Systematic Review

Outcomes after tricuspid transcatheter edge-to-edge repair: a systematic review and meta-analysis

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Background: Severe tricuspid regurgitation (TR) is associated with high morbidity and mortality. Tricuspid transcatheter edge-to-edge repair (T-TEER) improves TR severity and symptoms, yet survival benefit remains uncertain. This meta-analysis aims to evaluate 1-year outcomes after T-TEER and explore clinical and echocardiographic correlates of prognosis.

Methods: A systematic search of PubMed/MEDLINE, Web of Science, and Scopus was conducted through June 2025. Studies enrolling ≥100 patients undergoing T-TEER and reporting 1-year outcomes were included. Primary endpoints were 1-year all-cause mortality, heart failure (HF) hospitalization, and persistence of New York Heart Association (NYHA) class III–IV. Early residual TR (≥3+), assessed at the earliest post-procedural time point within 30 days, was a secondary endpoint.

Results: Ten studies, including 4,134 patients, were analyzed. At 1-year, pooled all-cause mortality was 14.0% [95% confidence interval (CI): 9.6–18.5%], HF hospitalization 16.9% (95% CI: 8.7–25.1%), and 30.9% of patients remained in NYHA class III–IV (95% CI: 22.1–39.7%). Early residual TR ≥3+ occurred in 19.1%. In meta-regression analysis, more contemporary recruitment periods were associated with lower 1-year mortality, whereas single-center design was associated with higher early residual TR ≥3+. Exploratory aggregate-level analyses suggested potential associations between comorbidity burden and mortality, right-sided dysfunction and HF hospitalization, and left-sided disease and persistent functional limitation.

Conclusions: T-TEER effectively reduces TR and improves functional status; however, 1-year mortality and HF hospitalization remain substantial. More contemporary recruitment periods were associated with lower 1-year all-cause mortality, suggesting improved outcomes over time. Systemic comorbidity burden, right-sided disease, and concomitant left-sided disease may contribute to residual risk after T-TEER; however, these associations should be considered hypothesis-generating and require validation in individual patient-level datasets.

Meta-analysis Registration: CRD420251155094.

Keywords: Right ventricle; tricuspid valve; tricuspid regurgitation (TR); echocardiography; survival

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Introduction

Severe tricuspid regurgitation (TR) is a progressive and debilitating disease associated with increased mortality, recurrent heart failure (HF) hospitalization, and impaired quality of life (1). Historically, severe TR was managed with medical therapy alone due to the high surgical risk of affected patients, who are typically elderly with multiple comorbidities (2).

The therapeutic landscape has evolved rapidly with the advent of transcatheter interventions, which offer a less invasive treatment option for patients deemed unsuitable for surgery (3). Among available approaches, tricuspid transcatheter edge-to-edge repair (T-TEER) has emerged as the most widely studied and clinically adopted technique and is now recommended by contemporary international guidelines (4,5). Randomized trials have confirmed that T-TEER reduces TR severity and improves quality of life and functional status, yet neither has shown a significant mortality benefit despite sustained hemodynamic improvement (6,7). This dissociation between effective TR reduction and survival benefit raises fundamental questions about patient selection and the optimal timing of intervention. As global adoption of T-TEER expands and longer follow-up data from both real-world practice and clinical trials become available, a synthesis of contemporary outcomes is needed. The present meta-analysis provides a comprehensive evaluation of 1-year outcomes following T-TEER and explores potential clinical and echocardiographic correlates of prognosis.

Methods

Literature search and study selection

A comprehensive systematic literature search was conducted across the PubMed/MEDLINE, Web of Science, and Scopus databases, from inception to June 2025. Studies were identified using the major Medical Subject Heading "Tricuspid Transcatheter Edge to Edge Repair". Only studies published in English were included. Both prospective and retrospective studies were eligible. Two investigators independently screened titles and abstracts and excluded irrelevant studies. The full texts of potentially eligible studies were retrieved, and any disagreements were resolved by discussion. The reference lists of relevant articles and systematic reviews were manually searched to identify additional studies. The study protocol was registered in the PROSPERO international register of systematic reviews.

Eligibility criteria

The inclusion criteria were defined as follows: (I) studies enrolling patients undergoing T-TEER; (II) reporting of clinical outcomes at 1-year follow-up; (III) a minimum cohort size of 100 patients; and (IV) publication as a full-text article in a peer-reviewed journal.

Studies were excluded if they involved concomitant mitral valve interventions or were non-original research articles. When multiple publications from the same center or registry reported overlapping patient populations, only the most recent or most comprehensive dataset was included in the analysis.

