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REVIEW ARTICLE

Comparative Efficacy and Safety of Transcatheter Mitral Valve Repair Versus Mitral-valve Surgery in Elderly Patients With Mitral Regurgitation: A Systematic Review and Meta-analysis

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Abstract

Objectives: **Mitral valve surgery is the reference treatment for severe symptomatic mitral regurgitation (MR). Percutaneous mitral valve interventions, such as the MitraClip procedure, offer an alternative, particularly for high-risk patients. The aim of this systematic review and meta-analysis was to analyze the safety and effectiveness of transcatheter mitral valve repair (TMVR) compared to surgical mitral valve repair or replacement (SMVR) in elderly patients with mitral regurgitation.**

Methods: **We searched PubMed, Scopus, Ovid, EBSCO, and ProQuest through July 2024. Eligible studies were randomized controlled trials and observational comparative studies of TMVR versus SMVR for patients with MR, reporting outcomes such as all-cause mortality, MR recurrence, stroke, myocardial infarction, and length of stay (LOS). Statistical analyses were performed using RevMan.**

Results: **Our search identified 3166 records, with 2756 screened and 21 studies included after review. The studies, comprising 20 retrospective cohorts and 1 randomized controlled trial with 20,900 patients, compared TMVR to SMVR. TMVR patients were significantly older than SMVR patients (MD 3.44 years; $P < 0.00001$). Mortality rates were similar at 30 days (relative risk (RR) 1.08; $P = 0.79$) and one year (RR 1.27; $P = 0.18$), but SMVR showed lower mortality at three years (RR 1.82; $P = 0.006$). SMVR also significantly reduced MR $\geq 3+$ recurrence at 30 days (RR 6.95; $P < 0.00001$), one year (RR 3.31; $P = 0.0001$), and three years (RR 4.37; $P < 0.00001$). TMVR was associated with higher myocardial infarction rates (RR 1.58; $P = 0.02$) but reduced LOS (MD -4.88 days; $P < 0.00001$). Sensitivity analysis showed consistent results for recurrence of MR $\geq 3+$ and variable outcomes for other metrics. Evidence of publication bias was noted for mortality at 30 days and LOS.**

Conclusion: **While TMVR with the MitraClip offers shorter hospital stays and is less invasive, SMVR provides better long-term survival and lower MR recurrence rates, emphasizing the need for a tailored approach based on patient risk profiles.**

Keywords: Mitral regurgitation, MitraClip, Transcatheter mitral valve repair, Surgical mitral valve repair, Mortality, Recurrence

1. Introduction

Mitral regurgitation (MR) is one of the most common valvular heart diseases, with its prevalence increasing with age, rising from 6.4% in patients aged 65–74 to >9% in those aged 75 and older [1].

Mitral valve surgery (MVS) is a recognized intervention for severe primary MR in symptomatic patients, as well as those with reduced left ventricular ejection fraction, dilated left ventricular end-systolic diameter, atrial fibrillation (AF), or elevated systolic pulmonary pressure, with surgical repair being preferred over replacement when possible [2,3].

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While MVS is effective for primary MR, its success has not extended to secondary MR, where treatment remains debated, making an unmet need for these patients and high-risk patients with severe MR [4,5].

Despite the high-risk nature of the patients treated, transcatheter mitral valve repair (TMVR) with the MitraClip System (Abbott Vascular, North Chicago, Illinois, USA) has demonstrated very good safety outcomes over the past ten years, though its reduction in MR is less than optimal [6–8].

MitraClip is now accepted as a treatment option for patients with severe symptoms who are at high risk or are not able to undergo surgery [2,9].

Results from the Everest II trial have shown that the procedure is safe and leads to improved clinical outcomes. Surgery still remains a well-established treatment, especially for patients with a EuroSCORE of less than 20% and preserved ejection fraction [10–12].

There is an existing systematic review on this topic [13]. However, the current review was considered necessary because it includes new studies published since the previous review that compare TMVR and MVS procedures. Additionally, this review examines more baseline characteristics such as gender and hypertension, allowing for a better understanding of factors influencing treatment outcomes. It also examined a broader range of outcomes, including the incidence of myocardial infarction (MI) and stroke, and length of hospital stay, providing a more complete evaluation of the benefits and risks of both procedures.

The purpose of this study was to perform a systematic review and meta-analysis comparing the outcomes of TMVR and surgical mitral valve repair or replacement (SMVR) approaches for elderly patients, aged over 60 years, with MR.

Abbreviation

AF	Atrial Fibrillation
CAD	Coronary Artery Disease
CABG	Coronary Artery Bypass Grafting
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CRF	Chronic Renal Failure
DM	Diabetes Mellites
HTN	Hypertension
LOS	Length of Stay
MD	Mean Difference
MI	Myocardial Infarction
MR	Mitral Regurgitation
MVS	Mitral Valve Surgery
NOS	Newcastle–Ottawa Scale
NYHA	New York Heart Association (classification)
PCI	Percutaneous Coronary Intervention
RCT	Randomized Controlled Trial
RR	Relative Risk
SD	Standard Deviation
SMVR	Surgical Mitral Valve Replacement or Repair
TMVR	Transcatheter Mitral Valve Repair

2. Methodology

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement guidelines (PRISMA) during the preparation of this systematic review in reporting our methodology and findings.

2.1. Criteria for considering studies for this review

For our systematic review and meta-analysis, we applied the following inclusion criteria: 1) observational comparative studies and randomized clinical trials (RCTs) that investigated TMVR using the MitraClip device as the intervention, compared to SMVR. 2) Patients with moderate to severe MR, including the following subtypes: primary MR, secondary MR, degenerative MR, functional MR. 3) High-surgical-risk patients, specifically those with comorbid conditions that significantly increase surgical risk. Examples of such patients include those with heart failure, left ventricular dysfunction, reduced left ventricular ejection fraction, or a dilated left ventricular end-systolic diameter. 4) Elderly patients aged over 60 years. The primary outcomes are mortality at 30 days, 1 year, and beyond 3 years; recurrence of mitral regurgitation at the same intervals. The secondary outcomes are the incidence of MI and the incidence of stroke as postoperative complications within the first year; and length of hospital stay. We excluded studies that did not meet these inclusion criteria, as well as animal studies, studies not written in English, case reports, case series, editorials, reviews, and theses without original data.

2.2. Search strategy

To identify relevant studies, we conducted comprehensive searches in several medical electronic databases through July 2024. The databases searched included: PubMed, Scopus, Ovid, EBSCO, and ProQuest, some studies were identified through searching the references of initially identified articles. The search strategy involved the use of specific keywords and Medical Subject Headings (MeSH) terms related to our study objectives. The search terms included: “Mitral Valve Insufficiency”, “Mitral Regurgitation”, “Mitral Insufficiency”,

"Transcatheter Mitral Valve Repair", "MitraClip", "Surgical Mitral Valve Repair", "Safety", "Effectiveness" Mortality", "Recurrence".

2.3. Selection of studies

Two authors independently (SA, RA) applied the selection criteria on all the records. Screening was performed in a two-step process: the first step was to screen titles and abstracts of the retrieved studies for relevance, and in the second step, full texts of potentially eligible studies were reviewed for inclusion. Disagreements were resolved through discussion.

2.4. Data extraction

Four authors extracted the data independently using an online data extraction form. The extracted data fell under the following categories: 1) study design and characteristics, 2) baseline characteristics of the population, 3) quality assessment using Newcastle−Ottawa scale (NOS) and Cochrane Risk of Bias (ROB 1) tool, 4) primary outcomes: mortality and recurrence of mitral regurgitation at 30 days, 1 year, and beyond 3 years, and 5) secondary outcomes: incidence of MI and stroke, and length of stay (LOS).

2.5. Quality assessment of the included studies

Four authors independently assessed the quality of the included cohort studies using the NOS. The EVEREST trial, the one RCT included in our review, was assessed using the Cochrane ROB 1 tool.

2.6. Dealing with missing data

When the mean and standard deviation (SD) were not provided, we calculated them using the median, first and third quartiles, range, and the sample size, following the method described by Wan et al. [14]. However, we did not conduct further assessment to eliminate risk of bias.

2.7. Data analysis and synthesis

Continuous variables are presented as mean ± SD, while categorical variables are shown as n (%). Meta-analyses were performed using relative risk (RR) for categorical variables and mean differences (MD) for continuous variables. Variables reported by two or more studies were pooled. Statistical pooling was conducted using the Mantel-Haenszel method for categorical variables and the inverse variance method for continuous variables. Heterogeneity was assessed through visual inspection of the forest plots and quantified using I-square and Chi-square tests. If significant heterogeneity was detected (Chi-square $P < 0.10$), sensitivity analyses were performed to address it. A random-effects model was applied when outcomes showed heterogeneity to account for potential variation in methodology and participant characteristics between studies; otherwise, a fixed-effects model was used. RR and MD with 95% confidence intervals (CIs) were computed using RevMan 5.3.

2.8. Publication bias

To assess publication bias, we generated funnel plots by plotting the pooled effect estimates against their standard errors using RevMan software. We performed Egger's and Begg's tests for continuous variables [15,16], while for categorical variables, we used the regression test to evaluate funnel plot asymmetry. The presence of publication bias was evaluated by examining the symmetry of the funnel plots and the results of the respective tests. Asymmetry in the funnel plots or significant test results indicated potential publication bias. Publication bias was assessed only when 10 or more studies were included.

3. Results

3.1. Search results

Our search yielded 3166 results (Fig. 1). After removal of duplicates, we screened 2756 records and reviewed 23 full-text reports of which 21 records were included. Two studies were excluded due to an inappropriate study design.

