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Comparative Effectiveness of MitraClip, TriClip, and PASCAL Systems for Moderate-to-Severe Tricuspid Regurgitation: A Systematic Review, Meta-Analysis, and Meta-Regression

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Abstract

Background: Tricuspid regurgitation (TR) is associated with progressive right-sided heart failure and increased mortality. Transcatheter tricuspid valve repair (TTVr) has emerged as a less invasive alternative to surgery, yet comparative evidence across device platforms remains limited.

Methods: A systematic review and meta-analysis was conducted following PRISMA guidelines. PubMed/MEDLINE, Embase, and Cochrane Library were searched from inception to March 2026. Studies reporting echocardiographic, functional, or clinical outcomes following TTVr using MitraClip, TriClip, or PASCAL systems were included. Pooled estimates were derived using random-effects models, with device-specific subgroup and REML-based meta-regression analyses performed to explore heterogeneity.

Results: Thirty-one studies enrolling several thousand patients were included. TTVr was associated with significant reductions in TR regurgitant volume (MD −17.60 mL; 95% CI: −18.85 to −16.35), vena contracta width (MD −6.27 mm; 95% CI: −7.41 to −5.14), and EROA (MD −0.21 cm²; 95% CI: −0.24 to −0.18). The proportion of patients with TR ≥ grade 3+ post-intervention was 27.3%. Six-minute walk distance improved significantly (MD +33.85 m; 95% CI: +23.11 to +44.59), and NYHA class ≥ III/IV was markedly reduced (OR 0.04; 95% CI: 0.03–0.07). TAPSE was broadly preserved. Subgroup analyses demonstrated consistent effects across all three device platforms, with no statistically significant between-device differences for most outcomes.

Conclusions: TTVr is associated with meaningful improvements in TR severity, echocardiographic parameters, and functional capacity across MitraClip, TriClip, and PASCAL systems. These findings support TTVr as an effective therapeutic option for patients with moderate-to-severe TR at high surgical risk. Adequately powered randomized trials with long-term follow-up are needed to establish comparative device efficacy and survival benefit.

Keywords: Tricuspid regurgitation; Transcatheter tricuspid valve repair; Edge-to-edge repair; MitraClip; TriClip; PASCAL; Structural heart disease; Meta-analysis.

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Background

Tricuspid regurgitation (TR) is a prevalent and clinically significant valvular heart disease associated with progressive right-sided heart failure, impaired functional capacity, and increased mortality. Once considered a benign condition, growing evidence has demonstrated that moderate-to-severe TR independently contributes to adverse outcomes, even after adjustment for comorbidities and left-sided heart disease [1].

Despite its substantial clinical burden, isolated surgical treatment for TR remains infrequently performed because many patients present at an advanced stage of disease with significant comorbidities and are therefore considered high-risk surgical candidates. As a result, conservative management continues to be the predominant treatment strategy for many individuals, often providing limited symptom control while allowing ongoing disease progression [2]. These challenges have accelerated the development of transcatheter tricuspid valve repair (TTVr) as a less invasive therapeutic alternative.

Among the currently available TTVr technologies, edge-to-edge repair devices have gained considerable attention. These include the MitraClip system (Abbott Vascular, Santa Clara, California, USA), which was originally designed for mitral valve repair and has been applied off-label for the treatment of TR; the TriClip system (Abbott Structural Heart, Santa Clara, California, USA), specifically engineered for tricuspid valve repair; and the PASCAL system (Edwards Lifesciences, Irvine, California, USA). Clinical studies have shown that these devices are technically feasible, demonstrate favorable procedural safety, and effectively reduce TR severity while improving patient outcomes [3-5]. Nevertheless, the current body of evidence is characterized by considerable heterogeneity arising from differences in study methodologies, patient characteristics, and reported endpoints. Furthermore, head-to-head comparisons between individual device platforms remain scarce, leaving uncertainty regarding their comparative effectiveness.

Accordingly, we performed a comprehensive systematic review and meta-analysis to assess the effects of transcatheter tricuspid valve repair on echocardiographic outcomes, functional capacity, and clinical endpoints, while also conducting subgroup analyses to compare the performance of the MitraClip, TriClip, and PASCAL systems.

Methods

Study Design and Reporting Standards

This systematic review and meta-analysis was performed in accordance with the **Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)** guidelines. A study protocol was established before the review commenced, with predefined objectives, eligibility criteria, and outcomes of interest. The review was prospectively registered in the **Open Science Framework (OSF)** database under DOI: **10.17605/OSF.IO/D4NWC**.

Search Strategy

A comprehensive literature search was performed across PubMed/MEDLINE, Embase, and Cochrane Library from database inception to March 2026. The search strategy combined controlled vocabulary (MeSH/Emtree terms) and free-text keywords related to "tricuspid regurgitation," "transcatheter tricuspid valve repair," "MitraClip," "TriClip," "PASCAL," and "edge-to-edge repair." No language restrictions were applied. Additionally, the reference lists of relevant articles and reviews were manually screened to identify further eligible studies.

Eligibility Criteria

Studies were included if they met the predefined eligibility criteria. The study population consisted of adults (≥18 years) with a diagnosis of moderate-to-severe or severe tricuspid regurgitation. Eligible interventions were transcatheter tricuspid valve repair (TTVr) performed using the MitraClip, TriClip, or PASCAL systems. To be eligible, studies had to report at least one outcome of interest, including TR severity or quantitative echocardiographic measures (regurgitant volume, effective regurgitant orifice area [EROA], or vena contracta), right ventricular function (e.g., tricuspid annular plane systolic excursion [TAPSE]), functional capacity assessed by the 6-minute walk test, or clinical outcomes such as New York Heart Association (NYHA) functional class. Both randomized controlled trials and observational studies, including prospective and retrospective designs, were considered eligible. Case reports, case series involving fewer than 10 patients, review articles, editorials, and conference abstracts without complete data were excluded. Studies lacking extractable quantitative data or containing overlapping patient populations were also excluded, with preference given to the most comprehensive or most recent dataset when duplication was identified.

Data Extraction

Two independent reviewers screened titles, abstracts, and full-text articles to determine eligibility. Data extraction was performed using a standardized form, capturing study characteristics (author, year, design, and sample size), patient demographics and baseline features, type of device used (MitraClip, TriClip, or PASCAL), and reported outcome measures including pre- and post-intervention values or event rates. Discrepancies between reviewers were resolved through discussion or consultation with a third reviewer.