Data extraction

Data extraction was performed independently by two investigators. Any discrepancies were resolved by consensus or, when necessary, through consultation with a third independent investigator. The following data were extracted: study design, baseline patient characteristics, echocardiographic parameters, and clinical outcomes.

Endpoints and definitions

The primary endpoints of this study were 1-year all-cause mortality, 1-year HF hospitalization, and persistence of advanced functional status, defined as New York Heart Association (NYHA) functional class III–IV at 1 year. The secondary endpoint was early residual TR (TR ≥3+), assessed at the earliest available post-procedural time point (≤30 days, including pre-discharge or 30-day evaluations according to the individual study protocol). In addition, the associations between baseline clinical characteristics and echocardiographic parameters, and both primary and secondary endpoints were explored using meta-regression analyses. All covariates were extracted and analyzed at the study level.

Quality assessment

Risk of bias in observational studies was assessed using the Newcastle-Ottawa Scale (8). This scale evaluates the internal validity of cohort studies included in a meta-

analysis across three domains: selection (adequate selection and definition of groups), comparability (comparability of two groups for a selected variable and comparability for other variables), and outcome (modality of assessment, adequacy of follow-up duration, and completeness of follow-up). Study quality was categorized according to the star-based scoring system.

Studies were considered to be at low risk of bias if they achieved the maximum score: four stars for selection, two for comparability, and three for outcome. A moderate risk of bias was assigned to studies with two to three stars for selection, one star for comparability, and two stars for outcome. Studies were classified as having a high risk of bias if they received only one star in either the selection or outcome domains, or no stars in any of the three domains.

Statistical analysis

An inverse variance-weighted study-level meta-analysis with a random-effects model was performed to estimate pooled rates of clinical outcomes across the included studies, including 1-year all-cause mortality, 1-year HF hospitalization, 1-year NYHA class III–IV, and early residual TR ≥3+. The results are presented as forest plots with corresponding 95% confidence intervals (CIs).

A random-effects model was selected because the included studies were expected to be heterogeneous with respect to study design, patient populations, baseline characteristics, and procedural techniques. The proportion of total variability attributable to between-study heterogeneity was assessed using the I^2 statistic. I^2 values of 25%, 50%, and 75% were considered indicative of low, moderate, and high heterogeneity, respectively. For descriptive purposes, pooled estimates of baseline characteristics were also calculated using inverse variance-weighted study-level meta-analytic methods, considering the precision of each study estimate. Continuous variables were summarized as pooled mean values with 95% CIs, while categorical variables reported as percentages were pooled using the same inverse variance approach.

To explore potential sources of heterogeneity, univariable meta-regression analyses were performed using study-level descriptors, including publication year, median recruitment year, recruitment duration, center design, study design, sample size, and device type. Additional meta-regression analyses with aggregate-level data were performed only as exploratory analyses and no causal inference was made from these associations. Each variable was analyzed separately. Meta-regression models were fitted using weighted least squares regression, with weights proportional to the sample size of each study. Regression coefficients (β), 95% CIs, and P values were reported.

For variables significantly associated with outcomes in meta-regression analyses ($P<0.05$), bubble plots were generated to illustrate the relationship between the covariate and the clinical outcome across studies. In these plots, each bubble represents an individual study, the x-axis represents the study-level covariate, the y-axis represents the outcome, and bubble size is proportional to the number of patients included in each study. The regression line represents the weighted meta-regression fit.

Statistical significance was defined as a two-sided $P<0.05$. All statistical analyses were performed using R statistical software (R Foundation for Statistical Computing) and OpenMetaAnalyst (Brown University).

Potential publication bias was assessed by visual inspection of funnel plots. When funnel plot asymmetry suggested possible publication bias, this was further evaluated using Egger's regression test, which assesses the relationship between study effect estimates and their standard errors.

Sensitivity analyses were performed to evaluate the robustness of the pooled estimates and to assess the potential impact of overlapping datasets. Subgroup and sensitivity analyses were performed using inverse-variance random-effects pooling of study-level proportions. This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results

Quantity of evidence

The database search identified a total of 1,254 studies, of which 473 were selected for title and abstract screening. Following full-text review, 10 studies met the inclusion criteria and were included in the meta-analysis, comprising a total of 4,134 patients undergoing T-TEER (Figure S1) (6,7,9-16). Most studies were retrospective, with two prospective observational registries (10,11) and two randomized controlled trials (6,7). Devices used for T-TEER included TriClip™ exclusively in three studies (6,7,11), while the remaining studies also utilized the PASCAL system. Only one study was exclusively dedicated to patients with primary TR (15); in all remaining cohorts, TR etiology was mixed with a predominance of secondary TR.

