Comparative Evaluation of the Incidence of Postoperative Pulmonary Complications After Minimally Invasive Valve Surgery vs. Full Sternotomy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials and Propensity Score-Matched Studies

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Background: Postoperative pulmonary complications remain a leading cause of increased morbidity, mortality, longer hospital stays, and increased costs after cardiac surgery; therefore, our study aims to analyze whether minimally invasive valve surgery (MIVS) for both aortic and mitral valves can improve pulmonary function and reduce the incidence of postoperative pulmonary complications when compared with the full median sternotomy (FS) approach.

Methods: A comprehensive systematic literature research was performed for studies comparing MIVS and FS up to February 2021. Randomized controlled trials (RCTs) and propensity score-matching (PSM) studies comparing early respiratory function and pulmonary complications after MIVS and FS were extracted and analyzed. Secondary outcomes included intra- and postoperative outcomes.

Results: A total of 10,194 patients from 30 studies (6 RCTs and 24 PSM studies) were analyzed. Early mortality differed significantly between the groups (MIVS 1.2% vs. FS 1.9%; p = 0.005). Compared with FS, MIVS significantly lowered the incidence of postoperative pulmonary complications (odds ratio 0.79, 95% confidence interval [0.67, 0.93]; p = 0.004) and improved early postoperative respiratory function status (mean difference −24.83 [−29.90, −19.76]; p < 0.00001). Blood transfusion amount was significantly lower after MIVS (p < 0.02), whereas cardiopulmonary bypass time and aortic cross-clamp time were significantly longer after MIVS (p < 0.00001).
Conclusions: Our study showed that minimally invasive valve surgery decreases the incidence of postoperative pulmonary complications and improves postoperative respiratory function status.

Keywords: cardiac surgery, minimally invasive, valve repair/replacement, meta-analysis (as topic), full sternotomy

INTRODUCTION

Full median sternotomy (FS) has long been the standard incision for cardiac surgery due to its excellent exposure of the heart and great vessels. However, to reduce the size of the sternotomy, cardiac surgeons have long pursued less extensive incisions to improve outcomes and thus have used minimally invasive approaches that have undergone rapid development in the last...
few decades (1–3). These approaches have multiple benefits over an FS because of a smaller surgical incision, reduced pain, earlier discharge, and quicker postoperative recovery (4, 5). On the other hand, some potential technical disadvantages tend to have prolonged cardiopulmonary bypass (CPB) and aortic cross-clamp time (6, 7).

Given such developments in surgical management and patients’ treatment over the years, postoperative pulmonary complications remain a leading cause of mortality and morbidity following cardiac surgery (8, 9). These complications contribute to longer hospital stays and more readmissions into the ICU, significantly affecting health care and increasing healthcare systems’ financial burden (8, 10). Atelectasis and pleural effusions, pneumonia, pneumothorax, diaphragm paralysis because of phrenic nerve damage, and pulmonary infection are the most common pulmonary complications (11).

Although considerable benefits were associated with the MIVS over FS, there is still ongoing debate about the advantage of MIVS on postoperative pulmonary complications (PPCs), and the associations remain unclear. To our knowledge, there is still limited evidence on PPCs and respiratory system function analysis of patients after MIVS compared with the FS approach has not been analyzed. Therefore, based on the existing clinical literature, we conducted this systematic review and meta-analysis of high-quality randomized controlled trials (RCTs) and propensity score-matched (PSM) studies to analyze the incidence of PPCs and respiratory function of patients who underwent a minimally invasive approach for mitral or aortic valve vs. FS.

### TABLE 1 | Characteristics of included studies.

| References | Country | Study interval | Study type | No. of patients MIVS/FS | Surgical approach | Quality assessment | LOE† | Median follow-up |
|------------|---------|----------------|------------|-------------------------|------------------|------------------|------|-----------------|
| Aris et al. (6) | Spain | NS | RCT | 20/20 | A ψ | 3/5 | 2b | 6 days |
| Machler et al. (28) | Austria | 1996–1997 | RCT | 30/30 | A ψ | 3/5 | 2b | 294 days<sup>MD</sup> |
| Bonacchi et al. (14) | Italy | 1999–2001 | RCT | 40/40 | A ψ | 4/5 | 1b | 9.7 ± 5.7 months<sup>MD</sup> |
| Dogan et al. (16) | Germany | 2003–2004 | RCT | 20/20 | M § | 2/5 | 3b | NS |
| Moustafá et al. (5) | Egypt | NS | RCT | 30/30 | A ψ | 2/5 | 3b | NS |
| Calderon et al. (15) | France | 2003–2007 | RCT | 39/39 | A ψ | 5/5 | 2b | NS |
| Albacker et al. (12) | US | 1995–2010 | PSM | 223/223 | A § | 7 | 4 | 2 years |
| Masiello et al. (29) | Italy | 1997–1999 | PSM | 100/100 | A ψ | 6 | 3b | 1 month |
| Farhat et al. (17) | France | 2000–2001 | PSM | 50/50 | A ψ | 7 | 3b | 1 month |
| Tabata et al. (37) | US | 1996–2005 | PSM | 41/41 | A ψ | 7 | 3b | NS |
| Iriarte et al. (25) | US | 2000–2008 | PSM | 382/382 | M § | 8 | 3b | 4.2 ± 2.4 yrs<sup>MD</sup> |
| Holzhey et al. (24) | Germany | 1999–2009 | PSM | 143/143 | M § | 8 | 1b | 2.4 ± 2.1 yrs<sup>MD</sup> |
| Bang et al. (13) | Korea | 1997–2010 | PSM | 73/73 | A ψ | 7 | 3b | NS |
| Murzi et al. (31) | Italy | 2006–2010 | PSM | 100/100 | A θ | 6 | 2b | 3 years |
| Sansone et al. (32) | Italy | 2008–2010 | PSM | 50/50 | A θ | 7 | 3b | NS |
| Johnston et al. (26) | US | 1995–2004 | PSM | 832/832 | A ψ | 8 | 3a | 6.5 ± 3.0 years<sup>MD</sup> |
| Gilman et al. (20) | Italy | 2004–2011 | PSM | 182/182 | A θ | 7 | 3b | Until patient discharge |
| Hiraoka et al. (23) | Japan | 2007–2012 | PSM | 36/36 | A ψ | 7 | 4 | NS |
| Ghanta et al. (19) | US | 2011–2013 | PSM | 289/289 | A ψ | 6 | 4 | NS |
| Gilman et al. (21) | Italy | 2001–2013 | PSM | 100/100 | A θ | 8 | 3a | 33.7 months<sup>MD</sup> |
| Merk et al. (30) | Germany | 2003–2012 | PSM | 477/477 | A ψ | 6 | 3a | 3.1 ± 2.7 years<sup>MD</sup> |
| Shehada et al. (34) | Germany | 2002–2012 | PSM | 585/585 | A ψ | 7 | 3b | NS |
| Stołniński et al. (35) | Canada | 2010–2013 | PSM | 211/211 | A θ | 8 | 3b | NS |
| Gasparovic et al. (18) | Slovakia | 2010–2013 | PSM | 34/34 | A ψ | 7 | 3a | 5 years |
| Levack et al. (27) | US | 1995–2014 | PSM | 483/483 | A ψ | 8 | 3b | NS |
| Stołniński et al. (33) | Poland | 2011–2014 | PSM | 212/212 | A θ | 8 | 3a | 3 months |
| Seitz et al. (33) | Australia | 2013–2016 | PSM | 53/53 | A θ | 7 | 3b | NS |
| Hawkins et al. (22) | US | 2011–2016 | PSM | 74/74 | M § | 7 | 3b | NS |
| Wang et al. (38) | China | 2012–2015 | PSM | 67/67 | M § | 6 | 3a | 2.8 years |
| Zhao et al. (39) | China | 2013–2016 | PSM | 91/91 | C θ | 8 | 3a | 1 year |

