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Research Article

Comparing Conventional and Minimally Invasive Sternotomy for Aortic Valve Replacement: A Systematic Review and Meta-Analysis

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ABSTRACT

Aim: We aimed to compare the safety and outcomes of the minimally invasive approaches *versus* conventional sternotomy procedure for aortic valve replacement.

Methods: We conducted a PRISMA-compliant systematic review and meta-analysis. We ran an electronic search of PubMed, Cochrane CENTRAL, Scopus, and Web of Science to identify the relevant published studies. Data were extracted and pooled in the DerSimonian Liard meta-analysis model as Standardized Mean Difference (SMD) or Risk Ratio (RR) using StataMP version 17 for macOS.

Results: Forty-one studies with a total of 15,065 patients were included in this meta-analysis (minimally invasive approaches n=7231 *vs.* conventional sternotomy n=7834). The pooled effect size showed that minimally invasive approaches had lower mortality rates [RR 0.76, 95%CI (0.59 to 0.99)], intensive care unit and hospital stays (SMD -0.16 and -0.31, respectively), ventilation time [SMD -0.26, 95%CI (-0.38 to -0.15)], 24 h chest tube drainage [SMD -1.03, 95%CI (-1.53 to -0.53)], RBCs transfusion [RR 0.81, 95%CI (0.70 to 0.93)], wound infection [RR 0.66, 95%CI (0.47 to 0.92)] and acute renal failure [RR 0.65, 95%CI (0.46 to 0.93)]

However, minimally invasive approaches had longer operative time, cross-clamp, and bypass times [SMD 0.47, 95%CI (0.22 to 0.72), SMD 0.27, 95%CI (0.07 to 0.48), and SMD 0.37, 95%CI (0.20 to 0.45)], respectively. There were no differences between the two groups in blood loss, endocarditis, cardiac tamponade, stroke, arrhythmias, pneumonia, pneumothorax, bleeding reoperation, tracheostomy, hemodialysis, or myocardial infarction, (all $p>0.05$).

Conclusion: Current studies have proved that minimally invasive aortic valve replacement has less mortality and better post-operative outcomes compared to the conventional approach. Future RCTs with long-term follow-ups are recommended.

Keywords: Aortic replacement; Aortic valve; Minimally-invasive; Sternotomy

INTRODUCTION

Aortic Valve Replacement (AVR) is a very common procedure worldwide, Minimally Invasive Aortic Valve Replacement (MIAVR) and Conventional Sternotomy Aortic Valve Replacement (CSAVR) are two different surgical techniques used for the replacement of the aortic valve, which is responsible for regulating blood flow from the heart to the rest of the body. AVR *via* median sternotomy remains the standard treatment for aortic valvular diseases [1].

However, the scientific world recently seeks less invasive procedures, so the development of less invasive approaches in general surgery has promoted the use of minimally invasive approaches within the field of cardiac surgery. [2].

Several approaches for Minimally Invasive Aortic Valve Replacement (MIAVR) have been described, but the most commonly used are the upper hemi-sternotomy and the right anterior mini-thoracotomy procedures, which have the advantage of feasible access to the aorta in addition to fewer requirements of specialized instrumentation [3]. MIAVR procedures aim to reduce surgical trauma, faster recovery, better aesthetic outcomes, decrease postoperative pain, decrease post-operative ventilation time and decrease blood loss [4]. Despite the advantages, during the procedures, access to the aortic valve through a smaller access

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portal leads to prolonged procedural times [5].

Minimally invasive AVR procedures support a patient's perception of less traumatic procedures but they do not eliminate the need for Cardiopulmonary Bypass (CPB).

Therefore, there is an ongoing debate about whether minimally invasive AVR procedures truly are less invasive treatment than the conventional surgical approach through full median sternotomy [6].

Through this systematic review and meta-analysis, we aim to evaluate the clinical outcomes of patients who performed AVR *via* minimally invasive approaches compared with those who performed AVR *via* conventional sternotomy.

MATERIALS AND METHODS

We followed the PRISMA statement guidelines when reporting this systematic review and meta-analysis [7]. All steps were done in strict accordance with the Cochrane handbook of systematic reviews and meta-analysis of interventions [8].

All steps of this study were prespecified, and the protocol was registered on PROSPERO before completion of full-text screening.

Search strategy

An electronic literature search was performed on PubMed, Cochrane CENTRAL, Scopus, and Web of Science to identify the relevant published studies.

The search strategy used was sternotomy or median sternotomy or full sternotomy or ministernotomy or open heart surgery or open-heart and valvular surgery or minimally invasive valvular surgery or valvular replacement or valvular implantation or Transcatheter Aortic Valve Replacement (TAVR) or aortic valve replacement or transcatheter aortic valve implantation or TAVI or Aortic valve implantation or Surgical Aortic Valve Replacement (SAVR).

Further, the references of the included studies were manually searched for any potentially eligible studies.

Study selection and data extraction

Studies were collected and organized by Endnote (Clarivate Analytics, PA, USA), duplications were removed and then a total number of 4720 articles were exported to start the study selection (screening) process.

Title and abstract screening of articles was done; this process was performed by five investigators separately. The inclusion criteria included (clinical trials and observational studies that compared the clinical outcomes of patients with aortic valvular diseases who performed MIAVR *versus* those who performed conventional sternotomy).

The exclusion criteria included (studies that were not in English, systematic reviews, literature reviews, case series, animal studies, non-comparative studies, and studies that did not report any of the relevant clinical outcomes, which are (mortality rate, intensive care unit and hospital stays, ventilation time, chest tube drainage, RBCs transfusion, wound infection, acute renal failure, operative time, cross-clamp and bypass times)). A second check was performed to check for any relevant studies to be added.

After the title and abstract screening phase was completed, we started the full-text screening phase which was performed by five separate investigators.

At the end of the full-text screening phase, the included studies have been identified and included for qualitative and quantitative synthesis.

Three independent investigators performed the data extraction process for each article. The data was extracted from full-text articles, tables, and figures. There were no major discrepancies between them, minor discrepancies have been resolved by the senior reviewer.

