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Repair or replacement for severe ischemic mitral regurgitation

A meta-analysis

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Abstract

Background: The best surgical option for severe ischemic mitral regurgitation (IMR) is still controversial. The aim of this study was to perform a meta-analysis to compare the clinical outcomes of mitral valve repair (MVP) with replacement (MVR).

Methods: A literature search was conducted in PubMed, Embase, and Medline using the terms "ischemic mitral regurgitation" and "repair or annuloplasty or reconstruction" and "replacement" in the title/abstract field. The primary outcomes of interest were perioperative mortality and long-term survival. Secondary outcomes were mitral regurgitation (MR) recurrence and reoperation.

Results: Of 276 studies, 13 studies met the inclusion and exclusion criteria. A total of 1993 patients were included in these studies, consisting of 1259 (63%) repair cases, and 734 (37%) replacement cases. Perioperative mortality was lower with MVP compared with MVR [OR 0.61; (95% CI, 0.43–0.87; $P < .05$)]. There was no difference with respect to long-term survival [HR 0.75; (95% CI, 0.52–1.09; $P = .14$)] and reoperation [OR 0.77; (95% CI, 0.38–1.57; $P = .47$)]. MVP is associated with a higher recurrence of MR [OR = 4.09; (95% CI, 1.82–9.19; $P < .001$)].

Conclusion: MVP is associated with a lower perioperative mortality but a higher recurrence of MR compared with MVR for severe IMR. No differences were found with respect to long-term survival and reoperation.

Abbreviations: CABG = coronary artery bypass grafting, CI = confidence interval, IMR = ischemic mitral regurgitation, LVEF = left ventricle ejection fraction, MR = mitral regurgitation, MVP = mitral valve repair, MVR = mitral valve replacement, NOS = Newcastle–Ottawa scale, NYHA = New York Heart Association, OR = odds ratio, RR = relative risk, SVA = subvalvular apparatus.

Keywords: coronary artery bypass grafting, meta-analysis, mitral valve repair, mitral valve replacement, severe ischemic mitral regurgitation

1. Introduction

Chronic ischemic mitral regurgitation (IMR) is a common and important complication after myocardial infarction. The presence of IMR is estimated to be 20% to 30% after acute myocardial infarction.[1] The pathophysiological mechanism of IMR includes adverse remodeling of left ventricle, mitral annular dilatation, and leaflet tethering.[2]

For less than severe IMR coronary artery bypass grafting (CABG) alone is recommended by guidelines as additional MV surgery would not add benefit to the short- and long-term outcome for patients.[3] However, the optimal surgery treatment for severe IMR is still debatable. There has been lots of studies comparing these 2 surgery techniques in the past few decades and the recommendation was divergent. Previous meta-analyses drew a conclusion that mitral valve repair (MVP) is associated with better short-term results but with a high recurrence of mitral regurgitation compared with replacement for IMR.[4–8] Wang and colleagues[9] failed to find a better operative mortality outcome with repair for patients undergoing concomitant CABG. On the reoperation rate and long-term survival, meta-analyses drew different conclusions.[4–9] In addition, these meta-analyses had included patients with less than severe IMR which could be not appropriate to apply the conclusion for patients with severe IMR. Although Wang and colleagues[10] had conducted a subgroup meta-analysis on severe IMR, they only included 3 studies which was not enough to draw a convincing result. So there is still need to perform a meta-analysis of the available evidence of the best option for severe IMR.

2. Materials and methods

2.1. Search strategy

We conducted a literature search in electronic databases including PubMed, Embase, and Medline for all relevant literature from the date of database inception to June 2017. The following search terms were searched in the title/abstract field: "ischemic mitral regurgitation" and "repair or annulo-

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plasty or reconstruction" and "replacement." Only English articles were included. The reference lists of relevant review articles were checked to identify extra relevant articles.

2.2. Inclusion and exclusion criteria

Articles are included if there is a direct comparison of repair versus replacement for severe IMR. Articles were excluded if they met the following criteria: no direct comparison between repair and replacement, nonischemic etiology of MR or ischemic etiology only in a subset of of the patients, part of patients with preoperative severity of MR lower than 3+ or 4+, (4) nonischemic dilated cardiomyopathy, and (5) concomitant ventricle restoration surgery.

2.3. Data extraction

Data were extracted independently by 2 authors (XW and BZ). If there was a disagreement, consensus was achieved by discussion. The following data were extracted from each included articles: first author, publication year, study design, patients' age and gender, comorbidities, New York Heart Association (NYHA) cardiac function, operation techniques, concomitant procedure, adjusted or crude odds ratio (OR), or hazard ratio (RR) with 95% confidence intervals (CIs).

