Atrial functional tricuspid regurgitation: a novel and underappreciated clinical entity

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Abstract: Functional or secondary tricuspid regurgitation (FTR) is a progressive disease with a significant negative impact on patient morbidity and mortality. Recently, atrial fibrillation (AF) has been recognized as a cause of FTR (with/without coexisting functional mitral regurgitation) by promoting right atrial (RA) remodeling and secondary tricuspid valve (TV) annulus dilation, even in the absence of right ventricular (RV) dilation or dysfunction. This distinct form of FTR has been called “atriogenic” or “atrial”. Recent evidence suggests that the RA is an important player in FTR pathophysiology not only for patients with AF, but also for those in sinus rhythm. Preliminary reports on atrial FTR show that cardioversion with doxycyclin promotes TV annulus and RA reverse remodeling and may significantly reduce FTR severity at follow-up. Large-scale studies on the prognostic benefits of rhythm vs control strategy in atrial FTR patients are needed to substantiate specific guidelines indications for this subset of patients.

Keywords: atrial functional tricuspid regurgitation; tricuspid valve; three-dimensional echocardiography; transthoracic echocardiography.

FUNCTIONAL OR SECONDARY TRICUSPID REGURGITATION

For years, the general belief has been that FTR is the hallmark of the disease of the RV, rather than the disease of the TV itself. According to current ESC/EACTS guidelines2, FTR develops as a result of the geometric changes of TV apparatus due to the dysfunction of the RV following pressure and/or volume overload. Nevertheless, there are often patients with significant FTR that may present with TV annulus dilation, despite a normal RV, and a dilated RA1. Recently, atrial fibrillation (AF) has been recognized as a cause of FTR (with/without coexisting functional mitral regurgitation) by promoting right atrial (RA) remodeling and secondary tricuspid valve (TV) annulus dilation, even in the absence of right ventricular (RV) dilation or dysfunction. This distinct form of FTR has been called “atriogenic” or “atrial”. Recent evidence suggests that the RA is an important player in FTR pathophysiology not only for patients with AF, but also for those in sinus rhythm. Preliminary reports on atrial FTR show that cardioversion with doxycyclin promotes TV annulus and RA reverse remodeling and may significantly reduce FTR severity at follow-up. Large-scale studies on the prognostic benefits of rhythm vs control strategy in atrial FTR patients are needed to substantiate specific guidelines indications for this subset of patients.

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fibrillation (AF) has been recognized as a cause of FTR (with/without coexisting functional mitral regurgitation) by promoting RA remodeling and secondary TV annulus dilation, even in the absence of RV dilation or dysfunction (type I of the Carpentier classification)⁴. This distinct form of FTR has been called “atriogenic” or “atrial”, and thanks to the use of three-dimensional echocardiography (3DE), its peculiar pathophysiologic mechanisms have now been described⁵–⁸.

However, both the 2017 ESC/EACTS Guidelines on the management of valvular heart disease⁹ and the recent 2020 ESC Guidelines on the diagnosis and management of AF¹⁰ do not even mention this distinct form of FTR that may typically affect patients with persistent AF. Current literature addressing atrial regurgitation of the TV or mitral valve (MV) has been calling it “neglected”, “an underappreciated cause”, “new entity”, “newly described disorder”⁷,¹⁰–¹². Only recently, in the newly published 2020 ACC/AHA Guidelines for the management of patients with valvular heart disease, has the atrial mechanism of FTR been given a distinct role¹³. Yet, as there is almost no evidence available on how to manage these patients, there are more open questions than answers. Atrial FTR may require different clinical management and the various interventional treatment options may have different outcomes than in the classical ventricular FTR due to RV dilation and dysfunction (type IIIb of the Carpentier classification)¹⁴,¹⁵. Since AF is the most common sustained arrhythmia (affecting ~33 million people worldwide) with an increasing prevalence due to the ageing of the population¹⁶, clinicians and echocardiographers will likely encounter patients affected by atrial FTR.

Therefore, we aimed to familiarize the reader with this “new” disease by providing an overview of the pathophysiology, and the key distinguishing features of atrial FTR that may help the clinicians and imaging specialists to differentiate it from the classical ventricular form of FTR.

