Original Article

Mitral valve repair versus replacement in elderly patients: a systematic review and meta-analysis

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Background: Although mitral valve repair (MVP) is generally accepted as the standard treatment for mitral valve disease, in older patients, there is increasing debate about whether MVP is superior to mitral valve replacement (MVR). We, therefore, performed a meta-analysis to compare MVP *vs.* MVR in the elderly population.

Methods: We systematically searched PubMed, the Cochrane Library, and Scopus up to February 2017 and scrutinized the references of relevant literatures. Only studies of MVP *vs.* MVR in the elderly patients (aged 70 years or older) that were published after 2000 were included.

Results: The retrieval process yielded seven observational clinical studies with 1,809 patients. Compared with MVR, MVP was associated with a significantly reduced 30-day mortality [risk ratio (RR): 0.40, 95% confidence interval (CI): 0.25–0.64], with shorter duration of postoperative hospital stay (days) (weighted mean difference: –1.47, 95% CI: –2.47–-0.48) and less postoperative complications (RR: 0.69, 95% CI: 0.56–0.86). In addition, our study also demonstrated improved 1-year (RR: 1.16, 95% CI: 1.08–1.24) and 5-year (RR: 1.26, 95% CI: 1.13–1.41) survival rates following MVP. There was no difference in reoperations between these two surgery approaches.

Conclusions: The present meta-analysis indicates that elderly patients who receive MVP have better early and late outcomes than those undergoing MVR. MVP may be the preferred strategy for mitral valve surgery in the elderly population.

Keywords: Mitral valve repair (MVP); mitral valve replacement (MVR); elderly; meta-analysis

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Introduction

Mitral valve repair (MVP) is the procedure of choice in adult patients with mitral valve disease, especially mitral insufficiency, as it has been shown to offer superiority over mitral valve replacement (MVR) in various clinical settings (1). Because of the demographic changes worldwide and a greater incidence of mitral valve disease, the elderly population constitutes an increasing proportion of patients referred for mitral valve surgery (2). A number of disorders may damage the valve in older patients, such as degeneration, ischemia, and rheumatic heart disease, resulting in mitral valve stenosis or regurgitation. Although it is generally accepted that surgical treatment should be implemented even in elderly patients, there remains debate

regarding whether MVP produces the equivalent benefits as in younger population (3).

Despite the advantages over MVR, in the elderly patients, MVP is less commonly performed when comparing with younger patients. According to the data from Medicare beneficiaries' database, less than 50% of elderly patients with mitral valve disease underwent MVP, and older age could predict a higher possibility of MVR (4). This reflects the perception that MVP may be associated with longer operative time and more complicated procedures. Besides, the long-term survival benefit after MVP is often believed to be attenuated in the elderly because of their shorter life expectancy. There is also a notion that elderly patients have more friable or calcified valvular tissues and poor left ventricular function as compared to younger patients, making repair technically more challenging, thus precluding the satisfaction of valve repair and increasing the risk of reoperation (5,6).

Although the outcomes following mitral valve surgery in older patients have improved significantly in recent years (7), it is still unclear which surgical approach should be performed preferentially. Moreover, innovative transcatheter mitral interventions are increasingly used to treat mitral valve disease (8) and, thus, should be evaluated against the outcomes of optimal surgical treatment. There are limited studies, however, regarding the efficacy of MVP *vs.* MVR in the elderly population, and their results are inconsistent. We, therefore, carried out a systematical review and meta-analysis to determine the optimum surgical treatment for mitral valve disease in elderly patients.

Methods

Search strategy

This study was conducted following the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement (9). We systematically searched databases of PubMed, the Cochrane Library, and Scopus through February 2017 to identify eligible publications, using the search terms as follows: "mitral valve repair", "mitral valve replacement", and "elderly" or "older" or "octogenarian". Moreover, the reference lists of all retrieved articles were also checked for inclusion of potentially relevant studies.

Eligibility criteria

To be included, the studies should meet all of the following requirements: (I) clinical trials or observational studies that compared MVP *vs.* MVR in patients aged 70 years or older; (II) with more than ten patients in either the MVP or MVR group; (III) have reported the early and late outcomes we focused on. All articles were limited to those involving human subjects and published in English. Reviews, editorials, duplications, abstracts, conference presentations, and expert opinions were excluded. In addition, the technique of MVP was not established and prevailed prior to 2000, and the outcomes in those eras were not as good as the current data. Therefore, we also discarded the studies that were published before 2000.

