



Impact of Concomitant Tricuspid Annuloplasty on Tricuspid Regurgitation, Right Ventricular Function, and Pulmonary Artery Hypertension After Repair of Mitral Valve Prolapse

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ABSTRACT

BACKGROUND For patients undergoing mitral valve (MV) repair, the indications for and results of concomitant tricuspid annuloplasty remain controversial.

OBJECTIVES This study was designed to compare a strategy of routine concomitant tricuspid annuloplasty for moderate tricuspid regurgitation (TR) or tricuspid annular dilation in patients undergoing degenerative MV surgery.

METHODS Of 645 consecutive patients (mean age 57 ± 13 years) undergoing primary repair of degenerative mitral regurgitation between 2003 and 2011, 419 (65%) underwent concomitant tricuspid annuloplasty for moderate TR and/or tricuspid annular dilation. These patients were retrospectively analyzed with longitudinal echocardiographic follow-up.

RESULTS Patients undergoing tricuspid valve repair were older (mean age 59.2 years vs. 52.3 years), had worse right and left ventricular function and higher pulmonary artery pressures, and were more likely to have had atrial fibrillation than patients undergoing isolated MV repair (all $p < 0.05$). No significant difference in 30-day mortality, morbidity, or permanent pacemaker requirement was seen between treatment groups. Freedom from moderate TR at 7 years was not significantly different in the 2 groups, but multivariate analysis showed that tricuspid annuloplasty was independently associated with freedom from late moderate TR ($p = 0.04$), and was an independent predictor of recovery of right ventricular function ($p = 0.02$).

CONCLUSIONS In patients with moderate TR or tricuspid annular dilation who were undergoing degenerative mitral repair, concomitant tricuspid annuloplasty is safe, effective, and associated with improved long-term right-sided remodeling. Routine treatment of moderate TR or tricuspid annular dilation at the time of MV repair appears to be beneficial. (J Am Coll Cardiol 2015;65:1931-8) © 2015 by the American College of Cardiology Foundation.

For patients with less than severe tricuspid regurgitation (TR) who are undergoing mitral valve (MV) repair, the indications for concomitant tricuspid annuloplasty remain subject to debate, with the reported frequency of concomitant tricuspid valve repair ranging from more than 60% to <6% (1-4). Evidence that MV repair or replacement alone

can improve functional TR (5) has led clinicians to pursue a conservative approach to concomitant tricuspid repair (6). Advocates of a more aggressive strategy point to the following: the relatively high incidence of significant TR after isolated MV operation (2,7,8); the adverse impact of TR on long-term mortality (7,9,10), morbidity (9,11), and functional

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**ABBREVIATIONS
AND ACRONYMS****AF** = atrial fibrillation**MV** = mitral valve**PAH** = pulmonary artery
hypertension**RV** = right ventricular**TR** = tricuspid regurgitation

outcome (7); and the safety and efficacy of tricuspid annuloplasty (11-13), particularly compared with the relatively high mortality associated with reoperative surgery for isolated TR. Data on the effect of concomitant tricuspid annuloplasty on progression of TR, ventricular remodeling, and pulmonary artery hypertension (PAH) after degenerative MV repair are lacking.

The aim of this study was to evaluate the outcomes of a strategy of routine concomitant tricuspid annuloplasty for moderate TR or significant annular dilation in patients undergoing surgical treatment of a degenerative MV.

