Original article

Three-dimensional Tricuspid Area. A New Criterion to Improve Patient Selection for Annuloplasty in Tricuspid Regurgitation



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Keywords: Three-dimensional echocardiography Tricuspid annulus Tricuspid valve Valve surgery ABSTRACT

Introduction and objectives: Late functional tricuspid regurgitation after rheumatic left-sided valve surgery is an important predictor of poor prognosis. This study investigated the usefulness and accuracy of 3-dimensional transthoracic echocardiography tricuspid area compared with conventional 2-dimensional diameter (2DD) for assessing significant tricuspid annulus dilatation, providing cutoff values that could be used in clinical practice to improve patient selection for surgery.

Methods: We prospectively included 109 patients with rheumatic heart disease in the absence of previous valve replacement. Tricuspid regurgitation was divided into 3 groups: mild, moderate, and severe. Optimal 3-dimensional area (3DA) and 2DD cutoff points for identification of significant tricuspid annulus dilatation were obtained and compared with current guideline thresholds. Predictive factors for 3DA dilatation were also assessed.

Results: Optimal cutoff points for both absolute and adjusted to body surface area (BSA) tricuspid annulus dilatation were identified (3DA: 10.4 cm^2 , $6.5 \text{ cm}^2/\text{m}^2$; 2DD: 35 mm, 21 mm/m^2); 3DA/BSA had the best diagnostic performance (AUC = 0.83). Three-dimensional transthoracic echocardiography tricuspid area helped to reclassify surgical indication in 14% of patients with mild tricuspid regurgitation (95%CI, 1%-15%; *P* = .03) and 37% with moderate tricuspid regurgitation (95%CI, 22%-37%; *P* < .0001), whereas 3DA/BSA changed surgery criteria in cases of mild tricuspid regurgitation (17%; 95%CI, 3%-17%; *P* = .01) compared with 2DD/BSA. On multivariable analysis, right and left atrial volumes and basal right ventricle diameter were independently correlated with 3DA.

Conclusions: The current 40 mm threshold underestimates tricuspid annulus dilatation. Although 21 mm/m^2 seems to be a reasonable criterion, the combination with 3DA assessment improves patient selection for surgery.

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Medida tridimensional del área del anillo tricúspide. Un nuevo criterio en la selección de candidatos a anuloplastia

RESUMEN

Introducción y objetivos: El desarrollo tardío de insuficiencia tricúspide funcional tras cirugía valvular izquierda de origen reumático es un importante predictor de mal pronóstico. Este estudio investiga la utilidad y precisión diagnóstica del área tricúspide evaluada por ecocardiografía transtorácica tridimensional en comparación con el diámetro bidimensional (D2D) convencional para evaluar la dilatación significativa del anillo tricúspide, proporcionando puntos de corte que podrían utilizarse en la práctica clínica para mejorar la selección de pacientes para cirugía.

Métodos: Se incluyeron prospectivamente 109 pacientes con valvulopatía reumática en ausencia de reemplazo valvular previo. La insuficiencia tricúspide se dividió en tres grupos: leve, moderado y grave. Se obtuvieron los puntos de corte óptimos del área tridimensional (A3D) y del D2D para la identificación de la dilatación significativa del anillo tricúspide y se compararon con los umbrales de las guías actuales. También se evaluaron los factores predictivos de la dilatación del A3D.

Resultados: Se identificaron los puntos de corte óptimos, absolutos y ajustados por el área de superficie corporal (ASC), de ambos parámetros (A3D: 10,4 cm², 6,5 cm²/m², D2D: 35 mm, 21 mm/m²) siendo el parámetro A3D/ASC el que obtuvo el mejor rendimiento diagnóstico (ABC = 0,83). El área tricúspide por ecocardiografía transtorácica tridimensional ayudó a reclasificar la indicación quirúrgica en el 14% de

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Palabras clave:

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pacientes con insuficiencia tricúspide leve (IC95%, 1-15%; p = 0,03) y en el 37% con insuficiencia tricúspide moderada (IC95%, 22-37%; p < 0,0001), mientras que el A3D/ASC cambió los criterios de cirugía en los casos de insuficiencia tricúspide leve (17%, IC95%, 3-17%; p = 0,01) en comparación con el D2D/ASC. En el análisis multivariable, los volúmenes de la aurícula derecha e izquierda y el diámetro del ventrículo derecho basal se correlacionaron independientemente con el A3D.

Conclusiones: El umbral del D2D actual propuesto de 40 mm infraestima la dilatación del anillo tricúspide. Aunque 21 mm/m² podría ser un criterio de selección razonable, la combinación con la evaluación del A3D mejora la selección de pacientes candidatos para cirugía.