**ANATOMY AND PATHOPHYSIOLOGY**

The TV apparatus consists of several components – valve leaflets, annulus, chordae tendineae, papillary muscles, and RV and RA walls. Compared to the MV complex, TV has greater anatomical variability, a more apically insertion of the septal leaflet, and chordal attachments directly inserted to the interventricular septum¹⁷. The normal TV annulus is an elliptical, saddle-shaped, and dynamic structure. In comparison to the mitral annulus, the TV annulus is larger (normal TV diameter in apical four-chamber view 19 ± 2 mm/m², and 3D area 7.6 ± 1.7 cm²/m²), and more dynamic (systolic fractional shortening of 25% and area change of 30-40%)¹⁸,¹⁹. The TV annulus is mostly a fatty structure, and its significantly smaller fibrotic component with respect to the MV annulus could explain why the TV annulus dilates more easily along with the right heart chamber enlargement and is the main mechanism responsible for the development of atrial FTR²⁰,²¹. TV papillary muscles send chordae to ipsilateral leaflet(s) and become more separated and apically displaced in the context of RV dysfunction, leading to TV leaflet tethering¹.

The classical (ventricular) form of FTR may occur in various cardiac conditions (left-sided valvular, myocardial, or pulmonary diseases) and includes three main mechanisms: 1) TV annulus dilatation due to RV remodeling; 2) changes in the geometry and dynamics of the annulus, becoming rounder, flatter and less contractile; 3) leaflet tethering as a consequence of the spatial displacement of the components of the TV apparatus resulting in loss of coaptation and secondary FTR²⁰,²². Among these mechanisms, TV leaflet tethering is the primary pathophysiological mechanism of ventricular FTR. It occurs with changes in RV geometry and function due to volume and/or pressure overload, such as an increase in RV volume, RV global or regional systolic dysfunction or shape abnormalities (increased sphericity, abnormal regional curvature, etc.)²³. Annular dilatation is an important contributor to the development of ventricular FTR, leading to edge-to-edge leaflet coaptation²⁰.

The importance of the RA has been ignored, despite the close anatomic relationship of the RA vestibule with the TV annulus. The RA vestibule is a smooth muscular rim that anchors the pectinate muscles and surrounds the TV orifice, with its thin musculature fibers inserting into the leaflet hinges¹. In contrast with the MV annulus, which is disconnected from the left atrial myocardium between both fibrous trigones at the base of the anterior leaflet, the TV annulus has a single right fibrous trigone keeping it in closer contact with RA myocardium over a larger part of its circumference. The muscular fibers of the RA vestibule are responsible for the “sphincteric-like” contraction of TA²⁴, and might explain the TV annular dysfunction in AF patients with RA remodeling and atrial FTR.

The proposed model of atriogenic regurgitation - typically with long-standing persistent AF - implies a significantly remodeled RA that promotes a mar-
ked and progressive dilatation of TV annulus in the presence of no or minimal dilation of the RV. TV annulus is considerably enlarged in AF patients, even with less than severe FTR, and independently of the presence of cardiac structural abnormalities, supporting that TA dilation is the direct consequence of AF itself, rather than the result of FTR. Compared with ventricular FTR patients and for similar FTR severity, patients with atrial FTR had increased dimensions and posterior displacement of the TV annulus, larger RA, and smaller RV. Moreover, in patients with so-called “idiopathic FTR” (most of them being actually atrial FTR due to AF), Topilsky observed that the RV assumes a triangular shape with dilation occurring at the basal level, resulting in a large TV annular area without leaflet tethering (Figure 1). In contrast, in patients with pulmonary hypertension and ventricular FTR, the RV becomes elliptical due to dilation occurring at the mid-ventricular level, resulting in significant valvular tethering with no or mild TV annular dilation (Figure 2). Thus, the tethering of TV leaflets is commonly seen in patients with a ventricular form of FTR (with/without significant annular dilation) due to pressure/volume RV overload, while in atrial FTR due to AF the tethering is characteristically absent because the RV is normal. Once the pathophysiological cascade is initiated (either by ventricular or atrial factors), a vicious cycle ensues, with progressive FTR and further dilatation of the TA due to either RA or RV volume overload, resulting in further FTR and ultimately a combination of both atrial and ventricular FTR. Therefore, in advanced stages with massive or torrential FTR, marked remodeling of TV apparatus, and secondary RA and RV dysfunction due to longstanding volume overload, it may be more challenging to distinguish the primary cause of FTR. However, the prognosis of

