Understanding right ventricular dysfunction and functional tricuspid regurgitation accompanying mitral valve disease

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Objectives: The study objective was to correlate the degree of tricuspid regurgitation with clinical indicators of right-sided heart failure and both qualitative and quantitative measures of right-sided heart morphology and function in patients with degenerative mitral valve disease.

Methods: From 2001 to 2007, 1833 patients with degenerative mitral valve disease, structurally normal tricuspid valve, and no coronary artery disease underwent surgery. Right-sided heart morphology (right ventricular base-to-apex length, tethering distance and area, and right atrial systolic area) and right ventricular function (tricuspid annular plane systolic excursion, myocardial performance index, and tricuspid valve annular shortening) were measured on preoperative transthoracic echocardiograms for 100 randomly selected patients from each of tricuspid regurgitation grades 0, 1+, and 2+, and for all 93 patients with tricuspid regurgitation grade 3+/4+. Multivariable regression was used to evaluate the association of left- and right-sided heart morphology and function with tricuspid regurgitation.

Results: Increasing tricuspid regurgitation grade was associated with higher right ventricular pressure ($P < .0001$), increased tethering distance ($P = .008$), larger right atrial size ($P = .0002$), and worsening right ventricular function, particularly when 3+/4+ tricuspid regurgitation was present. When tricuspid regurgitation was 3+/4+, both tricuspid annular plane systolic excursion and myocardial performance index were almost certainly abnormal. Changes in right-sided heart morphology and right ventricular dysfunction were synergistic in relation to severity of tricuspid regurgitation.

Conclusions: Functional tricuspid regurgitation accompanying mitral valve disease is associated with proportional changes in right-sided heart morphology; however, severe tricuspid regurgitation is nearly always associated with right ventricular dysfunction, suggesting a synergistic relationship. Right ventricular dysfunction is likely as important as tricuspid regurgitation because it offers an explanation for the negative prognostic impact of tricuspid regurgitation and has implications for the clinical management of patients. (J Thorac Cardiovasc Surg 2013;145:1234-41)

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Tricuspid regurgitation (TR) accompanying left-sided heart valve disease has long been recognized as a risk factor for early and late mortality after surgery.^{1,2} Although this TR

is simply considered secondary to right ventricular (RV) dilatation in response to left-sided events and is usually referred to as “functional,”³ its cause remains uncertain.⁴ We hypothesized that *left-sided events* resulting in TR also lead to RV dysfunction. If true, recognizing this has important implications for preoperative surveillance, operative timing, choice of procedure, and postoperative management. Therefore, the objectives of this study were to correlate the degree of TR with clinical indicators of right-sided heart failure and both qualitative and quantitative measures of right-sided heart morphology and function in patients with degenerative mitral valve disease.

PATIENTS AND METHODS

Patients

From January 2001 to January 2007, 2726 patients underwent primary mitral valve repair or replacement for degenerative mitral valve disease at Cleveland Clinic. Of these patients, 1833 had no structural tricuspid valve (TV) pathology and either no clinical suspicion of coronary artery disease or no angiographically significant (stenosis $< 50\%$) coronary artery disease; on the basis of clinical preoperative transthoracic echocardiogram assessment, 794 patients had no TR, 645 patients had grade 1+ TR, 301

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Abbreviations and Acronyms

LA	= left atrial
LV	= left ventricular
MELD	= Model for End-stage Liver Disease
MPI	= myocardial performance index
RA	= right atrial
RV	= right ventricular
RVSP	= right ventricular systolic pressure
TAPSE	= tricuspid annular plane systolic excursion
TR	= tricuspid regurgitation
TV	= tricuspid valve

patients had 2+ TR, 75 patients had 3+ TR, and 18 patients had 4+ TR. By using standard American Society of Echocardiography criteria, grading of TR included evaluation of the color TR jet area/right atrial (RA) area, vena contracta, proximal isovelocity surface area, and hepatic vein flow reversal.⁵⁻⁷

Study Design

Our strategy in studying the right side of the heart in relation to degree of TR was a quasi-experimental one, randomly sampling 100 patients from each TR grade 0, 1+, and 2+, but including all 93 patients with TR grades 3+ and 4+ (SAS PROC PLAN, SAS Institute Inc, Cary, NC). Thus, 393 patients formed the study cohort, 21% of the original 1833 patients (Figure E1).

