Systematic Review

Robotic versus conventional sternotomy mitral valve surgery: a systematic review and meta-analysis

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Background: Robotic-assisted mitral valve surgery (RMVS) is becoming an increasingly performed procedure in cardiac surgery, however, its true safety and efficacy compared to the gold standard conventional sternotomy approach [conventional sternotomy mitral valve surgery (CSMVS)] remains debated. The aim of this meta-analysis was to provide a comprehensive analysis of all available literature comparing RMVS to CSMVS.

Methods: An electronic search of five databases was performed to identify all relevant studies comparing RMVS to CSMVS. Pre-defined primary outcomes of interest included all-cause mortality, cerebrovascular accidents (CVA) and re-operation for bleeding. Secondary outcomes of interest included cross clamp time, cardiopulmonary bypass (CPB) time, intensive care unit (ICU) and hospital length of stay (LOS), post-operative atrial fibrillation (POAF) and red blood cell (RBC) transfusion.

Results: The search strategy identified fourteen studies qualifying for inclusion in this meta-analysis comparing RMVS to CSMVS. The outcomes of 6,341 patients (2,804 RMVS and 3,537 CSMVS) were included. RMVS had significantly lower mortality when compared to CSMVS group in both the unmatched [odds ratio (OR) 0.33; 95% confidence interval (CI): 0.19–0.57; P<0.001] and matched cohorts (OR 0.35; 95% CI: 0.15–0.80; P=0.01). There was no significant difference in rates of CVA or re-operation for bleeding between the two groups in either the entire included cohort or matched patients. CSMVS had significantly shorter cross clamp time by 28 minutes (95% CI: 19.30–37.32; P<0.001) and CPB time by 49 minutes (95% CI: 36.16–61.01; P<0.001) which remained significantly shorter in the matched cohorts. RMVS had shorter ICU [mean difference (MD) 26 hours; 95% CI: −34.31 to −18.52; P<0.001] and hospital LOS (MD 2 days; 95% CI: −2.66 to −1.37; P<0.001), which were again both significantly shorter in the matched cohort. RMVS group also had fewer RBC transfusions (OR 0.44; 95% CI: 0.28–0.70; P<0.001).

Conclusions: Current evidence on comparative outcomes of RMVS and CSMVS is limited with only low-quality studies currently available. This present meta-analysis suggests that RMVS may have lower mortality and shorter ICU and hospital LOS, however CSMVS may be associated with significantly shorter cross clamp and CPB times. Further analysis of high-quality studies with randomized data is required to verify these results.

Keywords: Mitral valve disease; mitral valve repair; mitral valve replacement; robotic cardiac surgery; robotic mitral valve surgery; conventional sternotomy

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Introduction

Robotic-assisted mitral valve surgery (RMVS) is an evolving technique under the umbrella of minimally invasive valve surgery, so developed out of a need for a less traumatic approach in comparison to the traditional sternotomy. Conventional sternotomy mitral valve surgery (CSMVS), however, remains the gold standard given the unhindered exposure, visual access, and procedural control over instrumentation in the operative site.

Minimally invasive mitral valve surgery, first pioneered by Carpentier and Chitwood in the mid to late-1990s (1), has developed over the subsequent two decades, and allowed cardiac surgeons to circumvent the need for conventional sternotomy at the expense of the degree of access and control these techniques allow. The various techniques developed for performing minimally invasive mitral valve surgery range from partial sternotomy, port-access thoracoscopic, right mini-thoracotomy, and RMVS (2). Although the benefits of minimally invasive surgery over CSMVS are incompletely understood, they are suggested to include better cosmesis, shorter lengths of hospital stay and use of fewer blood products without a significant difference in morbidity and mortality compared to conventional sternotomy (3-5). The downfalls of these more minimally invasive procedures have been consistently related to prolonged operative times which have been attributed to the steep learning curve that minimally invasive mitral valve surgery entails (6).

RMVS, although limited to highly specialized centers, has been undertaken internationally and hopes to boast similar perioperative benefits over traditional approaches; however, evidence for this has been largely limited to single-center studies, and long-term outcome data remains scarce. A 2015 meta-analysis of six retrospective studies performed by Cao *et al.* showed superior perioperative mortality for RMVS candidates but similar hospitalization and intensive care unit (ICU) stay rates (7). A recent meta-analysis by Takagi *et al.* analyzed seven propensity-matched studies comparing robotic and conventional sternotomy patients undergoing mitral valve surgery, and conversely found that ICU and hospital length of stay (LOS) were shorter in the robotic group with similar all-cause short-term mortality between the two groups (8). Both of these studies were constrained by the small volume of literature to appraise effectively and systematically. Additionally, the meta-analysis by Takagi *et al.* included a study which performed a population-based analysis using the National Inpatient Sample database (United States of America) comparing robotic mitral valve repair to non-robotic repair (9). The non-robotic cohort in this study was unable to be further differentiated by surgical approach, and thus included patients who underwent full sternotomy, partial sternotomy and minimally invasive mitral valve repair, therefore introducing bias to the results of that meta-analysis.

Since publication of these two meta-analyses, several single-center analyses have been performed comparing the surgical outcomes of RMVS and CSMVS. The purpose of this study is to perform a comprehensive and rigorous meta-analysis comparing the short-term outcomes of robotic and conventional sternotomy approaches for mitral valve surgery.

Methods

The methods for this meta-analysis adhered to the recommendations and guidelines set forth in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) updated Statement (10).

Literature search strategy

Five electronic databases were used to perform the literature search including Ovid MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CCRCT), Cochrane Database of Systematic Reviews (CDSR), and Database of Abstracts of Review of Effectiveness (DARE). These databases were searched from their inception to 12th March 2022. The search strategy included a combination of keywords and Medical Subject Headings (MeSH) including "Sternotomy" AND "Robotic" OR "Robo*" AND "Mitral valve" AND "Repair" OR "Replacement" OR "Annuloplasty". Reference lists from previous systematic reviews, meta-analyses and included articles were also

reviewed to ensure no additional publications were missed.

Study selection

Study eligibility for inclusion in this systematic review and meta-analysis included those which directly compared RMVS (repair or replacement) to those via conventional full median sternotomy for mitral valve disease. For this meta-analysis, cohorts that were either mixed without reporting separate outcomes, or those comparing partial sternotomy or minimally invasive right anterior thoracotomy mitral valve surgery to the robotically assisted approach were excluded. Studies assessing full cohorts comprised of patients undergoing redo-mitral valve surgery (either by conventional sternotomy or robotic approach) were excluded. If centers reported outcomes of overlapping patient series with either larger cohort size or extended follow-up, the most complete, contemporary series was included for analysis. Included studies were limited to those in English, unless data was easily extractable, and only those involving human subjects. Abstracts, case reports, conference presentations, editorials and reviews were excluded. Title and abstract screening followed by full-text review to determine included studies was performed independently by two reviewers (ML Williams and J Brookes) with any discrepancies discussed until consensus reached.

Outcomes of interest

The primary outcomes of interest were in-hospital/30-day mortality, cerebrovascular accidents (CVA) and re-operation for bleeding. Secondary outcomes of interest included standard operative and post-operative outcomes of interest, for example, renal insufficiency, post-operative atrial fibrillation (POAF), cross clamp time, cardiopulmonary bypass (CPB) time, length of ICU and hospital stay, and post-operative echocardiography results.

Data extraction

For all included studies, two independent reviewers (B Hwang and L Huang) extracted data directly from the reviewed text, tables and/or figures. All extracted data was checked by a senior author (ML Williams) independently, with any discrepancies reviewed, and consensus reached through means of discussion among all three reviewers. Where any indistinct or insufficient data was encountered, attempts were made to clarify these from corresponding authors of the included studies, if required. A priori subgroup analysis was to be performed on matched cohort data separately, therefore, this data was extracted separately to the larger unmatched cohort, where reported.

Statistical analysis

Meta-analysis of means or proportions was performed for categorical and continuous variables, as appropriate, to pool the patient characteristics across the included studies. To facilitate this statistical pooling, the methods described by Wan and colleagues were used to calculate means and standard deviations from the median (with range or interquartile range), where reported (11). This meta-analysis of proportions or means was conducted using Stata (version 17.0, StataCorp, Texas, USA) using a random effects model to account for the different patient populations in the included studies.

Comparative meta-analysis of operative and post-operative variables/outcomes was performed using Review Manager (Version 5.4, Cochrane Collaboration, Software Update, Oxford, United Kingdom). Again, where required for continuous data reported as median values (with range or interquartile range), the mean and standard deviation were estimated using the methods described by Wan *et al.* (11). A random effects model was used given variation would be present in terms of differing center/surgeon experience, different procedures (repair/replacement), and different operative and management protocols across the included studies. Summary measures were expressed as odds ratios (OR) for dichotomous variables and differences in mean (MD) for continuous data, as appropriate. Data significance and heterogeneity were assessed using the Cochrane Q statistic and the I^2 test statistic respectively, with significance set at P value <0.05. Thresholds for heterogeneity significance for I^2 values were considered as low, moderate and high heterogeneity at 0–49%, 50–74% and ≥75%, respectively (12). Publication bias was assessed through visual inspection of generated funnel plots.