Data abstraction and quality assessment

In general, two reviewers (X Shang and R Lu) independently extracted the study information, including study author, publication year, study period and design, location, inclusion criteria of age, sample size, follow-up duration, and patients' characteristics. Early outcomes in this meta-analysis were 30-day mortality, duration of postoperative hospital stay, and postoperative complications. Late outcomes included 1- and 5-year survival and reoperation during follow-up. Methodological quality of included studies was evaluated using Newcastle-Ottawa Scale (NOS), with the following three main aspects: study group selection, comparability between groups, and ascertainment of outcomes (10). A study with a NOS score of 7 or higher was regarded as of high quality. Any disagreements in data collection and quality evaluation were settled by consensus between the two reviewers or discussion with a third reviewer (M Liu).

Statistical methods

In the present study, categorical endpoints were reported as risk ratios (RRs) with corresponding 95% confidence intervals (CIs), while continuous outcomes were presented as weighted mean differences (WMDs). We calculated the pooled estimates using random effects model with DerSimonian-Laird method. Heterogeneity across studies was investigated by the Cochran Q test with a significant level of $P<0.1$. In addition, we used the I^2 statistic to quantify the heterogeneity, with an I^2 value >50% indicating substantial heterogeneity. Sensitivity analyses were performed by omitting each study in sequence. Publication bias was assessed by visual inspection of funnel plots and further confirmed by Egger's test. All data analyses were carried out using Review Manager 5.3 (RevMan, The Nordic Cochrane Center, The Cochrane Collaboration,

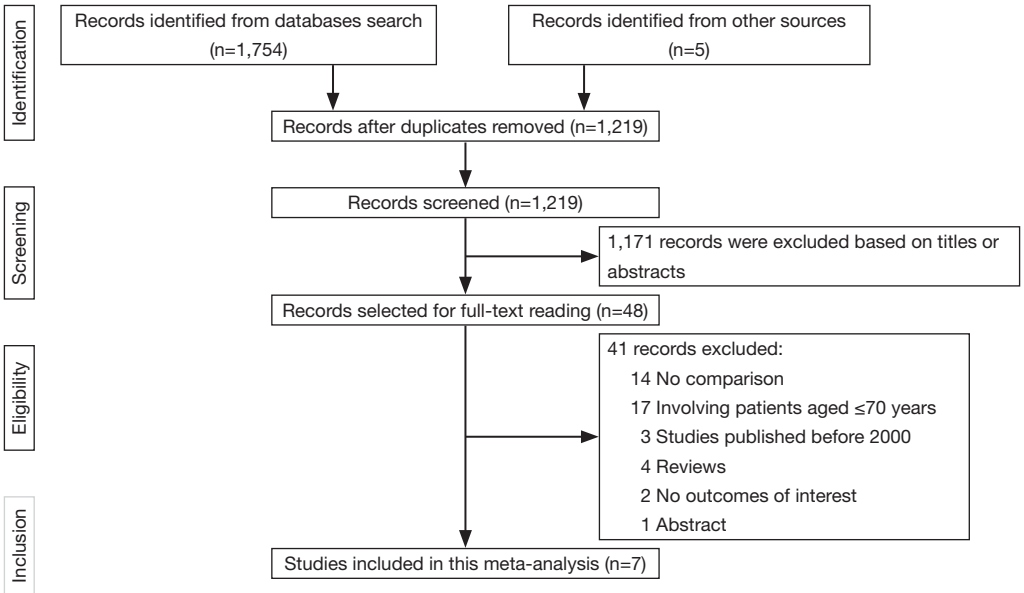

Figure 1 Flow diagram of study search process.