3.2. Characteristics of included studies and quality assessment

In total, the included studies had 22 samples, 20,900 Patients (10,471 TMVR and 10,429 SMVR), 20 retrospective cohorts and one RCT, eight studies involved secondary MR, three studies included primary MR patients, one study had both primary and secondary MR as separate samples, and nine studies did not specify a particular type of MR. In all the studies, TMVR was compared to SMVR. NOS was used for the quality assessment of the cohort studies, in which eight studies were of poor quality (0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain), two studies were of fair quality (2

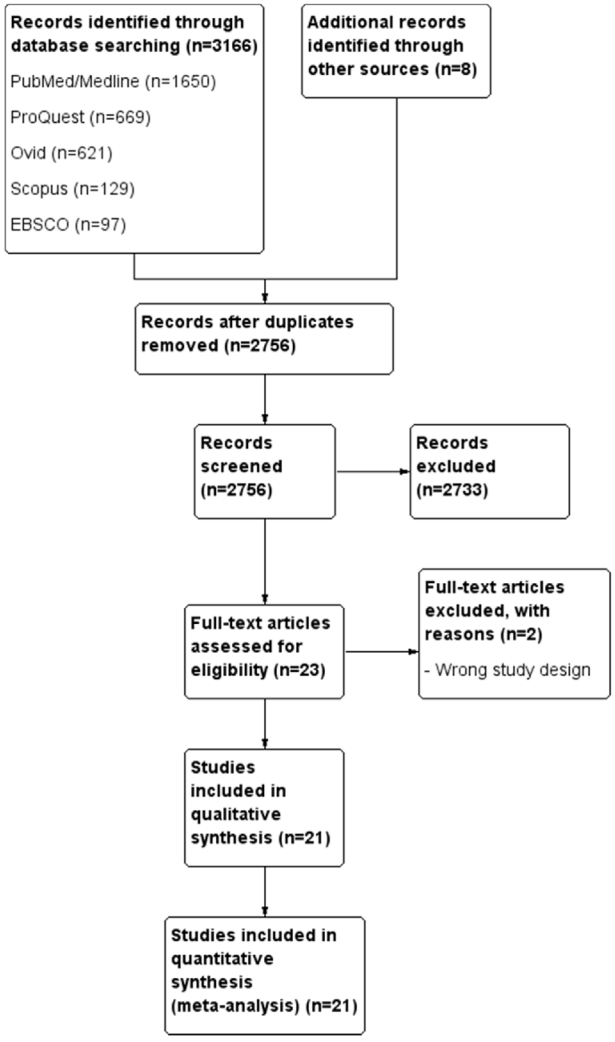

Fig. 1. PRISMA study flow diagram.

stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain) and ten studies were of good quality (3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain), while the EVEREST trial, the one RCT included in our review, was assessed using the Cochrane ROB 1 tool and was found to have moderate quality. See Supplementary Table S1 for detailed quality assessment scoring (see Table 1 for study characteristics).

3.3. Characteristics of included patients

A pooled analysis of the mean age between the TMVR (75.54 years) and SMVR (73.56 years) groups showed that it was significantly higher in the TMVR group than the SMVR group (MD 3.44 years; 95% CI 2.10−4.77 years; P < 0.00001) (figure S1). Gender was reported in all but one study. with pooled analysis showing that the percentage of males was equal between the two groups (RR 0.99, 95% CI 0.94 to 1.05, $P < 0.76$) (figure S2). The logistic EuroSCORE % was reported in 14 studies, where it ranged from as low as 1.8 to as high as 33.7. 14 studies reported the NYHA class III and class IV scores, with pooled results demonstrating a significantly higher percentage of combined NYHA class III/IV score in the TMVR group compared with SMVR group (RR 1.13, 95% CI 1.08 to 1.18, $P < 0.00001$) (figure S3). Regarding pre-existing conditions, 13 studies reported hypertension, 15 studies reported diabetes, 20 studies reported AF, 18 studies reported chronic obstructive pulmonary disease (COPD), 15 reported coronary artery disease (CAD), 13 studies reported chronic renal failure (CRF). The presence of pre-existing conditions varied across studies for the two groups. In 17 studies, the TMVR group had a higher percentage of preexisting conditions compared to the SMVR group. Conversely, one study found that the SMVR group had a higher prevalence of these conditions. Additionally, three studies reported that the prevalence of preexisting conditions was approximately equal between the two groups. Previous cardiac conditions were reported in 12 studies for percutaneous coronary intervention (PCI) and 14 studies for coronary artery bypass grafting (CABG). In most of these studies, the TMVR group had a higher percentage of prior PCI and CABG compared to the SMVR group. For detailed baseline characteristics of the included patients, refer to Table 2.

3.4. Analysis of primary outcomes

The primary outcomes of mortality and recurrence for MR patients undergoing TMVR compared to SMVR are illustrated in Figs. 2 and 3. 12 studies reported mortality at 30 days, with pooled results showing no significant differences between the two groups (RR 1.08, 95% CI 0.63 to 1.83, P = 0.79). 14 studies reported mortality at one year, with pooled results showing a not statistically significant difference (RR 1.27, 95% CI 0.90 to 1.78, P = 0.18). Eight studies reported mortality at three years, with pooled results showing that SMVR significantly reduced mortality compared with TMVR (RR 1.82, 95% CI 1.19 to 2.79, P = 0.006). Overall, the pooled results showed that SMVR significantly reduced mortality compared to TMVR (RR 1.38, 95% CI 1.07 to 1.77, P = 0.01). All the above pooled results demonstrated high heterogeneity ($I^2 \geq 74$), except for mortality at 30 days, which did not show significant heterogeneity. Eight studies reported recurrence of $MR \geq 3+$ at 30 days, with pooled

Table 1. Study characteristics.

Study ID	Study design	Sample size	Population	Intervention	Comparator	Findings
Niikura 2020 [25]	Retrospective study	875 (249 TMVR, 626 SMVR)	Patients who underwent surgical or commercial transcatheter therapy for MR	MitraClip®	Open surgical mitral valve repair or replacement	Commercial transcatheter mitral valve repair may increase cardiac surgery rates and improve clinical outcomes for patients with diverse surgical risks.
Alozie 2017 [26]	Retrospective study	84 (42 TMVR, 42 SMVR)	Patients ≥80 years of age with moderate/severe symptomatic MR	MitraClip®	Surgical mitral valve repair or replacement	Acceptable acute outcomes with either mitral valve surgery or the MitraClip device. Treatment decisions should be based on cumulative surgical risk rather than age.
Kortlandt 2018 [27]	Retrospective study	741 (568 TMVR, 173 SMVR)	Symptomatic high-surgical-risk patients with MR	MitraClip®	Surgical mitral valve repair or replacement	MitraClip has lower mortality than those on conservative treatment and similar survival to surgical patients.
Feldman 2015 [28]	Randomized trial	258 (178 TMVR, 80 SMVR)	Patients with moderately severe or severe (grade 3+ or 4+) MR	MitraClip®	Conventional surgical mitral valve repair or replacement	Percutaneous repair is less effective at reducing mitral regurgitation than conventional surgery but offers better safety and comparable clinical outcomes.
Deharo 2024 [29]	Retrospective study	4320 (2160 TMVR, 2160 SMVR)	Patients with severe MR	MitraClip®	Isolated surgical mitral valve repair or replacement	MitraClip results in lower long-term cardiovascular mortality and fewer instances of pacemaker implantation and stroke compared to mitral surgery.
Haberman 2021 [30]	Retrospective study	205 (99 TMVR, 106 SMVR)	Patients with secondary MR following acute MI	MitraClip®	Surgical mitral valve repair or replacement	Early intervention improves prognosis in post −MI MR patients. Percutaneous mitral valve repair is a viable alternative to surgery for high-risk patients.
Paranskaya 2013 [31]	Retrospective study	50 (24 TMVR, 26 SMVR)	Patients with EuroSCORE ≥20%, LVEF ≤45%, and grade 3/4 MR	MitraClip®	Surgical mitral valve repair	Surgical repair and MitraClip are valid treatments for severe MR when performed by experienced operators, with MitraClip reserved for nonsurgical patients.
Anwer 2019 [32]	Retrospective study	131 (56 TMVR, 75 SMVR)	Patients with severe MR due to degenerative MVP	MitraClip®	Open surgical mitral valve repair	Surgical repair is more durable than the percutaneous approach. While MitraClip use has increased, it still has higher rates of residual or recurrent MR.
Swaans 2014 [33]	Retrospective study	193 (139 TMVR, 53 SMVR)	High-surgical-risk patients with symptomatic severe MR	MitraClip®	Surgical mitral valve repair or replacement	TMVR resulted in similar survival rates to surgical treatment and better survival than conservative treatment.
Taramasso 2012 [34]	Retrospective study	143 (52 TMVR, 91 SMVR)	Symptomatic patients with severe FMR and severe LV dysfunction due to idiopathic or post-ischemic dilated cardiomyopathy	MitraClip®	Surgical mitral valve repair	MitraClip therapy results in lower hospital mortality and shorter stays compared to surgery but has higher early and 1-year recurrent MR rates.
Amabile 2023 [35]	Retrospective study	1100 (550 TMVR, 550 SMVR)	Patients with secondary MR	MitraClip®	Surgical mitral valve repair	Surgical repair showed significantly better survival rates and lower reintervention rates at 1 and 3 years compared to TMVR.