2.4. Quality assessment

The Newcastle–Ottawa scale (NOS) was used to access the quality of included studies, with the highest score of 9. The high-quality study was defined as a study with a score≥6. The assessment was performed independently by 2 authors (JZ and YY). If necessary, a third author (BC) was consulted to settle disagreements.

2.5. Statistical methods

Review Manager version 5.3 (The Cochrane Collaboration, Copenhagen, Denmark) and Stata (version 12.0; StataCorp, College Station, TX) were used to perform all statistical analyses. Heterogeneity was calculated by the Q-test and I^2 statistics.

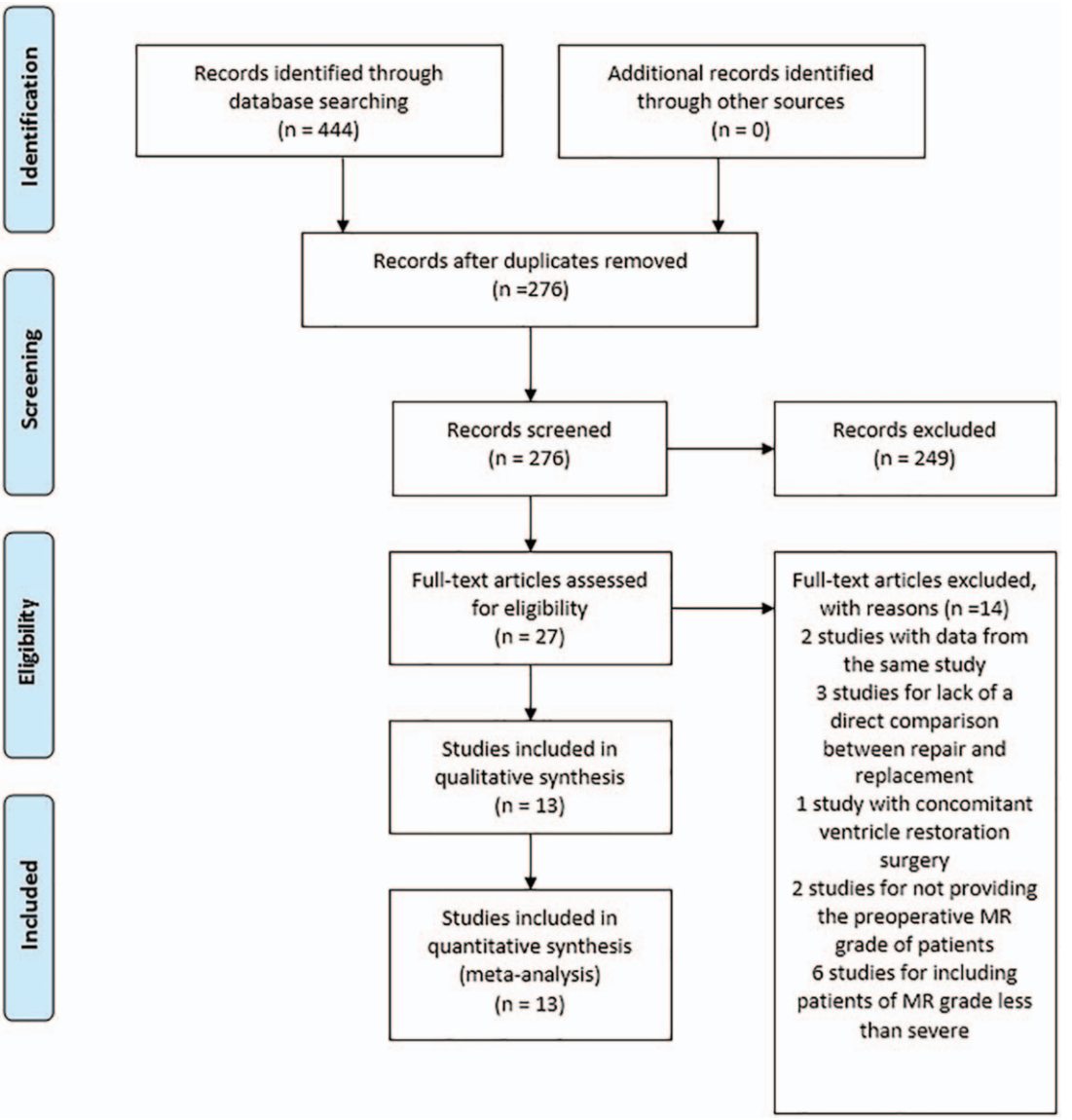

Figure 1. Flowchart of studies selection.