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METHODS

STUDY POPULATION. We retrospectively analyzed 646 consecutive patients with mitral regurgitation secondary to degenerative disease who underwent MV repair by a single surgeon (D.H.A.) at Mount Sinai Medical Center (New York, New York) between 2003 and 2011. One patient underwent MV replacement after repair complicated by atrioventricular groove hematoma; this patient was excluded from the analysis. All other patients underwent MV repair (99.8% repair rate). Patients with severe 3-vessel coronary artery disease, and patients who required concomitant aortic valve replacement or reoperative surgery were excluded from the analysis, to reduce the number of potential major confounders. Degenerative MV disease was defined as Carpentier type II mitral regurgitation resulting from chordal elongation or chordal rupture with excess leaflet motion. Barlow disease was defined by the presence of multisegment prolapse in a large valve; fibroelastic deficiency as the presence of single segment prolapse in a normal-sized valve; and forme fruste as valves sharing characteristics of both these etiologic factors. Connective tissue disorders were diagnosed pre-operatively on the basis of established diagnostic criteria. The research protocol was approved by the Icahn School of Medicine at Mount Sinai Institutional Review Board and was compliant with Health Insurance Portability and Accountability Act regulations and the ethical guidelines of the 1975 Declaration of Helsinki. The approval included a waiver of informed consent and a request to access data of decedents.

Indications for tricuspid valve repair were as follows: 1) the presence of moderate TR on either the pre-operative or the pre-bypass echocardiogram (whichever was the greater grade); 2) significant annular dilation assessed on pre-bypass echocardiography at end-diastolic diameter in the 4-chamber

view as an annulus >40 mm; or 3) in the case of equivocal findings, on the basis of direct assessment, intraoperative saline testing, and comparison of the anterior and posterior leaflet surface area with the annulus size (14) (Online Figure 1).

Patients undergoing tricuspid annuloplasty (65%; n = 419) received ring sizes ranging from 24 to 34; 83% of whom received a ring size of 28 or smaller. The tricuspid valve was evaluated directly via a right atriotomy for a mismatch between the leaflet surface area and the annulus size, when echocardiographic findings were equivocal and additional risk factors were present (e.g., atrial fibrillation [AF], PAH, or right ventricular [RV] dysfunction), as found in 301 patients (47%). Of this group, 221 underwent tricuspid annuloplasty. Techniques of tricuspid valve and MV repair have been previously described in detail (14). The tricuspid ring was sized according to the combined surface area of the posterior and anterior tricuspid leaflets extended using a right-angle hook and implanted with simple, interrupted mattress sutures sparing the septal annulus and conduction tissue in the region of the apex of the triangle of Koch.

DATA COLLECTION AND FOLLOW-UP. Operative mortality was defined as any death within 30 days or at any time during the same hospital stay. Post-operative morbidity was defined as stroke, new-onset renal failure, ventilation or reintubation for >72 h, new requirement for permanent pacemaker, surgical re-exploration, and deep sternal wound infection or sepsis. Pre-operative RV function was assessed qualitatively, mainly on the basis of wall motion abnormality and ventricular dilation by echocardiography pre-operatively or, if that was not available, by pre-bypass transesophageal echocardiography. Mitral regurgitation and TR were graded according to guideline-recommended standard quantitative and semiquantitative methods as none, mild, moderate, or severe (15). Pre-operative and pre-discharge echocardiography was obtained for all patients, of whom 85% (n = 535) also had post-discharge echocardiography available. A total of 1,432 echocardiograms were included in the analysis. Mean follow-up was 3.7 years (range 0.1 to 8.4 years). The earliest echocardiogram on which moderate or greater TR was indicated for each patient was used to designate recurrent TR. Post-operative RV function was defined as normal or decreased on the basis of the latest report available for each patient; mild, moderate, or severe dysfunction was grouped as decreased RV function. Survival data were obtained for all patients; for documented U.S. patients, this occurred by cross matching each patient's Social Security number with the Web-based Social Security death index.

DATA ANALYSIS. Continuous variables are expressed as mean ± SD. Categorical variables are presented as proportions. Differences between groups were evaluated using the chi-square test or Fisher exact test for categorical variables and independent samples Student *t* test or the Mann-Whitney *U* test for continuous variables. Paired samples Student *t* test was used to compare continuous variables with different follow-up occasions. The cumulative probability of survival, recurrent TR (defined as moderate or greater), and RV recovery were each estimated using the Kaplan-Meier method, and the predictors for each event were identified using Cox proportional hazards regression analysis. The proportional hazards assumption was met in all models. The predictors of post-operative mortality and morbidity were analyzed using logistic regression analysis. The variables with *p* value <0.25 in univariate analysis were entered into the final multivariate model. Results are presented as hazard ratios (HRs) or odds ratios (ORs) with corresponding 95% confidence intervals (CIs). All tests were 2-tailed. A *p* value <0.05 was considered to be statistically significant. The statistical analysis was performed using the Statistics Package for Social Sciences Statistics for Windows, version 19.0 (IBM Corporation, Armonk, New York).

