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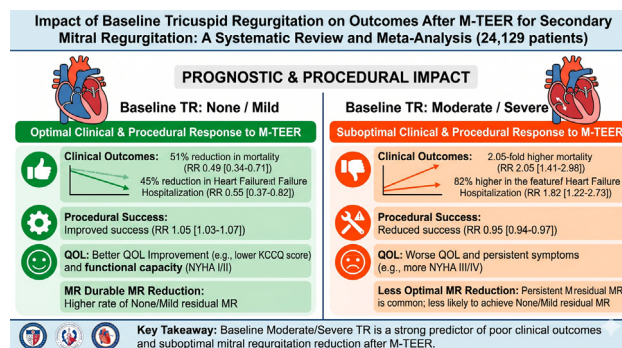
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Impact of baseline tricuspid regurgitation on outcomes after mitral transcatheter edge-to-edge repair: A systematic review and meta-analysis

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GRAPHICAL ABSTRACT



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ABSTRACT

Introduction: Mitral transcatheter edge-to-edge repair (M-TEER) has become a cornerstone for treating patients with mitral regurgitation (MR). However, the prognostic impact of baseline tricuspid regurgitation (TR) on outcomes after M-TEER remains uncertain. This systematic review and meta-analysis evaluates the influence of baseline TR in patients undergoing M-TEER.

Methods: We searched PubMed, Embase, SCOPUS, Cochrane Library, and Web of Science through January 2026. Studies comparing outcomes in patients with none/mild TR versus moderate/severe TR after M-TEER were included. Data were synthesized using random-effects models.

Results: Eight observational studies involving 24,129 patients were included. Compared to patients with none/mild TR, those with baseline moderate/severe TR had a 2.05-fold higher risk of all-cause mortality (RR 2.05; 95% CI:

Abbreviations: M-TEER, mitral transcatheter edge-to-edge repair; TR, tricuspid regurgitation; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; MD, mean difference; RR, risk ratio; MR, mitral regurgitation.

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1.41–2.98) and an 82% higher risk of heart failure rehospitalization (RR 1.82; 95% CI: 1.22–2.73). Moderate/severe TR was also associated with a 5% lower likelihood of procedural success (RR 0.95; 95% CI: 0.94–0.97). Regarding echocardiographic outcomes, patients with baseline moderate/severe TR had a 12% lower probability of achieving none/mild residual MR (RR 0.88; 95% CI: 0.80–0.97) and a 20% higher risk of moderate residual MR (RR 1.20; 95% CI: 1.05–1.38), though the risk of severe residual MR did not differ significantly between groups. Baseline moderate/severe TR was associated with a 48% higher risk of NYHA class $\geq$ III at follow-up (RR 1.48; 95% CI: 1.27–1.73). Although statistically significant, the pooled differences in follow-up sPAP (MD: 0.25 mmHg) and LVEF (MD: -0.08%) were clinically negligible, while no significant differences were observed in TAPSE.

Conclusions: Baseline moderate/severe TR is strongly associated with a worse prognosis and limited functional recovery following M-TEER. Further studies are warranted to determine whether simultaneous or staged TR interventions improve outcomes in patients undergoing M-TEER.

1. Introduction

Mitral transcatheter edge-to-edge repair (M-TEER) has emerged as an effective therapeutic approach for patients with severe MR, improving symptoms, functional capacity, health-related quality-of-life (QOL), and prognosis [1,2]. Baseline tricuspid regurgitation (TR) is common in patients with severe mitral regurgitation (MR), and when moderate or severe may also affect prognosis, influencing the response to M-TEER [1,2]. In this regard prior studies have reported that moderate/severe TR is reduced to none/mild in only 34–37% of patients after M-TEER [2,3].

However, the optimal management strategy for patients presenting with this concomitant valvular burden remains a critical clinical dilemma. Specifically, it is highly debated whether significant baseline TR should alter candidate selection for mitral intervention, or whether isolated M-TEER is inherently insufficient in patients with an advanced right-heart disease substrate. Furthermore, whether significant TR should be addressed simultaneously with dedicated transcatheter tricuspid devices or managed conservatively via a staged clinical strategy remains unresolved [1–3]. Given these uncertainties, the present systematic review and meta-analysis aims to evaluate the impact of baseline TR on the prognosis and QOL outcomes following M-TEER.

2. Methods

This systematic review and meta-analysis was conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [4,5] (Table S1). The study protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD420261300832).

2.1. Search strategy

A comprehensive search of PubMed, Embase, SCOPUS, the Cochrane Library, and Web of Science was performed by two independent reviewers (RP and JC) from database inception through January 2026. The search strategy combined the following terms using Boolean operators (“AND”, “OR”): (“Tricuspid Valve Insufficiency” OR “tricuspid regurgitation” OR “tricuspid insufficiency”) AND (“Mitral Valve surgery” OR “Mitral Valve Annuloplasty” OR “MitralClip” OR “Pascal” OR “M-TEER” OR “transcatheter mitral valve repair” OR “edge-to-edge repair”). No language or publication date restrictions were imposed. Additionally, the reference lists of included studies and relevant review articles were manually screened (snowballing method) to identify further eligible studies.

Articles were imported into the Rayyan platform (<https://www.rayyan.ai/>) [6]. All articles that did not directly relate to the topic of interest were excluded, and duplicate records were removed. This step was performed independently by two reviewers (RP and JC), and any uncertainties were resolved with the assistance of a third researcher (RSM).

2.2. Inclusion and exclusion criteria

The objective of this systematic review was to examine the impact of baseline TR on post-procedural outcomes after M-TEER. The PICOTT

strategy [7] was applied, encompassing the following components: Population (P): Patients with Tricuspid Regurgitation (TR), undergoing M-TEER; Intervention (I): Severe/Moderate TR; Comparison (C): None/Mild TR; O (Outcome): Echocardiographic outcomes; functional status (NYHA class); heart failure hospitalization (HFH) and mortality; T (Type of Study): randomized and observational; Time (T): No restriction.

Studies were excluded that: 1) Did not assess baseline TR, did not stratify outcomes by baseline TR, or exclusively evaluated patients without significant TR; 2) Compared M-TEER with other therapeutic modalities for MR (surgical or transcatheter) without specifically analyzing the impact of baseline TR; 3) Evaluated M-TEER in combination with other valvular interventions or device-based therapies (e.g., concomitant tricuspid intervention), without allowing isolated assessment of baseline TR; 4) Did not report (at a minimum) QOL outcomes using validated assessment instruments. In addition, case reports, conference abstracts, narrative or systematic reviews, editorials, letters to the editor, and other non-original research formats were excluded. Disagreements between reviewers were resolved through discussion with a third reviewer (RSM).

