



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).

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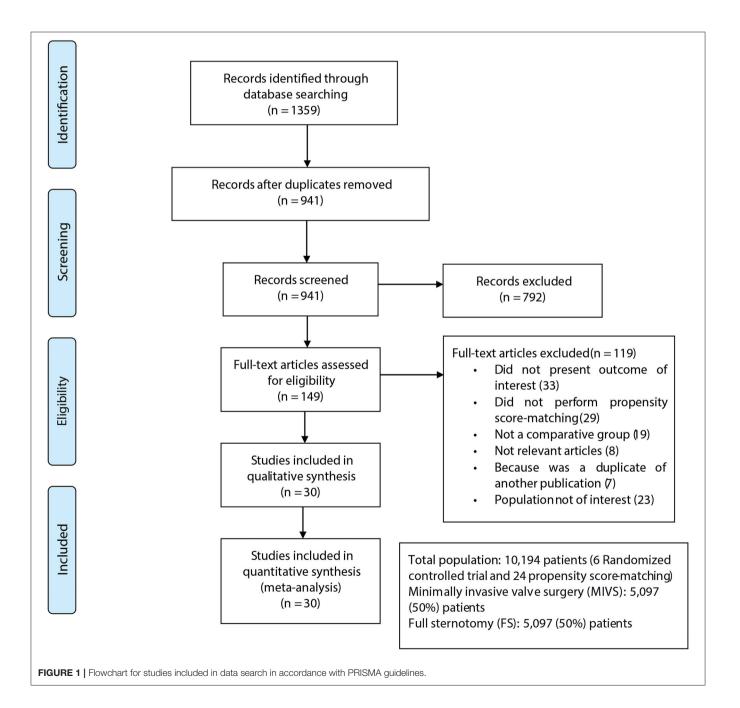
Conclusions: Our study showed that minimally invasive valve surgery decreases the incidence of postoperative pulmonary complications and improves postoperative respiratory function status.

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 it is 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 metaanalysis 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.

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	Aφ	3/5	2b	6 days
Machler et al. (28)	Austria	1996–1997	RCT	30/30	Aφ	3/5	2b	294 days ^M
Bonacchi et al. (14)	Italy	1999–2001	RCT	40/40	Αφ	4/5	1b	$9.7\pm5.7~\mathrm{months^{M}}$
Dogan et al. (16)	Germany	2003–2004	RCT	20/20	M§	2/5	Зb	NS
Moustafa et al. (5)	Egypt	NS	RCT	30/30	Αφ	2/5	Зb	NS
Calderon et al. (15)	France	2003-2007	RCT	39/39	Αφ	5/5	2b	NS
Albacker et al. (12)	US	1995–2010	PSM	223/223	Α§	7	4	2 years
Masiello et al. (29)	Italy	1997–1999	PSM	100/100	Αφ	6	3b	1 month
Farhat et al. (17)	France	2000-2001	PSM	50/50	Αφ	7	Зb	1 month
Tabata et al. (37)	US	1996–2005	PSM	41/41	Αφ	7	3b	NS
ribarne et al. (25)	US	2000-2008	PSM	382/382	M§	8	3b	$4.2\pm2.4~\rm yrs^{\rm M}$
Holzhey et al. (24)	Germany	1999–2009	PSM	143/143	M§	8	1b	$2.4\pm2.1~\rm yrs^{\rm M}$
Bang et al. (13)	Korea	1997–2010	PSM	73/73	Aφ	7	3b	NS
Murzi et al. (31)	Italy	2006-2010	PSM	100/100	Aθ	6	2b	3 years
Sansone et al. (32)	Italy	2008-2010	PSM	50/50	Aθ	7	3b	NS
Johnston et al. (26)	US	1995–2004	PSM	832/832	Aφ	8	3a	$6.5\pm3.0~{\rm years^{M}}$
Gilmanov et al. (20)	Italy	2004-2011	PSM	182/182	Aθ	7	3b	Until patient discharge
Hiraoka et al. (23)	Japan	2007-2012	PSM	36/36	Αφ	7	4	NS
Ghanta et al. (19)	US	2011-2013	PSM	289/289	Αφ	6	4	NS
Gilmanov et al. (21)	Italy	2001-2013	PSM	100/100	Aθ	8	3a	33.7 months ^M
Verk et al. (30)	Germany	2003-2012	PSM	477/477	Aφ	6	3a	$3.1\pm2.7~{\rm years^M}$
Shehada et al. (34)	Germany	2002-2012	PSM	585/585	Αφ	7	3b	NS
Stoliński et al. (36)	Canada	2010-2013	PSM	211/211	Aθ	8	3b	NS
Gasparovic et al. (18)	Slovakia	2010-2013	PSM	34/34	Αφ	7	За	5 years
_evack et al. (27)	US	1995–2014	PSM	483/483	Aφ	8	Зb	NS
Stolinski et al. (35)	Poland	2011-2014	PSM	212/212	Aθ	8	Зa	3 months
Seitz et al. (33)	Australia	2013-2016	PSM	53/53	Aθ	7	3b	NS
Hawkins et al. (22)	US	2011-2016	PSM	74/74	Μ§	7	3b	NS
Wang et al. (38)	China	2012-2015	PSM	67/67	Μ§	6	Зa	2.8 years
Zhao et al. (39)	China	2013-2016	PSM	91/91	Сδ	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; ^M, mean; NS, not specified; PSM, propensity score-matching; RCT, randomized control trial; θ, indicates aortic valve surgery right mini-thoracotomy; φ, indicates aortic valve surgery right mini-thoracotomy; φ, indicates aortic valve surgery right mini-thoracotomy; β, indicated mitral valve surgery right mini-thoracotomy; §, indicated mitral 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 riskof-bias using the Cochrane risk-of-bias (RoB2) tool. The riskof-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 \geq 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 \geq 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 \pm 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	Р	Study	heterog	eneity	
			WMD/OR (95% CI) [†]		chi ² -test	df	/ ² (%)	P-value
Postoperative respiratory	function state	us after 1 week						
Overall spirometry	6 (1,928)	964/964	MD -24.83 [-29.90,-19.76] [†]	< 0.00001	11770.40	13	100	< 0.00001
Subgroup analysis								
FEV1%	6 (722)	361/361	-74.06 [-89.14, -58.99] [†]	< 0.00001	1089.82	5	100	< 0.00001
FVC%	5 (642)	321/321	4.99 [1.23, 8.75] [†]	0.009	287.63	4	99	< 0.00001
TLC	3 (564)	282/2,282	8.39 [2.00, 14.78]†	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 insufficient	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; I², test of heterogeneity; FEV1, forced expiratory volume in 1 s; FVC, Forced vital capacity; TLC, total lung capacity; [†] 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).

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.