RESULTS

Baseline patient characteristics and operative information are summarized in **Table 1**. Patients undergoing concomitant tricuspid repair tended to be older (mean age 59.2 years [19 to 90 years] vs. 52.3 years [16 to 84 years]), with worse baseline left ventricular and RV function and higher pulmonary artery pressures, and they were almost twice as likely to have a history of AF compared with patients in the isolated mitral valve group (all *p* < 0.05).

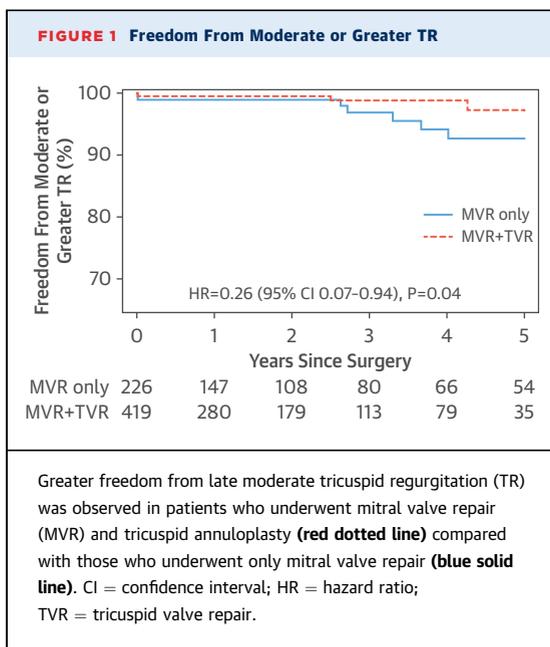
Overall operative mortality was 0.6% (*n* = 3 [75, 79, and 85 years of age] died in the hospital, and a fourth patient died suddenly of unknown causes 2 weeks post-discharge after an otherwise routine post-operative course). Tricuspid annuloplasty was not found to be associated with significantly increased operative mortality or morbidity in univariate analysis (*p* = 0.49) or multivariate analysis (*p* = 0.6). Specifically, there was no significant difference in implantation rate of permanent pacemakers post-operatively between the tricuspid annuloplasty group (2.4%; *n* = 10) and the control group (1.3%; *n* = 3) in either univariate analysis (*p* = 0.56) or multivariate analysis (*p* = 0.62). Seven-year survival for the tricuspid annuloplasty group was 91 ± 5% versus 97 ± 2% for the isolated mitral repair group (*p* = 0.1).

