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EDITORIAL COMMENT

Exploring Tricuspid Regurgitation in Treating Degenerated Bioprosthetic Aortic Valves*

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There has been growing interest in the impact of multivalvular disease on treatment strategies for valvular heart disease and in defining cardiac prognosis. Multivalvular disease, comprising a combination of stenotic and/or regurgitant lesions of 2 or more cardiac valves, is a highly prevalent clinical condition among patients with valvular heart disease (1). In the EuroHeart Survey, 20.2% of patients with native valve disease and 14.6% of those undergoing valvular surgery had multivalvular disease (2). Multiple valve surgery accounted for 10.9% of the 623,039 patients undergoing valve surgery between 1993 and 2007 in the Society of Thoracic Surgeons database (3). Among these patients, 57.8% underwent surgery on the aortic and mitral valves, 31.0% on the mitral and tricuspid valves, and 3.3% on the aortic and tricuspid valves, and 7.9% underwent triple-valve surgery. In the PARTNER (Placement of Aortic Transcatheter Valve) trial, the incidence of concomitant moderate-to-severe mitral regurgitation in patients with severe aortic stenosis (AS) undergoing transcatheter aortic valve replacement (TAVR) was approximately 20%, and the incidence of moderate to severe tricuspid regurgitation (TR) was 27% (4-7).

A newly proposed staging classification of AS pathology weighs the extent of cardiac damage and other valvular involvement (8). Patients with significant functional TR have been classified as stage 3 (of 4 grades of severity) with adverse prognostic clinical outcomes despite undergoing aortic valve replacement (AVR). Such an ordering characterizes the extent of secondary anatomic and functional cardiac damage associated with AS before AVR and has prognostic implications post-AVR.

There are various etiologies for coinciding TR among patients with aortic valve pathologies (stenosis or regurgitation). TR is often functional in etiology and caused by pulmonary hypertension or right ventricular (RV) pressure overload, and potentially aggrieved by left ventricular diastolic dysfunction and/or coexisting mitral insufficiency. Long-standing left-sided valvular pathology and/or ventricular failure may cause RV dysfunction with subsequent annular dilatation and secondary TR, though other causes (e.g., primary TR pathology, pacemaker leaflet function interruption) may be the predominant etiology (9).

Accordingly, functional TR is not infrequently found in conjunction with native-valve AS. The TR pathology often persists after AVR and is even progressive in some patients. According to 1 study, post-operative atrial fibrillation and exaggerated transvalvular aortic gradients may predict later TR persistence or even progression (10). In the PARTNER 2 trial, among patients undergoing TAVR, moderate or severe TR and RV enlargement were independently associated with increased mortality (11). Data analyzed from 34,576 patients who underwent TAVR at 365 U.S. hospitals (12) indicated that TR was present in 80% of TAVR patients, with mild TR in 56%, moderate TR in 19%, and severe TR in 5%. Increasing TR severity was associated with a number of comorbidities. Adjusted mortality at 1 year was significantly worse for patients with severe TR when left ventricular ejection fraction was >30% (hazard ratio: 1.29), as was heart failure readmission (hazard ratio: 1.27). Thus, the natural history of TR and its impact on the

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outcomes of native AS and/or AVR have been fairly well studied. However, until recently there was a paucity of data regarding the impact of catheter-based aortic valve-in-valve (VIV) interventions on TR frequency and the response to such a mode of treatment for degenerated surgical bioprosthetic aortic valves.

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In this issue of *JACC: Cardiovascular Interventions*, this background set the stage for Sathananthan et al. (13) to investigate the TR response in the multicenter PARTNER 2 aortic VIV trial, which enrolled patients with symptomatic degenerated surgical aortic bioprostheses who were at high risk for reoperation. The mode of bioprosthetic failure was AS in two-thirds of cases, and predominant aortic regurgitation was diagnosed in one-third. The investigators compared 237 patients with TR mild or less (n = 162) and those with TR moderate or greater (n = 75) using standard echocardiography and Doppler methods. Their results indicate that in the context of the trial, the presence of TR and/or TR severity was not a predictor of long-term adverse outcomes. Importantly, there was significant improvement in TR severity at both short (30-day) and long-term (1-year) follow-up.

The clinical significance of this study is 2-fold. First, it provides insight into TR response among patients undergoing aortic VIV interventions. The clinical evaluation of these patients is complex and challenging, and their prognostication is often unclear, as the impact of TR on the overall clinical scenario is sometimes ambiguous and difficult to resolve. Second, the study indicates for the first time that TR could be reversed in aortic VIV interventions, and it may not be associated with adverse clinical outcomes up to 1 year regardless of its severity. Although it is a reassuring message, I would not consider it robust, as only a few patients with truly severe TR were included in the present study, and the follow-up duration of the treated patients was probably too short. Also, the investigators have not reported the clinical outcomes of patients who were deemed from aortic VIV intervention because of overwhelming TR severity, especially in the context of severe RV failure or decompensated biventricular failure syndrome. Thus, more data are needed to validate the investigators' pivotal observation among "all comers" patients with failed aortic bioprosthetic valves and concomitant TR. These patients have a long-standing history of valvular heart disease, as they all underwent at least 1 open heart valve surgery; thus, the likelihood of TR with or without RV dysfunction and/or some degree of pulmonary hypertension is quite high.

I fully agree with the investigators' conclusion that this study addresses a knowledge gap and aids in making management decisions for patients undergoing aortic VIV TAVR with concomitant TR. Moreover, I think the present study is an important addition because it calls for a careful examination of the right side of the heart in planning for an aortic VIV intervention. The diagnosis of TR could pose a challenge to the clinician, and the severity of the valve pathology should be diagnosed precisely and quantified using Doppler echocardiography according to standardized methods (14). Patients planned for aortic VIV should be examined for right-sided failure symptoms, and invasive hemodynamic assessment is needed in the case of significant right-sided pathology to supplement the clinical evaluation. The need for additional tricuspid valve intervention is rare, though at present the catheter-based approach to TR correction is in its infancy and largely investigational. Importantly, patients with TR of any severity should not be excluded from aortic VIV TAVR.

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