A, Aortic valve; C, indicated both mitral and aorta valve; FS, full sternotomy; LOE, level of evidence; MIVS, minimally invasive valve surgery; M, mitral valve; MIVS/FS, minimally invasive valve surgery/FS; NS, not specified; PSM, propensity score-matching; RCT, randomized control trial; †, indicates aortic valve surgery right mini-thoracotomy; ψ, indicates aortic valve surgery upper mini-sternotomy; §, indicated aortic valve surgery right mini-thoracotomy and upper mini-sternotomy; θ, indicates both mitral and aorta valve surgery right mini-thoracotomy; ϕ, indicates aortic valve surgery right mini-thoracotomy and upper mini-sternotomy; ‡, indicates both mitral or aorta valve surgery right mini-thoracotomy; * Based on US Preventive Services Task Force grading system.
METHODS

Selection Criteria
We included all articles reporting clinical outcomes for MIVS (repair or replacement of the mitral valve, aortic valve, or both valves) via right/lateral mini-thoracotomy or mini-sternotomy, with either a camera or direct visualization, vs. traditional FS. Studies were considered using a PICOS (Population, Intervention, Comparison, Outcome, and Study) strategy if (1) articles were published in English, (2) articles reported RCTs or PSM studies, (3) articles compared the outcomes of MIVS and FS for either mitral or aortic valve disease, and (4) outcomes included postoperative pulmonary complications and early postoperative respiratory function.

Articles without a full report available, review studies, studies with previous cardiac surgery and concomitant surgical procedures (coronary artery bypass grafting, and procedure involving ascending aortic) other than isolated mitral and aortic or both valve surgery were excluded and studies with no comparison group were also excluded.

Information Sources
The following databases were used: PubMed, MEDLINE, Web of Science, Cochrane Central Register of Controlled Trials, Scopus, and Google Scholar. The reference lists of identified articles were also included in manual searches.

Search Strategy
We searched articles and studies comparing FS vs. MIVS using the following medical subject headings: aortic valve, aortic valve surgery, mitral valve or mitral valve surgery, minimally/partial invasive, full/conventional/partial sternotomy or mini-sternotomy, anterolateral/right mini-thoracotomy, partial upper Hemi-sternotomy or upper mini-sternotomy.

Study Selection
Search strategies, inclusion with exclusion criteria, statistical analysis, and outcomes were predefined. Thirty publications fulfilled our eligibility criteria (5, 6, 12–39). Two independent investigators (MA, SZ) reviewed all abstracts that fulfilled the search criteria. When there were differences of opinion between these investigators, other authors were included to resolve disagreements. Figure 1 summarizes the search strategy.

Data Extraction
Two reviewers independently extracted data from each included study and performed the quality assessment. Data extracted included the first author's name, year of publication, country, study interval, study type, the number of subjects who underwent MIVS or FS, and outcomes of interest. The following clinical outcomes of interest from each study were extracted to compare MIVS with FS: postoperative pulmonary complications (overall complications, pneumonia, pleural effusion, pneumothorax, pulmonary infection, and respiratory insufficiency), early postoperative pulmonary function variables after 1 week (forced expiratory volume...
in 1 second [FEV1], forced total lung capacity (TLC), and forced vital capacity [FVC%]). Secondary outcomes of interest included early mortality, blood transfusion and, cardiopulmonary bypass (CPB) time, aortic cross-clamp time, and operative time.

