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Mitral valve repair or replacement in native valve endocarditis? Systematic review and meta-analysis

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Abstract

Objective: The objective of this study is to review the morbidity and mortality associated with mitral valve repair versus replacement in infective endocarditis patients.

Methods: A comprehensive search was undertaken among the four major databases (PubMed, Embase, Scopus, and Ovid) to identify all available data comparing mitral valve repair or replacement in infective endocarditis. Databases were evaluated and assessed to March 2017. Data were analyzed using meta-analytical techniques including odds ratio and mean weighted difference.

Results: A total of 8978 patients were analyzed in a total of 14 articles. The average age of the cohort was 53 years. Results revealed a shorter CPB time in the mitral valve (MV) repair compared to replacement group ($P = 0.05$). Postoperative outcomes (30 days/in hospital events) such as bleeding ($P = 0.0047$) and recurrence of infective endocarditis (IE) ($P = 0.004$) were significantly lower in the MV repair group. Beyond 30 days, recurrence of IE was higher in the MV replacement than the repair group ($P < 0.0001$). Additionally, there were significantly less reoperations in the repair group ($P = 0.0021$). The MV repair group had significantly better survival at 1 and 5 years postop ($P < 0.0001$, $P < 0.0001$).

Conclusion: This meta-analysis shows that mitral valve repair has good clinical outcomes both in-hospital and at 1 and 5 years of follow-up. Mitral valve repair should be attempted in those patients in whom sufficient valve tissue is present for reconstruction after all infectious tissue has been resected.

KEYWORDS
endocarditis, mitral valve, repair, replacement

1 | INTRODUCTION

Surgical intervention for infective endocarditis of the mitral valve can involve repair (MV repair) or replacement (MV replacement). In the noninfectious endocarditis (IE) patient, MV repair results in superior perioperative mortality, preservation of left ventricular function, and decreased thromboembolic complications compared to MV replacement.[1–7] Furthermore, treatment with mechanical MV replacement requires lifelong anticoagulation which increases the risk of both thromboembolic events and major bleeding. Biological prostheses on the other hand demonstrate relatively poor durability and are

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therefore unsuitable for younger patients. However, MV replacement has been the standard procedure for acute IE, which leads to destruction of the leaflets and makes valve repair more challenging.[8]

Repair of the mitral valve in patients with native IE has been shown to be effective in several observational studies and is gaining popularity as an alternate to MV replacement in patients with acute native mitral valve IE.[7,9] The aim of this meta-analysis was to analyze and compare all available studies regarding MV repair and MV replacement for acute IE of the native mitral valve.

2 | METHODS

2.1 | Search strategy

An English language literature search was performed following the PRISMA guidelines.[10–11] An electronic search was performed utilizing four major databases, PubMed, Ovid, SCOPUS, and Embase from inception to March 2017. To obtain the maximum relevant output from the search strategy and identify all studies, we utilized the terms "Infective endocarditis" AND "mitral valve" OR "native" OR "mitral valve surgery" AND "replacement" OR "Repair" AND "mitral valve surgery" as key words or MeSH terms. Relevant articles have been screened with full reference checks for identification of relevant studies. All selected articles were assessed systematically; inclusion and exclusion criteria were applied.

2.2 | Eligibility criteria

Inclusion criteria included comparative studies in which the patients underwent surgical intervention with either mitral valve replacement or repair for native mitral valve endocarditis. Studies were excluded if they did not report outcomes, were noncomparative studies of mitral valve repair versus replacement, or involved prosthetic valve endocarditis.

2.3 | Data extraction and outcomes

The available data were extracted from full text articles, figures, and tables. Three independent investigators (AH, MG, AxH) selected the studies for inclusion, and any disagreements were resolved by consensus with a fourth reviewer (MB). The search strategy adopted is in accordance with the Meta-analysis of Observational Studies in Epidemiology guidelines.[11] Assessment for risk of bias for each selected study was performed according to the most updated Cochrane statement.[7] The data were analyzed according to the intention-to-treat principle.