2.3. Data extraction and outcomes

The following were extracted from the selected articles: authors, study location, study design (randomized controlled trial [RCT] vs. cohort studies), sample size and age, patient characteristics (including baseline TR severity), and duration of follow-up. Clinical, echocardiographic, and functional outcomes were assessed. Clinical outcomes were all-cause mortality, HFHs, and procedural success. Of note, given the nature of pooling multi-center and single-center cohorts spanning different publication timelines, procedural success was extracted as defined by the investigators of each primary study. This endpoint generally reflected a composite of successful transcatheter device deployment and reduction of residual mitral regurgitation to severe-grade-free status (typically $MR \leq 2+$) at discharge, without immediate procedural or in-hospital mortality. Echocardiographic outcomes were MR severity at follow-up (none/mild vs. moderate vs. severe), systolic pulmonary artery pressure (sPAP), tricuspid annular plane systolic excursion (TAPSE) and left ventricular ejection fraction (LVEF). Functional outcomes were New York Heart Association (NYHA) functional class.

Data extraction and management were independently performed by two reviewers (RP and JC) using a standardized Excel spreadsheet. Any disagreements or uncertainties were resolved through discussion with a third reviewer (RSM).

2.4. Quality assessment

The Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool was applied to non-randomized studies, focusing on bias related to study design, confounding factors, participant selection, and outcome assessment [8]. Two independent reviewers (RP and JC) conducted the risk-of-bias assessments, assigning judgments according to the established criteria for each ROBINS-I domain. Disagreements or uncertainties were resolved through discussion with a third reviewer (RSM).

2.5. Statistical analysis

Outcomes were analyzed according to the presence and severity of baseline TR (moderate or severe vs. none or mild) as reported in the original studies using R version 4.5.2 ('meta' package) for data synthesis [9]. Significance was set at two-sided $p < 0.05$. Both fixed and random-effects models were applied to estimate 95% CIs, addressing potential clinical heterogeneity. The choice of a random-effects framework was methodologically prioritized precisely to account for the anticipated clinical and temporal heterogeneity across cohorts, including substantial variations in individual study follow-up durations (ranging from 30 days to approximately 2 years), thereby allowing the underlying effect sizes to vary across different observation windows. The Mean Difference (MD) was employed for continuous outcomes, and the Risk Ratio (RR) was used as the effect measure for dichotomous variables. Heterogeneity was quantified using the I^2 statistic and Cochran's Q, with 40% and 75% serving as benchmarks for substantial and high variability, respectively. Data stability was tested through LIO sensitivity diagnostics. Finally, the influence of individual studies and the presence of publication bias were assessed using Baujat and Funnel plots. Of note, a formal meta-regression to quantitatively explore clinical drivers of heterogeneity such as device type, MR etiology, or baseline right ventricular function was not performed due to the aggregate nature of the available literature and because our analysis included 8

primary studies, falling short of the methodological recommendation of a minimum of 10 studies required to provide adequate statistical power for such meta-regression models.

3. Results

3.1. Study selection

The literature search identified 6431 records from five databases (PubMed ($n = 1253$), Scopus ($n = 1196$), Embase ($n = 2505$), Cochrane Library ($n = 57$), Web of Science ($n = 1420$)). After removal of 2890 duplicate records, 3541 articles were screened by title and abstract. Of these, 3489 were excluded due to irrelevance. A total of 52 reports were assessed for full-text eligibility, with no reports unavailable for retrieval. Among them, 44 studies were excluded, mainly due to insufficient data ($n = 32$), overlapping populations ($n = 7$), or other reasons ($n = 5$). Ultimately, 8 studies [10–17] met the inclusion criteria and were included in the qualitative and quantitative synthesis (Fig. 1).

3.2. Baseline characteristics of the included studies

The eight included studies were all observational in design, predominantly retrospective cohorts, and were conducted in Europe and the

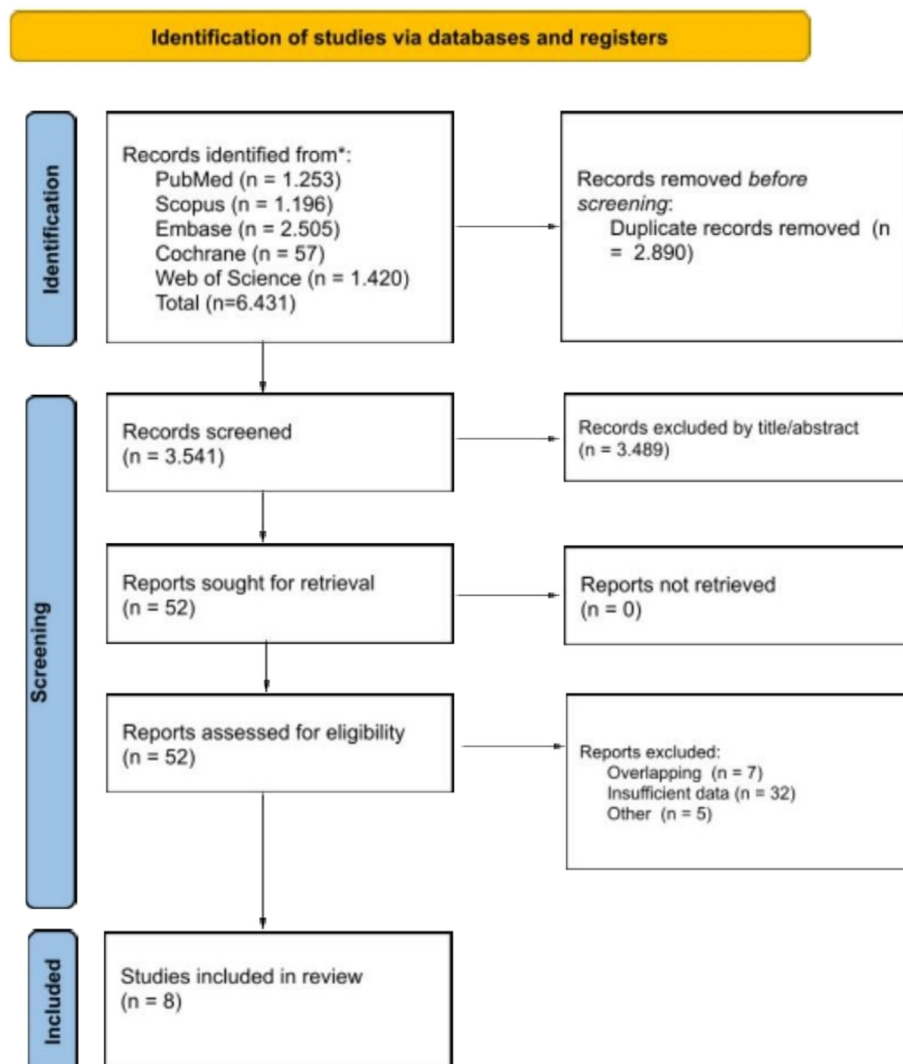


Fig. 1. PRISMA flow diagram.

Table 1
Baseline characteristics of the studies and patients.

