Determinants of Functional Tricuspid Regurgitation in Incomplete Tricuspid Valve Closure: Doppler Color Flow Study of 109 Patients

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Objectives. The aim of this study was to investigate the association between the pattern of incomplete tricuspid valve closure and the presence of tricuspid regurgitation and to identify factors that determine the severity of regurgitation associated with this pattern.

Background. The incomplete tricuspid valve closure pattern (defined as apical displacement of the leaflets) has been described by two-dimensional echocardiography. However, whether this pattern is universally associated with tricuspid regurgitation and the determinants of severity of regurgitation in its presence have not been studied by Doppler color flow mapping.

Methods. We identified 109 consecutive patients (mean age 62 ± 17 years) with incomplete tricuspid valve closure who were studied by Doppler color flow mapping. We measured the linear apical displacement of the coaptation point from the tricuspid annulus and the area of displacement between the leaflets and annulus. Right atrial, ventricular and annular dimensions were measured and compared with those in a group of normal subjects.

Results. Tricuspid regurgitation was present in all patients with the incomplete closure pattern; it was mild in 14%, moderate in 19% and severe in 67%. Apical displacement was significantly greater (p < 0.02) in those with severe regurgitation than in those with mild regurgitation or in normal subjects. Tricuspid annulus dilation was the only independent predictor of severity of regurgitation. The right ventricle was not significantly dilated in 32% of patients, and right ventricular systolic pressure was not correlated with the severity of regurgitation and was <30 mm Hg in 11% of patients.

Conclusions. Tricuspid regurgitation was associated with incomplete tricuspid valve closure in all patients studied and was moderate to severe in 86%. Impaired coaptation is best reflected by the displacement area between the leaflets and the annulus. High pulmonary pressure and significant right ventricular dilation are not prerequisites for functional tricuspid regurgitation. Annular dilation is the most consistent and important determinant of this lesion.

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this pattern in a large group of patients with a wide spectrum of underlying heart disease.

Methods

Study patients. During a 3-year period between January 1990 and December 1992, we identified 141 consecutive patients with a pattern of incomplete closure of the tricuspid valve. This pattern is distinctly different from normal, with the leaflet bodies displaced apical to a line connecting the annular hinge points in the apical four-chamber view and tented in an overall concave configuration toward the right atrium (as opposed to the normal double convexity of the curved leaflets toward the atrium). Of these patients, 32 were excluded from the analysis: 11 because of evident intrinsic abnormality of the tricuspid valve (thickening, doming or restricted motion), 18 because of imaging quality unsuitable for quantification and 3 because of pacemaker wires across the tricuspid valve. The remaining 109 patients constituted the study group. In these patients we confirmed that the coaptation point of the leaflets was displaced >6 mm relative to the line connecting the annular hinge points (displacement was >8 mm in >90%) because this value was consistent with prior work (7) and exceeded the 95% confidence limits of 15 normal subjects (7 men and 8 women, aged 19 to 53 years, with no more than trace tricuspid regurgitation) who served as a control group. (The normal leaflet bodies, as opposed to those in the patients, were always at or superior to the annulus line, but the coaptation point sometimes extended minimally to its apical side.)

Echocardiographic measurements. Complete two-dimensional and Doppler color flow examinations were performed in all patients with the 2.5-MHz transducer of a Hewlett-Packard phased array sector scanner (77020A). Echocardiographic images were obtained during quiet end-expiration in a standard apical four-chamber view optimized to obtain the longest right ventricular long axis and its largest short-axis diameters at the base and midventricular level, with the greatest visualized excursion of the tricuspid leaflets (16,17). The right ventricular end-systolic and end-diastolic cavity areas were traced in the same view, and the percent change in area was calculated (18). The maximal diastolic and minimal systolic annular diameters (8) were measured in the same beat from the insertion of the septal to the insertion of the anterior tricuspid leaflet (inner edge to inner edge), and the percent shortening was calculated. Right ventricular systolic pressures were estimated by continuous wave Doppler echocardiography using the modified Bernoulli equation (4 x [Peak tricuspid regurgitation velocity]²), adding 10 mm Hg for the estimated right atrial pressure (19-21). Maximal inferior cava diameter over both respiratory and cardiac cycles was measured approximately 5 mm distal to the right atrial—caval junction (22).