Studies with an I^2 statistics of >50% were considered of a high degree of heterogeneity. Heterogeneity was assessed by subgroup analysis. A summary of OR and its corresponding 95% CI were computed for the dichotomous outcomes using either random-effects models in the presence of large heterogeneity ($I^2 > 50\%$), or fixed-effects models. HR and the corresponding 95% CI were used for long-term mortality either directed provided by articles or indirectly calculated using the method of Tierney and colleagues[11] in each study. Publication bias was assessed qualitatively using funnel plots and quantitatively using Egger's linear regression method and Begg's rank correlation test. A P value < .05 was considered statistically significant.

2.6. Ethics

The article was a meta-analysis based on the results of studies published and the ethical approval was not necessary.

3. Results

The literature search identified a total of 276 studies for review. Based on the titles and abstracts, 27 articles were selected and reviewed for full text. Of these, 2 articles were excluded because the data were from the same study.[12,13] One article was eliminated because they included patients with concomitant restoration surgery.[14] Around 3 articles were excluded because they did not provide direct comparison between repair and replacement.[15–17] A total of 8 articles were eliminated because they either did not provide the MR grade of the patients or included patients of MR grade <3+.[18–25] Finally, 13 articles met the inclusion and exclusion criteria (Fig. 1).[26–38] Of the included articles, there were 12 retrospective observational studies and 1 randomized controlled study. These studies included a total of 1993 patients, 1259 of whom underwent repair and 734 of whom underwent replacement. Patient characteristics and operation details are summarized in Table 1. All the nonrandomized studies were assessed using the Newcastle–Ottawa scale for quality assessment and were of high quality (≥6 scores) (Table 2). Out of the 13 studies, age was reported in 10, gender in 11, hypertension in 6, diabetes in 9, preoperative mean left ventricle ejection fraction (LVEF) in 8, NYHA class in 9, subvalvular apparatus (SVA)-sparing techniques in 10, and concomitant CABG in 13. There were no significant differences in age except for 3 studies in which the replacement patients were 3 to 5 years older than repair patients. Only 1 study had significant more diabetes and 2 studies had significant better LVEF in MVP group. In addition, the 2 groups were similar with respect to hypertension and NYHA. Around 12 studies reported the use of annuloplasty ring and 9 studies reported the detail of SVA-sparing techniques.

3.1. Perioperative mortality

All the included studies reported perioperative mortality. The ORs ranged from 0.16 to 2.24 in studies (Fig. 2). The summary OR was 0.61 (95% CI, 0.43–0.87; $P < .05$) indicating there was a significantly lower perioperative mortality trend towards repair. $I^2 = 0$ indicated there was no potential heterogeneity across the studies. Funnel plot analysis showed symmetry (Fig. 3). No publication bias was found through Egger's linear regression method ($P = .92$) and Begg's rank correlation test ($P = .54$).

3.2. Long-term survival

A total of 11 studies reported long-term survival (Fig. 4). The overall HR was 0.75 (95% CI, 0.52–1.09; $P = .14$), suggesting

Table 1

Preoperative and operative characteristics of patients in included studies.

		Subjects		Mean Age		Female (%)		HTN (%)		Diabetes (%)		Mean LVEF (%)		NYHA III/IV (%)		Ring annuloplasty (%)	SVA sparing MVR (%)			Concomitant CABG (%)	
Author	Study type	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	None (%)	Posterior only (%)	Bileaflet (%)	MVP	MVR
Cohn et al[20]	Retrospective	94	56	65.5	68.6†	45	52	NR	NR	NR	NR	NR	NR	89	98	85	0	100	0	95	89
Grossi et al[21]	Retrospective	152	71	NR	NR	36	41	NR	NR	30	31	NR	NR	94.8	97.2	77	NR	NR	NR	89	80
Silberman et al[22]	Retrospective	38	14	62	67†	26	7	49	67	50	57	NR	NR	NR	NR	100	0	0	100	100	100
Bonacchi et al[23]	Retrospective	36	18	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	83	NR	100	NR	100	100
Micovic et al[24]	Retrospective	86	52	60.7	61.7*	27.9	26.9	74.4	65.4	21	15.3	29.0	35.9†	63.9	49.9	95	0	100	0	100	100
Qiu et al[25]	Retrospective	112	106	70.6	71.8	35.7	44.3	72.3	74.5	29.5	32.1	34.6	35.1	52.7	49.1	100	0	0	100	100	100
Maltais et al[26]	Retrospective	302	85	70.3	69.5	31.5	36.5	71.2	68.2	34.4	25.9	33.6	34.3	85.2	91.3	92	NR	NR	NR	100	100
Chan et al[27]	Retrospective	65	65	66.9	68.5	31	34	NR	NR	NR	NR	37.4	37.0	55	37	100	0	58	42	75	86
De Bonis et al[28]	Retrospective	85	47	64.3	66.1	27.1	23.5	NR	NR	30.5	29.7	30.8	33.6†	68.2	74.4	100	0	0	100	32.9	40.4
Roshanali et al[29]	Retrospective	31	26	56.9	57.1	16.1	23.1	NR	NR	NR	NR	37.9	40.0	NR	NR	100	0	0	100	100	100
Ljubacev et al[30]	Retrospective	34	41	NR	NR	NR	NR	85.3	80.5	32.4	56.1†	NR	NR	NR	NR	NR	NR	NR	NR	100	100
Lio et al[31]	Retrospective	98	28	64.8	69.7†	26.5	39.3	80.6	89.3	61.2	74.1	34.7	32.1	32.1	34.1	100	0	0	100	100	100
Acker et al[32]	prospecitve	126	125	69	68	38.9	37.6	NR	NR	38.1	32.8	42.4	40.0	24.6	16.8	100	0	0	100	73.8	75.2

