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# To repair or to replace in mitral valve infective endocarditis? an updated meta-analysis

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# **Abstract**

**Background** Valve infective endocarditis (IE) is a potentially life-threatening condition that affects patients' livelihoods. Current surgical options in mitral valve IE include mitral valve repair (MVr) or replacement (MVR). While each procedure boasts its merits, doubt remains as to which type of surgery is superior.

**Methods** We searched PubMed, Scopus, Web of Science, and Cochrane literature databases for studies comparing MVR and MVr in mitral valve IE. Any randomized controlled trial (RCT) or observational studies that compare MVR vs. MVr in mitral valve IE were eligible. Our dichotomous outcomes were extracted in the form of event and total, and risk and hazard ratio (RR)(HR) with 95% confidence interval (CI) and were pooled and calculated using RevMan 5.0.

**Results** Our study included 23 studies with a total population of 11,802 patients. Compared to MVR, MVr had statistically significant lower risks of both early mortality with RR [0.44; 95% CI, 0.38–0.51; p < 0.001] and long-term follow-up mortality with HR [0.70; 95% CI, 0.58–0.85; p = 0.0004]. Moreover, MVr was associated with a statistically significant lower risk of IE recurrence with RR [0.43; 95% CI, 0.32–0.58; p < 0.001]; however, no statistically significant differences between both groups in terms of re-operations with RR [0.83; 95% CI, 0.41–1.67; p = 0.60].

**Conclusion** Our results suggest that MVr was superior in terms of in-hospital mortality, long-term survival, and risk of recurrence without significance in valve reoperation. Therefore, MVr is appropriate as a primary treatment choice and should be considered whenever possible in most IE patients.

# **Key points**

- 1. MVr showed superiority in terms of in-hospital mortality.
- 2. MVr has better long-term survival.
- 3. MVr has a lower risk of recurrence and valve reoperation.

**Keywords** Infective endocarditis, Endocarditis, Mitral valve repair, Mitral replacement

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# **Background**

Valve infective endocarditis (IE) is a potentially life-threatening condition that affects patients' livelihoods through either its occurrence or high risk of recurrence. Bacteria target the endocardium, particularly the heart valves, compromising their integrity [1]. This results in the development of vegetations that adhere to the valves causing incompetence or obstruction. These vegetations most frequently attack the mitral valve. Patients may not respond adequately to medical treatment which renders surgery their preferred method of treatment. Valve surgery may be absolutely essential to preserve heart function and to correct underlying damage caused by the disease [1].

Searching through the literature yields two established surgical treatments: mitral valve repair (MVr) and replacement (MVR). A plethora of scientific studies have been conducted on each method with varying results. While each procedure boasts its merits, doubt remains as to which type of surgery is superior. This meta-analysis, therefore, builds upon the previous meta-analysis [2] updating it with five new studies and tripling the patient pool. We aim to compare characteristics such as mortality, survival, recurrence, and reoperation of both procedures.

# Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [3] and Meta-analyses Of Observational Studies in Epidemiology (MOOSE) [4] guidelines were followed during the conduction of this systematic review and meta-analysis. Our study was registered with ID: https://doi.org/10.17605/OSF.IO/JUETP.

# Search strategy

Our search strategy was applied till February 2023 on several databases including PubMed, Scopus, Web of Science, and Cochrane literature databases to include studies comparing MVR and MVr. Any randomized controlled trial (RCT) or observational studies were eligible with no restrictions made regarding the language or publication period. Our keywords were mitral valve repair, annuloplasty, mitral valve repair, infective endocarditis, and mitral endocarditis. Moreover, the included articles' references were searched manually for any relevant or missed eligible studies. We excluded Reviews, letters to editors, conference abstracts, and studies that investigate either operation solely, studies that include IE and non-IE mitral valves, studies that included patients with congenital heart diseases or don't satisfy the modified Duke criteria to diagnose IE.