The systolic configuration of the tricuspid valve was evaluated in the four-chamber view. The linear apical displacement of the coaptation point of the tricuspid leaflets into the right ventricle from the line connecting the tricuspid annulus hinge points toward the right ventricle was measured at the time of maximal systolic closure (Fig. 1). To integrate apical displacement over the entire width of the leaflets, the area between the atrial surface of the leaflets and the tricuspid annulus was traced at the same time (Fig. 1). Two-dimensional structural measurements were made before jet measurement and grading. Measurements were averaged in 3 beats during sinus rhythm and in 5 during atrial fibrillation.

Assessment of tricuspid regurgitation severity. Doppler studies. Tricuspid regurgitation was routinely assessed by integrating both Doppler color flow mapping images of the regurgitant jet and pulsed wave Doppler evidence of systolic flow reversal in the inferior vena cava or hepatic veins (23). Careful Doppler evaluation of the jet was performed in all obtainable views of the right ventricle and atrium, including the parasternal short-axis view at the aortic valve level, the right ventricular inflow view, the apical-four-chamber view and subcostal views. The color flow mapping display of reversed or mosaic signals originating from the tricuspid valve and extending into the right atrium during systole identified the presence of tricuspid regurgitation. The narrowest sector angle encompassing the regurgitant jet was used to obtain maximal frame rate. The area of disturbed flow that was traced (using a Sony off-line analysis system) included the aliased signals and the immediately contiguous nonturbulent velocities that were moving in the same direction. Right atrial area was traced from the same frame as maximal jet area.

Grading of regurgitation. Tricuspid regurgitation was then graded according to the following algorithm: 1) The view in which the spatial distribution of the jet was maximal was selected. 2) The severity of regurgitation was graded as mild if the jet area was estimated to occupy <20% of the right atrial area, as moderate if this value was between 20%
and 33% and as severe if this value exceeded 33%, based on correlations with surgical and angiographic severity in previous studies (24-26). 3) If the estimated ratio of jet area to right atrial area was close to a cutoff point, jet eccentricity increased the grade above that point to the next higher grade (because eccentric wall jets appear smaller than comparable free jets) (27-29). 4) Systolic flow reversal in the inferior vena cava or hepatic veins by pulsed wave Doppler study was considered to indicate at least moderate regurgitation regardless of the other findings (25).

Data analysis. Right heart dimensions were compared between patients and normal control subjects by unpaired Student t test, and the three patient subgroups (mild, moderate or severe tricuspid regurgitation) were compared by one-way analysis of variance. Right heart measurements were considered abnormal if they differed from the mean values measured in the control group by >2 SD. Multiple stepwise linear regression analysis was performed to identify predictors of the severity of tricuspid regurgitation (measured continuously as jet area). The following variables were entered into the model: right ventricular end-systolic and end-diastolic cavity areas, percent change in area, maximal diastolic and minimal systolic annular diameters, linear apical displacement, area of apical displacement, maximal inferior vena cava diameter and right ventricular systolic pressure. Forward stepping was used with the F-to-enter and F-to-remove any variable selected such that the corresponding significance level (outer tail area) was ≤0.05.

Observer variability. Two independent observers repeated 10 measurements of jet area and right atrial size. The measurements of the two observers were subtracted and the standard deviation of the differences was used to express interobserver variability.

Additional subsidiary analysis: incomplete mitral valve closure. To compare the distribution of mild, moderate and severe regurgitation in patients with incomplete mitral and tricuspid valve closure patterns, we reviewed the severity of mitral regurgitation routinely assessed by Doppler color flow mapping (30) in the 596 patients found to have incomplete closure of the mitral valve (defined as failure of the mitral leaflets to reach the level of the annulus) over the same 3-year period.

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Study Patients (n = 109)</th>
<th>Normal Subjects (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr) (mean ± SD)</td>
<td>62 ± 17</td>
</tr>
<tr>
<td>Male gender</td>
<td>61 (56%)</td>
</tr>
<tr>
<td>Rhythm</td>
<td></td>
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<tr>
<td>Sinus</td>
<td>49 (45%)</td>
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<tr>
<td>Atrial fibrillation</td>
<td>60 (55%)</td>
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<tr>
<td>Etiology</td>
<td></td>
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<tr>
<td>Myocardial dysfunction</td>
<td>54 (49%)</td>
</tr>
<tr>
<td>Left-sided valve disease</td>
<td>30 (27%)</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>14 (13%)</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>11 (10%)</td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Mild</td>
<td>15 (14%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>21 (19%)</td>
</tr>
<tr>
<td>Severe</td>
<td>73 (67%)</td>
</tr>
<tr>
<td>Visible gap*</td>
<td>15 (14%)</td>
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</table>

*Between the tips of the visualized leaflets at the time of maximal leaflet apposition.

