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EDITOR'S PAGE

Tricuspid Regurgitation

A Voyage of Discovery

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The real voyage of discovery consists not in seeking new landscapes, but in having new eyes.

—Marcel Proust (1)

The prevalence of tricuspid regurgitation (TR) is influenced by age as well as by sex and is likely to increase. Up to 5.6% of women and 1.5% of men have clinically significant TR by their eighth decade (2). This problem will get worse given an aging population in which the ≥65-year-old segment could reach 88 million by 2050 (3). Significant TR is not a benign disease; a recent natural history study reported a 42% mortality rate during a median follow-up of 2.9 years (4). Despite known TR's adverse outcomes, fewer than 8,000 of an estimated 1.6 million patients affected with moderate to severe TR undergo surgical interventions annually (2,5). In addition, current methods of treating severe TR seem to be suboptimal: operative mortality for isolated tricuspid valve surgery remains high, at 8% to 10% (6,7), and post-operative patient symptoms have improved but show no clear survival benefit. (5,8,9). Moderate or greater TR may be seen in approximately 34% of patients at 3 months following repair and in 45% by 5 years (10). The right side of the heart was considered an afterthought of left ventricular pathology until recently and has not been studied as extensively. *iJACC* has been doing its part to emphasize the unique importance of the right heart by showcasing some insightful aspects of RV-PA interactions using imaging in the past (11-14) and now by publishing a special, focused issue investigating the tricuspid valve itself. Mitigating the mortality and morbidity burdens of TR will require a better understanding of a whole slew of anatomic and physiologic relationships among various components of the right- and left-heart pathophysiologic interactions and the appropriate timing for and type of intervention. This issue of *iJACC* summarizes the field with a series of impactful papers that comprehensively cover a whole range of pressing questions in this space.

TR remains a significant problem in the community as well. Topilsky et al. (15) used the echocardiographic and clinical database of patients in Olmsted County, Minnesota, to evaluate the prevalence of TR phenotypes. In that community, the most common association with moderate and greater TR severity was left-sided valvular heart disease (49.5%), followed by pulmonary hypertension (23%), left ventricular dysfunction (12.9%), isolated TR (8.1%), primary TR (4.8%), and congenital disease (1.7%). Survival was 28.5 ± 1.3% at 5 years, 14.1 ± 1.1% at 10 years, and 10.2 ± 1.1% at 15 years, and it depended on the underlying cause. To appreciate the pathophysiology of the disease, it is essential to understand the anatomic underpinnings of the disease. The tricuspid valve is a complex structure, and imaging can help us gain insight into its anatomy. Dahou et al. (16) review the anatomy of the normal tricuspid valve and the right atrium and ventricle and discuss the anatomic changes associated with the TR secondary to pathology. Familiarity with normal and abnormal anatomy

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helps elucidate the challenges of transcatheter devices. The most recent American Society of Echocardiography guidelines for the evaluation of native regurgitation lists a number of qualitative, semiquantitative, and quantitative measurements of TR severity; however, these recommendations have not changed significantly since the previous version, highlighting the limited number of studies validating newer methods of assessing right-heart atrioventricular valve regurgitation. Hahn et al. (17) review the strengths and limitations of established and novel multimodality methods for assessing TR severity. Importantly, the color Doppler jet area depends on momentum, and using visual criteria similar to mitral regurgitation makes little physiologic sense and may significantly underestimate the severity of TR. Echocardiographers may need to reset their visual thresholds (or use quantitative methods) to prevent under-recognition of significant disease.

