

Unsolved questions in prophylactic tricuspid valve repair and the possible role of transcatheter tricuspid intervention

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Abstract

Tricuspid regurgitation progression after left-sided surgery and its correlation with worse postoperative and long-term outcomes is a highly debated topic. Some studies support prophylactic tricuspid repair based on annulus dimension rather than on tricuspid regurgitation severity only, while others are in favor of more conservative management. Furthermore, the advent of percutaneous tricuspid valve intervention and its promising short-term outcomes has introduced a new factor to be taken into account on the tricuspid intervention decision-making process. We present a review on prophylactic tricuspid valve intervention, covering currently available data, as well as the role of transcatheter tricuspid valve intervention in this equation.

Abbreviations:

Functional tricuspid regurgitation (FTR); mitral valve (MV); tricuspid regurgitation (TR); tricuspid valve (TV); transcatheter tricuspid valve intervention (TTVI); transesophageal echocardiogram (TEE); transthoracic echocardiography (TTE).

Introduction

The presence of some degree of tricuspid regurgitation (TR) can be considered the most common valvular heart disease, affecting 65-85% of the population¹. If considered only significant TR (moderate or severe), the condition is estimated to affect up to 1.6 million individuals in the United States², with secondary or functional tricuspid regurgitation (FTR) being responsible for almost 90% of the cases³.

Despite this prevalence, TR was during many years a forgotten and underappreciated disease^{4,5}. One of the reasons behind TR undertreatment was the concept, postulated by Braunwald in 1967⁶ that functional tricuspid regurgitation (FTR) would improve or disappear once the primary left-sided problem was treated. Another reason was the high surgical mortality rate associated with isolated tricuspid valve (TV) intervention, which, unfortunately, remains at least partially correct, since TR carries an impactful surgical mortality (8.8% – 9.7%)⁷. However, such high mortality is in part biased by the advanced stage that patients are referred to surgery, with severe right ventricle dysfunction and end-organ damage⁸.

Additionally, several publications have demonstrated that up to 74% of patients submitted to a successful mitral valve repair will exhibit significant tricuspid regurgitation (TR) over more than 3-year follow-up⁹, and one half will progress by more than two grades in a mean follow-up of 4.8 years¹⁰. It is also remarkable that, while isolated TV surgery due to residual TR after mitral valve (MV) intervention is associated with high mortality and poor outcomes^{11,7}, concomitant TV repair does not increase the operative mortality^{10,12}.

Based on these arguments and on the fact that FTR is associated with biventricular dysfunction, poor quality of life and, ultimately, death¹³⁻¹⁵, a more aggressive TR surgical approach was suggested. Hence, the concept of treating TR based on tricuspid annulus diameter rather than TR severity was raised¹⁰.

Prophylactic tricuspid intervention

Carpentier was one of the first authors to recommend tricuspid annular dilation as a more objective parameter to indicate TV repair. His evaluation method consisted in TV surgical exploration, checking the annulus ability to admit three fingerbreadths of the surgeon's hand, in which case TV repair would be indicated¹⁶.

Three decades later, Dreyfus et al. evaluated tricuspid annuloplasty performed concomitantly with MV surgery in the presence of intraoperative tricuspid annular diameter ≥ 70 mm, measured from the antero-septal commissure to the anteroposterior commissure, regardless the preoperative TR grade. In a 5-year follow-up, TR degree, as well as patients' functional status, was significantly lower in the TV treated group¹⁰.

Regarding echocardiographic measurement, evaluating 50 patients submitted to MV replacement due to rheumatic disease, Colombo et al. suggested that tricuspid annulus diameter > 21 mm/m² could be a reliable parameter to indicate concomitant TV repair in this specific patient population¹⁷.

Similarly, using a tricuspid annulus dimension ≥ 40 mm (> 21 mm/m²) measured preoperatively in transthoracic echocardiography (TTE) 4-chamber view as a cut-off to indicate concomitant TR intervention, Van deVeire et al. demonstrated better reverse right ventricular remodeling and less postoperative TR prevalence, when compared with isolated MV surgery¹⁸. Figure 1 illustrates echocardiographic tricuspid valve evaluation, and Figure 2 a TR surgical repair using an annuloplasty ring.