Study	Country	Design	Patients	Male (%)	Age	HTN	Diabetes	Prior PCI	Prior MI	Prior CABG	LVEF	Follow up (months)
Brooks [10]	United States	Multicenter retrospective	1838	48 (60.3%)	75.8 ± 10.3	714 (89%)	255 (31.8%)	308 (38.4%)	272 (33.9%)	196 (24.4%)	47.9 ± 15.4	30 days
Gröger [11]	Germany	Single-center retrospective observational	740	531 (51.3%) 173 (62.0%) 260 (56.4%)	78.4 ± 10.1 No/mild: 75.0 ± 8.8 Mod: 78.2 ± 8.1 Sev: 78.1 ± 8.1	963 (93%) NR	332 (32.0%) 91 (32.6%) 107 (23.2%)	334 (32.2%) NR	314 (30.3%) NR	276 (26.6%) NR	47.2 ± 15.6 No/mild: 43.2 ± 16.5 Mod: 45.0 ± 17.2 Sev: 44.5 ± 17.8	Up to 12 months
Meijerik [12]	Netherlands	Single-center retrospective observational	146	51 (54.3%) 24 (46.2%)	74.6 ± 10.4 78.4 ± 8.8	54 (57.4%) 37 (71.2%)	22 (23.4%) 14 (26.9%)	25 (26.6%) 8 (15.4%)	46 (48.9%) 20 (38.5%)	21 (22.3%) 11 (21.2%)	37.9 ± 12.4 39.5 ± 15.9	2 years
Sammour [13]	United States	Multicenter retrospective observational	19,593	5900 (57.7%) 3432 (33.6%)	No/mild: 76.2 ± 10.4 Mod: 77.5 ± 10.1 Sev: 77.9 ± 10.6	8,750 (85.6%) 8,193 (87.4%) 149 (67.7%)	971 (9.5%) 2753 (29.4%) 56 (25.5%)	3432 (33.6%) 2868 (30.6%) NR	2758 (27.0%) 2387 (25.5%) NR	NR	No/mild: 47.3 ± 15.4 Mod: 46.1 ± 15.8 Sev: 46.2 ± 15.7	1 year 721 ± 194 days
Schueler [14]	Germany	Single-center retrospective observational	261	155 (70.5%) 26 (63.4%)	80.5 ± 7.5 80.6 ± 8.3	149 (67.7%) 29 (70.7%)	13 (31.7%)	NR	NR	NR	43.5 ± 16.4 42.6 ± 15.5	Up to 1 year
Shechter [15]	United States	Single-center retrospective observational	1287	411 (66.0%) 365 (55.0%)	No/mild: 77 (68–84) Mod: 79 (72–86) Sev: 78 (68–85)	521 (83.6%) 551 (83.0%) 54 (84.4%)	158 (25.4%) 192 (28.9%) 17 (26.6%)	254 (40.8%) 273 (41.1%) 4 (6.3%)	254 (40.8%) 273 (41.1%) 10 (15.6%)	254 (40.8%) 273 (41.1%) 18 (28.1%)	54 (32–63) Mod: 52 (28–63) Sev: 45 (23–62)	Up to 1 year
Ueyama [16]	United States	Single-center retrospective observational	135	29 (45.3%) 23 (32.4%)	73 [65, 78] 73 [67, 79]	55 (77.5%) 44 (75.9%)	15 (21.2%) 18 (31%)	11 (15.5%) 28 (48.3%)	16 (22.5%) 28 (48.3%)	18 (25.4%) 11 (19%)	50 [40, 60] 43 ± 14	3 years
Yzeiraj [17]	Germany	Single-center retrospective observational	129	37 (63.8%) 48 (59.3%)	74.4 ± 7.9 77.8 ± 6.9	73 (90.1%)	27 (33.3%)	38 (46.9%)	35 (43.2%)	18 (22.2%)	45 ± 16	428 ± 386 days

Data are for none or mild/moderate or severe TR groups unless shown as 3-level. Data are presented as mean ± standard deviation, number (no.), or median (interquartile range). Abbreviations: BMI = body mass index; CABG = coronary artery bypass grafting; HTN = hypertension; LVEF = left ventricular ejection fraction (%); MI = myocardial infarction; MR = mitral regurgitation; PCI = percutaneous coronary intervention; TR = tricuspid regurgitation; NR = not reported; NA = not available.

United States. Sample sizes varied substantially, ranging from 129 to 19,593 patients per study. In total, 24,129 patients were included in the analysis. Across studies, the majority of patients were male and the median age ranged from the mid-70s to early 80s. The prevalence of cardiovascular comorbidities, including hypertension, diabetes mellitus, prior myocardial infarction, and prior coronary revascularization, was high. Baseline LVEF was generally preserved or mildly reduced. The severity of TR varied across cohorts, with a substantial proportion of patients having moderate to severe TR at baseline (Table 1).

3.3. Clinical outcomes

Median times to clinical follow-up across the studies ranged from 30 days to a mean follow-up interval of 721 ± 194 days. Six studies with 23,562 total patients reported data on all-cause mortality, including 11,516 patients with moderate/severe TR and 12,046 patients with none/mild TR. The pooled RR for mortality in patients with moderate/severe baseline TR compared with none/mild TR was 2.05 (95% CI: 1.41 to 2.98) using a random-effects model (Fig. 2). Heterogeneity across the studies was high ($I^2 = 82.7\%$, $p < 0.0001$).

Three studies with 21,450 total patients reported data on HFHs, including 10,328 patients with moderate/severe TR and 11,122 patients with none/mild TR. The pooled RR for HFHs in patients with moderate/severe baseline TR compared with none/mild TR was 1.82 (95% CI: 1.22–2.73) (Fig. 3). Heterogeneity across the studies was high ($I^2 = 89.6\%$, $p < 0.0001$).

Four studies with 22,059 total patients reported data on procedural success of M-TEER, including 10,637 patients with moderate/severe TR and 11,422 patients with none/mild TR. The pooled RR for M-TEER procedural success in patients with moderate/severe baseline TR compared with none/mild TR was 0.95 (95% CI: 0.94 to 0.97) (Fig. 4). Heterogeneity across the studies was low ($I^2 = 8.7\%$, $p = 0.35$).

3.4. Echocardiographic outcomes: recurrent MR post-intervention

Median times to echocardiographic follow-up across the studies ranged from 30 days to a mean follow-up interval of 721 ± 194 days. Seven studies with 23,060 total patients reported data on no/mild MR post-intervention, including 11,135 patients with moderate/severe TR and 11,925 patients with none/mild TR. The pooled RR for no/mild MR in patients with moderate/severe baseline TR compared with none/mild TR was 0.88 (95% CI: 0.80 to 0.97) (Fig. 5). Heterogeneity across the studies was moderate ($I^2 = 47.9\%$, $p = 0.07$).

Five studies with 2907 total patients reported data on moderate MR post-intervention, including 1471 patients with moderate/severe TR and 1436 patients with none/mild TR. The pooled RR for moderate MR in patients with moderate/severe baseline TR compared with none/mild TR was 1.20 (95% CI: 1.05 to 1.38) (Fig. 6). Heterogeneity across the studies was less than moderate ($I^2 = 33.5\%$, $p = 0.19$).