Quality of evidence

To assess the impact of study quality (risk of bias) on heterogeneity, we applied the Newcastle-Ottawa Quality Assessment Scale to the observational studies included in the meta-analysis. All studies included in this meta-analysis were assessed as having either low or moderate risk of bias (Table S1).

Funnel plot inspection showed overall symmetry for 1-year all-cause mortality and HF hospitalization, suggesting no relevant publication bias. In contrast, visual asymmetry was observed for 1-year NYHA class III–IV and early residual TR ≥3+, indicating potential small-study effects. These findings were consistent with Egger's test, supporting the presence of publication bias for these latter outcomes, which may lead to an overestimation of the observed effects and warrants cautious interpretation (Figure S2; Table S2).

Basic demographics

The included studies comprised of an elderly, high-risk population, with a pooled mean age of 79 years and 45% male patients. The burden of comorbidities was substantial. Atrial fibrillation was highly prevalent, affecting 90% of patients, followed by hypertension (81%). Most patients were symptomatic, with 79% in NYHA class III–IV, and nearly half had chronic kidney disease (48%) (*Table 1*).

Mean tricuspid annular plane systolic excursion (TAPSE) was 17.4 mm, and fractional area change (FAC) was 40%. Patients showed right ventricular dilatation (mean basal diameter 48 mm) and mildly elevated pulmonary artery systolic pressure (PAPs), with a mean value of 42 mmHg (*Table 2*). Full clinical and imaging characteristics are reported (Table S3).

Assessment of primary and secondary endpoints

At 1-year follow-up, pooled all-cause mortality was 14.0% (95% CI: 9.6–18.5%; I^2=94.4%). HF hospitalization occurred in 16.9% of patients (95% CI: 8.7–25.1%; I^2=92.9%). Despite overall improvement in functional status, 30.9% of patients remained in NYHA class III–IV (95% CI: 22.1–39.7%; I^2=97.2%). Early residual TR (TR ≥3+) was observed in 19.1% of patients (95% CI: 16.2–21.9%; I^2=78.8%) (Figure S3A-S3D). Because partial overlap between the EuroTR registry and the Stolz TRILUMINATE eligibility cohort could not be definitively excluded, these datasets were further assessed in predefined sensitivity analyses. Specifically, pooled estimates were recalculated in two scenarios: retaining EuroTR while excluding the Stolz TRILUMINATE eligibility cohort and retaining the Stolz TRILUMINATE eligibility cohort while excluding EuroTR. Sensitivity analyses showed consistent results across all outcomes (Table S4).

Meta-regression analyses

In meta-regression analyses, later median recruitment year was associated with lower 1-year all-cause mortality (β=–3.76, 95% CI: –6.55 to –0.97; P=0.015). For 1-year HF hospitalization and persistent NYHA class III–IV at 1 year, none of the evaluated study-level descriptors showed statistically significant associations. For early residual TR ≥3+, single-center design was associated with a higher rate of residual TR ≥3+ compared with multicenter design (β=7.49, 95% CI: 0.62–14.36; P=0.036). These study-level meta-regression findings are reported in *Table 3* and illustrated in *Figure 1* and Figure S4.

Subgroup analyses by study design are shown in Figure S5A-S5D. In these analyses, pooled 1-year all-cause mortality was lower in randomized controlled trials compared with observational registries [5.9% (95% CI: 0.8–11.0%) *vs.* 16.1% (95% CI: 11.5–20.7%); P for subgroup difference <0.001].

In exploratory aggregate-level meta-regression analyses, several baseline clinical and echocardiographic characteristics showed associations with 1-year outcomes. Male sex (β=0.77, 95% CI: 0.28–1.26; P=0.007), diabetes mellitus (β=1.16, 95% CI: 0.17–2.16; P=0.029), chronic obstructive pulmonary disease (β=1.22, 95% CI: 0.15–2.29; P=0.032), pacemaker/implantable cardioverter-defibrillator (β=0.58, 95% CI: 0.20–0.95; P=0.008), chronic kidney disease (β=0.24, 95% CI: 0.07–0.41; P=0.018), higher PAPs (β=1.24, 95% CI: 0.23–2.25; P=0.023), and larger tricuspid annular diameter (β=2.34, 95% CI: 1.22–3.46; P=0.022) were all associated with higher mortality rates. Lower FAC and higher tricuspid regurgitant volume were associated with an increased risk of hospitalization (β=–3.59, 95% CI: –3.89 to –3.29; P=0.004; β=0.13, 95% CI: 0.10–0.16; P=0.012, respectively).