| CARPENTIER CLASSIFICATION | ATRIAL FUNCTIONAL TRICUSPID REGURGITATION | VENTRICULAR FUNCTIONAL TRICUSPID REGURGITATION |
|----------------------------|------------------------------------------|---------------------------------------------|
| LEAFLET MOTION            | NORMAL                                   | RESTRICTED LEAFLET CLOSURE                   |
| LEAFLET TETHERING         | ABSENT/MILD                               | SEVERE                                       |
| ANNULUS SIZE              | SEVERE DILATION                          | NORMAL/MILD DILATION                         |
| VENTRICULAR SIZE          | NORMAL/MILD DILATION                      | SEVERE DILATION                             |
| VENTRICULAR FUNCTION      | NORMAL                                   | REDUCED                                       |
| ATRIAL SIZE               | SEVERE DILATION                          | MILD DILATION                                |
| ATRIAL FUNCTION           | SEVERELY REDUCED                         | MODERATELY REDUCED                           |

Figure 1. Comparison between atrial and ventricular functional tricuspid regurgitation; adapted from 5.
massive/torrential FTR is severe\textsuperscript{30,31} and there is likely little clinical benefit in clarifying the pathophysiological sequence at this advanced stage of the disease. Figure 3 presents the main imaging features that may help in differentiating the atrial FTR from the ventricular FTR.

Recent evidence suggests that the RA is important not only in AF patients but also in sinus rhythm. Indeed, RA could be a major player in the development of FTR and a key determinant of TV annular dilation\textsuperscript{32}, irrespective of its cause\textsuperscript{3}. We demonstrated that in all FTR groups (including atrial form due to AF and ventricular form due to both RV pressure and volume overload), as well as in healthy subjects, the TA area was more closely related to RA volume than to RV end-diastolic volume measured by 3DE\textsuperscript{3}.

**ECHOCARDIOGRAPHIC ASSESSMENT**

Transthoracic 2D-Doppler echocardiography is the primary imaging modality in the evaluation of FTR patients. By assessing TV morphology and annulus size, right-heart chambers’ size and hemodynamics, echocardiography generally provides the data needed to be integrated for evaluating the mechanisms and the severity of TR and to orient the subsequent clinical management\textsuperscript{22}. If unclear or conflicting results from transthoracic echocardiography, transesophageal echocardiography, cardiac magnetic resonance and cardiac computed tomography can be used for a comprehensive imaging assessment of the patient with FTR\textsuperscript{31}.

**TWO-DIMENSIONAL AND DOPPLER ECHOCARDIOGRAPHY**

The state-of-the-art echocardiographic evaluation of TR should follow several steps: 1) attesting the presence of pathological FTR; 2) evaluating the morphological characteristics of the TV; 3) assessing the key features of FTR (annulus dilation, leaflet coaptation, etc.); 4) discriminating between a ventricular and an atrial form of FTR; 5) quantifying the severity of FTR.

**Figure 2.** Atrial functional tricuspid regurgitation: RV-focused apical four-chamber color flow of the regurgitant jet (A); En face view of the tricuspid valve by 3D echocardiography (B); Tricuspid annulus geometry (C) and measurements (D) by 4D Auto-TVQ software (GE Healthcare, Horten, N).
and its hemodynamic impact on right-heart chambers. In clinical routine practice, TR assessment is performed by 2D and Doppler echocardiography as recommended by guidelines. When quantifying TR severity, different parameters (qualitative, semi-quantitative, or quantitative) should be evaluated (Figure 4). Structural parameters include TV morphology, IVC diameter, and RV and RA size. In some cases, 2D speckle-tracking echocardiography can detect the initial RV subclinical dysfunction. In advanced stages, RV dilatation is present, mainly due to chronic volume overload. Qualitative parameters consist of interventricular septal motion and Doppler ones such as regurgitant color flow and continuous wave jets and flow convergence zone’s characteristics (size and duration). A small and brief color flow jet is considered to be specific for mild regurgitation. However, grading of FTR severity based on this sole parameter is not recommended. The semi-quantitative parameters comprise regurgitant jet’s color flow area, PISA radius, vena contracta width, hepatic vein flow, and tricuspid inflow patterns. Quantitative parameters are PISA-derived EROA and regurgitant volume. Although the majority of Doppler methods used in grading left-sided valvular heart disease are applicable...
When evaluating FTR, it is important to remember that, in most cases, TR jet has lower pressure and velocity (strictly correlated to jet momentum) compared to MR. This has a direct impact on volumetric and jet analysis. In addition, the current criteria for FTR severity grading are seldom used in clinical practice due to paucity of validation studies and lack of prognostic data. Recently, newly validated prognostic cut-offs for grading FTR have been proposed by our group. By using patients’ outcome data as reference, we found that the threshold values to define severe TR were >6 mm, >0.30 cm², >30 mL, and >45% for vena contracta average, EROA, regurgitant volume and regurgitant fraction, respectively. Notably, these cut-off values are significantly smaller than those recommended by current guidelines.