Majmundar 2024 [36]	Retrospective study	4374 (2187 TMVR, 2187 SMVR) 4356 (2178 TMVR, 2178 SMVR)	Patients with primary MR and MR in HFrEF	MitraClip®	Surgical mitral valve repair	MitraClip showed better short-term outcomes, but had significantly higher medium-term MACE compared to SMVR in both cohorts.
De Bonis 2016 [37]	Retrospective study	120 (55 TMVR, 65 SMVR)	Patients with severe LV dysfunction and secondary MR	MitraClip®	Surgical edge-to-edge repair	MitraClip is safe for high-risk patients, but surgical repair is more effective post-operatively and at mid-term follow-up.
Buzzatti 2015 [7]	Retrospective study	60 (25 TMVR, 35 SMVR)	Octogenarian patients affected by isolated DMR	MitraClip®	Isolated surgical mitral valve repair or replacement	MitraClip patients had fewer postoperative complications despite being older and having more comorbidities. However, their two-year mortality was higher, likely due to comorbidities.
Gyoten 2020 [38]	Retrospective study	132 (85 TMVR, 47 SMVR)	Symptomatic patients with FMR and severe LV dysfunction (LVEF $\leqq$ 30%)	MitraClip®	Surgical mitral valve repair or replacement	MitraClip therapy resulted in lower perioperative complications and mortality than SMVR. Surgically treated patients had less residual MR, fewer re-hospitalizations for heart failure, and lower cardiac mortality.
Ondrus 2016 [39]	Retrospective study	72 (24 TMVR, 48 SMVR)	High-risk patients with significant FMR and severe heart failure	MitraClip®	Minimally invasive mitral valve repair	Despite differences in expertise and risk profiles, both surgical and MitraClip groups had similar 30-day and long-term outcomes.
Malik 2020 [40]	Retrospective study	2910 (1455 TMVR, 1455 SMVR)	Patients $\geq$80 years of age	MitraClip®	Surgical mitral valve repair or replacement	SMVR had a 4-fold higher mortality compared to TMVR and resulted in more cardiac, vascular, hemorrhagic, and respiratory complications.
Okuno 2021 [41]	Retrospective study	202 (101 TMVR, 101 SMVR)	Patients with secondary MR	MitraClip®	Surgical mitral valve repair	There was no significant difference in 2-year survival between TMVR and surgical repair. However, surgical repair resulted in greater and more durable SMR reduction and improved LVEF.
Buzzatti 2019 [42]	Retrospective study	306 (100 TMVR, 206 SMVR)	Low-intermediate risk elderly patients with DMR	MitraClip®	Isolated surgical mitral valve repair	MitraClip resulted in lower acute post-operative complications and better 1-year survival compared to surgery. However, it had greater MR recurrence and reduced survival beyond 1 year.
Conradi 2013 [43]	Retrospective study	171 (95 TMVR, 76 SMVR)	Patients with severe secondary MR	MitraClip®	Isolated surgical mitral valve repair	Surgery was more effective at reducing MR than MitraClip. However, many patients benefited from MitraClip.
Silaschi 2024 [44]	Retrospective study	98 (49 TMVR, 49 SMVR)	Elderly patients with MR	MitraClip®	Minimally invasive mitral valve repair	Patients undergoing TMVR had initially lower one-year survival compared to surgery, but this difference disappeared after matching. MR reduction was less effective.

Surgical mitral intervention (repair or replacement, SMVR); Secondary mitral regurgitation (SMR), Transcatheter mitral valve repair (TMVR), Mitral valve prolapse (MVP); Heart failure with reduced ejection fraction (HFrEF); Functional mitral regurgitation (FMR); Degenerative mitral regurgitation (DMR); Mitral regurgitation (MR); Left ventricular (LV); Left ventricular ejection fraction (LVEF); Major adverse cardiovascular events (MACE); Myocardial infarction (MI); EuroSCORE [European System for Cardiac Operative Risk Evaluation].

Table 2. Baseline clinical characteristics in TMVR versus. SMVR group.

Study ID	Group	Age	Male	European Score	NYHA III/IV	HTN	DM	AF	COPD	CAD	CRF	PCI	CABG
Niikura 2020 [25]	TMVR	82 ± 7.8	121 (48.6)			187 (75.1)	56 (22.5)	167 (67.1)	70 (28.1)	120 (48.2)		61 (24.5)	62 (24.9)
	SMVR	64.3 ± 12.4	388 (62)			346 (55.3)	97 (15.5)	181 (28.9)	71 (11.3)	195 (31.2)		68 (10.9)	29 (4.6)
Alozie 2017 [26]	TMVR	82.2 ± 1.65	24 (57.1)	11.3 ± 5.63	41 (89.3)		18 (42.9)	29 (69.0)	14 (33.3)	26 (61.9)	32 (76.2)	7 (16.7)	
	SMVR	81.7 ± 1.35	19 (45.2)	12.1 ± 10.6	34 (81)		14 (33.3)	23 (54.8)	10 (23.8)	31 (73.8)	26 (61.9)		16 (38)
Kortlandt 2018 [27]	TMVR	73.96 ± 10.45	321 (56.5)	8.03 ± 7.23	490 (86.3)	285 (50.2)	131 (23.1)	316 (55.6)	113 (19.9)	325 (57.2)	213 (38.4)	167 (29.5)	172 (30.3)
	SMVR	69.05 ± 9.84	95 (54.9)	4.36 ± 3.84	118 (68.2)	86 (50.0)	42 (24.3)	77 (44.5)	40 (23.1)	69 (39.9)	24 (16.3)	19 (11.0)	19 (11)
Feldman 2015 [28]	TMVR	67 ± 12.7	113 (63.5)		89 (50)	129 (72.5)	14 (7.9)	56 (32.9)	27 (15.3)	83 (46.9)		42 (23.7)	37 (20.8)
	SMVR	64.7 ± 12.6	53 (66.2)		40 (50)	66 (82.5)	1 (8.8)	29 (38.7)	11 (13.8)	35 (43.8)		13 (16.3)	13 (16.3)
Deharo 2024 [29]	TMVR	76.0 ± 8.5	1259 (58.3)	3.9 ± 1.2		1482 (68.6)	419 (19.4)	1566 (72.5)	303 (14.0)	1065 (49.3)	380 (17.6)	371 (17.2)	122 (5.7)
	SMVR	76.0 ± 8.5	1253 (58.0)	3.9 ± 1.2		1451 (67.2)	380 (17.6)	1568 (72.6)	285 (13.2)	1090 (50.5)	335 (15.5)	380 (17.6)	103 (4.8)
Haberman 2021 [30]	TMVR	71 ± 10	48 (48.5)	12.7 ± 10.5	99 (100)	70 (71)	47 (47)		16 (16)	80 (81)	30 (30)	94 (94)	28 (27)
	SMVR	68 ± 10	78 (73.6)	10.3 ± 8.3	106 (100)	67 (63)	36 (34)		9 (8)	78 (74)	13 (12)	37 (35)	1 (<1)
Paranskaya 2013 [31]	TMVR	80 ± 5	10 (41.7)	12.3 ± 3.7	21 (87.5)	24 (100)	12 (15)	15 (62.5)	5 (20.8)	14 (58.3)	15 (62.5)	2 (8.3)	
	SMVR	63 ± 12	17 (65.4)	3.9 ± 3.7	25 (96.2)	15 (57.7)	2 (7.7)	14 (53.8)	2 (7.7)	6 (23.1)	5 (19.2)	0 (0)	
Anwer 2019 [32]	TMVR	75.7 ± 8.6	45 (80.4)				43 (76.8)	40 (71.4)	32 (57.1)				51 (78.5)
	SMVR	68.6 ± 13.1	58 (77.3)				9 (12.0)	61 (81.3)	8 (10.6)				38 (50.7)
Swaans 2014 [33]	TMVR	74.6 ± 9.4	94 (67.6)	23.9 ± 16.0	123 (88.5)	74 (53.2)	32 (23)	74 (53.2)	31 (22.3)	89 (64.0)	55 (39.6)	41 (29.5)	59 (42.4)
	SMVR	70.2 ± 9.5	27 (50.9)	14.2 ± 8.9	47 (88.7)	28 (52.8)	10 (18.9)	27 (50.9)	15 (28.3)	28 (52.8)	9 (17.0)	5 (9.4)	9 (17)
Taramasso 2012 [34]	TMVR	68.4 ± 9.2	43 (82.7)	21.9 ± 4.8	44 (80.6)		14 (26.9)	37 (17.3)	11 (21.2)	37 (71.2)	30 (57.7)		12 (23.1)
	SMVR	64.9 ± 9.8	70 (76.9)	10.2 ± 7.4	61 (67)		9 (9.9)	29 (32)	3 (3.3)	44 (48.3)	16 (17.6)		9 (9.9)
Amabile 2023 [35]	TMVR	72.6 ± 10.1	366 (66.55)			455 (82.73)		324 (58.91)					
	SMVR	72.1 ± 9.1	356 (64.73)			453 (82.36)		323 (58.73)					
Majmundar 2024 [36] Primary MR	TMVR	72.5 ± 12	1113 (50.9)			1712 (78.3)	398 (18.2)	980 (44.8)	521 (23.80	160 (7.3)	35 (1.6)	147 (6.7)	77 (3.5)
	SMVR	72.3 ± 9.3	1089 (49.8)			1706 (78)	402 (18.4)	964 (44.1)	512 (23.40	175 (8)	35 (1.6)	168 (7.7)	107 (4.9)
MR in HFrEF	TMVR	68.1 ± 13.2	1239 (56.9)			1734 (79.6)	571 (26.2)	980 (45)	601 (27.60	255 (11.7)	35 (2.5)	209 (9.6)	107 (4.9)
	SMVR	68 ± 9.8	1257 (57.7)			1727 (79.3)	577 (26.5)	969 (44.5)	584 (26.80	285 (13.1)	35 (3.1)	253 (11.6)	166 (7.6)
De Bonis 2016 [37]	TMVR	68.3 ± 9.17	46 (83.6)	19.15 ± 3.82	45 (81.8)			19 (34.5)					
	SMVR	63.2 ± 10.05	45 (69.2)	11 ± 0.85	56 (86.1)			14 (21.5)					
Buzzatti 2015 [7]	TMVR	84.5 ± 3.2		19.725 ± 4.5	17 (68)			10 (40)	6 (24)	7 (28)	19 (76)		3 (12)
	SMVR	81.9 ± 2.0		8.475 ± 0.73	13 (37)			7 (20)	3 (9)	7 (20)	20 (57)		2 (6)
Gyoten 2020 [38]	TMVR	71 ± 8.2	21 (70)	29 ± 16	84 (99)	29 (97)	15 (50)	13 (43)	5 (17)		36 (42)	10 (3.3)	
	SMVR	71 ± 8.5	17 (61)	30 ± 24	46 (97)	27 (90)	7 (23)	20 (67)	5 (17)		12 (26)	6 (20)	13 (43)
Ondrus 2016 [39]	TMVR	75 ± 9	18 (75)	18 ± 14	21 (88)			18 (75)					15 (63)
	SMVR	76 ± 4	27 (56)	14 ± 11	44 (92)			33 (69)					15 (31)
Malik 2020 [40]	TMVR	83.7 ± 2.8	665 (46.7)			1106 (76)	226 (15.5)	1000 (68.7)	460 (31.6)		402 (27)		
	SMVR	83.7 ± 2.5	714 (49.1)			1100 (75.6)	230 (15.8)	1005 (69.1)	540 (37.1)		340 (23.4)		
Okuno 2021 [41]	TMVR	69.3 ± 12.03	64 (63.4)	8 ± 5.5	64 (63.4)	67 (66.3)	25 (24.8)	34 (33.7)	18 (17.8)	41 (42.6)	55 (54.5)	60 (59.4)	15 (14.9)
	SMVR	69.7 ± 6.8	70 (69.3)	6.2 ± 4.9	68 (67.3)	74 (73.3)	33 (32.7)	30 (29.7)		37 (36.6)	52 (51.5)	30 (29.7)	16 (15.8)
Buzzatti 2019 [42]	TMVR	82.9 ± 3.5	55 (55)		66 (66)			33 (33)	19 (19)	28 (28)			
	SMVR	78.8 ± 3.13	118 (57)		81 (39)			25 (12)	14 (6.8)	41 (20)			
Conradi 2013 [43]	TMVR	72.4 ± 8.1	61 (64.2)	33.7 ± 18.7	93 (97.9)	73 (76.8%)	38 (40)	55 (57.9)	27 (28.7)	50 (52.6)	9 (9.9)		
	SMVR	64.5 ± 11.4	34 (44.7)	10.1 ± 8.7	67 (88.2)	56 (73.7%)	19 (25)	35 (46.1)	12 (15.8)	22 (29)	5 (6.6)		
Silaschi 2024 [44]	TMVR	71.7 ± 8.57	28 (57.1)	2.3 ± 1.43				34 (69.4)	12 (24.5)	7 (14.3)		17 (34.7)	
	SMVR	70.0 ± 7.5	24 (49)	1.8 ± 1.43				20 (40.8)	6 (12.2)	4 (8.2)		3 (6.1)	