Outcomes

Primary Outcomes

The primary outcomes included changes in tricuspid

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regurgitation (TR) severity, assessed using both quantitative and categorical measures. Echocardiographic parameters were evaluated, including regurgitant volume, vena contracta width, effective regurgitant orifice area (EROA), and tricuspid annular plane systolic excursion (TAPSE).

Secondary Outcomes

The secondary outcomes comprised functional and clinical measures. Functional capacity was assessed using the 6-minute walk test (6MWT), while clinical status was evaluated based on the New York Heart Association (NYHA) functional class.

Statistical Analysis

Meta-analysis was conducted using a random-effects model based on the DerSimonian–Laird method to account for expected between-study variability. Continuous outcomes were pooled as mean differences (MD) with corresponding 95% confidence intervals (CI), while dichotomous outcomes were synthesized using risk ratios (RR) with 95% CI. Statistical heterogeneity across studies was evaluated using the I^2 statistic, with thresholds of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively. In the presence of substantial heterogeneity, potential sources were explored through subgroup and sensitivity analyses. A p-value of <0.05 was considered statistically significant for all analyses, and all statistical tests were two-sided.

Subgroup and Sensitivity Analyses

Prespecified subgroup analyses were performed according to the type of transcatheter device used, including MitraClip, TriClip, PASCAL, and other systems. Differences between subgroups were assessed using tests for subgroup interaction, with a p-value of less than 0.05 considered statistically significant. Sensitivity analyses were conducted where appropriate by sequentially excluding individual studies and reassessing pooled estimates. Publication bias was assessed using funnel plot visual inspection and Egger's regression test, provided that at least ten studies were available for a given outcome.

Risk of Bias Assessment

To evaluate the methodological quality of included studies, two validated tools were applied according to study design. For randomized controlled trials (RCTs), the Cochrane Risk of Bias 2 (ROB 2) tool was used, assessing five domains: randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting of results. For non-randomized studies, the Methodological Index for Non-Randomized Studies (MINORS) was applied universally, covering eight criteria: (1) a clearly stated aim, (2) inclusion of consecutive patients, (3) prospective collection of data, (4) endpoints appropriate to the study aim, (5) unbiased assessment of the study endpoint, (6) a follow-up period appropriate to the study aim, (7) loss to follow-up of less than 5%, and (8) prospective calculation of the study size. Each criterion is scored 0 (not reported), 1 (reported but inadequate), or 2 (clearly reported), yielding a maximum score of 16 for non-comparative studies. All assessments were conducted independently by two reviewers, with discrepancies resolved through discussion or adjudication by a third reviewer.

Results

Study Selection

A systematic search of **PubMed/MEDLINE, Embase, and the Cochrane Library** through **1 March 2026 yielded 527 records**, comprising **191** from PubMed, **124** from Embase, and 212 from the Cochrane Library. Following the removal of **112 duplicate** records, **415 unique studies** remained for title and abstract screening.

After the initial screening, **312 studies** were excluded because they did not meet the study objectives. These included **28 non-human studies, 96 review articles or editorials, 74 conference abstracts without complete data**, and 114 studies that did not evaluate transcatheter tricuspid valve repair or the relevant device platforms.

The full texts of **103 articles** were subsequently reviewed for eligibility. Of these, **72 studies** were excluded for one or more of the following reasons: **18** lacked sufficient or extractable outcome data, **14** did not report relevant clinical or echocardiographic endpoints, **11** evaluated surgical rather than transcatheter interventions, **10** did not investigate edge-to-edge repair systems (MitraClip, TriClip, or PASCAL), and 19 involved overlapping patient populations.

In total, **31 studies** satisfied the predefined eligibility criteria and were included in the final qualitative and/or quantitative synthesis. The study selection process is summarized in the **PRISMA flow diagram (Figure S1)**, while the detailed characteristics of the included studies are presented in **Table S1**.

Study Characteristics

A total of 31 studies met the inclusion criteria and were incorporated into the final qualitative and quantitative synthesis, representing several thousand patients treated across a wide range of clinical settings and geographic regions. Detailed study characteristics are summarized in Table S2.

Study design. The included studies represented a diverse range of methodological designs. Two investigations were randomized controlled trials (RCTs): Tri.Fr (2024) and TRILUMINATE Pivotal (2025). The remaining 29 studies were non-randomized and included prospective single-arm

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studies (Carpenito et al. 2022; Lurz et al. 2021; Nickenig et al. 2017 and 2019), multicenter prospective registries (Kalbacher et al. 2017; Stocker et al. 2021; Ruf et al. 2021), and retrospective cohort studies (Mahowald et al. 2021; Ohno et al. 2014; Karam et al. 2019; among others). Several studies also incorporated multiple treatment arms, including device-specific comparison groups (Kitamura et al. 2021; Low et al. 2021; Sugiura et al. 2020) or a medical therapy comparator arm (Cai et al. 2020).

Sample size. Study sample sizes varied considerably, ranging from 11 patients in Volz et al. (2022) to 766 patients in Kalbacher et al. (2017). The TRILUMINATE Pivotal trial enrolled 572 participants. Most single-center studies included between 11 and 50 patients, whereas larger multicenter investigations generally enrolled 60–305 participants.

Devices evaluated. The MitraClip system was the most frequently investigated device and served as the sole or primary intervention in most studies. TriClip was evaluated as the primary device in Carpenito et al. (2022), Lurz et al. (2021), Nickenig et al. (2019), Freixa et al. (2022), Donal et al. (2022), Tri.Fr, TRILUMINATE Pivotal, and Cepas-Guillen et al. (2021). The PASCAL and PASCAL Ace systems were examined in Kitamura et al. (2021), Kodali et al. (2021), Volz et al. (2022), Sugiura et al. (2020, 2021), Aurich et al. (2021), Fam et al. (2019), and Baldus et al. (2022). Mixed-device cohorts were described by Low et al. (2021), Stolz et al. (2022), Stocker et al. (2021), and Krikken et al. (2022).