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

	MIV		_ FS			Odds Ratio	Odds Ratio
Study or Subgroup	2 2240 101 142 1020			Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
1.3.1 Randomized c							
Aris 1999	1	20	0	20	0.2%	3.15 [0.12, 82.16]	
Bonacchi 2002	3	40	7	40	1.3%	0.38 [0.09, 1.60]	
Calderon 2009	0	39	0	39		Not estimable	
Dogan 2005	1	20	2	20	0.4%	0.47 [0.04, 5.69]	
Machler 1999	1	60	12	60	0.6%	0.07 [0.01, 0.54]	·
Moustafa 2007 Subtotal (95% CI)	0	30 209	1	30 209	0.2% 2.8%	0.32 [0.01, 8.24] 0.32 [0.12, 0.90]	
Fotal events	6		22				
Heterogeneity: Tau ² :	= 0.10; Cl	$1i^2 = 4.$	29, df =	4 (P =	0.37); I ² =	= 7%	
Test for overall effect	:: Z = 2.17	7 (P = C)	.03)				
1.3.2 Propensity-ma	tched ob	servati	onal stu	ıdies (F	POS)		
Albacker 2014	9	223	18	223	3.7%	0.48 [0.21, 1.09]	
Bang 2012	3	73	1	73	0.5%	3.09 [0.31, 30.38]	
arhat 2003	0	50	1	50	0.3%	0.33 [0.01, 8.21]	
Gasparovic 2017	3	34	4	34	1.0%	0.73 [0.15, 3.52]	
Ghanta 2015	26	289	25	289	7.1%	1.04 [0.59, 1.86]	
Gilmanov 2013	24	182	22	182	6.2%	1.10 [0.59, 2.05]	
Gilmanov 2015	24	100	22	100	5.6%	1.12 [0.58, 2.16]	_ _
Hawkins 2018	5	74	8	74	1.9%	0.60 [0.19, 1.92]	
Hiraoka 2014	1	36	0	36	0.3%	3.08 [0.12, 78.27]	
Holzhey 2011	22	143	22	143	5.8%	1.00 [0.53, 1.90]	
ribarne 2010	17	382	29	382	6.3%	0.57 [0.31, 1.05]	
ohnston 2012	24	832	45	832	9.0%	0.52 [0.31, 0.86]	
evack 2016	10	483	12	483	3.5%	0.83 [0.36, 1.94]	
Masiello 2002	7	100	5	100	1.8%	1.43 [0.44, 4.67]	
Merka 2014	52	477	67	477	14.0%	0.75 [0.51, 1.10]	
Murzi 2011	3	100	4	100	1.1%	0.74 [0.16, 3.41]	
Sansone 2012	6	50	0	50	0.3%	14.75 [0.81, 269.34]	· · · · · · · · · · · · · · · · · · ·
Seitz 2017	3	53	3	53	1.0%	1.00 [0.19, 5.19]	
Shehada 2015	50	585	69	585	14.2%	0.70 [0.48, 1.03]	
Stolinski 2016	28	211	36	211	8.1%	0.74 [0.44, 1.27]	
Stolinski 2017	0	212	0	212		Not estimable	
Tabata 2007	1	41	3	41	0.5%	0.32 [0.03, 3.18]	
Vang 2018	5	67	3	67	1.2%	1.72 [0.39, 7.51]	
Zhao 2018	18	91	13	91	4.0%	1.48 [0.68, 3.23]	- •
Subtotal (95% CI)		4888		4888	97.2%	0.80 [0.69, 0.94]	•
Total events	341		412				
Heterogeneity: Tau ² :	,		,	= 22 (P	= 0.52);	$l^2 = 0\%$	
Test for overall effect	:: Z = 2.82	2 (P = C)	.005)				
Fotal (95% CI)		5097		5097	100.0%	0.79 [0.67, 0.93]	•
Total events	347		434				
Heterogeneity: Tau ² :	= 0.01; Cł	$ni^2 = 28$	3.51, df =	= 27 (P	= 0.39);	$l^2 = 5\%$	0.01 0.1 1 10 100
Test for overall effect	: Z = 2.88	B (P = C)	.004)				Favours MIVS Favours FS
Fest for subaroup dif	ferences	Chi ² -	2 97 df	-1(P)	-0.08)	2 - 66 2%	

FIGURE 3 | Forest plot demonstrating the overall study incidence of postoperative pulmonary complications between MIVS and FS.

Study or Subgroup 1.2.1 Pneumonia	Events Total	Events To	al Weight	Odds Ratio M-H, Random, 95% Cl	M-H, Rand	om, 95% Cl
Dogan 2005	1 20	0	20 0.2%	3.15 [0.12, 82.16]		·
Gilmanov 2015	2 100	0 1	0.2%	5.10 [0.24, 107.62]		·
Hawkins 2018	1 74		74 0.4%	0.49 [0.04, 5.56]	• •	
Seitz 2017	1 53		53 0.4%	0.49 [0.04, 5.58]	• •	
Stolinski 2016 Subtotal (95% CI)	3 211 458	1 2		3.03 [0.31, 29.35] 1.42 [0.44, 4.55]		
Total events	8	5 7.	1.770	1.42 [0.44, 4.55]		
Heterogeneity: Tau ² = Test for overall effect:	= 0.00; Chi ² = 2.8	1, df = 4 (P	= 0.59); I ² =	• 0%		
1.2.2 Pleural effusior	n					
Aris 1999	1 20		20 0.2%	3.15 [0.12, 82.16]		·
Dogan 2005	0 20		20 0.2%	0.32 [0.01, 8.26]	• •	
Gasparovic 2017 Gilmanov 2013	3 34 10 182	4 5 1	340.9%321.9%	0.73 [0.15, 3.52] 2.06 [0.69, 6.14]		
Gilmanov 2015	4 100	5 1		0.79 [0.21, 3.04]	<u> </u>	
Machler 1999	1 60		50 0.5%	0.07 [0.01, 0.54]	←	
Masiello 2002	6 100	5 1		1.21 [0.36, 4.11]		•
Stolinski 2016 Subtotal (95% CI)	25 211 727	35 2	11 7.5% 27 14.2%	0.68 [0.39, 1.18] 0.81 [0.45, 1.45]		
Total events	50	67	17.2/0	0.01 [0.40, 1.40]		
Heterogeneity: Tau ² = Test for overall effect:	= 0.21; Chi ² = 10.	28, df = 7 ($P = 0.17$; I^2	= 32%		
1.2.3 Pneumothorax						
Bonacchi 2002	2 40		40 0.7%	0.65 [0.10, 4.11]		
Dogan 2005 Masiello 2002	0 20 1 100	1 1	20 0.2% 00 0.2%	0.32 [0.01, 8.26] 3.03 [0.12, 75.28]	· ·	`
Sansone 2002	6 50		00 0.2% 50 0.3%	3.03 [0.12, 75.28] 14.75 [0.81, 269.34]		
Subtotal (95% CI)	210	2		1.55 [0.30, 8.12]		
Total events Heterogeneity: Tau ² = Test for overall effect:		,	= 0.21); I ² =	- 33%		
1.2.4 Respiratory ins						
Albacker 2014	9 223	18 2		0.48 [0.21, 1.09]		
Bonacchi 2002 Ghanta 2015	1 40 26 289	2 -	10 0.4% 39 7.0%	0.49 [0.04, 5.60] 1.04 [0.59, 1.86]	· · · _	
Gilmanov 2015	14 100	10 1		1.47 [0.62, 3.47]		· · · · ·
Hiraoka 2014	1 24		24 0.2%	3.13 [0.12, 80.68]		·
Holzhey 2011	22 143	22 1		1.00 [0.53, 1.90]		
Johnston 2012 Merka 2014	24 832 52 477	45 8 67 4		0.52 [0.31, 0.86] 0.75 [0.51, 1.10]		-
Seitz 2017	2 53		53 0.4%	2.04 [0.18, 23.19]		
Shehada 2015	50 585	69 5		0.70 [0.48, 1.03]		
Wang 2018 Zhao 2018	3 67 2 91		57 1.1% 91 0.7%	0.58 [0.13, 2.54] 0.66 [0.11, 4.04]		
Subtotal (95% CI)	2924	292		0.75 [0.62, 0.91]	•	
Total events	206	267				
Heterogeneity: Tau ² = Test for overall effect:			P = 0.59); I ²	= 0%		
1.2.5 Pulmonary infe Bang 2012	ection 3 73	1	73 0.4%	3.09 [0.31, 30.38]		ļ,
Farhat 2003	0 50		50 0.2%	0.33 [0.01, 8.21]	· · · ·	
Subtotal (95% CI)	123	12		1.35 [0.16, 11.30]		
Total events Heterogeneity: Tau ² = Test for overall effect:			= 0.27); l ² =	- 19%		
1.2.7 Prolonged vent		1990 B				
Bonacchi 2002	0 40		40 0.2%	0.19 [0.01, 4.09]	· · ·	
Ghanta 2015 Cilmanov 2012	5 289	6 2		0.83 [0.25, 2.75]		
Gilmanov 2013 Gilmanov 2015	4 182 4 100	9 1 7 1		0.43 [0.13, 1.43] 0.55 [0.16, 1.95]		
Hawkins 2018	4 74		74 1.3%	0.65 [0.18, 2.40]	<u> </u>	
Iribarne 2010	17 382	29 3	6.1%	0.57 [0.31, 1.05]		ł
Levack 2016	10 483	12 4		0.83 [0.36, 1.94]		
Murzi 2011 Tabata 2007	3 100 1 41	4 1	00 1.0% 41 0.4%	0.74 [0.16, 3.41] 0.32 [0.03, 3.18]	· · · ·	
Zhao 2018	16 91		91 3.2%	1.73 [0.74, 4.04]		
Subtotal (95% CI)	1782	17		0.72 [0.51, 1.01]	+	
Total events Heterogeneity: Tau ² = Test for overall effect:			= 0.65); l ² =	- 0%		
Total (95% CI)	6224		24 100.0%	0.77 [0.66, 0.90]	•	
Total events	340	433 07 df - 40	$(\mathbf{P} = 0.60)$	2 - 0%	L	
Heterogeneity: Tau ² =	$= 0.00; Chi^2 = 37.$: Z = 3.39 (P = 0.		(r = 0.60); I	= 0%	0.05 0.2 Favours [MIVS]	1 5 20