CABG = coronary artery bypass grafting, HTN = hypertension, LVEF = left ventricular ejection fraction, MVP = mitral valve repair, MVR = mitral valve replacement, NR = no record, NYHA = New York Heart Association, SVA = subvalvular apparatus.

* Median.

† $P < .05$ between MVP and MVR.

Table 2

Quality assessment of the nonrandomized studies using the Newcastle-Ottawa Scale.

	Selection					Outcome			
Study	Representativeness of exposed cohort	Selection of nonexposed cohort	Ascertainment of exposure	Outcome of interest absent at start of study	Comparability (Based on design and analysis)	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow-up	Total score
Cohn et al[20]	1	1	1	1	1	1	1	1	8
Grossi et al[21]	1	1	1	1	1	1	1	1	8
Silberman et al[22]	1	1	1	1	1	1	1	1	8
Bonacchi et al[23]	1	1	1	1	2	1	1	1	9
Micovic et al[24]	1	1	1	1	1	1	1	1	8
Qiu et al[25]	1	1	1	1	2	1	1	1	9
Maltais et al[26]	1	1	1	1	2	1	1	1	9
Chan et al[27]	1	1	1	1	2	1	1	1	9
De Bonis et al[28]	1	1	1	1	1	1	1	1	8
Roshanali et al[29]	1	1	1	1	2	1	1	1	9
Ljubacev et al[30]	1	1	1	1	0	1	0	1	6
Lio et al[31]	1	1	1	1	1	1	1	1	8