TABLE 1 Characteristics of Patients With Degenerative Disease

	All Patients (n = 645)	Mitral Repair (n = 226)	Mitral and Tricuspid Repair (n = 419)	<i>p</i> Value
Patient characteristics				
Age, yrs	57.0 ± 13.2	52.3 ± 13.5	59.2 ± 12.3	<0.001
Female	236 (36.6)	93 (41.2)	143 (34.1)	0.077
Body surface area, m ²	1.90 ± 0.24	1.93 ± 0.23	1.88 ± 0.26	0.099
Hypertension	296 (45.9)	82 (36.3)	214 (51.1)	<0.001
Hypercholesterolemia	166 (25.7)	53 (23.5)	113 (27.0)	0.330
Diabetes mellitus	20 (3.1)	10 (4.4)	10 (2.4)	0.154
Coronary artery disease	77 (11.9)	28 (12.4)	49 (11.7)	0.795
Renal failure	2 (0.3)	0 (0)	2 (0.5)	0.298
Stroke	16 (2.5)	2 (0.9)	14 (3.3)	0.056
Etiology of mitral regurgitation				
Barlow disease	206 (31.9)	72 (31.9)	134 (32.0)	0.975
Forme fruste	137 (21.1)	49 (21.2)	88 (21.0)	0.944
Fibroelastic deficiency	299 (46.5)	104 (46.5)	195 (46.5)	0.985
Marfan syndrome	3 (0.5)	1 (0.4)	2 (0.5)	0.951
Echocardiographic parameters				
LV ejection fraction	60.7 ± 7.5	61.5 ± 6.9	60.2 ± 7.7	0.032
LV end-systolic diameter, mm	35.6 ± 6.7	34.7 ± 6.9	36.0 ± 6.6	0.011
Pulmonary artery systolic pressure, mm Hg	35.7 ± 14.0	31.8 ± 12.3	37.6 ± 14.4	<0.001
Atrial fibrillation	121 (18.8)	26 (11.5)	95 (22.7)	<0.001
Right atrium area, cm ²	18.8 ± 6.4	16.2 ± 3.6	20.4 ± 7.2	<0.001
Tricuspid annulus diameter, mm	37.8 ± 5.8	35.4 ± 5.5	38.8 ± 5.6	<0.001
RV dysfunction	105 (16.3)	21 (9.3)	84 (20.0)	<0.001
Tricuspid regurgitation grade				
None or trace		133 (58.8)	128 (30.5)	
Mild		93 (41.2)	219 (52.3)	
Moderate		0 (0)	63 (15.0)	
Severe		0 (0)	9 (2.1)	
Surgical details				
Concomitant surgery				
Coronary artery bypass grafts	59 (9.1)	22 (9.7)	37 (8.8)	0.704
Maze procedure	126 (19.5)	27 (11.9)	99 (23.6)	<0.001
Values are mean ± SD or <i>n</i> (%). LV = left ventricular; RV = right ventricular.				

There were no reoperations for recurrent TR during study follow-up.

Freedom from moderate TR at 7 years was 97 ± 2% in the tricuspid annuloplasty group compared with 91 ± 3% in the control group (*p* = 0.07) (**Figure 1**). In subgroup analysis limited to the patients with mild TR, freedom from moderate TR at 7 years was significantly better in the 219 patients who underwent concomitant tricuspid annuloplasty (97 ± 3%) than in the 93 patients who did not (97 ± 3% vs. 83 ± 7%; *p* = 0.004). In Cox proportional hazards regression analysis, tricuspid valve annuloplasty was shown to be an independent predictor of freedom from moderate or greater TR (hazard ratio [HR]: 0.26; 95% confidence interval [CI]: 0.07 to 0.94; *p* = 0.04).



(Table 2). Clinically significant tricuspid stenosis was not observed: the mean post-operative transtricuspid gradient was 2.0 mm Hg, and there was no significant difference between patients who received a ring size of 28 or less (mean gradient 2.1 mm Hg) or those who received a ring size greater than 28 (1.9 mm Hg) (p = 0.24). Type of annuloplasty ring had no significant influence on residual or recurrent TR.

TABLE 2 Determinants of Recurrent TR (Moderate or Greater)

	Univariate		Multivariate	
	p Value	HR	p Value	HR (95% CI)
Age	0.03	1.06	0.01	1.09 (1.02-1.16)
Female	0.31	1.76		
Hypertension	0.17	0.41	0.06	
Diabetes mellitus	0.08	6.87	0.12	
Coronary artery disease	0.12	2.58	0.42	
Etiology (Barlow disease as reference)				
FF	0.42	2.24	0.99	
FED	0.07	4.23	0.26	
LV ejection fraction <60%	0.91	1.07		
LV end-systolic diameter >40 mm	0.22	0.28	0.26	
Pulmonary artery systolic pressures >50 mm Hg	0.45	1.64		
Atrial fibrillation	0.98	1.02		
Tricuspid annulus diameter	0.58	1.06		
Pre-operative RV dysfunction	0.75	1.24		
Tricuspid annuloplasty	0.08	0.345	0.04	0.26 (0.07-0.94)

CI = confidence interval; FED = fibroelastic deficiency; FF = forme fruste; HR = hazard ratio; TR = tricuspid regurgitation; other abbreviations as in Table 1.