Data are n, mean ± SD, median (range), or n (%).

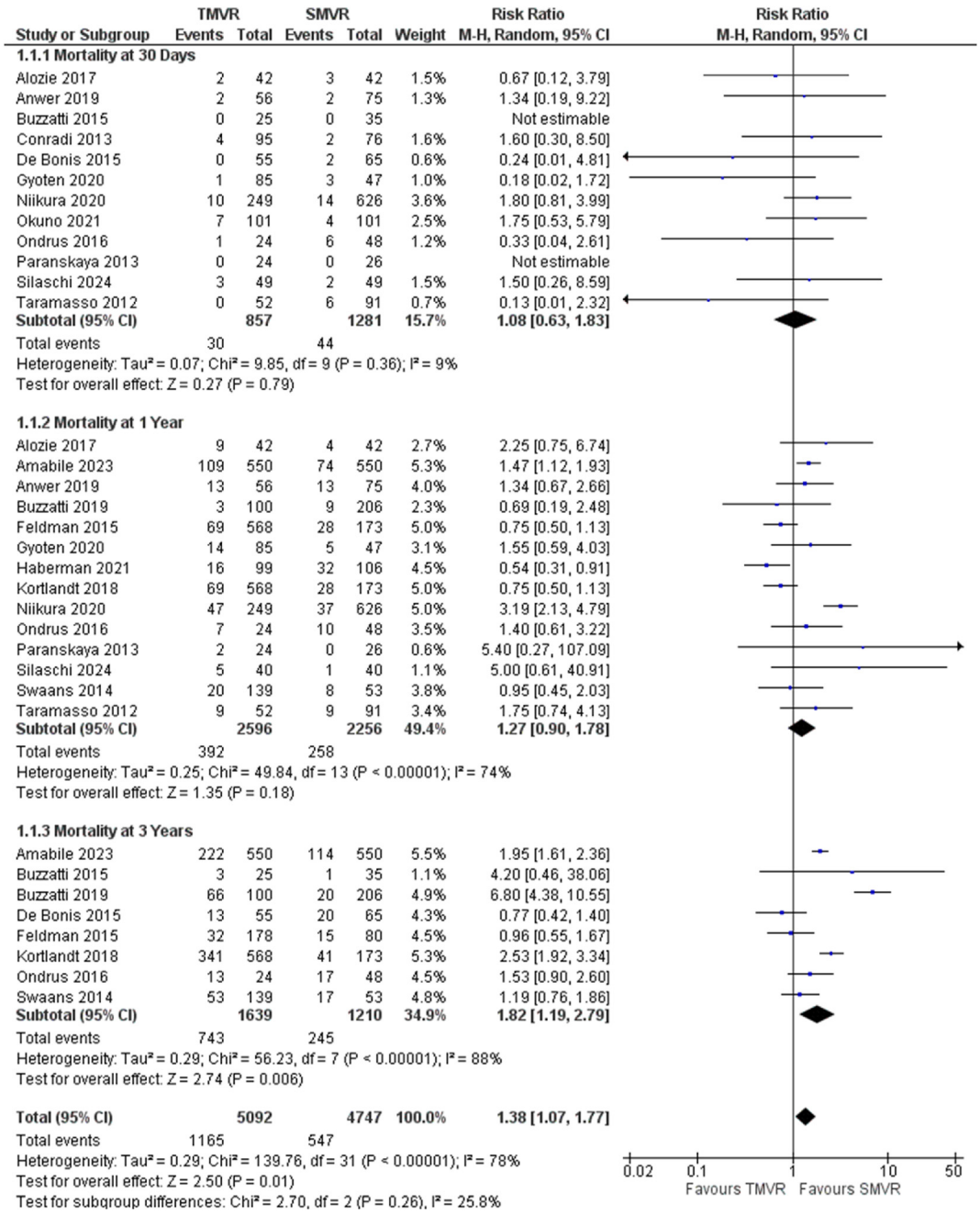

Fig. 2. Forest plot of risk ratios of mortality for MitraClip versus surgical mitral valve repair or replacement at 30 days, 1 year and 3 years. CI = confidence interval; M–H = Mantel-Haenszel.

results showing that SMVR significantly reduced recurrence compared to TMVR (RR 6.95, 95% CI 3.42 to 14.14, $P < 0.00001$). Nine studies reported recurrence of $MR \geq 3+$ at one year, with pooled results showing significantly lower rates of recurrence of $MR \geq 3+$ with SMVR compared to TMVR (RR 3.31, 95% CI 1.80 to 6.06, $P = 0.0001$). Five studies reported recurrence of $MR \geq 3+$ at three years, with pooled results showing significantly lower rates of recurrence of $MR \geq 3+$ with SMVR (RR 4.37, 95% CI 2.48 to 7.70, $P < 0.00001$). Overall, pooled results showed significantly lower rates of recurrence of $MR \geq 3+$ with SMVR (RR 4.09, 95% CI 2.74 to 6.10, $P < 0.00001$). All the pooled results for recurrence of MR $\geq$ 3 + were not heterogeneous, except for recurrence at one year and the overall results, which were highly heterogeneous ($I^2 \geq 61$). While high heterogeneity was observed in the pooled results for

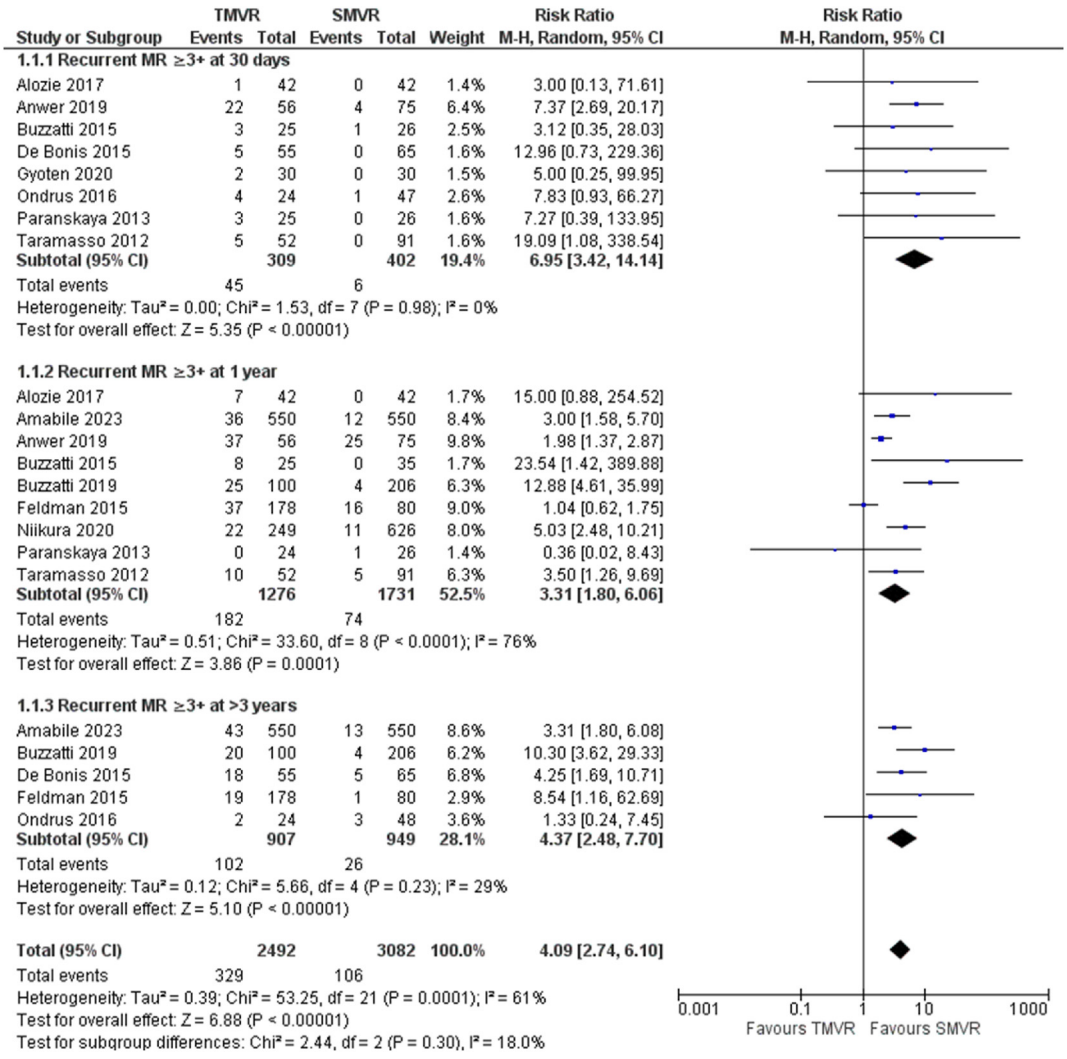

Fig. 3. Forest plot of risk ratios of MR recurrence for MitraClip versus surgical mitral valve repair or replacement at 30 days, 1 year, and >3 years. CI = confidence interval; M–H = Mantel-Haenszel.

mortality and recurrence outcomes, no specific measures were taken to control this heterogeneity, indicating a need for caution in interpreting these findings. Future studies may consider stratifying analyses by factors such as patient demographics, procedural techniques, or comorbidities to better understand the sources of heterogeneity and their impact on the outcomes.