Study quality appraisal

Study quality of the included studies was assessed using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool (13). This quality appraisal tool assesses bias in seven domains, including: bias due to confounding, selection of participants into study, classification of

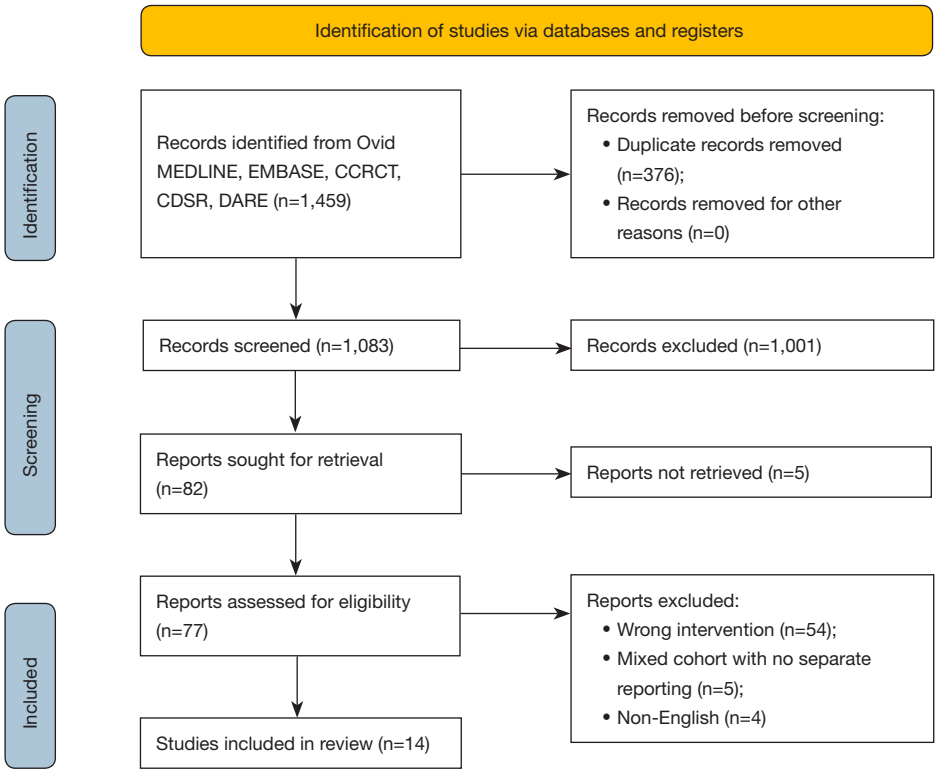

Figure 1 PRISMA flow-chart summarizing the search strategy for relevant publications. CCRCT, Cochrane Central Register of Controlled Trials; CDSR, Cochrane Database of Systematic Reviews; DARE, Database of Abstracts of Review of Effectiveness; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

interventions, deviations from intended interventions, missing data, measurement of outcomes and selection of the reported result. Using this tool, and assessing the seven domains of bias above, each study can then be classified as either low, moderate, serious or critical risk. Quality appraisal was undertaken independently by two investigators (B Hwang and ML Williams), with any discrepancies rectified through means of discussion until consensus was reached.

Results

The literature search identified a total of 1,459 articles (*Figure 1*). After exclusion of duplicates and title/abstract screening to remove irrelevant studies, 82 articles were deemed appropriate to undergo full-text review. After full-text review, 68 studies were excluded due to not meeting the inclusion criteria. Therefore, fourteen studies remained which fulfilled the pre-determined inclusion criteria (14-27), including a total of 6,341 patients of which 2,804 underwent RMVS and 3,537 patients underwent CSMVS.

Study characteristics

Of the fourteen included studies, thirteen were retrospective comparative studies (15-27) with the fourteenth paper not reporting exactly how the data accrual and analysis were performed (14) (*Table 1*). Eight studies either included or had separate data for matched patient cohorts, seven of which specifically indicated propensity score matching (PSM) (15,17,19,20,24,25,27), with the eighth study reporting that both cohorts were "matched" retrospectively with no statistical difference in any of the listed patient demographic data in the two cohorts (16). These eight studies included a total of 1,323 matched patients across both the robotic and conventional sternotomy groups. One of the included studies was published in Chinese, however, the published abstract and data listed in tables/figures within the text were in English and therefore included in this meta-analysis due to sufficiently meeting the inclusion

Table 1 Study characteristics

Primary author	Year	Country	Institution(s)	Study period	Type of study	Robotic (n)	Sternotomy (n)	Follow-up time (months), mean ± SD
Chemtob	2020	USA	Cleveland Clinic, Cleveland, Ohio	2014–2019	NR	605	395	NR
Coyan	2018	USA	University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania and West Virginia University, Morgantown, West Virgina	2013–2015	Retrospective PSM multicenter-center	91	91	12
Folliguet	2006	France	Institute Mutualiste Montsouris, Paris	2000–2005	Retrospective matched single-center	25	25	24
Hawkins	2018	USA	The Virginia Cardiac Services Quality Initiative (VCSQI) Database	2011–2016	Retrospective multi-center*	372	1,352	NR
Kam	2010	Australia	Epworth Hospital, Melbourne, Australia	2005–2008	Retrospective single-center	107	40	NR
Kesävuori	2018	Finland	University Central Hospital, Helsinki	2011–2015	Retrospective PSM single-center	142	142	35±17 robotic, 64±35 sternotomy
Mihaljevic	2011	USA	Cleveland Clinic, Cleveland, Ohio, USA	2006–2009	Retrospective PSM single-center	106	106	NR
Seo	2019	USA	University of California, Los Angeles, California	2008–2016	Retrospective single-center	175	259	NR
Sicim	2021	Turkey	University of Health Sciences, Gulhane Training and Research Hospital, Ankara	2014–2020	Retrospective single-center	64	66	NR
Stevens	2012	USA	East Carolina University Hospital, Greenville, North Carolina, USA	1992–2009	Retrospective single-center	447	377	76.8±54
Suri	2011	USA	Mayo Clinic, Rochester, Minnesota	2007–2010	Retrospective PSM single-center	95	95	1
Wang	2018	USA	Duke University Medical Center, Durham, North Carolina-The Society of Thoracic Surgeons (STS) database	2011–2014	Retrospective PSM multi-center database	503	503	21.36 (11.52–30.96)**
Woo	2006	USA	University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania	2002–2005	Retrospective single-center	25	39	NR
Zhao	2020	China	General Hospital of PLA, Beijing	2002–2014	Retrospective PSM single-center	47	47	6

*, study also includes PSM cohorts; **, median and interquartile range. n, number of patients; SD, standard deviation; NR, not report; PSM, propensity score matched.

Figure 2 Risk of bias assessment of included studies utilising the ROBINS-I tool. ROBINS-I, Risk Of Bias in Non-randomized Studies of Interventions.

criteria (27). The quality of the included studies, which was assessed using the ROBINS-I tool, was deemed to be moderate risk of bias in nine of the included studies (14-17,19,20,24,25,27) and serious risk of bias in the other five included studies (18,21-23,26) (*Figure 2*).

Patient baseline characteristics

The pooled mean age of patients who underwent RMVS was 63.5 years, slightly younger than those patients which had conventional sternotomy approach, who had a pooled mean age of 64.6 years (*Table 2*). Both groups had a slight male predominance with 65.5% and 61.8% of patients being male in the RMVS and CSMVS groups, respectively. Just under half of the patients in both groups had a history of hypertension (43.4% and 46.7% for RMVS and CSMVS groups, respectively). The RMVS and CSMVS groups had pooled mean pre-operative left ventricular ejection fraction of 61.5% and 60.5%, respectively. More patients were in New York Heart Association (NYHA) classification class III/IV in the CSMVS group compared to the RMVS group (26.8% and 19.4%, respectively). Myxomatous degenerative mitral valve disease was the main pathology of the mitral valve in both the RMVS and CSMVS groups with 94.6% and 90.5%, respectively. Full break down of underlying mitral valve pathology for surgery for each study can be seen in Table S1. Other pooled patient baseline characteristics can be seen in *Table 2*. The pooled patient characteristics for the matched patient cohorts can be seen in Table S2.