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Abbreviations

2DD: 2-dimensional diameter 3DA: 3-dimensional area TA: tricuspid annulus TR: tricuspid regurgitation TTE: transthoracic echocardiography TV: tricuspid valve

INTRODUCTION

Functional tricuspid regurgitation (TR) associated with left valvular disease, mainly related to rheumatic etiology, is quite common.¹ More than one-third of patients with mitral stenosis have at least moderate TR, and severe TR has been reported in 23% to 37% of patients after mitral valve replacement.²⁻⁵ The indication for surgery in TR at the same time as left-sided valvulopathy has moved toward a progressively more interventional attitude in the last few years because the presence of significant TR is closely related to late mortality, cardiac heart failure, and mortality after mitral valve surgery.^{4,6} Intervention in severe secondary TR is well established as a class I recommendation but is less supported by evidence when functional TR is mild/ moderate. In these cases, the presence of significant annulus dilatation (>40 mm or > 21 mm/m²) should be taken into account despite the absence of important TR at baseline (class IIa indication, level of evidence C for European Society of Cardiology and B for the American College of Cardiology guidelines).^{7,8} These recommendations, together with the frequent difficulty of correct TR evaluation, operator- and interpreter-dependency, and high variability in load conditions, have given rise to assessment of dilatation rather than regurgitation.9-13 Significant tricuspid annulus (TA) dilatation seems to be the underlying mechanism of severe TR but it could also be present in nonsignificant and moderate TR. It is well known that more than one-third of patients with previous nonsevere TR will develop it after surgery; therefore, the identification of significant annulus dilatation in this subgroup of patients is crucial. In patients with functional TR, the TA becomes more circular, planar and dilated in the anteroposterior diameter.¹⁴ Thus, TA dilatation might be underestimated with single linear measurements by 2-dimensional (2D) transthoracic echocardiographic (TTE) imaging measured from the apical 4-chamber view. Three-dimensional (3D) TTE offers accurate and real-time assessment of the shape and size of the TA.^{15–18} Assessment of 3D-TTE tricuspid area (3DA) by 3D-TTE could provide a more objective measurement of TA size; however, to date, no value has been described for this purpose. Thus, the aims of the present study were: a) to explore the influence of clinical and echocardiographic parameters on the severity of

functional TR; b) to assess cutoff points of TA dilatation associated with the presence of severe TR, identifying 3DA values that can be used in clinical practice; c) to determine the proportion of nonsevere TR with significant TA dilatation; d) to evaluate whether current guideline criteria properly classify patients for surgery in comparison with 3DA; and finally e) to identify the echocardiographic determinants of TA dilatation with this technology.

METHODS

Study Population

An initial sample of 115 consecutive patients referred to our echocardiography laboratory between September 2014 and December 2015 were evaluated with the following inclusion criteria: diagnosis of rheumatic heart valve disease without a history of previous mitral valve replacement, tricuspid valve (TV) repair, or organic TR. During recruitment, 6 patients were excluded due to inadequate echocardiographic images, resulting in a final study population of 109 patients. All patients underwent echocardiography because of clinical indications and gave written informed consent before undergoing echocardiography in accordance with a protocol approved by the institutional review board.

Two-dimensional Echocardiography

Two-dimensional TTE was performed using a commercially available ultrasound system (iE33; Philips Medical Systems, Andover, Massachusetts, United States) with a fully sampled matrix-array X5 transducer. Two-dimensional diameter (2DD) was measured in the 4-chamber view at the time of the maximum TV diastolic opening between the 2 hinge points of the valvular leaflets. Tricuspid regurgitation degree was graded in 3 groups: mild, moderate, and severe, evaluated by a combination of different echocardiographic parameters according to the recommendations for the echocardiographic assessment of native valvular regurgitation of the American Society of Echocardiography¹⁹ including vena contracta width and effective regurgitation orifice area by the proximal isovelocity surface area method. The 3 groups were reassigned in 2 categories: severe and nonsevere TR. Right ventricular diameters (RVD) were measured, adjusting the apical 4-chamber view to acquire the "right ventricular-focused view". Basal RVD (B-RVD), mid RVD and longitudinal RVD were evaluated.²⁰ Right ventricular systolic pressure (RVSP) was estimated from the TR velocity with the modified Bernoulli equation. Right ventricular (RV) systolic function was assessed by tricuspid annular plane systolic excursion and tissue Doppler-derived tricuspid lateral annular systolic velocity (S').

Three-dimensional Echocardiography

Using the fully sampled matrix-array X5-1 transducer, 3D volumes were obtained with zoomed acquisitions focused on the TV using electrocardiographic gating during a single breath and were digitally stored. In patients with stable sinus rhythm, 4 single-beat volumes were stitched together to create a single volumetric data set. It provides large data sets with high temporal and spatial resolution. The average 3D volume frame rate was 33 \pm 9 Hz. Full volume 3D images of the left atrium (LA) and right atrium (RA) were also obtained. For the calculation of left and right atrial volumes, a semiautomated tracing of the endocardial border was performed by marking 3 atrial points. Modifications were made to correct automatic tracings, if necessary. Measurement of 3DA was performed offline using commercial software (QLAB version 9.1; Philips Medical Systems). The 3D volume was sliced and analyzed using multiplanar reconstruction. The orthogonal and cross-sectional planes were adjusted to depict a cross section of the TA as viewed from the RV perspective. After careful orientation, cropping the plane of the TA at its junction with the valvular leaflets, 3DA was calculated by manual tracing at the time of maximum diastolic leaflet opening (Figure 1). Measurements were averaged in 5 cycles in patients with atrial fibrillation.

