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Review

The role of minimal access valve surgery in the elderly. A meta-analysis of observational studies

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HIGHLIGHTS

- Minimal access valve surgery is a safe alternative to the sternotomy approach in elderly patients.
- The approach demonstrates reduced mechanical ventilation time and reduced length of stay.
- Mortality is comparable to those undergoing a conventional sternotomy.
- Limitations for this approach include prolonged cardiopulmonary bypass and cross-clamp time.

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ABSTRACT

Background: Minimal access valve surgery, both mitral and aortic, may be related to improvement in specific post-operative outcomes, therefore may be beneficial for the subgroup of the elderly referred for valve surgery.

Methods: A systematic literature review identified several different studies, of which 6 fulfilled criteria for meta-analysis. Outcomes for a total of 1347 patients (675 conventional standard sternotomy and 672 minimally invasive valve surgery) were assessed with a meta-analysis using random effects modeling. Heterogeneity, subgroup analysis with quality scoring were also assessed. The primary endpoint was early mortality. Secondary endpoints included intra and post-operative outcomes.

Results: In the context of elderly patients, minimal access valve surgery conferred comparable early mortality to standard sternotomy (odd ratio (OR) 0.79, CI [0.40,1.56], $p = 0.50$) with no heterogeneity ($p = 0.13$); it was also associated with reduced mechanical intubation time (OR 0.48, CI [0.30,0.78], $p = 0.003$) and reduced post-operative length of stay (weighted mean difference (WMD) −2.91, CI [−3.09, −2.74] $p < 0.00001$), however both cardio-pulmonary bypass time and cross clamp time were longer (WMD 24.29, CI [22.97, 25.61] $p < 0.00001$ and WMD 8.61, CI [7.61, 9.61], $p < 0.00001$, respectively); subgroup analysis demonstrated statistically significant reduced post-operative length of stay for both minimally invasive aortic and mitral surgery (WMD −2.84, CI [−3.07, −2.60] $p < 0.00001$ and WMD −2.98, CI [−3.25, −2.71] $p < 0.00001$ respectively).

Conclusions: Despite a prolonged cardiopulmonary bypass and cross clamp time, minimally invasive valve surgery is a safe alternative to standard sternotomy in the elderly, with similar early mortality, and improvements in intubation time as well as length of stay.

1. Introduction

Population ageing is a long-term trend, which began several decades ago, moreover the 'very old segment population' is growing at a faster pace than any other age segment of the

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European population: those aged 65 years or over will account for 28.7% of the European population by 2080 [1]. It is clear that, in the future, cardiac surgeons will have to deal with an even larger number of elderly patients than today. These patients may be more prone to develop peri-operative adverse events [2], hence strategies that can ameliorate such outcomes are always sought.

Catheter based technologies, while being available, are still limited to very high-risk or inoperable patients. Nevertheless, cardiac surgeons have been offering minimally invasive valve surgery (MIVS), both aortic and mitral, for several years with favorable results in the general surgical population [3] - these benefits may be also evident in patients with co-morbidities [4].

Current drawbacks of MIVS consist of an increased incidence of stroke, aortic dissection, longer cardio-pulmonary bypass (CPB) and cross clamp time (CCT). Some of the aforementioned drawbacks may be related to technical reasons and/or learning curve; moreover, there are no prospective randomized trials so far, comparing in an unbiased way MIVS and sternotomy (ST) in a context of elderly. As such, the majority of evidences comes from observational studies [2].

Aims of this meta-analysis are to identify, in the context of elderly patients, whether MIVS 1) can be as safe as the counterpart ST in terms of mortality 2), can be still associated with certain post-operative benefits as in the general cardiac population despite the risk of prolonged cardiopulmonary bypass and cross clamp time.

2. Material and methods

2.1. Literature search

Literature search was performed using PubMed, Ovid, Embase, Medline, and Cochrane databases using the MeSH terms ‘minimally invasive/access mitral valve’, ‘minimally invasive/access aortic valve’, and we included in the MeSH entry terms ‘elderly’, ‘old’, ‘frail’, ‘elders’, ‘frail older’, ‘older adults’, ‘septuagenarian’, ‘octogenarian’, ‘nonagenarian’. In addition to this, our search was extended to include the clinicaltirals.gov database and ‘grey’ literature for further rigor. The ‘related articles’ function in PubMed was also used to ensure completeness. The literature search commenced on 06/11/2015 and the last date of the search was 1st December 2015 (Fig. 1); first paper scrutinized in Pubmed with mesh term ‘minimally invasive/access aortic valve’ was from 1966.

