Pathogenic structural heart changes in early tricuspid regurgitation

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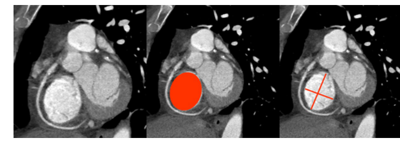
ABSTRACT

Objective: Severe, late functional tricuspid regurgitation is characterized by annulus dilation, right ventricular enlargement, and papillary muscle displacement with leaflet tethering. However, the early stages of mild tricuspid regurgitation and its progression are poorly understood. This study examined structural heart changes in mild, early tricuspid regurgitation.

Methods: Sequential patients undergoing cardiac computed tomography and transthoracic echocardiography with tricuspid regurgitation were identified and evaluated. The tricuspid annulus area and chamber volumes were measured by computed tomography angiography and categorized by tricuspid regurgitation severity.

Results: Patients (n = 622) were divided into 3 groups by tricuspid regurgitation severity: no/trace (n = 386), mild (n = 178), and moderate/severe tricuspid regurgitation (n = 58). Annulus area was highly dependent on and proportional to regurgitation severity and correlated with both right/left atrial enlargement. Annulus area most strongly correlated with right and left atrial volume, and the annulus shape changed from elliptical to circular in moderate/severe tricuspid regurgitation. Mild tricuspid regurgitation was associated with less right/left atrial enlargement than significant tricuspid regurgitation, normal right ventricular size, and annular dilation. Significant tricuspid regurgitation was associated with annular dilation, circularization, and right ventricular enlargement. Mild and significant tricuspid regurgitation were differentiated by annulus area and indexed right ventricular volume.

Conclusions: Tricuspid annular dilation and right/left atrial enlargement comprise early events in mild functional tricuspid regurgitation. Atrial enlargement occurs before right ventricular dilation, which occurs late, when tricuspid regurgitation is severe. Atrial volume and tricuspid annular dilation are early and sensitive indicators of tricuspid regurgitation significance. (J Thorac Cardiovasc Surg 2015;150:323-30)



Method of TAA measurement. TAA was measured in a plane defined by the tricuspid leaflets' most basal attachments. Measurements of area and major and minor diameters are shown.

Central Message

Early TR causes annular dilation and atrial enlargement, which may be useful in decision making for intervention.

Perspective

Functional TR is associated with late postoperative morbidity and mortality. Its early stages are associated with annular dilation and biatrial enlargement. RV enlargement occurs late, and each of these effects occurs in proportion to TR severity. Understanding longitudinal structural changes in TR may permit early intervention to prevent permanent structural changes.

See Editorial Commentary page 331.

Functional tricuspid regurgitation (TR) is a potent risk factor for all-cause mortality in valvular heart disease.[1] It typically results from left valve disease (LVD) and often fails to improve after successful left valve surgery despite beneficial postoperative hemodynamics. TR is also associated with increased late postoperative morbidity and mortality.[2-7] The timing of tricuspid valve surgery is important because patients with TR have anemia, organ dysfunction, and right ventricular (RV) dilatation, which also are associated with poor surgical outcomes.[8]

Structural heart changes in severe TR are well described and include tricuspid annular dilation and RV and right atrial (RA) enlargement. Tricuspid annuloplasty has favorable effects on right heart structure,[9-11] and early intervention can prevent right heart dilation and TR progression.[12]

Although structural changes in severe TR are well described, anatomic changes in early, mild TR are not well known. This study examined cardiac structural changes in

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Abbreviations and Acronyms

AF	= atrial fibrillation
CTA	= computed tomography angiography
LA	= left atrial
LV	= left ventricular
LVD	= left valve disease
LVEF	= left ventricular ejection fraction
PH	= pulmonary hypertension
RA	= right atrial
RV	= right ventricular
TAA	= tricuspid annulus area
TR	= tricuspid regurgitation

mild/early TR and compared them with late/severe TR. Recognizing these early structural changes in TR would be useful for therapy and its timing, especially as less-invasive tricuspid repair becomes available.[13]

MATERIALS AND METHODS

A total of 641 sequential patients with both computed tomography angiography (CTA) and transthoracic echocardiography were identified from the Minneapolis Heart Institute Advanced Imaging database. Institutional review board approval was obtained for data collection, analysis, and patient follow-up.

TR was assessed using categorization of Doppler color flow images.[14] Clinical data were collected from the electronic medical record, and patients were classified into 3 groups according to echocardiographic TR severity: none/trace, mild, and moderate/severe (Figure 1).