Two reviewers (MG, AxH) extracted the data. Immediate postoperative complications, mortality rate, recurrence of infective endocarditis, and five-year freedom from reoperation were the main outcome endpoints of this study. Immediate postoperative mortality was defined as any in-hospital or within 30-day mortality. In addition pooled analysis of intermediate survival was planned and the related data was extracted. One and five-year mortalities were analyzed as specified in each article. Acute surgery was defined as any operative procedure; either urgent or emergent, performed within 1 week of hospital admission.

2.4 | Statistical analysis

This meta-analysis performed in line with recommendations from the Cochrane Collaboration and Met-analysis of Observable Studies in Epidemiological (QUORUM) guidelines.[7] Where appropriate, the effect measures estimated were either relative risk (RR) or odds ratio (OR) for dichotomous data and weighted mean difference (WMD) for continuous data, both reported with 95% confidence intervals. The odds ratio represents the odds of an adverse event occurring in the MV repair compared to the MV replacement group. An odds ratio of less than one favored the MV replacement group. The point estimate of the odds ratio was considered statistically significant at the $P < 0.05$ level if the 95% confidence interval did not include the value one. Similarly, the RR represents the risk of an event occurring in the MV group compared to the MV replacement group.

For continuous variables, the relative risk was calculated with the Mantle-Haenszel Chi square method using a "random effects" meta-analytical technique as well as the "fixed model." In reporting for continuous variables such as time, statistical analysis was carried out using weighted mean difference as the summary statistic. WMD of negative value favored the MV replacement group. In reporting the results, the square is indicative of point estimates of the treatment effect (RR or MWD) with 95% confidence intervals (CIs) indicated by horizontal bars. The diamond represents the summary estimate from the pooled studies with 95% CIs. I^2 statistic was used to estimate the percentage of total variation across studies, owing to heterogeneity rather than chance, with values greater than 50% considered as substantial heterogeneity.

Where appropriate for continuous variables and comparison of the MV repair versus MV replacement group a paired Student's *t*-test was carried out to assess for degrees of significance.

Statistical analysis was performed using StatsDirect (Version 3.1.8, StatsDirect Ltd, Cambridge, UK) software.

3 | RESULTS

3.1 | Included studies and patients

The PRISMA statement flowchart describes the process of the literature search, study selection, and reasons for exclusion (Figure 1). The initial search results showed 2673 articles, of which 70 articles were retrieved for assessment in full-text. Eventually, results from 14 studies were eligible and were included in both the qualitative and quantitative meta-analysis.

3.2 | Study characteristics

The perioperative characteristics of the patients and the articles included in the analysis are summarized in Tables 1 and 2.[2,7,8,12–23]