Operative details

Where reported, the operative technique for the RMVS was performed through a varying 2- to 5-centimeter anterolateral mini-thoracotomy and varying number of other access ports. Eleven studies reported the robotic

Table 2 Pooled baseline characteristics for all included studies

Variable	Robotic (n=2,804)	Sternotomy (n=3,537)
Age (years), mean	63.5	64.6
Male, %	65.5	61.8
BMI (kg/m^2), mean	26.0	26.5
Hypertension, %	43.4	46.7
Diabetes, %	4.6	7.8
Cerebrovascular disease, %	3.0	4.8
Respiratory disease, %	4.6	8.2
LVEF, mean	61.5	60.5
Cardiac arrhythmia, %	13.9	18.4
PVD, %	3.4	3.7
NYHA III/IV, %	19.4	26.8
Valve pathology—myxomatous degeneration, %	94.6	90.5

BMI, body mass index; LVEF, left ventricular ejection fraction; PVD, peripheral vascular disease; NYHA, New York Heart Association.

surgical platform used (14-16,18,19,21-24,26,27), all of which used the da Vinci® Surgical System (Intuitive Surgical Inc., Sunnyvale, California, USA). Ten of the fourteen included studies reported the robotic cross clamp method. Five reported using solely a transthoracic aortic cross clamp (14-16,22,24), while the other five studies either reported using endoaortic balloon or a transthoracic aortic cross clamp (19,20,23,25,26). Nine studies reported details on cardioplegia delivery with four utilizing antegrade cardioplegia delivery only (14,16,22,24) and five studies reporting using antegrade and/or retrograde cardioplegia (19,20,23,25,26). Most procedures on the mitral valve were a mitral valve repair with 93.8% of patients in the RMVS group and 71.0% of the CSMVS group receiving a mitral valve repair. Concomitant surgical procedures such as left atrial appendage ligation, atrial fibrillation ablation and atrial septal defect closures were reported in seven studies (15,17,19,20,23-25). Eight studies reported events involving intra-operative conversion to sternotomy/thoracotomy (14-17,19-21,24). Forty-three patients across these eight studies converted to larger access incision out of a total 1,766 patients (2.4% conversion rate). Further information on the procedural details, mitral valve repair techniques and concomitant surgical procedures can be found in Table S3.

Mortality

All fourteen studies reported data on all-cause perioperative mortality, however, five studies had no deaths in either cohort. In total, there were 101 deaths (1.6%), of which 16 (0.6%) were in the RMVS group and 85 (2.4%) in the CSMVS. This resulted in a significant difference in all-cause mortality favoring the RMVS group [OR 0.33; 95% confidence interval (CI): 0.19–0.57; P<0.0001, I^2=0%] (*Figure 3A*). When assessing in-hospital all-cause mortality in the matched cohort, a significant difference remained in all-cause mortality favoring the RMVS group (OR 0.35; 95% CI: 0.15–0.80; P=0.01, I^2=0%) (Figure S1A). There was no evidence of publication bias on visual inspection of funnel plots.

CVA

CVA events were reported in twelve of the included studies, however, the distinction between transient ischemic attacks (TIA) and permanent strokes were heterogeneously reported so all CVA events were combined. There was a notable difference favoring the RMVS group in regards to rates of CVAs, however, this did not reach statistical significance (OR 0.62; 95% CI: 0.38–1.01; P=0.06, I^2=0%) (*Figure 3B*). When examining rates of CVAs in the matched cohorts (all eight studies), this difference was less noticeable (OR 0.84; 95% CI: 0.43–1.66; P=0.62, I^2=0%) (Figure S1B). There was no evidence of publication bias on visual inspection of funnel plots.

Re-operation for bleeding

Rates of re-operation for bleeding were reported in all fourteen studies with 77 patients (2.7%) and 90 patients (2.5%) in the RMVS and CSMVS groups, respectively, requiring re-operation for bleeding. There was no significant difference between the groups in either the total included patients (OR 1.10; 95% CI: 0.79–1.53; P=0.56, I^2=0%) (*Figure 3C*) or matched cohorts (OR 1.28; 95% CI: 0.80–2.03; P=0.30, I^2=0%) (Figure S1C). On visual inspection of generated funnel plots, there was no evidence of publication bias.

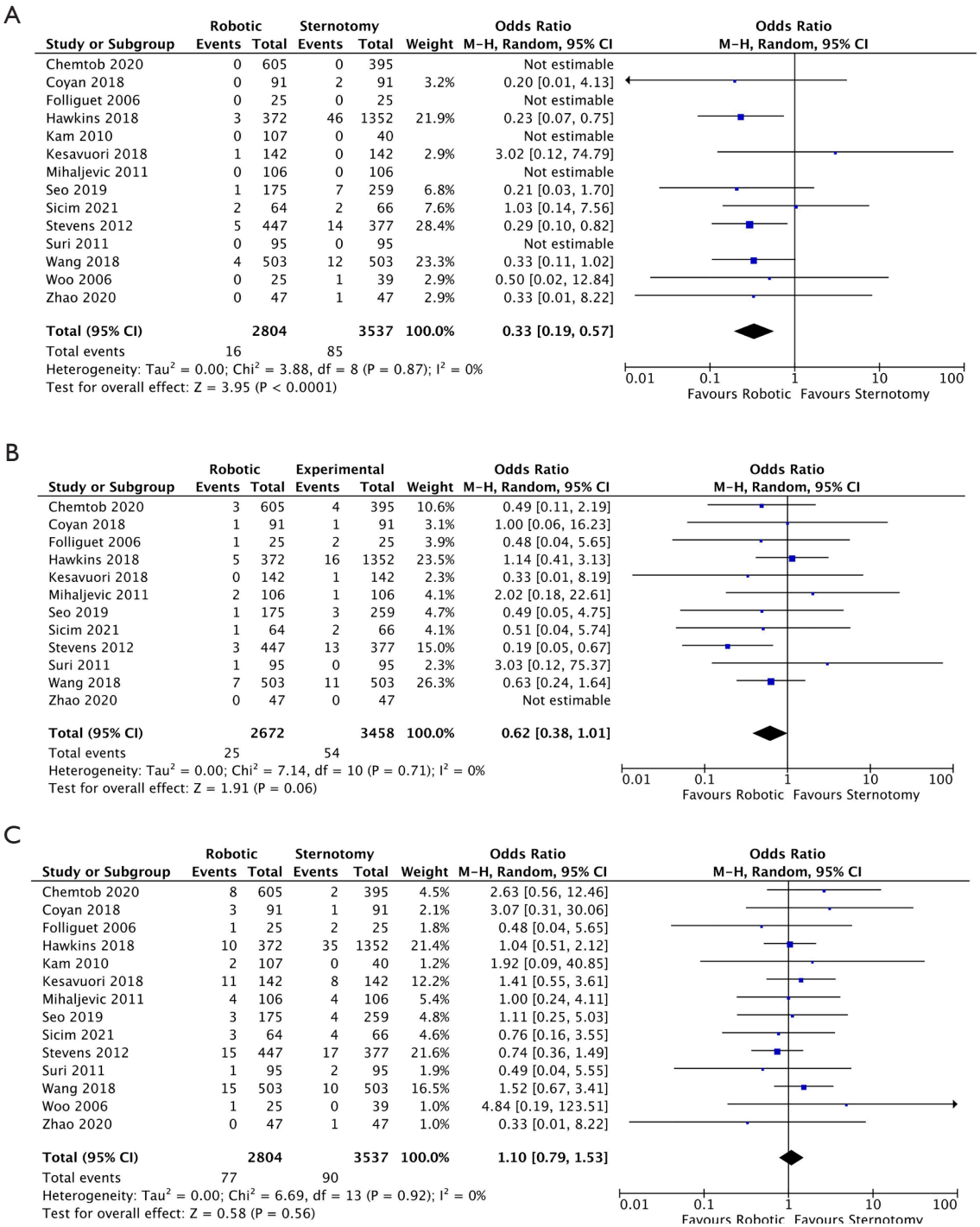

Figure 3 Forest plot of OR for all-cause mortality (A), CVA (B), and re-operation for bleeding (C) for robotic versus conventional sternotomy mitral valve surgery. M-H, Mantel-Haenszel test; CI, confidence interval; OR, odds ratio; CVA, cerebrovascular accidents.

