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Combined Transcatheter Edge-to-Edge Repair in Different Mitral and Tricuspid Regurgitation Combinations: A Contemporary and Comprehensive Review. Concomitant or Staged Procedure?

ABSTRACT

Transcatheter edge-to-edge repair (TEER) has become an effective treatment option for mitral regurgitation (MR) and tricuspid regurgitation (TR), with high procedural success and low complication rates. Moderate-to-severe MR and TR coexist in approximately 11% of patients with heart failure, and patients with both conditions have a worse prognosis than those with either lesion alone. Current guidelines recommend treatment of concomitant TR during mitral valve surgery when tricuspid annular dilation is present. However, there are no clear recommendations for combined TEER, as mitral and tricuspid TEER are addressed separately in the guidelines. In this review, the available evidence and current clinical approaches to combined vs. isolated TEER across different combinations and severities of MR and TR were evaluated.

Keywords: Combined TEER, mitral regurgitation, mitral TEER, tricuspid regurgitation, tricuspid TEER

REVIEW

INTRODUCTION

Over the last 10-15 years, transcatheter treatment of atrioventricular valve regurgitation has developed considerably. Most of the experience in this field has been gained with transcatheter edge-to-edge repair (TEER). Today, both mitral TEER (M-TEER) and tricuspid TEER (T-TEER) can be performed with high procedural success and low complication rates.

The coexistence of moderate-to-severe mitral regurgitation (MR) and moderate-to-severe tricuspid regurgitation (TR) is not uncommon. Data from the Heart Failure Association of the European Society of Cardiology (ESC-HFA) Heart Failure Long-Term Registry showed that 11% of patients with heart failure had both moderate-to-severe MR and moderate-to-severe TR.[1] Patients with both MR and TR also have a worse prognosis compared with those who have MR or TR alone.

Transcatheter edge-to-edge repair is an important treatment option for patients with severe MR and/or severe TR when surgical risk is high. In most patients, transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) are sufficient for patient selection, assessment of valve anatomy, procedural guidance, and follow-up. Therefore, anatomical suitability for TEER can usually be assessed without additional imaging. In some patients, however, further evaluation may be necessary. Cardiac magnetic resonance imaging, for example, may be useful when right ventricular function cannot be adequately assessed by echocardiography.

In patients undergoing left-sided valve surgery, leaving concomitant TR untreated may have a negative effect on prognosis.[2,3] The 2025 ESC/EACTS Guidelines recommend tricuspid valve intervention with a Class IIa indication in patients undergoing mitral valve surgery who have mild or moderate TR together with tricuspid

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annulus (TA) dilation (annular diameter ≥40 mm or ≥21 mm/m^2).[4] This is particularly relevant because TA dilation does not necessarily regress after mitral valve surgery. Thus, simply waiting to see whether TR improves after treatment of the mitral valve may not always be a relevant approach. This issue is especially important in atrial secondary MR, where left atrial enlargement and TA dilation may occur together and both valves may eventually require treatment.

While the guidelines provide recommendations for treating both valves during surgery, the situation is less clear for TEER. There is currently no clear recommendation on whether mitral and tricuspid TEER should be performed during the same session. In the ESC guidelines, M-TEER and T-TEER are considered separately, with Class I and Class IIa recommendations, respectively.[4] This leads to a practical question: if both valves were treated during the same surgical procedure, should treatment of both valves with TEER in the same session also be considered? This review analyzes the evidence and summarizes current approaches to combined vs. isolated TEER in various clinical scenarios and severities of MR and TR.

In this review, "combined TEER" refers to treatment of both the mitral and tricuspid valves using TEER within the same treatment strategy. When both procedures are performed during the same procedural session, this is referred to as "concomitant TEER." In contrast, "staged TEER" refers to sequential treatment of the 2 valves during separate procedural sessions, with clinical and/or echocardiographic reassessment between procedures.

DECISION-MAKING FOR COMBINED AND ISOLATED TRANSCATHETER EDGE-TO-EDGE REPAIR ACCORDING TO MITRAL REGURGITATION AND TRICUSPID REGURGITATION SEVERITY

When deciding between combined and isolated TEER for concomitant MR and TR, 4 different clinical combinations can be considered (Figure 1).

Severe Mitral Regurgitation (Grades 3 and 4) and Severe Tricuspid Regurgitation (Grades 3, 4, and 5)

As expected, most of the available evidence on combined TEER comes from patients with both severe MR and severe TR. The studies evaluating this approach can be summarized chronologically as follows.