Reproducibility

To assess the effect of observer variability and the reproducibility of 3DA, a second independent observer analyzed 10 randomly selected cases. On the same 3D acquisitions, each observer obtained 3DA, as described above. Intraobserver variability was assessed by comparing the measurements given by the same observer after an interval of more than a week between the 2 measurements. Both readers were blinded to previous measurements.

Statistical Analysis

Continuous variables are presented as mean \pm standard deviation and were compared using the Student *t* test. A nonparametric test was used when the data were not normally distributed. Categorical variables are reported as frequencies and were compared by the use of the chisquare and Fisher exact tests. Paired nominal data were compared with the McNemar test. Agreement between techniques was evaluated by the Cohen kappa coefficient. Optimal cutoff value for severe TR detection using both 3DA and 2DD, defined as the maximized value for the sum of sensitivity and specificity, were identified by receiver operating characteristic curves analysis. Interrater reliability was analyzed. Intraobserver and interobserver agreement for 3DA were evaluated by Bland-Altman analysis and intraclass correlation coefficients. Echocardiographic variables (B-RVD, mid RVD, longitudinal RVD, LA volume, RA volume, RVSP, and tricuspid annular plane systolic excursion) were entered in a stepwise multivariable analysis to determine predictors of 3DA dilatation. Statistical significance was defined with P < .05. Statistics were performed using SPSSS version 21 (IBM Inc. Chicago, Illinois, United States) and MedCalc version 10.0.1 (MedCalc Software, Mariakerke, Belgium).

RESULTS

Influence of Clinical and Traditional Echocardiographic Parameters on Functional Tricuspid Regurgitation Development

Demographic and 2D echocardiographic features are shown in Table 1. Severe functional TR was present in 25 patients (23%). Mean age was 68 ± 11 years, 87 patients (80%) were women and 76 (70%) were in atrial fibrillation. There was no difference in age, sex, body surface area, or heart rate between groups. A total of 43 patients (40%) had previous percutaneous mitral valvuloplasty or commissurotomy. The most common left valvular heart disease was mitral stenosis (53%),



Figure 1. Measurement of tricuspid annulus area using 3-dimensional transthoracic echocardiography. Sliced 3-dimensional volume. After careful orientation of the annular plane position using 2 orthogonal planes (A and B) the projection of the tricuspid annulus is obtained to measure tricuspid annulus area (C). Right lower panel (D) shows the multislice imaging of the tricuspid annulus.

Table 1

Clinical and 2-dimensional Echocardiographic Features of the Enrolled Participants

	Nonsevere TR (n=84)	Severe TR (n=25)	Р
Age, y	67 ± 10	72 ± 12	NS
Sex, % females	79	84	NS
BSA, m ²	1.7 ± 0.2	1.7 ± 0.2	NS
Heart rate, beats/min	75 ± 16	78 ± 17	NS
Atrial fibrillation, %	62	96	<.001
High blood pressure, %	43	52	NS
Diabetes, %	18	32	NS
Dyslipidemia, %	41	36	NS
Mitral stenosis, %	49	68	NS
Mitral regurgitation, %	44	36	NS
Aortic stenosis, %	16	8	NS
Aortic regurgitation, %	20	16	NS
Diuretics, %	52	80	0.02
Beta-blockers, %	56	52	NS
Echocardiographic parameters			
EROA, cm ²	$\textbf{0.23}\pm\textbf{0.08}$	$\textbf{0.62}\pm\textbf{0.43}$	<.001
VC, mm	$\textbf{0.43} \pm \textbf{0.12}$	$\textbf{0.95}\pm\textbf{0.30}$	<.001
LA diameter, mm	53.4 ± 10.5	$\textbf{62.3} \pm \textbf{7.9}$	<.001
Biplane LA volume/BSA, mL	56.7 ± 36.2	80.5 ± 27.3	<.001
Biplane RA volume/BSA, mL	$\textbf{18.3} \pm \textbf{9.9}$	27.6 ± 8.4	.03
B-RVD, mm	$\textbf{28.4} \pm \textbf{5.2}$	33.7 ± 5.4	<.001
M-RVD, mm	24.5 ± 5.1	31.0 ± 6.8	<.001
L-RVD, mm	49.0 ± 7.3	55.9 ± 9.2	<.001
RVSP, mmHg	41.8 ± 16.5	54.5 ± 22.9	.003
Pulmonary acceleration time (ms)	107.0 ± 32.8	90.9 ± 33.6	.04
TAPSE, mm	20.7 ± 5.0	18.3 ± 4.1	NS
RV DTI S wave, cm/sec	10.8 ± 2.6	10.1 ± 2.4	NS

BSA, body surface area; B-RVD, basal RV diameter; DTI, Doppler tissue imaging; EROA, effective regurgitant orifice area; LA, left atrium; L-RVD, longitudinal RV diameter; M-RVD, mid RV diameter; RA, right atrium; RV, right ventricular; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; VC, vena contracta.

followed by mitral (42%) and aortic regurgitation (19%), although there was no significant difference with respect to the type of predominant left-sided valvulopathy. The use of diuretics was higher in the group of severe TR. As expected, patients with severe TR had a significantly higher left atrial diameter, 3D left and right atrial volumes, RVSP and RV dimensions. However, no statistically significant differences were found regarding parameters of RV systolic function.

