Editorial Commentary

Functional tricuspid regurgitation: is prognosis mostly driven by phenotype or severity?

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Functional tricuspid regurgitation (FTR), which accounts for the majority of tricuspid regurgitation (TR) cases (>90%), is a highly heterogeneous condition encompassing various phenotypes. Increasingly, FTR has become a topic of interest, particularly in understanding how different phenotypes—atrial (A-FTR) and ventricular (V-FTR)—may influence patient prognosis and treatment outcomes.

In a recent study published in *JACC*: *Cardiovascular Interventions*, von Stein *et al.* conducted a multicenter study at three high-volume centers in Germany, demonstrating that percutaneous correction of TR using an annuloplasty technique (Cardioband by Edwards Lifesciences, a CE-approved system) yielded favorable results in reducing TR severity and improving 1-year survival in the overall population of patients with FTR. However, patients with A-FTR experienced a better prognosis than those with non-atrial functional tricuspid regurgitation (NA-FTR) (1). They also showed that A-FTR was associated with better procedural success, providing a potential mechanistic explanation for the observed differences in outcomes.

This study warrants several comments.

The first point to address is the definition of A-FTR. Recently it has been suggested to subdivide FTR into A-FTR and V-FTR. A-FTR corresponds to the Carpentier Type 1 classification, where leaflet structure and motion are normal, with tricuspid annulus dilation caused by right atrium enlargement and dysfunction, mostly associated with atrial fibrillation/heart failure with preserved ejection fraction. The current definition proposed by the Tricuspid Valve Academic Research Consortium and the PCR Tricuspid Focus Group suggests: clinically relevant FTR (≥ moderate), predominant tricuspid annulus dilation, predominant right atrium dilation with an increased end-systolic right atrium/right ventricle (RV) ratio, absence of significant tricuspid leaflet tethering, RV conical remodeling with predominant enlargement of the RV basal dimension, and preserved left ventricle (LV) and RV systolic function (2-4).

However, this classification is not widely agreed upon and is not applied consistently across the literature, with many researchers using their own definitions (5-7). This inconsistency is reflected in the current study, where the A-FTR population is defined using distinct criteria, characterized by the absence of tricuspid valve tenting (tenting height ≤10 mm), midventricular RV dilation (mid RV diameter ≤38 mm), and preserved LV ejection fraction (LV ejection fraction ≥50%). Patients not fulfilling all of these three criteria were assigned to the NA-FTR group (1). Interestingly, both definitions do not consider pulmonary hypertension and prior left-sided heart valve surgery as

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exclusion criteria for A-FTR.

Furthermore, applying this classification on an individual basis is challenging because patients show overlapping imaging features of A-FTR and V-FTR. This makes it difficult to clearly categorize them into one group or the other, raising the question of whether the authors selected true A-FTR cases or those with a less advanced stage of TR disease. To add complexity, it is likely that some patients labeled as having functional TR may actually present with organic TR, particularly those who previously underwent correction for left heart valve disease (13% of the population in this study). This is supported by a recent article that reported a 55% prevalence of tricuspid valve prolapse in patients with degenerative mitral regurgitation (8).

Second, recent studies have consistently shown that patients in the A-FTR group tend to have better outcomes than those in the V-FTR group, irrespective of the therapeutic approach, whether medical or percutaneous intervention (6,7,9). However, this raises a critical question: is the prognosis truly linked to the FTR phenotype, or is it more a reflection of the severity of TR and its hemodynamic consequences?

While the definitions of A-FTR and V-FTR vary across studies, the overall findings are strikingly consistent: A-FTR patients fare better. This study, despite being limited by a small sample size (165 patients) and a relatively short follow-up period of 1 year, confirms this trend (1). At first glance, the results appear to reinforce the importance of accurately identifying phenotypes to enhance prognostic prediction. However, a deeper look suggests that the difference in outcomes may be less about distinct disease mechanisms and more about the stage of disease progression.

Indeed, when comparing A-FTR and V-FTR patients, it becomes clear that A-FTR represents a less advanced stage of disease. Previous studies have highlighted that patients with A-FTR tend to be less symptomatic, with fewer cardiovascular comorbidities, and are less frequently prescribed loop diuretics (5,6,10). This distinction is even more pronounced in the current study (1). The baseline characteristics of A-FTR patients indicate a less advanced stage of the disease compared to NA-FTR patients, with lower bilirubin levels, a trend toward lower creatinine and N-terminal pro B-type natriuretic peptide (NT-proBNP) levels, less atrial fibrillation, smaller right heart dimensions (tricuspid annulus diameters and right atrium area), smaller coaptation gaps and tenting height, less frequent impairment of RV function, lower TR severity, higher LV ejection fraction and lower EuroSCORE II. All these differences are illustrated by a lower TRI-SCORE (4 *vs.* 5, P=0.038). These findings align with the idea that it is the severity of the disease rather than the underlying etiology that drives both procedural success and outcomes.

One of the objectives of the study was to evaluate the effectiveness of the Cardioband in patients with FTR based on their phenotype. The authors demonstrated its efficacy, as it significantly reduced TR in the majority of patients, achieving residual TR ≤ moderate. However, the authors' conclusion that «both phenotypes experienced similar symptomatic improvement, emphasizing the benefit of transcatheter tricuspid valve annuloplasty even in advanced disease stages» should be discussed as the results differed significantly depending on the phenotype, with residual TR ≤ moderate at discharge achieved in 85% of A-FTR patients versus 61% in NA-FTR patients (P=0.001). Thus, patients treated at an earlier stage had better procedural results and TR grade reduction. The two baseline parameters associated with residual TR ≤ moderate at discharge and 30 days were A-FTR type and lower TR grade. Additionally, although the follow-up period was short and the patient number small, A-FTR was associated with better 1-year survival.

This raises the possibility that the better outcomes observed in A-FTR patients are largely due to the fact that they represent a less advanced disease stage rather than being driven by fundamentally different pathophysiological mechanisms. It seems increasingly likely that the stage of TR severity is the primary determinant of both procedural success and outcomes. This perspective aligns with findings from other studies, which have demonstrated that the stage of the disease, as determined by the TRI-SCORE, significantly impacts mid- and long-term mortality across medical, percutaneous, and surgical populations (11-14). Therefore, accurate early phenotyping and timely intervention could play pivotal roles in improving prognosis in patients with FTR, regardless of the specific phenotype.

This study also reinforces the importance of achieving the best possible procedural result, defined by the lowest possible grade of residual TR, as previously demonstrated (15). The choice of therapeutic strategy is determined by a multidisciplinary heart valve team, primarily based on the disease stage, procedural risk, and the likelihood of procedural success based on TR severity and anatomy, including tricuspid valve and RV remodeling, with numerous therapeutic options currently available and many more in development, whether surgical or percutaneous, repair or replacement.

In conclusion, we believe the key message of this study

lies not in the underlying mechanism of TR, but in the importance of timely intervention and achieving optimal TR reduction, which are closely linked. Patients who undergo TR correction early in the disease course achieve better procedural results and consequently experience better survival than those treated at a more advanced stage. This study aligns with others advocating for early curative treatment. Numerous registries and randomized studies are currently underway to identify the best candidates and optimal treatment strategies for managing patients with severe FTR.

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Footnote

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