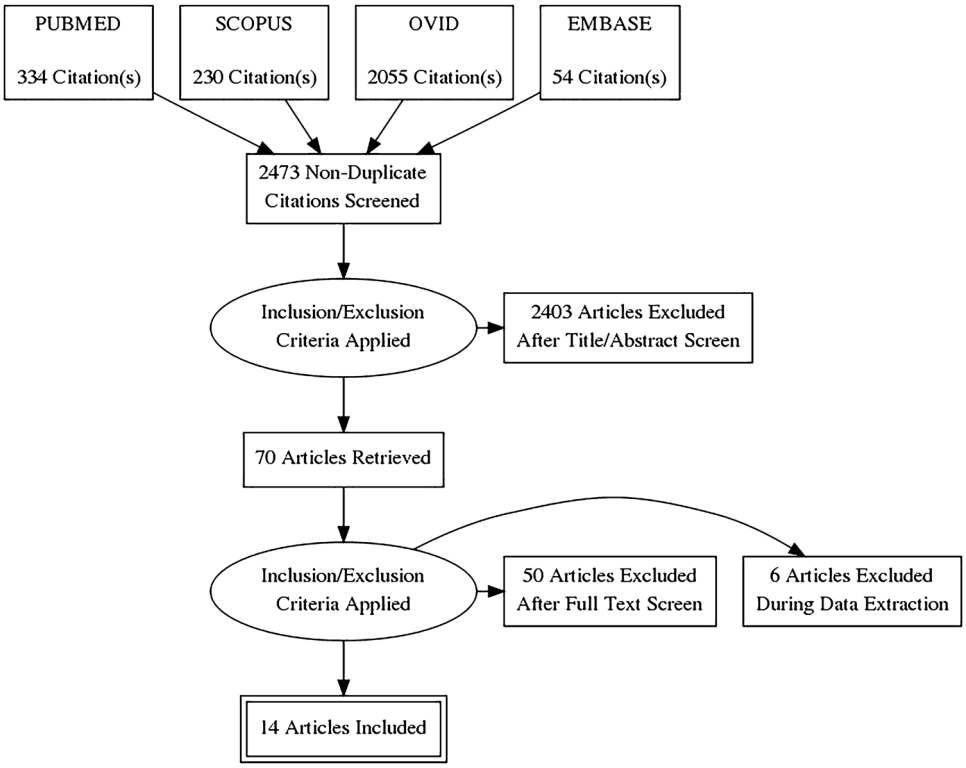

FIGURE 1 PRISMA flowchart of literature search

There were no randomized control trials comparing the two procedures. Each study had a MV repair group as control and a MV replacement group as an experimental arm of the study.

The 14 studies included a total of 8978 patients. A total of 2906 patients who had IE of the native mitral valve underwent the MV repair and a total of 6072 underwent the MV replacement. The mean age was 52 ± 8.21 for the MV repair group and 53 ± 4.8 for the MV replacement group; $P = 0.623$.

The mean cardiopulmonary bypass time (CPB) was 116.2 ± 28.3 min and 135.1 ± 41.6 min for the MV repair group and the MV replacement group, respectively; $P = 0.05$. The aortic cross clamp time (ACx) was 81.22 ± 22.6 min and 90.93 ± 29.80 min for the MV repair group and the MV replacement group, respectively; $P = 0.23$. Among the MV repair patients, 85% underwent urgent/emergent surgery while 15% were operated on electively. In comparison, the rate was 91% versus 9%, respectively, in the MV replacement group. Only 10 studies reported follow-up data at 1 and 5 years. The presence of large vegetations, acute heart failure, and severe sepsis were among the common indications for the MV replacement compared to MV repair group of patients. Severity of mitral regurgitation was a similar indication in both groups of patients (Figure 2). Only 11 studies reported the cultured organism responsible for the infective endocarditis; *Streptococcus* was significantly higher in the MV repair group, whereas staphylococci and culture-negative endocarditis were equal in both groups. Infective endocarditis with other organisms was higher in the MV replacement group of patients, but this was not statistically significant (Figure 3). The rate of concomitant coronary artery bypass graft surgery was higher in the MV replacement group, although this did not reach statistical significance (3% vs 2%, $P = 0.07$); similarly, the rate of aortic valve replacement and tricuspid valve repair were higher in the MV replacement group which was statistically significant (25% vs 16%, $P = 0.002$) and (18% vs 9%, $P = 0.0001$), respectively. Perioperative findings were reported in only nine papers; vegetation of the valves was the most common finding in both groups (Figure 4). Perforation and chordae rupture were the next most common findings and were also similar in both groups (Table 1).

3.3 | Clinical outcomes

3.3.1 | In-hospital results

Postoperative bleeding was higher in the MV replacement group ($P = 0.0047$) (Figure 5). Similarly, 30-day recurrence of IE ($P = 0.004$) was significantly higher in the MV replacement group (supplementary Figure S1). In-hospital stroke rates ($P = 0.1565$) revealed no difference following the two procedures. Although there was a higher 30-day mortality for the MV replacement group compared to the MV repair, this did not reach statistical significance ($P = 0.66$; Table 3).