Preoperative and operative data were retrieved from the Cardiovascular Information Registry (Table 1). Hemodynamic state at anesthesia induction was obtained from the Cardiothoracic Anesthesia Registry. Routine echocardiographic assessment of left ventricular (LV), RV, and atrial dimensions and functions were retrieved from the echocardiography database (Table 2). Data from these registries have been approved for use in research by the institutional review board, with patient consent waived.

Left-sided heart morphology and function. Left-sided heart evaluation was by the original routine clinical assessment only. Variables included quantitative measures of LV dimensions and volumes, hypertrophy, and function; left atrial (LA) dimensions; and RV systolic pressure (RVSP) estimated from TV regurgitant jet velocity (Appendix 1).⁸

Right-sided heart morphology and function. *Original clinical assessment.* Echocardiographic data retrieved from original clinical assessment (Appendix 1) included TR degree, qualitative assessment of RV and RA dilatation, and qualitative assessment of RV dysfunction.

Quantitative right-sided heart morphology. Quantitative assessment of right-sided heart morphology was performed de novo offline on recorded echocardiograms using ProSolv cardiovascular analyzer 3.5 (ProSolv Cardiovascular, Indianapolis, Ind). Measurements averaged over 3 beats were obtained from the apical 4-chamber view:

- RA end-systolic area: planimetric area at end systole (Figure E2, A)
- RV base-to-apex length: distance between midpoint of TV annular plane and RV apex at end diastole (Figure E2, B)
- TV tethering distance: distance between coaptation point of TV cusps and TV annular plane (Figure E2, C)
- TV tethering area: planimetric area between atrial surface of TV cusps and tricuspid annular plane at end diastole (Figure E2, D)

Quantitative right ventricular function. Quantitative assessment of RV function was performed de novo offline using the apical 4-chamber and parasternal RV inflow and outflow tract views.

- Tricuspid annular plane systolic excursion (TAPSE) (Figure E3): displacement of lateral portion of TV annulus from diastole to systole, averaged over 3 beats (cm).^{9,10} Normal TAPSE is 1.5 cm or more and decreases with diminishing systolic function.
- Myocardial performance index (MPI) (Figure E4): ratio of total isovolumetric contraction plus relaxation times and pulmonary ejection time^{8,11-14} averaged over 3 beats. Normal MPI is 0.4 or less and increases with diminishing global systolic and diastolic function.
- TV annular shortening (Figure E5): difference between diastolic and systolic TV annulus diameters. TV annulus diameter is the distance between points of attachment of anterior and septal TV cusps on the mural and septal endocardia, respectively.¹⁵
- TV annular fractional shortening: ratio of TV annulus shortening and diastolic TV annulus diameter.^{15,16}

Clinical indicators of right-sided heart failure. Variables constituting the Model for End-stage Liver Disease (MELD) score—creatinine, bilirubin, and international normalized ratio—and the MELD score itself were considered indicators of possible right-sided heart failure.¹⁷

Data Analysis**Multivariable analyses of tricuspid regurgitation grade.**

Multivariable analysis of TR grade, using variables listed in Appendix 1, was performed using cumulative logistic regression. Five sequential analyses of cardiac morphology and function were performed:

1. Analysis of left-sided heart variables: degree of mitral regurgitation, LV inner diameter and volume diastole and systole, posterior wall and septal thickness, relative wall thickness, calculated LV mass, LV fractional shortening, ejection fraction, RVSP, and LA diameter, volume, and systolic area.
2. Analysis of qualitative right-sided heart variables: qualitative RV and RA dilatation and RV dysfunction. Because of low frequencies in the mild-moderate-severe categories, we collapsed these, treating them as binary variables.
3. Analysis of quantitative right-sided heart morphology variables: RA systolic area in systole, RV base-to-apex length, and TV tethering distance and area.
4. Analysis of quantitative RV function variables: TAPSE, MPI, and TV annular and fractional shortening.
5. Analysis of all left- and right-sided heart variables: All these variables were included in a final analysis presented in this article.

Management of missing data and variable selection strategy.

Fivefold multiple imputation using a Markov Chain Monte-Carlo technique was performed to impute sporadic missing values under the assumption of missing at random.¹⁸ Multivariable analyses were then performed using the first imputed sample. Variable selection, with a *P* value retention criterion of .05, used bagging for 1000 bootstrap samples.^{19,20} Frequency of occurrence of individual variables and clusters of correlated variables was compiled, and those appearing in at least 50% of analyses were retained in final models. After variable selection, 4 additional imputed complete data sets were formed to estimate regression coefficients and their variance-covariance matrix.¹⁸

Data Presentation

Continuous variables are summarized by mean $\pm$ standard deviation, and categorical variables are summarized by frequencies and percentages. All analyses were performed using SAS statistical software (SAS V9.1). Uncertainty is expressed by confidence limits equivalent to ± 1 standard error (68%).

