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EDITORIAL COMMENT

Striding Forward on the Tricuspid Journey*

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Clinicians have recently developed a heightened awareness of tricuspid regurgitation (TR) as a meaningful clinical problem that requires a solution. No longer "the forgotten valve," in the last few years, the tricuspid valve has become a target for investigational transcatheter therapies. Why this newfound enthusiasm? With the advent of transcatheter aortic valve replacement (TAVR) and transcatheter mitral valve repair and replacement, we are increasingly challenged by patients with concomitant severe TR. Even after successful TAVR or transcatheter mitral valve repair and replacement, severe TR does not reliably "go away," and patients with severe TR have less clinical benefit, with higher death and rehospitalization rates. The development of structural heart teams and valve clinics has accelerated the referral of patients with concomitant and isolated TR for treatment. Patients with severe TR tend to be particularly symptomatic and challenging because surgery is almost always high risk, and diuretic therapy is at best palliative. There is also a sense within the interventional community that aortic stenosis has been conquered with mature TAVR devices, and that viable solutions to MR are here or on the near horizon. Naturally, the compass of attention and innovation now points to the tricuspid valve as a target for the next wave of transcatheter therapies.

There are numerous challenges to tricuspid transcatheter repair or replacement (Table 1). Merely imaging the tricuspid valve has required a renaissance in transesophageal echocardiographic techniques, and novel views of the tricuspid valve have been developed and are often device-specific. Not all patients can be adequately imaged by transesophageal echocardiography, and there is a clinical need for alternative valve imaging methods. Intracardiac echocardiography (ICE) has been used to help guide some of these procedures, but it is limited due to the need for a skilled ICE operator and some lack of control and stability of the ICE catheter. Quantification of TR has required a recalibration of the conventional mild, moderate, and severe categories, and newer classifications include categories of TR greater than severe including "submassive," "massive," and "torrential." The degree of leaflet separation and tricuspid annular dilation can be profound, and reapproximating the leaflets will require a robust system with adequate and durable forces to achieve lasting and meaningful TR reduction.

For devices whose mechanism is edge-to-edge repair, understanding the presence and number of leaflet scallops may be important in assessing optimal responders. Avoiding injury to adjacent structures such as the right coronary artery and atrioventricular node will be critical for procedural safety. Selecting patients for TR correction remains perhaps the most challenging question of all, because patients with functional TR by definition have TR secondary to other heart conditions including right ventricular dysfunction, pulmonary hypertension, atrial fibrillation, and left-sided myocardial or valvular disease. A population of patients with "pure" TR almost does not exist. Conventional endpoints such as TR reduction or ventricular remodeling may not be sufficient to capture the clinical impact of early transcatheter devices, and development of novel endpoints specific to these patients will be essential (such as diuretic dosage, the amount of ascites, liver function, calf circumference, and body weight).

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In the TriValve (Transcatheter Tricuspid Valve Therapies) registry published in this issue of *JACC: Cardiovascular Interventions*, we see early steps forward on the journey to transcatheter TR correction

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TABLE 1 Clinical Challenges to Transcatheter Tricuspid Valve Correction

Imaging with echocardiography (suboptimal windows)
Severity of TR quantification not standardized
Wide tricuspid leaflet coaptation gaps and marked annular dilation
Thin leaflets and variable chordal anatomy
Multiple leaflet scallops, particularly in the posterior leaflet
Proximity of the right coronary artery
Atrioventricular nodal injury
Diaphanous tricuspid annulus (narrow target zone for annular attachment)
Comorbid patient population, functional TR rarely exists in isolation
Nonstandard transcatheter alignment angles from IVC/SVC
Lack of evidence-based surgical indications for TR correction
Designing transcatheter clinical trials and endpoints

IVC = inferior vena cava; SVC = superior vena cava; TR = tricuspid regurgitation.

(1). This registry represents a collaborative effort of 11 international cardiac centers over a 2-year period, and reports the baseline characteristics and early outcomes of their initial experiences (in patients *outside* of any clinical trials) using 6 different transcatheter approaches to TR correction.