Table 2

Tricuspid Annulus Dimensions by 2D and 3D-TTE

	Nonsevere TR (n=84)	Severe TR (n=25)	Р
2D-TTE			
TA diameter, mm	$\textbf{32.8}\pm\textbf{0.5}$	$\textbf{38.2}\pm\textbf{0.9}$	<.001
TA diameter/BSA, mm/m ²	19.7 ± 0.3	23.0 ± 0.6	<.001
3D-TTE			
3D area, cm ²	9.3 ± 0.2	12.64 ± 0.5	<.001
3D area/BSA, cm ² /m ²	5.6 ± 0.2	$\textbf{7.6} \pm \textbf{0.3}$	<.001

2D, 2-dimensional; 3D, 3-dimensional; BSA, body surface area; TA, tricuspid annulus; TR, tricuspid regurgitation; TTE, transthoracic echocardiography.

Table 3

Sensitivity and Specificity of Echocardiographic Dimensions for Significant Tricuspid Annulus Dilatation Evaluation

	Cutoff point	Sensitivity, %	Specificity, %	AUC
2D-TTE				
TA diameter, mm	35	80	70	0.80
TA diameter/BSA, mm/m ²	21	80	63	0.78
3D-TTE				
3DA, cm ²	10.4	80	73	0.84
3DA/BSA, cm ² /m ²	6.5	80	76	0.83

2D, 2-dimensional; 3D, 3-dimensional; 3DA, 3-dimensional area; AUC, area under receiver operating characteristic (ROC) curve; BSA, body surface area; TA, tricuspid annulus; TR, tricuspid regurgitation; TTE, transthoracic echocardiography.

Assessment of Tricuspid Annulus Dilatation

Tricuspid annulus size obtained from 2DD and 3DA following the analysis of 3D-TTE images are summarized in Table 2. Twodimensional diameter and 3DA were significantly larger in patients with severe TR in both absolute values and those adjusted to body surface area. To evaluate significant TA dilatation (defined as that associated with the presence of severe TR), optimal cutoff points were identified by receiver operating characteristic curves analysis (Table 3). We found that a TA diameter of 35 mm and 21 mm/m² was the best value to differentiate severe from nonsevere TR groups. For 3DA, a cutoff point of 10.4 cm² and 6.5 cm²/m² proved to be just as sensitive as 2DD (80%) but with greater specificity to identify significant TA dilatation associated with severe TR (3DA/ BSA: 76% vs 2DD/BSA: 63%).

Significant Tricuspid Annulus Dilatation in Patients With Nonsevere Tricuspid Regurgitation

For this purpose, the degree of TR was classified into 3 groups: mild (n = 41), moderate (n = 43) and severe (n = 25). Using a cutoff value of 10.4 cm², 39% patients with moderate and 15% with mild TR had significant TA dilatation. Also, a nonnegligible percentage of patients, 41% with moderate and 5% with mild TR, had a 3DA \geq 6.5 cm²/m², indicative of evident TA enlargement.

Comparison of 2-dimensional Diameter and 3-dimensional Area Criteria to Select Patients for Tricuspid Valve Surgery

Figure 2 and Figure 3 show potential selection of candidates for surgery based on recommendations of the current guidelines in comparison with the use of 3DA area as a reference parameter for TA dilatation. Figure 2 shows patients who would potentially be referred to TV surgery according to guideline criteria based on absolute 2DD (> 40 mm) compared with those who would be selected by using our suggested reference value of 3DA for annular dilatation (\geq 10.4 cm²). Application of the current cutoff value for annuloplasty showed that 9% of patients (95% confidence interval [95%CI], 5%-16%) would have fulfilled absolute 2DD criteria in comparison with 39% (95%CI, 30%-49%) with our absolute 3DA criteria. The estimated difference in percentage was 19.75% (95%Cl, 11%-28%; P < .001). This reclassification was evident in all TR degrees. The agreement between the 2 parameters for annuloplasty indication was poor (kappa index: 0.268). Following the classic criteria, no patient with mild TR, only 2.3% with moderate TR, and 36% patients with severe TR would be candidates for



Figure 2. Comparison of absolute 2DD and 3DA for selecting candidates for TV surgery according to the guideline threshold of \geq 40 mm vs \geq 10.4 cm². All patients are represented according to the severity of TR in 3 groups (severe: black dots; moderate: white squares; mild: stars). Dashed lines represent the absolute cutoff points proposed by the guidelines (Y axis: 2DD) and the suggested in our work (X axis: 3DA). Following 2-dimensional criteria, most of the patients would be excluded from TV surgery. 2DD, 2-dimensional diameter; 3DA, 3-dimensional area; TR, tricuspid regurgitation; TV, tricuspid valve.