Seven studies with 23,070 patients reported data on severe MR post-intervention, including 11,135 patients with moderate/severe TR and 11,935 with none/mild TR. The pooled RR for severe MR post-intervention in patients with moderate/severe baseline TR compared with none/mild TR was 1.20 (95% CI: 0.90 to 1.60) (Fig. 7). Heterogeneity across the studies was substantial ($I^2 = 51\%$, $p = 0.05$).

3.5. Other echocardiographic outcomes

Two studies with 400 total patients reported data on sPAP, including 122 patients with moderate/severe TR and 278 patients with none/mild TR. The pooled MD was 0.25 mmHg (95% CI: 0.01 to 0.49) (Fig. 8). Heterogeneity across the studies was substantial ($I^2 = 0\%$). Four studies with 20,351 total patients reported data on LVEF, including 9595 patients with moderate/severe TR and 10,756 patients with none/mild TR. The pooled MD was −0.08% (95% CI: −0.10 to −0.05) (Fig. 9). Heterogeneity across the studies was low ($I^2 = 0\%$). Finally, three studies with 546 total patients

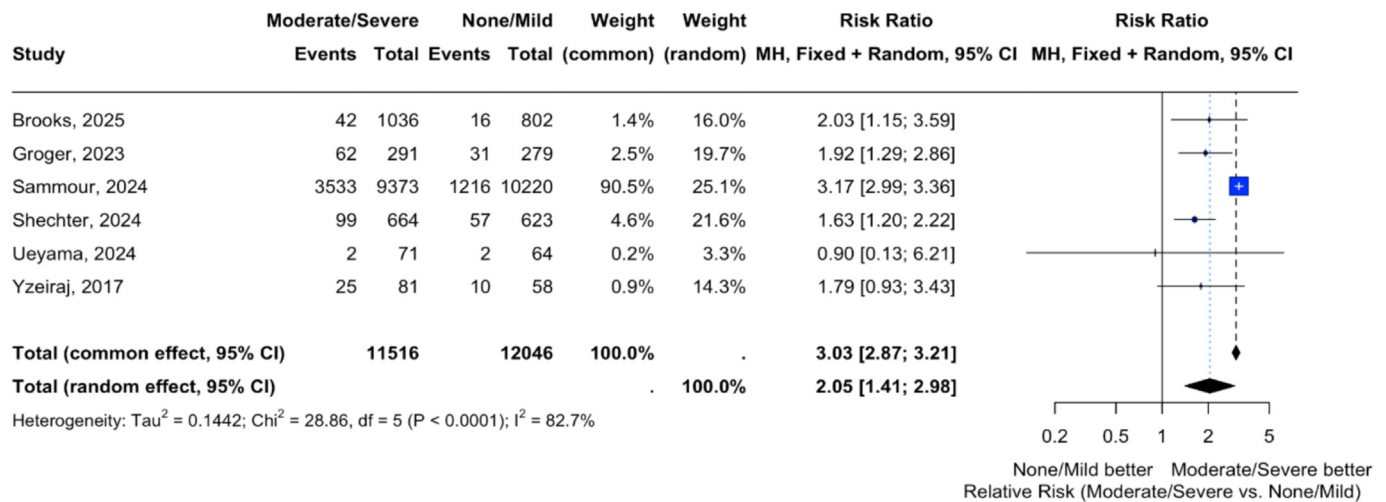


Fig. 2. Forest plot of the risk of all-cause mortality during follow-up following M-TEER in patients with moderate or severe vs. none or mild tricuspid regurgitation at baseline.

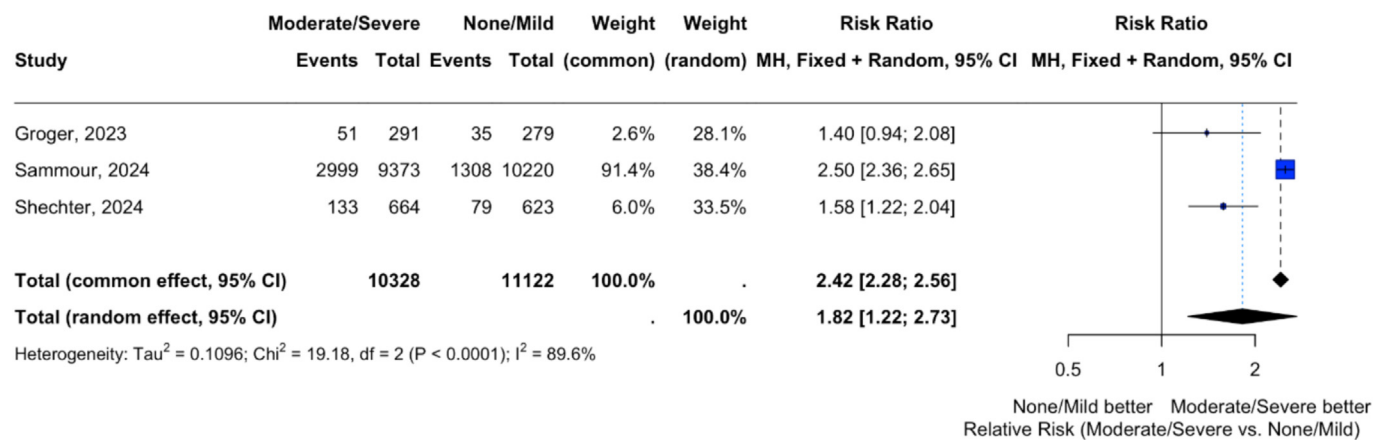


Fig. 3. Forest plot of the risk of heart failure rehospitalization during follow-up following M-TEER in patients with moderate or severe vs. none or mild tricuspid regurgitation at baseline.

reported data on TAPSE, including 174 patients with moderate/severe TR and 372 patients with none/mild TR. The pooled MD was -0.36 mm (95% CI: -1.35 to 0.63) (Fig. 10). Heterogeneity across the studies was high ($I^2 = 95.9\%$, $p < 0.0001$).

3.6. NYHA class

Five studies with 2404 total patients reported data on NYHA class at follow-up times ranging from 30 to 721 ± 194 days interval; 1124 patients



Fig. 4. Forest plot of procedural success following M-TEER in patients with moderate or severe vs. none or mild tricuspid regurgitation at baseline.

