vs 2.75 ± 5.64U in CARR, p = 0.01; Figure 6), but it is important to note that the denominator in this analysis was significantly smaller (286 and 407, respectively) than in previous analyses. Moreover, there was significant heterogeneity in the data (I^2 = 0.58, p = 0.03).

Neurologic Outcomes

Data on postoperative stroke was extracted from five of the eight included studies with a total of 2,083 patients. There was no significant difference in the rate of postoperative stroke following MIARR and CARR (0.85% in MIARR vs 0.8% in

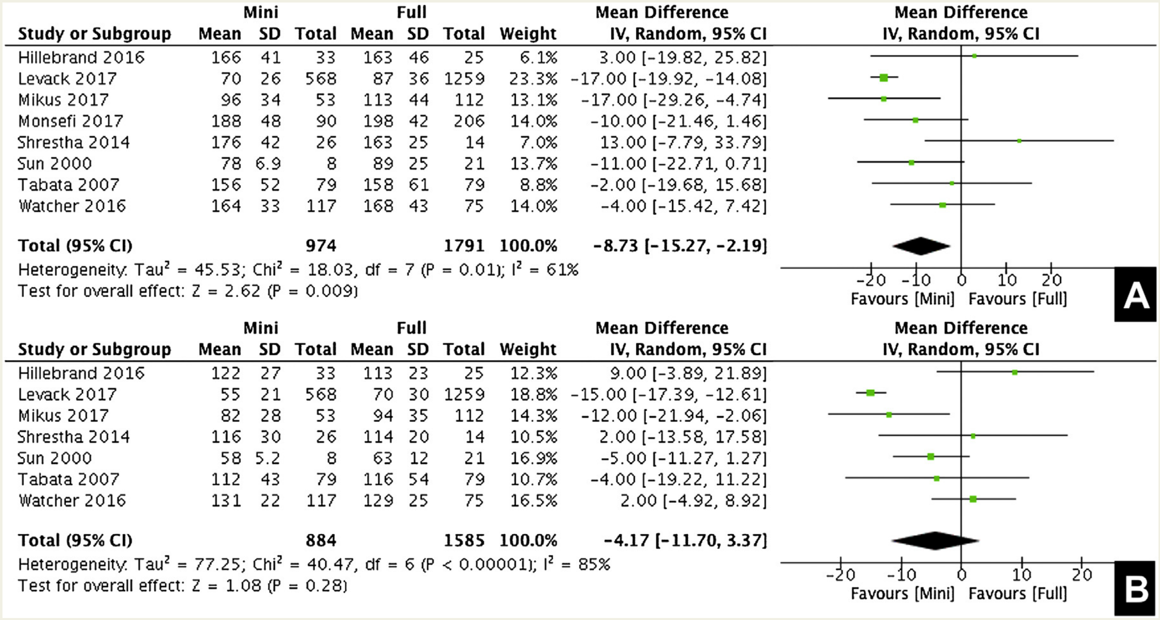

Figure 3 Forest plot of mean cardiopulmonary bypass (A) and aortic cross clamp time (B) of patients undergoing minimally invasive aortic root replacement (MIARR) vs conventional aortic root replacement (CARR) in included studies.
Abbreviations: CI, confidence interval; IV, inverse variance; SD, standard deviation.

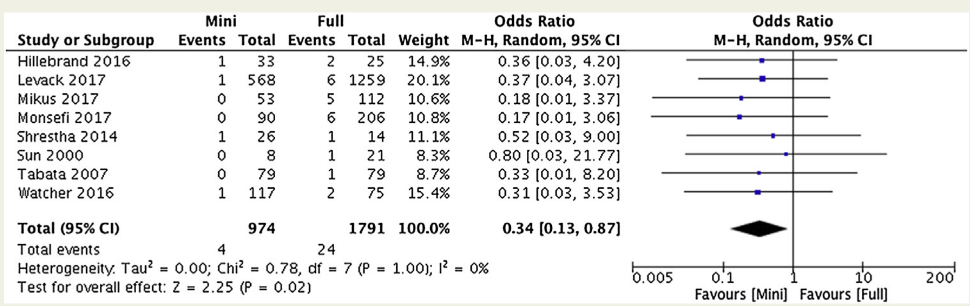

Figure 4 Forest plot of mortality rates in patients undergoing minimally invasive aortic root replacement (MIARR) vs conventional aortic root replacement (CARR) in included studies.
Abbreviations: CI, confidence interval; M-H, Mantel-Haenszel Test; SD, standard deviation.