The baseline characteristics reveal an older patient population (mean age 76.3 ± 8.9 years) that is predominantly female (60.4%). This differs from most valve studies that enroll a male majority. Subjects had elevated EuroSCOREs (7.6 ± 5.7), and 95% had functional TR, although 23.5% of subjects had concomitant transtricuspid pacing leads, which is interesting in that the reported mechanism of TR in most patients with pacing leads was functional (and not necessarily primary due to leaflet "trapping" or "pinning"). Most patients had atrial fibrillation (79%), which was certainly a contributor to TR by way of right atrial and tricuspid annular enlargement. Patients in the registry were highly symptomatic with very elevated pro-B-type natriuretic peptide levels (2,523 pg/ml), ascites (27.3%), and peripheral edema (81%), and 95% were in New York Heart Association functional class III/IV. By echocardiography, these patients had mostly preserved left ventricular ejection fractions (50.8 ± 12.6%), predominantly central TR (77%) with very severe TR by regurgitant volumes (62.9 ± 27 ml), large effective regurgitant orifice areas (0.87 ± 0.56 cm^2), and markedly dilated tricuspid annuli (45.4 ± 11 mm). Unexpectedly, these patients as a group did not have significant pulmonary hypertension by systolic pulmonary artery pressure (39.7 ± 13.9 mm Hg), although the true pulmonary vascular resistance may be underestimated due to depressed right ventricular function and diminished forward cardiac output.

This registry highlights the early device "leaders" in this journey. The MitraClip (Abbott Vascular, Santa Clara, California) has the largest global experience to date, primarily due its wide adoption, operator familiarity, and relative ease of placing the clip on the tricuspid valve leaflets. It is easy to envision "drive-by" or same-setting tricuspid valve clipping after MitraClip MR treatment. Other devices that target the tricuspid valve annulus are the next most prevalent in this series. These devices mimic various iterations of nonrigid surgical tricuspid valve annuloplasty. Finally, more unique solutions such as spacer and caval valve implantation complete this registry. The patient demographics are very similar between devices, and the main difference appears to be a higher prevalence of transtricuspid pacing leads in the MitraClip group.

Outcomes from this registry are thought provoking. Procedural success (defined as patient alive, device successfully implanted, with final TR grade ≤2) was 62%. Given the baseline severity of TR in these patients, this is an encouraging, but not optimal, result. The procedural safety profile was also favorable for an early experience with 30-day outcomes of mortality (3.7%), stroke (1.2%), bleeding (2.4%), rehospitalization for heart failure (8.6%), and 4 device failures (4.9%). Ascites was reduced in 13% of patients, and peripheral edema decreased in 41.9%. There were significant reductions in diuretic doses (furosemide dose reduced by 84%, and torasemide by 54.5%). At 30 days, only 40 of 107 patients had echocardiographic follow-up, and only 49% of those had final TR ≤2+. Although there was improvement in New York Heart Association functional class at 30-day follow-up, this registry did not include quality-of-life questionnaires or functional metrics such as the 6-min walk test, so it is difficult to gauge exactly how much better patients felt.

Several conclusions can be drawn from this first global registry. It is now clear that we have taken more than a few bold strides forward, with multiple devices having promising early clinical outcomes. Several technologies have since proceeded onto more formal safety and feasibility trials, with pivotal trials planned in the near future. Unanswered questions remain. Are the transcatheter approaches described in this registry robust enough to have sufficient and durable reductions in TR and lasting clinical benefit? Without longer and more complete follow-up, we will not know. The thoughtful design and execution of randomized clinical trials will be crucial for us to understand the types of patients that will derive meaningful clinical benefit, and to generate evidence-based clinical indications for TR correction. It is also provocative to note that none of the devices presented in this registry faithfully

mimic the current surgical standards for TR correction, which consist primarily of rigid ring annuloplasty, or TV replacement. Other technologies in development or new techniques will undoubtedly come forward in the future to address this mechanistic gap. Ultimately, the goal of reducing TR to mild or trace was not consistently achieved in this registry, and innovators should continue to strive for this goal.

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