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Effect of minimally invasive cardiac surgery on hospital length of stay: A systematic review and meta-analysis

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Abstract

Background: **Perioperative management using minimally invasive cardiac surgery (MICS), compared to full sternotomy (FS) cardiac surgery, is considered to improve postoperative recovery, and reduce hospital length of stay (LOS).**
Methods: **A comprehensive systematic search was conducted across MEDLINE/PubMed, Embase, and the Cochrane library to identify RCT comparing MICS to FS approach for aortic valve, mitral valve, and coronary artery bypass surgery. Meta-analysis of extracted data was performed using random effects models.**
Results: **A total of 33 RCTs including 2920 patients were identified. Overall MD (95% CI) for hospital and intensive care unit (ICU) LOS after MICS was significantly shorter compared to FS (-0.88 days (-1.55;-0.20), p<0.013; 2606 patients) and (-0.23 days (-0.41;-0.05), p=0.012; 2242 patients), respectively. Additionally, postoperative blood loss was reduced with the use of MICS, (-192.07 ml (-292.32;-91.82), p=0.002; 718 patients). There was no evidence for differences between both groups in terms of postoperative ventilation times, duration of surgery, reintervention rate, incidence of postoperative atrial fibrillation or stroke, hospital mortality, or 1-year mortality.**
Conclusion: **Within the limitations of a meta-analysis, MICS was found to be effective in promoting faster recovery by reducing postoperative blood loss, ICU, and hospital LOS.**

Keywords: **Enhanced recovery, minimally invasive, cardiac surgery, valve replacement, coronary bypass, ERACS.**

Introduction

In cardiac surgery, the classical access to the heart is via a median full sternotomy which is usually well tolerated postoperatively[1]. Nonetheless, sternotomy can result in moderate to severe postoperative pain affecting respiratory function, reducing ambulation and thus delaying hospital discharge[2]. Several surgical and technical innovations have led to a dramatic decrease in surgical invasiveness and contributed in some populations to an improved outcome (i.e., wound healing in diabetic and obese patients)[3-5]. In the early 1990s, off-pump coronary artery bypass grafting (OPCAB) surgery was introduced, followed by the development of minimally invasive direct coronary artery bypass grafting (MIDCAB) in 1995[6]. In 1996, mitral valve surgery (MVS) through a thoracotomy, hence avoiding sternotomy, was described[7,8]. Aortic valve replacement (AVR) through a right anterior thoracotomy was first presented in 1993 by Rao and Kumar[9], with the combination of femoral cannulation in 1996 by Cosgrove[10]. Each of these minimally invasive and/or access techniques have further evolved by reducing invasiveness with the aim to improve recovery, reduce length of stay and hasten return to normal activities[8].

The minimally invasive approaches described above are considered fundamental elements in Enhanced Recovery After (Cardiac) Surgery (ERA(C)S) concepts[11,12]. Mini thoracotomy, while a key element, may heighten the risk for intercostal nerve injury and postoperative pain[2]. Moreover, minimally invasive procedures often hinder surgical exposure, increase complexity and present significant challenges for the surgeon, perfusionist and anesthetist[13]. Associated drawbacks include longer operating times, duration of cardiopulmonary bypass (CPB), and aortic cross-clamp, increased rates of bleeding and vascular complications, and redo thoracotomies[2,14]. Consequently, there is concern about the heightened risks, such as stroke and aortic dissection/injury, particularly with femoral cannulation, emphasizing the need for careful consideration when opting for minimally invasive techniques[15,16].

Systematic reviews comparing minimally invasive cardiac surgery (MICS) to conventional surgery so far have generally stated that the evidence or quality of the included studies was generally poor[14,17]. Moreover, data on the risk of stroke are conflicting[2,16,18,19]. Furthermore, improved outcomes were often observed in only single or dual center studies[20]. In addition, several meta-analyses did not assess cardiovascular morbidity and recovery. Lastly, these meta-analyses were mostly limited to the comparison of aortic valve surgery comparing full to hemi-sternotomy.

The goal of the present systematic review was to update the available evidence by assessing the impact of MICS on hospital length of stay (LOS) when compared to conventional cardiac surgery with full sternotomy. We hypothesized that MICS would be associated with a reduced hospital LOS and would be equally safe when compared to 'conventional cardiac surgery' using a 'full sternotomy'. We analyzed this for a wide range of cardiac interventions: AVR, MVS, OPCAB and on-pump coronary artery bypass grafting (CABG) surgery.

Material and methods

Eligibility criteria

Based on the PICOS strategy we included studies if:

1. The population comprised patients undergoing AVR, MVS or coronary bypass surgery; and
2. The interventional or experimental group had this intervention using a minimally invasive surgical (non-full sternotomy) approach; and
3. The control group was undergoing a conventional surgical approach with full sternotomy; and
4. Outcomes of the selected studies included any of the following: Primary outcome was hospital LOS as defined from the day of cardiac surgery until the day of discharge (in days). Secondary outcomes included all-cause mortality (in hospital, at 30 days and 1 year after surgery), the incidence of major adverse cardiac and cerebrovascular events (MACCE) [(in-hospital and in the first 6 postoperative months); i.e., death from any cause; perioperative myocardial infarction, requirement of surgical revisions at the coronary arteries; postoperative coronary angioplasty; and stroke], re-intervention rates during total hospital LOS (such as re-exploration for bleeding), rates of other cerebrovascular accidents not included in MACCE (transient ischemic attacks, reversible ischemic neurologic deficit), duration of surgery (minutes), ICU LOS (days), pain scores (by measurement of the visual analogue scale (VAS) or numeric rating scale (NRS) for pain scale), postoperative blood loss (milliliters), incidence of new onset atrial fibrillation AF and postoperative ventilation times (minutes); and
5. These were randomized controlled trials.

Sources of information

A systematic literature search was performed on April 4th, 2021, and in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)[21] guidelines: Cochrane Central Register of Controlled Trials (CENTRAL) (2021, issue 4), PubMed, Embase and Web of Science. ClinicalTrials.gov database, World Health Organization international clinical trials registry platform search portal (ICTRP) and ResearchGate was searched for 'grey' literature and studies that were not yet identified. We double checked the reference lists of the included studies and related systematic reviews on the subject for additional references. We restricted our search to literature published in English, French, Dutch, or German. There were no restrictions on the date of publication.