# Eligibility criteria

Studies that investigate the mitral valve surgery repair versus replacement for mitral valve IE, published in peerreview journals reporting separate outcomes data for the two surgical groups were included. Our PICO (Patients, intervention, control, and outcome) was P; patients with mitral valve infective endocarditis, I; mitral valve repair/annuloplasty, C; mitral valve replacement, O; primary outcomes: early in-hospital mortality, long-term follow-up mortality, while secondary outcomes: risk of IE recurrence, and risk of reoperations.

# Data extraction and quality assessment

Both two independent authors (M.H.F, M.E) applied our eligibility criteria through first title and abstract screening and then full-text screening to select eligible articles. Any disagreement was solved by a third author (A.K.A). Articles had to have a baseline characteristics table for their patients with at least one of our primary or secondary outcomes. Baseline characteristics were extracted by two independent authors (K.W, M.H.F) along with mortality, survival, recurrent endocarditis, and valve reoperation as outcomes. The risk of bias was assessed using the Cochrane ROBINS-I tool [5] for observational studies. Two independent reviewers (A.K.A and M.A.A) screened the methodological quality of included studies and any discrepancies were resolved by a senior author (M.H.F).

# Data analysis

The inverse variance method was used to pool study estimates, and the restricted maximum-likelihood estimator was used to estimate between-study heterogeneity. The risk ratio (RR) or Hazard ratio (HR) with a 95% confidence interval (CI) are provided as effect size estimates. Random-effects meta-analysis models were utilized to investigate whether the results were sensitive to model choice. Forest plots were drawn, and the shaded boxes represent the point estimate for each individual trial, and the horizontal line extending from each box represents the upper and lower limits of the 95% CI. The diamonds represent the overall effect size. Meta-regression was used to explore the effects of mean age, gender, diabetes mellitus (DM), hypertension (HTN), and left ventricular ejection fraction (LVEF) on our outcomes. All analyses were performed using RevMan 5.0.2. and R software (version 4.2.0) [6, 7].

# Results

# Study selection

Our search strategy retrieved a total of 1817 studies. Following the title and abstract screening and removing the duplicates, 40 full-text articles were evaluated for eligibility. Following the full-text screening, 23 observational studies [8–30] met our criteria and were included in our

meta-analysis. Further details of the PRISMA flow chart can be found in Supplementary Fig. 1 and Table 1.

# Summary of the included studies

All our studies were observational studies with a total population of 11,802 patients, with 7,848 and 3,954 patients underwent MVR and MVr, respectively. Most of our patients were males with 84% in MVr and 86% in MVR group with a mean age of 55.2 (13.7) and 57.8 (14.2) in MVr and MVR groups, respectively. The most common indication for surgery was mobile vegetation in both MVr (46.3%) and MVR (42.7%) groups. Further details about our baseline can be found in Table 1.

# Risk of bias

Applying ROBINS-I tool to our observational studies, 20 reports have low risk of bias quality, while three have moderate risk of bias; two due to bias in the measurement of outcomes and one due to missing data. Further details of quality assessment can be found in Supplementary Table 2.

### Outcomes

In terms of early mortality, the analysis of 21 studies with 3543 patients in the MVR group and 7401 patients in the MVr group showed that patients who underwent MVr had a statistically significant lower risk of early in-hospital mortality with RR [0.44; 95% CI, 0.38–0.51; p<0.001] (Fig. 1). No heterogenicity was observed [p=0.48, I $^2$ =0%]. Moreover, in the analysis of 14 studies, MVr has also a statistically significant lower hazard ratio in terms of long-term follow-up mortality with RR [0.73; 95% CI, 0.63–0.85; p<0.0001] (Fig. 2) with moderate heterogeneity observed [p=0.11, I $^2$ =34%] which was solved by removing Brescia 2021 to [p=0.39, I $^2$ =5%] and RR [0.70; 95%CI, 0.60–0.80, p<0.00001].