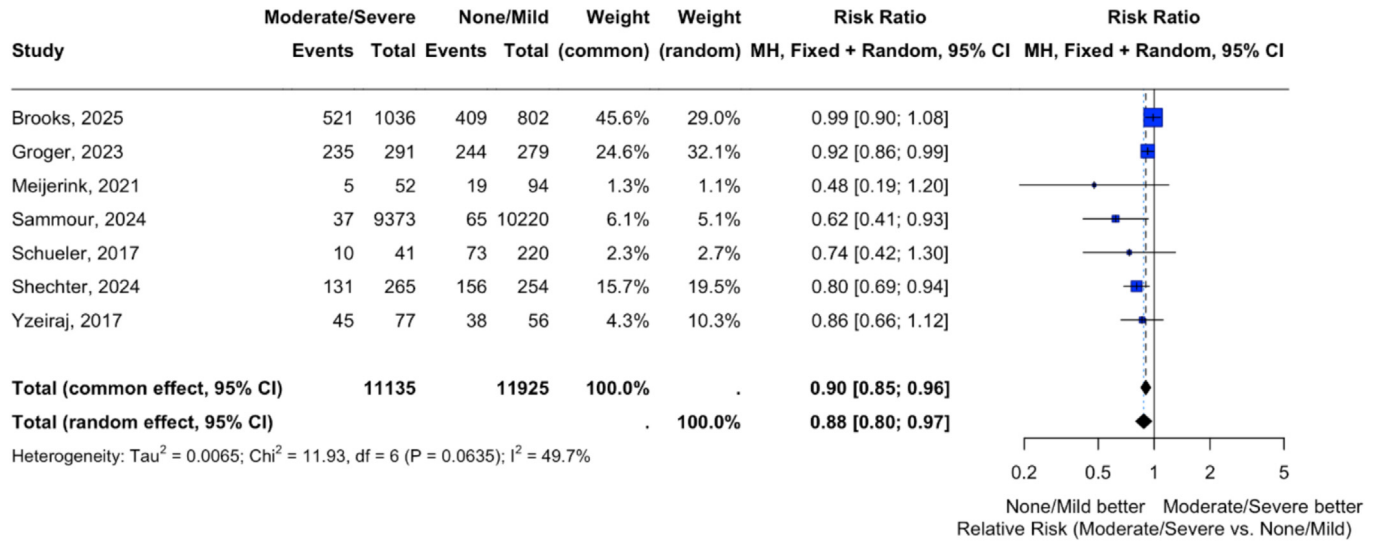


Fig. 5. Forest plot of none/mild mitral regurgitation during follow-up following M-TEER in patients with moderate or severe vs. none or mild tricuspid regurgitation at baseline.

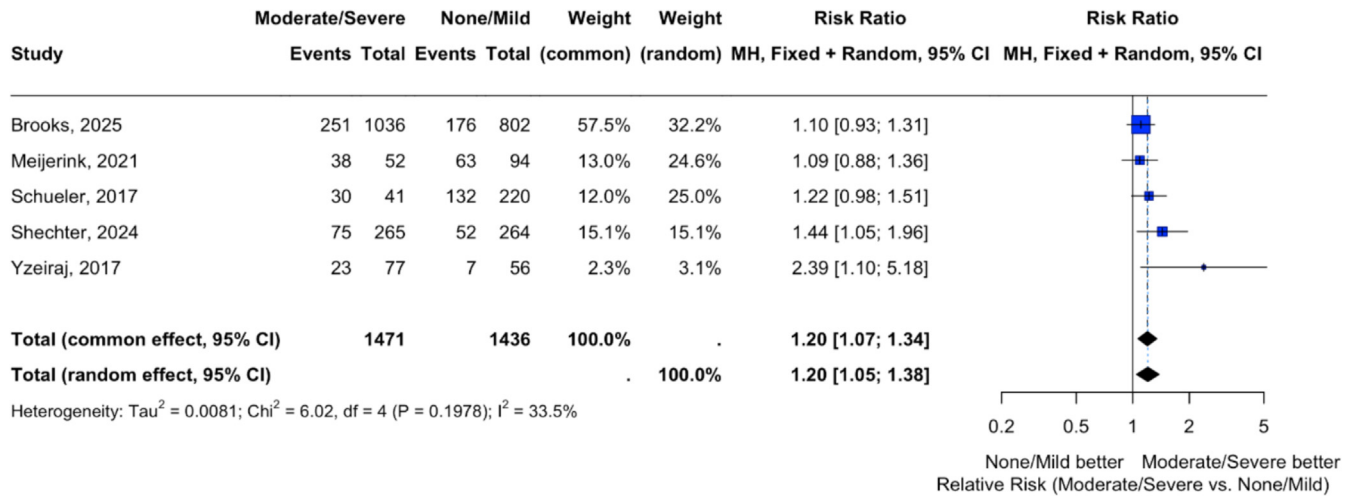


Fig. 6. Forest plot of moderate mitral regurgitation during follow-up following M-TEER in patients with moderate or severe vs. none or mild tricuspid regurgitation at baseline.

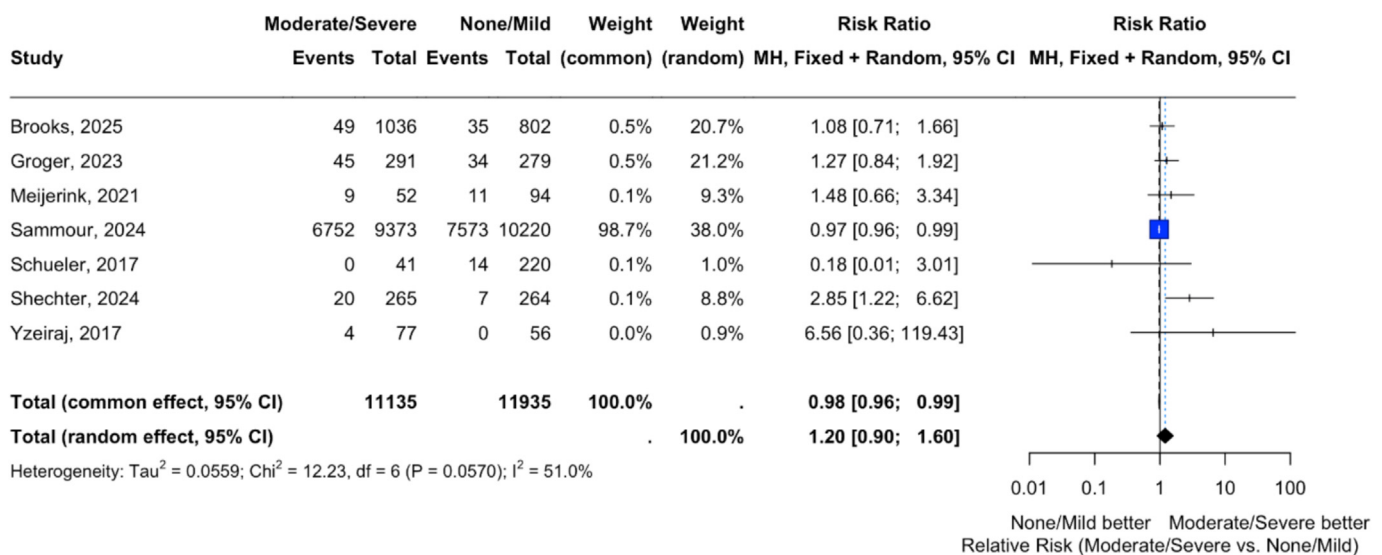


Fig. 7. Forest plot of severe mitral regurgitation during follow-up following M-TEER in patients with moderate or severe vs. none or mild tricuspid regurgitation at baseline.