TR can result from primary abnormalities of the leaflets, known as primary TR, or in the setting of intrinsically normal leaflets, known as secondary TR. Prihadi et al. (18) review the morphologic phenotypes, clinical characteristics, and outcomes of primary, secondary, and isolated TR. TR following endocardial lead placement, considered "organic" TR, is an increasingly recognized problem that poses adverse implications (19). In their prospective study of 153 patients, 25% of patients experienced an increase in TR severity at 12 months following lead placement. Any increase in TR (even if only an increase to mild) was associated with progressive increases in right-heart dimensions as well as right ventricular systolic pressure. Right-heart cardiomyopathies are considered a rare cause of secondary TR. In patients with arrhythmogenic right ventricular cardiomyopathy (ARVC), TR is a predictor of adverse events. In this issue of *iJACC*, Mast et al. (20) report using echocardiographic strain imaging to show that abnormal RV deformation in the subtricuspid region is associated with disease progression and was detected prior to typical guideline-recommended signs of ARVC.

To answer the question of whether TR has independent associations with outcomes in a heart failure population, Bartko et al. (21) studied 382 patients with heart failure and reduced ejection fraction with quantitated severities of TR. The authors used the proximal isovelocity surface area (PISA) method to calculate effective regurgitant orifice areas (EROA) and regurgitant volumes and showed that greater TR severity was associated with mortality in these patients (21). Similar to outcome studies using the same method to quantify functional mitral regurgitation (26), an EROA of ≥20 mm^2 and a regurgitant volume of ≥20 ml were the thresholds associated with increased mortality. Recent guidelines, however, have suggested that mitral EROA may be underestimated by PISA, and Dahou et al. (22) confirmed this for TR in their study of 160 patients by using quantitation of PISA, Doppler volumetric methods, and three-dimensional (3D) vena contracta area (VCA) measurements. A strong correlation between Doppler volumetric methods and 3D VCA measurement was found, whereas the correlation was modest between those measurements and the PISA method. The following EROA cutoff values for severe TR were 0.34 cm^2 for the PISA method, 0.65 cm^2 for the Doppler method, and 0.60 cm^2 for the 3D VCA method.

The development of secondary TR is determined by annular geometry, right- and left-heart sizes and functions, and the intervening pulmonary bed, and a keen understanding of RV-PA coupling is important. Hahn et al. (23) summarize these relationships and suggest a list of parameters which may be important for determining valve function and clinical outcomes. This complex valve requires advanced assessment, and real-time 3D imaging plays an increasingly important role (24). Khalique et al. (25) describe a comprehensive multimodality assessment of the tricuspid valve and right heart, which forms the cornerstone of pre-procedural analysis. Muraru et al. (26) clarify the use of 3D transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) imaging for assessing the valve and right-heart structures, removing much of the mystery surrounding the morphology of this complex valve and its ventricular relationship. Using customized software, Addetia et al. (27) used 3D TTE to describe the normal tricuspid annular morphology and dynamism, highlighting differences between standard 2D measurements of tricuspid annular size and those using more comprehensive 3D imaging.

Fueled by the success of transcatheter aortic valve replacement therapy for high- and now intermediate-risk surgical replacement, transcatheter solutions for TR have advanced rapidly (28). Given the surgical risk of nearly 4 times that of single left-valve surgery, isolated tricuspid valve surgery remains a high-risk procedure with a large unmet need. Imaging plays a crucial role (29–31) for pre-, intra-, and post-operative planning and monitoring. Current devices under investigation require intraprocedural echocardiography (both TEE and intracardiac echocardiography) for optimal assessment and guidance. Hahn et al. (32) review the complex imaging protocols and requirements for some of these procedures. The off-label use of mitral valve edge-to-edge repair devices

has become the most common tricuspid valve device to be implanted to date. Faletra et al. (33) show how transgastric TEE views are particularly useful for this procedure. Orban et al. (34) report the single-site 6-month clinical and echocardiographic outcomes of this procedure in 65 patients, probably the largest experience of this kind. Finally, Hahn et al. (35) report their early experience with transcatheter tricuspid valve replacement.

This is an exciting time for understanding the right heart and its pathophysiology and interventions for the tricuspid valve. Both conventional and advanced imaging will play pivotal roles in detecting the disease, quantifying severity, and guiding therapy for tricuspid pathology. We hope this *focus* issue helps our readers understand, evaluate, and tackle this important problem effectively.

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