surgery. The 3DA would reassign a significant proportion of mild, moderate and severe TR for surgical indication: 14% patients with mild TR (95%CI, 1%-27.5%; P < .001), 37% of moderate (95%CI, 22%-37%; P < .001) and 44% severe TR (95%CI, 19-44%; P < .001). Measurements adjusted by BSA are represented in Figure 3. When the $\ge 21 \text{ mm/m}^2$ threshold proposed by the guidelines was considered, differences with respect to the use of 3DA were less conspicuous. Surgical criteria agreement was acceptable (Kappa index: 0.55). The percentage of patients referred to surgery according to the 3DA/BSA changed in only 9% of patients (95%CI, -0.5%-16%; P = .064). This percentage was similar in patients with moderate TR: 9% (95%CI, -8% vs 22%; p = .380) or severe TR: 4% (95%CI, -14%-18%; P = .999). However, significant



Figure 3. Comparison of 2DD and 3DA (adjusted by BSA) for selecting candidates for TV surgery according to the guideline threshold of \geq 21 mm/m² vs \geq 6.5 cm²/m². All patients are represented according the severity of TR in 3 groups (severe: black dots; moderate: white squares; mild: stars). Dashed lines represent the absolute cutoff points proposed by the guidelines (Y axis: 2DD/BSA) and those suggested in our work (X axis: 3DA/BSA). Reclassification is evidenced in cases of mild TR. 2DD, 2-dimensional diameter; 3DA, 3-dimensional area; BSA, body surface area; TR, tricuspid regurgitation; TV, tricuspid valve.

Table 4

Univariable Analysis Results: Determinants of 3DA Dilatation ($\geq 6.5 \, cm^2/m^2$)

	Non-3DA dilatation (n=69)	3DA dilatation (n=40)	Р
Biplane LA volume/BSA, mL	53.7 ± 37.3	$\textbf{76.6} \pm \textbf{27.5}$	<.001
Biplane RA volume/BSA, mL	26.3 ± 20.6	50.0 ± 25	<.0001
B-RVD, mm	$\textbf{28.0} \pm \textbf{5.3}$	$\textbf{32.5} \pm \textbf{5.3}$	<.0001
M-RVD, mm	24.6 ± 5.1	$\textbf{28.4} \pm \textbf{7.0}$.001
L-RVD, mm	50.0 ± 7.5	51.4 ± 9.5	.41
RVSP, mmHg	40.2 ± 13.5	52.7 ± 23.8	.001
Pulmonary acceleration time, ms	109.9 ± 35.0	91.1 ± 26.5	.006
TAPSE, mm	21.0 ± 4.6	18.7 ± 5.1	.022
RV DTI S wave, cm/sec	11.0 ± 2.8	9.9 ± 2.1	.031

3DA: 3-dimensional area; BSA, body surface area; B-RVD, basal RV diameter; DTI, Doppler tissue imaging; LA, left atrium; L-RVD, longitudinal RV diameter; M-RVD, mid RV diameter; RA, right atrium; RV, right ventricular; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion.

reclassification was evidenced in patients with mild TR: 17% (95%CI, 3-17%; P = .01). Better specificity of 3DA would exclude from surgery 95% of patients with mild TR in contrast with 78% proposed by 2DD. This might avoid unnecessary interventions in these patients.

Determinants of 3-dimensional Area Dilatation

Variables associated with tricuspid 3DA dilatation (\geq 6.5 cm²/m²) in the univariate analysis are presented in Table 4. Stepwise multivariable analysis demonstrated that B-RVD, and left and right atrial volumes were the only echocardiographic independent determinants of TV annular dilatation evaluated with 3D-TTE (Table 5). The B-RVD had statistically the greatest association, with a continuous and direct relationship between B-RVD and 3DA (*r*: 0.470; *P* < .001).

Variability of Tricuspid Annulus 3-dimensional Area Measurements by Transthoracic Echocardiography

Mean intraobserver variability for 3DA measurement was 0.4 cm^2 (95%CI, -1.29 to 0.57), whereas mean interobserver variability was 0.7 cm^2 (95%CI, -1.88 to 0.52). Intraclass correlation coefficients for intraobserver and interobserver variability were 0.93 (95%CI, 0.84 to 0.99) and 0.87 (95%CI, 0.58 to 0.96), respectively.

Table 5

Multivariable Analysis: Determinants of 3DA dilatation

Coefficient	β	SE	t value	Р
	2.243	0.766	2.928	.04
B-RVD, mm	0.083	0.026	3.153	.02
RA volume, mm	0.019	0.007	2.662	.009
LA volume, mm	0.011	0.005	0.230	.021

3DA, 3-dimensional area; B-RVD, basal right ventricular diameter; LA, left atrium; RA, right atrium; SE, standard error. n = 109.