TABLE 1 Perioperative characteristics of patients included in the analysis

	Mitral valve repair	Mitral valve replacement	*P*-value
No. of patients			
2906	6072		
Mean age (yrs)	52 (8.21)	53 (4.8)	0.623
Male (%)	66%	59%	0.157
LVEF (%)	55.4%	55.5%	0.958
Severe MR (%)	75%	73%	0.015
HTN (%)	24%	24%	0.923
DM (%)	20%	16%	0.264
COPD (%)	27.4%	19%	0.356
Surgical acuity			
Acute (%)	85%	91%	0.04
Chronic (%)	15%	9%	0.035
Indication for surgery			
Severe heart failure	37.76 (16.21)	53.64 (20.27)	0.031
Large vegetation	60.73 (24.34)	47.30 (17.62)	0.054
Evidence of embolization	26.94 (23.22)	28.21 (21.74)	0.653
Severe sepsis	25.57 (25.03)	30.37 21.14	0.408
Severe MR	63.2 (21.7)	64.4 (21.1)	0.743
Abscess	7.97 (7.27)	13.30 (5.06)	0.201
Operative data			
CPB (mins)	116.2 (28.3)	135.1 (42.0)	0.05
Acx (mins)	81.22 (22.60)	90.93 (29.83)	0.230
Concomitant procedures (%)	27%	46%	
CABG (%)	2%	3%	0.07
AVR (%)	16%	25%	0.02
TVrepair (%)	9%	18%	0.0001
Perioperative finding			
Perforation	28.12 (10.42)	27.12 (19.92)	0.876
Vegetation	73.3 (23.2)	74.5 (25.7)	0.888
Chordae rupture	39.98 (18.01)	24.32 (6.42)	0.091
Abscess	11.00 (8.10)	21.33 (14.77)	0.178
Complete leaftleft destruction	13.0 (24.8)	22.9 (23.7)	0.184
Microbiology			
Streptococci species	44.67 (10.76)	32.58 (9.94)	0.028
Staphylococci species	34.07 (16.20)	34.93 (12.94)	0.841
Culture negative	12.13 (6.91)	19.03 (13.40)	0.126
Others	15.65 (16.55)	16.55 (13.18)	0.691

Values are mean figures ± standard deviation (SD), Acx, aortic cross clamp; AVR, aortic valve replacement; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; DM, diabetes mellitus; HTN, hypertension; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; TVrepair, tricuspid valve repair; yrs, years.

3.3.2 | At 1-year post discharge

Patients that had MV replacement had a higher rate of recurrence of infective endocarditis ($P < 0.0001$) (supplementary 2) and therefore a higher rate of reoperation for redo MV replacement ($P = 0.0021$) (supplementary Figure S3). The mortality rate in patients with MV replacement was also higher when compared with patients who underwent MV repair ($P < 0.0001$) (supplementary Figure S4; Table 4).

3.3.3 | Mean follow-up on 5-year mortality rate

Patients with mitral valve replacement had a mean follow-up of 10 years, while patients who underwent mitral valve repair had a slightly shorter follow-up period with a mean of follow-up of 9 years. The 5-year mortality rate was significantly higher in patients who had mitral valve replacement compared to repair ($P < 0.0001$) (supplementary Figure S5; Table 4).

TABLE 2 Study characteristics of the articles included in the systematic reviews and meta-analysis

Author	Year	Country	Type	No of patients	MVR (n)	MVRp (n)	Follow-up years	Primary end points
Jung et al[22]	2011	South Korea	Retrospective cohort	102	41	61	0-12 years	In hospital and long-term mortality & morbidity
Miura et al[20]	2014	Japan	Retrospective cohort	57	36	21	Average 5.3 years	In hospital and long-term mortality & morbidity
Muehrcke et al[8]	1997	United States of America	Retrospective cohort	146	102	44	Average 3.7	In hospital and long-term mortality & morbidity
Ruttmann et al[2]	2005	Austria	Retrospective cohort	68	34	34	Not available	Perioperative mortality and long-term event-free survival
Shang et al[18]	2009	United States of America	Retrospective cohort	87	56	31	Not available	In hospital and long-term mortality
Wang et al[16]	2014	New Zealand	Retrospective cohort	60	25	35	Average 3.9 years	In hospital and long-term mortality & morbidity
Feringa et al[12]	2007	Netherlands	Systematic review	1194	470	724	Not available	In hospital and long-term mortality & morbidity
Gammie et al[7]	2005	United States of America	Retrospective cohort	6627	1965	4462	Not available	In hospital and long-term mortality & morbidity
Wilbring et al[15]	2014	Germany	Retrospective cohort	89	14	75	Average 3 years (0-14)	In hospital and long-term mortality & morbidity
Wilhelm et al[14]	2004	Switzerland	Retrospective cohort	154	57	97	Average 7 years	In hospital and long-term mortality & morbidity
Mihaljevic et al[21]	2004	United States of America	Retrospective cohort	53	21	32	4 years (0-11)	In hospital and long-term mortality & morbidity
Musci et al[19]	2010	Germany	Retrospective cohort	280	61	219	0-21 years	In hospital and long-term mortality & morbidity
Yamaguchi et al[13]	2006	Japan	Retrospective cohort	21	14	7	Average 2 years	In hospital and long-term mortality & morbidity
Sternik et al[17]	2002	United States of America	Retrospective cohort	44	16	28	Average 3 years	In hospital and long-term mortality & morbidity

MVR, mitral valve replacement.

