Management of tricuspid regurgitation: time to adopt a lifetime perspective?

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During the past decade, advances in the understanding of pathophysiology, burden, and prognostic implications of tricuspid regurgitation (TR) have led to an in-depth transformation of its management. Transcatheter solutions have developed rapidly, with both repair and replacement devices now commercially available (1). Their use is supported by a class IIa, level of evidence A recommendation in the latest European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) Guidelines for the Management of Valvular Heart Disease (2). Treatment strategies for isolated TR remain, however uncertain regarding optimal timing of intervention and device selection. These considerations are particularly important for younger patients, who may require, and are now able to receive, repeated tricuspid interventions. In this context, the durability of TR reduction using various therapeutic approaches emerges as a key consideration for the patient's lifetime management.

Historically, TR treatment was limited to surgery, with tricuspid ring annuloplasty preferred over replacement when technically feasible. However, the long-term durability of surgical tricuspid valve (TV) repair is frequently suboptimal, with 25% of patients developing progressive moderate or severe TR within five years (3).

Surgical TV replacement is preferred in cases of advanced disease with severe annular dilatation and marked leaflet tethering (>10 mm). In contemporary practice, bioprosthetic valves are favored over mechanical valves due to their lower risk of thrombotic and hemorrhagic complications. Surgical studies have reported higher rates of thrombosis in tricuspid prostheses compared with left-sided valves, presumably due to lower pressure gradients, slow flow conditions and greater surface areas. Although not consistently defined across studies, surgical TV degeneration requiring re-intervention at 10 years ranges between 10% and 20% in contemporary cohorts (4). In summary, about one quarter of the patients undergoing any type of TV surgery will need a reintervention within 5–10 years.

Since repeat tricuspid surgery ranks among the highest risk operations (with 13% in-hospital mortality), transcatheter tricuspid valve-in-valve (ViV) and valve-in-ring (ViR) procedures have emerged as alternatives (5). ViV implantations are usually technically straightforward, while ViR interventions carry a higher risk of adverse events because of the nonplanar, and incomplete shape of tricuspid rings. A paravalvular leak in the open section of the rigid ring is frequently observed after ViR and may require supplemental plug implantation (6).

In real-world practice, isolated surgical TR correction remains uncommon (<5% of valve procedures in the United States), since most patients are referred late and present with high-risk characteristics (7). This unmet need likely explains the rapid completion of three randomized controlled trials investigating transcatheter solutions for TR treatment: tricuspid transcatheter edge-to-edge repair (T-TEER) with the TriClip device (Abbott Structural Heart) and transcatheter tricuspid valve replacement (TTVR) with the EVOQUE system (Edwards

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Lifesciences). Approval of the TriClip system by the Food and Drug Administration (FDA) in 2024 immediately followed the results of the TRILUMINATE pivotal trial, which randomly assigned 350 individuals with symptomatic severe TR to receive either T-TEER or optimal medical therapy (OMT) alone. T-TEER was superior to OMT in improving quality of life at one-year follow-up (8). A second investigator-initiated trial, TRI.Fr, confirmed the benefit of T-TEER over OMT among 300 patients, for a composite score driven by improved patient-reported outcomes (9). At one year, 71.0% of patients treated with T-TEER in TRI.Fr and 89% in TRILUMINATE had moderate TR or less. The TRISCEND II trial randomized 400 patients with symptomatic severe TR in a 2:1 ratio to either TTVR with the EVOQUE device or OMT alone. TR severity was reduced from severe to mild or less in 95.3% of patients treated with TTVR at one year. Consistent with the T-TEER trials, the main benefit in the device arm consisted of a greater improvement in quality-of-life at one-year compared to OMT (10).