**Risk-of-Bias and Study Quality Assessment**

Two independent reviewers (SZAS and NID) assessed the risk-of-bias using the Cochrane risk-of-bias (RoB2) tool. The risk-of-bias was categorized as low, high, or unclear risk-of-bias. The RoB2 Excel tool was applied to individual studies, and results were entered into Cochrane’s Review Manager 5.3 (40). The Newcastle–Ottawa Scale (NOS) was used to assess the methodological quality of all observational studies. The NOS assesses the following characteristics of a study: selection of the general population, comparability, and adequate assessment of outcomes, to evaluate the methodological quality of studies (41). Based on the NOS, a maximum of 9 points can be given to each study. In this review, the modified NOS scores ≥ 7 were considered to indicate high-quality publications. Furthermore, the methodological quality of RCTs was assessed using the Jadad scale, which evaluates RCT quality using a maximum score of 5. A Jadad score ≥ 3 was considered to indicate high-quality RCTs (42).

**Definitions of Outcomes**

MIVS was defined as any procedure not performed with an FS. A full sternotomy was performed from the sternal notch to the xiphoid process. The definitions of the postoperative outcomes mainly depend on the descriptions mentioned in the original articles (8, 18, 39, 43–45). Besides postoperative pulmonary complications were defined as complications occurring in the postoperative period and producing clinical diseases, such as pneumonia, pleural effusion, pneumothorax, pulmonary infection, and respiratory insufficiency (defined as the need for reintubation or tracheostomy after initial extubation), and prolonged ventilation time, which was defined as mechanical ventilatory support requirement for more than 24 h. Pulmonary function tests, represented by FEV1, TLC, and FVC, were assessed based on a spirometry test 1 week after surgery. The incidence of early mortality was defined as death in the hospital or within 30 days post-surgery.

**Statistical Analysis**

As per Cochrane Collaboration guidelines, all statistical meta-analyses were performed using Review Manager 5.3 software (Cochrane Collaboration, Copenhagen, Denmark). We calculated pooled odds ratios (ORs) with their 95% confidence intervals (CIs) for dichotomous data, which are presented as numbers and percentages. Weighted mean differences (WMDs) were used to assess continuous data, which are presented as means ± standard deviation or medians with interquartile ranges. We assessed the heterogeneity of studies by means of $I^2$ and chi-square test. As a sensitivity analysis, FS and MIVS from RCTs and from PSM studies were compared separately. The reported results all are two-sided, and a $p < 0.05$ was considered to indicate statistical significance.

**TABLE 2 | Overall and subgroup analysis of postoperative respiratory function and complications comparing MIVS and FS.**

| Outcome of interest | n/N | No. patients MIVS/FS | Overall effect | $P$ | Study heterogeneity |
|---------------------|-----|----------------------|---------------|-----|---------------------|
|                     |     |                      | WMD/OR (95% CI)$^\dagger$ |     | chi$^2$-test df $I^2$ (%) | $P$-value |
| **Postoperative respiratory function status after 1 week** |
| Overall spirometry  | 6 (1,928) | 964/964 | MD −24.83 [−29.90,−19.76]$^\dagger$ | <0.00001 | 11770.40 13 100 <0.00001 |
| Subgroup analysis   |     |                      |               |     |                      |
| FEV1%               | 6 (722) | 361/361 | −74.06 [−89.14,−58.99]$^\dagger$ | <0.00001 | 1089.82 5 100 <0.00001 |
| FVC%                | 5 (642) | 321/321 | 4.99 [1.23, 8.75]$^\dagger$ | 0.009 | 287.63 4 99 <0.00001 |
| TLC                 | 3 (564) | 282/282 | 8.39 [2.00, 14.78]$^\dagger$ | 0.01 | 72.03 2 97 <0.00001 |
| Overall PPCs        | 30 (10,194) | 5,097/5,097 | 0.79 [0.67, 0.93] | 0.004 | 28.51 27 5 0.39 |
| RCT                 | 6 (418) | 209/209 | OR 0.32 [0.12, 0.90] | 0.03 | 4.29 4 7 0.37 |
| PSM                 | 24 (9,776) | 4,888/4,888 | OR 0.80 [0.69, 0.94] | 0.005 | 20.98 22 0 0.52 |
| **Subgroup analysis** |
| Pneumonia           | 5 (916) | 458/458 | 1.42 [0.44, 4.55] | 0.56 | 2.81 4 0 0.59 |
| Pleural Effusion     | 8 (1,454) | 727/727 | 0.81 [0.45, 1.45] | 0.47 | 10.28 7 32 0.17 |
| Pneumothorax         | 4 (420) | 210/210 | 1.55 [0.30, 8.12] | 0.60 | 4.50 3 33 0.21 |
| Respiratory insufficiency | 12 (5,848) | 2,924/2,924 | 0.75 [0.62, 0.91] | 0.004 | 9.30 11 0 0.59 |
| Pulmonary infection  | 2 (246) | 123/123 | 1.35 [0.16, 11.30] | 0.78 | 1.24 1 19 0.27 |
| Prolonged ventilation time | 10 (3,564) | 1,782/1,782 | 0.72 [0.51, 1.01] | 0.06 | 6.92 9 0 0.65 |

$n$, number of studies; $N$, number of participants; MIVS, minimally invasive valve surgery; FS, full sternotomy; PPC, postoperative pulmonary complications; WMD, weighted mean difference; OR, odds ratio; CI, confidence interval; $^\dagger$, test of heterogeneity; FEV1, forced expiratory volume in 1 s; FVC, Forced vital capacity; TLC, total lung capacity; $^\ddagger$, Values of WMD.
RESULTS
Characteristics of Eligible Studies
Our literature search revealed 30 studies that met our selection criteria (5, 6, 12–39). The total number of patients in these studies was 10,194; 5,097 (50%) patients underwent MIVS, and 5,097 (50%) patients underwent FS. Six studies were RCTs (n = 418 patients) (5, 6, 14–16, 28) and 24 were PSM studies (n = 9,776 patients) (12, 13, 17–27, 29–39). The characteristics of these studies are shown in Table 1. Figure 1 shows the PRISMA flowchart of the search and selection strategy (46).