Patient demographics. The mean age of participants ranged from 71 years (Ohno et al. 2014; Volz et al. 2022) to 80.3 years (Baldus et al. 2022). Both randomized trials reported mean participant ages of approximately 78 years. Most non-randomized studies demonstrated a predominance of male participants, whereas female predominance was observed in Tri.Fr (65.5%), TRILUMINATE Pivotal (58.9%), Cepas-Guillen et al. (2021) (89%), Aurich et al. (2021) (75%), Freixa et al. (2022) (74%), and Volz et al. (2022) (73%). Left ventricular ejection fraction (LVEF) was generally preserved or mildly reduced, ranging from 33.2% in Ohno et al. (2014) to 59.4% in TRILUMINATE Pivotal. Tricuspid annular diameter, reported less frequently, ranged from 43.4 mm in Lurz et al. (2021) to 54 mm in Lurz et al. (2018). Mean systolic pulmonary artery pressure (sPAP) ranged from 28.2 mmHg (Freixa et al. 2022) to 50.3 mmHg (Ali et al. 2020), consistent with predominantly mild-to-moderate pulmonary hypertension.

Comorbidity profile. Atrial fibrillation was highly prevalent, exceeding 80% in most studies reporting this characteristic. The highest prevalence was observed in the PASCAL arm of Sugiura et al. (2020) (96%), followed by Baldus et al. (2022) (95.9%) and Otto et al. (2021) (95%). The lowest prevalence was reported by Ohno et al. (2014) (38.4%), reflecting a cohort with a greater proportion of non–atrial fibrillation-related tricuspid regurgitation. Functional TR accounted for 79% of cases in Freixa et al. (2022) and reached 100% in the MitraClip arm of Kitamura et al. (2021). The prevalence of diabetes mellitus ranged from 16% to 47%, while hypertension was reported in 59% to 91% of patients. Reported EuroSCORE II values ranged from 4.0% (Freixa et al. 2022; Cepas-Guillen et al. 2021) to 21.4% (Kalbacher et al. 2017), indicating that most patients were considered at high surgical risk.

Follow-up duration. Follow-up periods varied substantially across studies. Several investigations reported only in-hospital or 30-day outcomes (Freixa et al. 2022; Krikken et al. 2022; Baldus et al. 2022; Fam et al. 2019; Kodali et al. 2021, among others), whereas others provided follow-up at 3–6 months (Donal et al. 2022; Volz et al. 2022; Carpenito et al. 2022; Nickenig et al. 2019; Orban et al. 2018). Longer-term outcomes at 1 year were available from Sugiura et al. (2021), Kitamura et al. (2021), Lurz et al. (2021), Stocker et al. (2021), and Stolz et al. (2022). The TRILUMINATE Pivotal trial reported the longest follow-up of 24 months, while Kalbacher et al. (2017), Ohno et al. (2014), and Karam et al. (2019) presented extended follow-up durations ranging from approximately 187 to 660 days.

Outcomes reported. Echocardiographic assessment of TR severity was the most consistently reported endpoint across the included studies. Additional frequently reported outcomes included tricuspid annular plane systolic excursion (TAPSE), 6-minute walk distance, and New York Heart Association (NYHA) functional class. Other evaluated outcomes comprised all-cause mortality, cardiovascular mortality, major adverse cardiac and cerebrovascular events (MACCE), heart failure hospitalization, renal and hepatic function, procedural success, and tricuspid annular diameter. A comprehensive summary of all reported outcomes is provided in Table S2.

Tricuspid Regurgitation Severity and Echocardiographic Parameters

Echocardiographic Outcomes

Tricuspid Regurgitant Volume

Transcatheter tricuspid valve repair (TTVr) resulted in a significant reduction in tricuspid regurgitant volume (Figure S2), with a pooled mean difference (MD) of −17.60 mL (95% CI: −18.85 to −16.35; $I^2 = 73.8\%$; n = 452 across 15 studies; $p < 0.0001$). Moderate-to-high between-study heterogeneity was observed, likely reflecting differences in baseline TR severity, imaging techniques, and duration of follow-up. Device-specific subgroup analyses demonstrated significant reductions with all three repair systems, including MitraClip (MD −21.63 mL; 95% CI: −40.62 to −2.65; $I^2 = 80.4\%$),

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PASCAL (MD −17.49 mL; 95% CI: −31.32 to −3.66; I^2 = 37.5%), and TriClip (MD −17.51 mL; 95% CI: −19.67 to −15.35; I^2 = 82.0%). No statistically significant differences were identified between device subgroups (p for interaction = 0.33), suggesting a consistent reduction in regurgitant volume irrespective of device type, although the wider confidence intervals for the MitraClip and PASCAL subgroups likely reflect their comparatively smaller sample sizes.

Tricuspid Regurgitation Severity

Following TTVr, the pooled proportion of patients with residual TR ≥ grade 3+ was 27.3% (95% CI: 22.4–32.8%; I^2 = 80.9%; n = 1,151; p < 0.0001) (Figure S5), representing a marked reduction compared with the nearly universal prevalence of moderate-to-severe or severe TR at baseline. As these analyses were derived from single-arm pre–post studies, outcomes are presented as pooled post-procedural proportions rather than risk ratios. Similar reductions were observed across device subgroups, including MitraClip (25.7%; 95% CI: 18.9–34.0%; I^2 = 79.2%), TriClip (15.6%; 95% CI: 6.8–32.0%; I^2 = 85.2%), and PASCAL (33.2%; 95% CI: 11.3–66.1%; I^2 = 78.3%). There was no significant interaction between devices (p = 0.90), indicating comparable efficacy in reducing severe TR. Residual heterogeneity was likely attributable to variations in TR grading systems, echocardiographic imaging modalities, and baseline disease severity among the included studies.

Vena Contracta Width

A significant decrease in vena contracta width was observed after TTVr (Figure S8), with a pooled MD of −6.27 mm (95% CI: −7.41 to −5.14; n = 665; p < 0.0001). Between-study heterogeneity was absent (overall I^2 = 0.0%), and similarly low across the MitraClip, PASCAL, and TriClip subgroups, indicating highly consistent findings. Device-specific analyses demonstrated reductions of −5.46 mm (95% CI: −7.10 to −3.83) for MitraClip, −6.56 mm (95% CI: −12.64 to −0.47) for PASCAL, and −7.57 mm (95% CI: −12.18 to −2.95) for TriClip. No significant subgroup differences were detected (p for interaction = 1.00), supporting a consistent treatment effect across available edge-to-edge repair systems.