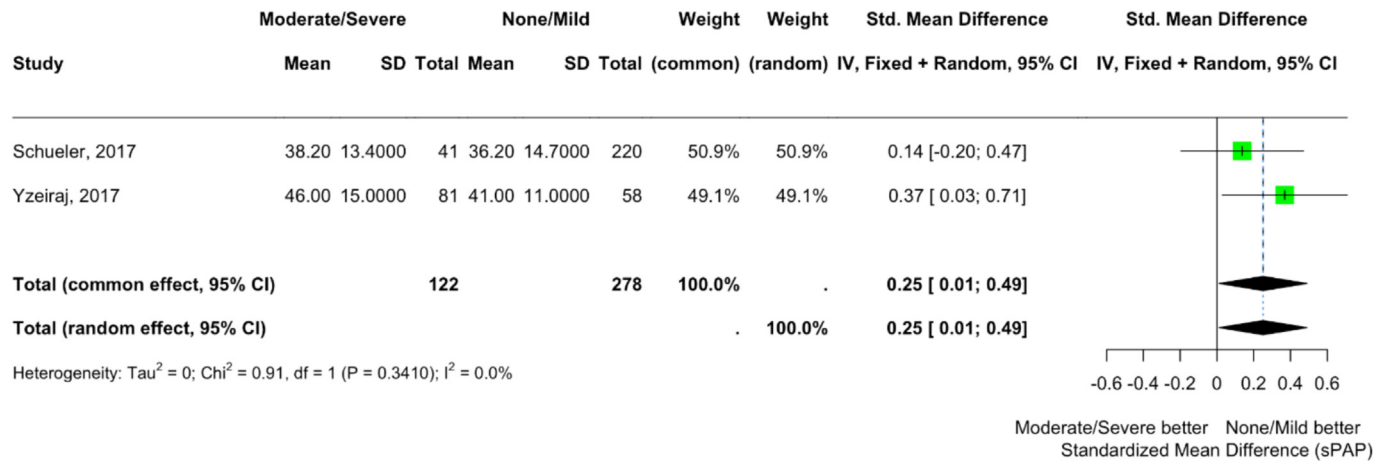


Fig. 8. Forest plot of systolic pulmonary artery pressure during follow-up following M-TEER in patients with moderate or severe vs. none or mild tricuspid regurgitation at baseline.

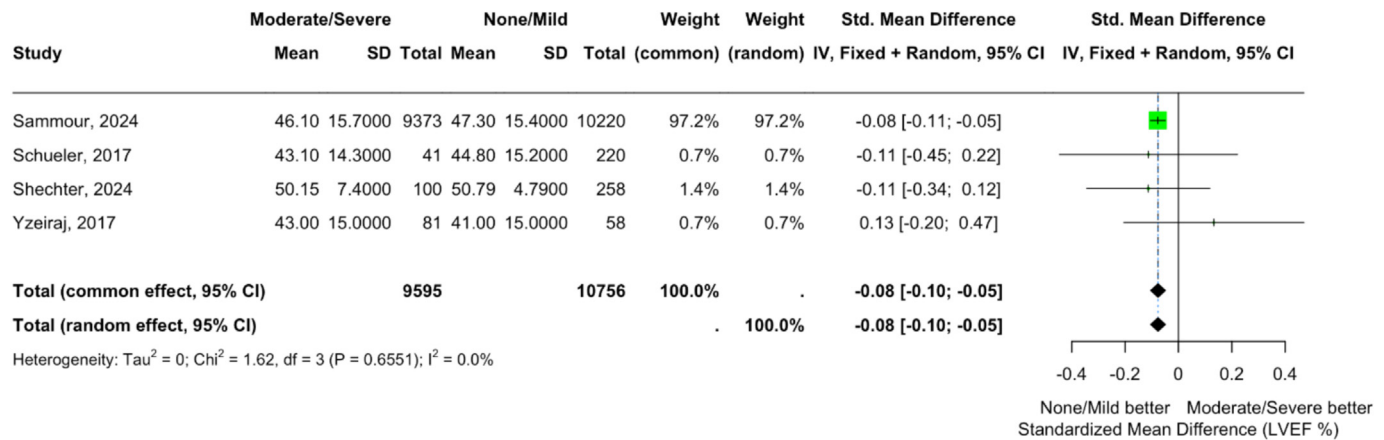


Fig. 9. Forest plot of left ventricle ejection fraction during follow-up following M-TEER in patients with moderate or severe vs. none or mild tricuspid regurgitation at baseline.

had moderate/severe TR and 1280 patients had none/mild TR. The pooled RR for NYHA $\geq$ III at follow-up was 1.48 (95% CI: 1.27 to 1.73) (Fig. 11). Heterogeneity across the studies was absent ($I^2 = 0.0\%$, $p = 0.57$).

3.7. Sensitivity analyses

Leave-one-out analyses (Figs. S1–S18) were performed to determine whether deleting selected studies would reduce heterogeneity. For most

outcomes, deleted single studies did not meaningfully reduce the degree of heterogeneity. Regarding the All-Cause Mortality, HFH and procedural success outcomes, excluding Sammour [13] diminished heterogeneity to 0% (Figs. S1–S3). For the moderate MR outcome post-M-TEER, excluding Yzeiraj [17] reduced the heterogeneity to 0% (Fig. S5). For the severe MR outcome post-M-TEER, excluding Shechter [15] reduced the heterogeneity to 15.6% (Fig. S6).

Funnel plot analyses (Figs. S9–S16) were evaluated qualitatively to assess publication bias and study asymmetry across endpoints. For the clinical

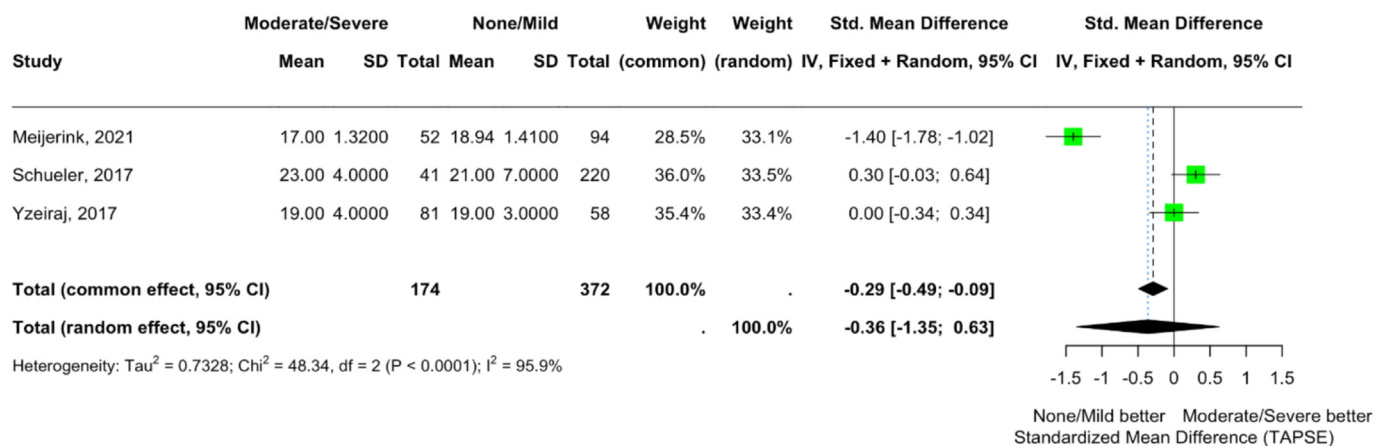


Fig. 10. Forest plot of tricuspid annular plane systolic excursion during follow-up following M-TEER in patients with moderate or severe vs. none or mild tricuspid regurgitation at baseline.