Search

The search was constructed with the aid of an information specialist using MeSH (medical subject headings) terms. A detailed search strategy is provided in the supplemental materials. The protocol was registered a priori in PROSPERO (CRD42021234941).

Selection of studies

The records identified were deduplicated with Endnote[22]. Thereafter, Rayyan QCRI[23] was used to screen and select abstracts. The selected titles were assessed for eligibility for final inclusion based on full text analysis. Studies were selected independently by two reviewers (DFH and FP). In case of conflict, a third author (SR) was consulted. This process is depicted in the PRISMA flow diagram (Figure 1)[24].

Data collection process and items

Two independent reviewers (DFH and FP) extracted study methodology, patient characteristics, procedural characteristics, outcomes, and key conclusions from the included studies.

Statistical plan:

Data collection process and items

A meta-analysis was conducted with randomized trials for our primary outcome and our secondary outcomes. Analyses were performed using the "metaphor" package (version 4.4-0) of R Statistical Software (version 4.3.1)[25].

Mean differences (MD) with 95% confidence interval (CI) were calculated for continuous outcomes, while odds ratios (OR) with 95% CI were assessed for binary outcomes[26]. In case only sample sizes, median, range and/or interquartile ranges were reported, we used the method described by Wan to estimate the sample means and standard deviations[27]. Forest plots were created to visually represent clinical outcomes.

Subgroup analysis

The following subgroups were further analyzed separately: aortic valve replacement (hemi sternotomy, mini sternotomy, thoracotomy or thoracoscopy vs full sternotomy), mitral valve surgery (minimally invasive approach vs full sternotomy) and coronary bypass surgery (MIDCAB vs OPCAB or CABG).

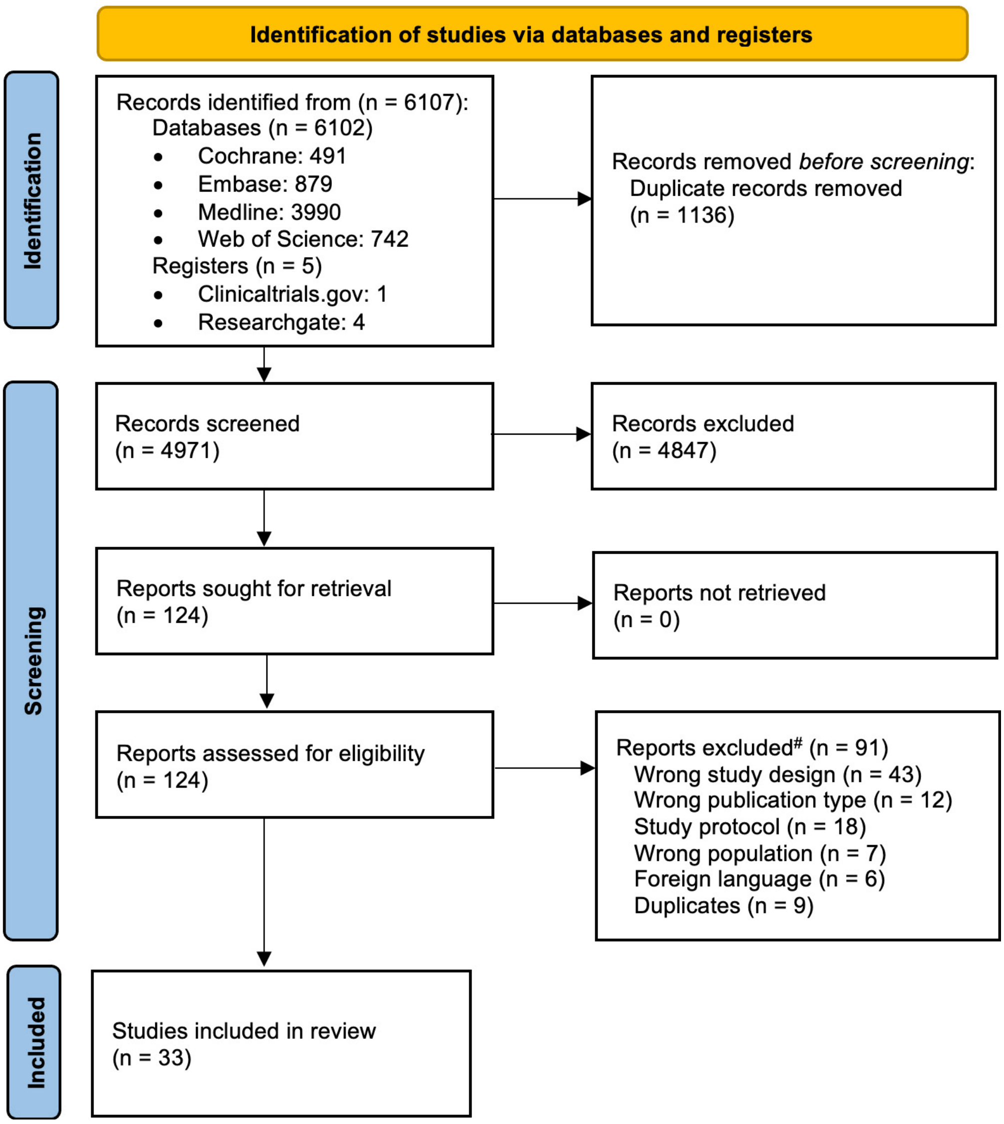

Fig. 1 — PRISMA 2020 flow diagram.
= overlap in reasons for exclusion.

Risk of bias in included studies

Two reviewers assessed possible bias of the included studies independently (DFH and FP). The criteria of the 'Cochrane handbook for systematic reviews of interventions' were used via the RoB 2 tool[28]. Bias was graded as 'yes', 'probably yes', 'probably no', 'no' and 'no information'. Once these questions were answered, a risk-of-bias judgement was made describing low risk of bias, some concerns or high risk of bias. Disagreement was solved by a third author (SR). Funnel plots represent the analysis of publication bias, statistically analyzed by Egger's test and Begg and Mazumdar's test.