The following data were extracted from the included studies (mortality, operative time, ventilation time, ICU stay, hospital stay, prolonged ventilation, blood loss ≥ 800 ml/24 h, postoperative bleeding, 24-h chest tube drainage, blood product transfusion, endocarditis, wound infection, acute renal failure, cardiac tamponade, stroke, new atrial fibrillation, new pacemaker, cross clamp time, bypass time, respiratory failure, pneumothorax, pneumonia, pleural effusion, bleeding reoperation, tracheostomy for respiratory failure, hemodialysis, reoperation for paravalvular regurgitation and myocardial infraction).

Methodological quality assessment of included studies

According to the Cochrane handbook of systematic reviews and meta-analysis of interventions, the quality of the retrieved RCTs was assessed.

The risks of bias assessment include the following domains: Sequence generation (selection bias), allocation sequence concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias) and other potential sources of bias. The authors' judgments are categorized as 'Low risk' or 'High risk' or 'Unclear risk' of bias. A qualitative assessment of the observational studies was performed using the Newcastle-Ottawa Scale (NOS). This scale uses a star-based rating system to assess the risk of bias in each study. This scale's maximum score is (9) which indicates the lowest risk of bias, and the minimum score is (0) which indicates the highest risk of bias. Scores above (7) indicate a lack of substantial bias. Quality of included studies was rated by two separate investigators. There were no major discrepancies, minor discrepancies have been resolved by a senior reviewer. Qualitative assessment of the non-randomized clinical trials was performed using ROBINS-I tool. It is a tool for evaluating risk of bias in estimates of the comparative effectiveness (harm or benefit) of interventions from studies that did not use randomization to allocate units (individuals or clusters of individuals) to comparison groups [9]. All included studies are summarized in Table 1. The forty-one eligible comparative studies included a total of (26,808) patients, (8,742) patients underwent MIAVR and (18,066) underwent conventional sternotomy. Results of the assessment are shown in Tables 2 and 3.

Statistical analysis

This meta-analysis was performed according to the recommendations of Quality of Reporting of Meta-analysis (QUOROM) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines [10,11].

Outcomes in continuous data were presented as Standardized Mean Difference (SMD) between the two groups, the SMD with the corresponding 95% confidence intervals were pooled in the DerSimonian Liard meta-analysis model using StataMP version 17 for macOS.

Table 1: Summary table of the included articles in this systematic review and meta-analysis.

Study design	Total patients (n)	MIAVR (n)	Conventional sternotomy (n)	Main findings	Reference
Prospective randomized study	80	40	40	MIAVR has important cosmetic advantages, beneficial effects in blood loss and transfusion, postoperative pain and earlier extubation and hospital discharge	[5]
Retrospective observational study	426	70	356	MIAVR can be sufficiently safe and effective. These surgeries reduce the duration of hospitalization, ventilation time, blood loss, and surgical trauma. they improve cosmetic results, and speed up patient rehabilitation	[12]
Retrospective observational study	1571	125	1446	MIAVR t has similar hospital outcomes compared to conventional sternotomy. The operation is quicker and does not confer any significant increase in complications or length of hospital stay	[13]
Prospectively cohort study	4163	307	3856	MIAVR is a safe alternative to CAVR concerning operative and 1-year mortality and is associated with a shorter post-operative stay	[14]
Retrospective observational study	506	232	274	MIAVR can be performed safely through a partial upper sternotomy on a routine basis for isolated aortic valve disease	[15]
Retrospective observational study	838	73	765	Both MIAVR and conventional sternotomy had comparable early clinical outcomes in patients undergoing primary isolated aortic valve replacement. MIAVR significantly decreases postoperative pain	[16]
Randomized multicenter trial	94	46	48	RDAVR by the MIS approach is associated with significantly reduced myocardial ischemic time and better valvular hemodynamic function than FS-AVR with a conventional stented bioprosthesis	[17]
Retrospective cohort study	39	20	19	Partial upper hemi-sternotomy for AVR avoids unnecessary lower mediastinal dissection, reducing blood loss, transfusion needs, and total operative duration.	[18]
Prospective randomized study	77	38	39	This study failed to show any improvement of respiratory function by a smaller chest incision. However, it showed a significant reduction in intraoperative bleeding	[19]
Retrospective cohort study	714	61	653	Minimally invasive rapid deployment AVR had reduced bypass and ACC times and reduced length of ICU stay.	[20]
Case-control-study	113	29	84	Both surgical techniques have comparable perioperative and mid-term results. MIAVR has better cosmetic results but longer duration of surgery	[21]
Prospective cohort study	100	30	70	Partial upper sternotomy is a safe and effective technique for AVR. Postoperative morbidity is not significantly reduced in patients undergoing AVR by this approach	[22]
Randomized trial	40	21	19	RV long-axis function was reduced after both mini-sternotomy and full sternotomy AVR, but the reduction was more pronounced in the full sternotomy group	[23]
Retrospective observational study	565	182	383	AVR through a mini-sternotomy with implantation of a sutureless bioprosthesis was associated with shorter ACC and cardiopulmonary bypass time and less transfusion of packed RBCs	[24]
Retrospective observational study	267	189	78	MIAVR with the sutureless Perceval bioprosthesis was a safe and reproducible procedure that was not associated with prolonged ACC or cardiopulmonary bypass time compared with a full sternotomy	[25]
Retrospective observational study	140	70	70	This study has failed to show any advantage of minimally invasive AVR in early or midterm follow-up	[26]