Postoperative Pulmonary Complications Outcomes
We analyzed data on postoperative pulmonary complications from 27 studies (6, 12–14, 16–34, 36–39). The overall complications were less in MIVS patients than in FS patients (OR

The RCTs scored at least 3 out of 5 on the Jadad scale, and most of the PSM studies scored at least 7 out of 9, based on a modified version of the NOS scale (Table 1 and Figure 2). Therefore, overall, the studies were considered to be of high quality.
Figure 4: Forest plot demonstrating the subgroup study of the incidence of postoperative pulmonary between MIVS and FS.
0.79; 95% CI [0.67, 0.93]; p = 0.004). The results of our meta-analysis are summarized in Table 2, and forest plots are shown in Figure 3.

In subgroup analysis, postoperative pulmonary complications differed significantly between the two groups (p = 0.0007) in terms of the incidence of postoperative respiratory insufficiency, reported by 12 studies (12, 14, 19, 21, 23, 24, 26, 30, 33, 34, 38, 39) (OR 0.75; 95% CI [0.62, 0.91]; p = 0.004). Two studies reported on pulmonary infection: MIVS was associated with a lower chance of infection, but this difference was not significant (OR 1.35; 95% CI [0.16, 11.30]; p = 0.78) (13, 17). The incidence of postoperative pleural effusion was reported in 8 studies; this was not significantly different between the groups (OR 0.81; 95% CI [0.45, 1.45]; p = 0.47) (6, 16, 18, 20, 21, 28, 29, 36).

We also compared the incidence of prolonged ventilation time based on data pooled from 10 studies; there was no significant difference between the groups (OR 0.81; 95% CI [0.51, 1.01]; p = 0.06) (6, 14, 19, 25, 27, 31, 37, 39). Although the observed proportions of patients with pneumonia (OR 1.42; 95% CI [0.44, 4.55]; p = 0.56) and pneumothorax (OR 1.55 95% CI; [0.30, 8.12]; p = 0.60) were less among MIVS patients, these were not significantly different between the groups. Subgroup analysis is summarized in Table 2 and forest plots are shown in Figure 4.

Six studies (5, 6, 14–16, 35) reported on postoperative respiratory function tests based on spirometry, revealing that the overall complications were significantly reduced with MIVS compared to FS (964 vs. 964, WMD = 24.83 95% CI [−29.90, −19.76]; p < 0.00001). Most pulmonary function tests showed that the MIVS group had better respiratory function than the FS group 1 week after surgery. There was significant heterogeneity among the studies (p < 0.00001).

A subgroup analysis of postoperative respiratory function identified that FEV1% (WMD: −78.06; 95% CI [−89.14, −58.99]; p < 0.00001), FVC% (WMD: 4.99; 95% CI [1.23, 8.75]; p = 0.009), and TLC (WMD: 8.39; 95% CI [2.00, 14.78]; p = 0.01) were all significantly better in the MIVS group. There was significant heterogeneity among the studies overall, as well as in the RCT and PSM subgroup (p < 0.00001) (Table 2 and Figure 5).

**Early Mortality Outcomes**

Early mortality was reported as an outcome in 30 studies (5, 6, 12–39), including 5 RCTs (6, 14–16, 28) and 25 PSM studies (12, 13, 17–27, 29–39). The incidence of early death was 1.2 and 1.9% with MIVS, and FS approaches, respectively. Thus, the early mortality rate after MIVS was significantly lower than that after FS (OR 1.58 95% CI: [1.15, 2.16]; p = 0.005). There was no significant heterogeneity between the groups (p = 0.97) (Figures 6A,B).

**Intraoperative Variable Outcomes**

MIVS was associated with a significantly prolonged CPB time (WMD: 11.06; 95% CI: 4.29, 17.84 min; p = 0.001) (Figure 7).
and aortic cross-clamping time (WMD: 23.28; 95% CI: 5.65, 40.87 min; \( p = 0.009 \)) (Figure 8). Thus, the MIVS approach took longer than the FS surgery, although there was no significant difference in the operative time (WMD: 0.39; 95% CI: –0.39, 1.77 h; \( p = 0.32 \)) between the groups (Figure 9). However, the overall heterogeneity between the two approaches was significantly different (\( p < 0.00001 \)). Table 3 provides a summary of these studies.

**Need for Blood Transfusion Outcomes**

Fourteen studies [2 RCTs (15, 16) and 12 PSM studies (19, 20, 22, 23, 26, 27, 30, 32, 33, 36, 37, 39)] reported on the need for blood transfusion in patients. Twenty-two percent of patients required red blood cell (RBC) transfusion after MIVS, compared to 28% after FS (OR 0.69, 95% CI 0.51, 0.93; \( p = 0.02 \)) (Figure 10).

Ten studies [3 RCTs (5, 13, 14) and 7 PSM studies (16–18, 24, 31, 36, 38)] reported the units of RBC transfused after MIVS and FS. Those who underwent MIVS used significantly fewer units of RBCs for transfusion than those who underwent FS (WMD: –0.59, 95% CI: [–2.08, 0.90] U; \( p = 0.44 \)). There was significant heterogeneity among the studies overall as well as for the RCTs and PSM studies (\( p < 0.00001 \)) (Figure 11).

**DISCUSSION**

Over the past decades, a steady evolution has taken place in the practice of MIVS, with excellent postoperative outcomes, according to the literature. The minimally invasive approach used for the aorta or mitral valve has advantages over the FS method in terms of decreased surgical trauma, postoperative blood loss, and length of ICU and hospital stay (4, 47). Nevertheless, postoperative pulmonary complications remain a common cause of postcardiac surgical morbidity, poor outcomes, increased cost, and hospital stays (48). Therefore, in the context of postoperative pulmonary complications and recovery of early respiratory system function, we considered it necessary to compare MIVS with FS.