Table 1 Characteristics of the included studies

Study author	Publication year	Study period	Design	Location	Age (years)	MVP (n)	MVR (n)	Follow-up (years)	NOS score
Ailawadi *et al.* (11)	2008	1998–2006	Retrospective OS	USA	≥75	70	47	4.2	7
Chikwe *et al.* (12)	2011	1998–2008	Retrospective OS	USA and Germany	≥80	227	95	2.4	9
DiGregorio *et al.* (13)	2004	1990–2000	Retrospective OS	USA	≥80	46	13	5.7	7
Gaur *et al.* (14)	2014	2002–2011	Retrospective OS	USA	≥70	556	102	4.1	8
Gogbashian *et al.* (15)	2006	1992–2002	Prospective OS	USA	≥70	147	36	6.3	9
Nloga *et al.* (16)	2011	1987–2007	Retrospective OS	France	≥80	75	54	3.4	7
Silaschi *et al.* (17)	2016	1994–2015	Retrospective OS	UK	≥75	221	120	5.3	8

MR, mitral regurgitation; MVP, mitral valve repair; MVR, mitral valve replacement; NA, not applicable; NOS, Newcastle-Ottawa Scale; OS, observational study.

2012, Copenhagen, Denmark) and STATA 12.0 software (Stata Corp, College Station, TX, USA), and a two-sided P value of <0.05 was considered statistically significant.

Results

Study search

The study selection process was summarized in *Figure 1*. In general, of the initial 1,759 publications, 1,171 were excluded based on the titles or abstracts. The remaining 48 articles were selected for full-text reading, of which 41 reports that failed to meet the eligibility criteria were eliminated. Consequently, seven observational studies (11-17) that were published from 2004 to 2016 were included in our meta-analysis.

Baseline characteristics

The study characteristics were exhibited in *Table 1*. Briefly, of the included observational studies, 6 were retrospective and 1 was prospective. These included data on a total of 1,809 patients with mitral valve disease, of which 1,342 patients receiving MVP and 467 undergoing MVR. Among the included studies, 4 were from USA, 2 were from Europe, and the

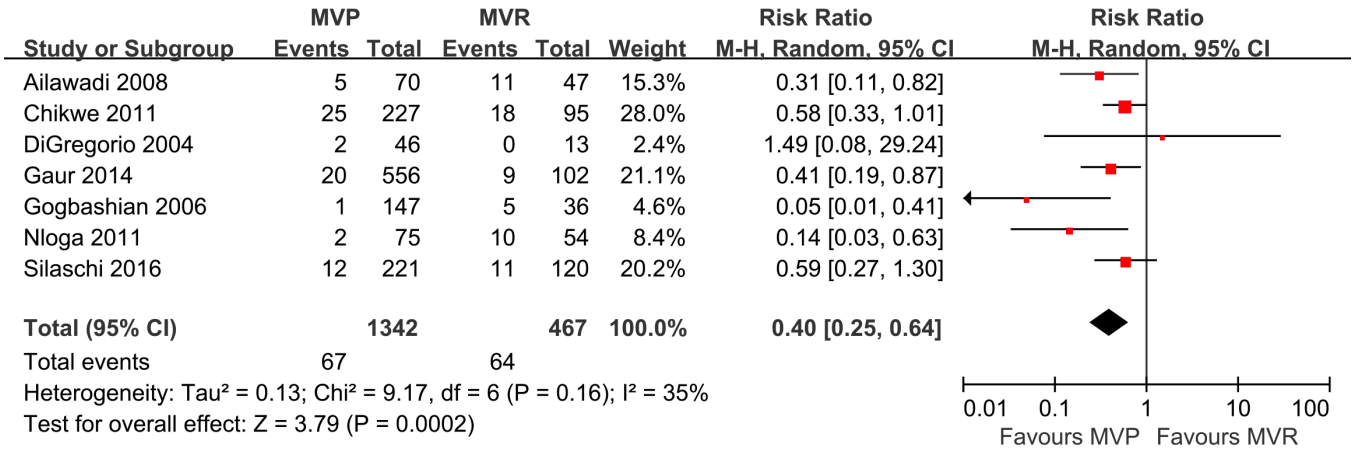

Figure 2 Meta-analysis for 30-day mortality between mitral valve repair *vs.* replacement. MVP, mitral valve repair; MVR, mitral valve replacement; CI, confidence interval.

remaining 1 was conducted in both USA and Europe, with the mean or median follow-up durations ranging from 2.4 to 6.3 years. The mean age of patients was 79 years, and men accounted for 51% of the total patients. Other patients' characteristics were shown in *Table S1*. Quality assessment showed a NOS score of 7 or higher for all studies, indicating the presence of high methodological quality.