TABLE 1. Preoperative patient characteristics according to tricuspid regurgitation grade

Variable	TV regurgitation grade								P‡
	0 (n = 100)		1+ (n = 100)		2+ (n = 100)		3+/4+ (n = 93)		
	n*	No. (%) or Mean ± SD	n*	No. (%) or Mean ± SD	n*	No. (%) or Mean ± SD	n*	No. (%) or Mean ± SD	
Demographics									
Age (y)	100	53 ± 10	100	57 ± 12	100	65 ± 12	93	68 ± 11	<.0001
Female	100	31 (31)	100	37 (37)	100	34 (34)	93	52 (56)	.002
Body surface area (m ²)	100	2 ± 0.23	100	2 ± 0.25	100	2 ± 0.23	93	1.9 ± 0.24	.001
Cardiac morbidity									
NYHA functional class	100		100		100		93		.04
I		33 (33)		28 (28)		36 (36)		18 (19)	
II		53 (53)		63 (63)		52 (52)		54 (58)	
III		14 (14)		8 (8)		11 (11)		20 (22)	
IV		0 (0)		1 (1)		1 (1)		1 (1.1)	
Noncardiac comorbidity									
Cholesterol (mg/dL)	93	200 ± 38	87	200 ± 43	92	190 ± 29	85	180 ± 35	<.0001
Bilirubin (mg/dL)	100	0.72 ± 0.59	97	0.74 ± 0.39	99	0.8 ± 0.41	89	0.87 ± 0.52	.03
Blood urea nitrogen (mg/dL)	99	17 ± 4.8	100	18 ± 5.3	100	19 ± 6	93	22 ± 8.8	<.0001
Creatinine (mg/dL)	100	0.93 ± 0.19	99	0.96 ± 0.23	99	1 ± 0.24	92	1.1 ± 0.7	.02
Hematocrit (%)	98	42 ± 3.5	99	41 ± 5.4	99	41 ± 4	90	40 ± 4.7	.0001
MELD score	100	7.2 ± 1.4	100	7.4 ± 1.6	100	8 ± 2.4	93	8.6 ± 2.4	<.0001

TV, Tricuspid valve; SD, standard deviation; NYHA, New York Heart Association; MELD, Model for End-stage Liver Disease. *Patients with data available. †For categorical variables, Mantel-Haenszel test of linear trend with increasing TV regurgitation grade; for continuous variables, equivalent test of Pearson correlation coefficient.

RESULTS

Tricuspid Regurgitation and Patient Factors

Increasing TR was associated with older age, female gender, smaller body surface area, impaired hepatic function (higher bilirubin and higher MELD score), lower serum cholesterol, higher blood urea nitrogen, and lower hematocrit. Severity of TR was also weakly associated with higher New York Heart Association functional class (Table 1).

Tricuspid Regurgitation and Left- and Right-Sided Heart Findings

Degree of TR was not correlated with degree of mitral regurgitation (by selection, all patients had at least moderate regurgitation) but was strongly positively correlated with higher RVSP (Figure E6) and LA diameter. TR was also weakly associated with lower LV ejection fraction and smaller LV end-diastolic volume, but not with LV hypertrophy (Table 2).

Degree of TR was closely correlated with degree of pulmonary valve regurgitation and both qualitative and quantitative measures of RV function (Table 2).

Routine qualitative echocardiographic assessment of right-sided heart morphology (Figure E7, A and B) and function (Figure E7, C), however, showed positive, but weak, correlations with degree of TR. In contrast, quantitative measurements of RA area (Figure E8, A), TV tethering distance (Figure E8, B) and area, and RV base-to-apex length were all positively correlated with degree of TR.