In 2012, Benedetto et al. conducted a randomized trial enrolling 44 patients with less-than-severe TR (≥ 2) and annular dilatation (≥ 40 mm) treated at the same time that MV surgery. Early results demonstrated the safety of the combined approach (1 case of 30-day mortality in each group), with just a discreet increase in cardiopulmonary bypass and aortic cross-clamping time. After 12 months, those patients who underwent TV intervention presented with significant TR reduction (TR absent in 71% vs. 19%; $p=0.001$), improvement in functional capacity (6 min walking test: $+115 \pm 23$ m vs. $+75 \pm 35$ m; $p=0.008$), and right ventricular reverse remodeling [right ventricle long-axis 71 ± 7 mm preoperative vs. 65 ± 8 mm postoperative ($p<0.01$) and short-axis 33 ± 4 mm preoperative vs. 27 ± 5 mm postoperative ($p=0.01$) in TV treated group; right ventricle long-axis 72 ± 6 mm preoperative vs. 70 ± 7 mm postoperative ($p=0.08$), and short-axis 34 ± 5 mm preoperative vs. 33 ± 5 mm postoperative ($p=0.1$) in TV non-treated group]¹⁹.

Two-years after this publication, Chikwe et al. tested the association of an aggressive concomitant prophylactic TV repair (annular dilatation ≥ 40 mm or \geq moderate TR) in patients undergoing MV repair for degenerative diseases. No increased 30-day mortality and morbidity, lower TR progression rate, reduced pulmonary hypertension and improvement in induced right ventricle recovery were observed at 7-year follow-up²⁰.

Regarding guideline recommendations, the American Heart Association/American College of Cardiology and the European Society of Cardiology/European Association for Cardio-Thoracic Surgery have recommended TR repair concomitant with left-sided surgery in the presence of annular size ≥ 40 mm (> 21 mm/m²), regardless of TR degree, as a Class IIa of recommendation^{21,22}, which still means a low level of evidence.

Controversial information

Despite the accumulated information reported, recent articles have presented opposite results. In a single-center retrospective cohort of 312 patients undergoing MV repair for degenerative diseases, David et al. demonstrated no association between tricuspid annulus size and subsequent FTR development, with a low rate of postoperative TR (at 7 years follow-up) in patients presenting annulus size < 40 mm (6.8%, 95% CI 4.6% – 10.4%), but also in those with annulus ≥ 40 mm (6.0%, 95% CI 2.9% – 12.2%)²³. The limitation of this study is that tricuspid annular size was measured intraoperatively, using transesophageal echocardiogram (TEE) under general anesthesia, while the current guidelines are based on TTE or direct intraoperative

measurement. Regardless this limitation, TR prevalence was similar to that previously described by Rajbanshi et al., in whose study only 6% of patients developed severe TR at 5-year follow-up after MV repair or replacement²⁴.

Furthermore, no advantage in terms of TV reoperation rate (HR 0.46; 95% CI 0.10 - 2.07; $p=0.31$); congestive heart failure (HR 1.12; 95% CI 0.37 - 3.36; $p=0.84$); and death (HR 1.41; 95% CI 0.82 - 2.42; $p=0.22$) when mild-to-moderate FTR was concomitantly managed was suggested by Ro et al.²⁵.

In terms of possible disadvantages of combined procedures, although prophylactic TV repair has not been associated with increased mortality rate, some authors have suggested association with longer operative times²⁶, higher pacemaker rates²⁷ and longer hospital length of stay²⁸.

Additional data comes from the results of a single-center prospective randomized trial published in 2019. In this study, prophylactic tricuspid annuloplasty performed concomitantly to MV repair in patients with less-than-severe FTR was able to reduce FTR recurrence, but did not affect functional capacity or right ventricular remodeling. Five-year freedom from cardiac-related mortality was similar in TV treated and non-treated patients (94.1 \pm 3.2% in treated-group vs. 89.7 \pm 4.3% in TV non-treated; $p=0.9$)²⁹.

When this new study was included in a meta-analysis, however, the conclusions went in the opposite direction. TV repair was associated with lower cardiovascular mortality, all-cause mortality and TR progression over a median of 5.3 years of follow-up (cardiovascular mortality: RR 0.46, 95% CI 0.28 - 0.75; $p=0.002$; all-cause mortality: RR 0.68, 95% CI 0.49 - 0.96; $p=0.03$; TR progression: RR 0.26, 95% CI 0.12 - 0.56; $p<0.001$)³⁰. Likewise, when the prevalence of TR after MV repair due to leaflet prolapse at a more extended follow-up are evaluated, even David et al. showed numbers that are more concerned. A 20.8% probability of persistent or new moderate or severe TR at 20 years made the author point that maybe a much longer follow-up than those previously reported is needed to observe changes in tricuspid annulus diameter³¹.