Early outcomes

The 30-day mortality was 5.0% in the MVP group and 13.7% in the MVR group, with no evidence of substantial heterogeneity across studies (I^2=35%, P=0.16). Compared with MVR, surgery with MVP was associated with a significantly decreased 30-day mortality in elderly patients (RR: 0.40, 95% CI: 0.25–0.64, P<0.001; *Figure 2*). The duration of postoperative hospital stay (days) was also shortened following MVP (WMD: −1.47, 95% CI: −2.47–−0.48, P=0.004; *Figure S1*). In addition, there was a reduction in total postoperative complications in patients receiving MVP than those undergoing MVR (RR: 0.69, 95% CI: 0.56–0.86, P<0.001; *Figure S2*). Among the complications, stoke and renal failure were nominally lower in the MVP than in the MVR groups (RR: 0.46, 95% CI: 0.20–1.09, P=0.08 and RR: 0.60, 95% CI: 0.36–1.01, P=0.05, respectively), while there was no difference in terms of bleeding between these two strategies.

Late outcomes

The meta-analytic results of late survivals were shown in *Figure 3*. The 1-year survival rate was 84.2% and 71.0% in the MVP and MVR groups, respectively, with no evident heterogeneity across studies (I^2=0%, P=0.63). Pooling data indicated that MVP was related to a significantly improved 1-year survival (RR: 1.16, 95% CI: 1.08–1.24, P<0.001). Likewise, the 5-year survival rate was 69.9% in the MVP group and 54.7% in the MVR group, without considerable heterogeneity among studies (I^2=0%, P=0.99). Meta-analytic pooling demonstrated that the 5-year survival was higher in patients treated with MVP than those treated with MVR (RR: 1.26, 95% CI: 1.13–1.41, P<0.001). However, the risk of reoperation during follow-up was similar between MVP and MVR (RR: 1.35, 95% CI: 0.42–4.36, P=0.62; *Figure S3*).

Sensitivity analysis and publication bias

Exclusion of each study in sequence had no influence on the overall results of 30-day mortality, duration of postoperative hospital stay, and 1- and 5-year survivals. The funnel plots for 30-day mortality and duration of postoperative hospital stay were visually symmetrical (*Figure S4*) with P values of Egger's test =0.20 and 0.38, respectively, suggesting the absence of publications bias. For other outcomes, publication bias test was not performed due to the limited number of included studies.

Discussion

Few studies have explored the comparison between MVP and MVR among the aging population. The present meta-analysis pooling available data demonstrated that compared