The first study comparing combined TEER with isolated M-TEER was reported by Besler et al.[5] In this study, published in 2018, 61 patients with severe MR and TR who were considered to be at high surgical risk underwent either combined TEER (n=27) or isolated M-TEER (n=34). Although mortality was similar between the 2 groups during 18 months of follow-up, hospitalization for heart failure was significantly lower in the combined TEER group. Cardiac magnetic resonance imaging and echocardiographic assessments showed a significant reduction in TR severity after combined TEER, together with increases in right and left ventricular stroke volumes and cardiac index. These hemodynamic changes were not seen in patients who underwent M-TEER alone. The combined TEER group also had better results in terms of New York Heart Association (NYHA) functional class, N-terminal fragment of pro-B-type natriuretic peptide (NT-proBNP) levels, and 6-minute walking distance. Overall, the study showed that treating both valves was associated with an early improvement in cardiac output and functional capacity, as well as better clinical outcomes during mid-term follow-up.

The effect of combined TEER in high-surgical-risk patients with severe MR and TR was also evaluated by retrospectively comparing data from the TriValve registry (n=122, combined TEER) and the Transcatheter Mitral Valve Interventions (TRAMI) registry (n=106, isolated M-TEER).[6] A total of 228 patients were included in the analysis. At 1-year follow-up, combined TEER was associated with an approximately 2-fold reduction in the risk of mortality compared with isolated M-TEER.

Basman et al[7] analyzed data from the Northwell TEER database and identified 107 patients with advanced TR (≥3+) among 479 patients who underwent M-TEER with MitraClip. The study focused on factors associated with residual TR after isolated M-TEER. During follow-up, an improvement in TR by more than one grade was observed in only 15% of patients. This study is important for 2 reasons: it shows that advanced TR is common among patients undergoing M-TEER for severe MR, and that TR regression after M-TEER is not uniform but depends on the underlying clinical and structural phenotype. In particular, factors such as atrial fibrillation (AF), right atrial and tricuspid annular dilation, pulmonary hypertension, and right ventricular remodeling may influence the likelihood of TR improvement after M-TEER. Another retrospective study reported the safety and 1-year clinical outcomes of combined TEER performed during the same session in 40 patients with heart failure and concomitant severe MR and TR treated at a tertiary center between 2019 and 2021.[8] Procedural success in both valves was achieved in 80% of patients. No intraprocedural stroke, myocardial infarction, or periprocedural death was reported. At 1 year, 80% of patients had a significant improvement in NYHA functional class.

Papadopoulos et al[9] reported the technical success and 1-year clinical outcomes of combined TEER performed using

HIGHLIGHTS

- Combined mitral and tricuspid TEER is feasible, with high procedural success and a low complication rate in appropriately selected patients with concomitant MR and TR.
- The choice between concomitant and staged TEER should be individualized according to TR phenotype, tricuspid annular dimensions, right ventricular function, pulmonary pressures, and the likelihood of TR regression after M-TEER.
- Although observational studies suggest improved clinical outcomes with combined TEER, randomized comparative trials are needed to establish its superiority over isolated or staged intervention.