2.2. Inclusion and exclusion criteria

All articles reporting outcomes for MIVS (experimental group) and ST (control group) were included. Studies were excluded from the review if: (1) Inconsistency of data did not allow valid extraction; (2) data was duplicated; (3) if the experimental or control group was robotic mitral or aortic valve intervention and (4) the trial/study was carried out on animal models. Based on these criteria, two assessors (SE, MM) independently selected studies for further examination by title and abstract review. All potentially eligible studies were retrieved in full for further evaluation. Any disagreement was resolved by discussion with three senior authors (TA-RC-KF). Statistical concordance testing was performed using Cohen's Kappa coefficient to measure of inter-rate agreement.

2.3. Data analysis

Two Authors (MM, SE) independently extracted the following data from each paper using a predefined protocol including: first author; year of publication; study type; number of subjects and study population demographics. Specific outcome data was where possible for the following: (i) Primary endpoints: early mortality

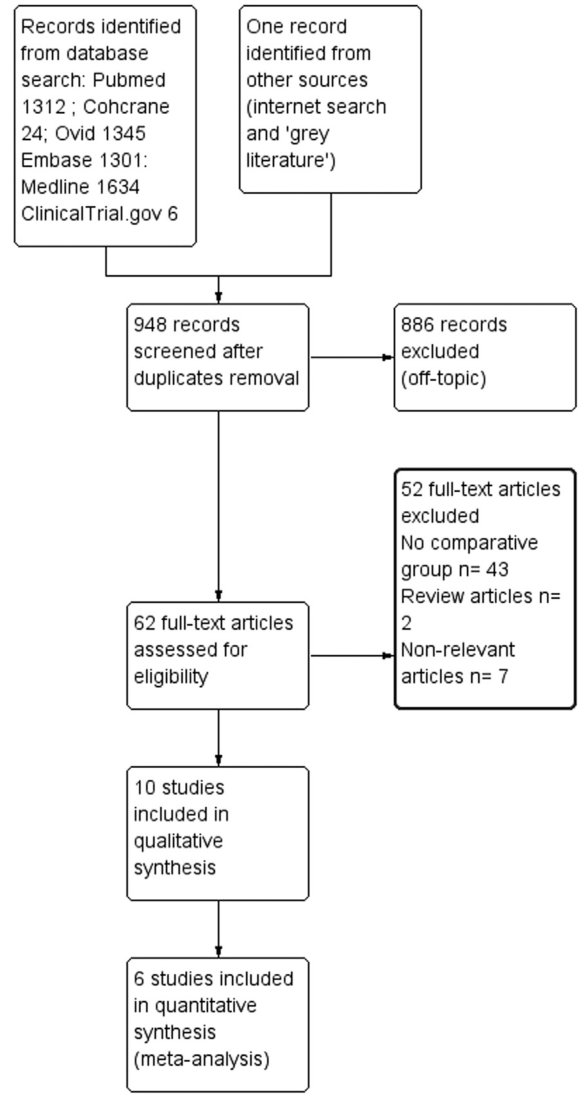

Fig. 1. Search strategy.

(including 30-day or in-hospital mortality) (ii) Secondary endpoints including: cardio pulmonary bypass time, cross clamp time, re-opening for bleeding, prolonged intubation time (defined as per more than 48 h), acute renal failure (defined as per creatinine >200 mg/dl or double the baseline value or need for dialysis), stroke, TIA, lung complications, post-operative length of stay.

Meta-analysis was performed in line with recommendations from the Cochrane Collaboration and in accordance with both PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and MOOSE (Meta-analysis Of Observational Studies in Epidemiology) guidelines [5,6]. Analysis was conducted by use of Review Manager® Version 5.1.7 for Windows (The Cochrane Collaboration, Software Update, Oxford, UK) and STATA v.11 statistical analysis software. Data was analyzed using a weighted DerSimonian–Laird with random effects model. Continuous data were investigated using weighted mean difference (WMD) as the summary statistic, reported with 95% confidence intervals (CI). The point estimate of the WMD was considered statistically significant at $p < 0.05$, if the 95% confidence interval did not include the value zero. Categorical variables were analyzed using the odds ratio (OR). An OR of <1 favored the treatment group and the point estimate of the OR is considered statistically significant at the $p < 0.05$ level, if the 95% confidence interval does not include the value 1.