Transcatheter tricuspid valve intervention

transcatheter tricuspid valve intervention (TTVI) has emerged as an attractive alternative approach for inoperable or high surgical risk candidates (STS-PROM $>8\%$)³² who cannot be submitted to a conventional open cardiac surgery.

Current available devices are designed for different anatomical and functional purposes, as follow (adapted from Curio J et al. and Kolte D et al.)^{33,34}:

- 1) Leaflet approximation or coaptation [MitraClip in the Tricuspid Position (Figure 3) or TriClip (Abbott Vascular, Santa Clara, CA, USA), Pascal system (Edwards Lifesciences Corp, Irvine, CA, USA), TriCinchTM Coil System (4Tech Cardio, Galway, Ireland), FormaTM Repair System (Edwards Lifesciences)];
- 2) Annuloplasty [Cardioband(r) Tricuspid Repair System (Edwards Lifesciences), IRIS Transcatheter Annuloplasty Ring (Millipede Inc, Santa Rosa, CA, USA), Trialign device (Mitralign Inc., Tewksbury, Mass., USA)];
- 3) Orthotopic [GATETM system self-expanding bioprosthesis (NaviGate Cardiac Structures, Lake Forest, CA, USA)] or heterotopic [Heterotopic caval valve implantation using the SAPIEN (Edwards Lifesciences Corp, Irvine, CA, USA), or the TricValve(r) (P&F Products GmbH, Vienna, Austria) systems].

In TTVI trials, technical feasibility and safety was proven, and TTVI showed a low periprocedural mortality (30-day mortality = 3.6%)³⁵, even when performed in high-surgical risk patients. Nonetheless, Taramasso et al. recently suggested an important benefit in terms of survival and rehospitalization rates when TTVI was compared with medical therapy [1-year mortality: 23 \pm 3% vs 36 \pm 3% in TTVI versus control group, respectively; $p=0.001$]; 1-year rehospitalization: 26 \pm 3% vs 47 \pm 3%, in TTVI versus control group, respectively; $p<0.0001$)³⁶.

Current Questions

Considering the information presented above, the following are meant to be discussion points:

1. Because TV annulus dilation as predictor of TR progression and criteria to indicate concomitant surgery is, still nowadays, controversial, is there a significant benefit of unrestricted prophylactic TV intervention? Or a watch-and-wait strategy with subsequent intervention, if necessary, could be a valuable alternative in some subgroup of patients? What patients' profile could benefit from a more conservative strategy?
2. Once one of the reasons to indicate concomitant TV repair is the assumption that a future reoperation would be associated with high surgical risk and poor outcomes, in a hypothetical scenario of TTVI providing significant lower procedural mortality, should this argument be reviewed?
3. If the indication of tricuspid prophylactic intervention based on annulus dilation is valid, should also TTVI be indicated in symptomatic, high-risk patients, based in annular dilation ([?] 40mm) rather than TR grade?

Conclusion

The comments in this document do not presume of answering the questions presented above, but to introduce in debate new issues, in order to stimulate a more in-depth discussion.

Tricuspid annular dilatation seems to play an important role as predictor of early and late outcomes after left-sided surgery, especially if other parameter such as leaflet coaptation and tethering are also present. However, controversial data regarding the role of prophylactic tricuspid valve repair concomitant with left-sided intervention make this procedure not as widespread as it could be. Nonetheless, with the advent of percutaneous tricuspid valve interventions, it turned into an interesting alternative approach in selected patients.

The decision-making process should be based on individual factors such as patient desire, clinical symptoms, response to medical management, quality of life, and life expectancy, as well as tricuspid valve morphology, currently available devices and procedural risks.

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Legend of Figures:

Figure 1: Echocardiographic tricuspid valve evaluation.

Figure 2: Tricuspid valve ring annuloplasty technique.

Figure 3: Tricuspid valve percutaneous repair using the MitraClip system. A. Preoperative tricuspid regurgitation. B. Intraprocedural Clip positioning between the anterior and the septal tricuspid leaflets. C. Tricuspid regurgitation after Clip implantation.