		MIVS			FS			Mean Difference	Mean Difference
Study or Subgroup		SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
l.1.1 FEV1% after 1 w	/eek								
Aris 1999	62	16	20	526	12	20	6.2%	-464.00 [-472.77, -455.23]	•
Bonacchi 2002	80.8	18.6	40	81.7	21.5	40	6.2%	-0.90 [-9.71, 7.91]	-+-
Calderon 2009	53.4	15.6	39	55	16	39	6.7%	-1.60 [-8.61, 5.41]	-+-
Dogan 2005	1.9	0.8	20	1.7	0.6	20	7.6%	0.20 [-0.24, 0.64]	•
Moustafa 2007	80.47	0.51	30	78.47	0.51	30	7.6%	2.00 [1.74, 2.26]	•
tolinski 2017	79.5	10.1		74	11.3	212	7.5%	5.50 [3.46, 7.54]	-
Subtotal (95% CI)			361			361	41.9%	-74.06 [-89.14, -58.99]	◆
Heterogeneity: Tau ² =	346.15	; Chi ²	= 1089	94.82, d	lf = 5	(P < 0.0)	00001); I ²	= 100%	
Test for overall effect:	Z = 9.6	53 (P <	0.000	01)					
L.1.2 FVC% after 1 we	eek								
Aris 1999	60	17	20	53	12	20	6.1%	7.00 [-2.12, 16.12]	+ ~
Calderon 2009	55.9	14.1	39	57.9	15.2	39	6.8%	-2.00 [-8.51, 4.51]	-+
Dogan 2005	2.5	0.9	20	2.1	0.8	20	7.6%	0.40 [-0.13, 0.93]	•
Aoustafa 2007	91.5	0.51	30	86.6	0.95	30	7.6%	4.90 [4.51, 5.29]	
Stolinski 2017	64.8	8.8	212	51.5	11.1	212	7.5%	13.30 [11.39, 15.21]	· ·
Subtotal (95% CI)			321			321	35.7%	4.99 [1.23, 8.75]	•
Heterogeneity: Tau ² = Test for overall effect:					4 (P <	0.0000	(1); $I^2 = 9$	9%	
1.1.3 TLC after 1 wee									
Bonacchi 2002	65.9		40			40	7.3%	6.30 [2.27, 10.33]	-
Aoustafa 2007		0.51	30	60.5		30	7.6%	5.00 [4.74, 5.26]	•
Stolinski 2017	67.1	7.5	212 282	53.3	13	212 282	7.5% 22.4%	13.80 [11.78, 15.82]	A
Subtotal (95% CI)	20.22	cl .2		16 0	(5)			8.39 [2.00, 14.78]	▼
leterogeneity: Tau ² =				, df = 2	(P < (J.00001	L); $I^2 = 97$	%	
Test for overall effect:	Z = 2.5	77 (P =	= 0.01)						
Total (95% CI)			964			964	100.0%	-24.83 [-29.90, -19.76]	♦
Heterogeneity: Tau ² =	87.70;	Chi ² =	= 11770).40, df	= 13	(P < 0.0)	00001); I ²	= 100%	
Test for overall effect:									Favours [MIVS] Favours [FS]
Test for subgroup diff	erences	: Chi ²	= 104.	02, df =	= 2 (P ·	< 0.000	$(01), I^2 =$	98.1%	

0.79; 95% CI [0.67, 0.93]; p = 0.004). The results of our metaanalysis 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 0.72; 95% CI [0.51, 1.01]; p = 0.06) (14, 19-22, 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 are 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)