Abnormal TAPSE and MPI separated patients with severe TR 3+/4+ from those with lower grades of TR. TAPSE

was substantially lower (worse function) for patients with TR 3+/4+ and, in this lower range, less variable than at lower grades of TR (Figure 1, A and B). MPI was considerably higher (worse function) for TR 3+/4+, but more variable than at lower grades (Figure 1, C and D). There were low to moderate correlations ($|r| > 0.1$) between quantitative measures of right-sided heart morphology and TAPSE and MPI (Figure E9, A and B).²¹

Higher values of TAPSE were associated with lower values of MPI (inverse relationship, $r = -0.74$, $P < .0001$) in a nonlinear fashion (Figure E10). At low TAPSE levels, MPI values stretched toward higher levels. The interaction between TAPSE and MPI in patients with severe TR 3+/4+ is illustrated in a 3-dimensional perspective plot (Figure E11).

Patient variables associated with lower TAPSE were older age, higher New York Heart Association class, larger LA volume, atrial fibrillation, lower creatinine clearance, lower cholesterol (Table 3), and with higher MPI, older age, increased heart rate, larger LA volume, lower creatinine clearance, lower cholesterol, higher MELD score, complete heart block, smaller LV end-diastolic volume, and lower hematocrit (Table 3).

Tricuspid Regurgitation and Multivariable Association With Cardiac Morphology and Right Ventricular Function

In multivariable analysis, cardiac morphologic variables associated with higher grade of TR included smaller LV and end-systolic volume, large RA systolic area, and larger

TABLE 2. Left- and right-sided heart echocardiographic findings according to tricuspid regurgitation grade

Variable	TV regurgitation grade								P†
	0 (n = 100)		1+ (n = 100)		2+ (n = 100)		3+/4+ (n = 93)		
	n*	No. (%) or Mean ± SD	n*	No. (%) or Mean ± SD	n*	No. (%) or Mean ± SD	n*	No. (%) or Mean ± SD	
MV regurgitation	100		100		100		93		.4
Moderate		0 (0)		1 (1)		0 (0)		0 (0)	
Moderately severe		7 (7)		8 (8)		4 (4)		10 (11)	
Severe		93 (93)		91 (91)		96 (96)		83 (89)	
LV mass index (g/m ²)	94	140 ± 110	95	130 ± 30	95	140 ± 36	87	130 ± 36	.5
LA diameter (cm)	87	4.6 ± 0.67	92	4.7 ± 0.81	93	5 ± 0.85	84	5.1 ± 0.94	<.0001
LV end-diastolic volume (mL)	95	160 ± 44	97	150 ± 46	95	150 ± 45	87	140 ± 40	.01
LV end-systolic volume (mL)	95	49 ± 24	97	50 ± 26	95	46 ± 20	87	46 ± 24	.2
LV mass (g)	94	280 ± 220	95	250 ± 73	95	270 ± 80	87	240 ± 69	.1
LV ejection fraction (%)	100	58 ± 7	99	59 ± 7.8	100	58 ± 5.7	93	56 ± 8.1	.05
RVSP (mm Hg)	61	31 ± 8.8	85	36 ± 12	94	45 ± 14	88	51 ± 20	<.0001
TV									
Regurgitation velocity (cm/sec)	62	250 ± 46	86	280 ± 49	94	310 ± 51	89	330 ± 71	<.0001
Tethering distance (cm)	99	0.44 ± 0.18	99	0.63 ± 0.23	98	0.55 ± 0.23	91	0.71 ± 0.30	<.0001
Tethering area (cm ²)	99	0.40 ± 0.32	99	0.59 ± 0.35	98	0.48 ± 0.33	91	0.74 ± 0.56	<.0001
Annular shortening (cm)	99	0.36 ± 0.27	99	0.37 ± 0.28	98	0.34 ± 0.26	91	0.40 ± 0.36	.6
Annular shortening fraction	99	0.11 ± 0.08	99	0.11 ± 0.08	98	0.10 ± 0.08	91	0.11 ± 0.10	.6
RV dilatation	98		95		92		89		.006
None		97 (99)		94 (99)		85 (92)		78 (88)	
Mild		1 (1)		1 (1.1)		5 (5.4)		4 (4.5)	
Moderate		0 (0)		0 (0)		2 (2.2)		6 (6.7)	
Severe		0 (0)		0 (0)		0 (0)		1 (1.1)	
RV base to apex length (cm)	99	6.8 ± 0.91	99	7.4 ± 0.98	98	7.4 ± 0.87	91	7.4 ± 0.96	<.0001
RA dilatation	98		95		92		84		<.0001
None		74 (76)		60 (63)		55 (60)		29 (35)	
Mild		24 (24)		28 (29)		29 (32)		29 (35)	
Moderate		0 (0)		7 (7.4)		8 (8.7)		23 (27)	
Severe		0 (0)		0 (0)		0 (0)		3 (3.6)	
RA systolic area (cm ²)	99	18 ± 4.4	99	19 ± 4.8	98	22 ± 5.9	91	28 ± 8.4	<.0001
Pulmonary valve regurgitation	100		100		100		93		<.0001
None		100 (100)		24 (24)		7 (7.0)		5 (5.4)	
Mild		0 (0)		75 (75)		7 (7.0)		4 (4.3)	
Moderate		0 (0)		1 (1)		86 (86)		5 (5.4)	
Moderately severe		0 (0)		0 (0)		0 (0)		64 (69)	
Severe		0 (0)		0 (0)		0 (0)		15 (16)	
Qualitative RV dysfunction	98		95		96		90		<.0001
None		97 (99)		93 (98)		85 (89)		72 (80)	
Mild		0 (0)		2 (2.1)		7 (7.3)		9 (10)	
Moderate		1 (1)		0 (0)		2 (2.1)		7 (7.8)	
Severe		0 (0)		0 (0)		2 (2.1)		2 (2.2)	
TAPSE	100	2.3 ± 0.45	100	2.2 ± 0.38	100	2.0 ± 0.39	93	1.1 ± 0.25	<.0001
MPI	100	0.28 ± 0.09	100	0.32 ± 0.06	100	0.38 ± 0.15	93	0.82 ± 0.28	<.0001