A total of 19 studies were assessed for the risk of IE recurrence with 3413 and 6025.

patients undergoing MVr and MVR respectively. Results showed MVr was associated with a statistically significant lower risk of IE recurrence when compared to MVR with RR [0.51; 95% CI, 0.36–0.72; p=0.0002] (Fig. 3) with low heterogeneity observed [p=0.21,  $I^2$ =20%]. We analyzed 15 studies for assessing the rate of reoperations with 1441 patients undergoing MVr and 1345 undergoing MVR and established that there were no statistically significant differences between both groups with RR [0.79; 95% CI, 0.45–1.40; p=0.42] (Fig. 4) with low heterogeneity observed [p=0.23,  $I^2$ =20%].

Moreover, we performed a meta-regression based on our baseline variables to further add to the robustness of our analysis and deal with any inter-group heterogeneity. In our meta-regression, LVEF showed significant affection of most of our outcomes, besides age which was significantly affecting IE recurrence and reoperation. Further details about our meta-regression can be found in Supplementary Table 3.

# Discussion

To the best of our knowledge, this comprehensive metaanalysis addressing this topic with 23 included studies with 11,802 patients, 7,848 patients in MVR and 3,954 patients in MVr. We found that opting for MVr over MVR entails significantly lower in-hospital mortality rates, higher long-term survival rates, lower risk of IE recurrence, and no difference in reoperation rates. Our findings support the results published earlier by Kang He MS et al. 2022 [2]; however, we reported an additional statistically significant lower rate of IE recurrence after MVr and lesser heterogeneity.

Although MVr's benefit in patients with IE has been previously established and included in recent guidelines, only 20% of cases are managed by repair [30, 31]. The decision to opt for MVr or MVR is influenced by preoperative patients' conditions, intraoperative findings, and technical complexity, particularly the surgeon's qualitative assessment of valvular damage [32, 33]. Other factors such as complex patient presentation, delayed diagnosis, and late surgical referral may also force surgeons to opt for replacing the infected valve. This is the case since the leading indicators of the feasibility of MVr are smaller vegetation dimensions and the absence of severe regurgitation [33, 34]. The choice of which surgery to perform remains multifactorial, and more guidelines now advocate for multidisciplinary decision-making with a specialized "endocarditis team" [35, 36]. It would be useful in this case to analyze certain variables and their eventual influence on the choice of surgery to perform like the preoperative condition of the patient using objective scores, timely nature of surgery; urgent, emergent, or elective, and the microorganism involved. Although mobile vegetation was the indication reported in most of our studies for surgery, current European society of cardiology (ESC) 2023 guidelines states that the most common indication is heat failure [37]. The challenge remains to accurately identify patients where MVr is feasible while outweighing the risks of a failed repair with the benefits of a successful one [32].

Acute bacterial endocarditis was a contraindication for valve repair until about 1990 [37]; however, it is now known that valve repair is not only possible but also safer than valve replacement [30]. The prosthetic mesh could be attributed to most of the feared complications following MVR. MVR not only removes valve tissue that is more resistant to infection than prosthetic mesh, but it also acts as a stimulus for new infection [30]. Even without being infected, mitral valve still has a debate going on between repair and replacement in various scenarios