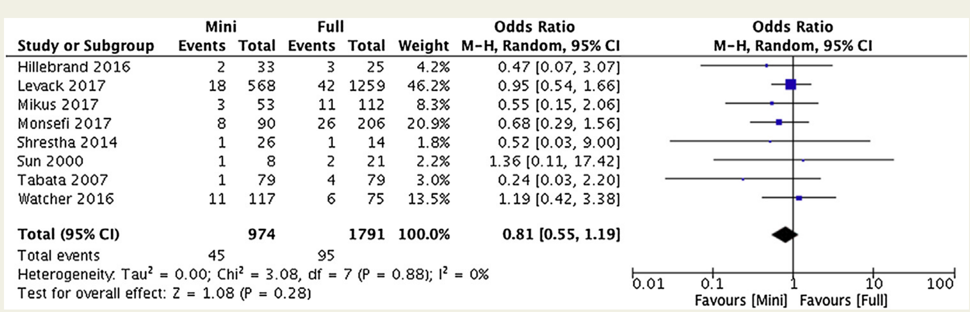

Figure 5 Forest plot of rate of re-exploration for bleeding in patients undergoing minimally invasive aortic root replacement (MIARR) vs conventional aortic root replacement (CARR) in included studies.
Abbreviations: CI, confidence interval; M-H, Mantel-Haeszel Test; SD, standard deviation.

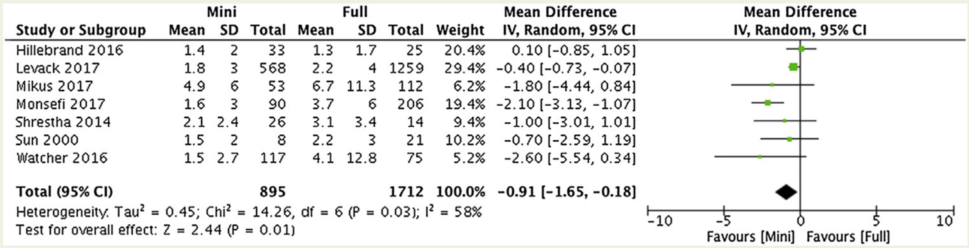

Figure 6 Forest plot of blood transfusion rates in patients undergoing minimally invasive aortic root replacement (MIARR) vs conventional aortic root replacement (CARR) in included studies.
Abbreviations: CI, confidence interval; IV, inverse variance; SD, standard deviation.

CARR, p = 0.90; Figure 7). The data was not significantly heterogeneous ($I^2 = 0.00$, p = 0.60). No other neurological deficit was specifically reported in any of the included studies.

Wound Infection and Renal Failure

Wound infection rates and the occurrence of postoperative renal failure requiring dialysis was reported by six (2,354 patients) and four (2,217 patients) studies, respectively. Whilst there was no significant difference in observed rates of wound infection (0.335% in MIARR vs 0.206% in CARR, p = 0.96; Figure 8), dialysis was more frequently required following CARR (2.78% in MIARR vs 3.36% in CARR, p = 0.001). Data for both variables were not significantly heterogeneous ($I^2 = 0.00$ (p = 0.50) and 0.00 (p = 0.47) respectively).

Duration of Ventilator Support, Intensive Care Stay and Total Hospital Stay

Postoperative mechanical ventilation times, intensive care stay and total hospital were extracted from four (455 patients), seven (2,607 patients), and seven (2,469 patients) studies, respectively. There was no difference in the mean length of mechanical ventilation (0.559 ± 1.28 days in MIARR vs 1.24 ± 3.46 days in CARR, p = 0.10). Nonetheless, there were small statistically significant differences in the mean length of intensive care stay (1.41 ± 1.75 days in MIARR vs 2.31 ± 2.28 days in CARR, p = 0.0009; Figure 9A) and mean total length of hospital stay (6.81 ± 3.76 days in MIARR vs 7.66 ± 4.41 days in CARR, p = 0.03; Figure 9B) favouring MIARR. Data for both variables were significantly heterogeneous ($I^2 = 0.70$ [p = 0.003] and 0.55 [p = 0.04], respectively). Duration of ventilator support analysis was, however, only based on a smaller denominator pool, highlighting the possibility of error secondary to a small sample size.