TV, Tricuspid valve; SD, standard deviation; MV, mitral valve; LV, left ventricular; LA, left atrial; RVSP, right ventricular systolic pressure; RV, right ventricular; RA, right atrial; TAPSE, tricuspid annular plane systolic excursion; MPI, myocardial performance index. *Patients with data available. †For categorical variables, Mantel-Haenszel test of linear trend with increasing TV regurgitation grade; for continuous variables, equivalent test of Pearson correlation coefficient.

tethering distance (Figure E12, A and B; Table 4). RVSP was proportionately higher in higher grades of TR. Lower (worse) TAPSE and higher (worse) MPI were associated with higher TR grade.

DISCUSSION

Study Design

Previous attempts to understand functional TR have focused on patients already exhibiting marked RV

FIGURE 1. TR and RV function. A, Cumulative distribution of TAPSE. Vertical dashed lines represent 95% confidence limits for patients without TR. Arrows point to median value for each TR grade. B, Box and whiskers plot of TAPSE and TR grade. Whiskers represent extreme values, boxes represent the 15th and 85th percentile of values, + sign represents the mean, and horizontal bar represents the median values. C, Cumulative distribution of MPI. Format is as in A. D, Box and whiskers plot of MPI and TR grade. Format is as in B. TR, Tricuspid regurgitation; RV, right ventricular.

enlargement²² or important TR.⁴ This approach presumes a mechanism for functional TR: RV dilatation. This study, in contrast, has taken a quasi-experimental approach, examining the entire spectrum of right-sided heart morphology and function in patients with no, mild, moderate, and severe TR. We were careful not to include patients with structural TV disease, intrinsic RV disease, or evidence of coronary artery disease. Our patients also had a homogeneous left-sided valve lesion: degenerative mitral valve disease with severe mitral regurgitation requiring operation.

Tricuspid Regurgitation and Right Ventricular Morphology and Function

Overall, with these exclusion criteria, 5% of patients undergoing surgery for degenerative mitral valve disease with mitral regurgitation had severe functional TR. The surgical mindset has been that functional TR is caused by changes in RV morphology during systole—size and shape of the annulus, distance from annulus to papillary muscles, and relative displacement of individual papillary muscles. Leaflet

tethering is a consequence of TV and RV dilatation.²³⁻²⁵ This concept of mechanism underlies the choice of repair procedure: annulus size reduction (annuloplasty, ring size), annulus reshaping (rigid vs flexible ring), valve replacement when papillary muscle splaying prevents annulus reduction, and reshaping from making the TV competent. Yet, no single repair technique has proven consistently effective in sustained elimination of functional TR, nor do surgeons believe that TV replacement leads to better prognosis. This study emphasizes associated RV dysfunction, which might not be cured with any TV procedure.