Case Control study	82	41	41	AVR is feasible through minithoracotomy. But, This approach increases surgical complexity and in this comparative study no significant benefit was shown	[27]
Prospective randomized trial	40	20	20	Safety and reliability of AVR *via* a partial upper sternotomy is reported. MIAVR can be performed with only slightly longer operative times, good cosmetic results and significantly less blood loss	[28]
Multicenter retrospective study	1057	622	435	Rapid-deployment bioprostheses allow the performance of MIAVR with similar surgical times and similar clinical and hemodynamic outcomes to conventional surgery	[29]
Retrospective, single-center study	150	74	76	Ministernotomy for AVR is a safe method and does not increase morbidity and mortality. It significantly reduces post-operative blood loss and hospital stay	[30]
Prospectively cohort study	984	436	548	AVR can be safely conducted through a partial ministernotomy. This approach is not associated with an increased rate of complications	[31]
Retrospective observational study	68	34	34	The minimal access aortic valve replacement can be performed safely with excellent long-term results in selected patients	[32]
Retrospective observational study	1341	442	899	Mortality and morbidity outcomes of MIAVR are equivalent to conventional AVR. MIAVR is associated with decreased ventilator time, blood product use, and early discharge	[33]
Retrospective observational study	1180	502	678	MIAVR surgery is a reproducible, safe and effective procedure with similar outcomes and no longer operative times compared to conventional sternotomy	[34]
Retrospective, observational, cohort study	709	338	371	MIAVR is a reproducible, safe, and effective procedure and reduces assisted ventilation duration, the need for blood product transfusion, and incidence of post-surgery atrial fibrillation	[35]
Single-blind RCT	270	135	135	MIAVR did not reduce RBCs transfusion within 7 days following surgery when compared with conventional sternotomy	[36]
Retrospective observational study	2095	1029	1066	MIAVR results in similar mortality, stroke, and reoperation rates for bleeding, , but shorter hospital length of stay compared to full sternotomy	[37]
Retrospective study	200	100	100	Upper partial sternotomy can be performed safely for AVR, without increased risk of death, stroke or re-admission in 3 years postoperatively	[38]
Retrospective observational study	2386	620	1766	MIAVR is a safe, effective and reproducible procedure providing as good results as FSAVR. It should be especially recommended to obese, diabetic patients with pulmonary and mobility disorders in order to improve their early recovery	[39]
Retrospective observational study	754	377	377	MIAVR is a reproducible, safe, and effective procedure with similar outcomes and operating times compared with full sternotomy	[40]
Open-label RCT	222	118	104	Ministernotomy AVR did not result in shorter hospital stay, faster recovery, or improved survival and was not cost-effective	[41]
Retrospective observational study	3021	1319	1702	MIAVR had decreased transfusion requirements, ventilation times, intensive care unit and hospital length of stay without compromising short and long term survival compared to conventional sternotomy	[42]
Retrospective observational study	627	453	174	MIAVR confers a protective effect against bleeding complications, but it is time-consuming. In addition, no differences in mortality were observed among groups	[43]
Retrospective, observational, cohort study	135	42	93	MIAVR is a reproducible, safe, and effective surgical option in patients candidate for isolated AVR, and it suggests a faster recovery when used in severely obese or older patients	[44]

Retrospective cohort study	236	118	118	The partial upper hemisternotomy shows similar perioperative outcome as the median sternotomy, whereas, the anterolateral minithoracotomy is associated with more perioperative complications	[45]
Single center retrospective study	653	137	516	Despite the longer CPB and AoX times in the MIAVR group, there was no significant difference in early complications, mortality and mid-term survival between MIAVR and conventional AVR	[46]
Retrospective observational study	511	56	455	MIAVR produces better wound cosmoses and less surgical trauma but requires more time to perform	[47]
Non-randomized prospective trial	42	24	18	Upper sternotomy approach is superior to the other approaches in MIAVR, because It brings cosmetic benefits, and excellent results in a postoperative course	[48]
Retrospective, nonrandomized review	100	50	50	The partial sternotomy offers a cosmetic benefit, but does not significantly reduce postoperative pain, length of stay, or cost	[49]
Prospectively cohort study	176	104	72	Minimal access AVR using MECC is feasible and provides excellent clinical results. Less pain and quicker recovery was experienced among patients in this group	[50]
Prospectively cohort study	36	18	18	MIAVR is associated with less blood loss, faster post-operative recovery, but increase operation time	[51]

Table 2: Results of quality assessment of the non-randomized clinical trials using ROBINS-I tool.

Study ID	Pre-intervention		At intervention	Post-intervention				
	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported results	Results
[48]	low risk	low risk	low risk	low risk	low risk	low risk	low risk	low risk of bias
[49]	low risk	low risk	low risk	low risk	low risk	low risk	low risk	low risk of bias

Table 3: Results of quality assessment of the observational studies using Newcastle-Ottawa Scale (NOS) tool.

Study ID	Selection			Comparability	Outcome			score/9
	Selection of patients receiving open surgery	Ascertainment of exposures	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 cohort	
[12]	*	*	*	**	*	*	*	8
[13]	*	*	*	**	*	*	*	8
[14]	*	*	*	**	*	*	*	8
[15]	*	*	*	*	*	-	*	7
[16]	*	*	*	**	*	*	*	8
[5]	*	*	*	**	*	*	*	8
[18]	*	*	*	**	*	*	*	8
[19]	*	*	*	**	-	-	-	5

[20]	*	*	*	*	*	*	*	7
[21]	*	*	*	*	-	*	-	5
[22]	*	*	*	*	*	-	-	5
[23]	*	*	*	**	*	*	*	8
[24]	*	*	*	**	*	*	*	8
[26]	*	*	*	**	*	*	*	8
[29]	*	*	*	**	-	*	*	7
[30]	*	*	*	**	*	*	*	8
[31]	*	*	*	**	*	*	*	8
[32]	*	*	*	**	*	*	*	8
[33]	*	*	*	**	*	-	-	6
[34]	*	*	*	*	*	-	-	5
[35]	*	*	*	*	*	-	-	5
[37]	*	*	*	**	*	*	*	8
[38]	*	*	*	**	*	*	*	8
[39]	*	*	*	**	*	*	*	8
[40]	*	*	*	**	*	-	-	6
[42]	*	*	*	**	*	-	-	6
[43]	*	*	*	**	*	-	-	6
[44]]	*	*	*	**	*	*	*	8
[45]	*	*	*	**	*	*	*	8
[46]	*	*	*	**	*	*	*	8
[47]	*	*	*	**	*	*	*	6
[50]	*	*	*	**	*	*	*	8
[51]	*	*	*	**	*	*	*	8

Note: *: Study controls for preoperative cardiac function; **: Cardiovascular co-morbidities

Outcomes in dichotomous data from prospectively designed studies were presented as Risk Ratio (RR) between the two groups, the RR with the corresponding 95% confidence intervals were pooled in the DerSimonian Liard (DSL) meta-analysis model using StataMP (SMP) version 17 for macOS [12].