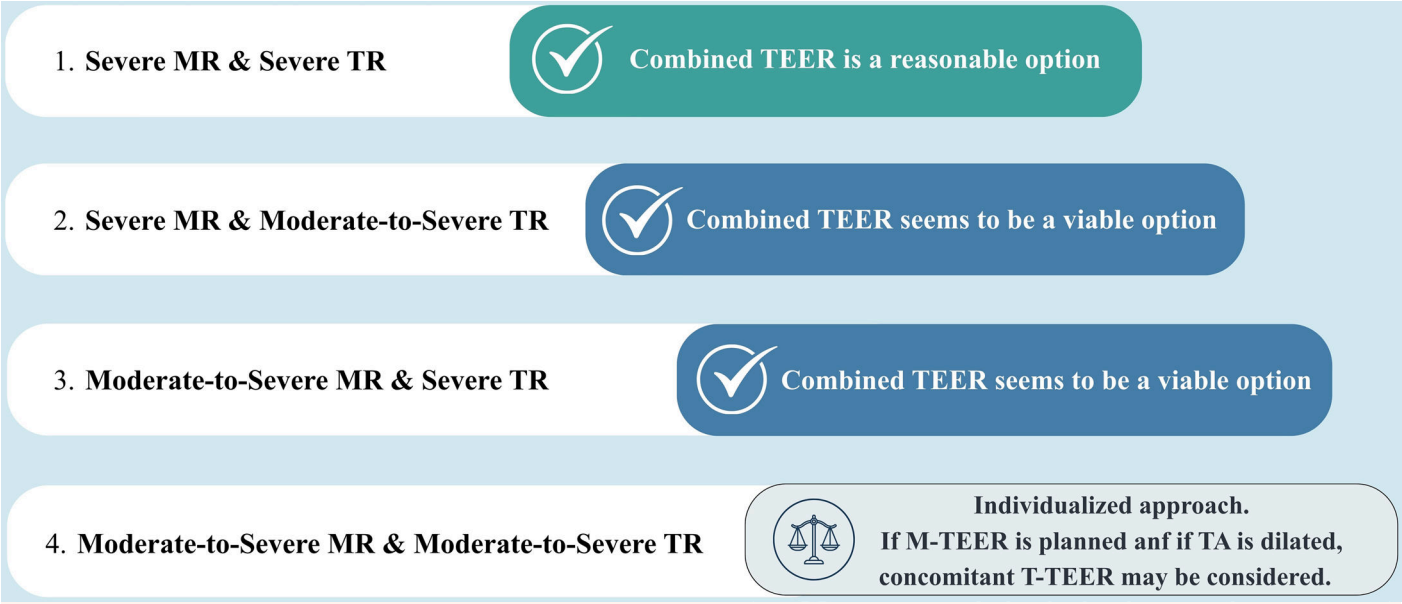


Figure 1. Recommendations for varying degrees of MR and TR combinations. MR, mitral regurgitation; TEER, transcatheter edge-to-edge repair; TR, tricuspid regurgitation.

a single TriClip device in 42 patients with NYHA class III or IV heart failure, severe MR and severe TR. Implantation was successful in all patients. The procedure lasted an average of 70 minutes, and no major adverse events, including death, stroke, or major bleeding, were observed either during the procedure or throughout the 30-day follow-up. Both MR and TR improved significantly on echocardiographic follow-up. No deaths occurred during the 1-year follow-up period, and only 7.1% of patients required rehospitalization. Notably, although 64.3% of the patients were in NYHA class IV at baseline, all patients were in NYHA class I or II at the end of the first year. The results of this recent study suggest that combined TEER using a single guiding catheter system is feasible, with reasonable completion time, high procedural success, a favorable safety profile, and marked clinical improvement.

Severe Mitral Regurgitation (Grade ≥3) and Moderate-to-Severe Tricuspid Regurgitation (Grade 2-3)

There are currently no studies directly comparing M-TEER with combined TEER specifically in this patient group. However, some data may help guide treatment decisions. Nickenig et al analyzed data from the TRAMI registry to assess the effect of baseline TR on clinical outcomes in 766 high-surgical-risk patients undergoing M-TEER.[10] At baseline, TR was absent or mild in 43.6% of patients, moderate in 42.6%, and severe in 13.8%. After isolated M-TEER, 1-year all-cause mortality was 14.6%, 21.0%, and 34.0% in these groups, respectively. These results clearly show that even moderate TR has prognostic importance in patients undergoing M-TEER, with mortality increasing further in those with severe TR.

A meta-analysis published by Chitturi et al[11] in 2022 also showed that baseline moderate/severe TR was associated with worse clinical outcomes in patients undergoing M-TEER for severe secondary MR. The analysis included 5 studies with a total of 1395 patients. Patients with moderate or severe TR before the procedure had more than twice the combined risk of all-cause mortality or hospitalization for heart failure at 1 year. M-TEER alone also had a limited effect on TR. Among patients who initially had moderate/severe TR, only 32% showed an improvement in TR grade after M-TEER. These data suggest that concomitant TR should not be considered simply a secondary finding in patients with severe MR. Its adverse effect on right-sided cardiac remodeling and clinical outcomes should be taken into account, and combined TEER may therefore need to be considered rather than treating the mitral valve alone.

Moderate-to-Severe Mitral Regurgitation (Grade 2-3) and Severe Tricuspid Regurgitation (Grade ≥3)

The EuroTR registry provides important data for this group. In this large European registry including 3100 patients, the effect of concomitant moderate MR was evaluated in patients undergoing T-TEER for severe TR. The study also examined the potential benefit of treating both valves during the same session.[12] Patients with untreated moderate MR had an almost 2-fold higher risk of death at 2 years compared with those without significant residual MR (37% vs. 23%), suggesting that moderate MR should not be overlooked in this setting.