All measures of altered right-sided heart morphology and RV dysfunction, qualitative and quantitative, correlated with the degree of TR. Even so, we were impressed by the poor correlation of routine quantitative measures of the right heart—RA dilatation and RV dilatation and dysfunction—with degree of TR. However, comparing our study with other studies of functional TR^{4,22} revealed several differences. The study populations are defined and selected differently. Our population was defined by

TABLE 3. Patient factors associated with worse right ventricular function

Factor	Coefficient ± SD	P	Reliability (%)*
Lower TAPSE			
Older age†	−0.12 ± 0.0403	.002	77
Higher NYHA‡ functional class	0.28 ± 0.104	.007	45
Larger LA volume index (mL/m ²)§	3.6 ± 1.5	.02	73
Atrial fibrillation	−0.27 ± 0.075	.0003	87
Lower creatinine clearance (mL/min)	0.24 ± 0.093	.009	68
Lower cholesterol (mg/dL)¶	0.036 ± 0.018	.04	47
Higher MPI			
Older age#	0.18 ± 0.041	<.0001	66
Increased heart rate (beats/min)**	0.13 ± 0.055	.02	70
Larger LA systolic area (cm ²)††	−7.7 ± 3.0	.01	94
Lower creatinine clearance (mL/min)‡‡	0.15 ± 0.044	.0008	80
Lower cholesterol (mg/dL)§§	0.40 ± 0.18	.02	55
Higher MELD score	−0.39 ± 0.092	<.0001	73
Complete heart block	0.38 ± 0.16	.02	61
Smaller LV diastolic volume (mL)¶¶	2.7 ± 1.3	.04	63
Lower hematocrit (%)###	2.7 ± 1.3	.04	63

SD, Standard deviation; TAPSE, tricuspid annular plane systolic excursion; NYHA, New York Heart Association; LA, left atrial; MPI, myocardial performance index; LV, left ventricular; MELD, Model for End-stage Liver Disease; LV, left ventricular. *Percent of time variable appeared in 1000 bootstrap models. †Exp(age/50), exponential transformation. ‡(1/NYHA functional class), inverse transformation. §(1/LA volume index), inverse transformation. ||Ln(creatinine clearance), logarithmic transformation. ¶[(Cholesterol/100)²], squared transformation. #[(Age/50)²], squared transformation. **[(Heart rate/75)²], squared transformation. ††[(1/LA systolic area), inverse transformation. ‡‡[(1/creatinine clearance)²], inverse squared transformation. §§[(100/cholesterol)²], inverse squared transformation. |||[(7/MELD score)²], inverse squared transformation. ¶¶[(1/LV diastolic volume), inverse transformation. ###[(Hematocrit/75)²], squared transformation.

a single diagnosis: degenerative mitral valve disease with severe regurgitation. Fukuda and colleagues⁴ studied patients with severe TR (>2+) accompanying any left-sided heart disease; Kim and colleagues²² studied patients with enlarged RVs with any diagnosis and any degree of TR. In these and the present study, leaflet tethering and dilatation were correlated with degree of TR, yet the weakness of the correlation suggests that the mechanism of TR is multifactorial and variable from case to case. Our study emphasizes the stronger correlation between severe TR and RV dysfunction assessed by the less frequently measured quantities, TAPSE and MPI. Kim and colleagues²² also found a correlation between TR and RV dysfunction using RV fractional area change as a measure of RV function.

TAPSE and MPI are considered standard assessment tools for RV function.²⁶ TAPSE is easily measured and reflects longitudinal excursion occurring during systole and has been validated as a measure of systolic RV function.^{7,9,27} It is more highly correlated with magnetic

TABLE 4. Left- and right-sided heart morphology and right and left ventricular function associated with higher grade of preoperative tricuspid valve regurgitation

Factor	Coefficient ± SD	P	Reliability (%)*
Morphology			
Smaller LV end-systolic volume (mL/m ²)†	−0.47 ± 0.22	.03	67
Larger RA area in systole‡	0.64 ± 0.17	.0002	85
Longer TV tethering distance (cm)§	0.74 ± 0.28	.008	82
Function			
Higher RVSP (mm Hg)	0.042 ± 0.0088	<.0001	99
Worse TAPSE	−7.1 ± 1.3	<.0001	96
Worse MPI¶	5.1 ± 0.92	<.0001	100
Interaction: TAPSE · MPI#	−3.9 ± 1.2	.0009	

SD, Standard deviation; LV, Left ventricular; RA, right atrial; TV, tricuspid valve; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion; MPI, myocardial performance index. *Percent of time variable appeared in 1000 bootstrap models. †(LV end-systolic volume/75)², squared transformation. ‡(RA area in systole/20)², squared transformation. §Log(TV tethering distance), logarithmic transformation. ||Log(TAPSE), logarithmic transformation. ¶Log(MPI), logarithmic transformation. #Interaction: log(TAPSE) · log(MPI).