Study at Subgrave versity Tail 1 and 2 2 20 1.8 Mergen VH. H. Random, 55% C VH. Rand	Chudu an Culan	MIVS	FS Function Trate	I Walaki •	Odds Ratio	Odds Ratio	
		Events Total	Events Tota	i weight M	1-H, Kandom, 95% CI	M-H, Kandom, 95% CI	—
$ \begin{array}{c} \text{Buscher 1002} & 1 & 40 & 2 & 40 & 108 & 0.610, 0.520 \\ \text{Cybern 2003} & 0 & 30 & 108 & 0.610, 0.520 \\ \text{Cybern 2003} & 0 & 20 & 0.20 & 108 & 0.610, 0.520 \\ \text{Marker 139} & 1.84 & 0.29 & 5.8 & 0.5010, 0.621 \\ \text{Hardrag 139} & 1.84 & 0.29 & 5.8 & 0.5010, 0.621 \\ \text{Test for weal effect 2 = 0.56 p - 0.51 \\ \text{Test for weal effect 2 = 0.56 p - 0.51 \\ \text{Hardrag 2012} & 0.73 & 2.73 & 1.28 & 0.1910, 0.1, 223 \\ \text{Hardrag 2012} & 1.50 & 1.48 & 1.0010, 0.5, 164 \\ \text{Cassaror 2013} & 1.28 & 0.59 & 2.58 & 0.5010, 0.0, 5.24 \\ \text{Hardrag 2014} & 1.90 & 1.48 & 1.0010, 0.5, 164 \\ \text{Cassaror 2013} & 1.28 & 2.8 & 2.23100, 2.13 \\ \text{Hardrag 2014} & 0.5 & 51 & 4.48 & 0.9010, 0.732 \\ \text{Hardrag 2014} & 0.7 & 322 & 7.3 & 1.38 & 0.1910, 0.1, 324 \\ \text{Hardrag 2014} & 0.5 & 51 & 3.48 & 0.9010, 0.732 \\ \text{Hardrag 2015} & 0.7 & 4.1 & 7.4 & 1.18 & 0.33100, 1.20 \\ \text{Hardrag 2015} & 0.7 & 4.2 & 1.38 & 0.2100, 1.31 \\ \text{Hardrag 2016} & 0.7 & 4.2 & 1.38 & 0.2100, 0.132 \\ \text{Hardrag 2016} & 0.7 & 4.2 & 1.38 & 0.2100, 0.132 \\ \text{Hardrag 2017} & 1.38 & 2.3 & 1.38 & 1.2400, 0.037, 2.48 \\ \text{Hardrag 2016} & 0.7 & 4.2 & 4.24 & 1.58 & 0.2010, 1.38 \\ \text{Hardrag 2017} & 1.83 & 3.5 & 1.38 & 0.9010, 0.32 \\ \text{Hardrag 2018} & 1.67 & 2.67 & 1.58 & 1.48 & 0.9010, 3.74 \\ \text{Hardrag 2016} & 1.67 & 2.67 & 1.58 & 0.4900, 5.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.57 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.57 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.58 \\ \text{Hardrag 2016} & 1.67 & 2.57 & 1.58 & 0.4900, 0.$		1 20		0 1.01/	0.47 [0.04 [. 60]		
Cubero 2009 0 39 1 39 1 39 1 18 0.22 [00], 22] Mulch 1999 1 60 0 60 118 35 [01,2,33] Subcati 2070 2 99 209 229 5.86 6.53 [01,6,2,53] Trail events 3 5 Henrygenety, Tarl - 0.07; Ch ² + 1.13, df - 2 (P - 0.57); f ² + 0.8; Text for event affect: 2 - 0.66 P - 0.51) Tarl 2091 1 209 2 33 88 0.59 [00,0,2,73] Henrygenety, Tarl - 0.07; Ch ² + 1.13, df - 2 (P - 0.57); f ² + 0.8; Tarl 2013 1 209 2 33 182 4.283 100 [00,0,1.42] Henrygenety, Tarl - 0.07; Ch ² + 1.13, df - 2 (P - 0.57); f ² + 0.8; Tarl 2003 1 1 59 1 45 138 4.284 100 [00,0,2,50] Gammaro 2013 2 106 4 4 10 3.79 4.049 [00,0,2,50] Gammaro 2013 2 106 4 4 10 3.79 4.049 [00,0,2,50] Gammaro 2013 2 106 4 4 10 3.79 4.049 [00,0,2,50] Gammaro 2013 2 106 4 4 10 3.79 4.049 [00,0,2,50] Gammaro 2013 3 182 4.284 120 [00,0,1,30] Henrygenety, Tarl - 100; Ch ⁴ - 1.17 4 115 4.33 [10,0,1,30] Henrygenety, Tarl - 4.00; Ch ⁴ - 1.17 4 18 6.38 [10,0,1,30] Henrygenety, Tarl - 4.00; Ch ⁴ - 1.17 4 18 6.48 [10,0,1,31] Henrygenety, Tarl - 4.00; Ch ⁴ - 1.17 4 18 6.48 [10,0,1,31] Henrygenety, Tarl - 4.00; Ch ⁴ - 1.17 4 18 6.48 [10,0,1,31] Henrygenety, Tarl - 4.00; Ch ⁴ - 1.17 4 18 6.48 [10,0,1,31] Henrygenety, Tarl - 4.00; Ch ⁴ - 1.25 4 - 2.29 + 0.50; f ² - 0.65 [1,7,38] Tarl 4055 (0) 5 55 1 18 6.045 [0,1,7,38] Tarl 4055 (0) 5 597 507 5097 10005 6.68 [0,49,055] Tarl 4055 (0) 5 597 507 10005 500 500 500 500 500						-	
Degra 205 0 20 0 20 0 20 we terminate Marker 139 0 0 20 0 20 5.8 663 [0.16, 2.51] Tail events 3 5 Hearganety, Tai 200, Ch - 11.4, di - 19 - 0.70; l ⁺ = 0K Hearganety, Tai 200, Ch - 11.4, di - 19 - 0.70; l ⁺ = 0K Hearganety, Tai 200, Ch - 11.4, di - 19 - 0.70; l ⁺ = 0K Hearganety, Tai 200, Ch - 11.4, di - 28 - 0.20; l ⁺ = 0K Hearganety, Tai 201 0 27 3 2 23 3.6K 0.59 [0.06, 2.78] Jan 201 0 73 2 73 1.28 0.19 [0.01, 21.4] Jan 201 1 28 6 29 258 0.106, 56.44 Cassaroro 2017 1 28 4 4 34 22.3 82 0.20 [0.02, 1.27] Jan 201 0 73 2 73 1.28 0.19 [0.01, 56.44 Hearganety, Tai 28 0 1.58 0.23 300, 12.00 Jan 2015 0 7 32 2 73 1.28 0.19 [0.00, 2.78] Jan 2010 0 73 2 2 73 1.28 0.19 [0.00, 2.78] Jan 2010 0 1 28 6 29 258 0.106, 56.44 Hearganety, Tai 28 0 58 1.00 3.78, 4.29 (0.00, 2.78] Jan 2010 0 73 82 7 38 1.28 2.38 1.28 2.30 0.00, 13.00 Hearganety, Tai 28 0 58 1.20 0.20 0.00, 13.08 Hearganety, Tai 28 0 58 1.20 0.20 0.00, 13.08 Hearganety, Tai 28 0 58 1.20 0.20 0.00, 13.08 Hearganety, Tai 28 0.59 1.28 0.20 0.00, 13.08 Hearganety, Tai 28 0.59 1.20 0.00, 13.08 Hearganety, Tai 28 0.00, Ch 31, 48 2 2.48 4.20 0.00, 13.08 Hearganety, Tai 28 0.00, Ch 31, 48 2 2.48 4.20 0.00, 13.08 Hearganety, Tai 28 0.00, Ch 31, 38 4.22 1.38 0.49 (0.01, 53.08) Hearganety, Tai 28 0.00, Ch 31, 38 4.22 1.38 0.49 (0.01, 53.08) Hearganety, Tai 28 0.00, Ch 31, 38 4.22 1.38 0.49 (0.01, 53.08) Hearganety, Tai 28 0.00, Ch 31, 38 4.22 4.48 4.49 (0.04, 55.08) Hearganety, Tai 28 0.00, Ch 31, 38 4.22 4.49 (0.04, 55.08) Hearganety, Tai 28 0.00, Ch 31, 38 4.22 4.49 (0.04, 55.08) Hearganety, Tai 28 0.00, Ch 31, 38 4.22 4.49 (0.04, 55.08) Hearganety, Tai 28 0.00, Ch 31, 38 4.22 4.49 (0.04, 55.08) Hearganety, Tai 28 0.00, Ch 31, 38 4.42 4.40 4.40 (0.04, 55.08) Hearganety, Tai 28 0.00, Ch 31, 38 4.42 4.40 4.40 (0.04, 55.08) Hearganety, Tai 28 0.00, Ch 32 4.22 4.49 (0.04, 55.08) Hearganety, Tai 28 0							
$ \begin{aligned} \begin{array}{lllllllllllllllllllllllllllllllllll$							
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Test for overall effect $Z = 0.66 p = 0.51$) 1142 PM Abacker 2014 2 223 4 223 88 050 [0.09, 2.73] Fanta 2003 1 50 1 50 1.80 0.130 [0.01, 4.12] Fanta 2005 1 2 210 0 4 100 3.7% 049 [0.03, 2.74] Hicko 2015 2 100 4 100 3.7% 049 [0.03, 2.74] Hicko 2015 2 100 4 100 3.7% 049 [0.03, 2.74] Hicko 2016 0 483 0 45 0 56 Not estimable Holzher 2011 11 143 9 143 133% 124 [0.50, 3.09] Hicko 2012 8 6322 1 48 10.00 [0.3, 1.83] Holzher 2011 0 100 1 100 1.9% 2.02 [0.13, 2.16] Hicko 2012 0 50 2 50 122 4 100 [0.3, 1.83] Hicko 2012 0 50 55 11.4% 100 [0.3, 1.83] Hicko 2013 0 55 10 1.88 [0.04, 0.85] State 2017 1 53 3 53 2.1% 0.33 [0.01, 6.20] Hicko 2016 2 211 3 211 34% 0.90 [0.3, 5.23] State 2017 1 53 3 53 2.1% 0.30 [0.03, 0.18, 0.04] Hicko 2016 2 211 3 211 3.4% 0.90 [0.3, 5.23] State 2017 1 53 3 53 2.1% 0.33 [0.01, 5.00] Hicko 2018 1 67 2 67 1.9% 0.49 [0.04, 5.56] State 2017 1 53 3 53 2.1% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 17 1.9% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 17 1.9% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 17 1.9% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 17 1.9% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 17 1.9% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 17 1.9% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 17 1.9% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 17 1.9% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 17 1.9% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 17 1.9% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 17 1.9% 0.49 [0.04, 5.56] Hicko 2018 1 67 2 2 10 - 0.03) Hicko 2018 1 61 - 7 2 50 - 12.9% 0.68 [0.49, 0.95] Hicko 2018 1 61 - 7 2 50 - 12.9% 0.68 [0.49, 0.95] Hicko 2018 Hicko 2 2.21 - 9 0.03); Hicko 2 0.56 [0.49, 0.95] Hicko 2018 Hicko 2 2.21 - 9 0.03); Hicko 2 0.56 [0.49, 0.95] Hicko 2018 Hicko 2 2.22 - 9 0.03); Hicko 2 0.56 [0.49, 0.95] Hicko 2018 Hicko 2 2.22 - 9 0.03); Hicko 2 0.56 [0.49, 0.95] Hicko 2018 Hicko 2 2.22 - 9 0.03); Hicko 2 0.56 [0.49, 0.95] Hicko 2018 Hicko 2 2.22 - 9 0.03); Hicko 2 0.56 [0.49, 0.95] Hicko 2018 Hicko 2 2.22 - 9 0.03); Hicko 2 0.56 [0.49, 0.95] Hicko 2018 Hicko 2 2.22 - 9 0.03); Hick				$= 0.76$; $ ^2 =$	0%		
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Abacker 2014 2 223 4 223 3.8% 0.50 (0.92, 273) Barg 2012 0 73 2 73 1.2% 0.19 (0.91, 4.12) Frant 2003 1 50 1.4% 1.4 2.4% 0.010 (0.6, 16.14) Gasparovi 2017 1 34 4 34 2.2% 0.23 (0.02, 2.15) Gilmanov 2013 3 182 3 182 4.2% 1.00 (10.05, 5.2.8) Gilmanov 2013 3 182 3 182 4.2% 1.00 (10.05, 5.2.8) Frider 2010 7 382 7 382 9.9% 1.00 (0.53, 2.88) Levak 2016 0 483 2 483 1.2% 0.020 (0.14, 4.16) Hinola 2014 0 36 0 36 Wet estimable Murz 2011 0 100 1 100 1.1% 0.33 (0.01, 8.20) Murz 2011 0 100 1 100 1.1% 0.33 (0.01, 8.20) Murz 2011 0 100 1 100 1.1% 0.33 (0.01, 8.20) Murz 2011 0 100 1 100 1.1% 0.33 (0.01, 8.20) Murz 2011 0 100 1 100 1.1% 0.33 (0.01, 8.20) Stele 2017 1 53 3 53 2.1% 0.22 (0.013, 3.18) Stele 2017 1 53 3 53 2.1% 0.29 (0.013, 3.18) Total events 55 9 2 Heterogenetity: Tarl = 0.0%, 0 ⁻¹ = 1.25, 5.6f = 22 (P = 0.93); i ¹ = 0% Test for overall effect: 2 = 2.19 (P = 0.03); i ¹ = 0% Test for overall effect: 2 = 2.19 (P = 0.03); i ¹ = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ² = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ³ = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ³ = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ³ = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ³ = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ³ = 0% Test for overall effect: 2 = 2.28 (P = 0.03); i ³ = 0% T							