Results

Patient characteristics. Important clinical characteristics of the study group are shown in Table 1. The underlying cardiac disease was myocardial dysfunction in 54 patients, left-sided valve disease in 30, pulmonary hypertension in 14 and congenital heart disease in 11. Tricuspid regurgitation was present in all patients; it was mild in 15 patients (14%), moderate in 21 (19%) and severe in 73 (67%).

Right heart measurements. Right heart measurements in the study and control groups are presented in Table 2. Right atrial area, right ventricular and annular size during systole and diastole, apical linear and area displacement of the tricuspid valve during systole, and inferior vena cava diameter were all significantly higher in patients with incomplete tricuspid valve closure than in the control group (p < 0.001 for all comparisons). Right ventricular function and percent annular constriction were significantly lower in the study patients than in the control group.

Table 2. Right Heart Measurements in Normal Subjects and Study Patients With Incomplete Tricuspid Valve Closure

<table>
<thead>
<tr>
<th>Study Patients (n = 109)</th>
<th>Normal Subjects (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV end-systolic area(cm²)</td>
<td>8.9 ± 2.2</td>
</tr>
<tr>
<td>RV end-diastolic area(cm²)</td>
<td>16.2 ± 3.7</td>
</tr>
<tr>
<td>RV area change(%)</td>
<td>46 ± 8</td>
</tr>
<tr>
<td>RA area(cm²)</td>
<td>11.8 ± 3</td>
</tr>
<tr>
<td>Annular diameter (systolic)(cm)</td>
<td>1.8 ± 0.35</td>
</tr>
<tr>
<td>Annular diameter (diastolic)(cm)</td>
<td>2.8 ± 0.5</td>
</tr>
<tr>
<td>Annular area change(%)</td>
<td>34 ± 8</td>
</tr>
<tr>
<td>Apical displacement(cm)</td>
<td>0.16 ± 0.17</td>
</tr>
<tr>
<td>Area displacement(cm²)</td>
<td>0.22 ± 0.26</td>
</tr>
<tr>
<td>Inferior vena cava diameter(cm)</td>
<td>1.5 ± 0.13</td>
</tr>
</tbody>
</table>

*p < 0.001. Data presented are mean values ± SD. RA = right atrial; RV = right ventricular.
Right heart measurements and underlying disease. Right heart measurements were also compared according to the underlying etiology. The severity of tricuspid regurgitation did not differ between patients with myocardial dysfunction and those with underlying left-sided valve disease. The mean end-diastolic area of the right ventricle was higher in patients with cardiomyopathy than in those with left-sided valve disease (20.1 ± 6.4 vs. 16.4 ± 5.4 cm², p < 0.001), whereas mean right atrial area was significantly higher in those with left-sided valve disease than in those with cardiomyopathy (26.8 ± 8.3 vs. 35 ± 14.2 cm², p < 0.001). There was no significant difference in linear or area displacement of the tricuspid valve among patients with different underlying diseases.

Tricuspid annulus diameter. When all right heart measurements were included in the multiple stepwise regression analysis, the tricuspid annulus diameter during diastole emerged as the only significant independent predictor of severity of tricuspid regurgitation. Right ventricular and right atrial size, tricuspid annulus diameter during systole and area of apical displacement were all significantly correlated with tricuspid regurgitation severity by univariate analysis but were displaced from the multivariate model. In contrast, mild tricuspid regurgitation was present in 14%, moderate regurgitation in 19% and severe regurgitation in 67% of patients with incomplete tricuspid valve closure.

Discussion

The primary goal of this study was to investigate the association between the pattern of incomplete closure of the tricuspid valve and the presence of functional tricuspid regurgitation and to identify factors that determine the severity of regurgitation associated with this pattern. Although several previous studies (6–10,31) described incomplete tricuspid valve closure, they were limited because color Doppler echocardiography was not available to assess the severity of tricuspid regurgitation. Combined two-dimensional and color Doppler echocardiography permit simultaneous evaluation of flow dynamics and morphologic features to provide greater insight into the mechanism of functional tricuspid regurgitation.

Incomplete tricuspid valve closure pattern and tricuspid regurgitation. The pattern of incomplete tricuspid valve closure was uniformly associated with tricuspid regurgita-
Incomplete Tricuspid Valve Closure

Figure 2. Top, Apical four-chamber view showing a relatively mild incomplete tricuspid valve closure pattern, with a modest area of apical displacement between the tricuspid leaflets and the line connecting the annular hinge points (dashed line). Bottom, Doppler color flow map in the same view showing a relatively mild tricuspid regurgitant jet.