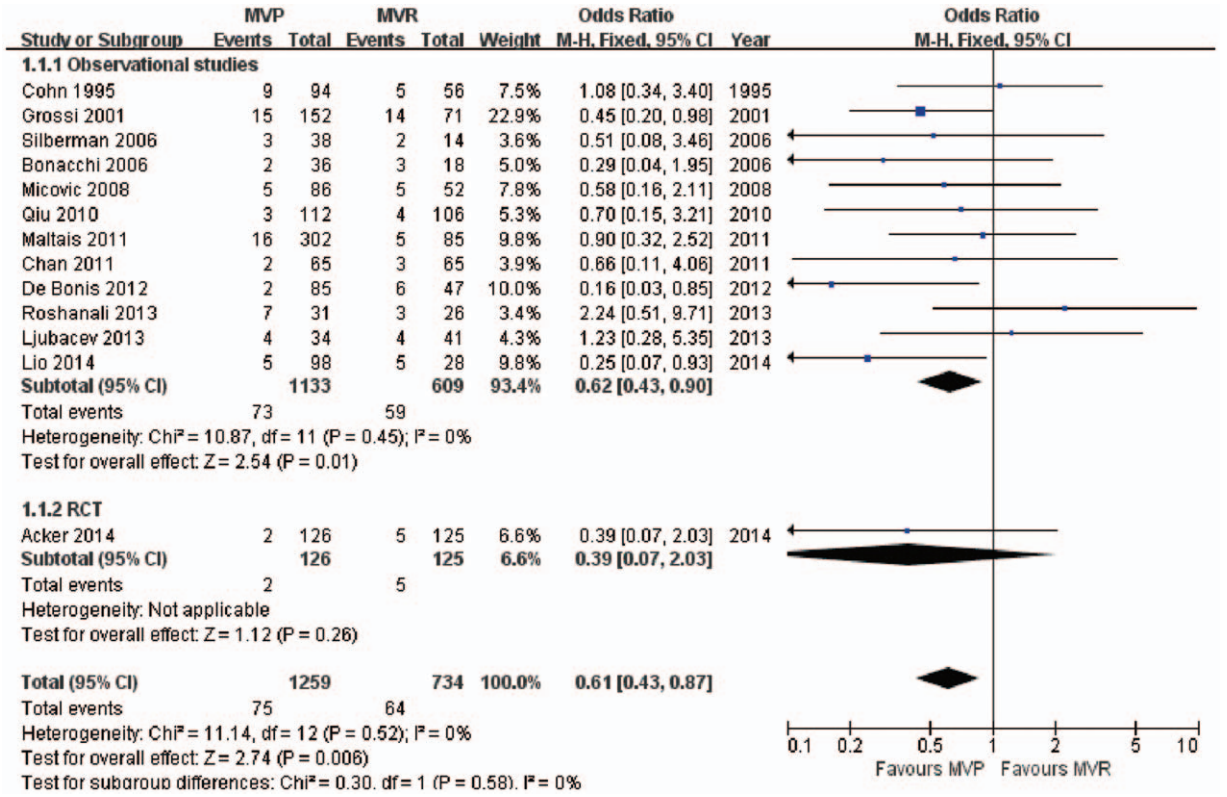

Figure 2. Mitral valve repair versus mitral valve replacement on perioperative mortality.

long-term survival was not significantly improved following repair. The heterogeneity was high ($I^2 = 58\%$). Subgroup analyses were conducted considering the high heterogeneity. Around 7 of 11 studies performing mitral valve surgery with concomitant CABG were pooled (Fig. 5). The subgroup HR was 0.81 (95% CI, 0.60–1.10; $P = .19$) with a moderate heterogeneity ($I^2 = 31\%$), which still indicated no significant difference between repair and replacement on long-term survival. 5 of 11 studies using SVA-sparing techniques in all MVR patients were analysed separately (Fig. 6), long-term survival still showed no significant difference between repair and replacement (HR = 0.58, 95% CI, 0.31–1.08; $P = .09$). As was the same when restricting studies to only posterior SVA preservation (HR = 0.92, 95% CI, 0.36–2.30; $P = .85$). However, there was a high heterogeneity among these studies, which adds a caution to these results.

3.3. Reoperation

About 7 studies involving a total of 805 patients reported reoperation during follow-up due to mitral regurgitation recurrence, thrombosis, paravalvular leak, endocarditis, et al (Fig. 7). The overall OR was 0.77, indicating the trend toward the preference of repair. However, there was no significant difference between repair and replacement (95% CI, 0.38–1.57; $P = .47$). There was no potential heterogeneity across the studies ($I^2 = 0$).

3.4. Mitral regurgitation recurrence

Around 5 studies involving a total of 449 patients provided data regarding recurrence of MR during the follow-up (Fig. 8). The repair group was associated with a significant increased

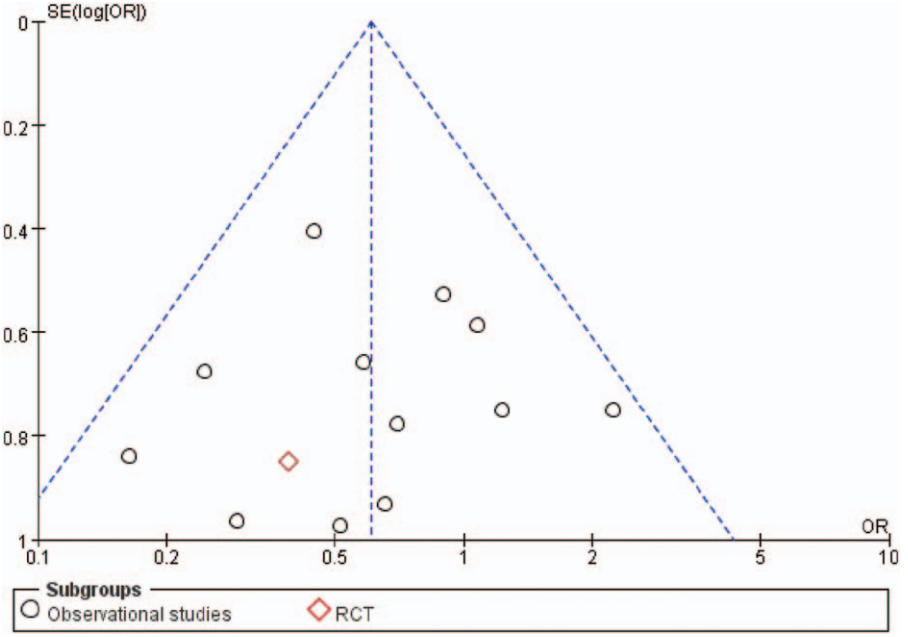

Figure 3. Funnel plot analysis.

recurrence rate of MR (OR = 4.09, 95% CI, 1.82–9.19; $P < .001$) with a low heterogeneity across the studies ($I^2 = 22\%$).