Discussion

Minimal access surgery is widely becoming a major area of research and commercial interest. Several original studies and meta-analyses of minimally invasive operations for valvular heart disease, particularly aortic and mitral valve surgery, have been published [1–3,5,20–23]. The number of studies evaluating the use of the minimal access incision in aortic root replacement surgery is significantly less with smaller sample sizes in each when compared to the studies published in aortic valve surgery. There is, therefore a clear need for an improved evidence base to help clinicians and patients make informed decisions. To the best of our knowledge, the present study represents the first meta-analysis evaluating comparative clinical outcomes of MIARR and CARR.

The most important finding of this study is that MIARR is a safe procedure that conferred a survival benefit with a clinically and statistically significantly reduced early mortality rate with no difference in risk of re-exploration, stroke, or wound infection when compared with CARR, the current standard of care. Although MIARR was associated with shorter CPB times, there was no statistically significant difference in ACx and total operation times. This could be attributed to performing more valve-sparing procedures

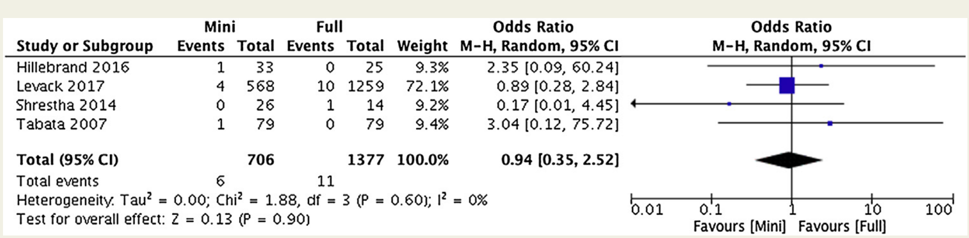

Figure 7 Forest plot of stroke rates in patients undergoing minimally invasive aortic root replacement (MIARR) vs conventional aortic root replacement (CARR) in included studies.
Abbreviations: CI, confidence interval; N-H, Mantel-Haenszel Test; SD, standard deviation.

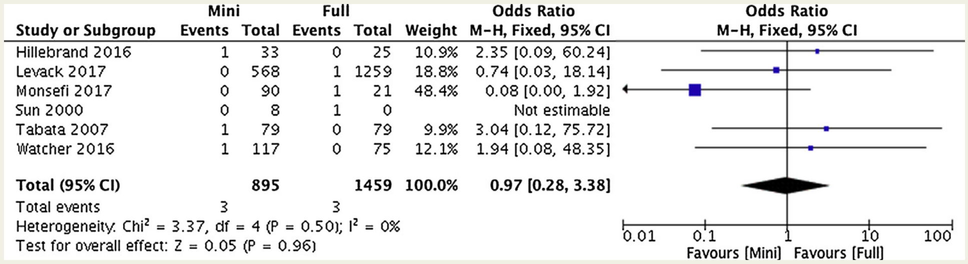

Figure 8 Forest plot of infection rates in patients undergoing minimally invasive aortic root replacement (MIARR) vs conventional aortic root replacement (CARR) in included studies.
Abbreviations: CI, confidence interval; M-H, Mantel-Haenszel Test; SD, standard deviation.