Effective Regurgitant Orifice Area (EROA)

TTVr was also associated with a significant reduction in effective regurgitant orifice area (EROA) (Figure S9), yielding a pooled MD of −0.21 cm² (95% CI: −0.24 to −0.18; I^2 = 94.1%; n = 526; p < 0.0001). Considerable heterogeneity was observed, likely reflecting differences in EROA measurement techniques, including variations in PISA assumptions and two-dimensional versus three-dimensional imaging, as well as differences in the underlying mechanism of TR. Device-specific analyses demonstrated reductions of −0.43 cm² (95% CI: −0.57 to −0.29; I^2 = 0%) for MitraClip, −0.29 cm² (95% CI: −0.48 to −0.09; I^2 = 0%) for PASCAL, and −0.20 cm² (95% CI: −0.25 to −0.15; I^2 = 95.5%) for TriClip. Despite the variability within the TriClip subgroup, no statistically significant differences were observed between devices (p for interaction = 0.94), indicating broadly comparable reductions in EROA.

Right Ventricular Function

Right ventricular systolic function, assessed using tricuspid annular plane systolic excursion (TAPSE), demonstrated an overall pooled improvement of +0.39 mm (95% CI: +0.21 to +0.58; I^2 = 89.9%; n = 709; p < 0.0001) (Figure S3), suggesting that RV longitudinal function was generally preserved or modestly enhanced following TTVr. Device-level analyses showed differing trends, with a small decline in the MitraClip subgroup (MD −0.98 mm; 95% CI: −1.93 to −0.02; n = 286), while TAPSE remained essentially unchanged in the PASCAL subgroup (MD −0.09 mm; 95% CI: −1.44 to +1.25; n = 129) and the TriClip subgroup (MD +0.11 mm; 95% CI: −1.65 to +1.88; n = 294). However, subgroup differences were not statistically significant (p = 0.50). The slight reduction observed with MitraClip may reflect differences in patient selection, procedural era, or baseline ventricular function rather than a true device-related effect. Overall, these findings indicate that edge-to-edge TTVr does not appear to adversely affect RV systolic performance during the available follow-up period. Nevertheless, interpretation should remain cautious given the substantial residual heterogeneity and the recognized limitations of TAPSE as a surrogate of global RV function.

Functional Capacity

The 6-minute walk distance (6MWD) improved significantly after TTVr (Figure S4), with a pooled MD of +33.85 meters (95% CI: +23.11 to +44.59; I^2 = 87.2%; n = 1,053; p < 0.0001). The magnitude of improvement exceeded the accepted minimum clinically important difference of approximately 25–30 meters, supporting the clinical relevance of these findings. Although heterogeneity was substantial, likely reflecting differences in baseline functional status and follow-up duration, all device platforms demonstrated improvement. Significant subgroup differences were observed (p for interaction = 0.004), with the largest gains reported for MitraClip (MD +71.65 m; 95% CI: +52.60 to +90.69; I^2 = 20.2%; n = 398), followed by PASCAL (MD +58.52 m; 95% CI: +7.81 to +109.23; I^2 = 0%; n = 102) and TriClip (MD +29.02 m; 95% CI: +16.66 to +41.38; I^2 = 77.6%; n = 553). These differences should be interpreted cautiously because they may reflect variations in baseline characteristics, follow-up intervals, and study era rather than true differences in device performance.

Health-related quality of life, measured using the Kansas City Cardiomyopathy Questionnaire (KCCQ), improved by

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a pooled mean of +15.78 points (95% CI: +12.21 to +19.35; I^2 = 65.6%; n = 613; p = 0.055) (Figure S11). Although the overall p-value narrowly missed conventional statistical significance, the magnitude of improvement substantially exceeded the established 5-point threshold considered clinically meaningful, suggesting important patient-perceived benefits despite moderate between-study heterogeneity.

NYHA Functional Class

Changes in New York Heart Association (NYHA) functional class were analyzed using odds ratios (ORs) because the available evidence consisted of single-arm pre–post data synthesized using logistic random-effects models, making this approach more appropriate than risk ratio estimation.

The pooled odds of remaining in NYHA class III/IV after TTVr were markedly reduced compared with baseline (Figure S6), with an OR of 0.04 (95% CI: 0.03–0.07; I^2 = 67.1%; n = 1,083; p < 0.0001). Comparable improvements were observed across all device subgroups, including MitraClip (OR 0.05; 95% CI: 0.02–0.10; I^2 = 70.8%), TriClip (OR 0.05; 95% CI: 0.04–0.07; I^2 = 0%), and PASCAL (OR 0.02; 95% CI: 0.00–0.09; I^2 = 79.5%), with no significant differences between devices (p = 0.23). These findings indicate a substantial and consistent reduction in advanced heart failure symptoms following TTVr. Conversely, the pooled odds of achieving NYHA class I/II after intervention were 21.30 (95% CI: 3.84–118.08; I^2 = 40.7%; n = 994; p = 0.134) (Figure S10). Although the direction and magnitude of effect favored substantial functional improvement, the overall estimate did not achieve statistical significance, primarily because of the very wide confidence interval, particularly within the TriClip subgroup (OR 12.53; 95% CI: 0.04–3,921.56). The MitraClip subgroup alone demonstrated a statistically significant improvement (OR 20.08; 95% CI: 8.80–45.81; I^2 = 42.4%; n = 856). Accordingly, interpretation of this outcome should be cautious, whereas the findings for the reduction in NYHA class III/IV are supported by a larger and more robust evidence base.

Risk of Bias Assessment

A total of 31 studies were included in the risk of bias assessment. 29 non-randomized studies were evaluated using MINORS (Table S5). MINORS scores ranged from 11 to 15 out of a maximum of 16, reflecting generally adequate methodological quality. Most studies clearly reported their aims, used appropriate endpoints, and achieved less than 5% loss to follow-up; however, prospective data collection and sample size justification were frequently scored as inadequate or unreported, representing the most consistent methodological limitations across this group. Unbiased outcome assessment — typically requiring blinded or independently adjudicated endpoints — was scored as inadequate across nearly all non-randomized studies, reflecting an inherent limitation of real-world single-arm registries and observational designs in the transcatheter tricuspid valve intervention literature. The two randomized controlled trials, TRILUMINATE Pivotal and TRI.FR, were assessed using the RoB 2 tool and both received an overall judgment of "some concerns," primarily related to open-label design and potential performance bias arising from the unblinded nature of device trials. These findings should be considered when interpreting the pooled estimates derived from this body of evidence.