resonance imaging–derived volumes²⁸ and radionuclide ejection fraction²⁹ than other previously described more complex measures, such as change in RV area during systole.^{9,30,31} MPI comprises energy-dependent periods of contraction, ejection, and relaxation.¹² RV isovolumetric relaxation time is prolonged with diastolic dysfunction, and isovolumetric contraction and ejection times increase with systolic dysfunction. MPI is correlated with invasive hemodynamic measures of RV function^{32,33} and ejection fraction by ventriculography.

TR is more than a simple consequence of RV dilatation. Unlike the linear relation of RVSP with increasing TR grade, there was a stepwise worsening of RV function, as reflected by TAPSE and MPI, from TR grade 2+ or less to severe 3+/4+. A threshold seems to exist above which severe TR did not occur without RV dysfunction. TAPSE and MPI were complementary: As TAPSE became abnormal, there was not much variation among the values; in contrast, MPI exhibited wide variation among abnormal values.

LV dysfunction has also been proposed as a mechanism for producing functional TR through interventricular septal interaction causing RV dysfunction.³⁴ In this study, we observed a reversed interaction in that the severe TR was associated with smaller LV end-diastolic volume, suggesting interventricular dependence with septal shift toward the left from high right-sided filling pressure and RV volume overload.

Clinical Implications

The strong correlation between TR and RV dysfunction has clinical implications beyond surgical technique and focuses attention on the indication for and timing of surgery,

postoperative management, and prognosis. It suggests that earlier surgery should be performed before RV function deteriorates. Surgeons must also develop greater awareness of the implications of RV dysfunction in postoperative management. TV repair might be of little help if the RV has limited capacity to take advantage of a competent valve. Such a scenario offers an explanation for TR as a predictor of early and late mortality in patients undergoing operation for left-sided heart disease.^{1,2}

Limitations

Severity of TR was evaluated qualitatively and not quantified; however, all clinical readers were using standard American Society of Echocardiography grading criteria. We did not assess intra- or interobserver variability in estimating severity of TR, but accepted the readings used for clinical decision-making. Although it is asserted that TAPSE and MPI are afterload and preload independent, we cannot discount the possibility that with severe TR, these measures may not solely reflect intrinsic RV function, making the correlations artificially stronger. Studies of RV strain and 3-dimensional echocardiography may enhance understanding the complex relationship between RV function and TR. Response to surgery is presented in a companion article.

CONCLUSIONS

Functional TR is associated with proportional changes in right-sided heart morphology; however, severe TR is nearly always associated with RV dysfunction, suggesting a synergistic relationship. RV dysfunction is likely to be as important as TR because it offers a credible explanation for the negative prognostic impact of TR and has implications for the clinical management of patients. Better evaluation of RV function requires adding quantitative echocardiographic measures, such as easily measured TAPSE and MPI, to preoperative assessment of these patients.

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APPENDIX TABLE 1. Variables used in statistical analyses

Patient	
Demographic	Age (y), gender, weight (kg), height (cm), body surface area (m ²), BMI (kg/m ²)
Symptoms	NYHA functional class (I–IV)
Valve pathology	Mitral valve regurgitation, aortic valve regurgitation
Coronary anatomy	Left main trunk disease (% stenosis), left anterior descending coronary artery system disease (maximum % stenosis), right coronary artery system disease (maximum % stenosis), left circumflex coronary artery system disease (maximum % stenosis)
Cardiac comorbidity	Atrial fibrillation, hypertension, history of cardiac disease, complete heart block/pacer, ventricular arrhythmia
Heart hemodynamics	Mean arterial pressure (mm Hg), central venous pressure (cmH ₂ O), heart rate (beats/min)
Noncardiac comorbidity	Treated diabetes, insulin-treated diabetes, peripheral arterial disease, history of smoking, carotid disease, popliteal disease, creatinine (mg/dL), blood urea nitrogen (mg/dL), bilirubin (mg/dL), creatinine clearance (mL/min), hematocrit (%), glomerular filtration rate (mL/min), history of renal disease, previous stroke, MELD score
Experience	Date of operation (years since January 1, 2001)
Left heart	
Ventricle	
Morphology	Inner diameter in diastole (cm), inner diameter in systole (cm), diastolic volume (mL), systolic volume (mL), diastolic volume index (mL/m ²), systolic volume index (mL/m ²), dilated left ventricle, mass (g), mass index (g/m ²), posterior wall thickness (cm), septal thickness (cm)
Function	Fractional shortening, ejection fraction (%), relative wall thickness (wall stress), LV dysfunction (grades: none, mild, mild to moderate, moderate, moderate to severe, severe)
Atrium	
Morphology	LA diameter (cm), volume (mL), volume index (mL/m ²), and systolic area (cm ²)
Right heart	
Ventricle	
Morphology	Qualitative RV dilatation (none, mild, moderate, severe) and base to apex length (cm), TV tethering distance (cm) and area (cm ²)
Function	Qualitative RV dysfunction (none, mild, moderate, severe), systolic pressure (mm Hg), TAPSE (cm) and MPI, TV diameter shortening (cm) and fractional shortening
Atrium	
Morphology	Qualitative RA dilatation (none, mild, moderate severe) at end systole (cm ²)