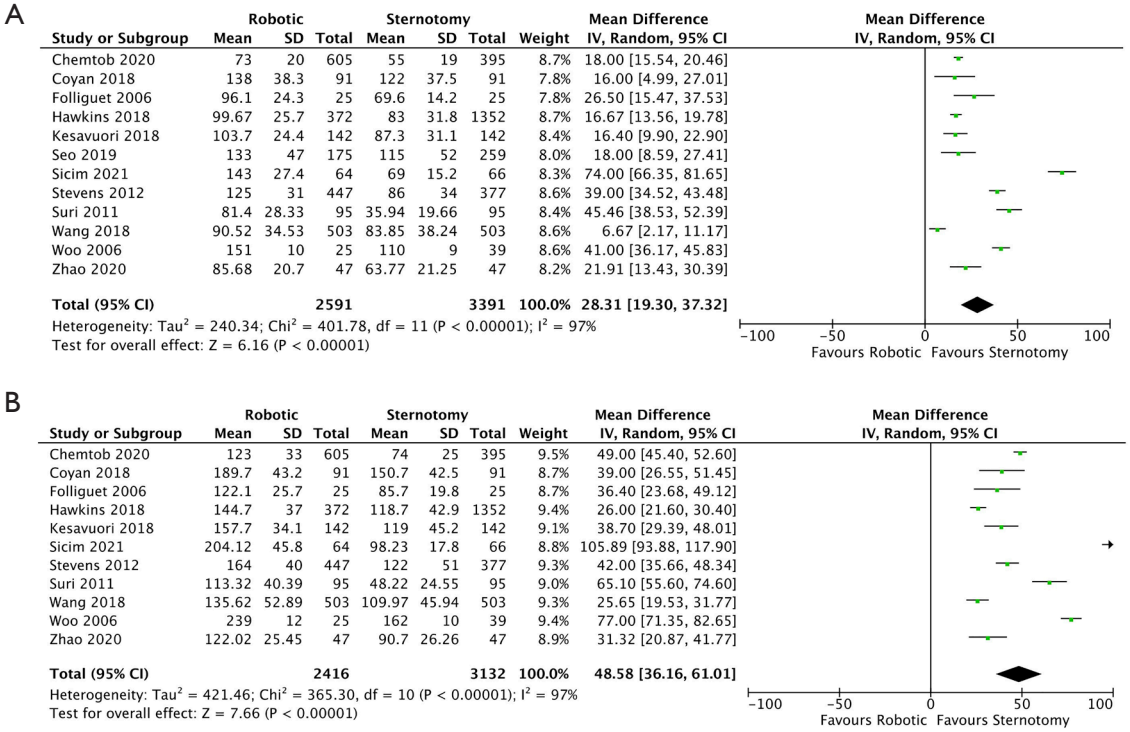

Figure 4 Forrest plot of MD for cross clamp (A), and CPB times (B) for robotic versus conventional sternotomy mitral valve surgery. MD, mean difference; CPB, cardiopulmonary bypass; SD, standard deviation.

Secondary outcomes

Sufficient data regarding cross clamp times were reported in twelve of the included studies (14-17,19,21-27). There was a significantly shorter cross clamp time by 28.31 minutes for patients who underwent CSMVS compared with RMVS (95% CI: 19.30–37.32; P<0.00001, I^2=97%) (*Figure 4A*). When assessing matched patient data from seven studies (15-17,19,24,25,27) there remained a statistically significant shortened cross clamp time by 21.54 minutes (95% CI: 12.08–31.00; P<0.00001, I^2=93%) (Figure S2A), favoring the CSMVS group. There was no evidence of publication bias on visual inspection via funnel plots.

CPB times were reported in eleven of the included studies totaling 5,548 patients (2,416 and 3,132 for RMVS and CSMVS, respectively). The MD between the two groups was statistically significant at 48.58 minutes favoring the CSMVS group (95% CI: 36.16–61.01; P<0.00001, I^2=97%) (*Figure 4B*). Seven studies (15-17,19,24,25,27) reported CPB times for matched patient cohorts and had a shorter MD of 37.81 minutes, favoring the CSMVS group, which was again statistically significant (95% CI: 28.04–47.58; P<0.00001, I^2=88%) (Figure S2B). On visual inspection of generated funnel plots, there was no evidence of publication bias.

Data regarding post-operative renal insufficiency was reported in eight studies (14,15,17,21,22,24,25,27). Only 0.7% of RMVS patients suffered from post-operative renal insufficiency, compared to 2.4% of CSMVS patients, resulting in a statistically significant difference between the two groups (OR 0.39; 95% CI: 0.21–0.73; P=0.003, I^2=0%) (Figure S3) favoring the RMVS group. There was no evidence of publication bias on visual inspection via funnel plots.

Nine studies reported data on POAF with 25.2% of RMVS patients and 28.3% of CSMVS patients experiencing POAF. When examining the data from the nine studies there was a noticeable difference favoring the RMVS group, however this did not reach statistical significance; importantly, there was a moderate amount of heterogeneity noted (OR 0.81; 95% CI: 0.65–1.01; P=0.06, I^2=57%) (Figure S4A). When examining matched cohort data from the five studies reporting POAF data, there was a significant difference favoring the RMVS group (OR 0.73; 95% CI:

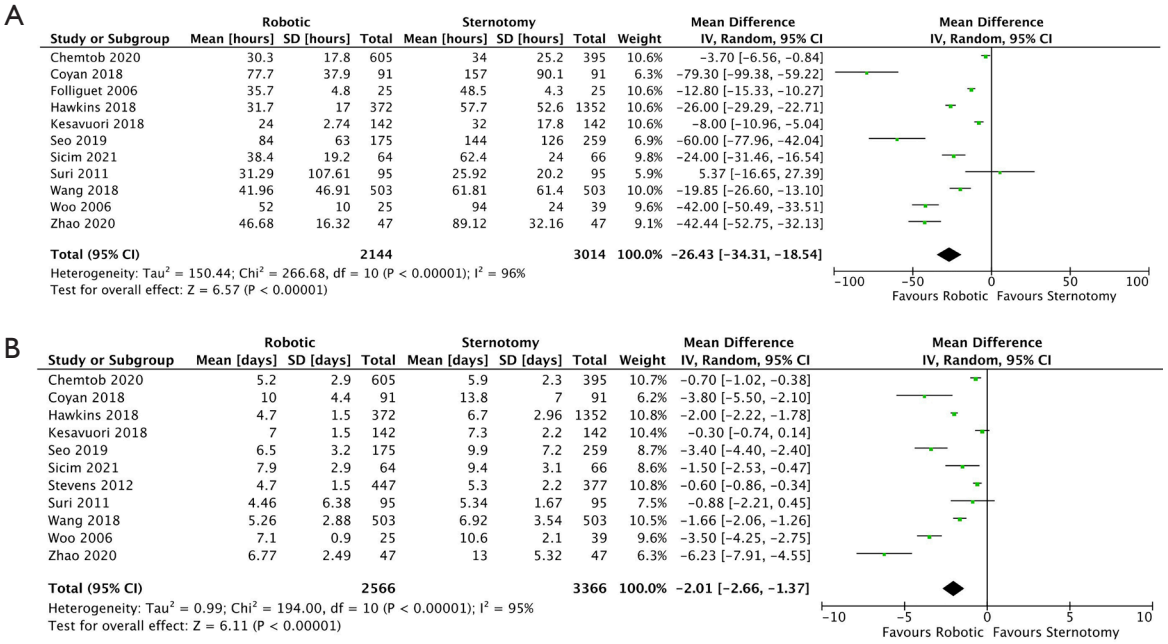

Figure 5 Forrest plot of MD for ICU stay (hours) (A), and length of hospital stay (days) (B) for robotic versus conventional sternotomy mitral valve surgery. ICU, intensive care unit; MD, mean difference; SD, standard deviation.

0.56–0.95; P=0.02, I^2=31%) (Figure S4B) with only a low level of heterogeneity. On visual inspection of generated funnel plots, there was no evidence of publication bias.

ICU LOS data was reported in eleven of the fourteen studies (14-17,19,21,22,24-27). ICU stay was significantly shorter by 26.43 hours (95% CI: −34.31 to −18.54; P<0.00001, I^2=96%) (*Figure 5A*) in the RMVS group compared with the CSMVS group. Matched cohort data regarding ICU LOS was available in seven studies (15-17,19,24,25,27). Again, there was a significantly shortened ICU length of admission in the RMVS group by 21.18 hours (95% CI: −29.20 to −13.16; P<0.00001, I^2=93%) (Figure S5A). There was no evidence of publication bias on visual inspection via funnel plots.

Eleven of the included studies reported data on total hospital LOS (14,15,17,19,21-27), six of which contained matched patient data (15,17,19,24,25,27). Hospital LOS was significantly shorter in the RMVS group compared to the CSMVS group by 2.01 days (95% CI: −2.66 to −1.37; P<0.00001, I^2=95%) (*Figure 5B*). When examining matched patient data, a significant difference between the two groups remained, with RMVS group having 1.90 days (95% CI: −2.85 to −0.95; P<0.0001, I^2=93%) shorter admission than the CSMVS group (Figure S5B). There was no evidence of publication bias on visual inspection via funnel plots.

Red blood cell transfusion (RBC) data was reported in nine studies (14,16,17,19-21,23-25). There was a significant difference between the two groups (OR 0.44; 95% CI: 0.28–0.70; P=0.0004, I^2=89%) (Figure S6A) favoring the RMVS group. This difference remained when assessing only patient-matched cohort data regarding RBC transfusion with lower heterogeneity (OR 0.65; 95% CI: 0.45–0.92; P=0.02, I^2=54%) (Figure S6B). There was no evidence of publication bias on visual inspection via funnel plots.

Ventilator time was reported in seven studies with only a total of 994 patients (489 patients RMVS group and 505 patients CSMVS group). The MD between the two groups was 2.6 hours, however, this did not reach statistical significance (95% CI: −6.74 to 1.49; P=0.21, I^2=96%) (Figure S7).