Both fixed and random effects models were tested and the random effect model was applied for outcomes because this random effect model assumes the included studies represent a random sample from the population and assigns a slightly higher weight to small studies on the expenses of larger studies.

Statistical heterogeneity among studies was evaluated by the Chi-square test (Cochrane Q test). Then, the chi-square statistic, Cochrane Q, was used to calculate the I-squared according to the equation: $I^2=[(Q-df)/Q] \times 100\%$

A chi-square p value less than 0.1 was considered as significant heterogeneity. I^2 values ≥ 50% were indicative of high heterogeneity.

RESULTS

Included studies and patient characteristics

Title and abstract screening of 4.720 articles was done and a total number of 4,565 studies were excluded in this phase, then the full-text screening phase was performed on 155 studies, 114 studies were excluded according to the exclusion criteria and 41 studies were included for qualitative and quantitative synthesis. Results are shown in the Prisma flow diagram (Supplementary Figure 1).

Data was pooled as Standardized Mean Difference (SMD) or Risk Ratio (RR) using StataMP version 17 for macOS. There was a statistically significant difference between the two methods in 13 outcomes (cardiopulmonary bypass time, aortic cross clamp time, operative time, ventilation time, hospital stay, ICU stay and postoperative bleeding, mortality, 24 h chest tube drainage, RBCs transfusion, wound infection, acute renal failure, and prolonged ventilation) (p value<0.05).

There was a non-statistically significant difference between the two methods in 13 outcomes (hemodialysis, myocardial infarction, endocarditis, cardiac tamponade, new atrial fibrillation, new pacemaker, stroke, respiratory failure, tracheostomy for respiratory failure, pneumonia, blood loss ≥ 800 ml/24 h, bleeding reoperation and reoperation for paravalvular regurgitation) (p value>0.05).

Results of quality assessment of the included studies

The forty-one included studies contained five RCTs, two non-randomized trials and 34 observational studies. Results of quality assessment of the RCTs according to the Cochrane handbook of systematic reviews and meta-analysis of interventions are shown in Supplementary Figure 2.

Mortality, ventilation time, hospital stay, ICU stay, postoperative bleeding and24 h chest tube drainage

Minimally invasive procedures showed clinically and statistically significant reduction in mortality, ventilation time, hospital stay, ICU stay, post-operative bleeding and 24 h chest tube drainage. Mortality was reported in 33 studies (total patients (n)=14059, MIAVR (n)=6731, full-sternotomy (n)=7328) and the overall risk ratio between the conventional sternotomy and the MIAVR favored the MIAVR, [polled risk ratio=0.76, 95% CI (0.59 to 0.99), p=0.04] (polled studies were homogenous, chi-square p=0.99, I-square=0%) (Supplementary Figure 3).

24-h chest tube drainage was reported in 10 studies (total patients (n)=2197, MIAVR (n)=1112, full-sternotomy (n)=1085) and the overall SMD between the conventional sternotomy and the MIAVR favored the MIAVR,([polled SMD=-1.03, 95% CI (-1.53, -0.53), p=0.00, polled studies were heterogeneous, chi-square p=0.00, I^2=95.78%) (Supplementary Figure 4).

Hospital stay was reported in 21 studies (total patients (n)=6810, MIAVR (n)=3618, full-sternotomy (n)=3192) and the overall SMD between the conventional sternotomy and the MIAVR favored the MIAVR, [polled SMD=-0.31, 95% CI (-0.49, -0.13), p=0.00, polled studies were heterogeneous, chi-square p=0.00, I^2=90.85%] (Supplementary Figure 5).

Ventilation time was reported in 25 studies (total patients (n)=7772, MIAVR (n)=4021, full-sternotomy (n)=3751) and the overall Standardized Mean Difference (SMD) between the conventional sternotomy and the MIAVR favored the MIAVR, [polled SMD=-0.26, 95% CI (-0.38, -0.15), p=0.00, polled studies were heterogeneous, chi-square p=0.00, I^2=80.06%] (Supplementary Figure 6).

Postoperative bleeding was reported in 12 studies [total patients (n)=2262, MIAVR (n)=1242, full-sternotomy (n)=1020] and the overall SMD between the conventional sternotomy and the MIAVR favored the MIAVR, [polled SMD=-0.13, 95% CI (-0.30, -0.03), p=0.00, polled studies were heterogeneous, chi-square p=0.00, I^2=66.43%] (Supplementary Figure 7).

ICU stay was reported in 27 studies (total patients (n)=10510, MIAVR (n)=5448, full-sternotomy (n)=5062) and the overall SMD between the conventional sternotomy and the MIAVR favored the MIAVR, [polled SMD=-0.16, 95% CI (-0.28, -0.04), p=0.00, polled studies were heterogeneous, chi-square p=0.00, I^2=86.15%] (Supplementary Figure 8).

RBCs transfusion, wound infection, acute renal failure and prolonged ventilation

Minimally invasive procedures showed clinically and statistically significant reduction in the post-operative RBCs transfusion, wound infections, acute renal failure and prolonged ventilation. RBCs transfusion was reported in 19 studies (total patients (n)=5496, MIAVR (n)=2552, full-sternotomy (n)=2944) and the overall risk ratio between the conventional sternotomy and the MIAVR favored the MIAVR [polled risk ratio=0.81, 95% CI (0.70 to 0.93), p=0.00, polled studies were homogenous, chi-square p=0.26, I^2=16.01%] (Supplementary Figure 9).

Prolonged ventilation was reported in 5 studies (total patients (n)=2143, MIAVR (n)=872, full-sternotomy (n)=1271) and the overall risk ratio between the conventional sternotomy and the MIAVR favored the MIAVR, [polled risk ratio=0.51, 95% CI (0.29 to 0.91), p=0.02, polled studies were heterogeneous, chi-square p=0.06, I^2=55.02%] (Supplementary Figure 10).