2.4. Heterogeneity

Inter-study heterogeneity was explored using the Chi [2]-statistic and the I^2 value was calculated to quantify the degree of heterogeneity across trials that could not be attributable to chance alone. When I^2 was more than 50%, significant statistical heterogeneity was considered to be present. Three strategies were used to assess data validity and heterogeneity: (1) Subgroup analysis of higher quality studies (quality score ≥ 8); (2) aortic and mitral valve surgery subgroup analysis (3) funnel plots to evaluate publication bias.

2.5. Sub-group analysis and quality scoring

Quality assessment of each study was performed by attributing a quality assessment score using a modification of the Newcastle–Ottawa scale [6] that included all the 17 EuroSCORE II risk factors. Studies attaining greater than the median score of 8 (out of a maximum 17) were defined to have 'higher matching quality'. Modified Newcastle–Ottawa scoring criteria are shown in Table 1.

2.6. Risk of bias analysis

A domain-based evaluation of risk of bias was performed in accordance with the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [7]. Two authors (MM, SE) subjectively reviewed all studies included in this review and assigned a value of 'yes', 'no', or 'unclear' to the following questions: (i) Was the allocation sequence adequately generated? (ii) Was allocation adequately concealed? (iii) Was there blinding of participants, personnel and outcome assessors? (iv) Were incomplete outcome data sufficiently assessed? (v) Are reports in the study free of the suggestion of selective outcome reporting? 'Risk of bias' plots were performed using Review Manager® Version 5.1.7 for Windows (The Cochrane Collaboration, Software Update, Oxford, UK).

2.7. Definition of 'elderly'

Definition of elderly is somewhat arbitrary; the common use of a calendar age to mark the threshold of old age assumes equivalence with biological age, yet at the same time, it is generally accepted that these two are not necessarily synonymous [8]. Nevertheless, all studies included had a mean population age equal or above 75 years old (y/o) (Table 2) with a total mean age of 79.2 y/o for both MIVS and ST groups. Thereby studies with a mean age below 75 y/o were not included [9,10].

2.8. Definition of 'minimal access'

Studies that adopted the Society of Thoracic Surgeons (STS) database definition of minimally invasive – minimal access cardiac surgery (as "any procedure not performed with a full sternotomy and CPB support) [11] were scrutinized in order to understand if eligible for inclusion in the meta-analysis. Operative strategies of each studies include are summarized in Table 3.

3. Results

Our search revealed six studies [12–17] fulfilling these inclusion criteria, producing a pooled data set of 1347 patients of whom 672 underwent MIVS and 675 underwent ST (Table 2/3). There was 100% concordance between reviewers equating to a Cohen's kappa coefficient of $\kappa = 1$. Three studies were retrospective observational [14–16] two studies were propensity matched [13,17] and one case control [12]. One study [14] reported amalgamated primary and secondary outcomes for minimally invasive mitral and aortic hence could not be included in the subgroup analysis.

3.1. Primary outcome

A summary of both primary and secondary endpoints is shown in Table 4. We observed no difference in terms of early mortality between MIVS and ST, 4.8% ± 2.6 vs 6.4% ± 2.6, $p = 0.86$ (OR 0.79, 95% CI [0.40, 1.56], $p = 0.150$) and no heterogeneity was observed (Chi [2] 8.51, $p = 0.13$, I^2 41%) (Fig. 2a/b).

3.2. Secondary endpoints

Minimal access valve surgery was associated with prolonged CPB time (WMD 24.29, CI [22.97, 25.61], $p < 0.00001$) and CCT (WMD 8.61, CI [7.61, 9.61], $p < 0.00001$), however as expected for continuous value, heterogeneity was observed ($p < 0.00001$ and 0.0005 CPB and CCT respectively). However MIVS led to reduced need for mechanical ventilation (OR 0.48, 95% CI [0.30, 0.78],

Table 1
Criteria for quality assessment. Modified Newcastle–Ottawa scoring criteria.