Higher baseline NYHA class III–IV (β=0.39, 95% CI: 0.04–0.74; P=0.034), larger tricuspid annular diameter (β=4.33, 95% CI: 0.34–8.32; P=0.039), at least moderate mitral regurgitation (β=2.10, 95% CI: 1.35–2.86; P=0.018),

Table 1 Baseline characteristics of included studies

First author	Year	N	Center/registry/trial	Age (years)	BMI (kg/m^2)	Sex (male, %)	DM (%)	HTN (%)	HLD (%)	AF (%)	COPD (%)	PM/ICD (%)	CKD (%)	NYHA III–IV (%)
Gröger	2023	180	Ulm University Heart Center	80±7	25.9±4.8	51	–	–	–	88	11	6	24	79
Hanses	2023	102	University of Lübeck	81±6	–	49	22	72	–	83	13	10	–	96
Echarte-Morales	2024	280	TRI-SPA Registry	77±7	26.5±4.3	30	19	68	47	91	16	10	41	70
Lurz	2024	511	bRIGHT Study	79±7	–	44	–	–	–	–	–	23	40	80
Stolz	2024	1,286	EuroTR Registry	78±9	26.1±4.9	46	26	80	48	90	18	28	–	84
Stolz	2024	962	Multicenter Registry	78±7	26.0±5.0	50	26	85	46	88	20	29	76	89
Vogelhuber	2024	262	University Hospital Bonn	79±7	–	49	23	84	–	93	–	31	–	15
Donal	2025	152	Tri-FR Trial	78±6	25.2±4.7	35	15	70	44	94	6	14	9	39
Sugiura	2025	114	Primary TR Registry	80±7	25.0±4.0	54	18	85	–	88	18	22	–	84
Tang	2025	285	TRILUMINATE Pivotal Trial	78±8	26.8±5.8	41	17	81	63	83	13	17	32	56

AF, atrial fibrillation; BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HLD, hyperlipidemia; HTN, hypertension; ICD, implantable cardioverter-defibrillator; N, number of patients; NYHA, New York Heart Association; PM, pacemaker; TR, tricuspid regurgitation.

Table 2 Imaging characteristics of included studies

First author	LVEF (%)	At least moderate MR (%)	TR secondary etiology (%)	RV EDD basal (mm)	TA (mm)	TAPSE (mm)	FAC (%)	PAPs (mmHg)	Vena contracta (mm)	EROA (cm^2)	TR Reg Vol (mL)
Gröger	50±12	24	87	–	44±8	–	–	49±13	12±4	0.6±0.2	–
Hanses	51±9	36	–	49±8	47±6	20.0±3.7	–	48±14	10±3	0.8±0.4	75±27
Echarte-Morales	59±5	26	79	–	39±6	18.0±3.0	40±11	38±12	11±2	0.7±0.2	–
Lurz	56±10	–	90	46±9	44±8	17.0±4.0	–	40±12	–	–	–
Stolz	54±11	–	84	49±10	45±8	17.1±4.5	39±11	43±15	11±4	0.7±0.5	52±33
Stolz	53±12	37	84	49±9	46±13	17.0±4.7	39±11	44±15	11±4	0.7±0.6	50±30
Vogelhuber	55±10	–	95	–	–	18.0±4.9	43±10	48±15	–	–	–
Donal	57±10	–	98	–	–	17.5±5.2	44±8	35±10	–	0.6±0.2	51±19
Sugiura	56±10	–	0	37±8	44±7	17.8±6.0	44±10	43±14	11±4	0.7±0.4	61±28
Tang	59±9	–	96	–	43±8	17.0±4.0	37±6	39±9	12±4	0.6±0.2	–

EROA, effective regurgitant orifice area; FAC, fractional area change; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; PAPs, pulmonary artery systolic pressure; Reg Vol, regurgitant volume; RV EDD, right ventricular end-diastolic diameter; TA, tricuspid annulus; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