Lion in the patients studied and the regurgitation was moderate to severe in 86%. Previous studies, which assessed tricuspid regurgitation by physical examination, ventriculography or pulsed Doppler echocardiography in smaller groups of patients, were limited in their ability to explore this association (7,9,10). Gibson et al. (9) reported tricuspid regurgitation by right ventriculography in only 5 of 21 patients with the incomplete closure pattern. They believed that tricuspid regurgitation was probably not recorded in other patients because of lack of attention paid to the abnormality both clinically and hemodynamically, and stated that “improved methods ... may settle whether tricuspid regurgitation is a universal finding in patients with this pattern” (9). Mikami et al. (7) failed to detect a regurgitant signal in 11 of 41 patients clinically thought to have functional tricuspid regurgitation, possibly reflecting the limited spatial appreciation of the pulsed Doppler method used, particularly for narrow or eccentric jets. Come and Riley (10) described five patients with severe tricuspid regurgitation who had a visible gap between the leaflets, which has been shown to coincide with severe tricuspid regurgitation with a laminar Doppler signal (31). Further, none of these studies investigated the severity of tricuspid regurgitation as a function of apical displacement (as continuous linear or area measures). In contrast, in the present study, the pattern of incomplete closure was always associated with tricuspid regurgitation and the severity of regurgitation was significantly correlated with the degree of apical displacement (p < 0.003), with a visible gap implying severe regurgitation. The area of displacement between the leaflets and tricuspid annulus is an index not previously described that incorporates both linear apical displacement and annular dilation. Therefore, unlike linear displacement alone, it was significantly correlated with the severity of tricuspid regurgitation as it more completely reflects the increased leaflet area required for complete valve closure because of altered leaflet geometry.

Functional tricuspid regurgitation: determinants of severity. Functional tricuspid regurgitation is a term used to describe valvular incompetence without evident structural abnormality of the tricuspid valve. The results of this study are consistent with prior reports that the most important
The present study also highlights an observation not previously discussed: Neither significant right ventricular dilation nor pulmonary hypertension is a prerequisite for functional tricuspid regurgitation in this context. Approximately one third of the patients studied had a right ventricular end-diastolic area that was within 2 SD of the mean for normal control subjects, albeit in the upper part of this range. Most of these patients had mild to moderate tricuspid regurgitation. In retrospect, this finding is also evident from the data of Gibson et al. (9). The incomplete leaflet closure pattern with relatively normal right ventricular size has several possible explanations: 1) The tricuspid annulus is shared by the right atrium and right ventricle, decreasing in size in early systole along with the ventricle and increasing in late systole along with the atrium (8). We can therefore propose that functional tricuspid regurgitation may result from annular dilatation due to right atrial dilation rather than from ventricular dilatation, a view supported by right atrial dilatation in all these patients. 2) Recently, left ventricular shape has been suggested (14,15) as the most likely substrate for the development of functional mitral regurgitation. Similar changes in right ventricular shape rather than size (for example, relative dilatation of its base or midportion) might therefore change annular or papillary muscle geometry in some patients to create incomplete leaflet closure. 3) Significant tricuspid regurgitation causes right ventricular volume overload. However, as long as right ventricular function is well maintained, right ventricular size can be normal or only slightly increased, especially early in the disease. This observation is consistent with the finding that in all of our patients with moderate to severe tricuspid regurgitation and normal right ventricular size, right ventricular function (percent area change) was normal or even relatively high.

Role of pulmonary hypertension. The relation between pulmonary pressure and tricuspid regurgitation in incomplete tricuspid valve closure has not been thoroughly investigated. The usual concept is that pressure overload will increase right ventricular and annular size and result in tricuspid regurgitation. However, pulmonary hypertension is not the only mechanism of functional tricuspid regurgitation. In this study, right ventricular systolic pressure did not significantly correlate with the severity of tricuspid regurgitation and was within normal limits (<30 mm Hg) in 11% of patients. This may relate to myocardial dysfunction being the most common underlying disease in the patients studied, with functional tricuspid regurgitation resulting from myocardopathic right ventricular and annular dilation. Additionally, pulmonary pressure may decrease in the late stage of severe tricuspid regurgitation because of low output failure. Although partial equilibration of pressures due to severe regurgitation may cause underestimation of right ventricular systolic pressure (21), partially obscuring the relation between pulmonary artery pressure and severity of tricuspid regurgitation, there was also no correlation between pressure and the severity of regurgitation in patients with mild to moderate lesions. Additionally there was no correlation even when pressure was calculated by using a regression equation to take into account variable right atrial pressure (32).