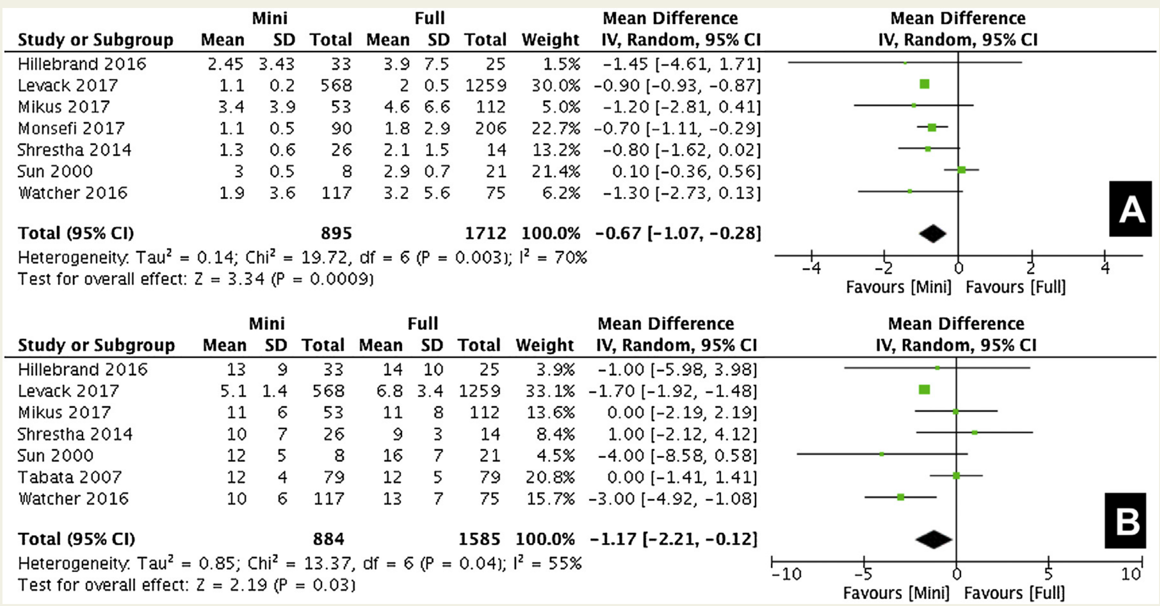

Figure 9 Forest plot of mean lengths of ICU (A) and total hospital (B) stays of patients undergoing minimally invasive aortic root replacement (MIARR) vs conventional aortic root replacement (CARR) in included studies.
Abbreviations: CI, confidence interval; IV, inverse variance; SD, standard deviation.

with full sternotomy, hence the longer CPB time. However, the surgical techniques were not clearly defined for the two groups in most papers. Thus, this cannot be said to be conclusively justifying this particular difference. Regardless, these were important findings pertinent to the postoperative outcomes. Aortic cross-clamp times in particular are known to increase the risk of severe cardiovascular morbidity by 1.4% per 1-minute increase and benefits of reduced ACx times are most clearly demonstrated in patients with impaired left ventricular ejection fraction and those with diabetes [24]. Analyses of operative, CPB and ACx times were, however, jeopardised by the presence of significant heterogeneity in CPB, ACx and total operative times. This heterogeneity can be attributed, in part, to the lack of standardisation of root procedures in included studies (combinations of valve sparing and valve replacement root procedures) with outcomes of various different types of root operations being reported collectively.

MIARR was associated with reduced blood transfusion use and shorter intensive care and in-hospital stay. This has been observed in minimally-invasive mitral valve surgery as well, as compared to conventional procedures [3]. Pain scores were not universally collected across all studies and those studies where pain data was collected, it had a lack of a clear, uniform pain scoring or pain management strategy nullifying the usefulness of pooled pain score estimates. Similarly, heterogeneity in cost calculations and reporting precluded cost data pooling and data synthesis.

Although MIARR was associated with reduced mortality, re-exploration rate, postoperative blood transfusion, and in-hospital stay and no difference in cross-clamp times, one must take into account the effect of the 'learning curve' when assessing the generalisability of these results. It is important to highlight that the greatest proportion of procedures were performed by centres with high experience in minimally invasive surgery and by experienced surgeons and, therefore, the exact of impact of the learning curve effect may not be clearly demonstrated [25]. Hence, extrapolating such data centres worldwide with either a low workload for root surgery or minimal experience with minimal access surgical techniques, is problematic. Shrestha et al. [13] particularly addressed the concern regarding the 'learning curve' effect. He advocates the use of a 'step-by-step' method of traversing this phenomenon in MIARR. Surgeons, by this method, should garner initial experience of minimally invasive cardiac surgery through performing simpler operations classically minimally invasive aortic valve replacements. After performing a large number of such procedures (>100 procedures) the surgeon can move to the next step in the form of isolated ascending aortic replacements and then finally progress to performing root replacements minimally invasively. Nonetheless, other studies on the learning curves of aortic valve surgeries yielded rather variable results [26,27]. As such, more studies in this area are needed before the effect of the learning curve may be commented on conclusively.

Data on length of intensive care stay and total hospital stay can, however, be used as a surrogate marker of cost as they have been shown to be major determinants of the cost of cardiac surgery [28,29]. In this study, we have shown small reductions in intensive care ($p = 0.0009$) and total length of stay ($p = 0.03$) but no statistically significant difference in ventilation times ($p = 0.10$). There was significant heterogeneity in length of intensive case and hospital stay which can be, in part, due to the lack of predefined and agreed protocols. As has been highlighted in previous studies of other minimally invasive operations [21], it is important to take into account the discrepancy in the reimbursement system, which varies from country to country, and institutional policy with regarding to early discharge.