DISCUSSION

Functional TR is an important lesion that leads to worse early and late outcomes after cardiac surgery.²¹⁻²⁴ Current society guidelines recommend increased recognition and surgical correction of TR at the time of the concomitant surgery; nevertheless, the presence of secondary tricuspid pathology is often not appreciated, especially if severe TR is not present. Considerable tricuspid dilatation may not always result in pronounced TR and while a general agreement exists for TV repair in cases of severe regurgitation, current guidelines provide more vague indications for patients with less severe TR.^{7,8} As tricuspid annular dilatation seems to be the underlying mechanism regarding functional TR, it may be a more reliable indicator of TV pathology than TR. Significant dilatation is defined by a diastolic diameter \geq 40 mm or \geq 21 mm/m².^{20,25} Of note, it has been demonstrated that the annular diameter, measured from the apical 4-chamber view, underestimates major and minor annular dimensions. We propose a new method for assessing tricuspid annular dimension, measuring the maximal diastolic area by 3D-TTE, and its application in the more relevant clinical scenario of functional TR, the rheumatic valve disease. The main results of the present study can be summarized as follows: a) 3DA measurement by TTE is reliable and reproducible; b) severe TR is related to a greater degree of TA expansion, but this enlargement may be present in minor grades of regurgitation but it is poorly identified with diameter measurement: c) 3DA allows a better identification of TA dilatation than 2DD evaluation: d) we defined pathological values of TA area that could be used in clinical practice to consider tricuspid annuloplasty in left-sided rheumatic heart disease: and e) the growth of both atria and the right ventricle are the major determinants of TA area.

Although guidelines and recent data support a proactive approach to surgical repair of TR at the time of mitral valve surgery, TV repair currently appears underused. This attitude comes from an erroneous and historic mistaken selection of patients, more based on the degree of regurgitation than on the evaluation of TA dimension. Since Dreyfus et al.¹⁰ notoriously remarked that there is no correlation between TR and tricuspid dilatation (88% of patients in their series with tricuspid dilatation had no or mild TR at preoperative echocardiographic assessment) and the importance of intraoperative TA diameter (>70 mm) as a criterion for TV repair, the evaluation of the annulus size has been of particular relevance. Because the decision to operate on the TV must be made when surgery is being planned, before patients enter the operating room, it has been proposed to treat, independently of the grade of TR, patients with TA dilatation on 2D echocardiography. However, thresholds for TA dilatation have been obtained from relatively small and heterogeneous patient populations. As can be inferred from our work, based on a larger and homogeneous population, and in agreement with previous literature, 9,26 a diameter $\geq 21 \text{ mm/m}^2$ seems to correspond to a significant degree of expansion, with a sensitivity of 80%, and a specificity of 63%. Nevertheless, it is important to note that the absolute diameter (regardless of BSA) deviates from the established cutoff points, reinforcing the idea suggested in previous works, in which it is stressed due to the need to better define the 40-mm threshold and it is strongly recommended that it should be lower with increasing degrees of TR and in rheumatic patients.⁵ In the present study, we found that a value \geq 35 mm fits more accurately with severe degrees of TR compared with the cutoff of \geq 40 mm, a very specific value but with a very poor sensitivity (sensitivity of 80% and 70% specificity vs 24% and 99%, respectively).

Therefore, 2 key findings of our study are the necessity to decrease the threshold of TA dilatation to \geq 35 mm, and the importance of adjusting to BSA. However, we have defined another crucial measurement in the management of these patients: the quantification of the diastolic area by 3D-TTE, which improves the diagnostic accuracy of significant TA dilatation, with greater specificity than 2DD measurement.

In addition, a $3DA > 10.4 \text{ cm}^2$ better identified significant TA dilatation in all TR degrees compared with the 40 mm value proposed by the guidelines and, more importantly, allowed reclassification of 14% of patients with mild TR, and 37% with moderate TR. Given that patients with severe TR are candidates for surgery regardless of the size of TA, this subgroup of patients with nonsevere degrees are those who would benefit the most from 3D measurements, especially those with diameters less than 40 mm. It is well known that in patients with less than severe TR, regurgitation might progress after surgery if the TV is untreated. The percentage of nonsevere TR that we could reclassify using 3DA is equivalent to the approximately one-third described by the literature that evolves into late severe TR after surgery follow-up.^{26,27} Although, according to our results, it seems clear that annular dilatation may be underestimated with single linear measurements, on the other hand, clinicians could wonder if this new measurement may lead to unnecessary interventions in mild degrees of TR. Conversely, this not only did not occur with 3DA estimation, but the better specificity of 3DA/BSA allowed us to reclassify surgical criteria in 17% of mild TR cases (95%CI, 3%-17%; P = .01) in comparison with the proposed > 21 mm/m² value. This fact might avoid unnecessary surgery in this subgroup of patients. It is important to highlight that the cutoff points obtained in this study are very similar to those recently described by Addetia et al.,²⁸ reinforcing our results. In their recent article, the authors used transthoracic 3D-TTE to characterize TA geometry and dynamics in healthy volunteers, defining the normal tricuspid 3DA as 8.6 ± 2.0 cm².