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Farfar 2003 1 50 1 4 50 1.4 $\frac{1}{2}$ 0.01 (0.06, 16.44) Grapsović 2017 1 3 44 34 2.2 $\frac{1}{2}$ 0.23 (0.02, 213) Glanarov 2013 3 182 3 182 4.2 $\frac{1}{2}$ 0.016 (0.02, 137) Glanarov 2013 3 182 4 2.8 0.16 (0.02, 137) Glanarov 2013 0 182 4 100 3.7 $\frac{1}{2}$ 0.4 (0.00, 27, 40 4) Harkins 2018 0 74 1 74 1.1 $\frac{1}{2}$ 0.3 (0.01, 20, 5.02) Glanarov 2013 0 74 1 74 1.1 $\frac{1}{2}$ 0.3 (0.01, 20, 5.02) Hibrare 2010 7 7 882 7 382 9.9% 100 [0.35, 2.88] Hothery 2011 11 143 9 143 13.3 $\frac{1}{2}$ 124 (1.50, 3.09) Hibrare 2010 7 7 882 7 382 9.9% 100 [0.35, 2.88] Hothery 2011 10 109 2.20 (0.13, 2.66] Hothery 2011 10 100 1.00 2.2 (0.01, 2.66] Hothery 2011 0 100 1.00 2.2 (0.01, 2.66] Hothery 2011 0 100 1.00 2.2 (0.01, 2.66] Hothery 2011 0 100 1.00 2.2 (0.01, 2.66] Hothery 2012 0 50 2 50 1.2 $\frac{1}{2}$ 0.19 [0.01, 4.10] Sansone 2012 0 50 2 50 1.2 $\frac{1}{2}$ 0.19 [0.01, 4.10] Sansone 2012 0 50 2 50 1.2 $\frac{1}{2}$ 0.29 (0.03, 2.21) Sansone 2012 0 50 2 50 1.2 $\frac{1}{2}$ 0.29 (0.03, 2.21) Sansone 2012 0 50 2 50 1.2 $\frac{1}{2}$ 0.29 (0.03, 2.21) Sansone 2012 0 50 2 50 1.2 $\frac{1}{2}$ 0.29 (0.03, 2.21) Sansone 2012 0 50 2 50 1.2 $\frac{1}{2}$ 0.29 (0.03, 2.21) Sansone 2013 1 91 2 91 1.9% 0.49 [0.04, 5.50] Wang 2018 1 67 2 67 1.9% 0.49 [0.04, 5.50] Sansone 2013 1 91 2 91 1.9% 0.49 [0.04, 5.50] Sansone 2013 1 91 2 91 1.9% 0.49 [0.04, 5.50] Sansone 2013 1 91 2 91 1.9% 0.49 [0.04, 5.50] Sansone 2013 1 91 2 91 1.9% 0.49 [0.04, 5.50] Sansone 2013 1 91 2 91 1.9% 0.49 [0.04, 5.50] Sansone 2013 1 91 2 91 1.9% 0.49 [0.04, 5.50] Sansone 2013 1 91 2 91 1.9% 0.49 [0.04, 5.50] Sansone 2013 1 91 2 91 1.9% 0.49 [0.04, 5.50] Sansone 2013 1 91 2 91 1.9% 0.49 [0.04, 5.50] Sansone 2012 5 50 7 100.0% 0.68 [0.49, 0.95] Total events 61 97 Heterogenety Tat ² = 0.00; (D ² = 1.4.3.2, d ² = 2.60 - 0.37); l ² = 0.68 Fettor overall effect 2 = 2.219 P = 0.03) Total events 61 97 Heterogenety Tat ² = 0.00; (D ² = 1.4.3.2, d ² = 2.60 - 0.37); l ² = 0.68 Fettor overall effect 2 = 2.219 P = 0.03) Total events 61 97 Heterogenety Tat ² = 0					0.50 [0.09, 2.73]		
Casparovic 2017 1 3 4 4 3 4 2.28 0.23 [0.02, 215] Chartar 2015 1 289 6 289 2.58 0.16 [0.02, 137] Chartar 2015 2 100 4 100 3.7% 0.49 [0.09, 2.4] Hawkins 2018 0 7 4 1 7 4 1.1% 0.33 [0.01, 81] Hinaka 2014 0 36 0 36 Not estimable Holzhe 2011 1 1 143 9 143 13.38 1.24 (0.05, 3.09] Inhiane 2010 7 382 2 88 120 (1.08, 2.26) Merka 2014 0 100 1.00 1.1% 0.38 (0.04, 0.8] Merka 2014 2 477 11 477 4.8% 0.03 [0.01, 82, 26] Merka 2014 2 477 11 477 4.8% 0.03 [0.01, 82, 26] Merka 2014 2 477 11 477 4.8% 0.038 (0.04, 0.8] Merka 2014 2 477 11 477 4.8% 0.038 (0.04, 0.8] Merka 2014 2 477 11 477 4.8% 0.038 (0.04, 0.8] Merka 2014 2 417 1.9% 0.49 [0.04, 5.6] Solinski 2015 9 585 10 585 13.4% 0.066 [0.14, 40] Sanone 2012 0 50 2 50 1.2% 0.019 [0.01, 4.10] Standard 2015 9 585 10 585 13.4% 0.066 [0.14, 40] Standard 2015 9 585 10 585 13.4% 0.066 [0.14, 40] Standard 2015 9 585 10 585 13.4% 0.066 [0.14, 60] Tabla 2007 1 41 2 411 1.9% 0.49 [0.04, 5.56] Merka 2017 3 212 4 212 4.9% 0.57 [0.15, 8] Tabla 2007 1 41 2 4 11 9.9% 0.49 [0.04, 5.56] Tabla 2007 1 41 2 4 11 9.9% 0.49 [0.04, 5.56] Tabla 2007 1 41 2 4 11 9.9% 0.49 [0.04, 5.56] Tabla 2007 1 41 2 4 11 9.9% 0.49 [0.04, 5.56] Tabla 2007 1 441 2 4 11 9.9% 0.49 [0.04, 5.56] Tabla 2007 1 441 2 4 12 9.9% 0.49 [0.04, 5.56] Tabla 2007 1 441 2 4 12 9.9% 0.49 [0.04, 5.56] Tabla 2007 1 441 2 4 12 9.9% 0.49 [0.04, 5.56] Tabla 2007 1 441 2 4 12 9.9% 0.49 [0.04, 5.56] Tabla 2007 1 441 2 4 14 1.9% 0.49 [0.04, 5.56] Tabla 2007 1 441 2 4 14 1.9% 0.49 [0.04, 5.56] Tabla 2007 1 442, df = 2 (0.9 - 0.97); l ⁺ - 0.% Test for oreall effect $z = 2.19 (P - 0.03);$ l ⁺ - 0.0 Table ents 61 97 Herorogenety Ta ⁻¹ = 0.00; Ch ⁺ = 1.4.32, df = 2 (P - 0.97); l ⁺ - 0.8 Test for oreall effect $z = 2.249 (P - 0.97);$ l ⁺ - 0.8 Test for oreall effect $z = 2.249 (P - 0.97);$ l ⁺ - 0.8 Test for oreall effect $z = 2.249 (P - 0.97);$ l ⁺ - 0.8 Test for oreall effect $z = 2.249 (P - 0.97);$ l ⁺ - 0.8 Test for oreall effect $z = 2.249 (P - 0.97);$ l ⁺ - 0.8 Test for oreall effect $z = 2.$					0.19 [0.01, 4.12] ←	· · · · ·	
Chaina 2015 1 289 6 289 2.5% 0.16 [0.02, 1.37] Glimanov 2013 3 182 4 2.4% 1.00 [0.05, 0.27] Hawkins 2016 0 74 1 74 1.1% 0.310 (0.1, 8.20) Hindrae 2010 7 382 7 382 9.9% 1.00 [0.3, 2.88] Hotchey 2011 11 143 9 143 13.3% 1.24 [0.50, 3.09] Hindrae 2010 7 382 7 382 9.9% 1.00 [0.3, 2.88] Johnston 2012 8 832 1.2% 0.20 [0.01, 4.16] Maxielo 2002 2 100 1 100 1.1% 0.310 (0.1, 8.20) Herka 2014 2 477 11 477 4.8% 0.18 [0.04, 8.26] Merka 2014 2 477 11 477 4.8% 0.18 [0.04, 8.26] Marielo 2002 2 100 1 100 1.1% 0.310 [0.1, 8.20] Marielo 2002 2 100 1 100 1.1% 0.310 [0.1, 8.20] Shethad 2015 9 585 10 585 13.4% 0.09 [0.36, 2.23] Shethad 2015 9 585 10 585 13.4% 0.09 [0.36, 2.23] Shethad 2015 9 585 10 585 13.4% 0.09 [0.36, 2.23] Shethad 2015 9 585 10 585 13.4% 0.09 [0.36, 2.23] Shethad 2015 9 585 10 585 13.4% 0.49 [0.04, 5.56] Thata 2007 1 4 1 2 41 1.9% 0.49 [0.04, 5.56] Thata 2007 1 4 1 2 421 1.9% 0.49 [0.04, 5.56] Thata 2007 1 4 1 2 421 1.9% 0.49 [0.04, 5.56] Thata 2007 1 4 1 2 421 1.9% 0.49 [0.04, 5.56] Thata 2007 1 4 1 2 421 1.9% 0.49 [0.04, 5.56] Thata 2007 1 4 1 2 41 2.4% 2.4% 0.68 [0.49, 0.95] Thata 2007 1 4 1 2 41 2.4% 0.48 [0.04, 5.56] Thata 2007 1 4 1 2 41 2.4% 0.48 [0.04, 5.56] Thata 2007 1 4 1 2 41 2.4% 0.48 [0.04, 5.56] Thata 2007 1 4 1 2 41 2.4% 0.48 [0.04, 5.56] Thata 2007 1 4 1 2 41 2.4% 0.48 [0.04, 5.56] Thata 2007 1 4 1 2 41 2.4% 0.48 [0.04, 5.56] Thata 2007 1 4 1 2 41 2.4% 0.48 [0.04, 5.56] Thata 2007 1 4 1 2 41 2.4% 0.68 [0.49, 0.95] Thata 2007 1 4 1 2 41 2.4% 0.68 [0.49, 0.95] Thata 2007 1 4 1 2 41 2.4% 0.68 [0.49, 0.95] Thata 2007 1 4 41 2 41 2.4% 0.68 [0.49, 0.95] Thata 2007 1 4 41 2 41 2.4% 0.68 [0.49, 0.95] Thata 2007 1 4 41 2 41 1.9% 0.49 [0.04, 5.56] Thata 2007 1 4 41 2 41 1.9% 0.49 [0.04, 5.56] Thata 2007 1 4 41 2 41 1.9% 0.49 [0.04, 5.56] Thata 2007 1 4 41 2 41 1.9% 0.49 [0.04, 5.56] Thata 2007 1 4 41 2 41 1.9% 0.49 [0.04, 5.56] That 2007 1 4 41 2 41 1.9% 0.49 [0.04, 5.56] That 2007 1 4 41 2 41 1.9% 0.49 [0.04, 5.56] That 2007 1 4 41 2 40 1.9% 0.48 [0.04, 5.56] Tha							····
Climanov 2013 3 182 428 100 1020, 5.02 Climanov 2015 2 100 4 100 3.78 0.49 [0.9, 2.74 Harkin 2018 0 7 4 1 74 1 174 118 0.33 [0.0] 8, 20 Harkin 2011 0 3 56 0 36 Not estimable Holzhey 2011 11 143 9 143 13.38 124 (0.50, 3.09) Holzhey 2011 11 143 9 143 13.38 124 (0.50, 3.09) Holzhey 2011 0 7 382 8 832 188 0.21 1.48 1.00 [0.37, 2.68] Leack 2016 0 483 2 483 128 0.20 [0.01, 4.16] Hariel 2020 2 1 100 1 100 1 190 1.30 0.32 (0.04, 8.81) Merka 2014 2 477 11 477 4.88 0.18 [0.04, 0.81] Marzi 2011 0 1 100 1 100 1.30 0.32 (0.04, 8.81) Sansone 2012 0 50 2 50 128 0.19 [0.01, 4.10] Sansone 2012 0 50 2 50 128 0.19 [0.01, 4.01] Sansone 2012 0 50 2 50 128 0.19 [0.01, 4.01] Sansone 2012 0 50 2 50 128 0.19 [0.01, 4.01] Sansone 2012 0 50 2 50 128 0.19 [0.01, 4.01] Sansone 2012 0 50 2 50 128 0.19 [0.01, 4.01] Sansone 2012 0 50 2 50 128 0.19 [0.01, 4.01] Sansone 2012 0 50 2 50 128 0.19 [0.01, 4.01] Sansone 2012 0 50 2 50 128 0.19 [0.01, 4.01] Sansone 2012 0 50 2 50 128 0.19 [0.01, 4.01] Sansone 2012 0 50 2 50 128 0.05 [0.10, 8.22] Total events 51 9 92 Heterogenety, Tau ² = 0.00, Ch ² = 14.42, df = 22 (P = 0.39); P ¹ = 0% Test for overall effect: 2 = 2.19 (P = 0.03) Total events 51 9 92 Heterogenety, Tau ² = 0.00, Ch ² = 14.42, df = 26 (P = 0.97); P ¹ = 0% Test for overall effect: 2 = 2.21 9 (P = 0.03) Total events MUSI Enource [S1]							
$\begin{array}{c} \text{Lineary 2013} & 5 & 182 & 4.28 & 1.00 \ 0.20, 50.2 \\ \text{Hirackz 2014} & 0 & 36 & 0 & 74 & 1 & 74 & 118 & 0.33 \ 0.01, 8.20 \ 0.1, 8.20 \ 0.1, 8.20 \ 0.1, 8.20 \ 0.1, 1.1 \ 1.41 & 39 & 143 \ 1.38 & 1.14 \ 0.50, 3.09 \ 0.1, 8.20 \ 0.1, 1.00 \ 1.5 \ 0.18 \ 0.28 \ 0.28 \ 0.28 \ 1.48 & 1.00 \ 1.5, 2.88 \ 0.18 \ 1.28 \ 0.20 \ 0.2 \ 2.1 \ 1.1 \ 1.48 & 0.18 \ 0.04 \ 0.04 \ 0.18 \ 0.$							
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	Test for subgroup dif	ferences: Chi ² =	0.01, df = 1 ($P = 0.91), I^2$	= 0%	raroara (mina) i raroara (ra)	