**Table 1** Baseline characteristics of included studies

Study	Country	Study	, Total	- <u>-</u>	Mean fol	ollow	Age (mean(SD))	SD))	Sex (female) n (%)	le) n (%)	OM n (%)	(9)	HTN n (%)	~	AF n (%)		LVEF (mean (SD))	ean (SD))
		5	size (n)	ξĒ	(years)	J												
			Ā	MVR	MVr	MVR	MVr	MVR	MVr	MVR	MVr	MVR	MVr	MVR	MVr	MVR	MVr	MVR
Scheggi 2019	Italy	RC	33	57	3	3	63.7(13.1)	63.6 (13.9)	6(18)	20(35)	4(12)	16 (28)	13 (39)	33 (58)	ΑN	ΥZ	58.5 (9)	60(10.5)
rutman 2005	Austria	PC S	34	34	3.14	3.70	51.5(17)	53.2(13.1)	12(35.2)	17(50)	6 (17.6)	6 (17.6)	ΑN	ΑN	ΑN	ΥZ	49 (12)	53(12)
Miura 2014	Japan	RC	36	21	5.3	5.3	57(17)	55(17)	27 (75)	8 (38)	6 (17)	2 (10)	ΑN	ΑN	2 (6)	2 (10)	ΑN	Α N
Lee 2018	China	RC	38	33	3.5	3.5	42.3(18.8)	53.7(15.6)	14 (36.8)	13 (39.4)	4 (10.5)	11	N A	N A	N A	Υ V	70.2(6.8)	69.8(14.5)
		7	-	7	7	7	(0 21)110	(0 1 (1 0)	(3 63)((	70/15 0)	(5,71)	(55.5)	(00)	(0 7 1 0)	<u> </u>	<u> </u>	(C 1) ( 1 )	((, 3))7 (3
Jung 2011 Deferma 2020	Korea Notherlands	۲ ک	4 6	<u> </u>	7.4	7.7	34.4(16.9)	43.1(14.9)	(5,02)27	28(45.9)	5 (12.2)	8 (13.1)	4 (9.8)	9 (14.8)	NA 19 (19 6)	AZ U	04.1(4.2)	02.7(6.2)
Derauw 2020	Netnerlands	Y V	6	75	ر: ر ر: ر	ر: ر:	5/ (13)	01 (13)	//(/9.3)	30(57.7)	(v: /) 8	(25.0)	35 (30.1)	20 (38.4)	(18.0)	(9.6)	K Z	¥ Z
cuerpo 2019	Spain	RC	89	301	_	-	61 (46–70)	63 (53–73)	16(23.5)	90(29.9)	N A	¥ Z	28 (41.2)	148 (49.2)	6 (8.8)	56 (18.6)	₹ Z	Y Y
helmers 2021	USA	RC	47	47	6.2	6.2	51.3 (13.6)	52.6 (18.0)	16 (34.0)	23 (48.9)	6 (12.8)	7 (14.9)	21 (44.7)	28 (59.6)	Ϋ́Z	₹Z	58.0	59.3
																	(11.6)	(12.0)
shang2009	USA	RC	99	33	ΥZ	ΑZ	NA	NA	30(33.7)	ΑA	17	12	ΝΑ	ĕ Z	ĕ Z	₹Z	ΥZ	ΝΑ
solari 2019	Belgium	RC	155	37	10.20	12.19	60.1 (13.8)	64.6 (11.5)	46(29.7)	19(51.4)	33 (21)	7 (18.9)	ΝΑ	ĕ Z	ĕ Z	₹Z	ΥZ	ΝΑ
tepsuwan 2019	Thailand	RC	38	9/	2.76	3.40	44.1 (15.8)	47.5 (15.0)	17(44.7)	21(25)	11	10	ΝΑ	Ϋ́Z	Ϋ́Z	₹Z	58.5 (9)	60(10.5)
tomisc 2018	Netherlands	RC	51	32	3.7	3.7	55 (14)	60 (13)	13 (26)	15 (47)	6 (12)	8 (25)	16 (31)	11 (34)	6 (12)	2 (6)	Ϋ́	ΝΑ
toyoda2017	USA	Z	367	1603	9.9	9.9	54.9 (15.3)	57.4 (14.6)	124(33.8)	703(43.9)	31 (8.4)	203	175	881	85 (23.2)	405	Ϋ́	Υ V
												(12.7)	(47.7)	(22.0)		(25.3)		
wang2014	New Zealand	RC	25	35	3.9	3.9	43.1 (16.3)	52.1 (15.7)	11(44)	14(40)	2 (8.0)	3 (8.6)	6 (24.0)	12 (34.3)	2 (8.0)	17	58.0	59.3
																(48.6)	(11.6)	(12.0)
Wilhelm 2004	Switzerland	R	22	26	7	7	NA	N A	NA	NA	¥ Z	Ϋ́Z	ΝΑ	Ϋ́	Ϋ́	Ϋ́Z	Ϋ́	ΝΑ
Mihaljevic 2004	USA	RC	21	32	4	4	NA	NA	N A	ΑN	¥.	ΥZ	ΥN	ΑN	ΑN	Ϋ́Z	ΥZ	Ϋ́
Sternik 2002	USA	RC	16	28	3.25	3.25	NA	NA	× N	Α A	¥ N	ΑN	ΑN	Ϋ́	Ϋ́	Ϋ́Z	ΥZ	× ×
yamaguchi 2006	Japan	PC	4	_	∢ Z	Υ N	55.5 (12)	61 (11)	4(28.6)	4(57.1)	Υ N	₹ Z	<b>⋖</b> Z	∢ Z	∢ Z	ΑN	₹ Z	Y Z
oliver 2022	France	2	115	37	2.33	2.33	59 (15)	58 (14)	37(32.2)	12(32.4)	15 (13)	9 (24)	ΑN	ΝΑ	13 (11.3)	2 (5.4)	ΥZ	ΑN
brescia 2021	USA	RC	181	79	3.7	2.7	54 (15)	54 (14)	53 (29)	35 (44)	28 (15)	25 (32)	71 (39)	46 (58)	Ϋ́	Ϋ́Z	56 (11)	(6) (9)
Musci 2010	Germany	RC	32	17	3.59	3.59	44.3 (11)	44.3 (11)	20	10	¥ Z	ΑN	ΝΑ	Ϋ́	Ϋ́	Ϋ́Z	ΥZ	Υ Y
Gammie 2005	USA	RC	1965	5 4662	6	6	99	29	N A	ΑN	Α V	ΑN	ΑN	ΑN	ΑN	Ϋ́Z	ΑN	ΑN
LEE 2024	Taiwan	RC	467	467	ΝΑ	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ΑN	NA	NA
						!												