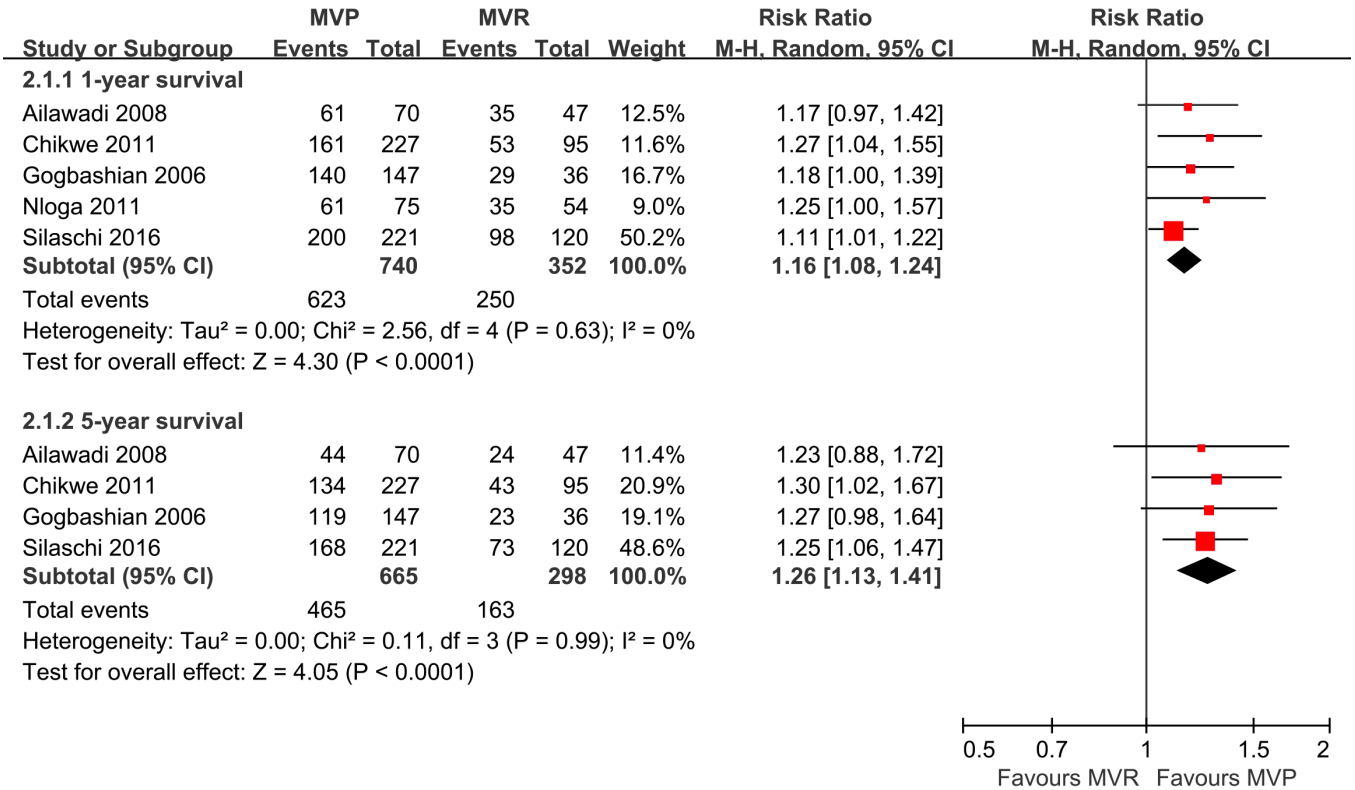

Figure 3 Meta-analysis for 1- and 5-year survivals between mitral valve repair *vs.* replacement. MVP, mitral valve repair; MVR, mitral valve replacement; CI, confidence interval.

with MVR, MVP was associated with a significantly lower 30-day mortality, with shorter duration of postoperative hospital stay and less postoperative complications. In addition, the 1- and 5-year survival rates have improved after MVP, with no difference regarding reoperation events during follow-up.

Our findings are consistent with a previous meta-analysis, which showed that MVP was correlated with improved early outcomes as compared to MVR in elderly patients (18). In that study, only four clinical studies were included, totaling 402 patients with mitral valve disease. The present work additionally included four observational studies and excluded studies prior to 2000, with nearly 4.5-fold increase in sample size, thus offering more reliable insights into the optimal mitral surgical procedures in older patients. In contrast, some studies of the aging population have reported similar long-term survival between MVP and MVR. For instance, a previous retrospective study (19) revealed that the 5-year survival of patients aged 60 years or older was not remarkably higher in patients undergoing MVP than those undergoing MVR (36% *vs.* 33%, P=0.34). However, the study cohort was historical involving patients treated between 1984 and 1997. Given the overall prolonged life expectancy and the improved perioperative management in cardiac surgery (20), MVP should have led to more favorable outcomes currently. In the present study, we did not specially explore the potential factor accounting for the improved outcomes after MVP; however, they can be summarized from the other available evidence. First of all, MVP allows better preservation of normal mitral or subvalvular apparatus than MVR that is important for ventricular contraction, thereby improving left ventricular function and remodeling (21-23). In addition, it has been suggested that there are fewer thromboembolic events and life-threatening hemorrhages in patients with MVP than those with MVR (24), thus reducing the deaths from these causes.