and a ortic 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 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

	I	MIVS			FS			Mean Difference	Mean Difference
tudy or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
5.1 RCT									
ris 1999	95	20	20	83	19	20	3.6%	12.00 [-0.09, 24.09]	
Calderon 2009	77.1	32.4	39	71.3	30.4	39	3.5%	5.80 [-8.14, 19.74]	- -
Oogan 2005	141.7	32.1	20	132.6	35.6	20	3.0%	9.10 [-11.91, 30.11]	
Aachler 1999	84	32.1	60	82	61.25	60	3.2%	2.00 [-15.50, 19.50]	
loustafa 2007	85.67	6.79	30	90	8.3	30	4.1%	-4.33 [-8.17, -0.49]	-
ubtotal (95% CI)			169			169	17.4%	3.26 [-4.83, 11.34]	•
leterogeneity: Tau ² =	43.08;	Chi ² =	= 9.03,	df = 4 (P = 0.0	6); I ² =	56%		
est for overall effect:	Z = 0.7	′9 (P =	0.43)						
.5.2 PSM									
ang 2012	106.3	45.3	73	101.9	39.6	73	3.5%	4.40 [-9.40, 18.20]	
arhat 2003	89	18	50	70	11	50	4.0%	19.00 [13.15, 24.85]	
Casparovic 2017	79.9		34	61.9	13.7	34	4.0%	18.00 [11.20, 24.80]	-
ilmanov 2013	117.5		100	104.1	34.6	100	3.7%	13.40 [2.75, 24.05]	
Gilmanov 2015		7.17	74	94	6.17	74	4.1%	-2.00 [-4.16, 0.16]	-
lawkins 2018	155	35	36	108	65	36	2.7%	47.00 [22.88, 71.12]	
liraoka 2014	129	28	36	125	47	36	3.2%	4.00 [-13.87, 21.87]	
lolzhey 2011	142	54	143	102	45	143	3.7%	40.00 [28.48, 51.52]	
ribarne 2010	139.7	2.6	382	117.1	2	382	4.1%	22.60 [22.27, 22.93]	
ohnston 2012	73	32	832	95	37	832		-22.00 [-25.32, -18.68]	+
evack 2016	70	26	483	87	36	483		-17.00 [-20.96, -13.04]	-
Aasiello 2002	82.4	22	100	66.8	16	100	4.0%	15.60 [10.27, 20.93]	
Aerka 2014	82.2	217	477	81	19.9	477	3.1%	1.20 [-18.36, 20.76]	
Aurzi 2011	119	30	100	106	32	100	3.9%	13.00 [4.40, 21.60]	
ansone 2012	101.4	35.2	50	62.8	18.3	50	3.7%	38.60 [27.60, 49.60]	
eitz 2017	112	44	53	98	25	53	3.5%	14.00 [0.38, 27.62]	
hehada 2015	93.5	25	585	88	28	585	4.1%	5.50 [2.46, 8.54]	-
tolinski 2016	111	25	211	97.6	19.4	211	4.1%	13.40 [9.13, 17.67]	-
tolinski 2017	109.3	26.5	212	97.6	19.6	212	4.1%	11.70 [7.26, 16.14]	-
abata 2007	122.2	48.5	41	112.1	39.8	41	3.1%	10.10 [-9.10, 29.30]	
Vang 2018	138.4	34.6	67	112.4	28.8	67	3.7%	26.00 [15.22, 36.78]	
hao 2018	112.5	12.9	91	103.5	12.2	91	4.1%	9.00 [5.35, 12.65]	-
ubtotal (95% CI)			4230			4230	82.6%	12.43 [4.97, 19.89]	•
leterogeneity: Tau ² =					= 21 (P	< 0.00	0001); I ² =	= 99%	
est for overall effect:	Z = 3.2	27 (P =	0.001))					
otal (95% CI)			4399				100.0%	11.06 [4.29, 17.84]	◆
leterogeneity: Tau ² =					= 26 (P	< 0.00	0001); I ² =	= 99%	-100 -50 0 50 10
est for overall effect:									Favours [MIVS] Favours [FS]
est for subgroup diff	erences	· Chi ²	= 2.67	df = 1	(P = 0)	$10), I^2 =$	= 62.6%		