Data regarding immediate post-operative or follow-up echocardiography results quantifying mitral regurgitation was reported in ten of the included studies (14-16,18-21,24-26). Due to either the inconsistent or heterogeneously reported data, statistical analysis was not performed. Most patients (where reported) in both the RMVS and CSMVS groups had no/trace/mild mitral regurgitation post-operatively. There was limited follow-

up echocardiography data reported in the included studies and where reported high numbers were lost to follow-up. Further details on post-operative echocardiography results can be found in Table S4.

Discussion

Minimally invasive approaches in cardiac surgery are becoming increasingly popular in the attempt to reduce short-term morbidity, and improve cosmesis and return to baseline functionality. However, the safety and efficacy of these minimally invasive approaches, especially in the field of mitral valve surgery, when compared to the gold standard surgical approach through full median sternotomy, remains debated. RMVS, especially robotic mitral valve repair, has more recently had excellent reported outcomes in large volume centers (28,29). However, due to the steep learning curve/operative complexity and higher associated costs, the uptake of robotically assisted approaches in mitral valve surgery has not been widely disseminated (30).

The aim of this meta-analysis was to provide the most updated and comprehensive review of all comparative studies in the existing literature comparing RMVS to CSMVS. Several meta-analyses have previously compared minimally invasive mitral valve surgery (mini-thoracotomy, mini-sternotomy and/or thoracoscopic) to CSMVS (3-5,31-33). However, only two previous meta-analyses have attempted to analyze RMVS and CSMVS (7,8), both of which had their own limitations as mentioned above.

The early all-cause mortality in the present meta-analysis favored the RMVS group in both the total included cohort (0.6% *vs.* 2.4%; P<0.0001) and matched (0.5% *vs.* 1.7%; P=0.01) patient cohorts. The meta-analysis of PSM studies by Takagi *et al.*, did not report a statistical difference between RMVS and CSMVS groups for the outcome of all-cause mortality (8). The meta-analysis by Takagi *et al.*, which included seven total PSM studies (six of which are included in the present analysis), included the study by Paul *et al.*, which was the largest PSM cohort included in that study (631 patients in each group) (9). That particular study was excluded from the present analysis as the "non-robotic" cohort included all other types of mitral valve approaches (i.e., full sternotomy, mini-sternotomy and other minimally invasive right thoracotomy approaches) as it was a population-based analysis. The study by Paul *et al.* reported an OR of 1.21 (95% CI: 0.4–3.62) trending towards the CSMVS group despite not reaching significance, but due to its large patient cohort, likely explains why there was no statistical significance in the all-cause mortality outcome in the meta-analysis by Takagi *et al.*

Cross clamp and CPB times have consistently been shown to be longer in minimally invasive cardiac surgery procedures when compared to the conventional sternotomy equivalent. Similar to the results seen in the current review, a meta-analysis of 119 studies comparing minimally invasive (not robotic) mitral valve surgery and CSMVS reported that both data from randomized control trials (RCTs) and observational studies showed significantly longer cross clamp and CPB times in the minimally invasive group (4). This meta-analysis reported a mean difference of only 9 minutes for cross clamp time (P<0.05) and 20 minutes for CPB time (P<0.05) when comparing the data from RCTs. The longer cross clamp and CPB times are likely attributable to both the operative complexity of robotic surgery (including docking/undocking and changing instrument arms) and the steep learning curve associated with these procedures. Two of the included studies in the present meta-analysis both reported that total operative, cross clamp and CPB times all reduced in length as operative case numbers increased (19,24). Suri and colleagues compared these times in the first and second half of their included robotic cases for comparison. They reported that the initial mean cross clamp and CPB times of 94.40 and 131.15 minutes, respectively, dropped to 68.67 and 95.85 minutes, respectively, in the second half of their robotic cohort (24). These dramatic improvements in cross clamp and CPB times with more operative experience likely partially explain the high heterogeneity seen in these results in the present meta-analysis, even in the matched patient data analysis.

One of the proposed benefits of minimally invasive cardiac surgery, including robotically-assisted cardiac surgery, is the reduced amount of surgical trauma allowing for a faster recovery to baseline functionality and in theory, shorter ICU and hospital LOS. In the present meta-analysis, RMVS patients had a significantly shorter ICU stay by 26.4 hours (P<0.0001) and a shorter hospital LOS by 2.01 days (P<0.0001); however, both outcomes had significant levels of heterogeneity. The high level of heterogeneity could be due to differing unit protocols for post-operative care and investigations. The shorter ICU and hospital LOS results are consistent with those reported in other meta-analyses comparing minimally invasive mitral valve surgery to CSMVS. A meta-analysis comparing randomized and matched observational studies of minimally invasive to conventional sternotomy for mitral valve repair reported

shorter ICU stay by 8.5 hours and hospital LOS by 1.3 days in the minimally invasive group, both results also having high heterogeneity (I^2>90%) (5).

Similar to the findings by Takagi *et al.*, this present meta-analysis found that the incidence of RBC transfusion was lower in the RMVS group than the CSMVS group in both the total included cohort (OR 0.44; P=0.0004) and matched cohort (OR 0.65; P=0.02). These results need to be interpreted with caution, as two of the included studies reporting data on RBC transfusion defined transfusion as greater than or equal to two units of RBCs, therefore introducing significant heterogeneity (19,24). However, reduced rates of RBC transfusion have been consistently reported across most meta-analyses comparing minimally invasive surgery to CSMVS (3-5).

There are a number of important limitations to consider when interpreting the results described in this present meta-analysis. Firstly, despite including fourteen studies comparing the safety and efficacy of RMVS to CSMVS, they were all retrospective observational series. Eight studies (15-17,19,20,24,25,27) included matched patient data which does to some degree minimize selection bias, however, as no studies were randomized, there inherently remains the risk of selection bias. Secondly, there was a heterogenous mix of procedures including mitral valve repair and replacement in most studies, with only six studies including cohorts of either purely mitral valve repair or replacement (16,18,21,22,24,27). Thirdly, along with the heterogenous procedures, the included studies also included heterogenous cohorts of mitral valve pathologies, which is an important consideration when interpreting the results. Fourthly, significant heterogeneity was detected in the analyses of cross clamp time, CPB time, RBC transfusion, ventilator time, along with ICU and hospital LOS. This may reflect the limited data, different surgical techniques, and specific unit protocols or operator experience across the included studies. Finally, data regarding post-operative echocardiography results were limited and heterogeneously reported. In future studies, direct comparison of mitral valve repair echocardiography results post-operatively between both surgical approaches with complete, long-term follow-up are required.

Conclusions

Both surgical approaches to mitral valve surgery have an adequate safety and efficacy profile. Current evidence on comparative outcomes of RMVS and CSMVS is limited, with only low-quality studies currently available with moderate-to-serious risk of bias. This present meta-analysis shows that RMVS may result in lower mortality, along with shorter ICU and hospital LOS compared to CSMVS in selected patients. On the contrary however, CSMVS may be associated with significantly shorter cross clamp and CPB times. Further high-quality studies with randomized data are required to verify these results and also necessary to assess differences in mitral valve repair quality and postoperative quality of life differences between the two surgical approaches.

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Footnote

Conflicts of Interest: TSG provides consultation for Edwards Lifesciences, Johnson & Johnson, and Intuitive Surgical. The other authors have no conflicts of interest to declare.

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Supplementary

Table S1 Summary of the underlying mitral valve pathology

Primary author	Approach	N	Myxomatous degeneration (%)	Ischaemic (%)	Infection (%)	Rheumatic (%)	Functional (%)	Other (%)
Chemtob, 2020	Sternotomy	395	100.0	0.0	0.0	0.0	0.0	0.0
	Robotic	605	100.0	0.0	0.0	0.0	0.0	0.0
Coyan, 2018	Sternotomy	91	NR	NR	11.0	NR	NR	NR
	Robotic	91	NR	NR	7.7	NR	NR	NR
Folliguet, 2006	Sternotomy	25	100.0	0.0	0.0	0.0	0.0	0.0
	Robotic	25	100.0	0.0	0.0	0.0	0.0	0.0
Hawkins, 2018 (unmatched)	Sternotomy	1,352	45.3	1.6	14.9	11.8	NR	14.3
	Robotic	372	80.9	0.8	5.7	7.0	NR	4.8
Hawkins, 2018 (PSM)	Sternotomy	314	78.0	1.0	6.4	7.3	NR	NR
	Robotic	314	79.0	1.0	6.4	7.0	NR	NR
Kam, 2010	Sternotomy	40	100.0	0.0	0.0	0.0	0.0	0.0
	Robotic	107	100.0	0.0	0.0	0.0	0.0	0.0
Kesävuori, 2018	Sternotomy	142	100.0	0.0	0.0	0.0	0.0	0.0
	Robotic	142	100.0	0.0	0.0	0.0	0.0	0.0
Mihaljevic, 2011	Sternotomy	114	100.0	0.0	0.0	0.0	0.0	0.0
	Robotic	261	100.0	0.0	0.0	0.0	0.0	0.0
Seo, 2019	Sternotomy	259	NR	NR	NR	NR	NR	NR
	Robotic	175	NR	NR	NR	NR	NR	NR
Sicim, 2021	Sternotomy	66	100.0	0.0	0.0	0.0	0.0	0.0
	Robotic	64	100.0	0.0	0.0	0.0	0.0	0.0
Stevens, 2012	Sternotomy	377	43.8	6.4	8.5	14.9	6.1	20.4
	Robotic	447	80.0	0.9	4.5	3.6	8.5	2.5
Suri, 2011	Sternotomy	95	100.0	0.0	0.0	0.0	0.0	0.0
	Robotic	95	100.0	0.0	0.0	0.0	0.0	0.0
Wang, 2018	Sternotomy	503	NR	NR	NR	NR	NR	NR
	Robotic	503	NR	NR	NR	NR	NR	NR
Woo, 2006	Sternotomy	39	NR	NR	NR	NR	NR	NR
	Robotic	25	NR	NR	NR	NR	NR	NR
Zhao, 2020	Sternotomy	47	17.0	0.0	4.3	76.6	0.0	2.1
	Robotic	47	12.8	0.0	4.3	76.6	0.0	6.4

PSM, propensity score matched cohort; N, number of patients.