BMI, Body mass index; NYHA, New York Heart Association; MELD, Model for End-stage Liver Disease; LV, left ventricular; LA, left atrial; RV, right ventricular; TV, tricuspid valve; TAPSE, tricuspid annular plane systolic excursion; MPI, myocardial performance index; RA, right atrial.

FIGURE E1. Consolidated Standards of Reporting Trials–type diagram showing study design and patient population. *TR*, Tricuspid regurgitation.

FIGURE E2. Transthoracic echocardiographic assessment of right-sided heart morphology using the apical 4-chamber view. A, RA systolic area shaded. B, RV base-to-apex length. C, TV tethering distance in systole. D, TV tethering area in systole (shaded). *RV*, Right ventricle; *LV*, left ventricle; *RA*, right atrium; *LA*, left atrium.

FIGURE E3. Transthoracic echocardiographic assessment of RV function: TAPSE. A, Annulus plane at end diastole (*dotted line*). B, TAPSE is measured at end systole. *Arrow* shows movement of tricuspid annular plane from end diastole to end systole. *RV*, Right ventricular.

FIGURE E4. Transthoracic echocardiographic assessment of RV function: MPI. Schematic representation of Doppler intervals for calculating MPI. $MPI = (C+R)/E$, calculated by measuring the interval between cessation and onset of flow across TV and pulmonary valve ejection time. *C*, Iso-volumetric contraction time; *R*, isovolumetric relaxation time; *E*, pulmonary ejection time; *TV*, tricuspid valve; *PV*, pulmonary valve.

FIGURE E5. TV annular shortening. TV plane in diastole is shown as *a* and in systole as *b*. *RV*, Right ventricle.

FIGURE E6. Box and whiskers plot of RVSP and TR grade. *Whiskers* represent extreme values, *boxes* represent the 15th and 85th percentile of values, + sign represents the mean, and *horizontal bar* represents the median values. *RVSP*, Right ventricular systolic pressure; *TR*, tricuspid regurgitation.

A

B

C

FIGURE E7. Bubble plots of qualitative clinical assessment of right-sided heart morphology and function associated with TR grade. Area of bubble corresponds to number of observations. A, RA dilatation grade. B, RV dilatation grade. C, RV dysfunction grade. *TR*, Tricuspid regurgitation.

FIGURE E8. Box and whiskers plots of right-sided heart morphology and TR grade. Format is as in Figure E6. A, RA systolic area. B, TV tethering distance. RA, Right atrial; TR, tricuspid regurgitation.

FIGURE E9. MPI and right-sided heart morphology. A, Scattergram of MPI and RA systolic area. Loess smoother shown as solid lines. B, Scattergram of MPI and TV tethering distance. RA, Right atrial; TV, tricuspid valve.

FIGURE E10. Scattergram of TAPSE and MPI. Loess smoother shown as solid lines. *TV*, Tricuspid valve.

A

B

FIGURE E12. Nomogram based on multivariable equation (analysis 2 in Table 4) relating percentage of patients in TR grades 3+/4+ to right-sided heart morphology. A, RA systolic area. B, Tethering distance. *TR*, Tricuspid regurgitation; *RA*, right atrial.

FIGURE E11. Three-dimensional perspective graph of TR grade, MPI, and TAPSE. *TR*, Tricuspid regurgitation; *MPI*, myocardial performance index; *TAPSE*, tricuspid annular plane systolic excursion.