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,

		MIVS			FS			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
.7.1 RCT									
Aris 1999	70	19	20	51	13	20	3.6%	19.00 [8.91, 29.09]	-
Bonacchi 2002	517	12.2	40	52.4	9.8	40	3.6%	464.60 [459.75, 469.45]	
Calderon 2009	55	9.3	39	50.6	11.9	39	3.6%	4.40 [-0.34, 9.14]	.
Dogan 2005	84.8	24.4	20	88	19	20	3.5%	-3.20 [-16.75, 10.35]	
Aachler 1999	60	20.25	60	60	19	60	3.6%	0.00 [-7.03, 7.03]	+
/loustafa 2007	85.67	6.79	30	90	8.3	30	3.6%	-4.33 [-8.17, -0.49]	-
Subtotal (95% CI)			209			209	21.4%	80.10 [-98.13, 258.32]	
Heterogeneity: Tau ² =	49595.7	0; Chi ²	= 2735	2.47, df	= 5 (P ·	< 0.000	01); l² = 1	00%	
Test for overall effect:	Z = 0.88	(P = 0.	38)						
.7.2 PSM									
Bang 2012	106.3	45.3	73	101.9	39.6	73	3.5%	4.40 [-9.40, 18.20]	- -
arhat 2003	66	15	50	49	10	50	3.6%	17.00 [12.00, 22.00]	-
Gasparovic 2017	63.4	12.7	34	50.3	11.6	34	3.6%	13.10 [7.32, 18.88]	-
Gilmanov 2013	83.8	28.5	182	71.3	27.5	182	3.6%	12.50 [6.75, 18.25]	-
Gilmanov 2015	59	4.667	100	63	4.333	100	3.6%	-4.00 [-5.25, -2.75]	
lawkins 2018	101	24	74	77	44	74	3.5%	24.00 [12.58, 35.42]	
Hiraoka 2014	91	22	36	90	30	36	3.5%	1.00 [-11.15, 13.15]	
lolzhey 2011	74	44	143	64	28	143	3.6%	10.00 [1.45, 18.55]	
ribarne 2010	83.7	1.9	382	79.6	1.5	382	3.6%	4.10 [3.86, 4.34]	•
lohnston 2012	58	25	832	71	28	832	3.6%	-13.00 [-15.55, -10.45]	÷
evack 2016	55	21	483	70	30	483	3.6%	-15.00 [-18.27, -11.73]	-
Aasiello 2002	63.8	17.2	100	50.2	13	100	3.6%	13.60 [9.37, 17.83]	-
Aerka 2014	59.4	16	477	56.9	14.6	477	3.6%	2.50 [0.56, 4.44]	-
Aurzi 2011	83	20	100	74	28	100	3.6%	9.00 [2.26, 15.74]	
Sansone 2012	74.6	26.7	50	44.8	13.4	50	3.6%	29.80 [21.52, 38.08]	
Seitz 2017	76	35	53	76	17	53	3.5%	0.00 [-10.48, 10.48]	+
Shehada 2015	65.6	18.4	585	64.3	19.8	585	3.6%	1.30 [-0.89, 3.49]	+
Stolinski 2016	78.2	13.6	211	63.4	12.9	211	3.6%	14.80 [12.27, 17.33]	-
Stolinski 2017	77.7	14.9	212	62.6	13.1	212	3.6%	15.10 [12.43, 17.77]	-
abata 2007	81.9	31.8	41	71.6	30	41	3.5%	10.30 [-3.08, 23.68]	<u>+</u>
Vang 2018	80.4	19.6	67	67.5	18.2	67	3.6%	12.90 [6.50, 19.30]	-
Zhao 2018	79.5	12.5	91	72.9	11.8	91	3.6%	6.60 [3.07, 10.13]	+
Subtotal (95% CI)			4376			4376	78.6%	7.21 [3.98, 10.43]	♦
Heterogeneity: Tau ² =	49.03: C	chi² = 72	29.99. 0	f = 21 (P < 0.00	0001):	² = 97%		
Test for overall effect:				(,,,			
otal (95% CI)			4585			4585	100.0%	23.28 [5.69, 40.87]	•
Heterogeneity: Tau ² =	2240.41	; Chi² =	35361	.85, df =	27 (P	< 0.000	01); l² = 1	- 00%	-100 -50 0 50 100
est for overall effect:	Z = 2.59	(P = 0.	009)				- 100		-100 -50 0 50 100 Favours [MIVS] Favours [FS]
est for subgroup diffe	erences:	Chi ² = 0).64, df	= 1 (P =	= 0.42),	$I^2 = 0\%$	6		

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 impact 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