Quality checklist
Selection
1. Assignment for treatment – any criteria reported? (If yes, 1-star)
2. How representative was the reference group (ST) in comparison to the general population for aortic/mitral surgery? (If yes, 1 star, no star if the patients were selected or selection of group was not described)
3. How representative was the reference group (MIVS) in comparison to the general population for aortic/mitral surgery? (If drawn from the same community as the reference group, 1-star, no star if drawn from a different source or selection of group was not described)
Comparability
Comparability variables: (1) age; (2) gender; (3) renal function; (4) extracardiac arteriopathy; (5) poor mobility; (6) previous cardiac surgery; (7) chronic lung disease; (8) active endocarditis; (9) critical preoperative state; (10) IDDM; (11) NYHA; (12) CCS IV; (13) LV function; (14) recent MI; (15) pulmonary hypertension; (16) urgency; (17) combined.
4. Groups comparable for 1, 2, 3, 4, 5, 6, 7, 8, 9 (If yes, 1-star was assigned for each of these. No star was assigned if the groups differed
5. Groups comparable for 10, 11, 12, 13, 14, 15, 16, 17(If yes, 1-star was assigned for each of these. No star was assigned if the two groups differed).
Outcome assessment
6. Clearly defined outcome of interest (If yes, 1-star).
7. Follow-up (1-star if described).

IDDM = insulin dependent diabetes mellitus; MIVS = minimally invasive valve surgery; NYHA = New York Heart Association; ST = standard sternotomy.
Comparability includes all the EuroSCORE II risk-factors.

Table 2
Study characteristics.

Author, year (total patients) study type	Inclusion criteria	MIVS/ ST (n)	Mean age (y/o)		Sex (female)(n)		Ejection fraction (%)		Infective endocarditis (n)		Chronic renal failure (n)		COPD (n)		CCF - NYHA (n)		Re-do (n)	
			MIVS	ST	MIVS	ST	MIVS	ST	MIVS	ST	MIVS	ST	MIVS	ST	MIVS	ST	MIVS	ST
Gilmanov 2015 (n = 200) Propensity matched	a	100§/100	83 ± 2.1	82.5 ± 2.2	64	67	60 (5.8)	55 (10)	1	0	4	3	11	15	2.4 ± 0.6	2.4 ± 0.6	0	2
Kaneko 2013 (n = 105) Retrospective observational	a	51∞/54	83.3 ± 2.7	82.4 ± 4.6	15	27	55 (10)	57 (10)	NS	NS	1	4	NS	NS	32 (NYHA 3–4)	34 (NYHA 3–4)	51	54
Iribarne 2012 (n = 175) Retrospective observational	b	70/105	78.6 ± 3.3	79.4 ± 3.9	27	35	51.9 ± 1.2	50.7 ± 1.2	3	4	0	2	4	13	NS	NS	0	0
Holzhey 2011 (n = 286) Propensity matched	b,c	143/143	76 ± 3.9	76 ± 3.6	41	45	58 ± 15	58 ± 15	6	8	NS	NS	13	12	NS	NS	21	22
Lamelas 2011 (n = 203) Retrospective observational	a,b	119§/84	79 (6)	80 (60)	72	47	58 (13)	55 (14)	NS	NS	NS	NS	NS	NS	43 (NYHA 3–4)	47 (NYHA 3–4)	20	18
Sharony 2003 (n = 378) Case control	a	189§,∞/189	75.3 ± 6.4	75.3 ± 6.7	93	136	NS	NS	NS	NS	4	5	25	24	57 (NYHA 3–4)	64 (NYHA 3–4)	32	32

NS = not specified; MIVS = minimally invasive valve surgery; ST = sternotomy.
Value are expressed as mean ± sd or median and IQR (inter quartile range).
Inclusions: *a*-aortic valve; b; -mitral valve; c-aortic and mitral; d-associated tricuspid.
§: indicates AVR right mini-thoracotomy.
∞: indicates AVR upper mini-sternotomy.

Table 3
Operative strategies.

Author/year		Approach	Aortic cannulation site	Venous cannulation site	Clamping	Conversion (n)
Gilmanov 2015	Mini-aortic n = 100 (ST = 100)	Right anterior mini-thoracotomy (6–7 cm) 2nd intercostal space	Direct aortic cannulation	Right femoral vein	Direct clamping	2§
Kaneko 2013	Mini-aortic n = 51 (ST = 54)	Upper mini-sternotomy	Direct aortic cannulation (n = 6) Axillary artery (n = 34) Femoral artery (n = 11)	Right femoral vein (n = 48) Direct RA cannulation (n = 3)	Direct clamping	0
Iribarne 2012	Mini-mitral n = 70 (ST = 105)	Right mini-thoracotomy	Direct aortic cannulation	Right femoral vein	Direct clamping	0
Holzhey 2011	Mini-mitral n = 143 (ST = 143)	Right mini-thoracotomy	Femoral artery cannulation	Right femoral vein	Direct clamping	NS
Lamelas 2011	Mini- aortic/ mitral n = 119 (ST = 84)	Mitral: Right mini-thoracotomy (fourth to fifth IS) Aortic: Right anterior mini-thoracotomy (second to third IS)	Femoral artery cannulation	Right femoral vein	Direct clamping Fibrillatory arrest (for re-do)	NS
Sharony 2003	Mini-aortic N = 189 (ST = 189)	Right anterior mini-thoracotomy (n = 169) Upper mini-sternotomy (n = 20)	Direct aortic cannulation (n = 128) Femoral artery cannulation (n = 41)	Right femoral vein (n = 134) Direct RA cannulation (n = 55)	Direct clamping	NS