4 | DISCUSSION

Mitral valve replacement has been the standard surgical therapy for patients with mitral valve endocarditis.[14] More recently, attempts have been undertaken to repair the mitral valve in the setting of infective endocarditis.[17,21,22] The advantage of mitral valve repair includes avoiding insertion of a prosthetic valve in infected tissue compared to the use of an annuloplasty ring.[12] The operative strategy is determined by the severity of the infection, the amount of valve tissue available after debridement of infected tissue, and the hemodynamic status of the patient.[21]

The results from this meta-analysis that involved 14 published cohort studies with a total of 8978 patients showed

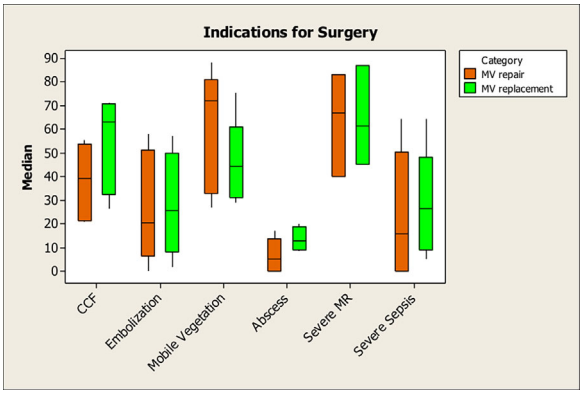

FIGURE 2 Indication for surgery in both MV repair and MV replacement groups. Mobile vegetation and sever MR rank high in both groups. CCF, congestive cardiac failure; MR, mitral regurgitation; MV, mitral valve

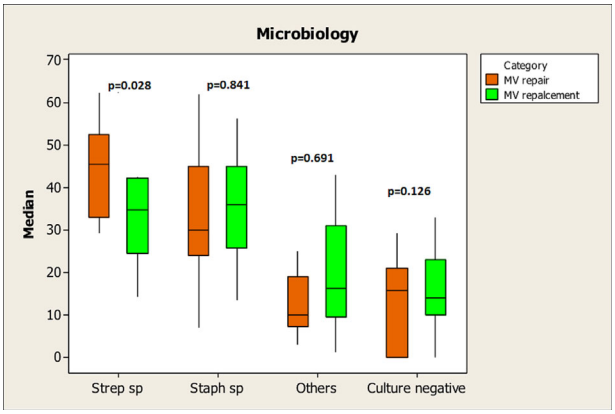

FIGURE 3 Microbiological organisms responsible for infective endocarditis in both groups

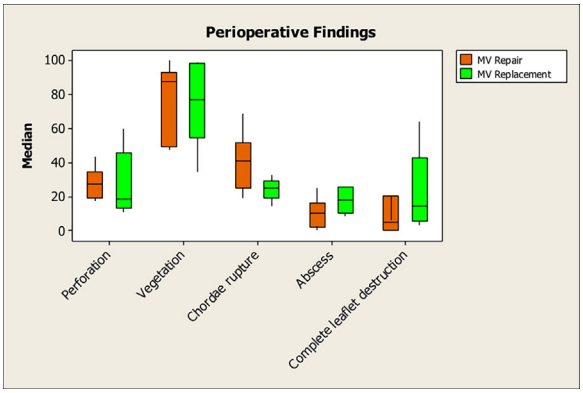

FIGURE 4 Perioperative finding for MV REPAIR and MV replacement group. MV, mitral valve