	1	MIVS			FS			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.9.1 RCT									
Calderon 2009	159	51.2	39	173.1	48.8	39	0.1%	-14.10 [-36.30, 8.10]	←
Dogan 2005	253.9	50.3	20	239.4	55.5	20	0.1%	14.50 [-18.33, 47.33]	· · · · · · · · · · · · · · · · · · ·
Moustafa 2007	2.55	0.422		3.583	0.695	30	30.7%	-1.03 [-1.32, -0.74]	
Subtotal (95% CI)			89			89	30.9%	-1.36 [-6.81, 4.09]	
Heterogeneity: Tau ² =	8.41; C	$hi^2 = 2$.19, df	= 2 (P =	= 0.33);	$I^2 = 9\%$,		
Test for overall effect:	Z = 0.4	9 (P = 0	0.63)						
1.9.2 PSM									
Bonacchi 2002	3.7	46	40	3.4	0.6	40	0.3%	0.30 [-13.96, 14.56]	
Farhat 2003	2.8	0.4	50	2.7	0.4	50	31.7%	0.10 [-0.06, 0.26]	•
Hawkins 2018	291	46	74	234	64	74	0.2%	57.00 [39.04, 74.96]	,
Hiraoka 2014	235	35	36	272	73	36	0.1%	-37.00 [-63.45, -10.55]	←──
Holzhey 2011	186	61	143	169	59	143	0.3%	17.00 [3.09, 30.91]	│
Merka 2014	156.9	33.4	477	145.1	30.5	477	3.3%	11.80 [7.74, 15.86]	│
Stolinski 2016	197.1	27.6	211	183	51.2	211	1.0%	14.10 [6.25, 21.95]	
Stolinski 2017	195	212	212	184	55.7	212	0.1%	11.00 [-18.51, 40.51]	· · · · · · · · · · · · · · · · · · ·
Wang 2018	246.5	38.4	67	227.6	45.3	67	0.3%	18.90 [4.68, 33.12]	· · · · · · · · · · · · · · · · · · ·
Zhao 2018	4	0.4	91	4.1	0.3	91	31.9%	-0.10 [-0.20, 0.00]	
Subtotal (95% CI)			1401			1401	69.1%	0.97 [0.07, 1.87]	◆
Heterogeneity: Tau ² =				df = 9 (P < 0.0	0001);	$^{2} = 92\%$		
Test for overall effect:	Z = 2.1	0 (P = 0)	0.04)						
Total (95% CI)			1490			1490	100.0%	0.39 [-0.39, 1.17]	◆
Heterogeneity: Tau ² =	0.49; C	$hi^2 = 1$	53.09,	df = 12	(P < 0.	00001);	$I^2 = 92\%$		
Test for overall effect:			,						Favours [MIVS] Favours [FS]
Test for subgroup diff	erences	Chi ² =	0.68,	df = 1 (P = 0.4	1), $ ^2 =$	0%		
URE 9 The forests pla	ot demor	nstrates	operat	ive time	(hours)	betwee	n MIVS ar	nd FS.	

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

Variables	n(N)	No. patients	Overall effect WMD/OR	Р		Study I	neterogen	eity
		MIVS/FS	(95% CI)†		chi ² -test	df	I ^{2(%)}	р
Age, y \pm SD	30 (10,194)	5,097/5,097	-0.43 [-1.05, -0.18] [†]	0.17	91.87	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 %, \pm SD	23 (2,910)	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) \pm SD	10 (1,536)	768/768	-0.59 [-2.08, 0.90] [†]	0.44	166.69	9	95	< 0.00001
Blood transfusion (patient), %	14 (5,756)	2,878/2,878	0.69 [0.51, 0.93]	0.02	48.53	13	73	< 0.00001
CBP time \pm 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 \pm 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 \pm SD	13 (2980)	1,490/1,490	0.39 [–0.39, 1.17] [†]	0.32	153.09	12	92	< 0.00001

COPD, chronic obstructive pulmonary disease; CBP, cardiopulmonary bypass; CI, confidence interval; FS, Full sternotomy; I², 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

	Experim		Contr			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight M	I-H, Random, 95% CI	M-H, Random, 95% CI
1.19.1 RCT							
Calderon 2009	18	39	20	39	6.0%	0.81 [0.33, 1.98]	
Dogan 2005	8	20	8	20	3.9%	1.00 [0.28, 3.54]	
Subtotal (95% CI)		59		59	9.8%	0.87 [0.42, 1.80]	
Total events	26		28				
Heterogeneity: Tau ² =				(P = 0.	79); $I^2 = 0$	%	
Test for overall effect	:: Z = 0.37	(P = 0.7)	71)				
1.19.2 PSM							
Ghanta 2015	71	289	92	289	10.5%	0.70 [0.48, 1.00]	
Gilmanov 2013	1	182	2	182	1.4%	0.50 [0.04, 5.53]	
Hawkins 2018	6	74	12	74	5.0%	0.46 [0.16, 1.29]	
Hiraoka 2014	15	36	24	36	5.5%	0.36 [0.14, 0.93]	
Johnston 2012	202	832	286	832	11.7%	0.61 [0.49, 0.76]	
Levack 2016	26	483	34	483	9.0%	0.75 [0.44, 1.27]	
Merka 2014	134	477	94	477	11.0%	1.59 [1.18, 2.15]	- - -
Sansone 2012	13	50	25	50	6.3%	0.35 [0.15, 0.81]	
Seitz 2017	14	53	14	53	6.1%	1.00 [0.42, 2.37]	
Stolinski 2016	103	211	142	211	10.2%	0.46 [0.31, 0.69]	
Tabata 2007	19	41	13	41	5.9%	1.86 [0.76, 4.57]	
Zhao 2018	16	91	34	91	7.5%	0.36 [0.18, 0.71]	
Subtotal (95% CI)		2819		2819	90.2%	0.67 [0.48, 0.93]	\bullet
Total events	620		772				
Heterogeneity: Tau ² =	= 0.21; Chi	$i^2 = 48.2$	21, df =	11 (P <	0.00001);	$I^2 = 77\%$	
Test for overall effect	:: Z = 2.41	(P = 0.0))2)				
Total (95% CI)		2878		2878	100.0%	0.69 [0.51, 0.93]	•
Total events	646		800				
Heterogeneity: Tau ² =	= 0.19; Chi	$i^2 = 48.5$	53, df =	13 (P <	0.00001);	$I^2 = 73\%$	0.05 0.2 1 5 20
Test for overall effect							Favours [experimental] Favours [control]
Test for subgroup dif	ferences: ($Chi^2 = 0$.42. df =	1 (P =	(0.52) $I^2 =$	0%	ravous [experimental] ravous [control]

FIGURE 10 | Forest plot of patients transfused red blood cells between MIVS and FS.

	MIVS			FS			Mean Difference		Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
1.21.1 RCT										
Bonacchi 2002	157	98	40	293	172	40	0.1%	-136.00 [-197.35, -74.65]	•	
Dogan 2005	200	309.9	20	421.1	514.1	20	0.0%	-221.10 [-484.18, 41.98]	←	
Moustafa 2007	1.77	0.68	30	3.13	0.78	30	20.7%	-1.36 [-1.73, -0.99]		
Subtotal (95% CI)			90			90	20.7%	-88.29 [-212.15, 35.56]		
Heterogeneity: Tau ² =	= 8912.4	0; Chi ²	= 21.1	8, df =	2 (P < 0	0.0001)	$l^2 = 91\%$			
Test for overall effect	: Z = 1.4	0 (P = 0)	0.16)							
1.21.2 PSM										
Bang 2012	680	826	73	633	738	73	0.0%	47.00 [-207.09, 301.09]	•	
Farhat 2003	394	219	50	465	318	50	0.0%	-71.00 [-178.02, 36.02]	•	
Gasparovic 2017	1.2	1.2	34	1.3	1.5	34	20.1%	-0.10 [-0.75, 0.55]	+	
Holzhey 2011	3.6	6.2	143	3.9	4.6	143	18.2%	-0.30 [-1.57, 0.97]	+	
Murzi 2011	0.7	1.1	100	2	3	100	20.2%	-1.30 [-1.93, -0.67]	•	
Stolinski 2016	298.1	317.1	211	527.7	427	211	0.0%	-229.60 [-301.36, -157.84]	•	
Wang 2018	2.2	1.2	67	1.1	0.8	67	20.7%	1.10 [0.75, 1.45]		
Subtotal (95% CI)			678			678	79.3%	-0.27 [-1.93, 1.38]	•	
Heterogeneity: Tau ² =	= 2.69; C	$2hi^2 = 8$	8.86, d	f = 6 (P)	< 0.00	001); I ²	= 93%			
Test for overall effect	Z = 0.3	3 (P =)	0.75)							
Total (95% CI)			768			768	100.0%	-0.59 [-2.08, 0.90]		
Heterogeneity: Tau ² =	2 77.0	· h:2 1						-0.55 [-2.00, 0.50]		
Test for overall effect				ui = 9 (P < 0.0	0001),	= 95%		-20 -10 0 10 20	
Test for subgroup dif		· •		JE 1/1	0.1	2) 12	10 10/		Favours [MIVS] Favours [FS]	
rest for subgroup an	rerences	. Cni= =	1.94,	ui = 1 (i	r = 0.10	s), i [_] =	40.4%			
URE 11 Forest plot	of units o	of red bl	ood tra	nsfusec	l betwe	en MIVS	S and ES			

disease and chronic obstructive pulmonary disease undergoing mitral or/and aortic valve operations (12, 56). 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

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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.

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