Limitations

One of the most important limitations of this meta-analysis was the presence of significant heterogeneity in many of the variables analysed (7 out of 14). The possible reasons for these have been alluded to in previous sections. Overall, this represented significant differences in study designs and variable controlling, most prominently different surgical techniques. Studies had confirmed the influence of surgical techniques on intra-operative and postoperative outcomes [30,31]. Unfortunately, there was no clearly defined and stratified data of the distribution of cases with different surgical techniques and MIARR or CARR respectively, making detailed analysis of the influence of surgical techniques impossible.

Moreover, apart from one large single-centre observational study, all studies included in this meta-analysis had significantly smaller sample sizes. Moreover, several clinical outcomes were reported inconsistently across the studies therefore the denominator pool for such analyses. The largest study was therefore most heavily weighted and exerted most impact on the overall results.

Furthermore, not all variables were reported in all studies. Data on blood transfusion use, total operation times, and ventilation times were only extractable from smaller studies leading to a small denominator pool for their respective analyses. The lack of reportable statistical differences in total operation times and ventilation times may, therefore, be secondary to a type II error. It would be most useful if further studies could report on these important clinical outcomes consistently. An international clinical registry, akin to the International Registry of Acute Aortic Dissection, might well be useful [32].

In addition, blinding for patients, surgeons, and surgical staff was not exercised in all included studies. Although minimally invasive aortic valve replacement procedures have become more widespread, as highlighted earlier the learning curve for root operations is steeper and hence its widespread adoption has yet to be witnessed. Although this meta-analysis suggests favourable outcomes with MIARR, its application in included studies has been solely in the context of elective first-time root surgery. Emergency and reoperative scenarios still mandate surgery by the conventional full sternotomy.

Conclusion

Current evidence suggests that minimally invasive aortic root procedures are safe and effective alternatives to conventional full sternotomy aortic root replacement procedures in patients undergoing elective first-time operations. However, this is based on suboptimal non-randomised studies with significant heterogeneity and well-designed blinded prospective randomised studies are required to justify the use of such technique more often.

Disclaimer

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References

[1] Johnston DR, Atik FA, Rajeswaran J, Blackstone EH, Nowicki ER, Sabik JF, et al. Outcomes of less invasive J-incision approach to aortic valve surgery. J Thorac Cardiovasc Surg 2012;144:e3 852–8.

[2] Atik FA, Svensson LG, Blackstone EH, Gillinov AM, Rajeswaran J, Lytle BW. Less invasive versus conventional double-valve surgery: a propensity-matched comparison. J Thorac Cardiovasc Surg 2011;141:e4 1461–6.

[3] Svensson LG, Atik FA, Cosgrove DM, Blackstone EH, Rajeswaran J, Krishnaswamy G, et al. Minimally invasive versus conventional mitral valve surgery: a propensity-matched comparison. J Thorac Cardiovasc Surg 2010;139:e2 926–32.

[4] Woo YJ. Minimal-incision cardiac surgery. Introduction. Semin Thorac Cardiovasc Surg 2007;19:279–80.

[5] Phan K, Xie A, Di Eusanio M, Yan TD. A meta-analysis of minimally invasive versus conventional sternotomy for aortic valve replacement. Ann Thorac Surg 2014;98:1499–511.

[6] Javadikasgari H, Suri RM, Tappuni B, Gillinov AM. Minimally invasive mitral valve repair. Heart 2018;104:861–7.

[7] Glauber M, Ferrarini M, Miceli A. Minimally invasive aortic valve surgery: state of the art and future directions. Ann Cardiothorac Surg 2015;4:26–32.

[8] Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred Reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097.