Certainty of Evidence (GRADE Assessment)

To facilitate clinical interpretation and guide evidence-based recommendations, the certainty of evidence for all nine pre-specified outcomes was formally evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework (Table S7). Domains assessed included risk of bias, inconsistency (heterogeneity), indirectness, and imprecision, with the overall certainty rated as High, Moderate, Low, or Very Low. The full domain-level justifications are presented in Table S7.

Echocardiographic and Haemodynamic Outcomes

Vena contracta width and 6-minute walk distance were rated as Moderate certainty evidence. For vena contracta (MD −6.27 mm; 95% CI: −7.41 to −5.14; Table S7), the Moderate rating reflects the absence of statistically significant between-study heterogeneity (I^2 = 0.0% across all device subgroups), consistent directional effects across MitraClip, PASCAL, and TriClip, and non-serious indirectness, with the sole downgrade driven by the observational-only study design and the absence of an active comparator in most contributing studies.

The remaining echocardiographic outcomes—TR severity proportion (pooled proportion 27.3%; 95% CI: 22.4–32.8%), EROA (MD −0.21 cm^2; 95% CI: −0.24 to −0.18), and TR regurgitant volume (MD −17.60 mL; 95% CI: −18.85 to −16.35)—were all rated as Low certainty. For TR severity and TR regurgitant volume, the primary downgrades were applied for serious risk of bias (predominantly single-arm observational designs, without active comparator arms in most studies) and serious inconsistency, with I^2 values of 80.9% and 73.8%, respectively. For EROA, very high heterogeneity (overall I^2 = 94.1%; TriClip subgroup I^2 = 95.5%) constituted a serious inconsistency downgrade, in addition to the observational study design limitation.

TAPSE was also rated Low certainty (MD +0.39 mm; 95% CI: +0.21 to +0.58; I^2 = 89.9%). Although the pooled estimate excludes the null and directionally supports preservation of RV longitudinal function, the high heterogeneity—driven in particular by divergent device-level effects (MitraClip subgroup showing −0.98 mm versus neutral effects in

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PASCAL and TriClip subgroups)—constituted a serious inconsistency downgrade. Additionally, TAPSE as a single-plane surrogate of RV function introduces measurement indirectness relative to volumetric or global RV functional assessment, which was noted as a consideration in domain scoring, though not sufficient to apply a formal indirectness penalty given the consistency of TAPSE as the field-standard RV metric in TTVr trials.

Functional and Patient-Reported Outcomes

6-Minute Walk Distance (6MWD) was rated Moderate certainty (MD +33.85 m; 95% CI: +23.11 to +44.59; I^2 = 87.2%). The rating reflects inclusion of four randomized controlled trials (Tri.Fr, TRILUMINATE Pivotal, TRISCEND II, TRICAVAL) alongside observational data (N = 1,053), providing higher-level evidence for this endpoint than for purely observational outcomes. The overall CI excludes the null and the pooled estimate exceeds the minimum clinically important difference (MCID) of approximately 25–30 meters. Downgrade for inconsistency was considered but not applied at the Moderate threshold given the overall robustness of the directional effect across device subgroups, despite high I^2. Two of the four RCTs (TRISCEND II Pivotal and TRICAVAL) received high RoB 2 ratings, contributing a partial risk-of-bias downgrade that was balanced against the trial-level evidence from TRILUMINATE and Tri.Fr.

NYHA Class > III was rated Low certainty (OR 0.04; 95% CI: 0.03–0.07; I^2 = 67.1%). Despite the large effect size and a confidence interval that clearly excludes the null, the certainty was downgraded for serious risk of bias—predominantly unblinded observational designs, with two of the four contributing RCTs (TRISCEND II and TRICAVAL) rated high risk of bias on RoB 2—and for serious inconsistency, in particular the markedly elevated heterogeneity in the PASCAL subgroup (I^2 = 79.5%).

NYHA Class < III (proportion achieving functional improvement) was similarly rated Low certainty (OR 21.30; 95% CI: 3.84–118.08; I^2 = 40.7%; p = 0.134). Although between-study heterogeneity was more acceptable for this outcome (I^2 = 40.7%), the extremely wide confidence interval in the TriClip subgroup (OR 12.53; 95% CI: 0.04–3,921.56) constituted a serious imprecision downgrade, and the failure of the overall pooled estimate to reach conventional statistical significance (p = 0.134) further limited certainty.

KCCQ score change was rated Low certainty (MD +15.78 points; 95% CI: +12.21 to +19.35; I^2 = 65.6%; p = 0.055). The pooled improvement well exceeds the KCCQ MCID of 5 points and suggests clinically meaningful quality-of-life benefit. However, the borderline statistical significance, moderate-to-high heterogeneity, and predominantly observational design resulted in downgrades for risk of bias and imprecision, yielding a Low overall certainty rating.

Summary and Clinical Implications

Across all nine outcomes, no outcome achieved High certainty evidence, two achieved Moderate certainty (vena contracta and 6MWD), and seven were rated Low certainty (Table S7). The predominance of Low certainty evidence reflects the field-wide reliance on single-arm observational and registry-based data, which, while informative regarding feasibility and directional efficacy, cannot provide the degree of causal inference afforded by adequately powered, properly controlled randomized trials. Reviewers and guideline committees should interpret the consistent directional effects across outcomes as supportive of TTVr efficacy, while recognising that the certainty of evidence remains insufficient to draw definitive conclusions about the magnitude of benefit or the comparative effectiveness of individual device platforms.

Meta-Regression Analyses

To explore potential sources of between-study heterogeneity and to assess whether key study-level covariates moderated treatment effects, REML-based meta-regression analyses were performed for functional and structural outcomes where a sufficient number of studies contributed data. Results are summarized in Table S3. Covariates examined included follow-up duration (log-transformed days), the proportion of patients with functional TR aetiology, the proportion of patients treated with a specific device (MitraClip or TriClip), and baseline TR severity proportion. All analyses used REML estimation, and the R^2 analogue is reported as the proportion of between-study variance explained by each covariate.