IS = intercostal space; NS = non specified; RA = right atrium.
§ = Intention to treat analysis.

Table 4
Results of overall meta-analysis.

Outcome	N			Mean difference	Overall effect			Heterogeneity		
	Studies	MIVS	ST		Odds ratio	95% CI	p	Chi^2	p	I^2
Primary outcome										
Early Mortality	6	672	675		0.79	0.40, 1.56	0.50	8.51	0.13	41%
Secondary outcomes										
CPB time[a]	6	672	675	24.29		22.97, 25.61	<0.00001	69.28	<0.00001	93%
CCT[a]	6	672	675	8.61		7.61, 9.61	<0.00001	21.90	0.0005	77%
Stroke/TIA	5	572	575		1.24	0.51, 3.01	0.63	5.33	0.25	25%
Reopening for bleeding	6	672	675		0.48	0.71, 1.89	0.48	4.48	0.48	0%
Prolonged intubation[a]	3	289	289		0.48	0.30, 0.78	0.003	1.16	0.56	0%
Lung complication	5	553	591		1.41	0.94, 2.09	0.09	3.50	0.48	0%
Acute renal failure	6	672	675		0.42	0.15, 1.13	0.09	13.9	0.02	62%
Total LOS[a]	6	672	675	−2.91		−3.09, −2.74	<0.00001	32.49	<0.00001	92%

AV = atrio-ventricle; CCT = cross clamp time; CPB = cardio-pulmonary bypass; LOS = length of stay; MIVS = minimally invasive valve surgery; ST = sternotomy; TIA = transient ischemic attack.
[a] Denote significance.