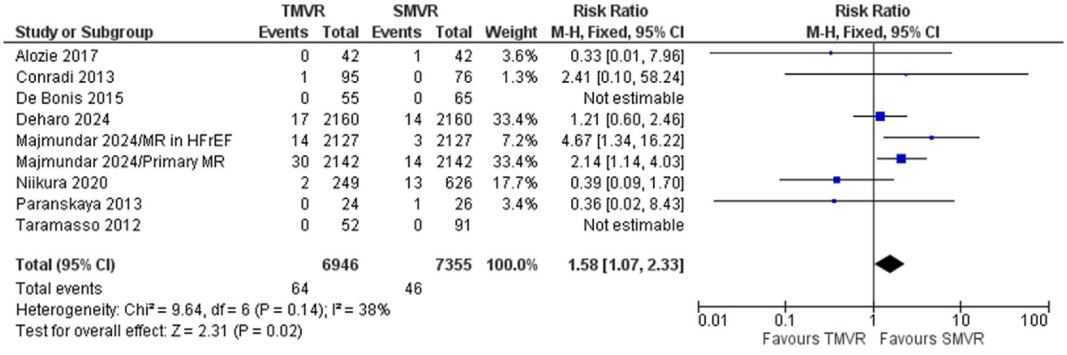

Fig. 4. Forest plot of pooled risk ratios of MI for MitraClip versus surgical mitral valve repair or replacement. CI = confidence interval; M–H = Mantel-Haenszel.

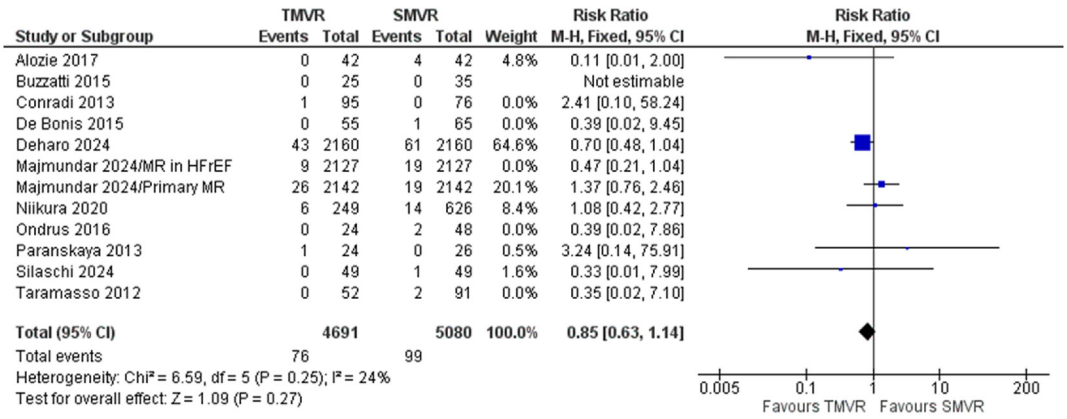

Fig. 5. Forest plot of pooled risk ratios of stroke for MitraClip versus surgical mitral valve repair or replacement. CI = confidence interval; M–H = Mantel-Haenszel.

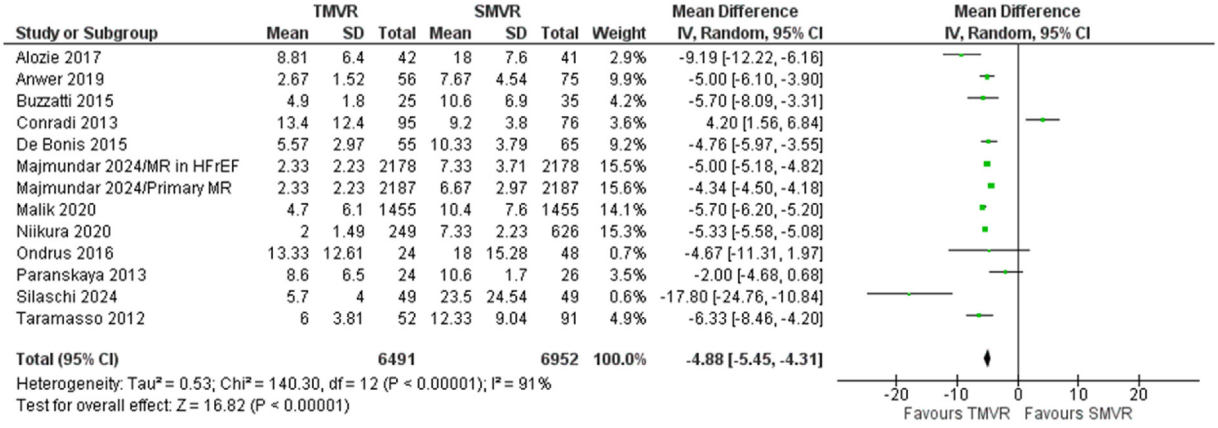

Fig. 6. Forest plot of pooled effect estimates comparing length of stay for MitraClip versus surgical mitral valve repair or replacement. CI = confidence interval; IV = inverse variance.

3.5. Analysis of secondary outcomes

All secondary outcomes are displayed in Figs. 4–6. Eight studies reported MI as a post-procedural complication, with pooled results showing a significantly higher incidence of MI with TMVR compared to SMVR (RR 1.58, 95% CI 1.07 to 2.33, $P = 0.02$). 11 studies reported stroke as a postprocedural complication, with pooled results showing no statistically significant difference between the two groups in stroke incidence (RR 0.78, 95% CI 0.59 to 1.02, $P = 0.07$). 12 studies reported LOS, with pooled results showing that TMVR significantly reduced LOS compared to SMVR (MD -4.88, 95% CI -5.45 to −4.31, $P < 0.00001$). All pooled results were not heterogeneous, except for LOS, which showed high heterogeneity ($I^2 = 92$).

3.6. Sensitivity analysis

Results of the sensitivity analysis are shown in Supplementary Figure S4-S8. When restricting the analysis to studies with secondary MR, the pooled results for mortality at 30 days (12 studies) and one year (14 studies) remained insignificant. However, the meta-analysis outcomes for mortality at three years (8 studies) and overall mortality became insignificant under the same restriction. The pooled results of recurrence of $MR \geq 3+$ remained significant when the analysis was restricted to secondary MR studies. After the restriction, pooled results for mortality at 30 days remained homogeneous, while the heterogeneity for mortality at one year, three years, and overall mortality decreased ($I^2 = 74$ *to* 67, $I^2 = 88$ *to* 77, and $I^2 = 78$ *to* 64, respectively). For recurrence of MR ≥ 3 +, the results at 30 days and three years remained homogeneous after restriction, while those at one year and the overall results became homogeneous. The pooled results of MI incidence and LOS remained significant, whereas stroke incidence became significant after the restriction. The meta-analysis outcomes of MI and stroke incidence remained homogenous while those for LOS remained heterogeneous following the restriction.

3.7. Publication bias

The funnel plots for mortality at 30 days and at one year, LOS and stroke are shown in Supplementary Figure S9-S12. The bias indicators for mortality at 30 days demonstrated evident publication bias (Regression test for funnel plot asymmetry, P = 0.041), while there was no evident publication bias for mortality at one year and stroke (Regression test for funnel plot asymmetry, P = 0.216 and P = 0.697, respectively). There was an evident publication bias for LOS (Egger's Regression and Begg's and Mazumdar Rank Correlation, P = 0.735 and P = 1.000, respectively).

4. Discussion

This systematic review and meta-analysis compared the safety and efficacy of TMVR with those of SMVR. In terms of mortality, we found no significant differences between the two groups at 30 days, consistent with previous meta analyses conducted by Khader et al. [17], Felbel et al. [18], Oh et al. [19], Takagi et al. [20], Wan et al. [21], and Yuan et al. [13]. At one year, our results align with Felbel et [18], Takagi et [20], and Kaddoura et al. [22], but different from the findings of Oh et al. [19] and Yuan et al. [13] who reported an increased risk with TMVR, which could be, in part, due to the higher comorbidity burden and higher calculated logistic EuroSCORE among TMVR patients in these studies.

The pooled results at three years indicated a significant reduction in mortality for the SMVR group compared to TMVR, which aligns with Yuan et al. [13] but contrasts with Cardoso et al. [23] and Takagi et al. [20] where the study found no significant differences between the two groups, which could be attributed to the much smaller sample sizes and fewer studies included in these meta-analyses. Therefore, SMVR should be considered for patients who are expected to live longer and can withstand the surgical procedure (low surgical risk), as it offers a better chance of long-term survival.

In regard to recurrence of $MR \geq 3+$, the study found significantly lower rates of recurrence with SMVR at 30 days, one year and three years, consistent with Cardoso et al. [23], Khader et al. [17],Takagi et al. [20], and Yuan et al. [13] but different from Felbel et al. [18] and Wan et al. [21] where no significant difference was found, which could be a result of the smaller sample sizes in these studies not being able to detect the difference between the groups, so for patients where preventing the recurrence of MR is crucial, SMVR might be the preferred treatment to ensure lasting valve repair and reduce the need for re-interventions.