Functional and Symptomatic Outcomes

For NYHA ≥ III/IV (log OR), meta-regression against follow-up duration (log days) yielded a regression slope (β1) of +0.262 (p = 0.456; df = 9; R^2 analogue = 0.0%), indicating that longer follow-up did not significantly predict the odds of remaining in NYHA ≥ III/IV post-intervention (Table S3). The R^2 analogue of 0.0% confirms that follow-up duration explains none of the residual between-study variance for this outcome. This suggests that the symptomatic benefit of TTVr, as reflected in NYHA class reduction, is not systematically attenuated or amplified by the duration of follow-up across the range represented in included studies.

For the broader NYHA outcome (log OR), meta-regression against the proportion of patients with functional TR (β1 = +12.48; p = 0.433; df = 3; R^2 analogue = 0.0%) similarly found no statistically significant moderating effect. The functional TR proportion did not explain variability in NYHA improvement across studies, suggesting that the symptomatic response to TTVr is not contingent on the proportion of functional versus other TR aetiologies

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represented in a study population, at least within the aetiology mix present in the included studies.

A device-specific meta-regression for NYHA ≥ III/IV within the MitraClip subgroup examined the MitraClip proportion as a covariate (β1 = +1.304; p = 0.887; df = 5; R^2 analogue = 0.0%). No significant relationship was identified, indicating that the proportion of MitraClip-treated patients within a study did not explain between-study variability in NYHA ≥ III/IV outcomes in the MitraClip subgroup.

Structural Outcomes

For EROA mean change (cm^2), meta-regression against baseline TR severity proportion yielded a slope of −0.900 (p = 0.230; df = 2; R^2 analogue = 44.0%; Table S3). Although this regression did not reach statistical significance, the R^2 analogue of 44.0% suggests that baseline TR severity proportion may explain a meaningful share of the between-study variance in EROA reduction. Studies enrolling patients with a higher proportion of severe TR at baseline tended towards greater absolute EROA reduction, consistent with the expectation that greater regurgitant burden provides more room for measurable echocardiographic improvement. This finding should be interpreted cautiously given the small number of studies contributing to this regression (df = 2).

The most statistically robust meta-regression finding was for TR severity binary outcome (log OR) within the MitraClip subgroup. Baseline TR severity proportion was a significant negative predictor (β1 = −15.30; p = 0.003; df = 8; R^2 analogue = 78.8%; Table S3). This indicates that studies with a higher baseline proportion of patients with severe TR were associated with lower post-intervention odds of residual TR ≥ grade 3+, explaining 78.8% of the between-study variance in this subgroup. This finding is clinically interpretable: patients presenting with more severe baseline TR may benefit disproportionately from MitraClip-based edge-to-edge repair, achieving greater categorical TR grade reduction. It also suggests that baseline TR severity is a substantial driver of the heterogeneity observed in the MitraClip TR severity outcome, and that future analyses should stratify by or adjust for baseline TR grade distribution.

For TR regurgitant volume within the TriClip subgroup, meta-regression against baseline TR severity proportion yielded β1 = −48.28 (p = 0.086; df = 2; R^2 analogue = 92.3%; Table S3). While this did not meet the pre-specified significance threshold of $p < 0.05$, the trend-level p-value and the exceptionally high R^2 analogue of 92.3% suggest that baseline TR severity proportion is a near-complete explanation of between-study variability in TR regurgitant volume reduction in the TriClip subgroup. The low degrees of freedom (df = 2) substantially limits statistical power for this regression, and the finding should therefore be interpreted as hypothesis-generating. Nonetheless, the consistent pattern across both the MitraClip and TriClip subgroups—where baseline TR severity proportion explains a large proportion of variance in structural outcomes—provides a coherent mechanistic signal: greater baseline TR burden predicts greater absolute echocardiographic benefit.

Summary and Interpretation

Taken together, the meta-regression analyses (Table S3) demonstrate that follow-up duration and functional TR proportion do not significantly moderate NYHA functional outcomes, suggesting that symptomatic improvements following TTVr are relatively stable across the range of follow-up durations and TR aetiologies represented in the current evidence base. In contrast, baseline TR severity proportion emerges as a consistent and clinically meaningful moderator of structural outcomes, particularly TR severity and TR regurgitant volume, most prominently within the MitraClip and TriClip subgroups. The significant finding for TR severity binary outcome in the MitraClip subgroup (R^2 = 78.8%; p = 0.003) is the strongest meta-regression result in this analysis and has direct implications for patient selection: patients with higher baseline TR severity may achieve more pronounced categorical improvements in TR grade following edge-to-edge repair.

These findings should be interpreted in the context of several limitations inherent to meta-regression. Most regressions were constrained by small numbers of studies per covariate (df ranging from 2 to 9), limiting statistical power and increasing susceptibility to ecological fallacy. The covariates examined represent aggregate study-level characteristics rather than individual patient-level data, and therefore cannot establish causal relationships or substitute for individual patient data meta-analysis. Future prospective analyses with consistent covariate reporting across studies would substantially strengthen the meta-regression evidence base for TTVr.

Cardioband (Direct Annuloplasty) Outcomes: Narrative Synthesis

Because Cardioband and other direct annuloplasty systems differ mechanistically from edge-to-edge repair devices, data from these studies were extracted separately and are reported here as a narrative synthesis rather than pooled within the primary quantitative meta-analysis. Three studies reporting clinical outcomes with the Cardioband tricuspid system were identified.[18,32,43] In the United States Early Feasibility Study (EFS), 30 patients with severe or greater symptomatic functional TR (mean age 77 years, 80% women, 97% atrial fibrillation, 70% NYHA class III–IV, mean LVEF 58%) underwent Cardioband implantation, with device success in 93% of patients and no 30-day mortality. Between baseline and 30 days, septolateral annular diameter decreased by 13% (p<0.001), 85% of patients achieved at least a one-

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grade reduction in TR and 44% achieved ≤moderate TR, 75% improved to NYHA class I–II (p<0.001), and KCCQ score improved by 16 points.[18]

The European TriBAND post-market study reported 30-day outcomes in 61 patients with predominantly severe or greater functional TR (mean age 79 years, 85% NYHA class III–IV, mean EuroSCORE II 6.8%, mean LVEF 53%). Device success was 96.7%, and all-cause mortality and composite major adverse event rates at 30 days were 1.6% and 19.7%, respectively. Septolateral annular diameter was reduced by 20% (p<0.001), with 69% of patients achieving ≤moderate TR and 85% achieving at least a one-grade TR reduction. Early right heart remodeling was reflected by reductions in mid-right ventricular end-diastolic diameter (−10%, p=0.005), right atrial volume (−21%, p<0.001), and inferior vena cava diameter (−11%, p=0.022). Functional status improved substantially, with 74% of patients in NYHA class I–II at 30 days compared with 15% at baseline, and KCCQ score improved by 17 points (both p<0.001). Right coronary artery injury requiring intervention occurred in 6.6% of patients, underscoring a device-specific procedural risk related to anchor deployment adjacent to the annulus.[43]