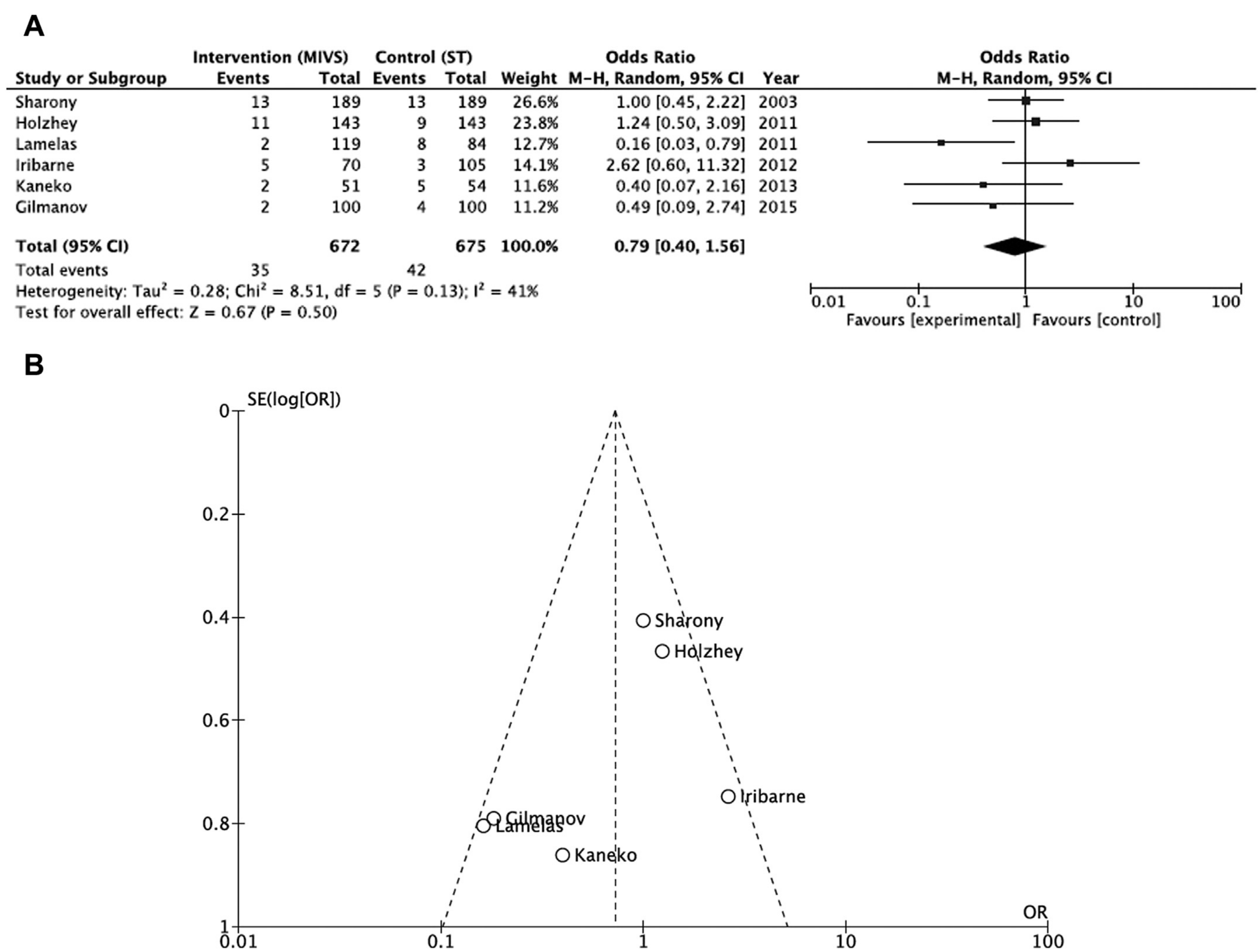

Fig. 2. **(a)**. Forest plot MIVS vs ST (Overall Early Mortality); **(b)** Funnel plot MIVS vs ST (Overall Early Mortality).

p = 0.003) with no heterogeneity (p = 0.56) and to reduced post-operative length of stay (WMD −2.91, CI [−3.09, −2.74], p < 0.00001) nonetheless heterogeneity was observed (p < 0.00001). There was no significant difference with regard to all the other secondary outcomes considered and heterogeneity was found only with regards to acute renal failure (p = 0.002) (Table 4).

3.3. Subgroup and quality scoring analysis

Three studies [12,16,17] included specifically minimally invasive aortic valve and two studies [13,15] minimally invasive mitral surgery valve and were meta-analyzed separately. One study [14] did not separate outcomes therefore was not part of the subgroup analysis. Analysis of both sub-groups did not demonstrate a significant difference in terms of the primary outcome early mortality (OR 0.59, CI [0.32, 1.10] p = 0.10 and OR 1.53, CI [0.71, 3.31] p = 0.28, minimally invasive aortic and mitral valves surgery respectively) (Tables 5 and 6).

In terms of secondary outcomes, as per overall analysis, both subgroups were associated to reduced post-operative length of stay (WMD −2.84, CI [−3.07, −2.60], p < 0.00001 and WMD −2.98, CI [−3.25, −2.71], p < 0.00001, aortic and mitral surgery respectively); however, heterogeneity was observed (p < 0.00001) (Tables 5 and 6). Both CPB and CCT were significantly prolonged in the minimally invasive mitral subgroup (p < 0.00001 CPB and CCT, with heterogeneity only for CCT), however no differences were found in the aortic subgroup (p = 0.65 and 0.50 CPB and CCT respectively with no heterogeneity).

By using a modified version of the Newcastle-Ottawa scale, we assigned 1 point for each EuroSCORE II risk factors included and comparable in between the two MIVS and ST groups. The overall quality of studies is outlined in Table 7. All of the 6 studies included in this review were considered to be of high quality, scoring above the median of 8 (Table 5) [12–17] thereafter the overall analysis (Table 4) may be considered high-quality meta-analysis.

3.4. Heterogeneity assessment: bias exploration

In accordance with Cochrane guidelines, risk of bias analysis was performed for all studies included in this review (Fig. 3). Overall, high level of bias was detected, due to non-randomized, un-blinded nature of the majority of studies. In addition to established bias assessment, a score was also given for each of the following: (1) multicenter trial, (2) propensity matched study and (3) confounder adjustment. No study fulfilled all 3 of these criteria (Fig. 3). Two studies were propensity matched [13,17] and one was case control [12]; however the general level of population comparability between groups was high even in the retrospective observational studies as it is shown in the quality scoring analysis (Table 6).