In this meta-analysis, we analyzed data of 10,194 patients (5,097 [50%] vs. 5,097 [50%] patients in MIVS vs. FS groups, respectively), from 30 studies (6 RCTs and 24 PSM studies) to evaluate postoperative pulmonary functions status and pulmonary complications after MIVS vs. FS. We also assessed early mortality, CPB time, aortic cross-clamp time, procedure time, and need for blood transfusion between the MIVS and FS. Using the best available level of evidence based
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FIGURE 7 | Forest plot of cardiopulmonary bypass time (minutes) between MIVS vs. FS.

on RCTs and PSM studies, our meta-analysis added to the literature that the MIVS is safe and had a significantly reduced overall incidence of postoperative pulmonary complications and respiratory insufficiency and decreased mechanical ventilation time compared with FS.

Moreover, the overall findings for the secondary outcomes suggested that MIVS, both aortic and mitral, significantly reduced early mortality and blood transfusion requirements. To the best of our knowledge, no previous meta-analyses have indicated whether the incidence of pulmonary complications is lower after MIVS compared with FS. Most studies that describe the effect of cardiac surgery on pulmonary complications were related to patients who underwent a coronary bypass operation through full median sternotomy (49).

It has been reported that the MIVS showed better preserved early postoperative respiratory function status and reduced the time needed to make a full recovery of pulmonary status compared with FS (50). However, there has not been explained this improved respiratory function in the MIVS group so far.

This study found that patients undergoing MIVS had a reduced incidence of postoperative pulmonary complications and better postoperative respiratory function outcomes than patients undergoing valve surgery via full median sternotomy. Therefore, we believe that our finding of a reduced incidence of pulmonary complications after the MIVS group may explain the improved lung function than patients with a full median sternotomy. As a result, we believe these phenomena are more likely caused by preserving the chest wall's integrity and reduced surgical trauma. Because of their improved respiratory condition, patients could begin mobilization quicker and perform pulmonary bronchial tree ventilation and cleaning more adequately.

Several risk factors may influence the impairment of spirometry and change in pulmonary gas exchange after cardiac surgery performed via a sternotomy; these include surgical trauma, prolonged operative and CPB time (6, 12, 14, 51). CPB causes an inflammatory cascade of compounds associated with the systemic inflammatory syndrome due to blood interaction with the CPB circuit and decreased pulmonary regeneration,
mostly because of insufficient surfactant release triggered by poor perfusion of the alveolar epithelium during CPB (49). Because of the more technical problem, patients in the MIVS group had a longer mean CPB duration than those in the FS group. However, we believe that this variation has no influence on postoperative pulmonary complications.

However, if CPB duration were the underlying cause, we would predict the MIVS group to have more significant postoperative pulmonary complications. This study found that patients who underwent MIVS had significantly longer cardiopulmonary bypass time, which may have contributed to the lower number of pulmonary complications observed in this group. A randomized clinical trial would be the only approach to analyze the influence of these independent factors on the incidence of postoperative pulmonary problems. MIVS did not result in an adverse postoperative pulmonary complication. It is likely that patients in whom the MIVS approach was used tended to have better early recovery and more favorable improvement of postoperative pulmonary function because of the shorter mechanical ventilation time, preservation of the chest wall integrity, and reduced postoperative pain, as compared with FS (50, 52, 53). Previous studies drew a similar conclusion to ours: there is less impaired respiratory function among patients who underwent surgery using the MIVS approach (11).

However, other investigators found no significant differences between the MIVS and FS regarding postoperative respiratory function system improvement (14, 15, 36, 54).

Moreover, we found that patients who underwent MIVS had a significant reduction in the incidence of early mortality (1.2%) compared with FS (1.9%). This finding was in line with that of previously published studies. A study by Mark et al. (30), who analyzed 477 PSM patients who underwent MIVS or FS, showed...
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FIGURE 9 | The forests plot demonstrates operative time (hours) between MIVS and FS.

TABLE 3 | Overall analysis of demographic, intraoperative, and postoperative outcomes comparing MIVS and FS.

| Variables | n(N) | No. patients | Overall effect WMD/ OR (95% CI) | P | Study heterogeneity |
|-----------|------|--------------|---------------------------------|---|---------------------|
| Age, y ± SD | 30 (10,194) | 5,097/5,097 | 0.43 [-1.05, -0.18] | 0.17 | 0.9187 29 68 <0.00001 |
| Male, % | 27 (9,628) | 4,814/4,814 | 1.01 [0.95, 1.12] | 0.48 | 9.61 26 0 1.00 |
| LVEF, % ± SD | 23 (9,628) | 3,455/3,455 | 0.65 [-0.09, 1.39] | 0.09 | 1288.37 22 98 <0.00001 |
| COPD, % | 17 (8,132) | 4,066/4,066 | 0.87 [0.74, 1.03] | 0.11 | 4.51 15 0 1.00 |
| Early mortality, % | 30 (10,194) | 5,097/5,097 | 0.68 [0.49, 0.95] | 0.02 | 14.42 26 0 0.97 |
| Blood transfusion (unit) ± SD | 10 (1,536) | 768/768 | -0.59 [-2.08, 0.90] | 0.44 | 166.69 9 96 <0.00001 |
| Blood transfusion (patient), % | 14 (6,756) | 2,878/2,878 | 0.69 [0.51, 0.93] | 0.02 | 48.53 13 73 <0.00001 |
| CBP time ± SD | 27 (8,798) | 4,399/4,399 | 11.06 [4.29, 17.84] | 0.001 | 1924.40 26 99 <0.00001 |
| Cross clamping time, minutes ± SD | 28 (9,170) | 4,585/4,585 | 23.28 [5.69, 40.87] | 0.009 | 35361.85 27 100 <0.00001 |
| Operative time, minutes ± SD | 13 (2980) | 1,490/1,490 | 0.39 [-0.38, 1.17] | 0.32 | 153.09 12 92 <0.00001 |