Wound infection was reported in 24 studies (total patients (n)=5795, MIAVR (n)=3033, full-sternotomy (n)=2762) and the overall risk ratio between the conventional sternotomy and the MIAVR favored the MIAVR, [polled risk ratio=0.66, 95% CI (0.47 to 0.92), p=0.02, polled studies were homogenous, chi-square p=0.47, I^2=0.00%] (Supplementary Figure 11).

Acute renal failure was reported in 15 studies (total patients (n)=6622, MIAVR (n)=3266, full-sternotomy (n)=3356) and the overall risk ratio between the conventional sternotomy and the MIAVR favored the MIAVR, [polled risk ratio=0.65, 95% CI (0.46 to 0.93), p=0.02, polled studies were homogenous, chi-square p=0.35, I^2=9.04%] (Supplementary Figure 12).

Operative time, cardiopulmonary bypass time, and Aortic Cross Clamp (ACC) time

Conventional sternotomy showed clinically and statistically significant reduction in operative time, cardiopulmonary bypass time and Aortic Cross-Clamp (ACC) time. Operative time was reported in 19 studies (total patients (n)=3813, MIAVR (n)=2049, full-sternotomy (n)=1764) and the overall SMD between the conventional sternotomy and the MIAVR favored the conventional sternotomy [polled SMD=0.47, 95% CI (0.22, 0.72), p=0.00, polled studies were heterogeneous, chi-square p=0.00, I^2=91.51%] (Supplementary Figure 13).

Cardiopulmonary bypass time was reported in 35 studies (total patients (n)=12547, MIAVR (n)=5973, full-sternotomy (n)=6574) and the overall SMD between the conventional sternotomy and the MIAVR favored the conventional sternotomy [polled SMD=0.37, 95% CI (0.20, 0.54), p=0.00, polled studies were heterogeneous, chi-square p=0.00, I^2=94.43%] (Supplementary Figure 14).

Aortic cross-clamp time was reported in 36 studies (total patients (n)=12147, MIAVR (n)=6068, full-sternotomy (n)=6079) and the overall SMD between the conventional sternotomy and the MIAVR favored the conventional sternotomy [polled SMD=0.27, 95% CI (0.07, 0.48), p=0.00, polled studies were heterogeneous, chi-square p=0.00, I^2=96.4%] (Supplementary Figures 15-23).

Hemodialysis, myocardial infarction, endocarditis, cardiac tamponade, new atrial fibrillation, new pacemaker, stroke, respiratory failure, tracheostomy for respiratory failure, pneumonia, blood loss ≥ 800 ml/24 h, bleeding reoperation and reoperation for paravalvular regurgitation.

The overall risk ratio between the conventional sternotomy and the MIAVR doesn't favor any of the two groups in all of these outcomes. Hemodialysis [polled risk ratio=0.97, CI (0.68 to 1.42), p=0.86, polled studies were homogenous, chi-square p=0.78], myocardial infarction [polled risk ratio=0.98, CI (0.51 to 1.87), p=0.95, polled studies were homogenous, chi-square p=0.91], endocarditis [polled risk ratio=0.97, CI (0.45 to 2.11), p=0.94, polled studies were homogenous, chi-square p=0.61], cardiac tamponade [polled risk ratio=0.90, CI (0.60 to 1.35), p=0.61, polled studies were homogenous, chi-square p=0.81], new atrial fibrillation [polled risk ratio=0.93, CI (0.79 to 1.09), p=0.37, polled studies were heterogeneous, chi-square p=0.03], new pacemaker [polled risk ratio=1.07, CI (0.75 to 1.48), p=0.66, polled studies were homogenous, chi-square p=0.31], stroke [polled risk ratio=0.64, CI (0.65 to 1.10), p=0.21, polled studies were homogenous, chi-square p=1.00], respiratory failure [polled risk ratio=0.97, CI (0.62 to 1.50), p=0.89, polled studies were homogenous, chi-square p=0.90], tracheostomy for respiratory failure [polled risk ratio =0.39, CI (0.07 to 2.21), p=0.28, polled studies were homogenous, chi-square p=0.68], pneumonia [polled risk ratio=1.51, CI (0.87 to 2.62), p=0.14, polled studies were homogenous, chi-square p=0.91], blood loss ≥ 800 ml/24 h [polled risk ratio=0.86, CI (0.59 to 1.24), p=0.41, polled studies were homogenous, chi-square p=0.45], bleeding reoperation [polled risk ratio=1.14, CI (0.91 to 1.43), p=0.26, polled studies were homogenous, chi-square p=0.37] and reoperation for paravalvular regurgitation [polled risk ratio=0.71, CI (0.38 to 1.31), p=0.27, polled studies were homogenous, chi-square p=0.67] (Table 4).

DISCUSSION

Minimally invasive aortic valve replacement surgeries have been gaining acceptance for the last decades. Lots of studies have shown that they can be done safely with mortality and morbidity similar to the conventional sternotomy aortic valve replacement surgeries. These procedures have become a major area of research and commercial interest. This systematic review is analyzing the clinical outcomes of 41 observational and interventional studies

Table 4: Summary of the included patients' numbers, relative risks and 95% confidence intervals of the non-statistically significant outcomes.