RC; retrospective cohort, PC; prospective cohort, MVr; mitral valve repair, MVR; mitral valve replacement. DM; diabetes milletus, HTN; hypertension, AF; atrial fibrillation, LVEF; left ventricular ejection fraction; SD; standard deviation; N; number of patients, NA; not available

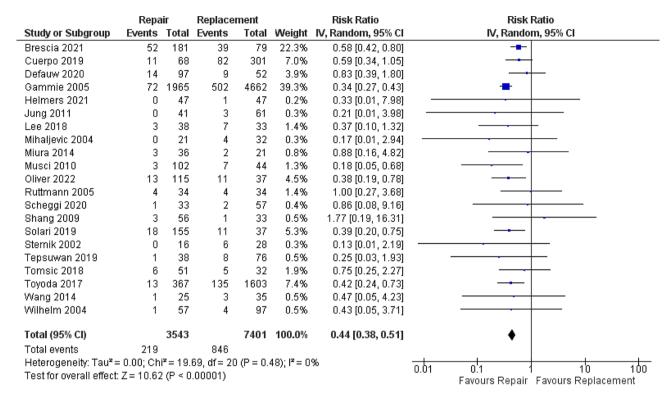


Fig. 1 Forrest plot analysis of early mortality

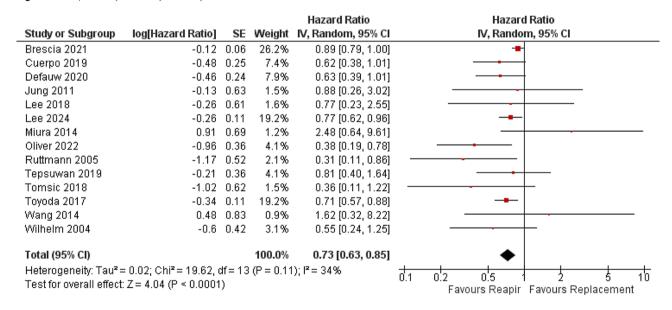


Fig. 2 Forrest plot analysis of late mortality

especially after failure of initial repair. In a meta-analysis published by Veerappan et al., there was no difference of whether to re-repair or replacement following failure initial repair in terms of post-operative outcomes [39]. Thus, every modality has its pros and cons making the choice of which is best is solely the surgeons decision based on the patient status as for example the need for anticoagulation following repair increases the incidence