Funnel plots were used to assess for publication bias for all primary and secondary outcomes. Minor funnel plot asymmetry was identified for primary outcome (Fig. 2b); and minor funnel plot asymmetries were observed for the secondary outcomes: stroke, TIA, acute renal dysfunction, lung complication, prolonged ventilation time, post-operative length-of-stay and re-opening for bleeding.

3.5. Comment

This meta-analysis compares elderly patients (mean age 79.2 y/o) undergoing either MIVS or ST and allowed inclusion of 1347 patients who would be difficult to accumulate prospectively for this

Table 7
Quality scoring.

Authors (no of patients)	Selection			Comparability		Outcome		Total
	1	2	3	4	5	6	7	
Gilmanov 2015 (n = 200)	–	–	–	********	******	*	*	16
Kaneko 2013 (n = 105)	–	–	–	****	***	*	*	9
Lamelas 2011 (n = 203)	–	–	–	*****	**	*	–	8
Iribarne 2012 (n = 175)	–	–	–	****	**	*	*	8
Holzhey 2011 (n = 286)	–	–	–	*******	***	*	*	12
Sharony 2003 (n = 378)	–	–	–	******	***	**	–	11

Quality scoring system based on EuroSCORE II modified Newcastle-Ottawa scale.

Table 5
Results of minimally invasive aortic valve meta-analysis.

Outcome	N			Mean difference	Overall effect			Heterogeneity		
	Studies	MIAVS	ST		Odds ratio	95% CI	p	Chi^2	p	I^2
Primary outcome										
Early Mortality	3	340	343		0.59	0.32, 1.10	0.10	4.07	0.13	51%
Secondary outcomes										
CPB time	3	340	343	1.35		−4.52,7.22	0.65	0.83	0.66	0%
CCT	3	340	343	1.35		−2.57, 5.27	0.50	1.91	0.38	0%
Stroke/TIA	2	240	243		2.07	0.70, 6.15	0.19	0.22	0.64	0%
Reopening for bleeding	3	340	343		1.08	0.53, 2.22	0.83	1.79	0.41	0%
Lung complication	2	340	343		1.40	0.82, 2.38	0.22	0.39	0.82	0%
Acute renal failure	3	340	343		0.56	0.26, 1.21	0.14	3.66	0.16	45%
Total LOS[a]	3	340	343	−2.84		−3.07, −2.60	<0.00001	54.05	<0.00001	96%

CCT = cross clamp time; CPB = cardio-pulmonary bypass; LOS = length of stay; MIAVS = minimally invasive aortic-valve surgery; ST = sternotomy; TIA = transient ischemic attack.
[a] Denote significance.

Table 6
Results of minimally invasive mitral valve meta-analysis.

Outcome	N = 2			Mean difference	Overall effect			Heterogeneity		
	Studies	MIMVS	ST		Odds ratio	95% CI	p	Chi^2	p	I^2
Primary outcome										
Early Mortality		213	248		1.53	0.71, 3.31	0.28	0.72	0.40	0%
Secondary outcomes										
CPB time[a]		213	248	25.58		23.99, 27.17	<0.00001	31.58	<0.01	84%
CCT[a]		213	248	9.21		8.18, 10.25	<0.00001	0.03	0.86	0%
Stroke/TIA		213	248		1.14	0.38, 3.41	0.82	3.51	0.06	72%
Reopening for bleeding		213	248		1.08	0.53, 2.23	0.48	2.70	0.83	63%
Acute renal failure		213	248		0.78	0.38, 1.62	0.51	1.54	0.22	35%
Total LOS[a]		213	248	−2.98		−3.25, −2.71	<0.00001	2.18	0.14	54%

CCT = cross clamp time; CPB = cardio-pulmonary bypass; LOS = length of stay; MIMVS = minimally invasive mitral-valve surgery; ST = sternotomy; TIA = transient ischemic attack.
[a] Denote significance.