COPD, chronic obstructive pulmonary disease; CBP, cardiopulmonary bypass; CI, confidence interval; FS, Full sternotomy; P, test of heterogeneity; LVEF, left ventricular ejection fraction; MIVS, minimally invasive valve surgery; n, number of studies; N, number of participants; OR, odds ratio; SD, standard deviation; WMD, weighted mean difference; † Values of WMD.

that MIVS was associated with lower hospital mortality (0.4 vs. 2.3%, respectively). This result was also in line with the results of Paparella et al. (55), who reported on 5,801 patients from different centers who underwent mini-aortic valve replacement vs. conventional aortic valve replacement.

Shehada et al. and Johnston et al. (26, 34) reported on 2,103 and 2,689 patients, respectively, in PSM analyses that compared minimally invasive to conventional aortic valve surgery. They reported a significantly lower incidence of the need for blood transfusion, as well as respiratory insufficiency in MIVS patients. Similarly, we found that the number of patients who required blood transfusion and the number of units of RBC required for transfusion were significantly reduced in MIVS than in FS.

Our observations provide evidence for the value of MIVS as an acceptable alternative option to traditional FS for patients at higher risk of developing pulmonary complications and for patients with chronic lung
Nevertheless, our study has certain limitations. Most studies did not report similar outcomes, and there was limited information about the pulmonary effects of MIVS. Follow-up
for most studies was limited; hence, we were unable to compare long-term results.

CONCLUSIONS

Based on the above findings in our meta-analysis, MIVS, both mitral and aortic, seem to provide better clinical and surgical outcomes than FS, particularly the benefits of early recovery of postoperative respiratory system functions and reduced incidence of postoperative pulmonary complications. Moreover, MIVS was not associated with an increased incidence of early mortality or a greater need for blood transfusion than FS. We believe that our findings might help surgeons in patient selection, particularly when dealing with patients with a high risk of pulmonary disease undergoing cardiac valve surgical repair or replacement. Finally, further studies comparing MIVS and FS are recommended to validate our findings.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

MM and SA: data analysis/writing. MM and SD: data collection/writing. RL, ND, CC, and XW: reviewers/editing. All authors contributed to the article and approved the submitted version.

REFERENCES

1. Doll N, Borger MA, Hain J, Bucerius J, Walther T, Gummert JF, et al. Minimal access aortic valve replacement: effects on morbidity and resource utilization. *Ann Thorac Surg.* (2002) 74:S1318–22. doi: 10.1016/S0003-4975(02)03911-5

2. Chitwood WR, Wilson CL, Elbeery JR, Moran JF, Chapman WWH, Lust RM. Video-assisted minimally invasive mitral valve surgery. *J Thorac Cardiovasc Surg.* (1997) 114:773–80. doi: 10.1016/S0022-5223(97)70081-3

3. Boix-Garibo R, Uzzaman MM, Bapat VN. Review of minimal invasive aortic valve surgery. *Inter J Cardiol.* (2015) 10:144–48. doi: 10.15420/icr.2015.10.03.144

4. Bouhout I, Morgant MC, Bouchard D. Minimally invasive heart valve surgery. *Can J Cardiol.* (2017) 33:1129–37. doi: 10.1016/j.cjc.2017.05.014

5. Moustafa MA, Abdelsamad AA, Zakaria G, Omarah MM. Minimal vs median sternotomy for aortic valve replacement. *Asian Cardiovasc Thorac Ann.* (2007) 15:472–5. doi: 10.1111/j.1475-9773.2007.00605.x

6. Aris A, Camara ML, Montiel J, Delgado LJ, Galan J, Litvan H. Minimally versus median sternotomy for aortic valve stenosis: a prospective, randomized study. *Ann Thorac Surg.* (1999) 67:1583–7. doi: 10.1016/S0022-5223(99)00362-8

7. Cheng DC, Martin J, Lal A, Diegeler A, Folliguet TA, Nifong LW, et al. Minimally invasive versus conventional open mitral valve surgery: a meta-analysis and systematic review. *Innovations.* (2011) 6:84–103. doi: 10.1097/IMI.0b013e3182167fe6

8. Miskovic A, Lumb AB. Postoperative pulmonary complications. *Br J Anaesth.* (2017) 118:317–34. doi: 10.1093/bja/aex002

9. Weissman C. Pulmonary complications after cardiac surgery. *Semin Cardiothorac Vasc Anesth.* (2004) 8:185–211. doi: 10.1053/j.ctva.2004.08.0303

10. Canet J, Gallart L, Gomar C, Paluzie G, Valles J, Castillo J, et al. Prediction of postoperative pulmonary complications in a population-based surgical cohort. *Anesthesiology.* (2010) 113:1338–50. doi: 10.1097/ALN.0b013e3181f6cd0a

11. Weissman C. Pulmonary function after cardiac and thoracic surgery. *Curr Opin Anaesthesiol.* (2000) 13:47–51. doi: 10.1097/00000539-199909600-00014

12. Albacker TB, Blackstone EH, Williams SJ, Gillinov AM, Nivia JL, Roselli EE, et al. Should less-invasive aortic valve replacement be avoided in patients with pulmonary dysfunction? *J Thorac Cardiovasc Surg.* (2014) 147:355–61. doi: 10.1016/j.jtcvs.2012.12.014

13. Bang JH, Kim JW, Lee JW, Kim JR, 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) 45:80–4. doi: 10.5090/kjtcs.2012.45.2.80