4. Discussion

Although several meta-analyses had reported their results on MVR versus MVP, these analyses had included studies involving patients with less severe IMR (MR $\leq$ 2+).[4–9] Wang and colleagues[10] reported a subgroup analysis about repair versus replacement for severe IMR, only 3 included studies were not enough to compare these 2 techniques. Our study is the first meta-analysis which included 13 articles to compare repair with replacement for severe IMR.

It has been well established mitral valve repair is superior to replacement for degenerative mitral valve disease. Mitral valve repair has an advantage of lower operative mortality, higher long-term survival, fewer valve-related complications and better preservation of ventricular function.[39–46] However, the benefit of MVP over MVR for severe IMR is not clear.

In our meta-analysis of 13 studies, MVP was found to be with significant lower perioperative mortality. There was no significant difference regarding long-term mortality and reoperation. Mitral repair was associated with a significant higher incidence of mitral regurgitation.

Our meta-analysis confirms the advantage of repair compared with replacement in perioperative mortality for severe IMR. Our result should be considered as a good supplement to the conclusion that repair was superior to replacement for IMR which was reported by previous meta-analyses. The superiority of repair over replacement for degenerative valve disease has been

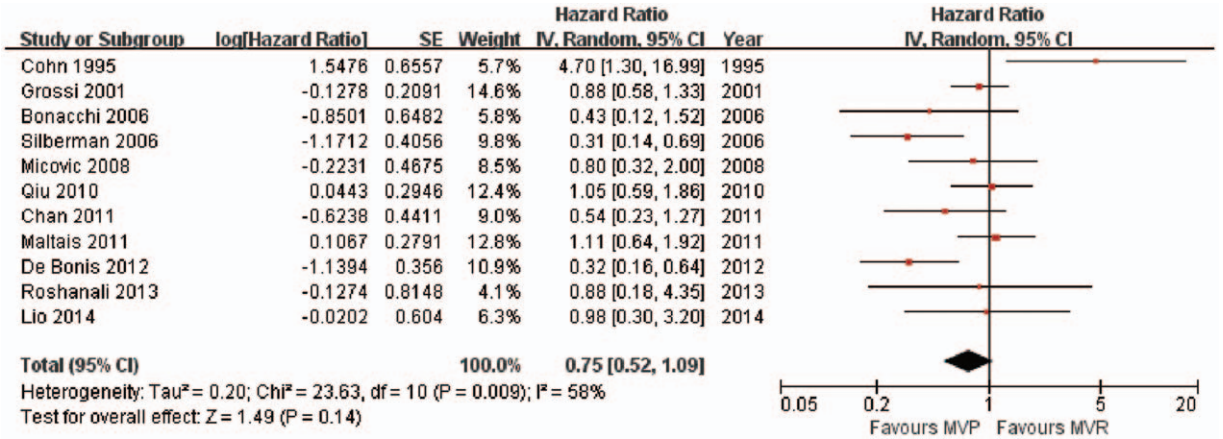

Figure 4. Mitral valve repair versus mitral valve replacement on long-term survival.