Even though FTR severity grading remains a challenging task, there have been formulated several specific severity indices (severe valve lesions such as flap leaflet, large, holosystolic flow convergence zone, and systolic flow reversal in the hepatic veins).

THREE-DIMENSIONAL ECHOCARDIOGRAPHY

When quantifying the right-chambers’ sizes by 2D echocardiography (2DE), significant underestimation may occur due to foreshortening or geometrical assumptions. The 3D-derived methods allow a more accurate and reliable measure of both the RV and the RA, which is one of the key prerequisites in differentiating atrial FTR from ventricular FTR. 3DE allows the simultaneous visualization of all three valve leaflets to reliably exclude any structural abnormalities and the quantitative automated analysis of all components of the TV apparatus accounting for their complex three-dimensional shape.

An important benefit of 3DE is increased accuracy in sizing the TV annulus. Currently, the indication for TV annulus repair in the context of left-sided valvular disease surgery is based on a cut-off value of >40mm or >21mm/m² measured from the apical four-chamber view by 2DE, assuming that the annulus is symmetrical, flat, and circular. Due to the complex, three-dimensional configuration, with variable spatial orientation, of the tricuspid annulus, 3DE should be the first-line modality in imaging the patient with FTR. Another key parameter to evaluate is the tethering of TV leaflets. The coaptation of TV normally occurs at the leaflets’ body, at the annulus level, or just below it. With tethering of the valves, the coaptation takes place on the leaflets’ free edges with consequent FTR (Figure 5). The measurements of the tethering distance and tenting area by 3DE assume a symmetrical tethering pattern and that the longest distance to the coaptation point of the three leaflets occurs exactly in the 4-chamber view plane (i.e. displaying two out of three leaflets), which is unlikely in patients with FTR. Tenting volume measured by 3DE is a more precise parameter in grading FTR severity, as it does not depend on any plane posi-
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reports show that cardioversion in atrial FTR with documented maintenance of sinus rhythm promotes TV annulus and RA reverse remodeling and may significantly reduce the severity of FTR at follow-up 26,44,45.

However, current recommendations are largely based on expert opinion and large-scale studies on the prognostic benefits of rhythm vs rate-control strategy in atrial FTR patients are needed to substantiate specific guideline indications for this subset of patients.

CONCLUSIONS

Functional tricuspid regurgitation is a common finding in several cardiac conditions, either isolated or in association with left-heart valvular diseases. Emerging evidence suggests a novel pathophysiological model of atrial functional tricuspid regurgitation in patients with long-standing AF. Three-dimensional echocardiography has revolutionized the noninvasive imaging of the tricuspid valve apparatus, conferring new insights and better understanding of the pathophysiology of functional tricuspid regurgitation. Awareness about the atrial tricuspid functional regurgitation is key to identify

CLINICAL IMPLICATIONS AND UNMET NEEDS

The key message for cardiologists and echocardiographers is that atrial TR should nowadays be recognized as one of the potential complications of AF and one of the contributing factors for heart failure symptoms. Up to 25% of patients with non-valvular AF develop significant atrial FTR, with 33% of lone AF cases occurring in young patients 42,43. The awareness regarding atrial FTR and the known adverse prognostic implications of isolated severe FTR may intuitively justify a more aggressive rhythm control in patients with persistent AF that present an associated FTR. Preliminary
the appropriate management and treatment strategies for these patients.

Conflict of interest: none declared.

Financial support: Dr. D.R.F. was supported by an Erasmus+ traineeship grant.