Results

Results of the search

We identified a total of 6107 citations, of which 124 studies were considered relevant based on title and abstract. Based on full text assessment, we identified 33 publications that fulfilled our eligibility criteria (Figure 1). However, 3 publications reported on the same patient population but differed regarding exclusion criteria and outcomes[29-31]. Therefore, from these three studies, we primarily used the data from Gąsior et al, unless the relevant outcome was not reported but was included in one of the other two studies[30].

Study characteristics

The study and patient characteristics are reported in Table I and Supplementary Table I. A total of 2920 unique patients (MICS: 1464 patients, FS: 1456 patients) were included in 33 trials[29-61]. The trials had randomized between 36 and 270 participants and had been performed between 1995 and 2021 in 18 countries (Austria, Brazil, Czech Republic, Egypt, France, Germany, India, Italy, The Netherlands, Poland, Russia, Serbia, South Korea, Spain, Sweden, Turkey, United Kingdom, and USA). A total of 16 trials had been performed on AVR, 7 trials on MVS and 8 trials on CABG surgery. Only 5 studies were multicenter trials[33,35,38,39,57]. The intervention procedure (minimally invasive technique) had been performed through a 'mini sternotomy or upper sternotomy' in 16 studies, through a thoracotomy (lateral/anterolateral/right/left/anterior) or thoracoscopy in 15 studies. In 58 patients the surgical procedure was converted from minimally invasive to full sternotomy due to technical, anesthetic or surgical complications. In the trial of Nair et al. eight patients were diverted from MICS to the FS group prior to surgical incision based on findings derived from intraoperative transesophageal ultrasound, nonetheless, these were analyzed based on intention-to-treat[39]. Two trials excluded 3 patients each due to inability for single lung ventilation or inability of positioning the experimental valve[42,57]. Further details can be found in Supplementary Table II.

Risk of bias in the included studies

Application of the RoB 2 tool suggested that several trials had some concerns of bias (Figure 2). Considering that specific outcomes might have been reported differently, we assessed reporting bias at the study-level as has been recommended[28]. We found that all studies included information on outcome measures that are considered important for the type of intervention. Detailed information regarding allocation, blinding, incomplete outcome data, and selective reporting can be found in supplementary material.

Synthesis of results

Length of stay

Hospital LOS was reported in 28 studies (2606 patients) but none of the studies reported any discharge criteria (Figure 3). The overall MD (95% CI) showed a significant reduction in hospital LOS in patients undergoing MICS compared to patients having a conventional full sternotomy (-0.88 days (-1,55;-0.20), p=0.013) (Table II). Amongst these studies, there was an important heterogeneity of treatment effect for hospital LOS (I^2 91%, p < 0.001). Subgroup analysis revealed that this effect was largest following MVS and non-significant following CABG or AVR surgery. No publication bias was observed (Figure 4).

Duration of ICU LOS was reported in 25 trials including 2242 patients. Overall MD (95% CI) showed that the patient group having MICS, compared to those operated on by conventional full sternotomy, had a shorter ICU LOS (-0.23 days (-0.41;-0.05), p=0.012) (Figure 3). There was evidence of important heterogeneity of treatment effect (I^2 88%, p<0.001). Subgroup analysis revealed that this effect was largest following MVS and non-significant following CABG or AVR surgery. Funnel plot assessment suggested potential publication bias (Figure 4).

Duration of surgery

Twenty-one studies (2036 patients) reported duration of surgery. Compared to patients who had a conventional full sternotomy, MD (95% CI) for surgical time showed no difference in patients with MICS (15.67 minutes (-0.91;32.32), p=0.064) (Supplementary figure S1). These studies showed an important heterogeneity of treatment effect. Funnel plot assessment did not show any publication bias (Supplementary figure S2).

Table I. — Study characteristics of relevant studies identified for meta-analysis comparing minimally invasive with full sternotomy approach for patients undergoing aortic valve replacement, mitral valve surgery or coronary artery bypass surgery.

Author	Country	Procedure	Study period	Intervention	Control	Multicentric	Reported outcomes
				MICS (N)	FS (N)	Yes/No	
Ahangar et al[61]	India	AVR	09/2010-08/2012	30	30	No	Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Postoperative pain;
Aris et al[60]	Spain	AVR	1999, 4 months	20	20	No	Ventilation time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Mortality; Postoperative pain; Atrial fibrillation
Bauer et al[59]	Germany	CABG	NR	50	50	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL;
Bonacchi et al[58]	Italy	AVR	01/1999 - 07/2001	40	40	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Re-exploration rates; Mortality; Postoperative pain; Atrial fibrillation;
Borger et al[57]	USA, Germany	AVR	05/2012 - 08/2015	46	48	Yes	Re-exploration rates; Mortality; Major adverse cardiac and cere-brovascular events;
Calderon et al[56]	France	AVR	01/2002 - 12/2006	39	38	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Postoperative pain;
Chahal et al[55]	India	MVS	NR	25	25	No	Ventilation time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Major adverse cardiac and cere-brovascular events;
Dalén et al[54]	Sweden	AVR	10/2016 - 08/2015	19	21	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Major adverse cardiac and cere-brovascular events; Stroke; Atrial fibrillation;
Dias et al[53]	Brazil	AVR	06/1997 - 08/1998	20	20	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Postoperative pain;