Because of the rapid demographic changes and the high prevalence of mitral valve disease in the elderly population, our findings are of great clinical importance. Older patients are often considered as poor candidates for MVP owning to the difficulty of repair and the conception that they may not tolerate a longer cardiopulmonary bypass time for achieving

an adequate repair (14). However, out data suggest that both early and late outcomes have improved with MVP, certainly when compared with MVR, pointing towards that MVP should be the preferred procedure for mitral valve surgery in the elderly group of patients. In addition, the available treatment strategies for mitral valve disease is developing rapidly towards interventional strategies to repair or replace the mitral valve with aims to reduce the surgical trauma and to improve outcomes, particularly in the elderly patients (8). However, new techniques to be introduced into clinical practice should have to be measured against the optimum conventional treatment, such as MVP in our study.

There are several limitations that should be acknowledged in our work. Firstly, all included studies are designed as prospective or retrospective observational studies with relatively small sample size, which may increase the risk of selection bias and reduce the statistical power for some complications. Secondly, because of insufficient data, we cannot perform stratified analyses by some important confounders, such concomitant surgical procedures and prosthesis for replacement. Furthermore, data in the present meta-analysis were obtained from studies conducted in USA or Europe. Thus, generalization of our findings to other populations should be used with caution.

Conclusions

Taken together, our meta-analysis shows that MVP is associated with significantly improved early and late outcomes as compared to MVR in the elderly patients. However, these findings should be considered within the observational nature of current evidence. Future larger studies, or perhaps randomized trials, are required to enhance the benefit of MVP *vs.* MVR in the aging population.

Acknowledgements

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: All analyses were based on previously published studies, thus no ethical approval and patient consent are required.

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Supplementary

Table S1 Baseline characteristics of included patients

Study author	Age (years)	Male (%)	HTN (%)	DM (%)	CAD (%)	AF (%)	LVEF (%)	NYHA class III–IV (%)	Prior MI (%)	IE (%)	Concomitant surgery (%)		
											CABG	TVS	AVS
Ailawadi *et al.* (11)	78/79	51/38	56/45	17/19	57/34*	36/51	NA	26/27	NA	0/2	46/32	7/15	3/11
Chikwe *et al.* (12)	83/83	52/59	NA	22/20	NA	NA	52/56	NA	15/11	2/14*	47/48	36/20*	0/0
DiGregorio *et al.* (13)	82/82	61/46	NA	2/8	NA	52/46	63/63	80/77	NA	4/8	0/0	20/31	0/0
Gaur *et al.* (14)	77/78	50/54	69/76	17/19	NA	NA	55/60	NA	NA	1/9*	49/50	17/27	0/0
Gogbashian *et al.* (15)	75/77	51/42	39/31	5/6	13/6	NA	57/58	62/61	8/0	0/0	33/51	8/28*	NA
Nloga *et al.* (16)	82/81	59/70	NA	1/17*	7/15	12/7	NA	47/67	NA	0/0	12/20	9/2	8/32*
Silaschi *et al.* (17)	79/78	57/48	63/53	11/12	25/29	NA	NA	46/65*	21/8*	0/0	44/32*	15/14	0/0

Data were provided as mitral valve repair/replacement groups. *, significant differences between study groups. AF, atrial fibrillation; AVS, aortic valve surgery; CABG, coronary artery bypass grafting; CAD, coronary artery disease; DM, diabetes mellitus; HTN, hypertension; IE, infective endocarditis; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NA, not applicable; NYHA, New York Heart Association; TVS, tricuspid valve surgery.