that both short- and long-term outcomes in patients with mitral valve repair in the setting of acute infective endocarditis are much more favorable than mitral valve replacement. Patients who underwent MV repair had a shorter CPB time of 116 versus 135 min, respectively ($P = 0.047$). The shorter CPB time in the mitral valve repair group may be attributable to these patients having much smaller areas of infective endocarditis with less need for annular reconstruction. Additionally there was a higher rate of concomitant procedures in the MV replacement group (46% vs 27%) which contributed to the longer CPB times. In addition MV repair patients also had a much lower rate of postoperative complications such as bleeding ($P = 0.0047$) and recurrence of infection ($P = 0.004$). Our analysis also showed an advantage toward a higher survival rate in the mitral valve repair group at both 1 and 5 years post-surgery ($P = 0.03$ and $P < 0.0001$, respectively). Furthermore, recurrence of infective endocarditis at 1-year follow-up was also lower in the repair group compared to the replacement group ($P < 0.0001$).

During the early stages of IE, the patient's condition is frequently critical, and reconstructive surgery in inflammatory tissue may be difficult. The feasibility of repairing infected mitral valves for acute endocarditis has been demonstrated to vary from 33% to 78% and has been attributed to demographic variation and the surgeon's technical experience in mitral valve surgery (repair vs replacement).[14,17,21,23]

Mitral valve repair is a reliable option when the valve damage is limited. Mihaljevic et al showed that MV repair outcomes are durable when the remaining valvular tissue can be reconstructed, the results from his study showed freedom from reoperation and reinfection at 5 years was 90%.[21] Previous studies have demonstrated that the feasibility of MV repair is dependent on the extent of tissue destruction and that earlier intervention helps in ensuring valve reparability.[9,10]

A recent study by Rostagno et al showed that mitral valve repair is a feasible and reliable procedure in patients with native mitral valve endocarditis.[24] The study involved 34 consecutive patients who were admitted for infective endocarditis of the native mitral valve. MV repair had a long-term survival rate of 96.7% with a dramatic improvement in functional status (93.2% were at New York Heart Association class I-II at time of follow-up) and none of the patients developed severe mitral regurgitation at long-term follow-up. They recommended earlier surgery for IE when only a small portion of valvular tissue is destroyed and the chance of valve repair is high.[24]

On the contrary, devastating complications after mitral valve surgery for infective endocarditis include cerebrovascular accidents and recurrent endocarditis.[25] Recurrent infective endocarditis is frequently associated with the presence of a prosthetic mechanical

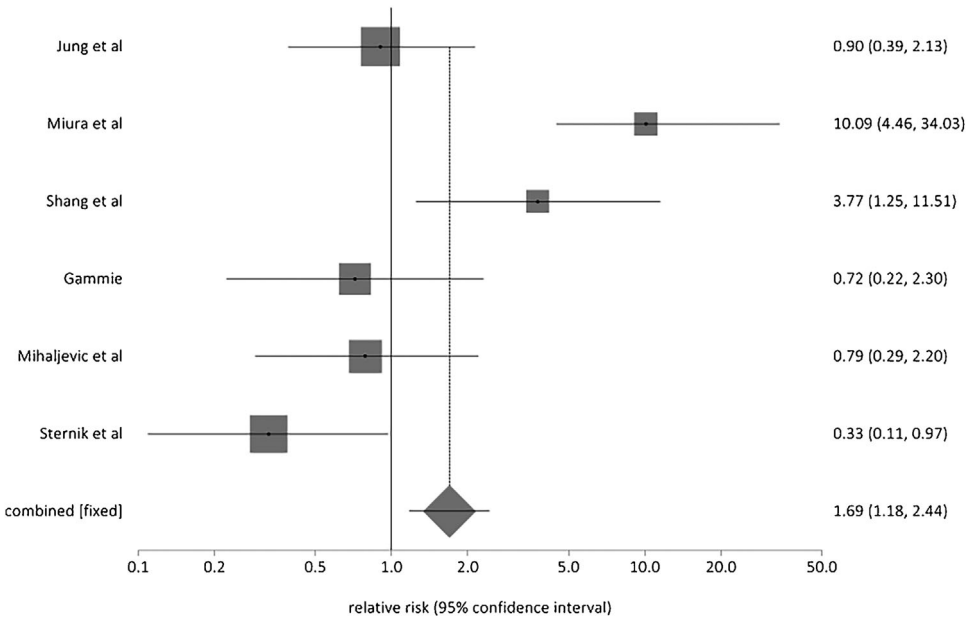

FIGURE 5 Forest plot for postoperative bleeding (<30 days bleed) ($P = 0.0047$)