of intracranial hemorrhage while the thrombogenic effect of the replaced valve increases the incidence of intracranial embolism [30, 39] thus repair can be contraindicated in patients which a must indication in others. Failure of complete or proper repair has constitute many problems as further surrounding tissue damage or involvement or abscess formation, thus may provide a plausible explanation for why replacement entails a lower risk of IE

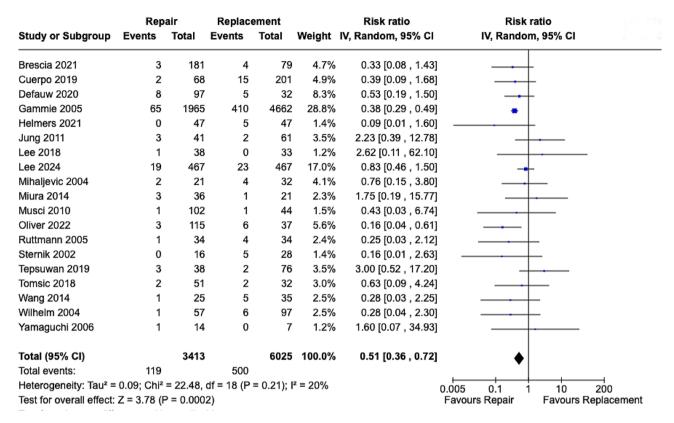


Fig. 3 Forrest plot analysis of infective endocarditis recurrence

	Repair		Replace	ement		Risk ratio	Risk ra	tio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random	, 95% CI
Brescia 2021	10	181	4	79	14.8%	1.09 [0.35 , 3.37]	_	_
Cuerpo 2019	2	68	0	301	3.2%	21.88 [1.06 , 450.72]	_	<del></del>
Defauw 2020	5	97	1	52	5.9%	2.68 [0.32 , 22.34]		-
Jung 2011	3	41	0	61	3.3%	10.33 [0.55 , 194.91]	+	
Lee 2024	14	467	20	467	24.2%	0.70 [0.36 , 1.37]	-	
Mihaljevic 2004	2	21	1	32	5.0%	3.05 [0.29 , 31.53]		-
Miura 2014	0	36	1	21	2.9%	0.20 [0.01, 4.66]		_
Musci 2010	1	102	1	44	3.8%	0.43 [0.03, 6.74]		
Oliver 2022	2	115	2	37	6.9%	0.32 [0.05, 2.20]		
Ruttmann 2005	1	34	5	34	6.0%	0.20 [0.02 , 1.62]		
Shang 2009	2	56	0	33	3.2%	2.98 [0.15, 60.30]		
Solari 2019	3	155	3	73	9.5%	0.47 [0.10 , 2.28]		
Sternik 2002	0	16	5	28	3.6%	0.16 [0.01 , 2.63]		_
Tepsuwan 2019	0	38	5	76	3.5%	0.18 [0.01 , 3.16]		_
Yamaguchi 2006	1	14	1	7	4.1%	0.50 [0.04 , 6.86]		_
Total (95% CI)		1441		1345	100.0%	0.79 [0.45 , 1.40]		
Total events:	46		49			- · · · · ·	T	
Heterogeneity: Tau <sup>2</sup> = 0.22; Chi <sup>2</sup> = 17.55, df = 14 (P = 0.23); l <sup>2</sup> = 20% 0.005 0.1 1 10 200								
Test for overall effect:	Z = 0.80 (F	P = 0.42)					Favours Repair	Favours Repalcement

Fig. 4 Forrest plot analysis of reoperation

recurrence and significantly lower in-hospital and longterm mortality rates [40–42]. However, a multi-centric study with more than 10 years follow up showed unfavorable long term outcomes for mitral valve replacement with significant higher risk of mortality and major bleeding in patients with infective endocarditis [43].