Dogan et al[50]	Germany	CABG	NR	19	20	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Postoperative pain;
Dogan et al[51]	Germany	AVR	NR	20	20	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Postoperative pain;
Dogan et al[52]	Germany	MVS	NR	20	20	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Stroke;
El-Fiky et al[49]	Egypt	MVS	NR	50	50	No	Surgery time in minutes; Hospital stay in days; Blood loss in mL;
Foik et al[29]	Poland	CABG	11/2009 - 12/2013	92	108	No	Mortality; Atrial fibrillation;
Ganyukov et al[48]	Russia	CABG	12/2012 - 11/2017	52	50	No	Hospital stay in days; Mortality; Major adverse cardiac and cere-brovascular events;
Gasior et al[30]	Poland	CABG	11/2003 - 10/2013	98	102	No	Hospital stay in days; Blood loss in mL; Mortality; Major adverse cardiac and cere-brovascular events;
Gofus et al[47]	Czech Re-public	AVR	05/2017 - 11/2019	20	20	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Stroke; Atrial fibrillation
Gu et al[46]	The Nether-lands	CABG	06/1995 - 06/1996	31	31	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Blood loss in mL;
Gulielmos et al[45]	Germany	CABG	NR	17	19	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Mortality; Atrial fibrillation;
Hancock et al[44]	United King-dom	AVR	03/2014 - 07/2016	135	135	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Re-exploration rates; Mortality; Major adverse cardiac and cere-brovascular events; Postoperative pain; Stroke; Atrial fibrillation

Iyigün et al[43]	Turkey	CABG	05/2013 - 01/2015	33	29	No	Hospital stay in days; Intensive care unit stay in days;
Kang et al[42]	South Korea	MVS	11/2010 - 03/2011	50	50	No	Ventilation time in minutes; Intensive care unit stay in days;
Mächler et al[41]	Austria	AVR	07/1996 - 12/1997	60	60	No	Surgery time in minutes; Blood loss in mL; Mortality; Major adverse cardiac and cerebrovascular events;
Moustafa et al[40]	Egypt	AVR	NR	30	30	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates;
Nair et al[39]	United Kingdom	AVR	01/2010 - 04/2015	118	104	Yes	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Mortality; Major adverse cardiac and cerebrovascular events; Postoperative pain;
Nasso et al[38]	Italy	MVS	01/2008 - 01/2012	80	80	Yes	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Mortality; Major adverse cardiac and cerebrovascular events;
Nourelden et al[37]	Egypt	MVS	05/2017 -04/2019	25	25	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Postoperative pain; Atrial fibrillation
Rodriguez-Caulo et al[36]	Spain	AVR	03/2016 - 05/2018	50	50	No	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Major adverse cardiac and cerebrovascular events; Atrial fibrillation
Rogers et al[35]	United Kingdom, Italy	CABG	02/2007 - 11/2009	91	93	Yes	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Major adverse cardiac and cerebrovascular events; Postoperative pain; Stroke; Atrial fibrillation
Schneider et al[34]	Russia	AVR	2012 - 2017	56	56	No	Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Re-exploration rates; Mortality; Major adverse cardiac and cerebrovascular events;

Speziale et al[33]	Italy	MVS	01/2006- NR	70	70	Yes	Ventilation time in minutes; Surgery time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Major adverse cardiac and cerebrovascular events; Postoperative pain;
Tajstra et al[31]	Poland	CABG	11/2009 - 10/2013	94	97	No	Mortality; Major adverse cardiac and cerebrovascular events;
Vukovic et al[32]	Serbia	AVR	02/2016 - 11/2017	50	50	No	Ventilation time in minutes; Hospital stay in days; Intensive care unit stay in days; Blood loss in mL; Re-exploration rates; Mortality; Major adverse cardiac and cerebrovascular events; Atrial fibrillation

			D1	D2	D3	D4	D5	Overall
Ahangar et al	2013	AVR	!	+	+	+	!	!
Aris et al	1999	AVR	+	+	+	+	!	+
Bauer et al	2001	CABG	+	+	+	+	!	+
Bonacchi et al	2002	AVR	+	+	+	+	+	+
Borger et al	2016	AVR	!	!	+	!	+	!
Calderon et al	2009	AVR	+	+	+	+	-	!
Chalal et al	2016	MVS	+	+	+	+	!	+
Dalen et al	2018	AVR	+	+	+	+	+	+
Dias et al	1999	AVR	+	+	+	+	!	+
Dogan et al 2002	2002	CABG	!	+	+	+	!	!
Dogan et al 2003	2003	AVR	!	+	+	+	+	+
Dogan et al 2005	2005	MVS	!	+	+	+	!	+
El-Fiky et al	2000	MVS	+	+	+	+	!	+
Ganyukov et al	2020	CABG	+	+	+	+	+	+
Gasior et al	2014	CABG	+	-	+	+	+	-
Gofus et al	2020	AVR	!	+	+	+	!	!
Gu et al	1999	CABG	!	+	+	+	!	!
Gulielmos et al	1999	CABG	!	!	+	+	!	!
Hancock et al	2021	AVR	+	+	+	+	+	+
Iyigun et al	2017	CABG	+	+	+	+	!	+
Kang et al	2011	MVS	+	+	+	+	!	+
Mächler et al	1999	AVR	!	+	+	+	!	!
Moustafa et al	2007	AVR	!	+	+	+	!	!
Nair et al	2018	AVR	+	!	+	+	+	!
Nasso et al	2014	MVS	+	+	+	+	!	+
Nourelden et al	2020	MVS	!	+	+	+	+	!
Rodriguez-caulo et al	2020	AVR	+	+	+	+	+	+
Rogers et al	2012	CABG	+	!	+	+	+	!
Shneider et al	2020	AVR	!	+	+	+	!	!
Speziale et al	2011	MVS	+	+	+	+	!	+
Vukovic et al	2019	AVR	+	+	+	+	!	+

+ Low risk
! Some concerns
- High risk

D1 Randomisation process
D2 Deviations from the intended interventions
D3 Missing outcome data
D4 Measurement of the outcome
D5 Selection of the reported result

Fig. 2 — Risk of bias summary.
AVR, aortic valve replacement; CABG, coronary artery bypass grafting; MVS, mitral valve surgery.

Ventilation time

Twenty-three studies reported ventilation time, including 2071 patients. The MD (95% CI) showed that ventilation time tended to be reduced in patients who had MICS compared to full sternotomy, although this was non-significant (-183,19 minutes (-379.1;10,72), p=0.063) (Supplementary figure S1). These studies showed an important heterogeneity of treatment effect. Funnel plot assessment did not show any publication bias (Supplementary figure S2).