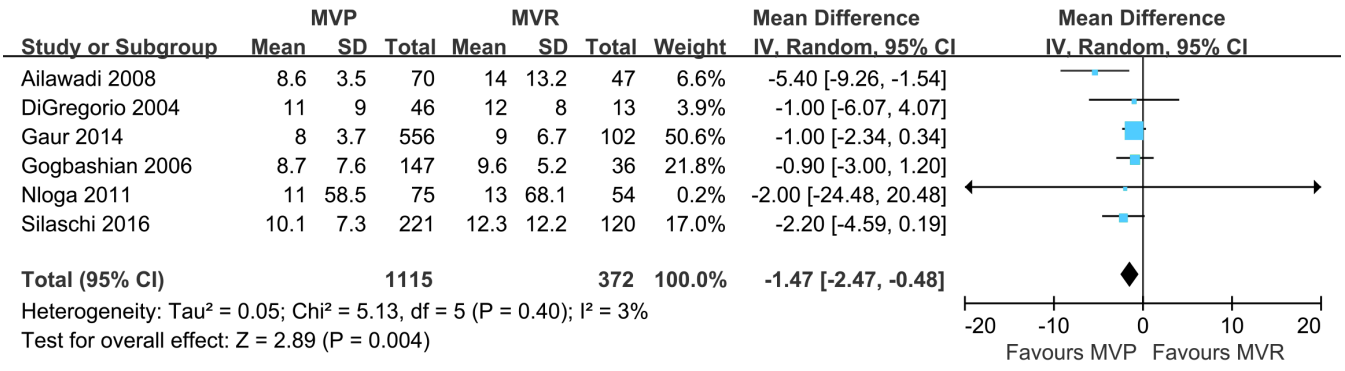

Figure S1 Meta-analysis for duration of postoperative hospital stay. MVP, mitral valve repair; MVR, mitral valve replacement; CI, confidence interval; SD, standard deviation.