Overall freedom from greater than moderate mitral regurgitation in all patients at 7 years was 96 ± 2% and was not different between the treatment groups (p = 0.2). Longitudinal changes in echocardiographic estimates of mean pulmonary artery systolic pressure and right atrium area, as well as the percentage of patients with RV dysfunction, are shown in Figures 2 to 5. In all these parameters, the tricuspid annuloplasty group had worse baseline parameters (all p < 0.001). After tricuspid annuloplasty, pulmonary artery systolic pressure and right atrium area improved significantly by the time of pre-discharge echocardiography (both p < 0.001). It continued to improve during follow-up, so that at midterm follow-up there was no significant difference in these parameters between the 2 groups (p = 0.97 and 0.50, respectively). RV dysfunction initially deteriorated post-operatively in both groups (both p < 0.001). This change was more marked in the tricuspid annuloplasty group, in whom the rate of post-operative RV dysfunction before discharge was almost 70%. During follow-up, however, recovery of RV function occurred more rapidly in the tricuspid annuloplasty group, and by 5 years post-operatively, the proportion of patients with normal RV function was similar in both groups (Figure 5). Tricuspid annuloplasty was the main independent positive predictor of late RV recovery in the subgroup of patients with pre-discharge RV dysfunction (HR: 1.4; 95% CI: 1.06 to 1.96; p = 0.02) (Table 3).

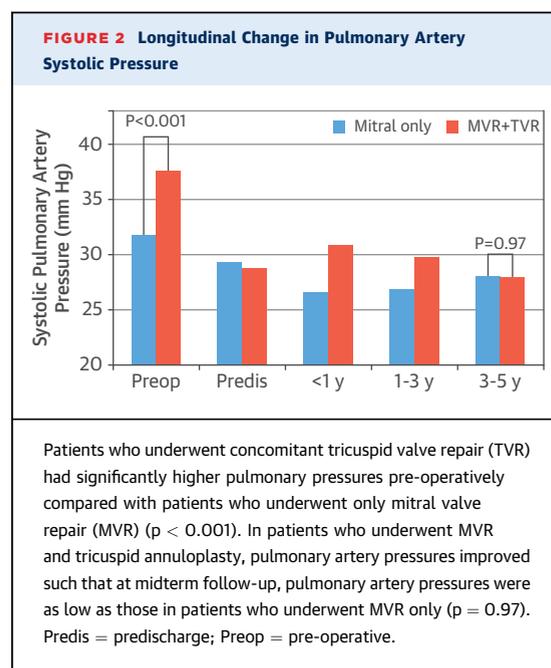
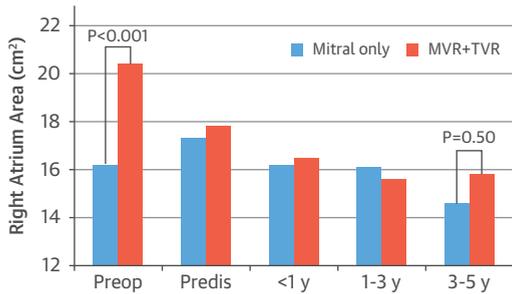
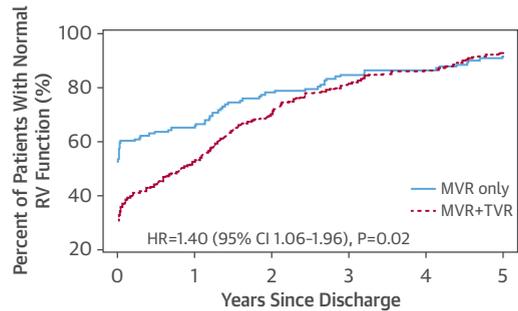


FIGURE 3 Longitudinal Change in Right Atrium Area



Patients who underwent concomitant tricuspid valve repair (TVR) had significantly larger right atria pre-operatively compared with patients who underwent mitral valve repair (MVR) only ($p < 0.001$). In patients who underwent MVR repair and tricuspid annuloplasty, right atrial size decreased to the point that at midterm follow-up, right atrial size was the same as in those patients who underwent MVR only ($p = 0.50$). Abbreviations as in Figure 2.