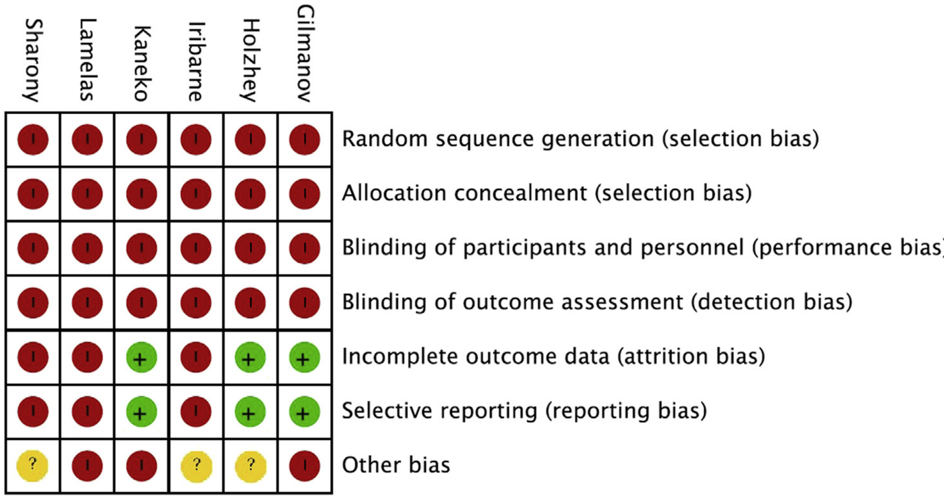

Fig. 3. Risk of bias assessment.

particular topic. We demonstrated that MIVS is at least as safe as the standard approach in terms of early mortality, moreover in the MIVS groups, both aortic and mitral, there was a significant reduced mechanical ventilation time and post-operative length of stay. Cardiopulmonary bypass time and CCT were significantly higher in the MIVS, however that has not translated to any adverse events. Subgroup aortic analysis did not show differences in terms of CPB and CCT with the counterpart ST and that may be related to the use of fast-release valve in the Gilmanov series [17] (weight 18.9%). Beside elderly patients, there was a consistent number of re-do operation in four series (Table 2) [12–14,16]. In line with previous meta-analysis on high-risk patients [2], we did not observe any differences in terms of stroke and both femoral (retrograde) and central-aortic or axillary (antegrade) were used in the series (Table 3); however no endo-clamping were used.

The hypothesis of this meta-analysis is that patients in the MIVS group could have the same chance to survive at surgery as the ST group, however we expected differences in the secondary outcomes such as lung function test, lung atelectasis and consequent chest infection within 2–3 months post discharge which affect both quality of life and costs favoring the MIVS to the ST group. However, such outcomes were not consistently reported so could not be meta-analyzed. Thereby, in a context of elderly, there is the need of comparative studies MIVS vs ST with particular focus on early and mid-term post-operative outcomes. If it is possible to establish that MIVS performs better over ST, then a comparison against catheter based procedures might be of particular interest.

We acknowledge several limitations of this study. Definition of elderly is somewhat conventional, and studies that included patients above certain calendar age were considered, with no mention to biological or functional age. As such, the impact of MIVS on frailty could not be assessed. However, we included studies where the mean age was 75 y/o or above.

Although a relatively low level of statistical heterogeneity was observed throughout the analysis, clinical heterogeneity has to be considered since two different types of surgery were included (aortic and mitral); however, the common denominator was the minimally invasive approach.

Similarly, minimally invasive aortic valve surgery included two different means of access; the right mini-thoracotomy and upper sternotomy (Table 3). Moreover, in one series fast release valve were also used. Amongst the 6 studies included, there were no randomized controlled trials. Although MIVS is associated with a significant learning curve and volume–outcome relationship, it was not possible to quantify the impact of this on the outcomes reported in this study; nevertheless, bias in favor to ST technique cannot be ruled out. Cost-effective and quality of life analysis could not be performed. However, in saying that - if we assess cost-effectiveness from a quicker return to work perspective, then we would need to consider a younger patient cohort for a rational analysis.

Another limitation of this study is that it does not include mid or long-term outcomes.

In conclusion, with this meta-analysis we contribute to demonstrating that in a context of elderly patients, MIVS, both aortic and mitral, is a safe alternative to standard sternotomy. There was no difference in terms of early mortality; additionally, MIMVS led to improvements in certain post-operative outcomes such as reduced mechanical ventilation time and reduced post-operative length of stay. Ultimately, further studies are needed in order to better investigate pros and cons of MIMV in such a cohort of patients.

Ethical approval

Not applicable for this study.

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Author contribution

Data analysis/writing: Marco Moscarelli.
Data collection/writing: Sam Emmanuel.
Reviewers/writing: Thanos Athanasiou, Giuseppe Speziale, Khalil Fattouch, Roberto Casula.

Conflict of interest

None.

Guarantor

Sam Emmanuel.

Glossary

CCT cross clamp time
CPB cardiopulmonary by-pass
MIAVS minimally invasive aortic valve surgery
MIMVS minimally invasive mitral valve surgery
MIVS minimally invasive valve surgery
ST sternotomy

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