[9] Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting: Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008–12.
[10] Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses n.d. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. (Accessed 15 August 2018).
[11] Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement Quality of Reporting of Meta-analyses. Lancet (London, England) 1999;354:1896–900.
[12] Sun L, Zheng J, Chang Q, Tang Y, Feng J, Sun X, et al. Aortic root replacement by ministernotomy: technique and potential benefit. Ann Thorac Surg 2000;70:1958–61.
[13] Shrestha M, Krueger H, Umminger J, Koigeldiyev N, Beckmann E, Haverich A, et al. Minimally invasive valve sparing aortic root replacement (David procedure) is safe. Ann Cardiothorac Surg 2015;4:148–53.
[14] Mikus E, Micari A, Calvi S, Salomone M, Panzavolta M, Paris M, et al. Mini-Bentall: an interesting approach for selected patients. Innov Technol Tech Cardiothorac Vasc Surg 2017;12:41–5.
[15] Levack MM, Aftab M, Roselli EE, Johnston DR, Soltesz EG, Gillinov AM, et al. Outcomes of a less-invasive approach for proximal aortic operations. Ann Thorac Surg 2017;103:533–40.
[16] Wachter K, Franke UFW, Yadav R, Nagib R, Ursulescu A, Ahad S, et al. Feasibility and clinical outcome after minimally invasive valve-sparing aortic root replacement. Interact Cardiovasc Thorac Surg 2016;24. ivw362.
[17] Tabata M, Khalpey Z, Aranki SF, Couper GS, Cohn LH, Shekar PS. Minimal access surgery of ascending and proximal arch of the aorta: a 9-year experience. Ann Thorac Surg 2007;84:67–72.
[18] Hillebrand J, Alshakaki M, Martens S, Scherer M. Minimally invasive aortic root replacement with valved conduits through partial upper sternotomy. Thorac Cardiovasc Surg 2018;66:295–300.
[19] Monsefi N, Risteski P, Miskovic A, Moritz A, Zierer A. Midterm results of a minimally invasive approach in David procedure. Thorac Cardiovasc Surg 2018;66:301–6.
[20] Brown ML, McKellar SH, Sundt TM, Schaff HV. Ministernotomy versus conventional sternotomy for aortic valve replacement: a systematic review and meta-analysis. J Thorac Cardiovasc Surg 2009;137:670–9. e5.
[21] Shehada S-E, Elhmidi Y, Mourad F, Wendt D, El Gabry M, Benedik J, et al. Minimal access versus conventional aortic valve replacement: a meta-analysis of propensity-matched studies†. Interact Cardiovasc Thorac Surg 2017;25:624–32.
[22] Phan K, Zhou JJ, Niranjan N, Di Eusanio M, Yan TD. Minimally invasive reoperative aortic valve replacement: a systematic review and meta-analysis. Ann Cardiothorac Surg 2015;4:15–25.
[23] Modi P, Hassan A, Chitwood WR. Minimally invasive mitral valve surgery: a systematic review and meta-analysis. Eur J Cardio-Thoracic Surg 2008;34:943–52.
[24] Ranucci M, Frigiola A, Menicanti L, Castelvecchio S, de Vincentiis C, Pistuddi V. Aortic cross-clamp time, new prostheses, and outcome in aortic valve replacement. J Heart Valve Dis 2012;21:732–9.
[25] Hughes GC, Zhao Y, Rankin JS, Scarborough JE, O'Brien S, Bavaria JE, et al. Effects of institutional volumes on operative outcomes for aortic root replacement in North America. J Thorac Cardiovasc Surg 2013;145:166–70.
[26] Murzi M, Cerillo AG, Gilmanov D, Concistrè G, Farneti P, Glauber M, et al. Exploring the learning curve for minimally invasive sutureless aortic valve replacement. J Thorac Cardiovasc Surg 2016;152: e1 1537–4.
[27] Murzi M, Cerillo AG, Bevilacqua S, Gilmanov D, Farneti P, Glauber M. Traversing the learning curve in minimally invasive heart valve surgery: a cumulative analysis of an individual surgeon's experience with a right minithoracotomy approach for aortic valve replacement. Eur J Cardio-Thoracic Surg 2012;41:1242–6.
[28] Hamilton A, Norris C, Wensel R, Koshal A. Cost reduction in cardiac surgery. Can J Cardiol 1994;10:721–7.
[29] Doll N, Borger MA, Hain J, Bucerius J, Walther T, Gummert JF, et al. Minimal access aortic valve replacement: effects on morbidity and resource utilization. Ann Thorac Surg 2002;74:S1318–22.
[30] Khaladj N, Leyh R, Shrestha M, Peterss S, Haverich A, Hagl C. Aortic root surgery in septuagenarians: impact of different surgical techniques. J Cardiothorac Surg 2009;4:17.
[31] Badiu CC, Deutsch MA, Sideris C, Krane M, Hettich I, Voss B, et al. Aortic root replacement: comparison of clinical outcome between different surgical techniques. Eur J Cardio-Thoracic Surg 2014;46:685–92.
[32] Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL, et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. JAMA 2000;283:897–903.