References

1. Badano LP, Muraru D, Enríquez-Sarano M. Assessment of functional tricuspid regurgitation. Eur Heart J. 2013;34(25):1875-1884. doi:10.1093/eurheartj/ehs474
2. Helmut Baumgartner (ESC Chairperson) (Germany), Volkmar Falk1 (EACTS Chairperson) (Germany) JBF (The Netherlands), Michele De Boni1 (Italy) CH (Germany), Per Johan Holm (Sweden), Bernard Junglue (France), Patrizio Rizzoli (Belgium), Emmanuel Lansac1 (France), Daniel Rodriguez Mun-oz (Spain), Raphael Rosenhek (Austria), Johan Stognier1 (Sweden), Pilar Tornos Mas (Spain), Alec Vahanian (France), Thomas Wilt Jilz (Spain). 2017 ESC/ EACTS Guidelines for the management of valvular heart disease. Eur Heart J 38, 2739–2791. Published online 2017. doi:10.1093/eurheartj/ehx391
3. Muraru D, Addetia K, Guta AC, Roberto C, Genovesi D, Veronesi F, Basso C, Illiceto S, Badano LP, Lang RM. Right atrial volume is a major determinant of tricuspid annulus area in functional tricuspid regurgitation: a three-dimensional echocardiographic study. Eur Hear J - Cardiovasc Imaging. 2020:1-9. doi:10.1093/ehjci/jea286
4. Utsunomiya H, Harada Y, Mihara H, Berdejo J, Kobayashi S, Siegel Rj, Shiota T. Functional Tricuspid Regurgitation Caused by Chronic Atrial Fibrillation: A Real-Time 3-Dimensional Transesophageal Echocardiography Study. Circ Cardiovasc Imaging. 2017;10(1):1-11. doi:10.1161/CIRCIMAGING.116.004897
5. Muraru D, Guta AC, Ochoa-Jimenez RC, Bartos D, Aruta P, Mihaila S, Popescu BA, Illiceto S, Basso C, Badano LP. Functional Regurgitation of Atrioventricular Valves and Atrial Fibrillation: An Elusive Pathophysiological Link Deserving Further Attention. J Am Soc Echocardiogr. 2020;33(1):42-53. doi:10.1016/j.echo.2019.08.016
6. Utsunomiya H, Harada Y, Susawa H, Ueda Y, Izumi K, Ikataura K, Hidaka T, Shiota T, Nakano Y, Hikaya Y, Spitzer RJ, Steigen TK, Komar M, De Moura Branco LM. Popescu BA, Usansky V, Foscoli M, Jovicic M, Simkova I, Bunc M, de Prada JAV, Stagno M, Kaufmann BA, Mahdhaoui A, Bockzurt E, Nesukay E, Brecker SJ. 2017 ESC/EACTS Guidelines for the Management of Valvular Heart Disease. Eur Heart J Vol. 38; 2017. doi:10.1093/eurheartj/ehx391
7. Lancellotti Patrizio, Zamorano José Luis, Habib Gilbert BL. The EACVI Textbook of Echocardiography.; 2017. https://www.oupjapan.co.jp/en/node/16697
8. Muraru D, Parati G, Badano LP. The tale of functional tricuspid regurgitation: when atrial fibrillation is the villain. Eur Heart J Cardiovasc Imaging. 2020;21(10):1079-1081. doi:10.1093/ehjci/jea223
9. Lancellotti P. Tribouilloy C, Hagedornoff A, Popescu BA, Edvardsen T, Pierard LA, Badano L, Zamorano JL. Recommendations for the echocardiographic assessment of native valvular regurgitation: An executive summary from the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2013;14(7):611-644. doi:10.1093/ehjci/jet105
10. Basso C, Muraru D, Badano LP. Thieme. Anatomy and Pathology of Right-Sided Atrioventricular and Semilunar Valves. In: Rajamannan NM, ed. Cardiac Valvular Medicine. Springer London; 2013:21-221. doi:10.1007/978-1-4471-4132-7_19
11. Miglioranza MH, Mihaila S, Muraru D, Cucchinì U, Illiceto S, Badano LP. Variability of Tricuspid Annulus Diameter Measurement in Healthy Volunteers. JACC Cardiovascular Imaging. 2015;8(7):864-866. doi:10.1016/j.jcmg.2014.09.010
12. Spinner EM, Shannon P, Buice D, Jimenez JH, Veledar E, Del Nido PJ, Adams DH, Yogathanathan AP. In vitro characterization of the mechanisms responsible for functional tricuspid regurgitation. Circulation. 2011;124(8):920-929. doi:10.1161/CIRCULATIONAHA.110.03897
13. Messer S, Moseley E, Marinescu M, Freeman C, Goddard M, Nair S. Histologic analysis of the right atrioventricular junction in the adult human heart. J Heart Valve Dis. 2012;21(3):368-373.
14. Badano LP, Hahn R, Zanella A, Araiza Garaygordobil D, Ochoa-Jimenez RC, Muraru D. Morphological Assessment of the Tricuspid Apparatus and Grading Regurgitation Severity in Patients With Functional Tricuspid Regurgitation: Thinking Outside the Box. JACC Cardiovascular Imaging. 2019;12(4):652-664. doi:10.1016/j.jcmg.2019.02.061
15. Deferm S, Bertrand PB, Verbrugge FH, Verhaert D, Rega F, Thomas JD, Vandervoort PM. Atrial Functional Mitral Regurgitation: JACC Review Topic of the Week. J Am Coll Cardiol. 2019;73(19):2465-2476. doi:10.1016/j.jacc.2019.02.061
16. Hoit BD. Atrial functional mitral regurgitation. Curr Opin Cardiol. 2020;35(5):474-481. doi:10.1097/HCO.0000000000000761
17. Kagyama N, Mondillo S, Yoshida K, Mandoli GE, Camelli M. Subtypes of Atrial Functional Mitral Regurgitation: Imaging Insights Into Their Mechanisms and Therapeutic Implications. JACC Cardiovascular Imaging. 2020;13(3):820-835. doi:10.1016/j.jcmg.2019.01.040