Despite the demonstrated efficacy of both transcatheter therapies to reduce TR, promote reverse right ventricular remodeling and improve symptoms, important limitations persist. First, none of the three trials showed a survival benefit at 1- or 2-years. The lack of impact on mortality might be explained by the high crossover rate after the first year, as well as the relatively low risk profile of the patients included, with fewer events than anticipated. An 18-month subanalysis of TRISCEND II showed, however, a lower incidence of heart failure (HF) hospitalization among patients with massive or torrential TR treated with TTVR (23.6% *vs.* 38.8% in the control arm) (11). Similarly, in the extended 2-year follow-up of the TRILUMINATE trial, T-TEER was associated with a 28% reduction in the risk of HF hospitalization compared to OMT (12). Second, procedural limitations need to be acknowledged. After T-TEER, single-leaflet device attachment (SLDA) occurs in 6.5% of cases, and 16% of patients have residual TR > moderate at two years (12). Although TTVR offers more consistent TR elimination and lower procedural complexity, it carries specific risks, including conduction disturbances (18%), dysfunction of pre-existing pacemaker leads (6–7%), and bleeding complications (14%) (9). Third, current device requirements impose relatively narrow anatomical inclusion criteria, which may limit patient eligibility. In a multimodality imaging assessment of screening eligibility for TTVIs, including both computed tomography (CT) and echocardiography, screening failure rates ranged from 30% to 50% depending on the device selected (13). Fourth, in analogy to surgery, the issues of hypoattenuated leaflet thickening (HALT) and bioprosthetic valve thrombosis remain relevant for transcatheter valves, with recent studies demonstrating moderate or severe HALT in 27% of the patients undergoing CT within 30 days after TTVR (14). This phenomenon might be reversible either spontaneously or after intensification of the anticoagulation regimen, and its impact on valve durability remains unknown. Indeed, data on mid- and long-term durability of transcatheter valves, as well as the rate of recurrent TR after T-TEER over the same timeframe are currently lacking.

Since patients with severe residual TR after failed transcatheter intervention have dismal prognosis (possibly even worse than those under OMT alone), transcatheter bailout strategies need to be developed and offered at expert centers. While redo T-TEER may be a viable option for selected cases, TTVR after failed T-TEER has also been recently reported in small series, with or without prior leaflet modification. Electrosurgical laceration creating iatrogenic SLDA(s) might be required for T-TEER devices that are >7 mm away from the nearest commissure (15). In the scenario of early transcatheter valve failure, the design of the EVOQUE valve (28 mm) allows for easy ViV implantation of a balloon-expandable bioprosthesis.

Therefore, lifetime management of patients with TV disease still puts physicians in front of several challenges, which can be summarized as follows:

(I) The current design of tricuspid rings complicates ViR procedures after failed surgical repair. Innovations in ring design will be required to better accommodate consecutive transcatheter procedures.

(II) Bioprostheses in tricuspid position may have higher thrombogenicity and lower durability, with ViV as a potential option in case of valve degeneration.

(III) The management of failed T-TEER cases is complex and may require leaflet modification.

(IV) Interaction between right ventricular lead and transcatheter prostheses can cause lead malfunction. Pacing strategies in patients with or at risk of developing TR, as well as the device design more tailored to the specificities of the TV, will need to be refined to minimize the risk of lead-related complications.

Beyond these technical considerations, decision-making regarding the lifetime management of patients with TR should incorporate individualized factors such

as age, estimated life-expectancy, TR mechanism and anatomical parameters (in particular the severity of annular dilation). While in the rare scenario of primary TR, repair techniques are usually preferred, the choice of the most appropriate treatment of secondary TR should be based on anatomical eligibility and its ability to adequately and durably reduce TR balancing clinical risks (e.g., pacemaker need, right ventricular dysfunction, bleeding etc.). In addition, the clinical consequences of long-lasting TR, including renal and liver dysfunction due to non-treatable venous congestion have been identified as main drivers of adverse events (16). It is now well established that late TR correction is associated with higher procedural risk and may no longer improve symptoms. Conversely, intervening too early may expose patients to an increased lifetime risk for recurrent TR or valve degeneration without established clinical advantage. Recent EuroTR and TRIGISTRY analyses showed no survival benefit in patients treated at too early or very advanced stages, while TR correction was associated with a significant reduction in one-year mortality in those with intermediate disease stage (16,17).

Future progress will therefore depend as well on earlier patient referral to improve clinical outcomes. Indeed, low disease awareness and delayed recognition remain the major challenges limiting therapeutic options and lifetime perspectives of patients with TR.

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