As for postprocedural stroke, we found no statistically significant difference between the groups, which agrees with Barros da Silva et al. [24], Cardoso et al. [23], Khader et al. [17], OH et al. [19], and Yuan et al. [13]. However, we found a significantly higher incidence of postprocedural MI with TMVR, indicating the need for careful patient selection and monitoring. The higher incidence of postprocedural MI in TMVR patients may be due to several factors. One possible reason is the increased mechanical stress on the mitral apparatus during the deployment of the MitraClip device, which can result in incomplete leaflet coaptation or device-related trauma. These factors can lead to elevated left ventricular pressures, promoting myocardial ischemia. Furthermore, residual mitral regurgitation, which is more common following TMVR, may exacerbate left ventricular overload, contributing to myocardial oxygen demand and ischemic events. Additionally, TMVR patients typically present with a higher cardiovascular risk profile, including pre-existing coronary artery disease (CAD), advanced age, and poorer left ventricular function compared to those undergoing SMVR. These baseline characteristics likely predispose them to a higher risk of postprocedural MI. Specifically, patients with prior MI or severe CAD are particularly vulnerable to ischemic complications following the procedure. Given these risks, careful preoperative evaluation, including coronary artery assessments and optimization of medical management, is essential for TMVR candidates. The use of perioperative strategies such as antiplatelet agents and statins could potentially mitigate the risk of MI in these high-risk patients. Moreover, closer postprocedural monitoring is recommended for early detection and management of ischemic events.

As for LOS, our study found that it was significantly lower with TMVR, consistent with Cardoso et al. [23], Khader et al. [17] and Oh et al. [19]. This suggests that while SMVR may be more beneficial for long-term outcomes, TMVR offers advantages in terms of recovery and shorter hospital stays. However, this study has several limitations that must be considered when interpreting the findings. A key limitation is that only one randomized controlled trial (RCT) was included, with the rest of the data coming from retrospective studies. The predominance of non-randomized studies introduces potential selection biases, which may impact the overall quality and reliability of the data. Additionally, there were significant differences in comorbidity burden between patients undergoing SMVR and those receiving MitraClip procedures. Specifically, the MitraClip cohort had a higher logistic

EuroSCORE, indicating a higher risk profile due to its use in patients considered high risk for surgery. This disparity in baseline characteristics could have influenced the comparative outcomes. In particular, TMVR patients tend to have higher logistic EuroSCOREs, reflecting a higher surgical risk due to advanced age, greater comorbidity burden, and poorer baseline cardiovascular health. These factors, combined with a higher prevalence of prior myocardial infarction, reduced left ventricular function, and other cardiovascular risk factors such as diabetes and hypertension, increase the likelihood of adverse postoperative outcomes. The selection of TMVR in high-risk patients underscores its role as a less invasive alternative for individuals who are not suitable candidates for open surgery. However, this also means that such patients are inherently more prone to complications like MI, stroke, and residual MR. Identifying these risk factors is crucial for tailoring the therapeutic approach and improving patient outcomes in both TMVR and SMVR populations.

Another limitation is the moderate to considerable heterogeneity observed in the meta-analyses, largely due to variations in patient demographics such as age and comorbidity levels. While we performed a sensitivity analysis to reduce heterogeneity in some outcomes, variability remained in others, underscoring the complexity of comparing these treatment options.

Given these limitations, the findings should be interpreted with caution. They highlight the necessity for further research, particularly through well-designed and adequately powered RCTs, to confirm and strengthen these results.

To overcome the limitations of this review, future research should focus on several strategies. First, the need for more RCTs is critical, as our analysis relied heavily on retrospective studies, introducing selection bias. Well-powered RCTs with balanced patient characteristics between TMVR and SMVR will provide stronger, more reliable evidence.

Second, longer follow-up periods are needed to better capture the long-term outcomes of these procedures. While SMVR has been studied extensively, the long-term durability of TMVR, particularly its impact on survival and MR recurrence, requires further investigation through extended follow-up studies.

The heterogeneity in our analysis highlights the need for standardization in future studies. The variability in patient demographics, study designs, and outcome reporting complicates comparisons and limits the ability to draw firm conclusions. Future research should aim to standardize protocols and outcome measures, such as defining consistent criteria for MR severity and post-procedural complications. Reducing this variability will allow for more meaningful comparisons and improve the quality of pooled results in future meta-analyses.

Lastly, future research should focus on patient-specific risk factors to help guide treatment selection between TMVR and SMVR. Tailoring interventions based on individual risk profiles can optimize outcomes and improve clinical decision-making.

5. Conclusion

In conclusion, this systematic review and meta-analysis demonstrate that while TMVR and SMVR have comparable short-term survival rates, SMVR offers better long-term survival and lower rates of MR recurrence. TMVR patients, who are typically older and at higher surgical risk, face a higher risk of postprocedural MI but benefit from shorter hospital stays. A personalized treatment approach is crucial to improve outcomes for these patients.

Ethical approval

As this systematic review does not involve primary data collection from human participants, ethical approval was not required. The review adheres to the guidelines and principles of evidence synthesis and analysis.

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Conflict of interest

The authors of this study declare no conflict of interest.

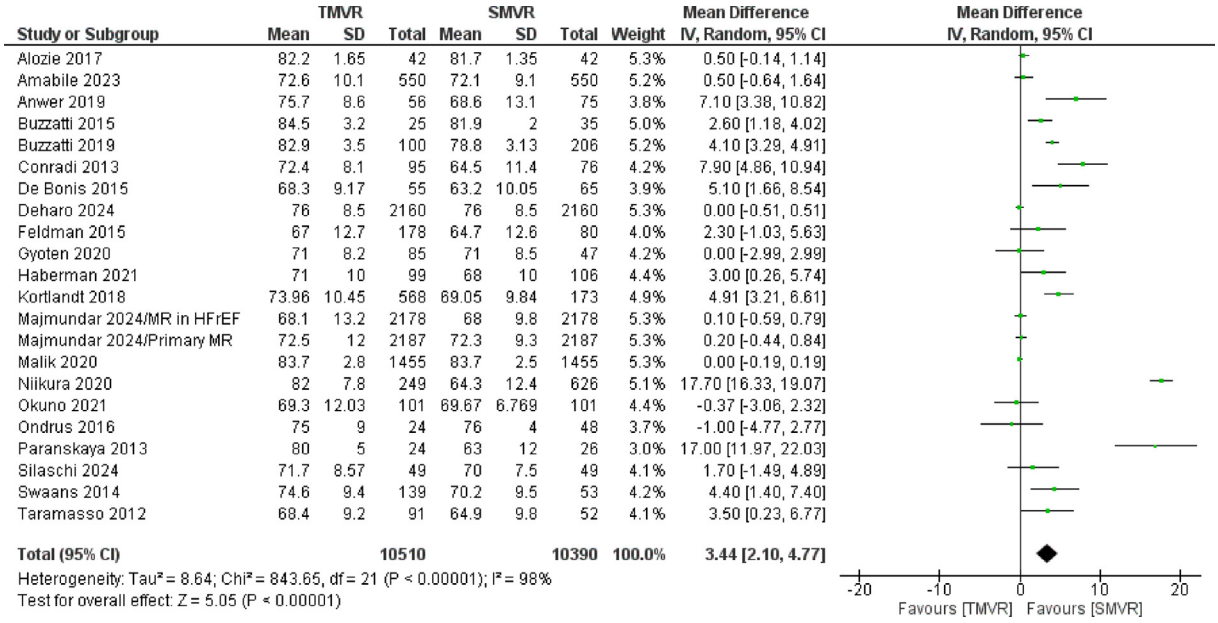
Author contributions

Conception and design of Study: SA. Literature review: SA, ML, RA, Acquisition of data: SA, ML, RA. Analysis and interpretation of data: SA, ML, SA. Research investigation and analysis: SA, ML. Data collection: SA, ML, RA, SA. Drafting of manuscript: SA, ML, RA, SA. Revising and editing the manuscript critically for important intellectual contents: SA, ML. Data preparation and presentation: SA, ML, RA, SA. Supervision of the research: SA. Research coordination and management: SA.

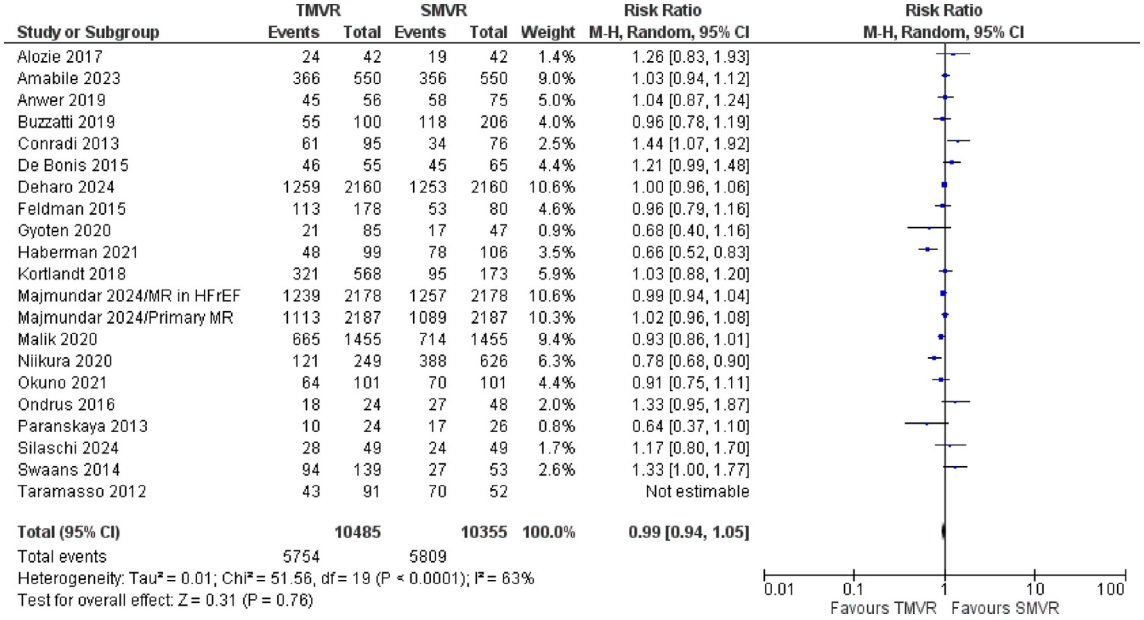
Appendix

Supplementary Table S1. The Newcastle–Ottawa Scale (NOS) quality assessment of the included studies in this meta-analysis (details).