Table 3 Meta-regression analysis for 1-year clinical outcomes

Covariate	1-year all-cause mortality			1-year HF hospitalization			1-year NYHA class III–IV		
	β	95% CI	P value	β	95% CI	P value	β	95% CI	P value
Study-level									
Publication year	–4.17	–13.63 to 5.28	0.34	6.31	–18.43 to 31.05	0.48	–9.98	–34.99 to 14.06	0.36
Median recruitment year	–3.76	–6.55 to –0.97	0.015	–5.19	–31.50 to 21.11	0.57	–4.19	–12.47 to 4.09	0.27
Recruitment duration	1.87	–0.25 to 4.00	0.08	0.10	–11.85 to 12.05	0.98	3.67	–1.03 to 8.39	0.11
Single-center *vs.* multicenter	3.30	–9.62 to 16.22	0.57	–6.44	–67.34 to 54.45	0.76	–13.37	–45.83 to 19.09	0.36
Log (sample size)	2.98	–2.04 to 7.98	0.21	2.79	–25.36 to 30.93	0.77	9.08	–0.89 to 19.05	0.07
Device	3.06	–1.63 to 7.74	0.17	–4.23	–25.41 to 16.96	0.57	7.18	–2.62 to 16.98	0.13
Aggregate-level									
Age (years)	2.03	–3.53 to 7.59	0.43	–6.54	–23.91 to 10.82	0.32	–0.53	–14.68 to 13.61	0.93
Sex (male, %)	0.77	0.28 to 1.26	0.007	–0.42	–3.80 to 2.96	0.72	0.98	–0.58 to 2.53	0.18
BMI (kg/m^2)	–2.75	–19.19 to 13.69	0.69	14.63	–6.77 to 36.02	0.07	–15.41	–44.20 to 13.37	0.21
DM (%)	1.16	0.17 to 2.16	0.029	–0.11	–15.94 to 15.72	0.98	2.00	–0.27 to 4.27	0.07
Hypertension (%)	0.78	–0.01 to 1.58	0.051	1.06	–4.29 to 6.41	0.48	0.49	–1.66 to 2.63	0.60
AF (%)	0.05	–1.86 to 1.96	0.95	–1.88	–7.25 to 3.49	0.27	0.37	–3.66 to 4.40	0.83
COPD (%)	1.22	0.15 to 2.29	0.032	0.66	–8.41 to 9.74	0.78	1.44	–1.55 to 4.43	0.27
PM/ICD (%)	0.58	0.20 to 0.95	0.008	–0.39	–4.24 to 3.46	0.77	0.82	–0.53 to 2.17	0.20
CKD (%)	0.24	0.07 to 0.41	0.018	0.14	–11.12 to 11.40	0.90	0.39	–0.27 to 1.06	0.16
NYHA III–IV (%)	0.05	–0.17 to 0.27	0.60	–0.20	–1.15 to 0.75	0.55	0.39	0.04 to 0.74	0.034
LVEF (%)	–1.41	–2.93 to 0.11	0.06	3.09	–2.46 to 8.64	0.18	–4.20	–6.85 to –1.54	0.007
At least moderate MR (%)	1.13	–0.05 to 2.31	0.054	–	–	–	2.10	1.35 to 2.86	0.018
RV EDD basal (mm)	0.33	–1.06 to 1.73	0.50	0.30	–3.65 to 4.26	0.51	1.56	–2.60 to 5.71	0.32
TA (mm)	2.34	1.22 to 3.46	0.022	–5.05	–26.33 to 16.24	0.42	4.33	0.34 to 8.32	0.039
TAPSE (mm)	0.62	–7.84 to 9.08	0.87	–3.81	–23.28 to 15.65	0.58	–4.30	–21.64 to 13.04	0.58
FAC (%)	0.18	–3.37 to 3.72	0.90	–3.59	–3.89 to –3.29	0.004	–1.01	–8.14 to 6.12	0.73
PAPs (mmHg)	1.24	0.23 to 2.25	0.023	–0.44	–5.88 to 5.00	0.81	1.20	–2.05 to 4.45	0.41
Vena contracta (mm)	–6.30	–20.13 to 7.53	0.28	–	–	–	–1.70	–39.33 to 35.92	0.90
EROA (cm^2)	83.20	–38.87 to 205.26	0.14	13.20	–12.50 to 38.90	0.10	–4.31	–25.83 to 24.97	0.96
TR Reg Vol (mL)	0.22	–1.17 to 1.61	0.65	0.13	0.10 to 0.16	0.012	–0.13	–0.83 to 0.56	0.59

AF, atrial fibrillation; BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; EROA, effective regurgitant orifice area; FAC, fractional area change; HF, heart failure; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NYHA, New York Heart Association; PAPs, pulmonary artery systolic pressure; PM, pacemaker; Reg Vol, regurgitant volume; RV EDD, right ventricular end-diastolic diameter; TA, tricuspid annulus; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