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Table S2 Pooled baseline characteristics for matched patients only

Variable	Robotic matched (n=1,323)	Sternotomy matched (n=1,323)
Age (years), mean	68.4	68.6
Male, %	65.0	65.3
BMI (kg/m^2), mean	26.2	26.4
Hypertension, %	46.5	45.2
Diabetes, %	6.8	7.1
Cerebrovascular disease, %	3.3	3.6
Respiratory disease, %	4.1	5.4
LVEF, mean	60.1	60.0
Cardiac arrhythmia, %	17.8	19.3
NYHA III/IV, %	26.4	29.5
Valve pathology—myxomatous degeneration, %	87.4	88.0

BMI, body mass index; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

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Table S3 Procedural details

Primary Author	Robotic access method	Robotic XC method	Cardioplegia strategy	Replacement—sternotomy	Replacement—robotic	Repair—sternotomy	Repair—robotic	Repair details	Concomitant surgery—robotic	Concomitant surgery—sternotomy	Conversion to sternotomy/thoracotomy
Chemtob	Access ports placed through the right chest, including a 4-cm mini-thoracotomy working port	Transthoracic aortic cross-clamp	Antegrade	4 (1%), 2 were failed repairs	0 (0%)	391 (99%)	605 (100%)	Resectional techniques, artificial chordae, or both along with flexible annuloplasty band	0 (0.0%)	0 (0.0%)	0 (0%)
Coyan	4-cm right lateral mini-thoracotomy and access ports	Transthoracic aortic cross-clamp	NR	17 (18.7%)	13 (14.3%)	74 (81.3%)	78 (85.7%)	NR	TVR/r, closure of ASD, or surgical ablation procedures	TVR/r, closure of ASD, or surgical ablation procedures	0 (0%)
Folliguet	Two ports and a 4–5 cm intercostals lateral incision in the right chest	Transthoracic aortic cross-clamp	Antegrade	0 (0%)	0 (0%)	25 (100%)	25 (100%)	Posterior leaflet resection and open band or a closed annuloplasty ring	NR	NR	1 (4%)—thoracotomy
Hawkins—PSM group	NR	NR	NR	77 (24.5%)	30 (9.5%)	237 (75.5%)	284 (90.5%)	Leaflet resection and/or neochords and ring annuloplasty	LAAL 18 (5.7%)	LAAL 46 (14.7%)	0 (0%)
Hawkins—larger cohort	NR	NR	NR	655 (48.4%)	36 (9.7%)	697 (51.6%)	336 (90.3%)	Leaflet resection and/or neochords and ring annuloplasty	LAAL 21 (5.7%)	LAAL 19 (3.3%)	0 (0%)
Kam	Right thoracotomy (<4 cm) and a number of smaller ports	NR	NR	0 (0%)	0 (0%)	40 (100%)	107 (100%)	NR	0 (0.0%)	0 (0.0%)	NR
Kesävuori	Camera port was placed near the mammilla (4th intercostal space), service port was placed laterally same or adjacent intercostal space, 3 other access ports	Endoaortic balloon primarily, but transthoracic aortic cross-clamp used in some operations	Antegrade and retrograde	3 (2.1%)	2 (1.4%)	139 (97.9%)	140 (98.6%)	Neochord implantation and/or leaflet resection and/or commissuroplasty	AF ablation 35 (24.6%), TVr 6 (4.2%), PFO closure 14 (9.9%), LAAL 32 (22.5%), myxoma excision 1 (0.7%), pericardial cyst excision 1 (0.7%)	AF ablation 30 (21.1%), TVr 17 (12.0%), PFO closure 7 (4.9%), LAAL 26 (18.3%), thymoma excision 1 (0.7%)	14 (9.9%)
Mihaljevic	Mini-thoracotomy fourth intercostal space in the mid-axillary line and other access ports	Endoaortic balloon or transthoracic aortic clamp	Antegrade and retrograde	1 (0.9%)	0 (0%)	113 (99.1%)	261 (100%)	Annuloplasty and leaflet resection or chordal procedure or edge-to-edge repair	ASD or PFO closure 34 (13%), left-sided ablative lesions for AF 22 (8.4%)	ASD or PFO closure 7 (6.1%), Left-sided ablative lesions for AF 31 (27%)	24 (9.1%)
Seo	NR	NR	NR	0 (0%)	0 (0%)	259 (100%)	175 (100%)	NR	0 (0.0%)	0 (0.0%)	4 (2.3%)
Sicim	4-cm anterolateral thoracotomy incision	Transthoracic aortic cross-clamp	Antegrade	66 (100%)	64 (100%)	0 (0%)	0 (0%)	NR	0 (0%)	0 (0%)	NR
Stevens	3- to 4-cm working port in the right inframammary fold through the fourth intercostal space	Transthoracic aortic cross-clamp primarily, endoaortic balloon occlusion used infrequently	Antegrade and/or retrograde	169 (44.8%)	5 (1.1%)	208 (55.2%	442 (98.9%)	Techniques involving combination or isolated annuloplasty, leaflet resection and chordal procedure	AF ablation 84 (19%)	AF ablation 22 (6%)	NR
Suri	2- to 3-cm working port lateral to the camera port in the right 4th intercostal space	Transthoracic aortic cross-clamp	Antegrade	0 (0%)	0 (0%)	95 (100%)	95 (100%)	Triangular resection for posterior leaflet disease, neochords for anterior leaflet prolapse and all repairs partial annuloplasty band	ASD/PFO closure or Maze/modified Maze procedures	ASD/PFO closure or Maze/modified Maze procedures	0 (0%)
Wang	NR	Endoaortic balloon or transthoracic aortic clamp*	Antegrade and/or retrograde*	49 (9.7%)	8 (1.6%)	454 (90.3%)	495 (98.4%)	Combination or isolated annuloplasty, leaflet resection, sliding plasty, neochords, edge-to-edge repair and chordal procedure	PFO or ASD repair	PFO or ASD repair	NR
Woo	Right chest was entered in the fourth intercostals space and other port access	Endoaortic balloon or transthoracic aortic clamp	Antegrade and retrograde	16 (41%)	8 (32%)	23 (59%)	17 (68%)	Ring annuloplasty and indicated leaflet, chordal, and annular reconstruction	0 (0.0%)	0 (0.0%)	NR
Zhao	NR	NR	NR	Mechanical 33 (70.2%)/ bioprosthetic 14 (29.8%)	Mechanical 35 (84.5%)/ bioprosthetic 12 (25.5%)	0 (0%)	0 (0%)	NR	NR	NR	NR

*, one operation (robotic) performed beating heart and four (3 robotic and 1 sternotomy) performed utilising fibrillatory arrest. NR, not reported; TVR/r, tricuspid valve replacement/repair; ASD, atrial septal defect; PFO, patent foramen ovale; LAAL, left atrial appendage ligation; AF, atrial fibrillation.