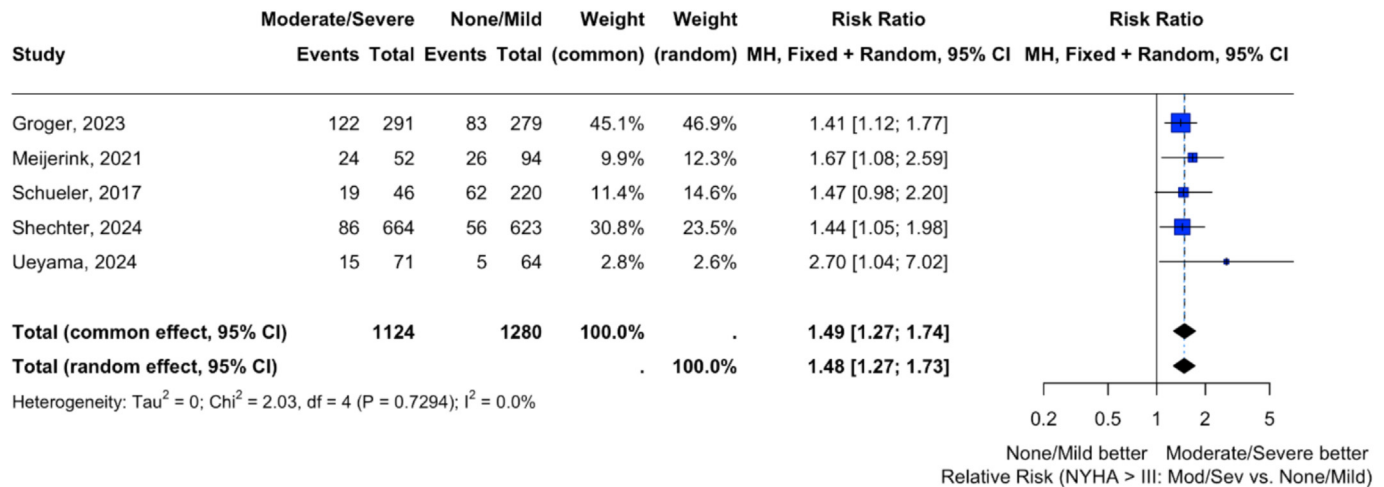


Fig. 11. Forest plot of the risk of New York Heart Association (NYHA) class $\geq$ III during follow-up following M-TEER in patients with moderate or severe vs. none or mild tricuspid regurgitation at baseline.

outcomes of All-Cause Mortality and HFH, the plots displayed a generally symmetrical distribution of studies within the pseudo-95% confidence intervals, suggesting a low likelihood of dominant publication bias (Figs. S9–S10). Regarding the procedural success and NYHA class $>$ III outcomes, studies were symmetrically distributed around the pooled effect size, indicating robust data consistency (Figs. S11 and S16). For continuous echocardiographic measures, including sPAP, LVEF, and TAPSE, minor asymmetry was visually noted, reflecting the clinical diversity and sample size variations among the included cohorts (Figs. S12–S15). Formal statistical testing for funnel plot asymmetry (such as Egger's or Begg's tests) was intentionally not performed, given that our meta-analysis included eight primary studies; this falls below the methodological consensus recommending a minimum of ten studies to provide adequate statistical power for quantitative asymmetry models.

3.8. Risk of bias

The quality of the eight included observational studies was rigorously evaluated using the ROBINS-I tool across seven specific domains (Supplementary Table 2 and Fig. S17). The domains driving the highest methodological concern were bias due to confounding (D1) and bias in the selection of participants (D2). Given the non-randomized, real-world registry nature of the primary evidence, baseline clinical differences, such as the severity of underlying heart failure, frailty, and renal function, introduced a moderate-to-serious risk of confounding, as multivariable adjustments could not uniformly erase baseline disparities across all cohorts. Additionally, selection bias was classified as moderate-to-serious in several single-center retrospective studies where consecutive enrollment parameters or precise structural heart team allocation criteria were poorly documented. Conversely, low risk of bias was consistently observed for the domains of intervention classification, deviations from intended interventions, missing data management, and objective outcome measurement. Overall, four studies were classified as carrying a moderate overall risk of bias, while four single-center retrospective cohorts were judged to have a serious overall risk of bias due to unadjusted confounding elements.

4. Discussion

In this systematic review and meta-analysis of 8 observational studies including 24,129 patients undergoing M-TEER, the presence of moderate or severe TR at baseline was consistently associated with worse outcomes during follow-up. Clinically, patients with moderate/severe TR had substantially higher risks of all-cause mortality and HFHs after M-TEER than those with none/mild TR, while also showing a modestly lower likelihood of procedural success. Baseline TR severity also was associated with higher

sPAP during follow-up and a signal toward greater residual MR, although TAPSE did not show a consistent between-group difference in pooled estimates. Patients with baseline moderate/severe TR were also more likely to have NYHA functional class $\geq$ III symptoms during follow-up compared with those with none/mild TR. Collectively, these findings support (at a minimum) the role of baseline TR as a marker of advanced disease and worse prognosis after M-TEER, and questions whether treating TR would improve the prognosis of these high-risk patients.

Mechanistically, TR in patients undergoing mitral intervention is frequently functional and reflects the combined burden of left-sided heart disease, pulmonary hypertension, and progressive right-heart remodeling (with right atrial and right ventricular dilation and tricuspid annular enlargement). This advanced disease complexity and adverse ventricular remodeling can structurally impair optimal mitral leaflet coaptation, providing a clear mechanistic explanation for why baseline moderate/severe TR associates with a modest increase in residual moderate MR, though absolute differences remain low and severe residual MR did not differ significantly [18]. Moderate or severe TR may thus be a marker of more severe disease due to MR ($\pm$ ischemic cardiomyopathy and other conditions), providing a plausible explanation for why increasing baseline TR severity associates with worse clinical outcomes after M-TEER [18]. Importantly, TR may partially improve after effective MR reduction ("mitral unloading"), but this response is variable and depends on the stage of right-heart disease and pulmonary vascular load [18]. Thus, early post-procedure (residual) TR may be particularly informative for ongoing risk stratification after MTEER, as supported by previous observational evidence [19–21].