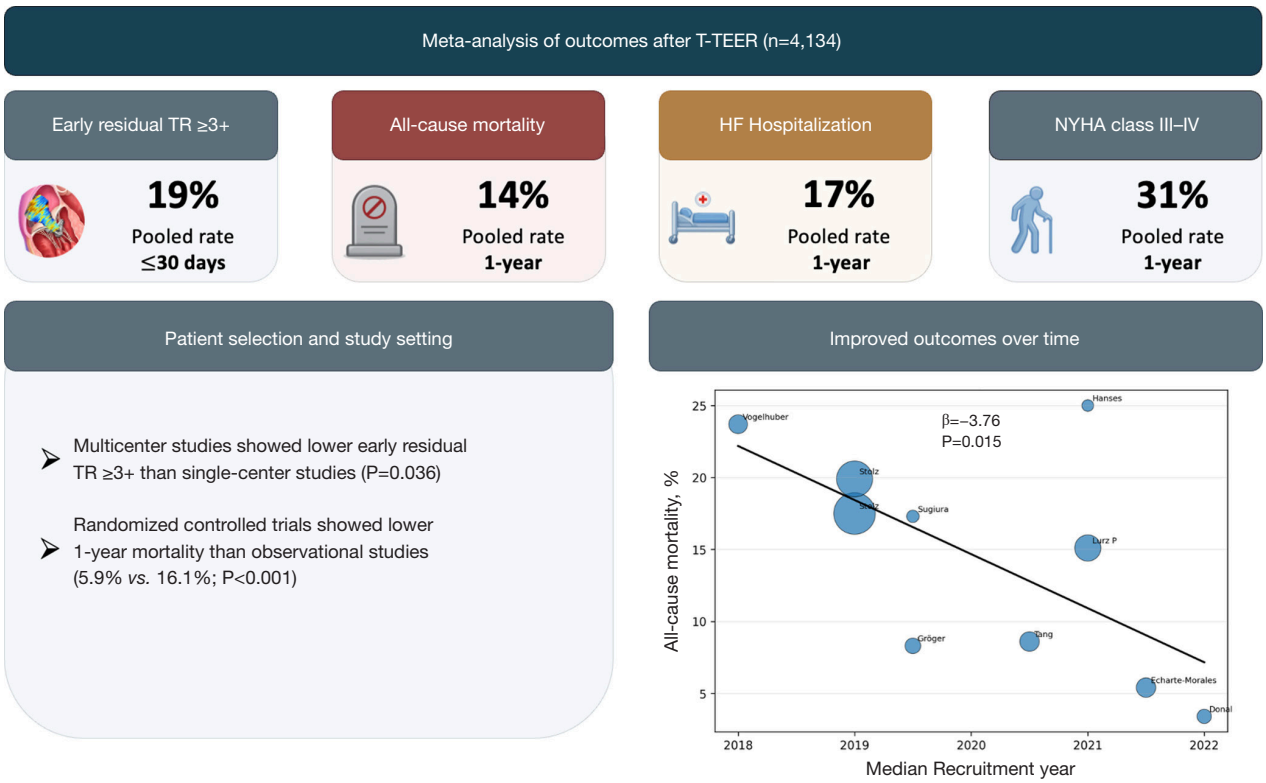

Figure 1 Contemporary outcomes after T-TEER. T-TEER effectively reduces TR but does not eliminate residual risk. In a meta-analysis of 4,134 patients, 1-year mortality, HF hospitalization, and persistent functional limitation remain substantial. Multicenter studies showed lower rates of early residual TR ≥3+ than single-center studies, whereas 1-year mortality was lower in randomized controlled trials than in observational registries, highlighting the potential impact of patient selection, center experience, and study setting on observed outcomes. More contemporary recruitment periods were associated with lower 1-year all-cause mortality, suggesting improved outcomes over time. Bubble size is proportional to study sample size. HF, heart failure; NYHA, New York Heart Association; T-TEER, tricuspid transcatheter edge-to-edge repair; TR, tricuspid regurgitation.

and lower left ventricular ejection fraction (LVEF) (β=–4.20, 95% CI: –6.85 to –1.54; P=0.007) were significantly associated with 1-year NYHA class III–IV. These exploratory analyses are reported in *Table 3* and illustrated in *Figure 2*. No significant association was observed between any clinical or echocardiographic parameter and early residual TR (TR ≥3+) (Table S5).

Discussion

This systematic review and meta-analysis yields three findings of direct clinical relevance. First, despite effective reduction of TR in approximately 80% of patients, residual clinical burden remains substantial, with 1-year all-cause mortality of 14%, HF hospitalization of 17%, and nearly one-third of patients remaining functionally impaired. Second, study-level analyses suggested that more contemporary recruitment periods were associated with lower 1-year mortality, whereas single-center design was associated with higher early residual TR ≥3+. Third, exploratory aggregate-level clinical and echocardiographic analyses suggested potential associations between systemic comorbidity burden, right-sided dysfunction, left-sided disease, and different outcome domains.