Indicator	Total patients (n)	MIAVR (n)	Full-sternotomy (n)	Relative risk	95% CI	p value
Hemodialysis (n)	7301	3154	4147	0.97	[0.68, 1.42]	0.86
Myocardial infarction (n)	3605	1895	1710	0.98	[0.51,1.87]	0.95
Endocarditis (n)	2215	1085	1130	0.97	[0.45, 2.11]	0.94
Cardiac tamponade (n)	2884	1404	1480	0.9	[0.60,1.35]	0.61
New atrial fibrillation (n)	7687	3320	4367	0.93	[0.79,1.09]	0.37
New pacemaker (n)	7323	3556	3767	1.07	[0.78,1.48]	0.66
Stroke (n)	12223	6274	6894	0.84	[0.65,1.10]	0.21
Respiratory failure (n)	1582	747	835	0.97	[0.62,1.50]	0.89
Tracheostomy for respiratory failure (n)	1220	293	927	0.39	[0.07, 2.21]	0.28
Pneumonia (n)	1882	898	984	1.51	[0.87,2.62]	0.14
Blood loss ≥ 800 ml/24 h, (n)	2597	1391	1206	0.86	[0.59,1.24]	0.41
Bleeding reoperation (n)	9467	4648	5143	1.14	[0.91,1.43]	0.26
Reoperation for paravalvular regurgitation (n)	5614	2880	2734	0.71	[0.38, 1.31]	0.27

comparing the conventional full sternotomy *versus* the minimally invasive procedures in aortic valve replacement.

Summary of the findings

The most important finding of this study is that MIAVR are safe procedures that conferred a survival benefit with clinically and statistically significant reduction in mortality rate as the overall risk ratio between the conventional sternotomy and the MIAVR favored the MIAVR [polled risk ratio=0.76, 95% CI (0.59 to 0.99), p=0.04] [polled studies were homogenous, chi-square p=0.99, I^2=0%] (Supplementary Figures 23-28).

Minimally invasive procedures showed clinically and statistically significant reduction in ventilation time, hospital stay, ICU stay, postoperative bleeding, 24-h chest tube drainage, post-operative RBCs transfusion, wound infections, acute renal failure and prolonged ventilation as the overall risk ratio between the conventional sternotomy and the MIAVR favored the MIAVR.

However, the conventional sternotomy showed clinically and statistically significant reduction in operative time, cardiopulmonary bypass time and Aortic Cross Clamp (ACC) time, as the overall Standardized Mean Difference (SMD) between the conventional sternotomy and the MIAVR favored the conventional.

The overall risk ratios between the conventional sternotomy and the MIAVR don't favor any of the two groups in hemodialysis, myocardial infarction, endocarditis, cardiac tamponade, new atrial fibrillation, new pacemaker, stroke, respiratory failure, tracheostomy for respiratory failure, pneumonia, blood loss ≥ 800 ml/24 h, bleeding reoperation and reoperation for paravalvular regurgitation (p value>0.05).

Explanation of the study findings

Minimally invasive approaches for AVR like the right anterior thoracotomy and mini-sternotomies allow smaller surgical incisions during operations compared to conventional sternotomies, which decrease the risk of bleeding and the need for post-operative blood product transfusion. That also decreases the risk of post-operative acute renal failure. Smaller surgical wounds decrease the risks of post-operative prolonged ventilation and wound infections, they also allow better cosmetic results, and speed up patient rehabilitation [12].

Minimally invasive approaches for AVR showed statistically significant increase in operative times, ACC, and cardiopulmonary bypass times compared to conventional sternotomies; that may be due to the learning curve of the new procedures. Some analyzing studies proved that with experience, the duration of surgery as well as ACC time decreased significantly and became similar between both groups [21]. Patients who performed AVR through the minimally invasive approaches had less time on the ventilator, shorter ICU and hospital length of stays with comparable short and long-term survival compared to the conventional sternotomy group.

Many studies have shown that these improved in-hospital outcomes likely result from decreased post-operative pain, facilitating quicker return of pulmonary function and mobilization [42]. Better post-operative clinical outcomes in the minimally invasive group led to lower mortality rates in this group compared to the conventional sternotomy group. This experience was also made by others, when new operative techniques were introduced. They demonstrated, that time for surgery may approximate to usual values for conventional AVR with increasing experience [52].

Significance of the work

This study expands the literature by providing strong evidence that minimally invasive approaches in aortic valve replacement are superior to the conventional sternotomy as they have lower mortality rate and, in addition, they have better post-operative prognosis and fewer post-operative complications compared to the conventional sternotomy. In this study, we analyzed data from 41 studies (7 clinical trials and 34 observational studies) with a total of (26,808) patients, making it, to the best of our knowledge, the largest and most comprehensive meta-analysis addressing this comparison to date.

Strength points

This study has lots of strong points including (1) Comprehensive research was done on multiple databases finding and including more studies than previously published systematic reviews. (2) All steps were conducted according to the guidelines of Cochrane handbook of systematic reviews and meta-analysis of interventions. (3) This manuscript is reported according to the PRISMA guidelines. (4) Methodological quality assessment of the included studies was done according to their study designs. (5) This meta-analysis includes 41 eligible comparative studies which include a total of (26,808) patients, (8,742) patients underwent MIAVR and (18,066) underwent conventional sternotomy so this large number of included patients indicates a reliable significant results.

CONCLUSION

This systematic review and meta-analysis proves that minimally invasive aortic valve replacement procedures have lower mortality rates, better post-operative clinical outcomes and fewer post-operative complications compared to conventional sternotomy. However, the conventional sternotomy has less operative time, aortic cross clamp and cardiopulmonary bypass times. Future well-designed blinded RCTs with long term follow- up are recommended.

LIMITATIONS

The most important limitation of this meta-analysis is the presence of significant heterogeneity in many variables analyzed such as (ventilation time, hospital stay, ICU stay, post-operative bleeding, 24-h chest tube drainage, operative time, cardiopulmonary bypass time and aortic cross-clamp time). The possible reasons for heterogeneity in these outcomes are the variability of the minimally invasive surgical techniques, sample size of each study and variable study designs.

CONFLICT OF INTERESTS

All authors have no conflict of interests.

REFERENCES

1. Bonow RO, Carabello BA, Chatterjee K, de Leon AC, Faxon DP, Freed MD, et al. 2008 Focused update incorporated

into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: A report of the American college of cardiology/American heart association task force on Practice guidelines (writing committee to revise the 1998 guidelines for the management of patients with valvular heart disease) endorsed by the society of cardiovascular anesthesiologists, society for cardiovascular angiography and interventions, and society of thoracic surgeons. Circulation. 2008;52(13):1-42.