FIGURE 5 Recovery of RV Function



MVR only	226	48	30	20	18	11
MVR+TVR	419	144	84	49	33	17

The percentage of patients who normalized right ventricular (RV) function after surgical treatment is stratified by the presence of concomitant tricuspid valve repair (TVR) (red dotted line) versus mitral valve repair (MVR) only (blue solid line). Abbreviations as in Figure 1.

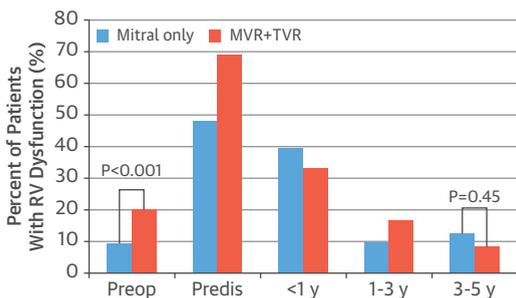
DISCUSSION

This study reveals that a strategy of routine repair of moderate or greater TR or significant annular dilation, or both, at the time of MV repair in patients with degenerative disease (Central Illustration) almost eliminates residual and recurrent TR without incremental risk. Importantly, tricuspid valve repair achieved superior freedom from TR and improved RV

function and PAH in patients with worse baseline risk factors, compared with MV repair only.

POST-OPERATIVE PROGRESSION OF TRICUSPID REGURGITATION. Data on the post-operative course and clinical sequelae of TR are conflicting (2,6,8,11,12,16-22). The reason may be, in part, that most previous studies reported on groups with heterogeneous mitral disease etiology or surgical management. In a study that focused exclusively on patients with degenerative disease who were undergoing isolated