The temporal association between recruitment year and 1-year mortality represents one of the principal study-level findings of the present analysis and may reflect progressive improvements in patient selection, advances in imaging guidance, operator experience, device technology, and post-procedural care. Similarly, the association between single-center design and higher rates of early residual TR ≥3+ may also reflect differences in center-level expertise. Multicenter

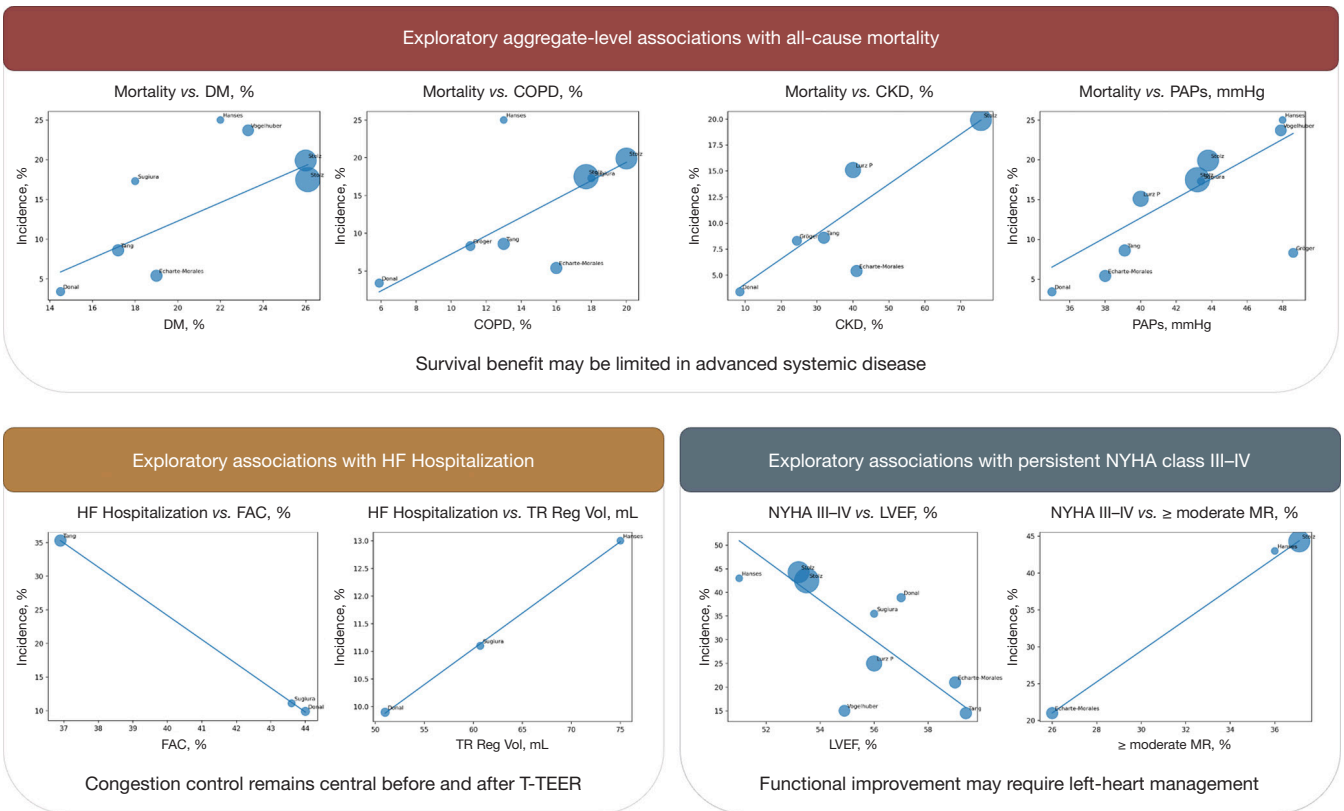

Figure 2 Exploratory aggregate-level meta-regression analyses. Exploratory aggregate-level meta-regression analyses suggested potential associations between comorbidity burden, right-sided dysfunction, left-sided disease, and clinical outcomes. CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; FAC, fractional area change; HF, heart failure; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; NYHA, New York Heart Association; PAPs, pulmonary artery systolic pressure; Reg Vol, regurgitant volume; T-TEER, tricuspid transcatheter edge-to-edge repair; TR, tricuspid regurgitation.

studies may be more likely to involve higher-volume centers, apply standardised screening and procedural protocols, and select patients more consistently for transcatheter tricuspid intervention.

Along the same lines, the lower mortality observed in randomized controlled trials compared with observational registries may partly reflect the more selective inclusion criteria, procedural standardization, treatment in highly experienced centers, and closer follow-up that are typical of randomized trials.

The association between comorbidity burden and 1-year mortality is clinically plausible and suggests that residual mortality after T-TEER may not be determined by TR severity alone, but also by multiorgan involvement. This finding is consistent with a staged model of the disease, in which the potential survival benefit of T-TEER may be greatest when intervention is performed before irreversible multiorgan dysfunction has developed (17,18).

In contrast, HF hospitalization appeared more closely related to right-sided dysfunction and baseline regurgitant volume. This finding is biologically coherent: severe TR increases stressed blood volume, right ventricular wall tension, systemic venous congestion, and susceptibility to recurrent decompensation (19,20).