A separate multicenter real-world experience with the Cardioband system in 60 patients with predominantly severe-to-torrential secondary TR (median age 76 years, 82% NYHA class III–IV, 78% heart failure with preserved ejection fraction) reported a more modest primary efficacy endpoint, with ≥2-grade TR reduction achieved in 45% of patients, although 60% had less-than-severe TR at discharge. The more modest efficacy signal in this cohort likely reflects the inclusion of a higher-risk, anatomically more complex real-world population, including patients with massive or torrential TR, relative to the earlier feasibility cohorts.[32]

Taken together, these descriptive data indicate that Cardioband-based direct annuloplasty achieves consistent, if numerically more modest, reductions in TR severity compared with the pooled edge-to-edge repair outcomes reported above, alongside meaningful gains in NYHA functional class and quality of life and low short-term mortality. However, because patient populations, echocardiographic reporting conventions, and follow-up durations differed appreciably from the edge-to-edge repair cohorts, and because study-level variance estimates required for formal random-effects pooling were not uniformly reported across these studies, these findings are presented narratively rather than combined with the primary quantitative synthesis of this meta-analysis.

Discussion

In this comprehensive systematic review and meta-analysis, we found that transcatheter tricuspid valve repair (TTVr) was associated with significant improvements in echocardiographic, functional, and patient-centered outcomes among individuals with moderate-to-severe tricuspid regurgitation (TR). Across the pooled analysis, TTVr significantly reduced regurgitant volume, vena contracta width, effective regurgitant orifice area (EROA), and the proportion of patients with residual severe TR. These anatomical improvements were accompanied by clinically meaningful gains in functional capacity, including improvements in New York Heart Association (NYHA) functional class, six-minute walk distance (6MWD), and health-related quality of life. Collectively, these findings support the expanding role of transcatheter edge-to-edge repair as an effective therapeutic option for patients who are at high or prohibitive surgical risk.

One of the principal findings of this meta-analysis is the consistency of treatment benefit across currently available edge-to-edge repair systems. Device-specific subgroup analyses demonstrated significant reductions in TR severity and favorable changes in quantitative echocardiographic parameters with the MitraClip, TriClip, and PASCAL systems. Importantly, formal subgroup analyses showed no statistically significant differences between devices for regurgitant volume, TR severity, vena contracta width, EROA, TAPSE, or NYHA functional outcomes. Although numerical differences were observed for selected endpoints, these findings should not be interpreted as evidence of superiority because subgroup analyses were limited by unequal sample sizes, differences in patient characteristics, procedural era, and study design. Instead, the overall findings support a potential class effect of edge-to-edge repair technologies, consistent with previous registry and clinical trial data demonstrating substantial TR reduction and symptomatic improvement following transcatheter intervention.[3–4]

The observed improvements in quantitative echocardiographic parameters further strengthen the mechanistic basis of TTVr. Significant reductions in regurgitant volume, vena contracta width, and EROA indicate effective restoration of leaflet coaptation and reduction of regurgitant burden across different device platforms. Although moderate-to-high heterogeneity was present for several outcomes, this variability is expected given differences in imaging methodology, TR grading systems, baseline disease severity, and follow-up duration among the included studies. Nevertheless, the direction and magnitude of treatment effect remained remarkably consistent, supporting the robustness of the overall findings.

An important aspect of our analysis relates to right ventricular (RV) function. Contrary to some earlier reports suggesting deterioration in RV longitudinal mechanics following successful TR reduction, our updated pooled analysis demonstrated that TAPSE was largely preserved,

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with a small overall increase. Device-specific analyses showed a modest decline in the MitraClip subgroup, whereas essentially neutral changes were observed with TriClip and PASCAL. These subgroup differences were not statistically significant. The slight reduction observed in some studies may reflect altered loading conditions after elimination of severe TR rather than intrinsic deterioration in myocardial contractility. Acute reduction of severe regurgitation increases effective forward stroke volume and RV afterload, potentially resulting in transient reductions in longitudinal shortening despite preserved or improved global ventricular performance. Because TAPSE reflects only one component of RV function and is highly load dependent, its interpretation following TTVr should be made cautiously and ideally alongside additional indices of RV remodeling and systolic performance.

The improvements in functional capacity observed in this study are particularly noteworthy. Patients experienced a pooled increase in 6MWD that exceeded the accepted minimum clinically important difference for patients with heart failure and valvular disease, suggesting that the observed benefits are clinically meaningful rather than merely statistically significant. Similarly, KCCQ scores improved by more than 15 points, substantially exceeding the established threshold for clinically important improvement in health-related quality of life. Although significant subgroup differences were identified for 6MWD, with numerically greater improvements in the MitraClip and PASCAL subgroups than in the TriClip subgroup, these findings should be interpreted cautiously because they likely reflect differences in baseline functional status, follow-up duration, patient selection, and procedural experience rather than true device-related superiority. Likewise, while improvement in NYHA functional class was observed across all platforms, statistical precision varied between device-specific analyses owing to differences in sample size and available data.

These findings are broadly consistent with contemporary evidence from prospective registries and randomized trials. Studies such as TRILUMINATE Pivotal and Tri.Fr have demonstrated significant improvements in symptom burden, exercise capacity, and quality of life following edge-to-edge tricuspid repair while maintaining favorable procedural safety profiles. Similarly, investigations evaluating the PASCAL system have reported meaningful reductions in TR severity accompanied by improvements in functional status. Our meta-analysis extends these observations by integrating data across multiple device platforms and demonstrates that these favorable outcomes appear consistent throughout the currently available evidence base.

Clinical Significance and Mechanistic Correlation

The clinical implications of these findings extend beyond echocardiographic improvement alone. Persistent severe TR is associated with progressive right-sided heart failure, repeated heart failure hospitalization, impaired quality of life, hepatic and renal dysfunction, and increased mortality. By consistently reducing regurgitant burden while simultaneously improving exercise tolerance, symptom severity, and patient-reported quality of life, TTVr addresses several clinically meaningful aspects of disease burden in patients who frequently have limited treatment options because of excessive operative risk.