In the propensity score-matched analysis, patients who underwent combined TEER had better 2-year survival than those treated with T-TEER alone (81% vs. 70% respectively). Recurrent hospitalization for heart failure was also less frequent (13% vs. 22%), together with greater improvement in exercise capacity and symptom control. Importantly, performing combined TEER during the same session did not increase the procedural risk within the first 30 days. Taken together, these findings indicate that combined TEER was

associated with better survival and clinical outcomes than T-TEER alone in this observational analysis; however, these findings should not be interpreted as evidence of a causal treatment effect.

Moderate-to-Severe Mitral Regurgitation (Grade 2-3) and Moderate-to-Severe Tricuspid Regurgitation (Grade 2-3)

Data for this combination are quite limited. The available literature indicates that the evidence is derived mainly from TEER studies that included patients with moderate to severe MR.

The recently published multicenter randomized Randomised Study of the MitraClip Device in Heart Failure Patients with Clinically Significant Functional Mitral Regurgitation (RESHAPE-HF2) trial compared M-TEER with optimal medical therapy (OMT) in patients with moderate-to-severe functional MR.[13] Over 24 months of follow-up, patients treated with M-TEER had fewer heart failure hospitalizations and cardiovascular deaths, together with an improvement in quality of life. Unlike previous landmark trials such as Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT) and Percutaneous Repair with the MitraClip Device for Severe Functional/Secondary Mitral Regurgitation (MITRA-FR), which mainly focused on patients with more advanced MR (grades 3-4), RESHAPE-HF2 was the first randomized controlled trial to directly include a group of patients with moderate to severe MR. Subgroup analyses suggested that the clinical benefit of M-TEER may also extend to patients with moderate to severe MR. However, these findings provide evidence only for the treatment of the mitral valve and should not be directly extrapolated to support combined mitral and tricuspid TEER in patients with moderate MR and moderate TR. The optimal management of patients with moderate disease affecting both valves remains uncertain and requires further prospective and randomized evaluation.

Why, then, might M-TEER be beneficial even in patients with moderate MR? One possible explanation is the dynamic nature of MR. A patient with grade 2-3 MR at rest may develop more severe regurgitation even with mild exercise. Earlier treatment may also have a favorable effect on left ventricle (LV) remodeling before marked ventricular dilation develops. In addition, some patients remain markedly symptomatic and have elevated natriuretic peptide levels despite having only moderate MR at rest. In such patients, moderate MR itself may still contribute significantly to the clinical picture. These factors may partly explain why M-TEER can provide clinical benefit even when MR is not severe at baseline.

Asgar et al[14] evaluated the safety and effectiveness of M-TEER in moderate secondary MR (SMR) using data from the EXPAND and EXPAND G4 registries. A total of 335 patients with moderate SMR (2+) were compared with 525 patients with severe SMR (≥3+). Baseline characteristics were similar between the 2 groups, and a marked reduction in MR was achieved after the procedure in both groups. Patients with moderate SMR also showed improvements in quality of life and favorable LV remodeling after M-TEER, with results comparable to those seen in patients with severe SMR.

For isolated moderate TR (grade 2), there are currently no data on T-TEER. Follow-up studies, however, clearly show that moderate TR is not a benign condition. In the LOCOMOTRI study, 250 patients with moderate TR were followed for a mean of 3.6 years, regardless of the underlying etiology.[15] During follow-up, TR progressed to severe in 34% of patients, and AF and right ventricular dilation were independent predictors of progression. TR progression was also independently associated with all-cause mortality and hospitalization for heart failure.

Although there is currently no guideline recommendation for M-TEER in patients with moderate or moderate-to-severe MR (grades 2 and 2-3), the available evidence suggests that it may be considered in selected patients. This may be particularly relevant in patients who remain symptomatic despite OMT, given the favorable safety and efficacy profile of M-TEER. When M-TEER is planned in a patient with moderate MR who also has moderate-to-severe TR, the presence of a dilated tricuspid annulus and AF may support consideration of a concomitant TEER approach. However, evidence supporting T-TEER for moderate TR remains limited, and the use of concomitant TEER in this setting should be regarded as an author-proposed strategy rather than an evidence-based recommendation. Further randomized studies are needed to determine whether this approach provides clinical benefit.

Although randomized data are still limited, the studies summarized above show that combined TEER can be performed with high procedural success and a low rate of complications. Performing both interventions during the same session may offer several practical advantages.

First, both valves can be treated using a single guiding catheter system, and procedure times can now be kept below 90 minutes in experienced centers. Growing experience with intraprocedural imaging, a multidisciplinary heart team approach, and advances in device technology have made combined procedures easier to perform. Features such as independent leaflet grasping and the availability of different clip sizes also provide greater flexibility when treating both valves. A multi

Second, treating both valves in the same session avoids a second exposure to anesthesia and eliminates the need for another invasive procedure.