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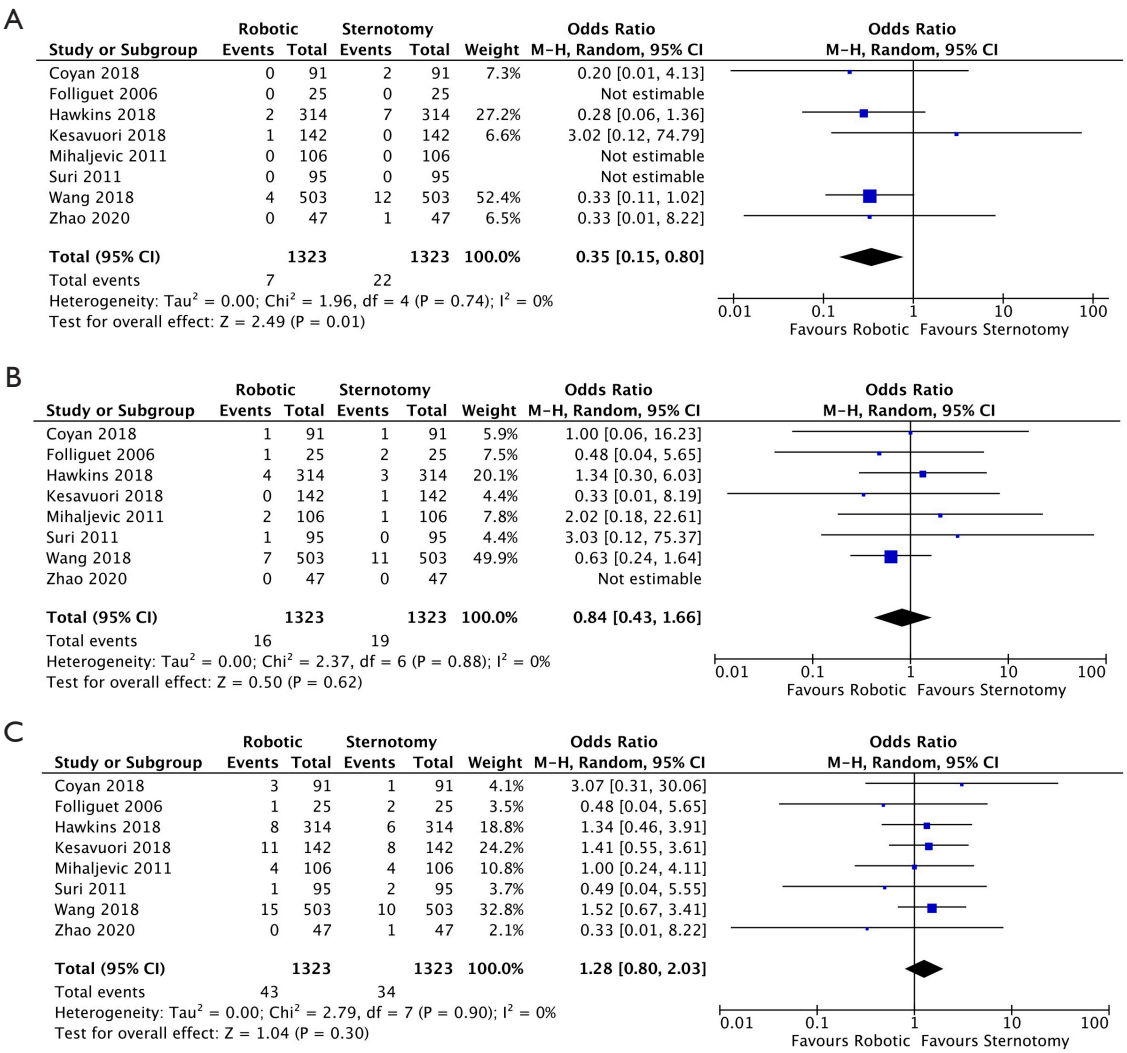

Figure S1 Forrest plot of OR of matched cohort studies for all-cause mortality (A), CVA (B), and re-operation for bleeding (C) for robotic versus conventional sternotomy mitral valve surgery. OR, odds ratio; CI, confidence interval; CVA, cerebrovascular accidents; M-H, Mantel-Haenszel test.

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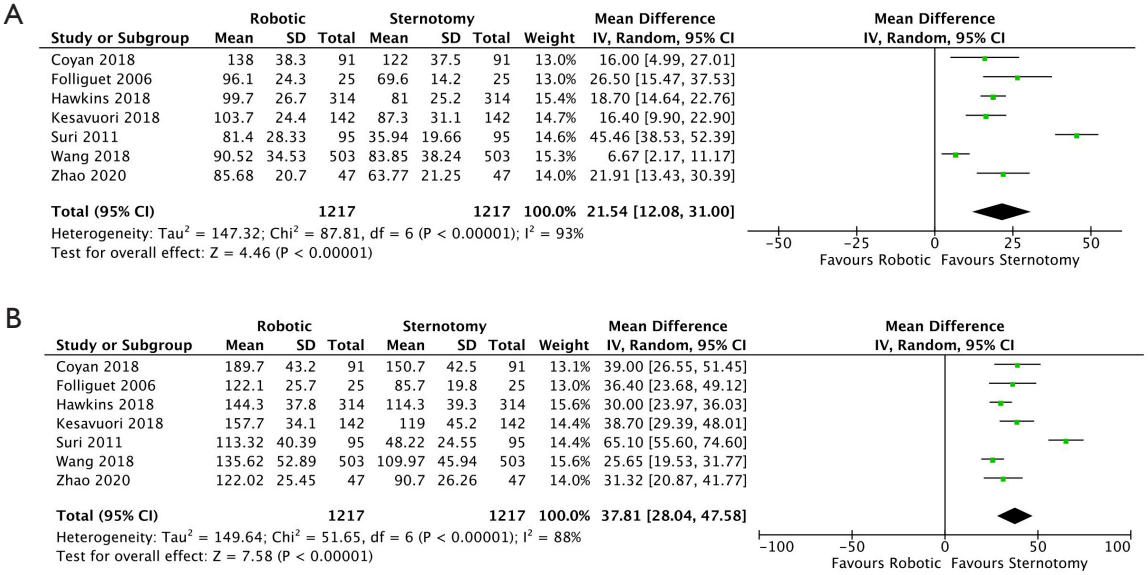

Figure S2 Forrest plot of MD of matched cohort studies for cross clamp (A), and CPB times (B) for robotic versus conventional sternotomy mitral valve surgery. MD, mean difference; CPB, cardiopulmonary bypass; CI, confidence interval.

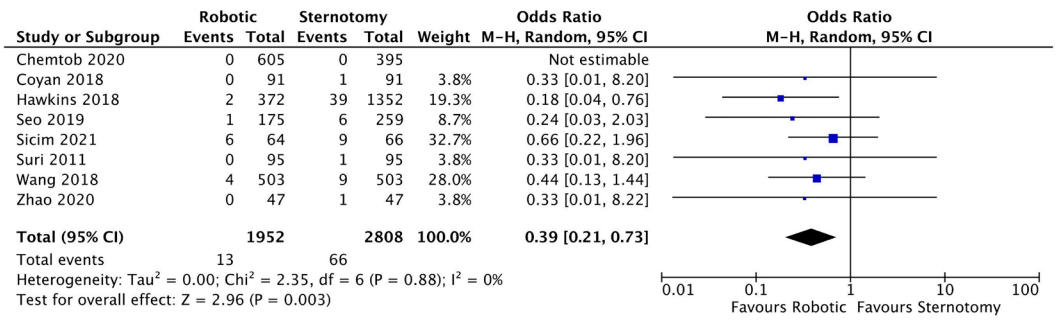

Figure S3 Forrest plot of OR for post-operative renal insufficiency for robotic versus conventional sternotomy mitral valve surgery. OR, odds ratio; CI, confidence interval; M-H, Mantel-Haenszel test.

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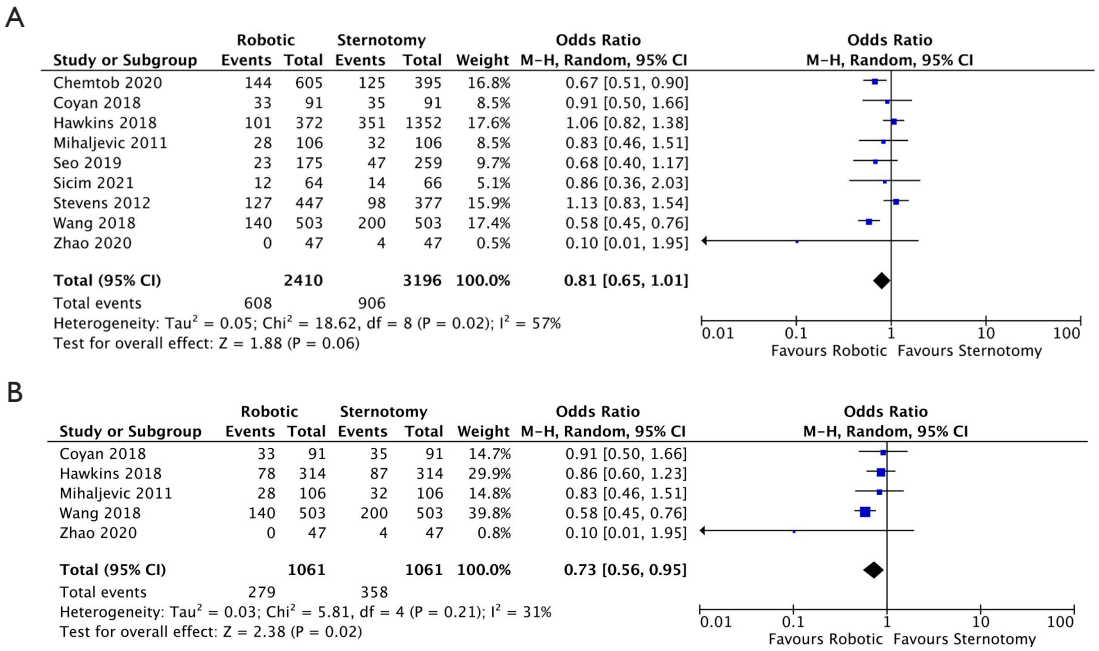

Figure S4 Forrest plot of OR for POAF in all studies (A) and POAF in matched patient cohorts (B) for robotic versus conventional sternotomy mitral valve surgery. POAF, post-operative atrial fibrillation; OR, odds ratio; CI, confidence interval; M-H, Mantel-Haenszel test.