FIGURE 4 Longitudinal Change in the Proportion of Patients With RV Dysfunction

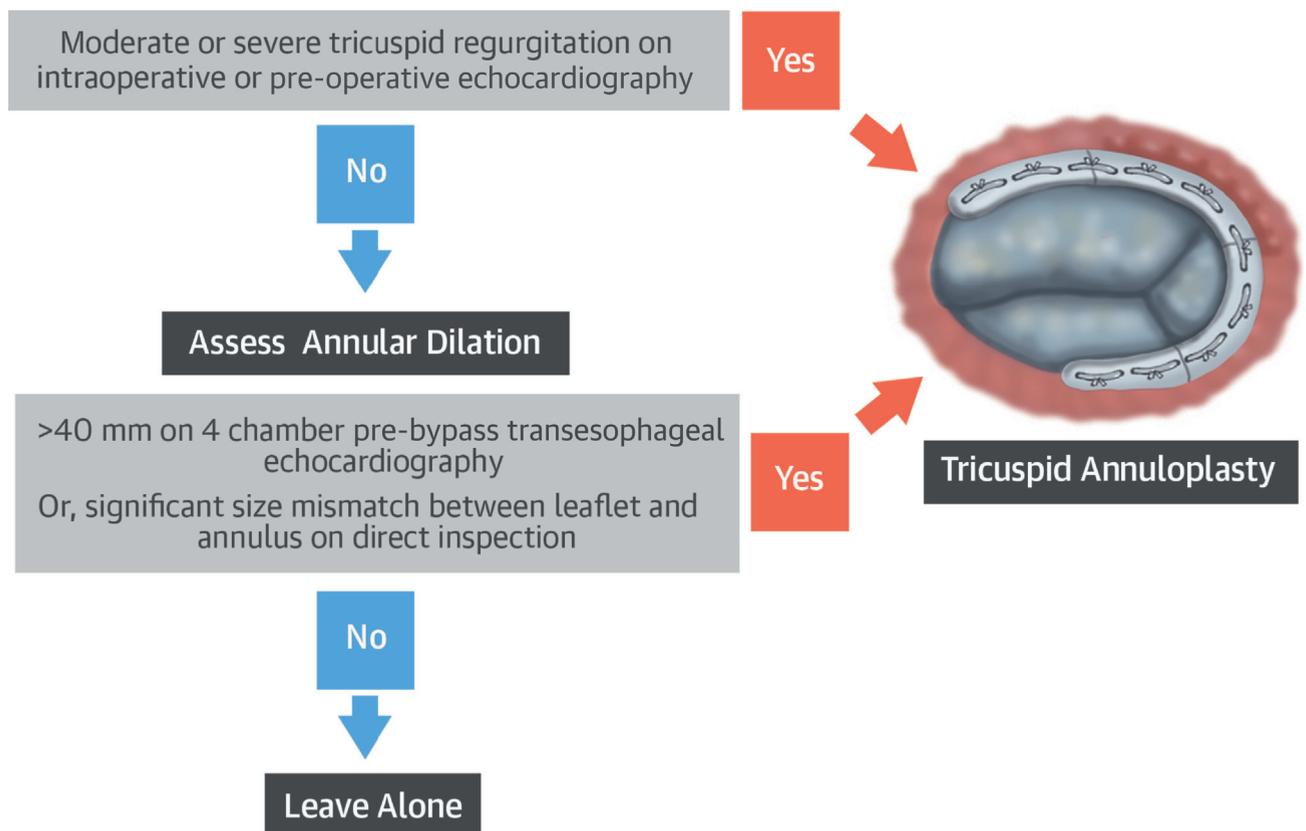


Right ventricular (RV) dysfunction initially deteriorated after surgical treatment in patients who underwent mitral valve repair (MVR) only, as well as in patients who underwent concomitant tricuspid valve repair (TVR) (both $p < 0.001$). During follow-up, recovery of RV function occurred in both groups, and by 5 years post-operatively, the proportion of patients with normal RV function was similar in both groups ($p = 0.45$). Abbreviations as in Figure 2.

TABLE 3 Determinants of RV Function Recovery During Follow-Up

	Univariate		Multivariate	
	p Value	HR	p Value	HR (95% CI)
Age	0.04	0.99	0.16	
Female	0.49	0.91		
Hypertension	0.94	0.99		
Diabetes mellitus	0.97	0.98		
Coronary artery disease	0.06	0.66	0.18	
LV ejection fraction <60%	0.82	0.97		
LV end-systolic diameter >40 mm	0.85	0.97		
Pulmonary artery systolic pressure >50 mm Hg	0.27	0.82		
Atrial fibrillation	0.01	0.64	0.02	0.68 (0.50-0.95)
Tricuspid annulus diameter	0.09	0.98	0.22	
Pre-operative RV dysfunction	0.10	0.76	0.43	
Pre-operative tricuspid regurgitation moderate or more	0.43	0.86		
Tricuspid annuloplasty	0.04	1.38	0.02	1.4 (1.06-1.96)

Abbreviations as in Tables 1 and 2.

CENTRAL ILLUSTRATION Role of Tricuspid Annuloplasty in Mitral Repair

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The indications for and effectiveness of concomitant tricuspid annuloplasty in patients with less than severe tricuspid regurgitation who are undergoing mitral valve repair remain under debate. Patients undergoing mitral valve repair who demonstrated the presence of moderate tricuspid regurgitation on either the pre-operative or the pre-bypass echocardiogram had concomitant tricuspid annuloplasty. Those patients who did not have moderate tricuspid regurgitation underwent further assessment of annular dilation to determine the appropriateness of concomitant tricuspid annuloplasty.