Complications

Postoperative blood loss

Eleven studies (718 patients) reported postoperative blood loss. Compared to patients operated on by full sternotomy, MD (95% CI) postoperative blood loss was significantly reduced in patients with MICS (-192.07 ml (-292.32;-91.82), p=0.002) (Supplementary figure S3). These studies showed an important heterogeneity of treatment effect. Funnel plot assessment did not show any publication bias (Supplementary figure S4).

Re-intervention

Twenty studies (1899 patients) reported re-intervention rate. Compared to patients operated on by full sternotomy, re-intervention rate was not different in patients with MICS (Supplementary figure S3). There was no evidence of heterogeneity of treatment effect. Funnel plot assessment did not show any publication bias (Supplementary figure S4).

Mortality

In-hospital mortality was reported by 19 studies including 1655 patients. No significant difference was observed in in-hospital mortality between patients with MICS or full sternotomy (Figure 5). Seven studies, including 692 patients, reported 30-day mortality. Compared to patients who had a conventional full sternotomy, no significant difference was observed in 30-day mortality in patients with MICS (Figure 5). Ten studies, including 1282 patients, reported 1-year mortality. No significant difference was observed in 1-year mortality between the groups (Figure 5). No evidence of heterogeneity of treatment effect was observed in the mortality analyses. Funnel plot assessment did not show any publication bias (Supplementary figure S5).

New onset atrial fibrillation

Eleven studies (1102 patients) reported the incidence of new onset AF. Incidence of new onset AF was not different between the two groups (Supplementary figure S6). There was no evidence of heterogeneity of treatment effect. Funnel plot assessment did not show any publication bias (Supplementary figure S7).

Major adverse cardiac and cerebrovascular events

Only 1 study reported on MACCE. Seventeen studies, including 2013 patients reported stroke, and seven studies (996 patients) reported cerebrovascular accidents not included in MACCE. No significant difference was observed in the occurrence of either outcome in patients with MICS compared to those operated on by conventional full sternotomy (Supplementary figure S6). There was no evidence of heterogeneity of treatment effect for stroke or cerebrovascular accidents not included in MACCE. Assessment of funnel plots did not show any publication bias (Supplementary figure S7).

Postoperative pain

Six studies (973 patients) described pain scores between the two groups for pain scores on postoperative day 1. These studies showed an important heterogeneity of treatment effect. Subgroup analysis identified a low heterogeneity following AVR surgery with a statistically significant reduction in pain scores in favor of MICS (Supplementary figure S8).

Five studies (749 patients) reported pain scores between the two groups for pain scores on postoperative day 2. Subgroup analysis, including 4 studies, identified a low heterogeneity following AVR surgery without any difference in pain scores. Two studies (492 patients) described pain scores on postoperative day 3 following AVR surgery and three studies (312 patients) on postoperative day 5. No significant difference was observed in pain scores at the given time points (Supplementary figure S8). Assessment of funnel plot did not show any publication bias (Supplementary figure S9).

Discussion

Summary of main results

General belief is that MICS ensures better outcomes when compared to traditional full sternotomy surgery. Given the ongoing technological advancements and the widespread awareness of these options among the general population, surgeons nowadays find themselves compelled to adopt these techniques, despite the long learning curves[4,5].

The findings of our systematic review and meta-analysis indicate that MICS is linked to a reduction in ICU and hospital LOS. Moreover, there is a significant decrease in postoperative blood loss following MICS whilst no difference can be detected in procedural and postoperative ventilation time. Additionally, the results demonstrate no differences in reintervention rates, incidences MACCE, new onset AF, or mortality (Table II).

Resource restraints have prompted changes in postsurgical management, aiming to “fast-track” cardiac surgical patients[62]. Traditionally, next to the use of minimal access, early postoperative extubation was a key component in this approach, suggested to reduce ICU LOS. Although we did not identify a reduction in postoperative ventilation times, we found a modest yet significant reduction in ICU