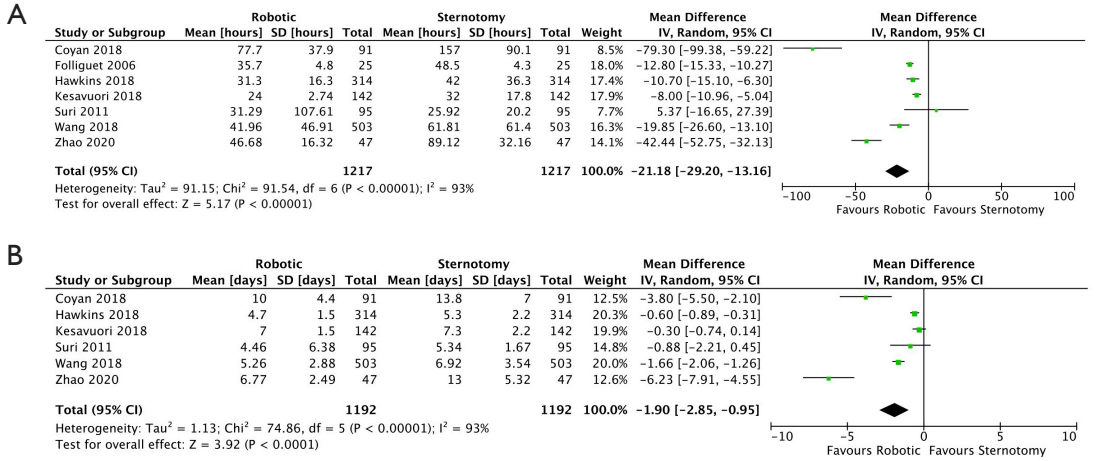

Figure S5 Forrest plot of MD of matched cohort studies for (A) intensive care unit stay (hours), and (B) length of hospital stay (days) for robotic versus conventional sternotomy mitral valve surgery. MD, mean difference; CI, confidence interval.

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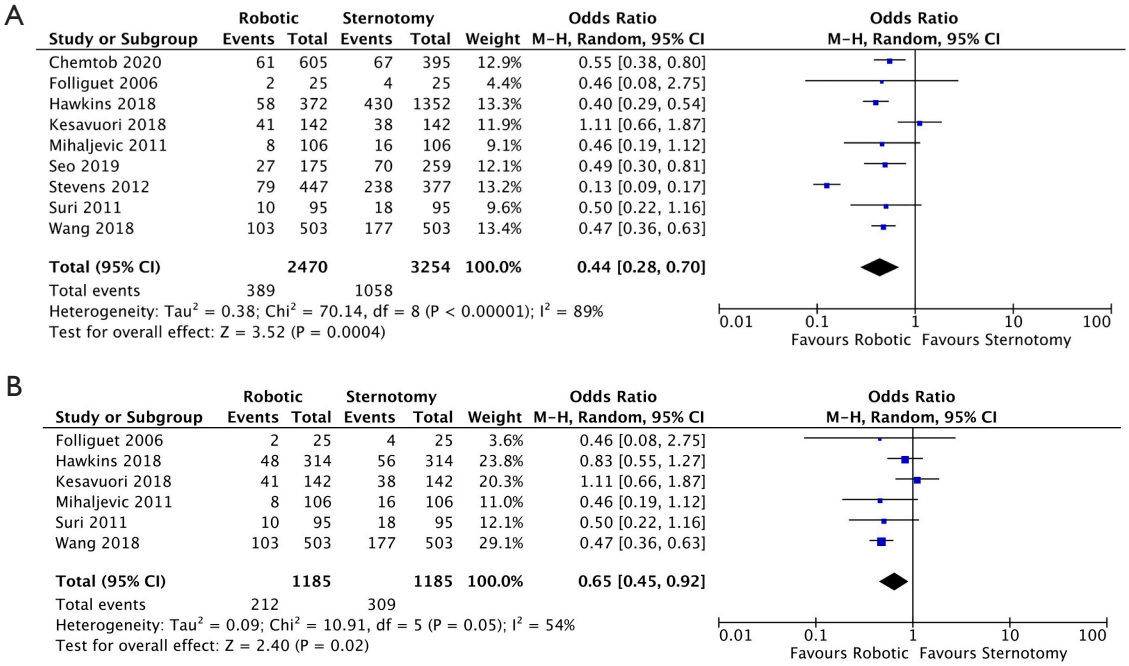

Figure S6 Forrest plot of OR for RBC transfusion in all studies (A) and RBC transfusion in matched patient cohorts (B) for robotic versus conventional sternotomy mitral valve surgery. RBC, red blood cell; OR, odds ratio; CI, confidence interval; M-H, Mantel-Haenszel test.

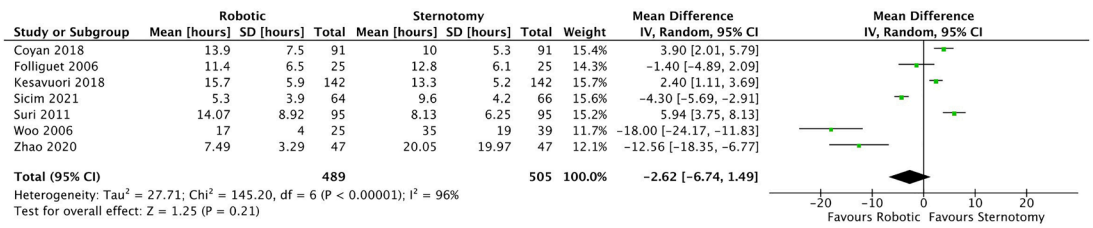

Figure S7 Forrest plot of MD for ventilation time (hours) for robotic versus conventional sternotomy mitral valve surgery. MD, mean difference; CI, confidence interval.

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Table S4 Echocardiography results post-operatively

Primary author	Approach	In-hospital/early follow-up					Latest follow-up				
		None (%)	Trace (%)	Mild (%)	Moderate (%)	Severe (%)	None (%)	Trace (%)	Mild (%)	Moderate (%)	Severe (%)
Chemtob, 2020	Sternotomy	92.9		7.1	0.0	(0.0	NR	NR	NR	NR	NR
	Robotic	86.3		13.6	0.1	0.0	NR	NR	NR	NR	NR
Coyan, 2018	Sternotomy	100.0		0.0	0.0	0.0	NR	NR	NR	NR	NR
	Robotic	100.0		0.0	0.0	0.0		91%*		NR	NR
Folliguet, 2006	Sternotomy	92.0	0.0	0.0	8.0	0.0	NR	NR	NR	NR	NR
	Robotic	92.0	0.0	0.0	8.0	0.0	NR	NR	NR	NR	NR
Hawkins, 2018	Sternotomy	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
	Robotic	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Kam, 2010	Sternotomy	82.1	17.9	0.0	0.0	0.0	NR	NR	NR	NR	NR
	Robotic	82.1	14.2	2.8	0.9	0.0	NR	NR	NR	NR	NR
Kesävuori, 2018	Sternotomy	NR	NR	NR	NR	NR		84.7		5.1	0.8
	Robotic	NR	NR	NR	NR	NR		86.3		7.6	1.5
Mihaljevic, 2011	Sternotomy		99.0		1.0	NR	NR	NR	NR	NR	NR
	Robotic		98.1		1.9	NR	NR	NR	NR	NR	NR
Seo, 2019	Sternotomy	78.7		15.7	4.7	0.9	58.2*		27.8*	12.7*	1.3*
	Robotic	74.4		19.8	5.2	0.6	39.5*		31.6*	21.1*	7.9*
Sicim, 2021	Sternotomy	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
	Robotic	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Stevens, 2012	Sternotomy	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
	Robotic	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Suri, 2011	Sternotomy	82.1		16.8	1.1	0.0	NR	NR	NR	NR	NR
	Robotic	82.1		17.9	0.0	0.0	NR	NR	NR	NR	NR
Wang, 2018	Sternotomy	48.2	35.4	9.8	4.3	1.2	NR	NR	NR	NR	NR
	Robotic	45.3	38.2	14.7	1.2	0.6	NR	NR	NR	NR	NR
Woo, 2006	Sternotomy	82.6	8.7	8.7	0.0	0.0	NR	NR	NR	NR	NR
	Robotic	82.4	0.0	17.6	0.0	0.0	NR	NR	NR	NR	NR
Zhao, 2020	Sternotomy	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
	Robotic	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

*, one year follow-up data. NR, not reported.

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