14. Bonacchi M, Prifti E, Giunti G, Frati G, Sani G. Does minimi sternotomy improve postoperative outcome in aortic valve operation? A prospective randomized study. *Ann Thorac Surg.* (2002) 73:460–5. doi: 10.1016/S0003-4975(01)03402-6

15. 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 minimi sternotomy or total median sternotomy. *J Cardiothorac Vasc Anesth.* (2009) 23:795–801. doi: 10.1053/j.jvca.2009.03.011

16. Dogan S, Aybek T, Risteski PS, Detho F, Rapp A, Wimmer-Greinecker G, et al. Minimally invasive port access versus conventional mitral valve surgery: prospective randomized study. *Ann Thorac Surg.* (2005) 79:492–8. doi: 10.1016/j.athoracsur.2004.08.006

17. Furtat F, Lu Z, Lefevre M, Montagna P, Mikaeloff P, Jegaden O. Prospective comparison between total sternotomy and minimi sternotomy for aortic valve replacement. *J Card Surg.* (2003) 18:396–401. doi: 10.1016/j.jtcvs.2003.12.007.x

18. 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) 118:479–84. doi: 10.4149/BLL_2017_092

19. Ghanta RK, Lapar DJ, Kern JA, Kron IL, Speir AM, Fonner 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) 149:1060–5. doi: 10.1016/j.jtcvs.2015.01.014

20. Gilmanov D, Bevilacqua S, Murzi M, Cerillo AG, Gasbarri T, Kallush E, et al. Minimally invasive and conventional aortic valve replacement: a propensity score analysis. *Ann Thorac Surg.* (2013) 96:837–43. doi: 10.1016/j.jatlsur.2013.04.102

21. Gilmanov D, Farneti PA, Ferrarini M, Santarelli F, Murzi M, Miceli A, et al. Full sternotomy versus right anterior minithoracotomy for isolated aortic valve replacement in octogenarians: a propensity-matched study dagger. *Interact Cardiovasc Thorac Surg.* (2015) 20:732–41. doi: 10.1093/icvts/ivt030

22. Hawkins RR, Mehaffey JH, Kessel SM, Dahl JJ, Kron IL, Kern JA, et al. Minimally invasive mitral valve surgery is associated with excellent resource utilization, cost, and outcomes. *J Thorac Cardiovasc Surg.* (2018) 156:611–16. doi: 10.1016/j.jtcvs.2018.03.108

23. Hiraoka A, Totsugawa T, Koshino M, Nakajima K, Chikazawa G, Tamura K, et al. Propensity score-matched analysis of minimally invasive aortic valve replacement. *Circ J.* (2014) 78:2876–81. doi: 10.1253/circj.CJ-14-0861

24. Holzhey DM, Shi W, Borger MA, Seeburger J, Garbade J, Pfannmu ller B, et al. Minimally invasive versus sternotomy approach for mitral valve surgery in patients greater than 70 years old: a propensity-matched comparison. *Ann Thorac Surg.* (2011) 91:101–5. doi: 10.1016/j.athoracsur.2010.08.006

25. Iribarne A, Russo MJ, Easterwood R, Hong KN, Yang J, Cheema FH, et al. Minimally invasive versus total median sternotomy. *J Thorac Cardiovasc Surg.* (2011) 142:1533–40. doi: 10.1016/j.jtcvs.2011.01.062

26. Johnston DR, Atik FA, Rajeswaran J, Blackstone EH, Nowicki ER, Sabik JF, et al. Outcomes of less invasive J-incision approach to aortic valve surgery.
Machler HE, Aftab M, Roselli EE, Johnston DR, Soltesz EG, Gillinov AM, et al. Outcomes of a less-invasive approach for proximal aortic operations. *Ann Thorac Surg.* (2017) 103:33–40. doi: 10.1016/j.athoracsur.2016.06.008

Machler HE, Bergmann P, Anelli-Monti M, Dacar D, Rehak P, Knez I, et al. Minimally invasive versus conventional aortic valve operations: a prospective study in 120 patients. *Ann Thorac Surg.* (1999) 67:1001–5. doi: 10.1016/s0003-4975(99)00722-7

Masiello P, Coscioni E, Panza A, Triumbi F, Preziosi G, Di Benedetto G. Surgical results of aortic valve replacement via partial upper sternotomy: comparison with median sternotomy. *Cardiovasc Surg.* (2002) 10:333–8. doi: 10.1093/scr/10.4.333

Merk DR, Lehnmann S, Holzhey DM, Dohmen P, Candolfi P, Misfeld M, et al. Minimal invasive aortic valve replacement surgery is associated with improved survival: a propensity-matched comparison. *Eur J Cardiothorac Surg.* (2015) 47:11–7. doi: 10.1093/ejcts/ezu068

Murzi M, Cerillo AG, Bevilacqua S, Gilmanov D, Farneti P, Glauber M. Traversing the learning curve in minimally invasive heart valve surgery: a cumulative analysis of an individual surgeon's experience with a right minithoracotomy approach for aortic valve replacement. *Eur J Cardiothorac Surg.* (2012) 41:1422–6. doi: 10.1093/ejcts/ezz230

Sansone F, Punta G, Parisi F, Dato GM, Zingarelli E, Flocco R, et al. Right minithoracotomy versus full sternotomy for the aortic valve replacement: preliminary results. *Heart Lung Circ.* (2012) 21:69–73. doi: 10.1016/j.hlc.2011.10.004

Seitz M, Goldblatt J, Paul E, Marcus T, Larobina M, Yap CH. Minimally invasive aortic valve replacement via right anterior mini-thoracotomy: propensity matched initial experience. *Heart Lung Circ.* (2019) 28:320–26. doi: 10.1016/j.hlc.2017.11.012