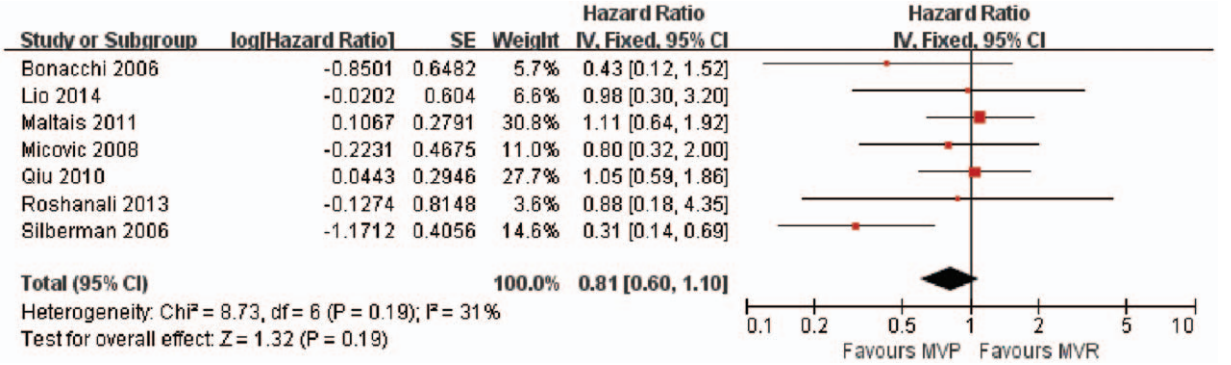

Figure 5. Mitral valve repair versus mitral valve replacement with concomitant coronary artery bypass graft on long-term survival.

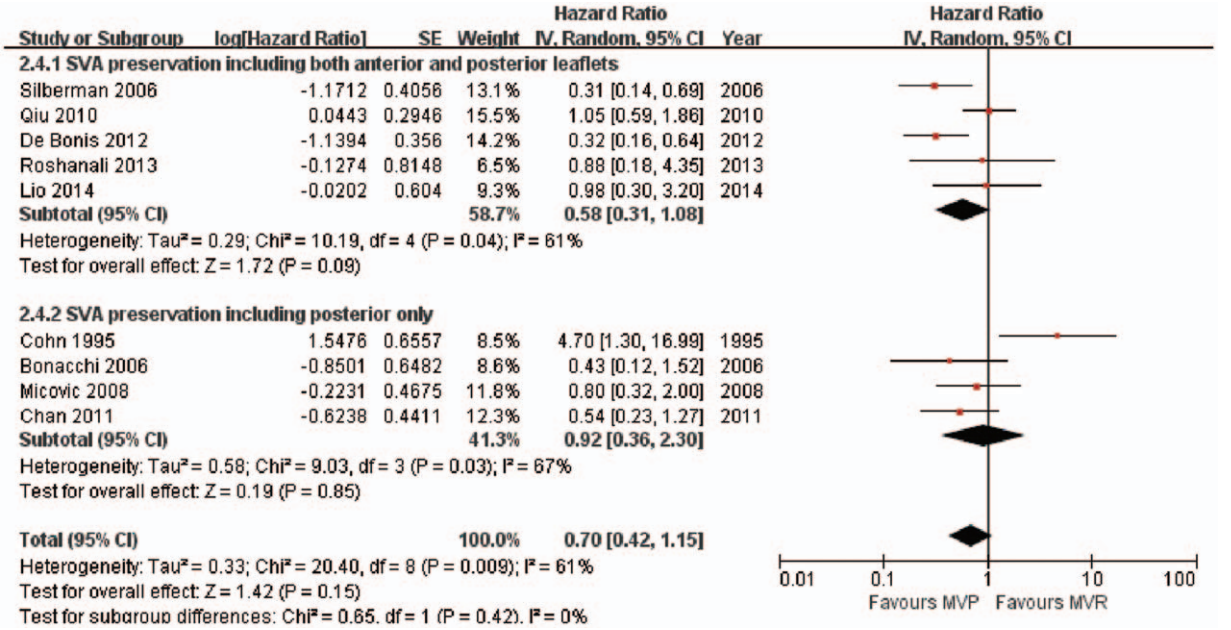

Figure 6. Mitral valve repair versus mitral valve replacement with different subvalvular apparatus preservation techniques on long-term survival.

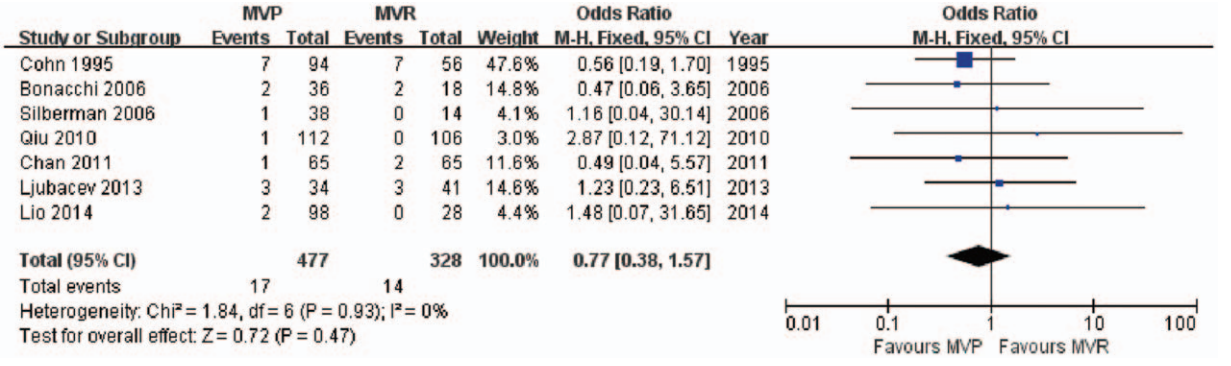

Figure 7. Mitral valve repair versus mitral valve replacement on reoperation during follow-up.