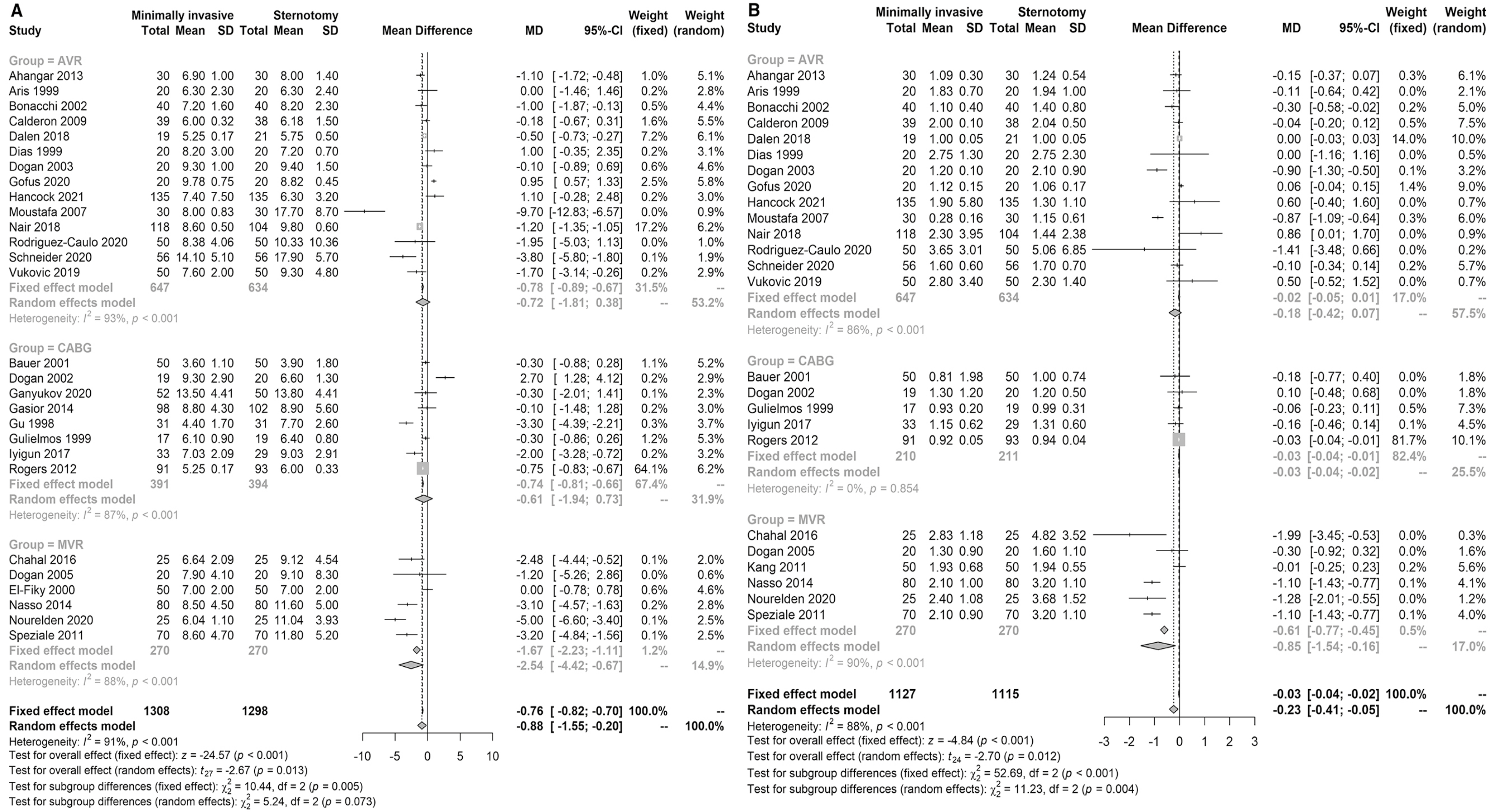

Fig. 3 — Forrest plots with pooled mean difference for (A) hospital and (B) intensive care unit length of stay.
AVR, aortic valve replacement; CABG, coronary artery bypass grafting; CI, confidence interval; MD, mean difference; MVR, mitral valve replacement/repair.

Table II. — Summary of findings: Full sternotomy compared to minimally invasive cardiac surgery in adults.
Patient or population: adult patients requiring aortic valve replacement, mitral valve surgery or coronary artery bypass surgery.
Settings: Cardiac surgical care; Intervention: minimally invasive cardiac surgery (partial sternotomy, thoracotomy or thoracoscopic access).; Comparison: full sternotomy cardiac surgery.

Outcomes No of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects[#] (95% CI)			Certainty of the evidence (GRADE)	Comments
		Risk with FS	Risk with MICS	Difference		
Hospital LOS Follow-up: In-patient stay 2606 (28 studies)	-	Mean hospital LOS was 9 days	-	0.88 days shorter hospital LOS (1.55 to 0.20 fewer)	Low[1,2,3,4] Due to risk of bias, indirectness, and inconsistency	May decrease the hospital LOS.
ICU LOS 2242 (25 studies)	-	The mean ICU LOS was 2 days	-	0.23 days shorter ICU LOS (0.41 to 0.05 fewer)	Very low[1,2,3,4] Due to risk of bias, indirectness, and inconsistency	May reduce the ICU LOS.
Duration of surgery (min) 2036 (21 studies)	-	The mean surgery time was 189 minutes	-	15.67 minutes longer surgery time (0.97 fewer to 32.32 more)	Very low[1,3] Due to inconsistency and variations in perioperative management	There may be an increase in surgery time.
Postoperative ventilation time (min) 2071 (23 studies)	-	The mean postoperative ventilation time was 803 minutes	-	184 minutes shorter postoperative ventilation time (379.10 fewer to 10.72 more)	Very low[1,3] Due to inconsistency and variations in perioperative management	May decrease postoperative ventilation time.
Postoperative blood loss (ml) Follow-up: until removal of drains 718 (11 studies)	-	The mean postoperative blood loss was 573 mL	-	192 mL fewer postoperative blood loss (292 to 92 lower)	Moderate[3] Due to inconsistency	Probably decreases the incidence of postoperative blood loss.
Reintervention rate Follow-up: In-patient stay 1899 (20 studies)	OR 0.82 (0.53 to 1.26)	53 per 1000	44 per 1000 (29 to 66)	1.0 % fewer reinterventions (2.6 fewer to 1.5 more)	Moderate[4]	There may be little or no difference in reintervention rate.

In-hospital mortality 1955 (19 studies)	OR 0.93 (0.39 to 2.19)	12 per 1000	11 per 1000 (5 to 26)	0.08 % fewer in-hospital mortality (0.74 fewer to 1.47 more)	Moderate[4]	There may be little or no difference in in-hospital mortality.
30-day mortality 692 (7 studies)	OR 0.98 (0.46 to 2.11)	20 per 1000	20 per 1000 (9 to 41)	0.04 % fewer 30-day mortality (1.09 fewer to 2.32 more)	Moderate[4]	There may be little or no difference in 30-day mortality.
1-year mortality 1282 (10 studies)	OR 1.10 (0.61 to 1.99)	31 per 1000	34 per 1000 (19 to 60)	0.32 % more 1-year mortality (1.23 fewer to 3.27 more)	Moderate[4]	There may be little or no difference in 1-year mortality.
New onset AF Follow-up: In-patient stay 1102 (11 studies)	OR 1.01 (0.72 to 1.41)	252 per 1000	253 per 1000 (195 to 322)	0.34 % more new onset AF (8.62 fewer to 16 more)	Low[5] Due to imprecision	There may be little or no difference in new onset AF.
Postoperative day 1 pain score Follow-up: first day after surgery 973 (6 studies)	-	The mean pain score was 3.44	-	0.55 lower postoperative day 1 pain score (1.31 lower to 0.21 higher)	Very low[1,3,6] Due to indirectness	There may be little or no difference in postoperative pain scores.
Stroke 2013 (17 studies)	OR 1.05 (0.51 to 2.17)	13 per 1000	14 per 1000 (7 to 28)	0.07 % more stroke (0.64 fewer to 1.57 more)	Moderate[4] Due to imprecision	There may be little or no difference in mortality.
Cerebrovascular accidents not included in MACCE 996 (7 studies)	OR 1.39 (0.57 to 3.37)	20 per 1000	28 per 1000 (11 to 64)	0.80 % more non-MACCE (0.87 fewer to 5.08 more)	Moderate[4] Due to imprecision	There may be little or no difference in cerebrovascular accidents not included in MACCE occurrence.