Romanian Journal of Cardiology
Vol. 31, No. 1, 2021
Echocardiography. 2012;29(2):140-146. doi:https://doi.org/10.1111/j.1540-8175.2011.01565.x

26. Ortiz-Leon AX, Posada-Martinez EL, Trejo-Paredes MC, Ivey-Miranda JB, Pereira J, Crandall I, DaSilva P, Bouman E, Brooks A, Gerardi C, Ugono I, Chen W, Houle H, Akar JG, Lin BA, McNamara RL, Lombo-Lievano B, Arias-Godinez JA, Sugeng L. Understanding tricuspid valve remodelling in atrial fibrillation using three-dimensional echocardiography. Eur Heart J Cardiovasc Imaging. 2020;21(7):747-755. doi:10.1093/ehjci/jea058

27. Topilsky Y, Khanna A, Le Toumeau T, Park S, Michelenia H, Suri R, Mahoney DW, Enriquez-Sarano M. Clinical context and mechanism of functional tricuspid regurgitation in patients with and without pulmonary hypertension. Circ Cardiovasc Imaging. 2012;5(3):314-323. doi:10.1161/CIRCIMAGING.111.967919

28. Nemoto N, Lesser JR, Pedersen WR, Soraja P, Spinner E, Garb-erich RF, Vock DM, Schwartz RS. Pathogenic structural heart changes in early tricuspid regurgitation. J Thorac Cardiovasc Surg. 2015;150(2):323-330. doi:10.1016/j.jtcs.2015.05.009

29. Yamazaki N, Kondo F, Kubo T, Okawa M, Matsumura Y, Kitaoka H, Yabe T, Furuno T, Doi Y. Severe tricuspid regurgitation in the aged: atrial remodeling associated with long-standing atrial fibrillation. J Cardio. 2006;48(6):315-323.

30. Santoro C, Marco Del Castillo A, González-Gómez A, Monteguido JM, Hinojor R, Lorente A, Abellás M, Viteitez JM, García Martín A, Casas Rojo E, Ruiz S, Barrios V, Luis Moya J, Jimenez-Nacher JJ, Zamorano Gomez JL, Fernández-Gollin C. Mid-term outcome of severe tricuspid regurgitation: Are there any differences according to mechanism and severity? Eur Heart J. Cardiovasc Imaging. 2019;20(9):1035-1042. doi:10.1093/ehjci/jez024

31. Kebed KY, Addetta K, Henry M, Yamat M, Weinert L, Besser SA, Mor-Avi V, Lang RM. Defining Severe Tricuspid Regurgitation Definition by Echocardiography with a New Outcomes-Based “Massive” Grade. J Am Soc Echocardiogr. 2020;33(9):1087-1094. doi:10.1016/j.echo.2020.05.007

32. Prihadi EA, Delgado V, Hahn RT, Leipsic J, Min JK, Bax JJ. Imaging Needs in Novel Transcatheter Tricuspid Valve Interventions. JACC Cardiovasc Imaging. 2018;11(5):736-754. doi:10.1016/j.jcmg.2017.10.029