Regarding the relationship between 3DA and conventional echocardiographic parameters, the stronger association of RA volume, basal RV and LA volume with TA size found in our study lends support to recent studies conducted with 3D echocardiography, confirming that TA dilatation is an on-going process, which includes the right chambers.^{14,16,29,30} On the contrary, the absence of an association between RVSP and TA dimensions shows that this phenomenon is not necessarily linked to the presence of pulmonary hypertension, emphasizing the idea that the correction of pulmonary hypertension does not always lead to a decrease in TA size. The absence of significant differences related to RV function between both groups could be related to the limitation of conventional parameters in the presence of preload increase. Probably, the evaluation of other, less preload-dependent parameters (such as ventricular function estimated by deformation parameters) could have shown some discrepancies with these parameters.

The good inter- and intraobserver reproducibility confirms the feasibility and reproducibility of 3D-TTE in assessing TA area, even in the presence of atrial fibrillation.

Finally, this study demonstrates that although $2DD > 21 \text{ mm/m}^2$ seems to be a reasonable criterion of marked dilatation of TA in functional TR, the combination with 3DA assessment might improve the selection of candidates for TV surgery. We believe that this approach, based on tricuspid dilatation through the incorporation of this new parameter, and not only on TR degree, allows a more adequate evaluation of secondary TR, a serious and progressive condition that determines the long-term survival of our patients. Future randomized prospective studies are needed to validate these new thresholds in patients who undergo mitral valve surgery.

Limitations

Despite including all degrees of TR, we did not incorporate healthy participants in our work for comparison with patients. Although it would have been of great interest to have normal values, there are recent works that have provided reference values of the TV area by 3D-TTE that support our findings.¹⁹ Despite the use of a rigorous method of quantification of the TR. most parameters are influenced by load conditions that can interfere with the correct determination of regurgitation severity. We assessed intra- and interobserver variability of 3DA measurement but not those related to image acquisition, performing all the studies with the same equipment, although acquisition protocols are well standardized and do not substantially differ among vendors. Finally, although we only selected functional TR, excluding cases with organic involvement of the TV, we cannot rule out that there was discrete rheumatic involvement of the TV not visualized by TTE.

CONCLUSIONS

Tricuspid annulus dilatation is present in a high percentage of patients with nonsevere TR degrees. Although a 2DD cutoff value of 21 mm/m² seems to be a reasonable criterion, the current 40 mm threshold underestimates real TA dilatation. We provide new parameters with better diagnostic performance related to TA morphology than 2DD, identifying 3DA values $\geq 10.4 \text{ cm}^2 \text{ or } \geq 6.5 \text{ cm}^2/\text{m}^2$ as new indicators of significant TA dilatation. This approach might improve the selection of candidates for TV annuloplasty, decreasing the incidence of late TR after rheumatic left-sided valve surgery.

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CONFLICTS OF INTEREST

None declared.

WHAT IS KNOWN ABOUT THE TOPIC?

- It is well known that more than one-third of patients with previous nonsevere TR will develop it lately after surgery; therefore, the identification of significant annulus dilatation in this subgroup of patients is crucial. Tricuspid annulus dilatation might be underestimated with single linear measurements by 2D-TTE.

WHAT DOES THIS STUDY ADD?

 Tricuspid annulus dilatation is present in a high percentage of patients with nonsevere TR degrees. The main finding of the present study is that current 40 mm threshold underestimates TA dilatation. We provide new 3D parameters with better diagnostic performance. This approach might improve the selection of candidates for TV annuloplasty, decreasing the incidence of late TR after rheumatic left-sided valve surgery.