The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
AF, atrial fibrillation; CI, confidence interval; FS, full sternotomy; ICU, intensive care unit; LOS, length of stay; MACCE, Major adverse cardiac and cerebrovascular events; MICS, minimally invasive cardiac surgery; OR, odds ratio;
GRADE working group quality of evidence:
Very low: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.
Low: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Moderate: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Strong: We are very confident that the true effect lies close to that of the estimate of the effect.
Explanations: 1 Downgraded for high risk of bias: outcome measure sensitive to lack of blinding in study; 2 Downgraded for indirectness: length of stay is a surrogate marker of quality and (inter)national variations exist in discharge criteria; 3 Downgraded for inconsistency: variations in discharge criteria, anesthetic management and/or surgical technique might lead to a high heterogeneity; 4 Downgraded for imprecision: sample size did not meet Optimal Information Size criteria; 5 Downgraded for imprecision: wide 95% confidence intervals overlapping no effect; 6 Downgraded for indirectness: different measures of pain used across studies.

LOS in patients undergoing MICS, primarily driven by patients undergoing mitral valve surgery[33,37,38,42,52,55]. This finding aligns with a recent review describing a significant reduction in ICU LOS[63]. Patients undergoing surgery through minimally invasive access, as opposed to full sternotomy, face fewer mobility restrictions. This influences the behavior of healthcare personnel, potentially leading to patients being extubated at the end of surgery, expediting their ICU course and hospital LOS. Unfortunately, none of the included studies reported any discharge criteria.

Nevertheless, there is a prevailing belief that a minimal access limits visibility and increases complexity, consequently prolonging the duration of surgery[63]. These challenges may counterbalance any potential advantages derived from MICS. Dieberg et al.'s review lends support to this perception by noting longer durations spent on CPB and in the operating theatre[64]. In contrast, our analysis revealed no disparity in surgical times, not even in the subgroup analysis. We suggest that this finding can be most likely attributed to the increasing familiarity of the surgical community with the different MICS techniques. Another commonly cited criticism is the tendency to select only low-risk cases for MICS. However, the demographics of patients in the included randomized controlled studies were well balanced, and most trials used an intention-to-treat analysis.

Our analysis revealed comparable postoperative ventilation times for patients undergoing MICS and those undergoing full sternotomy cardiac surgery. The review of Dieberg et al. identified similar results with no significant differences between the two groups[64]. Clearly, achieving blinding of healthcare providers for surgical access is challenging (if not impossible), so that the assessed outcomes are prone to bias, which might explain the large intergroup differences in several studies[33,38]. Additionally, this difference may also reflect various institutional standard practices, given that MICS is considered a core intervention of enhanced recovery after surgery, often coupled to early postoperative extubation[65].

Early morbidity, including postoperative bleeding, is not uncommon after cardiac surgery, exposing patients to potential disruption in recovery and prolonging hospital LOS. The finding of reduced blood loss in patients undergoing MICS is thus promising. Elimination of the need for sternotomy has been suggested as the reason for reduced blood loss[63]. However, our subgroup analysis revealed that hemi-sternotomy (as compared to full sternotomy for AVR), also resulted in reduced blood loss. Another possible explanation could be heightened attention to meticulous hemostasis in case of MICS, partially due to the increased risk of tamponade from minor blood loss following the procedure.

New onset AF post cardiac surgery is a frequent adverse event. The etiology of AF is considered multifactorial, with a causal link to systemic inflammatory response following valve surgery[66,67]. Importantly, new onset AF has been linked to an increase in ICU LOS, hospital LOS and additional postoperative complications, including mortality. Our review found no difference between MICS or conventional full sternotomy surgery.

Overall completeness, quality, and applicability of evidence

We conducted a comprehensive search and uncovered several RCTs that were overlooked in Dieberg et al.'s search[64]. Despite similarities in inclusion criteria, Dieberg et al.'s review encompassed prospective non-randomized studies and RCTs comparing MICS to conventional full sternotomy, while excluding hybrid procedures[64]. In adhering to these criteria, we pinpointed eleven additional RCTs that meet their inclusion/exclusion criteria, indicating the depth of our search to be more exhaustive.

The population included in the different trials typically were exposed to surgical techniques consistent with standard practice. Nonetheless, ERACS programs, goal-directed cardiopulmonary bypass perfusion strategies, hybrid revascularization and/or transcatheter techniques are emerging

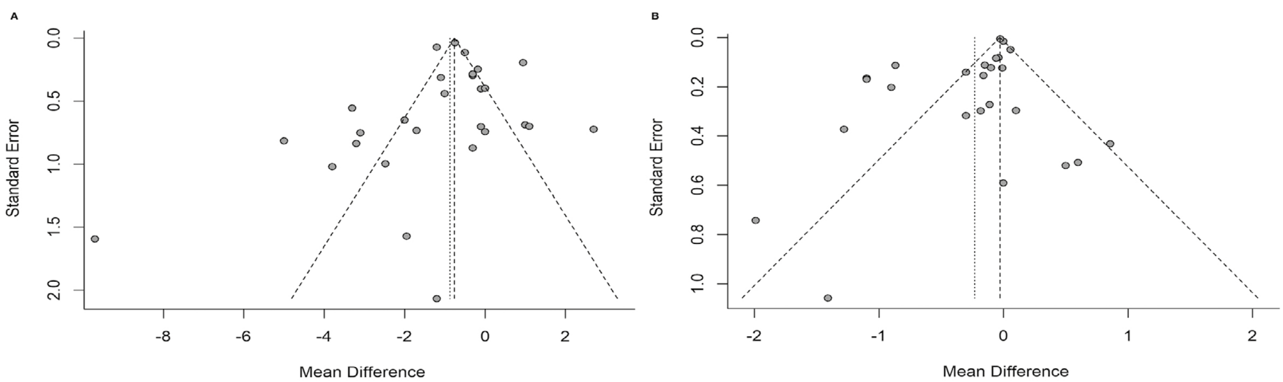

Fig. 4 — Funnel plots representing publication bias for (A) hospital and (B) intensive care unit length of stay.