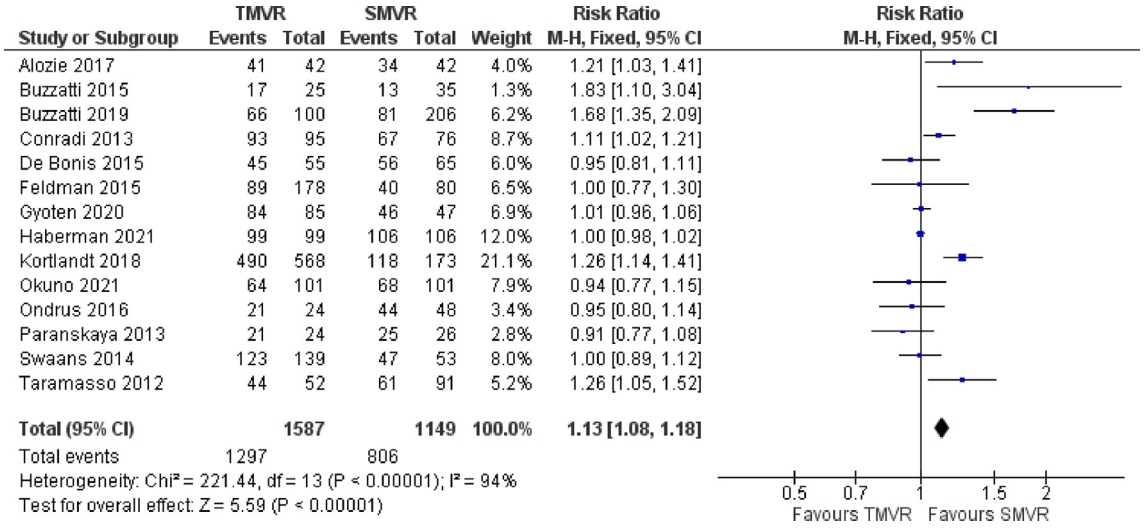
Study	Selection of cohorts				Comparability of cohorts	Outcome		
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts based on the design or analysis	Assessment of outcome	Was follow up long enough for outcomes to occur	Adequacy of follow up of cohorts
Niikura 2020 [25]			☆	☆		☆	☆	☆
Alozie 2017 [26]		☆	☆	☆	☆	☆	☆	☆
Kortlandt 2018 [27]			☆	☆	☆	☆	☆	☆
Deharo 2024 [29]	☆	☆	☆	☆	☆☆	☆	☆	☆
Haberman 2021 [30]			☆	☆	☆	☆		
De Bonis 2016 [37]			☆	☆		☆		☆
Buzzatti 2015 [7]		☆	☆	☆	☆	☆		☆
Gyoten 2020 [38]		☆	☆	☆	☆	☆		☆
Ondrus 2016 [39]		☆	☆	☆	☆	☆		☆
Malik 2020 [40]		☆	☆	☆	☆☆	☆		
Okuno 2021 [41]		☆	☆	☆	☆	☆		☆
Paranskaya 2013 [31]			☆	☆		☆		☆
Anwer 2019 [32]		☆	☆	☆	☆	☆		☆
Swaans 2014 [33]		☆	☆	☆	☆	☆		☆
Taramasso 2012 [34]			☆	☆	☆	☆		☆
Amabile 2023 [35]			☆	☆	☆☆	☆		
Majmundar 2024 [36]	☆	☆	☆	☆	☆	☆		☆
Buzzatti 2019 [42]	☆	☆	☆	☆	☆	☆	☆	☆
Conradi 2013 [43]		☆	☆	☆		☆		☆
Silaschi 2024 [44]		☆	☆	☆	☆☆	☆		☆



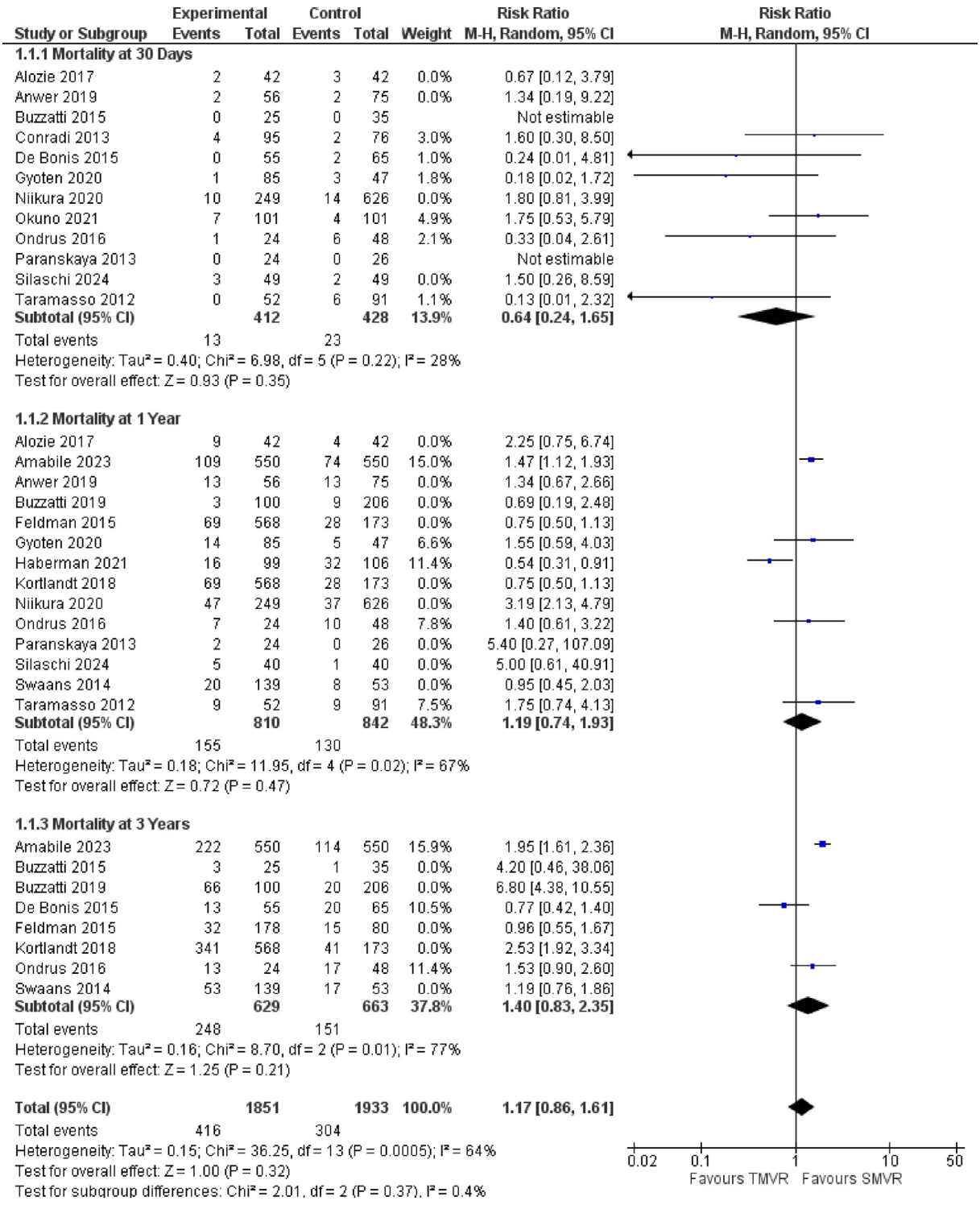
Supplementary Figure S1. Forest plot of pooled effect estimate comparing the mean age of patients for MitraClip versus surgical mitral valve repair or replacement. CI = confidence interval; IV = inverse variance.



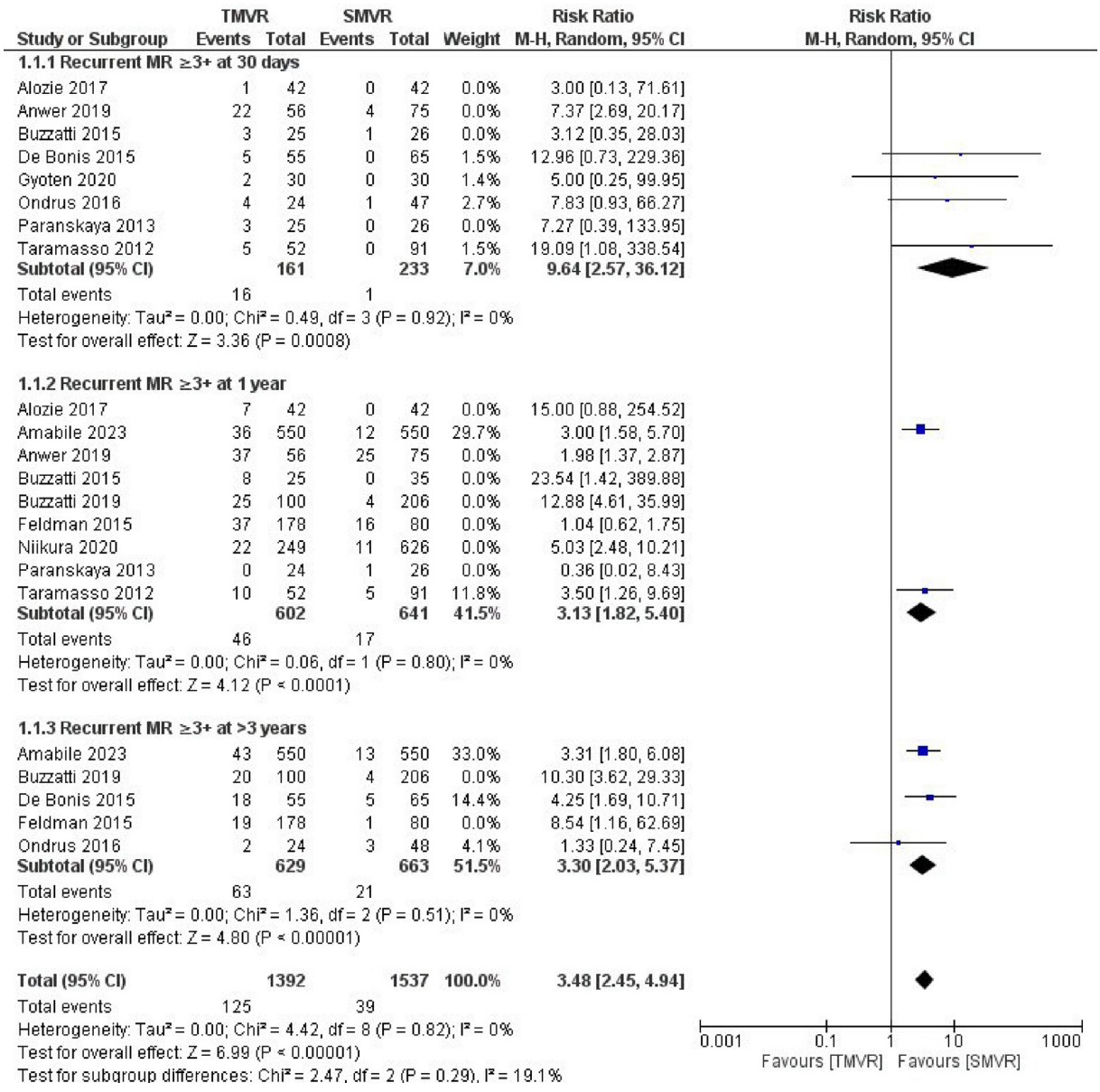
Supplementary Figure S2. Forest plot of pooled effect estimate comparing the gender (male) proportion of patients for MitraClip versus surgical mitral valve repair or replacement. CI = confidence interval; M–H = Mantel-Haenszel.