The association between lower LVEF, concomitant significant mitral regurgitation, and persistent functional impairment at 1 year is particularly relevant for clinical decision-making. It suggests that, in patients in whom TR is part of a broader left-sided heart disease, isolated T-TEER may be insufficient to achieve meaningful symptomatic recovery (21).

In patients with concomitant significant mitral regurgitation or left ventricular dysfunction, isolated

T-TEER may be insufficient to fully address symptoms. Instead, the pre-procedural work-up should explicitly define the relative contribution of left-sided disease to the patient's symptoms to guide patient selection and set realistic expectations for functional recovery. Combined or staged mitral and tricuspid transcatheter strategies may be appropriate in selected patients, although the optimal timing, sequencing, and patient selection criteria remain uncertain and require prospective evaluation (22).

Taken together, the present findings support an individualized approach to patient selection and counselling before T-TEER. In patients with a high comorbidity burden, residual mortality risk may remain substantial despite effective TR reduction. In patients with right-sided dysfunction and severe volume overload, careful optimization of congestion before and after the procedure remains important. In patients with concomitant left ventricular dysfunction or significant mitral regurgitation, persistent symptoms may reflect the contribution of left-sided disease and may require an integrated management strategy.

Importantly, these observations should not be interpreted as three discrete or mutually exclusive patient phenotypes. In clinical practice, comorbidity burden, right ventricular dysfunction, venous congestion, left-sided valve disease, and left ventricular dysfunction frequently coexist within the same patient.

Early residual TR ≥3+ was observed in approximately one in five patients. Although reduction to TR ≤2+ has historically been considered a threshold for procedural success, contemporary data increasingly suggest that residual TR ≤1+ may represent a more desirable target when anatomically feasible (16,23). Therefore, the observed rate of residual TR ≥3+ should not be considered fully acceptable in contemporary practice and supports continued evaluation of alternative transcatheter strategies, including transcatheter tricuspid valve replacement in selected patients. While transcatheter replacement may enable more consistent near-complete TR elimination in patients with anatomy unsuitable for repair, it also introduces distinct clinical considerations, including right ventricular afterload mismatch, device durability, and interactions with pacing leads (24). Accordingly, the present findings should not be interpreted as favoring one treatment over another, but rather as underscoring the need for continued refinement of procedural techniques, patient selection, and device technology to maximize procedural success and long-term clinical benefit. As in other valvular heart disease, accurate phenotyping may be the key for risk stratification and defining timing and type of intervention for patients with significant TR (25).

The high heterogeneity observed across endpoints is clinically expected in the current T-TEER literature. Included studies differed in study design, patient selection, baseline TR etiology and severity, imaging protocols, device type, procedural experience, and follow-up definitions. Therefore, pooled estimates should be interpreted as contemporary benchmarks rather than as a uniform treatment effect applicable to all T-TEER candidates.

Future studies should move beyond aggregate study-level analyses. Individual patient-level datasets are needed to validate whether the observed patterns persist after adjustment for confounders, to distinguish overlapping mechanisms within the same patient, and to identify subgroups most likely to derive survival, hospitalization, or symptomatic benefit. In addition, the identification of imaging predictors of procedural success remains a key priority to improve patient selection and optimize clinical outcomes, and, for this task, the use of artificial intelligence could be instrumental (26).

Several limitations should be acknowledged. First, most available data were derived from observational registries, and the included studies differed in study design, patient selection, TR etiology and severity, and device type. This heterogeneity limits the generalizability of the pooled estimates. Second, this analysis was based on study-level aggregate data rather than individual patient-level data. Accordingly, meta-regression analyses are susceptible to ecological bias, limited statistical power, and potential overfitting, and should be considered exploratory and hypothesis-generating. Third, detailed anatomical and procedural variables were not consistently available, limiting the identification of predictors of early residual TR ≥3+. Fourth, although potentially overlapping publications were systematically assessed and sensitivity analyses were performed, residual patient overlap across registries cannot be definitively excluded. Finally, HF rehospitalization data were available from only five studies, reducing statistical power for this endpoint, and publication bias was detected for NYHA class III–IV and early residual TR ≥3+, warranting cautious interpretation.

Conclusions

T-TEER is associated with significant TR reduction and improved functional status; however, 1-year mortality

and HF hospitalization rates remain substantial. More contemporary recruitment periods were associated with lower 1-year all-cause mortality, suggesting improved outcomes over time. Systemic comorbidity burden, right-sided disease, and concomitant left-sided disease may contribute to residual risk after T-TEER; however, these associations should be considered hypothesis-generating and require validation in individual patient-level datasets.

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Footnote

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