MV repair, Yilmaz et al. (6) reported that after a small decrease in TR in the immediate post-operative period, mean TR grade subsequently increased, but by less than a single grade of regurgitation over 5 years, to a mean grade of mild to moderate TR. The investigators concluded that their findings justified a conservative approach to concomitant tricuspid valve repair; their own reported rate of concomitant tricuspid annuloplasty was 7% for patients with degenerative MV disease during the study period. However, by reporting mean TR grade, these investigators understated the risk of post-operative progression of TR observed in their patients, almost one-third of whom had either moderate or severe TR by 5-year follow-up (compared with 16% pre-operatively) (6). Notably, this high prevalence of progressive TR occurred even though the investigators

excluded from their study the patients most at risk of progression of TR (e.g., patients with pulmonary disease, significant RV dysfunction, or right-sided heart failure). As such, their data offer valuable insight into the high rate of progression of untreated TR in patients with degenerative MV disease.

CLINICAL SIGNIFICANCE OF POST-OPERATIVE TRICUSPID REGURGITATION. Moderate TR is not benign. It appears to be a predictor of reduced survival independent of PAH or RV and left ventricular dysfunction (10); additionally, it has been shown to be an independent risk factor for decreased functional outcome and survival after mitral repair (7). Although it is possible that TR is simply a more sensitive marker of RV dysfunction (which may be underestimated by reliance on echocardiographic assessment of RV contractility, particularly in the

presence of tricuspid valve insufficiency), this may not be the whole story. In a detailed quantitative echocardiographic analysis of pre-operative patients with a degenerative MV, a “synergistic relationship” between TR and RV dysfunction was described (23). Our findings are consistent with those of Desai et al. (24), who reported sustained improvement in RV function after MV surgery with concomitant tricuspid repair. TR results in progressive abnormalities of right atrial and ventricular structure and function, and this finding may explain why our strategy, designed to eliminate significant TR, resulted in enhanced long-term remodeling of both the right ventricle and the right atrium in patients who had impaired baseline characteristics.

Thus, the results of this investigation confirm current guideline recommendations for routine tricuspid valve repair for mild, moderate, or greater functional TR with tricuspid annular dilation at the time of MV repair (25).

STUDY LIMITATIONS. This is an analysis of a relatively large cohort of patients undergoing repair of a degenerative MV with comprehensive echocardiographic follow-up, providing an insight into RV remodeling, TR grade, and PAH. The main limitations of this study stem from its retrospective nature. Although multivariate analysis was used to adjust for RV dysfunction and PAH, among other variables, we could not account for other potential confounders, such as intraoperative myocardial protection or variation in the performance and interpretation of echocardiograms performed outside our institution. Specifically, because of the lack of a consistently used standardized grading system, RV function was classified as normal or decreased on the basis of qualitative reports; we could not quantify the degree of dysfunction or reliably distinguish among mild, moderate, or severe dysfunction—all of which were therefore grouped together as decreased function. Our study does not provide information on the functional sequelae of TR and was not designed to determine differences in long-term efficacy of the different annuloplasty techniques employed. However, it does provide new evidence supporting the benefits of eliminating TR from patients undergoing repair of a degenerative MV.

CONCLUSIONS

TR can be nearly eliminated by a strategy of routine ring annuloplasty at the time of MV repair in patients with moderate TR or tricuspid annular dilation, without adverse clinical consequences and with evidence of enhanced long-term right-sided remodeling. Further, in patients with risk factors for post-operative TR, such as AF, PAH, or RV dysfunction, and equivocal echocardiographic findings, our data support a strategy of direct intraoperative evaluation of tricuspid annular dilation.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Routine tricuspid annuloplasty at the time of MV repair in patients with moderate tricuspid regurgitation or tricuspid annular dilatation minimizes the long-term risk of developing TR and may enhance long-term right-sided remodeling.

COMPETENCY IN PATIENT CARE: Routine treatment of moderate TR or tricuspid annular dilation at the time of MV repair appears to be beneficial. Direct intraoperative evaluation of the tricuspid annulus can be useful when echocardiographic findings are equivocal.

TRANSLATIONAL OUTLOOK: Studies of larger numbers of patients undergoing MV repair are necessary to establish whether routine tricuspid valve annuloplasty improves survival and reduces the likelihood of late tricuspid valve reoperation.

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KEY WORDS annular, dilation, remodel

APPENDIX For a flow diagram showing the distribution of patients in each study arm, please see the online version of this article.