Shehada SE, Ozturk O, Wotthe M, Lange R. Propensity score analysis of outcomes following minimal access versus conventional aortic valve replacement. *Eur J Cardiothorac Surg.* (2016) 49:464–9. doi: 10.1093/ejcts/eov061

Stolinski J, Musial R, Plicner D, Fijorek K, Medryczyk M, Andres J, et al. Respiratory functional status after conventional and minimally invasive aortic valve replacement surgery - a propensity score analysis. *Kardiochir Torakochirurgia Pol.* (2017) 14:5–9. doi: 10.5114/ktp.2017.66922

Stolinski J, Plicner D, Grudzien G, Wasowicz M, Musial R, Andres J, et al. A comparison of minimally invasive and standard aortic valve replacement. *J Thorac Cardiovasc Surg.* (2016) 152:1030–9. doi: 10.1016/j.jtcvs.2016.06.012

Tabata M, Umasanthan R, Cohn LH, Bolman RM, 3rd, Shekar PS, Shen FY, et al. Early and late outcomes of 1000 minimally invasive aortic valve operations. *Eur J Cardiothorac Surg.* (2008) 33:537–41. doi: 10.1016/j.ejcts.2007.12.037

Wang Q, Xi W, Gao Y, Shen H, Min J, Yang I, et al. Short-term outcomes of minimally invasive mitral valve repair: a propensity-matched comparison. *Interact Cardiovasc Thorac Surg.* (2018) 26:805–12. doi: 10.1093/icvts/ivx402

Zhao D, Wei L, Zhu SJ, Zhang Z, Liu H, Yang Y, et al. Combined mitral and aortic valve procedure via right mini-thoracotomy versus full median sternotomy insights from a single-center study of propensity-matched data. *Int Heart J.* (2019) 60:336–44. doi: 10.1536/ihj.18-18

Higgins JPT, Altman DG. Assessing risk of bias in included studies. In: Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions.* Chichester: Wiley (2008). p. 187–241.

Ontario Hospital Research Institute. The Newcastle-Ottawa Scale (nos) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses. (2019). Available online at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed August 14, 2019).

Jadad AR, Carroll D, Glynn CJ, Moore RA, McQuay HJ. Morphine responsiveness of chronic pain: double-blind randomised crossover study with patient-controlled analgesia. *Lancet.* (1992) 339:1367–71. doi: 10.1016/0140-6736(92)91194-d

Galatt L, Canet J. Post-operative pulmonary complications: understanding definitions and risk assessment. *Best Pract Res Clin Anaesthesiol.* (2015) 29:315–30. doi: 10.1016/j.bpa.2015.10.004

Szelkowski LA, Puri NK, Singh R, Massimiano PS. Current trends in preoperative, intraoperative, and postoperative care of the adult cardiac surgery patient. *Curr Problems Surg.* (2014) 52:531–69. doi: 10.1016/j.cpsurg.2014.10.001

Tanner TG, Colvin MO. Pulmonary complications of cardiac surgery. *Lung.* (2020) 198:889–96. doi: 10.1007/s00408-020-00405-7

Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* (2009) 6:e1000097. doi: 10.1371/journal.pmed.1000097

Coughtrie DM, 3rd, Sabik JF. Minimally invasive approach for aortic valve operations. *Ann Thorac Surg.* (1996) 62:596–7.

Badenes R, Lozano A, Belda FJ. Postoperative pulmonary dysfunction and mechanical ventilation in cardiac surgery. *Crit Care Res Pract.* (2015) 2015:420513. doi: 10.1155/2015/420513

Chetta A, Bobbio A, Aiello M, Del Donno M, Castagnaro A, Comel A, et al. Changes in lung function and respiratory muscle strength after sternotomy vs. laparotomy in patients without ventilatory limitation. *Eur Surg Res.* (2006) 38:489–93. doi: 10.1159/000096008

e Silva AM, Saad R, Stirbulov R, Rivetti LA. Off-pump versus on-pump coronary artery revascularization: effects on pulmonary function. *Interact Cardiovasc Thorac Surg.* (2010) 11:42–5. doi: 10.1510/icvts.2009.229617

Ragnarssdottr M, KristjAnsdottir A, Ingvarsrdottir I, Hannesson P, Torfason B, Cahalin L. Short-term changes in pulmonary function and respiratory movements after cardiac surgery via median sternotomy. *Scand Cardiovasc J.* (2004) 38:46–52. doi: 10.1080/1401430310016658

Shenkman Z, Shir Y, Weiss YG, Bleiberg B, Gross D. The effects of cardiac surgery on early and late pulmonary functions. *Acta Anaesth Scand.* (1997) 41:1193–9.

Khosbin E, Prayaga S, Kinsella J, Sutherland FW. Mini-sternotomy for aortic valve replacement reduces the length of stay in the cardiac intensive care unit: meta-analysis of randomised controlled trials. *BMJ Open.* (2011) 1:e000266. doi: 10.1136/bmjopen-2011-000266

Lim JY, Deo SV, Altarabsheh SE, Jung SH, Erwin PJ, Markowitz AH, et al. Conventional versus minimally invasive aortic valve replacement: pooled analysis of propensity-matched data. *J Card Surg.* (2015) 30:125–34. doi: 10.1111/jocs.12493

Paparella D, Malvindi PG, Santarpino G, Moscarelli M, Guida F, Fattouch K, et al. Full sternotomy and minimal access approaches for surgical aortic valve replacement: a multicentre propensity-matched study. *Eur J Cardiothorac Surg.* (2020) 57:709–16. doi: 10.1093/ejcts/ezz286

Santana O, Reyna J, Benjo AM, Lamas GA, Lamelas J. Outcomes of minimally invasive valve surgery in patients with chronic obstructive pulmonary disease. *Eur J Cardiothorac Surg.* (2012) 42:648–52. doi: 10.1093/ejcts/ezs098

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