33. Khalique OK, Cavalcante JL, Shah D, Gupta AC, Zhan Y, Piazza N, Muraru D. Multimodality Imaging of the Tricuspid Valve and Right Heart Anatomy. JACC Cardiovasc Imaging. 2019;12(3):516-531. doi:10.1016/j.jcmg.2019.01.006

34. Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, Hahn RT, Han Y, Hung J, Lang RM, Little SH, Shah DJ, Sherman S, Thavendiranathan P, Thomas JD, Weissman NJ. Recommendations for Noninvasive Evaluation of Native Valvular Regurgitation: A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Magnetic Resonance. J Am Soc Echocardiogr. 2017;30(4):303-371. doi:10.1016/j.echo.2017.01.007

35. Hahn RT, Thomas JD, Khaliique OK, Cavalcante JL, Praz F, Zoghbi WA. Imaging Assessment of Tricuspid Regurgitation Severity. JACC Cardiovasc Imaging. 2019;12(3):469-490. doi:10.1016/j.jcmg.2018.07.033

36. Hahn RT. State-of-the-art review of echocardiographic imaging in the evaluation and treatment of functional tricuspid regurgitation. Circ Cardiovasc Imaging. 2016;9(12):1-15. doi:10.1161/CIRCIMAGING.16.11.005332

37. Muraru D, Previtero M, Ochoa-Jimenez RC, Guta AC, Figliozzi S, Gregori D, Bottigliengo D, Parati G, Badano LP. Prognostic validation of partition values for quantitative parameters to grade functional tricuspid regurgitation severity by conventional echocardiography. Eur Heart J Cardiovasc Imaging. Published online November 2020. doi:10.1093/ehjci/jea282

38. Muraru D, Spadotto V, Cucchietto A, Romeo G, Aruta P, Ermacora D, Jenei C, Cucchini U, Liceto S, Badano LP. New speckle-tracking algorithm for right ventricular volume analysis from three-dimensional echocardiographic data sets: validation with cardiac magnetic resonance and comparison with the previous analysis tool. Eur Heart J Cardiovasc Imaging. 2016;17(11):1279-1289. doi:10.1093/ehjci/jev309

39. Addetta K, Muraru D, Badano LP, Lang RM. New Directions in Right Ventricular Assessment Using 3-Dimensional Echocardiography. JAMA Cardiol. 2019;4(9):936-944. doi:10.1001/jamacardiol.2019.2424

40. Moreno J, De Isla LP, Campos N, Guinea J, Domínguez-Perez L, Saltijeral A, Lennie V, Quezada M, De Agustín A, Marcos-Alberca P, Mahia P, García-Fernández MA, Macaya C. Right atrial indexed volume in healthy adult population: Reference values for two-dimensional and three-dimensional echocardiographic measurements. Echocardiography. 2013;30(6):667-671. doi:10.1111/echo.12121

41. Song J-K, Muraru D, Guta A-C, Badano LP. Functional Tricuspid Regurgitation. In: Badano LP, Lang RM, Muraru D, eds. Textbook of Three-Dimensional Echocardiography. Springer International Publishing; 2019:285-297. doi:10.1007/978-3-030-14032-8_21

42. Abe Y, Akamatsu K, Ito K, Matsumura Y, Shimeno K, Naruko T, Takahashi Y, Shibata T, Yoshimaya M. Prevalence and prognostic significance of functional mitral and tricuspid regurgitation despite preserved left ventricular ejection fraction in atrial fibrillation patients. Circ J. 2018;82(5):1451-1458. doi:10.1253/circj.CJ-17-1334

43. Lévy S, Maarek M, Cournel P, Guize L, Lekiefre J, Medvedovsky JL, Sebaoun A. Characterization of different subsets of atrial fibrillation in general practice in France: The ALFA study. Circulation. 1999;99(23):3028-3035. doi:10.1161/01.CIR.99.23.3028

44. Muraru D, Caravita S, Guta AC, Mihalcea D, Branzi G, Parati G, Badano LP. Functional Tricuspid Regurgitation and Atrial Fibrillation: Which Comes First, the Chicken or the Egg? Case. Published online 2020. doi:10.1093/ehjci/jea058

45. Fender EA, Zack CJ, Nishimura RA. Isolated tricuspid regurgitation: Outcomes and therapeutic interventions. Heart. 2018;104(10):798-806. doi:10.1136/heartjnl-2017-311586