REFERENCES

- Dreyfus GD, Martin RP, Chan KM, Dulguerov F, Alexandrescu C. Functional tricuspid regurgitation: a need to revise our understanding. J Am Coll Cardiol. 2015;65:2331– 2336.
- King RM, Schaff HV, Danielson GK, et al. Surgery for tricuspid regurgitation late after mitral valve replacement. *Circulation*. 1984;70:1193–1197.
- Groves PH, Hall RJ. Late tricuspid regurgitation following mitral valve surgery. J Heart Valve Dis. 1992;1:80–86.
- Kwak JJ, Kim YJ, Kim MK, et al. Development of tricuspid regurgitation late after left-sided valve surgery: a single-center experience with long-term echocardiographic examinations. Am Heart J. 2008;155:732–737.
- Shiran A, Sagie A. Tricuspid regurgitation in mitral valve disease incidence, prognostic implications, mechanism, and management. J Am Coll Cardiol. 2009;53:401–408.
- Song H, Kim MJ, Chung CH, et al. Factors associated with development of late significant tricuspid regurgitation after successful left-sided valve surgery. *Heart.* 2009;95:931–936.
- Baumgartner H, Falk V, Bax JJ, et al. ESC Scientific Document Group. 2017 ESC/ EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2017;38:2739–2791.
- Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2017;70:252–289.
- **9.** Colombo T, Russo C, Ciliberto GR, et al. Tricuspid regurgitation secondary to mitral valve disease: tricuspid annulus function as guide to tricuspid valve repair. *Cardiovas Surg.* 2001;9:369–377.
- Dreyfus GD, Corbi PJ, Chan KM, Bahrami T. Secondary tricuspid regurgitation or dilatation: which should be the criteria for surgical repair? *Ann Thorac Surg.* 2005;79:127–132.
- 11. Antunes MJ, Barlow JB. Management of tricuspid valve regurgitation. *Heart*. 2007;93:271–276.
- 12. Benedetto U, Melina G, Angeloni E, et al. Prophylactic tricuspid annuloplasty in patients with dilated tricuspid annulus undergoing mitral valve surgery. *J Thorac Cardiovasc Surg.* 2012;143:632–638.
- **13.** Van de Veire NR, Braun J, Delgado V, et al. Tricuspid annuloplasty prevents right ventricular dilatation and progression of tricuspid regurgitation in patients with tricuspid annular dilatation undergoing mitral valve repair. *J Thorac Cardiovasc Surg.* 2011;141:1431–1439.
- 14. Ton-Nu TT, Levine RA, Handschumacher MD, et al. Geometric determinants of functional tricuspid regurgitation: insights from 3-dimensional echocardiography. *Circulation*. 2006;114:143–149.
- **15.** Fukuda S, Saracino G, Matsumura Y, et al. Three-dimensional geometry of the tricuspid annulus in healthy subjects and in patients with functional tricuspid regurgitation: a real-time, 3-dimensional echocardiographic study. *Circulation*. 2006;114:1492–1498.
- Miglioranza MH, Mihaila S, Muraru D, Cucchini U, Iliceto S, Badano LP. Dynamic changes in tricuspid annular diameter measurement in relation to the echocardiographic view and timing during the cardiac cycle. J Am Soc Echocardiogr. 2015;28:226–235.
- 17. Addetia K, Yamat M, Mediratta A, et al. Comprehensive Two-Dimensional Interrogation of the Tricuspid Valve Using Knowledge Derived from Three-Dimensional Echocardiography. J Am Soc Echocardiogr. 2016;29:74–82.
- Dreyfus J, Durand-Viel G, Raffoul R, et al. Comparison of 2-Dimensional, 3-Dimensional, and Surgical Measurements of the Tricuspid Annulus Size: Clinical Implications. *Circ Cardiovasc Imaging*, 2015;8:e003241.
- Zoghbi WA, Adams D, Bonow RO, et al.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;30:303–371.
 Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber
- 20. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2015;16:233–270.
- Chan V, Burwash IG, Lam BK, et al. Clinical and echocardiographic impact of functional tricuspid regurgitation repair at the time of mitral valve replacement. *Ann Thorac Surg.* 2009;88:1209–1215.
- 22. Jhawar MB, Chan AK, Baig SZ, Calaluce ME, Senthilkumar A, Xie GY. Prognostic variables for clinical outcomes in valvular heart disease patients with moderate to severe secondary tricuspid regurgitation. J Heart Valve Dis. 2013;22:418–424.
- Groves PH, Ikram S, Ingold U, Hall RJ. Tricuspid regurgitation following mitral valve replacement: an echocardiographic study. J Heart Valve Dis. 1993;2:273–278.
- 24. Nath J, Foster E, Heidenreich PA. Impact of tricuspid regurgitation on long-term survival. J Am Coll Cardiol. 2004;43:405–409.
- **25.** Chopra HK, Nanda NC, Fan P, et al. Can two-dimensional echocardiography and Doppler color flow mapping identify the need for tricuspid valve repair? *J Am Coll Cardiol.* 1989;14:1266–1274.

- **26.** Ro SK, Kim JB, Jung SH, Choo SJ, Chung CH, Lee JW. Mild-to-moderate functional tricuspid regurgitation in patients undergoing mitral valve surgery. *J Thorac Cardiovasc Surg.* 2013;146:1092–1097.
- 27. Tang GH, David TE, Singh SK, Maganti MD, Armstrong S, Borger MA. Tricuspid valve repair with an annuloplasty ring results in improved long-term outcomes. *Circulation.* 2006;114:1577–1581.
- 28. Addetia K, Muraru D, Veronesi F, et al. 3-Dimensional Echocardiographic Analysis of the Tricuspid Annulus Provides New Insights Into Tricuspid Valve Geometry and

Dynamics. JACC Cardiovasc Imaging. 2017. http://dx.doi.org/10.1016/ j.jcmg.2017.08.022. Accessed 16 May 2018.

- 29. Yiu KH, Wong A, Pu L, et al. Prognostic value of preoperative right ventricular geometry and tricuspid valve tethering area in patients undergoing tricuspid annuloplasty. *Circulation*. 2014;129:87–92.
- Shiran A, Najjar R, Adawi S, Aronson D. Risk factors for progression of functional tricuspid regurgitation. Am J Cardiol. 2014;113:995–1000.