The improvements in KCCQ score and 6MWD further suggest that successful reduction of TR translates into measurable benefits from the patient's perspective. Improvement in forward cardiac output, reduction of systemic venous congestion, and reversal of right-sided volume overload likely contribute collectively to these favorable clinical outcomes. However, whether these short-term physiological improvements ultimately translate into improved survival or reductions in heart failure hospitalization remains uncertain because long-term outcome data remain limited.

The considerable heterogeneity observed across several pooled analyses likely reflects differences in patient selection, TR etiology, imaging methodology, baseline RV function, procedural techniques, operator experience, and duration of follow-up. Despite this variability, treatment effects consistently favored TTVr across nearly all outcomes examined, increasing confidence in the overall conclusions.

Alternative Approaches: Direct Annuloplasty (Cardioband)

In addition to edge-to-edge leaflet approximation, direct annuloplasty represents a mechanistically distinct transcatheter strategy for tricuspid valve repair. The Cardioband Tricuspid System employs a contractible band anchored circumferentially along the tricuspid annulus, reducing annular dilation and restoring leaflet coaptation through annular remodeling rather than direct leaflet capture. Conceptually closer to surgical ring annuloplasty, this approach may in theory avoid certain limitations of edge-to-edge devices, such as residual multi-jet regurgitation or iatrogenic leaflet tethering, although it introduces its own procedural considerations, including anchor deployment adjacent to the right coronary artery and the atrioventricular conduction system.

Early feasibility data have shown encouraging results with this technology. The Early Feasibility Study of the Cardioband system reported significant reductions in TR severity and annular dimensions at 30 days with an acceptable procedural safety profile.[18] These findings were corroborated by 30-day outcomes from the TriBAND study, which similarly demonstrated significant TR reduction and functional

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improvement following Cardioband implantation in patients with symptomatic functional TR.[43] Complementary evidence from a related direct annuloplasty platform has further supported the feasibility of transcatheter annular reduction as a therapeutic strategy in secondary TR.[32]

Because these studies differ substantially from edge-to-edge repair trials in device mechanism, patient selection, and reported outcome metrics, Cardioband and other annuloplasty-based devices were not incorporated into the primary quantitative synthesis of this meta-analysis. The available evidence nonetheless suggests that direct annuloplasty represents a complementary rather than competing strategy within the expanding transcatheter tricuspid repair landscape. Future comparative studies, ideally randomized, are warranted to clarify the relative efficacy, durability, and safety of annuloplasty-based versus edge-to-edge repair approaches, as well as their potential combined or staged use in patients with complex tricuspid valve pathology and marked annular dilation.

Strengths and Limitations

Strengths

This study has several important strengths. First, it represents one of the most comprehensive syntheses of contemporary evidence evaluating transcatheter edge-to-edge tricuspid valve repair across multiple commercially available device platforms. Second, a broad range of clinically relevant outcomes was examined, including quantitative echocardiographic parameters, right ventricular function, exercise capacity, quality of life, and functional status. Third, predefined subgroup analyses enabled assessment of device-specific outcomes while maintaining an overall pooled estimate. Finally, inclusion of a large cumulative patient population across diverse clinical settings enhances the precision and generalizability of the findings.

Limitations

Several limitations should be considered when interpreting these results. Most included studies were observational and single-arm in design, increasing susceptibility to selection bias, confounding, and uncontrolled baseline differences. Only two randomized controlled trials were available, limiting the overall certainty of comparative evidence. High between-study heterogeneity persisted for several endpoints because of differences in patient populations, imaging techniques, outcome definitions, procedural experience, and follow-up duration. Individual patient-level data were unavailable, precluding adjustment for important clinical variables or more detailed subgroup analyses. Furthermore, direct head-to-head comparisons between MitraClip, TriClip, and PASCAL systems remain scarce; therefore, the absence of statistically significant subgroup differences should not be interpreted as evidence of therapeutic equivalence. Finally, most available evidence focuses on surrogate echocardiographic and short-term functional outcomes, whereas robust data regarding long-term durability, heart failure hospitalization, reintervention, and survival remain limited.

Future Directions

Future investigations should prioritize adequately powered randomized controlled trials directly comparing currently available TTVr systems to better define their relative efficacy and safety. Extended follow-up studies are required to determine the durability of TR reduction, long-term right ventricular remodeling, structural valve integrity, and survival benefit. Greater standardization of imaging protocols, TR grading systems, and clinical endpoint definitions would improve comparability across future studies and reduce methodological heterogeneity.

Further research should also focus on optimizing patient selection through integration of multimodality imaging, RV functional assessment, and clinical phenotyping to identify patients most likely to benefit from intervention and determine the optimal timing of treatment before irreversible right ventricular dysfunction develops. Finally, future studies should clarify whether observed changes in TAPSE represent true alterations in myocardial performance or simply physiological adaptation to changing loading conditions following successful TR reduction.

Conclusions

This systematic review and meta-analysis demonstrates that transcatheter tricuspid valve repair using the MitraClip, TriClip, and PASCAL systems is consistently associated with significant reductions in tricuspid regurgitation severity and quantitative echocardiographic measures, accompanied by meaningful improvements in functional status, exercise capacity, and health-related quality of life among patients with moderate-to-severe TR who are at elevated surgical risk. The consistency of benefit observed across device platforms supports the concept of a shared therapeutic effect of edge-to-edge repair technologies. Nevertheless, these findings should be interpreted in the context of important limitations, including the predominance of observational single-arm studies, substantial between-study heterogeneity, and relatively short follow-up durations. Furthermore, the absence of statistically significant subgroup differences should not be interpreted as evidence of equivalent efficacy between devices because the currently available evidence is insufficient for definitive comparative effectiveness assessment.

Although the available data consistently demonstrate improvements in surrogate echocardiographic and functional outcomes, robust evidence regarding long-term mortality, heart failure hospitalization, right ventricular remodeling,

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and durability of repair remains limited. Overall, TTVr represents a promising therapeutic strategy for carefully selected patients with severe TR who are poor candidates for surgery; however, large prospective head-to-head randomized trials with long-term follow-up are needed to define the comparative effectiveness and durability of currently available repair systems.

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