2. Fudulu D, Lewis H, Benedetto U, Caputo M, Angelini G, Vohra HA. Minimally invasive aortic valve replacement in high risk patient groups. J Thorac Dis. 2017;9(6):1672.
3. Ramlawi B, Bedeir K, Lamelas J. Aortic valve surgery: Minimally invasive options. Methodist Debakey Cardiovasc J. 2016;12(1):27.
4. Schmitto JD, Mokashi SA, Cohn LH. Minimally-invasive valve surgery. JACC. 2010;56(6):455-462.
5. Bonacchi M, Prifti E, Giunti G, Frati G, Sani G. Does ministernotomy improve postoperative outcome in aortic valve operation? A prospective randomized study. Ann Thorac Surg. 2002;73(2):460-465.
6. Salenger R, Gammie JS, Collins JA. Minimally invasive aortic valve replacement. J Card Surg. 2016;31(1):38-50.
7. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. Prisma 2020 checklist prisma 2020 checklist. BMJ 2021;372:71.
8. C. B. Series, Cochrane Handbook for systematic reviews of interventions.
9. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. BMJ.2016;355.
10. 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. JAMA. 2000;283(15):2008-2012.
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. Br J Surg. 1999;354(9193):1896-1900.
12. Aliahmed HM, Karalius R, Valaika A, Grebelis A, Semėnienė P, Čypienė R. Efficacy of aortic valve replacement through full sternotomy and minimal invasion (ministernotomy). Medicina. 2018;54(2):26.
13. Ariyaratnam P, Loubani M, Griffin SC. Minimally invasive aortic valve replacement: Comparison of long-term outcomes. Asian Cardiovasc Thorac Ann. 2015;23(7):814-821.
14. Attia RQ, Raja SG. Surgical pericardial heart valves: 50 years of evolution. Int J Surg. 2021;94:106121.
15. Bakir I, Casselman FP, Wellens F, Jeanmart H, de Geest R, Degrieck I, et al. Minimally invasive *versus* standard approach aortic valve replacement: A study in 506 patients. Ann Thorac Surg. 2006;81(5):1599-1604.
16. Bang JH, Kim JW, Lee JW, Kim JB, Jung SH, Choo SJ, et al. Minimally invasive approaches *versus* conventional sternotomy for aortic valve replacement: A propensity score matching study. Korean J Thorac Cardiovasc Surg. 2012;45(2):80.
17. Borger MA, Moustafine V, Conradi L, Knosalla C, Richter M, Merk DR, et al. A randomized multicenter trial of minimally invasive rapid deployment *versus* conventional full sternotomy aortic valve replacement. Ann Thorac Surg. 2015;99(1):17-25.
18. Byrne JG, Aranki SF, Couper GS, Adams DH, Allred EN, Cohn LH. Reoperative aortic valve replacement: Partial upper hemisternotomy *versus* conventional full sternotomy. J Thorac Cardiovasc Surg. 1999;118(6):991-997.
19. Calderon J, Richebe P, Guibaud JP, Coiffic A, Branchard O, Asselineau J, et al. Prospective randomized study of early pulmonary evaluation of patients scheduled for aortic valve surgery performed by ministernotomy or total median sternotomy. J Cardiothorac Vasc Anesth. 2009;23(6):795-801.
20. Chien S, Clark C, Maheshwari S, Koutsogiannidis CP, Zamvar V, Giordano V, et al. Benefits of rapid deployment aortic valve replacement with a mini upper sternotomy. J Cardiothorac Surg. 2020;15:1-6.
21. Christiansen S, Stypmann J, Tjan TD, Wichter T, van Aken H, Scheld HH, et al. Minimally-invasive versus conventional aortic valve replacement–perioperative course and mid-term results. Eur J Cardiothorac Surg. 1999;16(6):647-652.
22. Corbi P, Rahmati M, Donal E, Lanquetot H, Jayle C, Menu P, et al. Prospective comparison of minimally invasive and standard techniques for aortic valve replacement: Initial experience in the first hundred patients. J Card Surg. 2003;18(2):133-139.
23. Dalén M, Oliveira Da Silva C, Sartipy U, Winter R, Franco-Cereceda A, Barimani J, et al. Comparison of right ventricular function after ministernotomy and full sternotomy aortic valve replacement: A randomized study. Interact Cardiovasc Thorac Surg. 2018;26(5):790-797.
24. Dalén M, Biancari F, Rubino AS, Santarpino G, Glaser N, de Praetere H, et al. Aortic valve replacement through full sternotomy with a stented bioprosthesis *versus* minimally invasive sternotomy with a sutureless bioprosthesis. Eur J Cardiothorac Surg. 2016;49(1):220-227.
25. Kasama K, Juvonen T, Deste W, Pollari F, Meuris B, Fischlein T, et al. Ministernotomy *versus* full sternotomy aortic valve replacement with a sutureless bioprosthesis: A multicenter study. Ann Thorac Surg. 2015;99(2):524-530.
26. Detter C, Deuse T, Boehm DH, Reichenspurner H, Reichart B. Midterm results and quality of life after minimally invasive *vs.* conventional aortic valve replacement. Thorac Cardiovasc Surg. 2002;50(6):337-341.
27. Vaumas C, Philip I, Daccache G, Depoix JP, Lecharny JB, Enguerand D, et al. Comparison of minithoracotomy and conventional sternotomy approaches for valve surgery. J Cardiothorac Vasc Anesth. 2003;17(3):325-328.

28. Dogan S, Dzemali O, Wimmer-Greinecker G, Derra P, Doss M, Khan MF, et al. Minimally invasive *versus* conventional aortic valve replacement: A prospective randomized trial. J Heart Valve Dis. 2003;12(1):76-80.

29. D'Onofrio A, Tessari C, Lorenzoni G, Cibin G, Martinelli G, Alamanni F, et al. Minimally invasive *vs.* conventional aortic valve replacement with rapid-deployment bioprostheses. Ann Thorac Surg. 2021;111(6):1916-1922.