Third, a single-session strategy may reduce resource utilization by avoiding a second invasive procedure, including the associated procedural and hospitalization requirements.

COMBINED TRANSCATHETER EDGE-TO-EDGE REPAIR: CONCOMITANT OR STAGED APPROACH?

The large-scale analysis from the OCEAN registry (N = 3666) in Japan showed that among patients with TR at baseline undergoing M-TEER, TR persisted in 63%.[16] Residual TR independently increased the composite endpoint of cardiovascular death or hospitalization for heart failure. In this study,

2 important parameters determining TR persistence after M-TEER were a TA diameter index >21 mm/m^2 and the presence of AF/flutter.

Takeuchi et al[17] aimed to identify 3-D echocardiographic predictors of TR regression in 61 patients with moderate or greater functional TR undergoing M-TEER. Tricuspid regurgitation severity had regressed in 43% of patients. Multivariate analysis identified TA perimeter (≤13.75 cm), TA area (≤13.55 cm^2), and area change (≥17.5%) as significant predictors of post-procedure TR regression. They concluded that M-TEER may lead to TR regression in patients with a non-dilated tricuspid annulus and a significant change in tricuspid annulus area.

Pooled analysis from the EXPANDed cohort (EXPAND and EXPAND G4 studies) evaluated natural TR progression after M-TEER in patients with severe MR and TR.[18] Among 160 patients with evaluable 30-day TR data, 73% improved to ≤moderate TR, and this group had less AF, lower left ventricular ejection fraction, and larger LV dimensions at baseline. Ventricular secondary MR combined with pulmonary hypertension–mediated TR responded more favorably to the reduction in afterload/pulmonary pressure achieved by M-TEER. In contrast, TR associated with AF and RA/TA dilation predominantly represented secondary atrial TR, which tended to persist after M TEER. Consequently, phenotype emerged as a key determinant.

The Table 1 summarizes the main factors that may favor a concomitant or staged TEER approach, with the underlying TR phenotype being an important consideration. AF-related atrial TR with marked right atrial and TA dilatation may favor concomitant T-TEER, whereas TR associated with pulmonary hypertension and potentially reversible right ventricular dysfunction may favor an initial M-TEER followed by clinical and echocardiographic reassessment. When the anatomy of both valves is suitable and RV function is preserved, concomitant TEER can be considered. A staged approach may be more appropriate in patients with high pulmonary pressures and impaired RV function, particularly in the presence of RV–pulmonary artery uncoupling. In these patients, M-TEER can be performed first, followed by reassessment during follow-up. If pulmonary artery pressure decreases and RV function improves after M-TEER, the need for T-TEER can then be reconsidered.

Table 1. Combined TEER, Concomitant vs Staged Approach

A. Factors Favoring Concomitant Approach	B. Factors Favoring Staged Approach
Significant coaptation gap	PAP is high and seems associated with MR
Severe leaflet tethering	Potentially reversible RV dysfunction
Right heart failure signs	TA index <21 mm/m^2
TA index >21 mm/m^2	TA 3D perimeter <13.75 cm
TA 3D perimeter >13.75 cm	TA not exhibiting fixed remodeling
Hepatic vein flow reversal	Annulus area change preserved ≥17.5%
RA severely dilated	RA not severely dilated
Persistent/Permanent AF	No AF or paroxysmal AF

AF, atrial fibrillation; RA, right atrium; RV, right ventricle; TA, tricuspid annulus; TEER, transcatheter edge-to-edge repair.

CONCLUSION

However, the available evidence remains largely observational or registry-based, and the reported associations between combined TEER and lower mortality, fewer heart failure hospitalizations, and improved clinical outcomes should not be interpreted as evidence of a causal treatment effect or definitive superiority over an isolated or staged strategy. Until randomized comparative data become available, the decision between concomitant and staged TEER should therefore be individualized according to valve anatomy, right ventricular function, pulmonary pressures, tricuspid annular dimensions, and the likelihood of TR improvement following M-TEER. The principles established for concomitant valve surgery may provide a useful framework for clinical decision-making, but they should not be directly extrapolated to TEER in the absence of randomized evidence. In patients with suitable anatomy and an appropriate clinical profile, a single-session combined procedure may offer practical advantages by avoiding a second invasive procedure and additional anesthesia exposure. If venous access has already been obtained, both valves can be treated with a single guiding catheter system, and the additional procedural risk is low; there is a practical question worth asking: why not treat both valves during the same session?

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