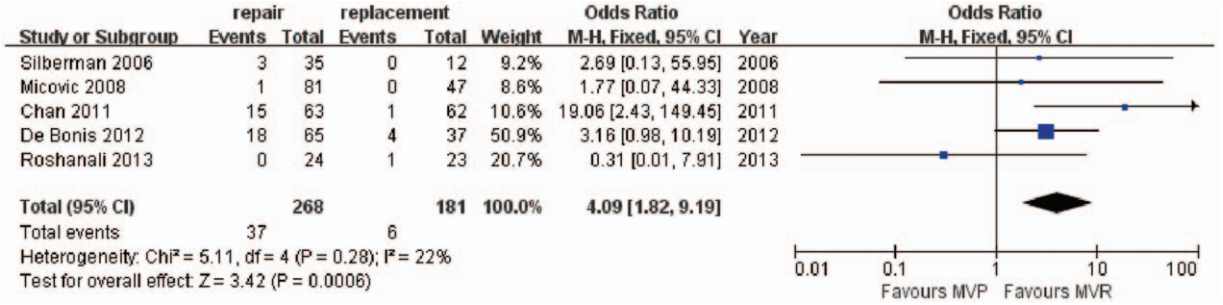

Figure 8. Mitral valve repair versus mitral valve replacement on mitral regurgitation recurrence during follow-up.

explained partly with the preservation of the subvalvular apparatus and the subsequent protection on left ventricular function. Since Lillehei et al[47] introduced the concept of preservation of posterior subvalvular apparatus for mitral valve replacement in 1964, the contribution of the subvalvular apparatus to protection of postoperative ventricular function has been confirmed by large amount of studies.[48–50] Recently, preservation of both the anterior and posterior leaflets confirmed a greater benefit over the preservation of posterior leaflet alone in left ventricle remodeling and reducing systolic afterload, and improving ventricle performance.[51,52] In our subgroup analysis according to the preservation of subvalvular apparatus, we still confirmed the preference of MVP over MVR in the long-term survival although it was not statistically significant. This adds to the validity of our results on long-term survival after repair compared with replacement in patients with severe IMR.

Recurrence of MR has been found to be a common complication for MVP in the treatment of IMR and degenerative MR.[53,54] Our study contributes further evidence to the high recurrence of MR after MVP. However, we didn't find a significant difference in reoperation rate between these 2 treatments. It could be explained for several possible reasons. Firstly, the reasons for repeat operation were not restricted to the recurrence of MR. Other reasons for repeat operation were endocarditis, thrombosis, paravalvular leak and structural deterioration of bioprosthetic valve, most of which were related to MVR.[23,25,31,33] Secondly, although there was an indication for repeat operation for the recurrence of MR, risks may be substantial considering the underlying myocardial disease and surgeons tend to take conservative measures to treat these high-risk patients.[55] Thirdly, the recurrence of MR was defined to be MR of 2+ or greater. Some of the patients with recurrence of MR may not reach the indication for repeat operation.

4.1. Limitations

Our study has several limitations. Firstly, this meta-analysis include observational, retrospective studies with the inherent biases of study design. The publications except one random controlled study were relatively small nonrandomized studies. Secondly, the follow-up data of changes on NYHA class, LVEF and left ventricle remodeling were not provided in most of the studies which prevented the further analysis of these 2 surgical techniques in these aspects. Thirdly, the confounding factors such as age, EF, SVA preservation techniques and concomitant CABG were not adjusted in the studies. Well-designed multi-center RCTs are still needed to draw a convincing conclusion.

5. Conclusion

We draw a conclusion that MVP is associated with a significant lower perioperative mortality compared with MVR for severe IMR. There is no significant difference with respect to long-term survival and reoperation between these 2 surgical techniques. However, MVP is associated with a higher recurrence of MR.

Author contributions

Funding acquisition: Yongquan Ying.
Methodology: Jian Zhang.
Project administration: Chengchu Zhu.
Resources: Bo Zhang.
Writing – original draft: Xinxin Wang.
Writing – review & editing: Baofu Chen.

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