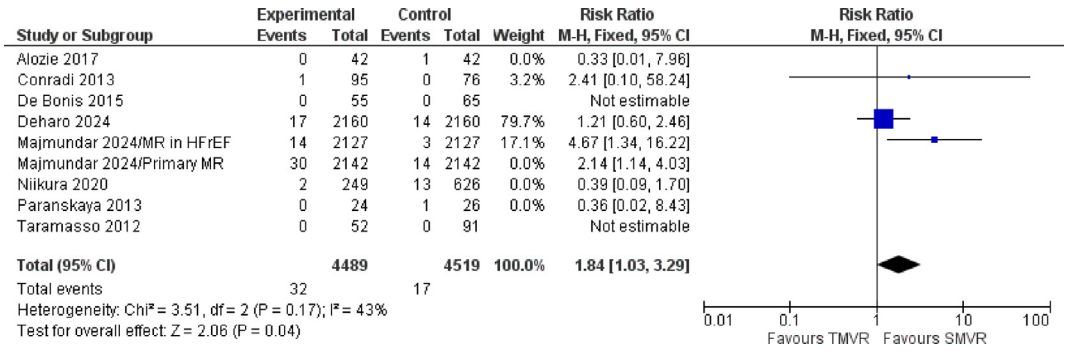
Supplementary Figure S3. Forest plot of pooled effect estimate comparing the NYHA class III/IV score of patients for MitraClip versus surgical mitral valve repair or replacement. CI = confidence interval; M–H = Mantel-Haenszel.



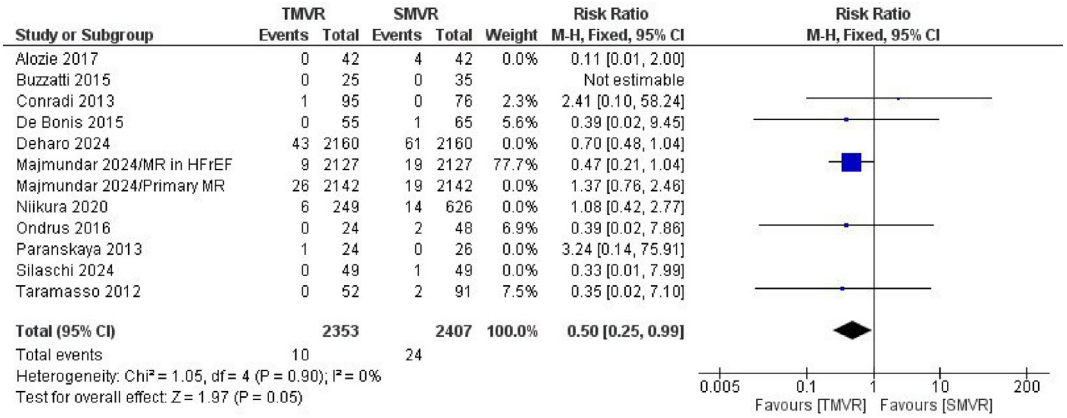
Supplementary Figure S4. Forest plot showing sensitivity analysis of mortality after restricting the analysis to studies with secondary MR. CI = confidence interval; M–H = Mantel-Haenszel.



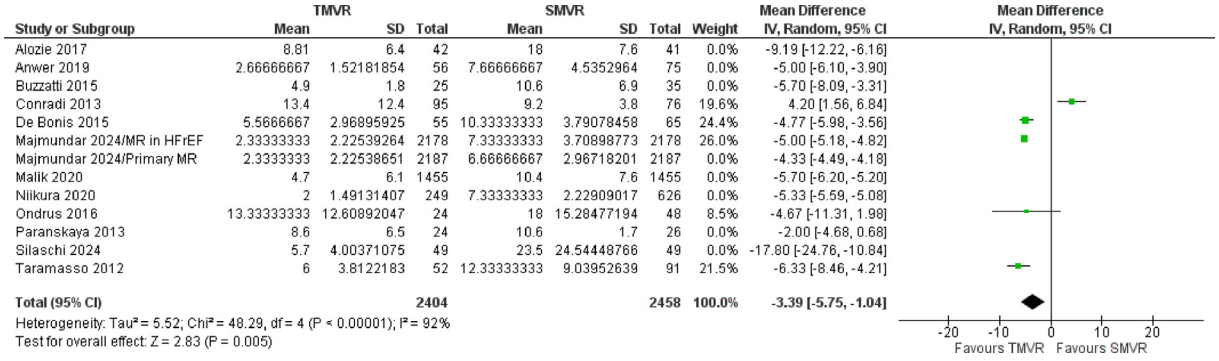
Supplementary Figure S5. Forest plot showing sensitivity analysis of recurrent MR after restricting the analysis to studies with secondary MR. CI = confidence interval; M–H = Mantel-Haenszel.



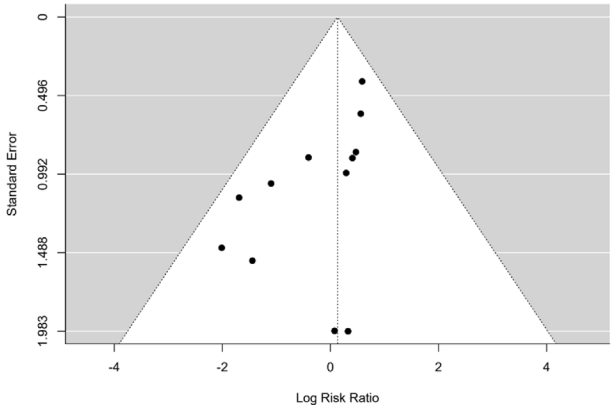
Supplementary Figure S6. Forest plot showing sensitivity analysis of MI after restricting the analysis to studies with secondary MR. CI = confidence interval; M–H = Mantel-Haenszel.



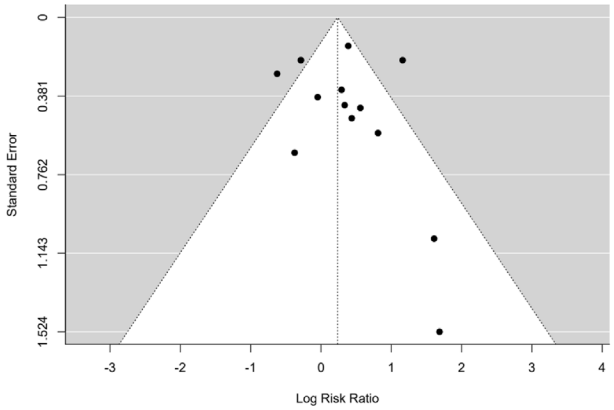
Supplementary Figure S7. Forest plot showing sensitivity analysis of stroke after restricting the analysis to studies with secondary MR. CI = confidence interval; M–H = Mantel-Haenszel.



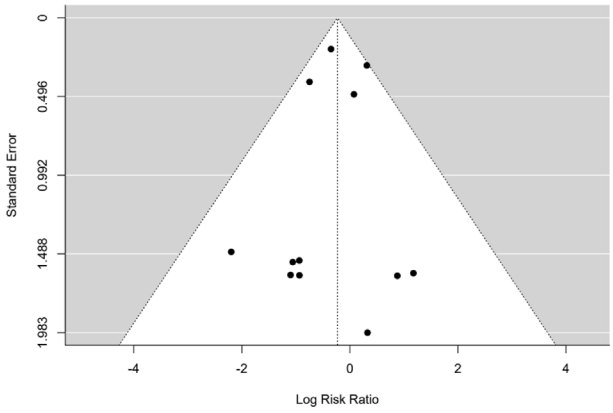
Supplementary Figure S8. Forest plot showing sensitivity analysis of length of stay after restricting the analysis to studies with secondary MR. CI = confidence interval; IV = inverse variance.



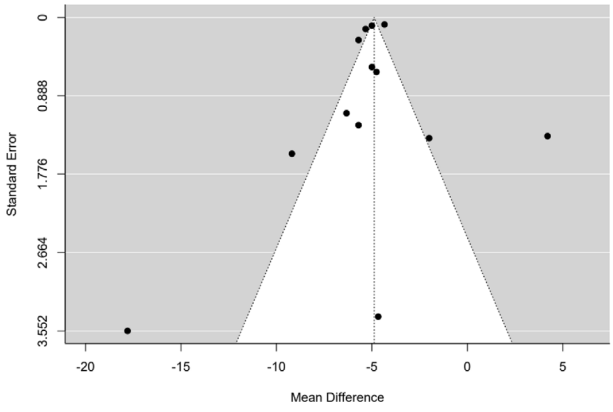
Supplementary Figure S9. Funnel plot of mortality at 30 days for publication bias assessment.



Supplementary Figure S10. Funnel plot of mortality at 1 year for publication bias assessment.



Supplementary Figure S11. Funnel plot of incidence of stroke for publication bias assessment.



Supplementary Figure S12. Funnel plot of length of stay for publication bias assessment.

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