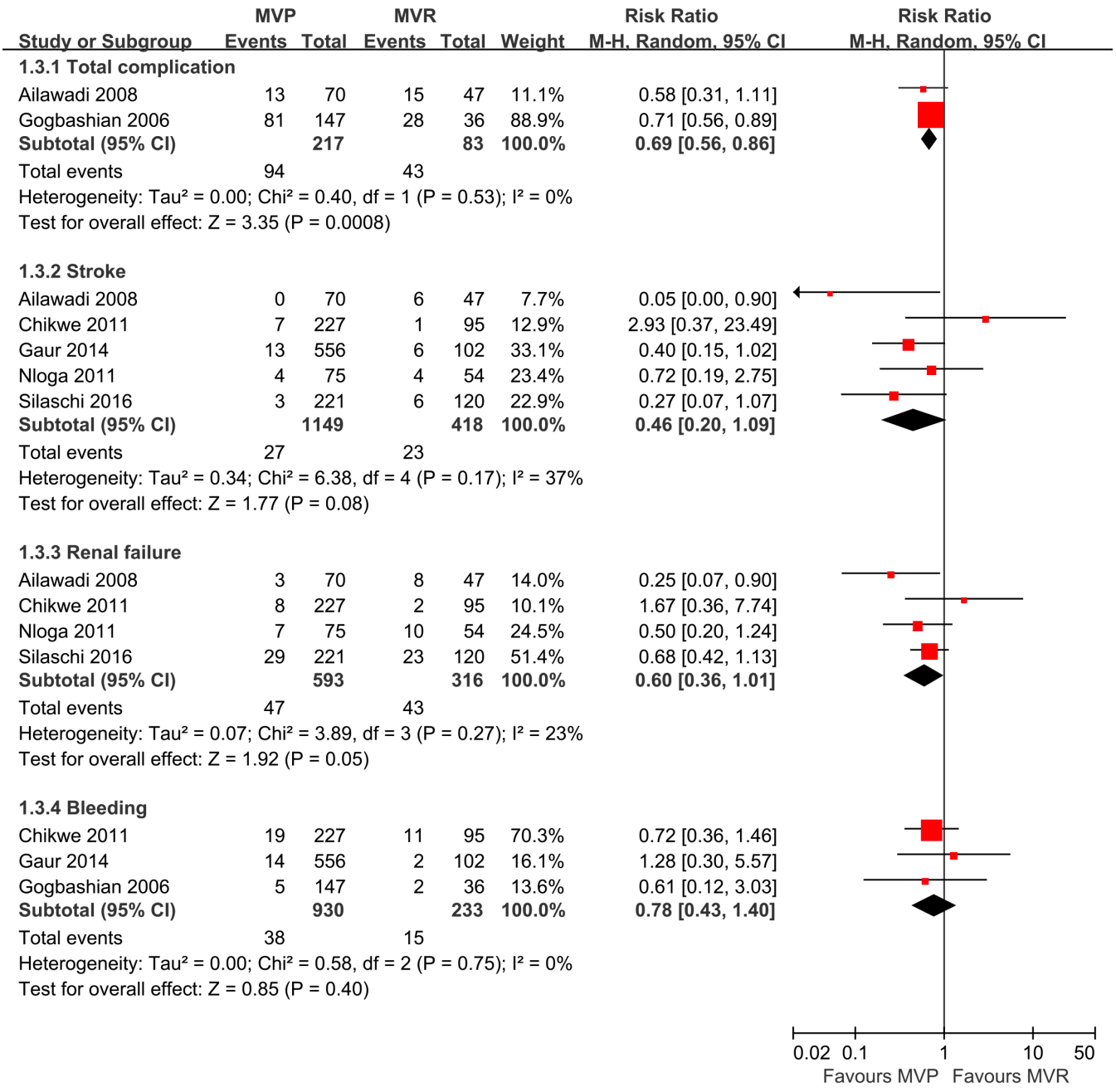

Figure S2 Meta-analysis for postoperative complications. MVP, mitral valve repair; MVR, mitral valve replacement; CI, confidence interval.

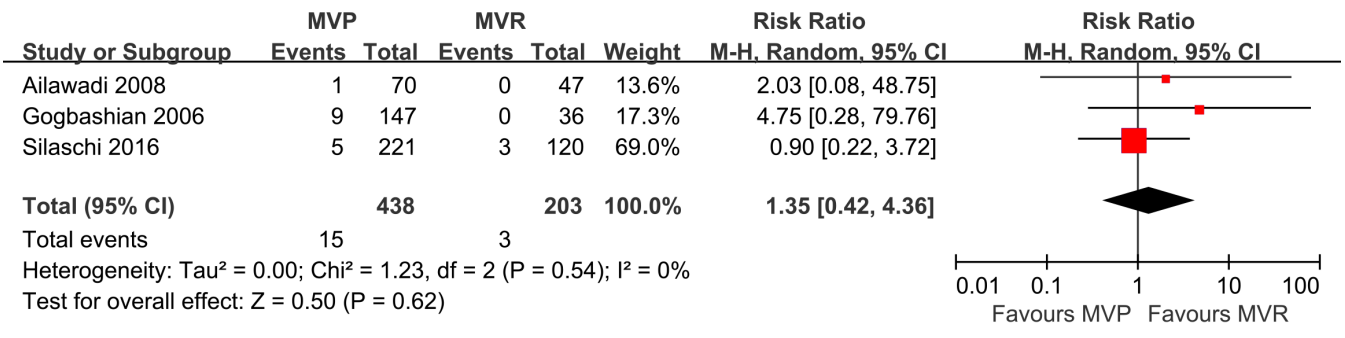

Figure S3 Meta-analysis for reoperation during follow-up. MVP, mitral valve repair; MVR, mitral valve replacement; CI, confidence interval.

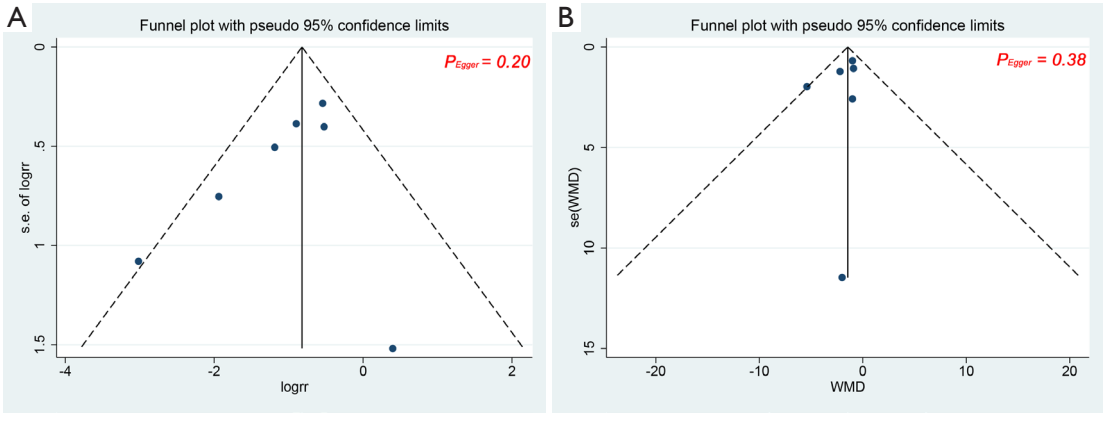

Figure S4 Funnel plots for (A) 30-day mortality and (B) duration of postoperative hospital stay. WMD, weighted mean difference.