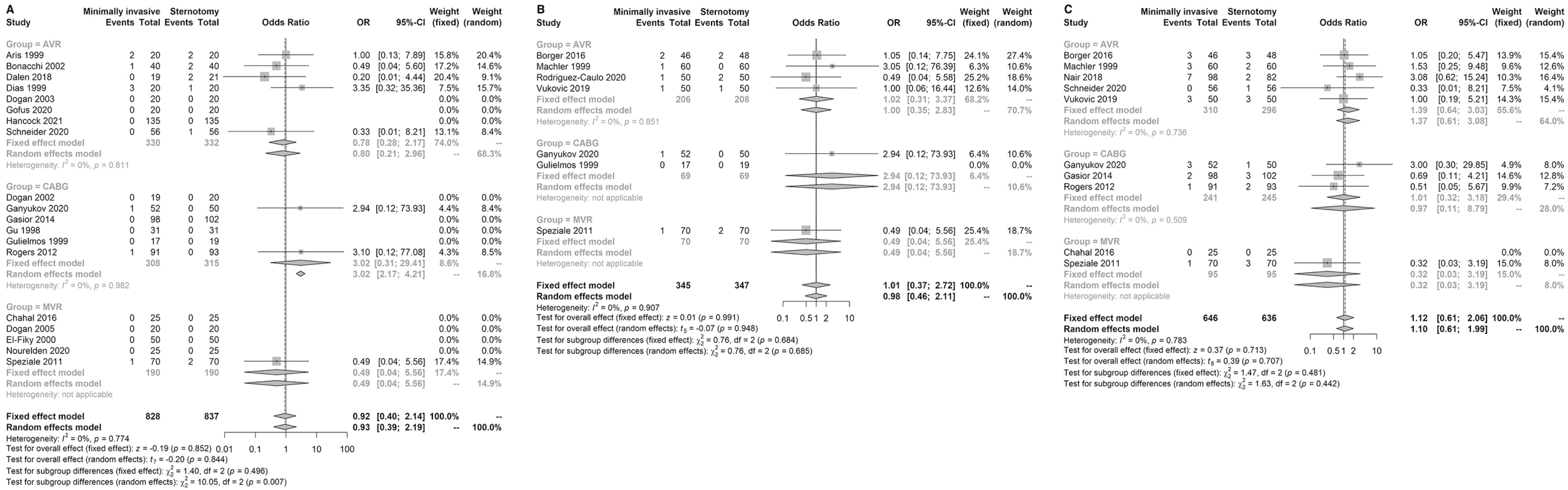

Fig. 5 — Forrest plots with pooled odds ratio for (A) in-hospital, (B) 30-day, and (C) 1-year mortality.
AVR, aortic valve replacement; CABG, coronary artery bypass grafting; CI, confidence interval; MVR, mitral valve replacement/repair; OR, odds ratio.

options that had not been implemented routinely in the trials that were included in this review. Most trials reported outcome rates which correlate with equivalent data in the literature. This suggests that the teams involved (surgeon, anesthesiologist, and nurses) had sufficient experience with the different surgical techniques.

Limitations and strengths

The current meta-analysis has several limitations. Firstly, our analysis revealed significant heterogeneity, primarily stemming from variations in surgical techniques (e.g., robotic assistance), perioperative practices, and the definitions employed. While the inclusion and exclusion criteria across different trials were similar, variations in pathology (aortic, mitral, or coronary) or CPB techniques may have introduced additional differences. Furthermore, trials in CABG surgery generally excluded patients for participation if anatomy was unfavorable for either treatment arm, limiting generalizability. None of the trial protocols or published papers provided details on transfusion triggers, extubation criteria, ERACS concepts, or discharge criteria from the ICU or hospital, although these aspects were expected to be consistent within studies. Moreover, multiple of the assessed outcomes are prone to observer bias, downgrading the certainty of the evidence (Table II). Last, we cannot exclude the possibility of publication bias, as multiple trials have been registered but are either not completed or were unsuccessful regarding MICS. Last, absence of evidence does not necessarily indicate evidence of absence. The majority of included studies were probably underpowered to detect significant differences, at least in the secondary outcomes. Hence, our findings must be interpreted with caution.

This review has also several strengths. The current meta-analysis has been performed in a transparent and reproducible manner. The protocol for this meta-analysis was registered prior to the literature search and should have reduced any risk of bias in this review. Secondly, in contrast to Dieberg et al., we only included RCTs whereas these authors also included prospective trials in which patients were assigned to either treatment arm depending on preferences of the surgeon and patient[68]. This seriously affects outcome assessment due to selection bias.

Conclusion

Implications for practice

This meta-analysis demonstrates that MICS reduces ICU and hospital LOS when compared to conventional cardiac surgery. Prolonged procedural times and increased neurological complications are frequently brought forward as a major disadvantage of MICS. However, our review shows that these arguments are unfounded. Reduced postoperative blood loss, ICU, and hospital LOS, suggest that MICS is effective in promoting faster recovery.

Implications for research

The study suggests that minimally invasive techniques may reduce hospital and intensive care unit LOS without increasing mortality or morbidity in cardiac surgery. However, overall quality of evidence is rated as generally low to moderate, primarily due to small sample sizes, clinical heterogeneity, and, in some cases, statistical heterogeneity. While hospital LOS is considered a useful (surrogate) marker of postoperative recovery, the current trials have failed to describe their discharge criteria. Last, future research should focus on quality-of life assessments, well defined discharge criteria, and cost analysis to enhance the robustness of these findings.

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TvB: Validation, writing - original draft
FP: Data curation, investigation, writing – original draft.
PV: Writing - review & editing.
WO: Writing - review & editing.
JVdE: Formal analysis, visualization, writing - review & editing.
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