The dominant role of annular dilatation as opposed to pulmonary hypertension was recently highlighted by studies demonstrating substantial increases in functional tricuspid regurgitation during application of a left ventricular assist device (35,36). In such patients, tricuspid regurgitation remains the same or increases in the presence of decreasing pulmonary pressures when the left ventricle becomes smaller and the tricuspid annulus dilates.

Previous clinical reports (4,37) have suggested that in patients with rheumatic valve disease, a systolic pulmonary pressure that is only mildly elevated (<40 mm Hg) favors the diagnosis of primary or organic tricuspid valve disease, whereas a systolic pulmonary pressure >60 mm Hg favors secondary or functional regurgitation. In the 30 patients with left-sided valve disease (mostly rheumatic) in this study, 7 (23%) had systolic pulmonary pressure <40 mm Hg and still had functional tricuspid regurgitation. In addition, 31% of patients with myocardial dysfunction had a pulmonary pressure <40 mm Hg and functional tricuspid regurgitation. The distinction between organic and functional tricuspid regurgitation therefore cannot be based solely on systolic pulmonary pressure.

Comparison with incomplete closure and functional regurgitation of the mitral valve. Although this study was not originally designed to compare functional regurgitation between the two atrioventricular valves, some observations are of interest. The finding that significant ventricular enlargement, as opposed to shape change, is not a prerequisite for the development of tricuspid regurgitation also seems to be true for functional mitral regurgitation (14,15,38). The degree of severity of mitral regurgitation associated with incomplete mitral valve closure was significantly less than the severity of tricuspid regurgitation associated with incomplete tricuspid valve closure. Possible explanations for this difference include 1) the different geometric structure of the valves (trileaflet versus bileaflet, with the tricuspid papillary muscles located on different sides of the ventricle, potentially pulling the leaflets apart with ventricular or annular dilation, whereas the two mitral papillary muscles are located posteriorly); and 2) the difference in pressure between the left and the right ventricle. In addition, the greater tendency of the tricuspid valve to leak even in structurally normal hearts (39,40) may make it more susceptible to increased regurgitation in heart disease. However, further studies are needed to investigate these differences.

Advantages and limitations of the study. The availability of color Doppler echocardiography enabled us to quantify tricuspid regurgitation in a more objective way than that used in previous work, and we studied a larger number of patients with a wide spectrum of underlying diseases. De-
spite the potential for bias between imaging and color Doppler data, almost one third of the patients had a right ventricle of normal size, contrary to the expected bias. One important limitation of our study is the known difficulty in measuring right ventricular size and function accurately. To date, there is no universally accepted technique (echocardiographic, radionuclide or angiographic) for accurately assessing the size and function of the right ventricle because of its shape and the difficulties in tracing endocardial borders. Right ventricular size may also appear different if the transducer is placed over the right or the left ventricular apex. We tried to overcome these limitations by including only patients with an imaging study of reasonable quality and by using measures of right ventricular area that are independent of the geometric assumptions used to derive volumes and in views that optimized that area. Further studies would be of interest to compare apical displacement in the four-chamber view with that in the two-chamber view, which contains the largest annular dimension (8) but appears more difficult to obtain routinely.

Potential clinical implications. The correlation between annular dilation, apical linear and area displacement and the severity of tricuspid regurgitation may be of additional use in assessing the severity of tricuspid regurgitation, particularly when color Doppler echocardiography is unavailable or limited in its ability to visualize the entire jet. In addition, a better understanding of the mechanism of functional tricuspid regurgitation may identify factors (such as annular dilation) that could potentially predict irreversible tricuspid regurgitation and therefore the need for simultaneous tricuspid valve repair in patients undergoing corrective left-sided valve surgery. In that context, the association between annular dilation and regurgitation supports the current surgical policy of tricuspid annuloplasty for patients with severe functional tricuspid regurgitation (41,42). This observation in this study also provide greater insight into the failure of significant tricuspid regurgitation to resolve even after successful balloon mitral valvotomy in patients with mitral stenosis despite reduced pulmonary pressures (43); this failure may possibly reflect irreversible tricuspid annular and right ventricular dilation.

Conclusions. Tricuspid regurgitation was associated with the incomplete closure pattern in all patients studied and was moderate to severe in the majority. Impaired coaptation is best reflected by the displacement area between the leaflets and the annulus, incorporating both apical linear displacement and annular dilation. Neither pulmonary hypertension nor significant right ventricular dilation is a prerequisite for functional tricuspid regurgitation. Annular dilation, which can impair coaptation, is the most consistent finding and is the most important determinant of functional tricuspid regurgitation.

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References
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