TABLE 3 In-hospital postoperative outcomes

	Mitral valve repair (%)	Mitral valve replacement (%)	*P*-value
Bleeding (%)	4	8	0.0047
Stroke (%)	3	7	0.15
Endocarditis (%)	1	5	0.004
Mortality (%)	5	10	0.66

or biological valve. The use of anticoagulation therapy is most likely responsible for the higher rate of late cerebrovascular events after mitral valve replacement compared with mitral valve repair.[12]

Published rates of prosthetic valve endocarditis after mitral valve replacement for IE ranges from 8% to 27% at long-term follow-up.[7] In contrast, reinfection of the repaired mitral valve is uncommon.[7] In our meta-analysis, the rate of recurrence of infective endocarditis was much lower in the MV repair group.[7,8]

Sternik et al reported that 16 (36%) of 44 patients with active native mitral valve infective endocarditis underwent repair.[17] Gammie et al reported that the overall frequency of MV repair was 15.9% (423 of 2654 patients) in active infective endocarditis patients.[7] Rostagno et al reported that 60% of patients admitted for mitral valve endocarditis underwent mitral valve repair.[24] Omoto et al[25] performed valve repair in 68% of patients with mitral valve endocarditis and 50% of patients underwent mitral valve repair in the study by Ruttmann et al.[2] In our systematic review, 32% (2906) of the patients underwent a MV repair.

It has been previously shown that IE patients undergoing MV replacement have increased early and late mortality when compared to MV repair.[19] Patients in the MV repair group were older, required more emergency operations and more frequent and higher doses of inotropic support, and had a higher rate of severe cardiac decompensation.[19,20] In our systematic review, the surgical acuity was higher in the mitral valve replacement group (91% vs 85%; $P < 0.05$). Patients with sepsis and unstable hemodynamics had poorer outcomes.[19,26–28] The major concern related to MV repair is the possibility of recurrent IE due to incomplete resection of the infected tissue and therefore decreased durability of the repair.[29,30] Our analysis suggests that when all infected valvular tissue is resected, and a repair is technically possible, it should be performed.

TABLE 4 Rate of reoperation, recurrence of infection, 1- and 5-year mortality in both groups of patients

	Mitral valve repair (%)	Mitral valve replacement (%)	*P*-value
Reoperation (%)	6.7	12.4	0.002
Recurrent endocarditis (%)	2.9	8.9	<0.0001
Mortality (%) at 1 year	8.3	17.3	0.03
Mortality (%) at 5 year	20.5	29.7	<0.0001

5 | CONCLUSION

In conclusion, the present meta-analysis identified a significant survival benefit for mitral valve repair in infective endocarditis of the native mitral valve compared to mitral valve replacement. Mitral valve repair is durable and resistant to reinfection in the setting of either acute or healed endocarditis. However, it is important to realize that not all patients are candidates for mitral valve repair because of the variable extent of mitral valve tissue destruction caused by endocarditis.

6 | LIMITATIONS

Despite the advantages of a pooled analysis, such as increased statistical power, there are several limitations of the current analysis.

First, publication bias may have influenced our study outcomes, as observational studies with a poor outcome may not have been published. Second, surgical techniques and approaches have improved over last three decades and may have influenced the current results. The shorter cardiopulmonary bypass time in the repair group could potentially be due to very limited valve leaflet destruction. Third, no randomized control trial was identified for this meta-analysis and the data was collected from observational studies. These studies did not control for confounding factors in treatment selection; that may have also influenced the results of this pooled data analysis. As a result, the differences in survival and outcomes could represent the patient characteristics rather than the surgical intervention. Fourth, the studies have not reported the rate of intravenous drug abusers among each cohort of the patients which could have effected both long- and short-term outcomes regardless of the type of surgical procedure.

Mitral valve replacement is often reserved for the sickest patients in whom mitral valve repair cannot be performed. Therefore, poorer postoperative outcomes are anticipated in such patients. Finally, the choice of mitral valve repair or replacement in the present study may have been affected by surgeon preference or experience with valve repair.

DISCLOSURE

None.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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