On the other hand, the current ESC 2023 guidelines reported directly that "it cannot be concluded that mitral valve repair is superior to replacement due to the high probability of selection patients bias. Valve preservation in acute IE should only be attempted if a durable repair is anticipated and complete eradication of infected tissue can be achieved" [37] which further emphasize that repair is still a very valid and potential option for IE patients when performed in the suitable time, as interventional time has been shown to be a cornerstone in the outcome of these patients as delaying surgery may rise questions and carries hemodynamic instability risks. In a study conducted by Kang et al [44], showed that the earlier the repair the better the outcome of IE patients, yet the patients don't receive earlier treatment which was evident in the results presented by Gammie et al as only 10-20% of acute cases of IE underwent repair with still showing promising results favoring mitral valve repair [28].

Further patient subgroup analysis by comparing MVr and MVR outcomes in patients with different comorbidities, age groups, or disease severity could provide valuable insight into which patient populations may benefit more from either surgical approach. Additionally, including patient-reported outcomes such as quality of life, satisfaction with surgical outcomes, and impact on daily activities could help understand the patient's experiences and preferences regarding both surgical approaches. Our results also encourage the need to understand why MVr rates remain low and suggest possible solutions in order to increase its adoption. This could be done by comparing surgical data in different centers, taking into account the number of MVr and MVR surgeries performed, surgeon expertise, and hospital resources. This also introduces the limitation of how factors associated with the choice of MVr or MVR could have biased the comparative results associated with each procedure given that all studies included were observational studies. A pooled analysis would also minimize selection bias however controlling for confounding factors through randomized controlled trials would be optimum. Finally, in addition to MVr's established clinical benefits, we must also consider its economic implications. A cost-effectiveness analysis could compare the results of both MVr and MVR including factors like follow-up care, rehabilitation, and any necessary reoperations. This could provide insight into improving outcomes and taking advantage of MVr's benefits in different centers.

### Limitations

It is important to note that the included studies in this meta-analysis had large variabilities in terms of sample size, patient baseline characteristics, disease severity, surgeons' expertise, and centers' volume. This is due to the fact that all the included studies are observational studies beside the younger nature of patients undergoing repair might attributed to its favorable ouctomes. Moreover, we couldn't access individual patients data from the included studies and this may attributed to our high heterogeneity observed beside the difference in baseline characteristics, yet we tried to solve them by sensitivity analysis once found to ensure robustness of our presented results. Thus, the limitations of this study call for further randomized control trials or matching observational studies to be conducted to address the differences in safety and efficacy between MVr and MVR in IE.

# **Conclusions**

Our results suggest that MVr showed superiority in terms of in-hospital mortality and long-term survival. Furthermore, it has a lower risk of recurrence and valve reoperation. Therefore, MVr is a potentially effective treatment choice that could be considered in most IE patients whenever possible.

# Abbreviations

MVr Mitral valve repair MVR Mitral valve replacement IE Infective endocarditis

# **Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s13019-024-02767-y.

Supplementary Material 1

# Acknowledgements

Not available

# **Author contributions**

A.K.A and M.H.F formulated the research idea and prepared the search strategy. A.K.A, M.A.E, K.W and M.E performed the screening and data extraction, A.K.A did the analysis, and A.K.A, M.H.F, and M.E wrote the primary draft, which was further edited and modified by A.K.A and K.W. All authors reviewed and agreed to the final version of the manuscript.

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Not available

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# Data availability

All data are available and attached.

# **Declarations**

# Ethics approval and consent to participate

Our paper is a meta-analysis that doesn't require an ethical approval.

### Consent for publication

All authors reviewed and agreed on the final version of the manuscript. Human ethics and consent to participate statement: our manuscript was not applied on human beings and thus requires no ethical approval.

### Competing interests

The authors declare no competing interests.

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