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Editorial

Residual Tricuspid Regurgitation After Mitral Transcatheter Edge-to-Edge Repair: Accomplice or Bystander?

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Tricuspid regurgitation (TR) has been associated with worse outcomes with increasing severity. Community-based echocardiographic studies of asymptomatic patients demonstrated the prevalence of at least moderate TR or greater can range from 3% to 8%, with 1-year–adjusted mortality rates for moderate TR at 29.5% and severe TR at 45.6%.[1,2] The 2020 ACC/AHA guidelines define a staging system for TR with 3 principal stages: progressive TR (stage B), asymptomatic severe TR (stage C), and symptomatic severe TR (stage D).[3] It is a class I recommendation that concomitant tricuspid valve surgery be performed in patients with stage C or D TR undergoing left-sided valvular surgery. Progressive stage B TR by definition is clinically asymptomatic with no hemodynamic consequences. A study examining patients with stage B TR who underwent isolated left-sided valvular surgery showed that those with a tricuspid annular diastolic diameter of >40.0 mm (or >21.0 mm/m^2) who did not undergo concomitant tricuspid annuloplasty had worse New York Heart Association functional class and worsening TR by more than 2 grades in 5-10 years of follow-up.[4] This supported a class 2a recommendation for patients with stage B TR to undergo concomitant tricuspid valve surgery at the time of left-sided valve surgery.

For patients who are not suitable conventional surgical candidates for concomitant mitral and tricuspid valve repair/replacement, transcatheter therapies may be considered. Currently, no commercially available FDA-approved transcatheter therapy exists for TR in the United States. Therefore, these patients are often evaluated for isolated mitral transcatheter edge-to-edge repair (m-TEER) with the goal of improving TR by reducing pulmonary arterial (PA) pressures due to severe mitral regurgitation (MR). Unlike the strength of recommendations guiding surgical intervention, rigorous evidence on the transcatheter management of coexisting MR and TR is lacking. Approximately 60% of patients undergoing m-TEER also have moderate or greater TR with significantly decreased 1-year survival in patients with residual severe TR compared with those with lesser degrees of TR after m-TEER.[5] This is consistent with subgroup analyses from the Transcatheter Mitral Valve Interventions (TRAMI) and Getting Reduction of Mitral Insufficiency by Percutaneous Clip Implantation (GRASP) registries that showed worse 12-month outcomes of mortality, rehospitalization for heart failure, and major adverse cardiovascular and cerebrovascular events.[6,7]

Basman et al[8] present prospectively collected registry data analyzed retrospectively in a single-hospital system comprising 4 high volume m-TEER centers. Their goal was to identify predictors of severe TR at the 1-month follow-up transthoracic echocardiography (TTE) after m-TEER. TR improvement was defined as a reduction in TR grade by at least 1+ resulting in moderate (2+) or less TR. Approximately half of the patients who underwent successful MR reduction also experienced significant TR reduction. Multivariate analyses showed MR reduction of ≥3+ as the only predictor of significant TR reduction. Univariate predictors of severe residual TR were right atrial area and unsuccessful m-TEER. Other factors such as atrial arrhythmia, previous cardiac implantable electronic device, mechanism of MR, tricuspid annular dilation, right ventricular (RV) function, PA systolic pressure, and left ventricular (LV) dimensions did not reach statistical significance.

The authors should be commended on their report of the largest analysis to date on significant predictors of severe TR after m-TEER. However, several limitations should be noted. First, methodologic challenges and the small sample size in a single-system limit the study's potential larger scale effect. The number of operators and their experience is not known, which may affect procedural success and outcomes. In addition, all baseline covariates were TTE-based parameters although all patients underwent transesophageal echocardiography (TEE) guidance for m-TEER. Baseline TEE mitral and tricuspid valve parameters were a potential valuable missed repository of important analyzable predictors. For example, baseline tricuspid coaptation gap, although not directly studied in this context, has been shown to affect tricuspid-TEER procedural strategy and success.[9] Because >90% of the TR pathology in the study Basman et al was functional, baseline coaptation gap and its correlation with ultimate TR reduction could be very relevant. In addition, other pertinent baseline TEE covariates could have been examined such as quantification of TR by proximal isovelocity surface area and tricuspid annular

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measurements. For degenerative MR, qualitative and quantitative characterization of the MR pathology on TEE such as myxomatous disease and flail width/gap are important to understand the severity of degenerative MR in this cohort and contextualize the observed outcomes. Even though 45% of the cohort had functional MR, the degree of LV systolic dysfunction was not quantified. Rather, LV dysfunction was analyzed as a binary variable that does not accurately capture the effect of varying degrees of baseline cardiomyopathy on MR reduction after m-TEER and consequent TR outcomes. Procedural information is also not available such as average number of clips per case, type of clip(s), and end-procedural/short-term follow-up mitral mean gradient. Iatrogenic mitral stenosis from m-TEER could significantly increase resultant TR. Regarding the span of the study, only 30-day follow-up was analyzed when 12-month outcomes would have had more significance. Pre-procedure and post-procedure brain natriuretic peptide levels and TTE inferior vena cava assessment could also be an important gauge of volume status that could affect follow-up TR assessment. Finally, quantifying TR based on the ACC/AHA staging system instead of the routinely cited 5-grade system may have more relevance in future guideline derivation.

The authors' primary conclusion of significant MR reduction as a predictor of significant TR reduction is intuitive but not necessarily additive. Physiologically, it can be explained by the effective reduction of left atrial pressure leading to consequent reduction in mean PA pressure and TR reduction. The authors acknowledge the inability to account for the presence of intrinsic PA hypertension. Although PA systolic pressure was not found to be a significant risk factor for severe residual TR, TTE-derived pulmonary vascular resistance could have been explored as an important covariate. The authors also report that right atrial area was a predictor of severe residual TR in univariate analyses, but not RV dysfunction. RV dysfunction, similar to the LV, was also treated categorically (moderate or severe). Quantification of RV ejection fraction, RV area, and tricuspid annular dilation assessed by pre- and post-cardiac magnetic resonance imaging may help refine our understanding on the role of right atrioventricular remodeling on TR reduction. Strain analyses could have also strengthened the study findings. One study demonstrated improvement in RV free-wall global longitudinal strain at 12 months after m-TEER, but not LV strain.[10] This may suggest that the RV may be more able to reverse remodel in response to improvements in PA pressure. Longitudinal changes in RV strain may play an important role in predicting residual TR after m-TEER.

The recently published 5-year COAPT trial data and the ongoing REPAIR-MR and PRIMARY trials may expand m-TEER to larger patient populations.[11] If m-TEER in the future reaches a comparable ubiquity with transcatheter aortic valve replacement, studies similar to the one reported by Basman et al are warranted to identify salient predictors of significant TR reduction in patients with severe MR treated with m-TEER. The generalizability of this study is confined by the sample size and single-system experience. Limited clinical and TTE-based covariates and the absence of longer-term follow-up cap the study's ability to be practice-changing. Despite these limitations, Basman et al provide essential insight into predicting severe TR after m-TEER. Future studies in larger cohorts using hemodynamic parameters and multimodality imaging will help elucidate in which patients residual TR after m-TEER is a bystander responsive to reduction in PA pressure or an accomplice to severe MR that will continue to portend a poor prognosis even after successful m-TEER.

Declaration of competing interest

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