Importantly, our study cannot determine whether baseline or residual TR acts as a direct driver of adverse outcomes or merely as a bystander reflecting advanced systemic disease, an important distinction as such a relationship would support a potential benefit for treating severe TR, either simultaneously during the M-TEER procedure or sequentially if it persists during follow-up. Dedicated RCTs are required to address this uncertainty. Until such studies are complete, the present observations support guideline/consensus emphasis on systematic TR assessment and heart team planning in patients with left-sided valve disease, recognizing that significant TR identifies higher-risk patients who may warrant closer follow-up and consideration of advanced therapies when symptoms persist [22].

The substantial statistical heterogeneity observed in our clinical endpoints (all-cause mortality, $I^2 = 82.7\%$; HF hospitalizations, $I^2 = 89.6\%$) mirrors the clinical diversity of real-world M-TEER programs. Clinically, contemporary cohorts encompass highly heterogeneous populations with variations in MR etiology (primary vs. secondary) and TR mechanisms (functional vs. degenerative), which inherently modify long-term responses

to isolated mitral repair. Methodologically, the included studies span different procedural eras, technological iterations, and device types (e.g., MitraClip vs. Pascal platforms). Furthermore, differences in baseline right ventricular (RV) dysfunction severity, a wide range of clinical follow-up intervals (30 days to over 2 years), and shifting institutional criteria for quantitative TR grading further contribute to this variance. While sensitivity diagnostics isolated specific landmark cohorts that heavily weighted the pooling, this mathematical heterogeneity primarily reflects the complex, real-world spectrum of structural heart disease [18–23].

In our pooled echocardiographic analysis, greater baseline TR severity was associated with a statistically significant but clinically minimal increase in pulmonary artery pressures (sPAP) (MD: 0.25 mmHg) and a negligibly lower LVEF (MD: -0.08%) during follow-up after M-TEER, although RV systolic function (TAPSE) did not show a consistent difference between groups. These effects are concordant with data in M-TEER populations linking TR severity with the pulmonary pressure/RV load axis and showing that the prognostic implications of severe TR may correlate with RV-PA coupling rather than being fully explained by RV dysfunction alone [23]. It is also consistent with the interpretation that greater TR reflects advanced cardiopulmonary disease burden rather than isolated valve anatomy [24]. Our observation that baseline TR severity also was associated with worse NYHA class during follow-up is also consistent with the interpretation that worse baseline TR reflects a higher-burden phenotype rather than an incidental echo finding [25].

These findings align with guidelines that stress comprehensive hemodynamic and imaging assessment (including pulmonary pressures and RV performance) when evaluating TR severity in patients undergoing left-sided valve surgery or transcatheter interventions [22]. In practice, our findings support a structured approach to TR grading before mitral intervention and systematic clinical and echocardiographic reassessment after M-TEER to guide follow-up intensity, optimize medical therapy, and prompt early heart team re-evaluation regarding potential tricuspid-targeted therapies in appropriate high-risk patients [22].

4.1. Limitations

Several limitations should be acknowledged when interpreting these findings. Because the included evidence is observational, unmeasured confounding cannot be excluded and the observed associations should not be considered causal. Specifically, residual confounding remains highly probable across the pooled cohorts, as primary studies could not fully adjust for critical unmeasured prognostic variables, such as right ventricular (RV) function parameters beyond TAPSE, RV-pulmonary arterial (RV-PA) coupling, baseline atrial fibrillation burden, baseline renal dysfunction, pulmonary vascular resistance (PVR) metrics, the optimization of guideline-directed medical therapy, clinical frailty, and the precise clinical timing of the intervention. In addition, heterogeneity varied across endpoints, being low for procedural success and NYHA class but higher for outcomes including mortality, HFHs, sPAP, TAPSE, and residual MR. This high statistical variance underscores the presence of critical unmeasured clinical trial disparities, including variations in MR and TR etiologies (primary vs. secondary), differing utilization of transcatheter device types (MitraClip vs. Pascal), and shifts in procedural eras. Furthermore, definitions for procedural success lacked strict standardization across the included cohorts, presenting minor variations regarding residual MR thresholds and peri-procedural complication tracking; nevertheless, the exceptionally low statistical heterogeneity ($I^2 = 8.7\%$) observed for this outcome supports the clinical reliability of our pooled estimate.

TR was only grouped as none/mild vs. moderate/severe, whether more granular classification of TR severity or standardized quantification protocols would have provided greater precision is unknown. Importantly, due to the aggregate nature of the available literature, we were unable to perform stratified sub-analyses or meta-regressions for baseline RV dysfunction severity or specific follow-up cutoff points, as these metrics were inconsistently reported across the original cohorts. As mentioned, serial measures of TR severity were not assessed. Furthermore, the substantial

variance in follow-up durations across the primary literature (ranging from 30 days up to 2 years) presents a potential source of temporal bias, as acute post-procedural events and long-term heart failure progression operate under completely different clinical dynamics. While these different durations in follow-up undoubtedly added to the observed heterogeneity, some echocardiographic measures were informed by a limited number of studies, reinforcing the value of prospective, standardized reporting and systematic follow-up imaging to refine effect estimates and improve comparability across cohorts. Finally, absent access to individual patient data, the multivariable determinants of prognosis could not be evaluated.

5. Conclusions

In patients undergoing M-TEER, moderate or severe TR at baseline should be considered an important marker of advanced disease and a poor prognosis after MR correction, not just an incidental secondary echocardiographic finding. Given the observational nature of the current evidence, this association primarily reflects a higher-burden phenotype characterized by advanced right ventricular remodeling, pulmonary hypertension, and cumulative clinical frailty. Our results support incorporating TR severity into pre-procedural risk assessment and post-procedural surveillance, with consideration that residual TR may contribute to persistent symptoms and adverse events. Future prospective randomized trials should determine whether TR-guided strategies, such as simultaneous or staged transcatheter tricuspid interventions in selected patients, can improve clinical outcomes beyond mitral repair alone.

CRediT authorship contribution statement

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Declaration of competing interest

Dr. Stone has served as a consultant to Apollo Therapeutics, Occlutech, Oxitope, Elixir, Impulse Dynamics, Asceneuron, Myochron, Vesalio, HeartFlow, Colibri, Bioventrix, Abbott, Aria, Adona Medical, Curie Bio, Cardiac Success, Remote Cardiac Enablement, Valfix, Zoll, Shockwave, HighLife, Elucid Bio, Alleviant, FBR Medical, MedHub, Biotyx Medical, Ablative Solutions; and has equity/options from Cardiac Success, Ancora, Cagent, Applied Therapeutics, Biostar family of funds, SpectraWave, Orchestra Biomed, Valfix, Xenter, Vascentis. Dr. Stone's employer, Mount Sinai Hospital, receives research grants from Shockwave, Biosense-Webster, Bioventrix, Abbott, Abiomed, Cardiovascular Systems Inc., Phillips, Pulnovo, V-wave and PCORI (via Weill Cornell Medical Center). The other authors report no relationships.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.carrev.2026.06.002>.

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