30. Filip G, Bryndza MA, Konstanty-Kalandyk J, Piatek J, Wegrzyn P, Ceranowicz P, et al. Ministernotomy or sternotomy in isolated aortic valve replacement? early results. Kardiochirurgia i torakochirurgia polska/polish. J Thorac Cardiovasc Surg. 2018;15(4):213-218.

31. Furukawa N, Kuss O, Aboud A, Schönbrodt M, Renner A, Hakim Meibodi K, et al. Ministernotomy *versus* conventional sternotomy for aortic valve replacement: Matched propensity score analysis of 808 patients. Eur J Cardiothorac Surg. 2014;46(2):221-227.

32. Gasparovic I, Artemiou P, Hudec V, Hulman M. Long-term outcomes following minimal invasive *versus* conventional aortic valve replacement: A propensity match analysis. Bratisl Lek Listy. 2017;118(8):479-484.

33. Ghanta RK, Lapar DJ, Kern JA, Kron IL, Speir AM, Fonner Jr E, et al. Minimally invasive aortic valve replacement provides equivalent outcomes at reduced cost compared with conventional aortic valve replacement: A real-world multi-institutional analysis. J Thorac Cardiovasc Surg. 2015;149(4):1060-1065.

34. Giglio M, Mikus E, Nerla R, Micari A, Calvi S, Tripodi A, et al. Right anterior mini-thoracotomy *vs.* conventional sternotomy for aortic valve replacement: A propensity-matched comparison. J Thorac Dis. 2018;10(3):1588.

35. Gilmanov D, Bevilacqua S, Murzi M, Cerillo AG, Gasbarri T, Kallushi E, et al. Minimally invasive and conventional aortic valve replacement: A propensity score analysis. Ann Thorac Surg. 2013;96(3):837-843.

36. Hancock HC, Maier RH, Kasim A, Mason J, Murphy G, Goodwin A, et al. Mini-sternotomy *versus* conventional sternotomy for aortic valve replacement: A randomised controlled trial. BMJ open. 2021;11(1): 041398.

37. Hirji SA, Funamoto M, Lee J, Del Val FR, Kolkailah AA, McGurk S, et al. Minimally invasive *versus* full sternotomy aortic valve replacement in low-risk patients: Which will stand against transcatheter aortic valve replacement?. Surgery. 2018;164(2):282-287.

38. Hlavicka J, Janda D, Budera P, Tousek P, Maly M, Fojt R, et al. Partial upper sternotomy for aortic valve replacement provides similar mid-term outcomes as the full sternotomy. J Thorac Dis. 2022;14(4):857.

39. Kaczmarczyk M, Pacholewicz J, Kaczmarczyk A, Filipiak K, Hrapkowicz T, Zembala M. Ministernotomy for aortic valve replacement improves early recovery and facilitates proper wound healing–forced propensity score matching design with reference full sternotomy. Kardiochirurgia i torakochirurgia polska/polish. J Thorac Cardiovasc Surg. 2022;19(1):1-10.

40. Mikus E, Calvi S, Campo G, Pavasini R, Paris M, Raviola E, et al. Full sternotomy, hemisternotomy, and minithoracotomy for aortic valve surgery: Is there a difference? Ann Thorac Surg. 2018;106(6):1782-1788.

41. Liu R, Song J, Chu J, Hu S, Wang XQ. Comparing mini-sternotomy to full median sternotomy for aortic valve replacement with propensity-matching methods. Front Surg. 2022;9:972264.

42. Neely RC, Boskovski MT, Gosev I, Kaneko T, McGurk S, Leacche M, et al. Minimally invasive aortic valve replacement *versus* aortic valve replacement through full sternotomy: The Brigham and Women's Hospital experience. Ann Cardiothorac Surg. 2015;4(1):38.

43. Pfeiffer S, Dell'Aquila AM, Vogt F, Kalisnik JM, Sirch J, Fischlein T, et al. Efficacy of sutureless aortic valves in minimally invasive cardiac surgery: An evolution of the surgical technique. J Cardiovasc Surg. 2016;58(5):731-738.

44. Pisano C, Totaro P, Triolo OF, Argano V. Advantages of minimal access *versus* conventional aortic valve replacement in elderly or severely obese patients. Innovations. 2017;12(2):102-108.

45. Semsroth S, Gothe RM, Raith YR, de Brabandere K, Hanspeter E, Kilo J, et al. Comparison of two minimally invasive techniques and median sternotomy in aortic valve replacement. Ann Thorac Surg. 2017;104(3):877-883.

46. Oo S, Khan A, Chan J, Juneja S, Caputo M, Angelini G, et al. Propensity matched analysis of minimally invasive *versus* conventional isolated aortic valve replacement. Perfusion. 2023;38(2):261-269.

47. Stamou SC, Kapetanakis EI, Lowery R, Jablonski KA, Frankel TL, Corso PJ. Allogeneic blood transfusion requirements after minimally invasive *versus* conventional aortic valve replacement: A risk-adjusted analysis. Ann Thorac Surg. 2003;76(4):1101-1106.

48. Suenaga E, Suda H, Katayama Y, Sato M, Fujita H, Yoshizumi K, et al. Comparison of limited and full sternotomy in aortic valve replacement. Jpn J Thorac Cardiovasc Surg. 2004;52:286-291.

49. Szwerc MF, Benckart DH, Wiechmann RJ, Savage EB, Szydlowski GW, Magovern Jr GJ, et al. Partial *versus* full sternotomy for aortic valve replacement. Ann Thorac Surg. 1999;68(6):2209-2213.

50. Yilmaz A, Sjatskig J, van Boven WJ, Waanders FG, Kelder JC, Sonker U, et al. J-shaped *versus* median sternotomy for aortic valve replacement with minimal extracorporeal circuit. Scand Cardiovasc J.2011;45(6):379-384.

51. Zallé I, Son M, El-Alaoui M, Nijimbéré M, Boumzebra D. Minimally invasive and full sternotomy in aortic valve replacement: A comparative early operative outcomes. Pan Afr Med J. 2021 Sep 30;40(1).

52. Svensson LG, D'Agostino RS. "J" incision minimal-access valve operations. Ann Thorac Surg. 1998;66(3):1110-1112.