CTA is a validated, accurate method for measuring right heart volumes[15,16] and was used to measure chamber volumes and annulus area using Vital Images (Toshiba, Minato, Tokyo) VITREA software. The tricuspid annulus plane was identified from 3-dimensional multiplanar reformatted CTA data in diastole. Major and minor diameters, and annulus area were measured (Figure 2). RA, RV, left atrial (LA), and left ventricular (LV) long axes and areas were measured using CTA 4-chamber and orthogonal 2-chamber views (Figure 3). RA, RV, and LA volumes were calculated at mid-diastole using Simpson's method. Chamber volume indices were defined as volume normalized to body surface area. Pulmonary hypertension (PH) was defined as Doppler RV-RA pressure gradient 40 mm Hg or greater, and severe PH was defined as 60 mm Hg or greater. The presence/absence and TR severity were assessed using multiple transthoracic echocardiography windows. Patients were hemodynamically stable at the time of computed tomography and echocardiography imaging.

All patients underwent comprehensive 2-dimensional echocardiography, including Doppler examination of aortic stenosis severity. TV leaflet anatomy and hepatic venous flow patterns were assessed using the parasternal RV inflow, parasternal short-axis, apical 4-chamber, and subcostal views. Mild TR was defined as a small central jet, moderate TR was defined as an intermediate jet, and severe TR was defined as a large jet in the presence of TV leaflet malcoaptation or systolic hepatic vein flow reversal. Pulmonary artery systolic pressure was estimated from the TR jet using the view with maximal velocity, and RA pressure was estimated from inferior vena cava diameter, inspiratory collapse, or direct jugular vein examination. The average TR jet value was assessed during 30 seconds in all atrial fibrillation (AF) cases. Echocardiographic TR was classified into 3 grades: none/trace, mild, or moderate/severe, as noted earlier. The time between CTA and echocardiography was 30 days or less.

Statistical Analysis

Variables were summarized by TR group as median (25th, 75th percentile) for continuous covariates and number and percentage with characteristic for categoric variables. Comparisons between the TR groups were done using the Kruskal–Wallis test for continuous covariates and Pearson's chi-square or Fisher exact tests for categoric variables. The Pearson correlation between cardiac chamber volumes and tricuspid annular area (TAA) was computed.

Univariable and multivariable polytomous (multinomial) logistic regression analysis identified independent and co-predictors of mild TR and moderate/severe TR. We graphically assessed the linearity assumption using restricted cubic splines to flexibly model the relationship between the covariate and the log odds. The linearity assumption was reasonable for all covariates except age and ejection fraction. We found that the relationship could be adequately modeled using a linear spline with knot points at 50 years and 65%, respectively. Covariates in the multivariable model were selected using stepwise variable selection (P value for reentry and to stay $\leq$.05). All statistical analyses were performed with SAS software version 9.3 (SAS Institute Inc, Cary, NC).

RESULTS

A total of 641 patients with CTA and echocardiography studies were identified. Patients were excluded from the study for the following reasons: prior tricuspid annuloplasty (n = 1), implanted LV assist device (n = 2), RV tumor (n = 1), congenital heart disease (n = 2), insufficient or uninterpretable echocardiography data (n = 10), and suboptimal computed tomography image quality (n = 3). The resulting 622 cases were divided into 3 groups by TR severity: no/trace TR (n = 386), mild TR (n = 178), and moderate/severe TR (n = 58).

Clinical Characteristics

Table 1 shows the clinical characteristics of the 3 patient groups. The median age and percentage of patients with AF and LVD were significantly lower for no/trace TR than the other 2 TR groups. Median body surface area decreased in proportion to increasing TR severity, whereas PH ($\geq$40 mm Hg) increased proportionally to increasing TR severity. In moderate/severe TR, left ventricular ejection fraction (LVEF) was lower and PH was more prevalent.

Annulus Comparison

Table 2 compares TAA and shape by TR group. In no/trace and mild TR the annulus maintained an elliptical shape, whereas in moderate/severe TR there was annular circularization (less eccentric) according to the minor/major tricuspid annulus diameter quotient. TAA was larger in moderate TR than in mild TR and proportional to TR severity ($P <$ .0001). TAA in moderate/severe TR was larger than in trace and mild TR. TAA thus progressively enlarged and circularized with increasing TR severity.

Atrial and Ventricular Volumes

Table 2 shows RA and LA volumes by TR severity. RA and LA volume and respective volume indices each