

## Fate of functional tricuspid regurgitation in aortic stenosis after aortic valve replacement

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**Objective:** Functional tricuspid regurgitation (TR) is found not infrequently in conjunction with aortic stenosis. The aim of the present study was to evaluate the changes in TR and to identify the predictors of late progression after aortic valve replacement.

**Methods:** We evaluated 354 patients who had undergone aortic valve replacement for aortic stenosis from January 1995 to December 2009. Patients with mitral regurgitation were excluded. Of the 354 patients, 54 had TR greater than mild. The mean follow-up duration was  $4.4 \pm 4.3$  years (maximum, 15). The serial echocardiographic and clinical data were analyzed.

**Results:** No early mortality occurred, and the late cardiac mortality rate was 3.9% (14 of 354). In the 48 patients with TR greater than mild, TR did not improve in 23 (49.1%) during the follow-up period. Freedom from cardiac mortality at 10 years was lower in those with TR greater than mild than in patients without TR ( $61.6\% \pm 16.7\%$  vs  $93.0\% \pm 2.9\%$ ,  $P = .008$ ). Left ventricular diastolic function correlated with right ventricular systolic pressure ( $P < .001$ ) and the degree of TR during follow-up ( $P = .001$ ). Multivariate analysis showed that postoperative atrial fibrillation (odds ratio, 6.8;  $P = .001$ ) and the aortic transprosthetic mean pressure gradient (odds ratio, 1.1;  $P = .028$ ) predicted late TR greater than mild.

**Conclusions:** Not only did TR in patients with aortic stenosis frequently persist after aortic valve replacement, it was progressive in some. This finding was associated with left ventricular diastolic dysfunction. A concomitant tricuspid valve procedure could be considered in selected patients with aortic stenosis to avoid late TR. (*J Thorac Cardiovasc Surg* 2014;148:1328-33)

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Functional tricuspid regurgitation (FTR) is common in patients with left-sided valve disease, and its development has been associated with increased morbidity and mortality after surgery.<sup>1,2</sup> Several studies have reported on the risk factors related to FTR and its prognostic implications.<sup>3-5</sup> Recently, guidelines have been issued for the management of FTR; however, the indications and optimal strategy have remained controversial.<sup>6-8</sup> Most studies have been confined to tricuspid regurgitation (TR) associated with mitral valve disease, because this is more common than TR associated with aortic stenosis.

In patients with aortic stenosis, TR is frequently a manifestation of right ventricular failure and a generalized distortion of ventricular geometry, especially in the setting of pulmonary hypertension and atrial fibrillation.<sup>9</sup> Whether management of FTR associated with aortic stenosis should be undertaken just as is done for TR in mitral valve disease has not been determined, because its clinical significance and natural history are unknown. Because aortic valve replacement (AVR) for aortic stenosis is the most frequently performed surgery for valvular heart disease, FTR associated with aortic stenosis at AVR deserves the same careful consideration as FTR associated with mitral valve disease.

Our goals in the present study were to observe the changes in TR in those with aortic stenosis after AVR and its clinical effects. We also tried to identify the predictors for late progression of TR during the follow-up period.

### METHODS

#### Patients

We reviewed the data from 448 consecutive patients with aortic stenosis who had undergone AVR from January 1995 to December 2009. Of the 448 patients, we excluded those with rheumatic aortic stenosis, combined mitral valve disease and/or tricuspid valve disease requiring valve procedures, and coronary artery disease. Patients with a history of cardiac surgery were also excluded; thus, 354 patients were enrolled. Of the 354 patients, 54 had FTR greater than mild (TR group) and 300 had no or trivial FTR (no-TR group). Our institutional review board approved the present

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### Abbreviations and Acronyms

AVR	= aortic valve replacement
FTR	= functional tricuspid regurgitation
NYHA	= New York Heart Association
TMPG	= transprosthetic mean pressure gradient
TR	= tricuspid regurgitation

study and waived the requirement for individual consent from the patients or relatives.

### Operative Technique

AVR was performed using standard cardiopulmonary bypass with bicaval cannulation. The basic surgical procedures and principles of AVR have been previously described and were maintained throughout the present study.<sup>10</sup> Antegrade and retrograde blood cardioplegia were used for myocardial protection. Retrograde blood cardioplegia was infused by direct coronary sinus cannulation. Spaghetti or pledgeted 2-0 sutures were placed in a horizontal mattress fashion. The types of prostheses used were determined by surgeon preference. Modified ultrafiltration was routinely used.

### Follow-up

Standard guidelines were used to define mortality and morbidity.<sup>11</sup> An early event was defined as an event that occurred during the initial hospitalization (including >30 days), and all later events were defined as late events. Major adverse valve-related events included any structural or nonstructural prosthesis dysfunction, valve thrombosis, embolism, bleeding events, and prosthetic valve endocarditis. The postoperative outcomes and events after discharge were acquired by reviewing the medical records, by direct telephone interviews with the patients or their families, and from the National Registry of Births and Deaths. Follow-up data were available for 349 of the 354 patients (98.6%). The mean follow-up period was  $4.4 \pm 4.3$  years (maximum, 15).

Transthoracic echocardiography was performed before discharge and at 1, 3, 5, and >7 years after surgery. The left ventricular end-systolic and end-diastolic dimensions were obtained in the parasternal view according to the American Society of Echocardiography guidelines.<sup>12</sup> For 331 of 354 patients (93.5%), echocardiographic assessments were performed not less than 1 year after AVR. Early diastolic mitral inflow and the mitral annular velocity ratio (E'/E) were measured by scanning the tips of the mitral valve leaflets with a pulse-wave Doppler unit. The aortic transprosthetic mean pressure gradients (TMPGs) were calculated using the Bernoulli equation. The degree of TR was assessed using the vena contracta width and the ratio of the maximal jet area to the corresponding right atrial area averaged on the parasternal and apical views. For statistical analysis, TR was graded from 0 to 4. Late FTR was defined as TR greater than mild at any time postoperatively using color-flow Doppler analysis.

### Statistical Analysis

For comparisons between the 2 groups, the  $\chi^2$  test or Fisher exact test was used for categorical variables and the unpaired Student *t* test for continuous variables. Repeated measures analysis of variance was used to compare the values at different measurement points. Cox regression analysis was used to identify the risk factors related to the clinical outcomes and FTR progression. The patients who had undergone tricuspid valve repair were excluded from this Cox regression analysis to remove the effect of valve repair on late FTR. The variables entered into the model were age, gender, New York Heart Association (NYHA) functional class, hemoglobin level, total bilirubin level, effective glomerular filtration rate, diabetes, hypertension, stroke, atrial fibrillation, bicuspid aortic valve, and the

preoperative and postoperative echocardiographic parameters, including indexed the effective orifice area and E'/E. If the *P* value of a variable was <.20 on univariate analysis, the variable was entered into the multivariate analysis model. Survival and cardiovascular event-free curves were constructed to compare cardiac-related mortality and cardiovascular events in the 2 groups. The Statistical Package for Social Sciences, version 18.0 (SPSS, Chicago, Ill), was used for statistical analyses.

## RESULTS

### Patient Baseline Characteristics and Operative Data

The patient profiles are summarized in [Table 1](#). The mean age was 64  $\pm$  10 years (range, 30-85), and the incidence of bicuspid aortic valve was 64.6% (248 of 384). The preoperative transaortic mean pressure gradient was  $58.9 \pm 17.9$  mm Hg, and the E'/E ratio had increased to 15.6. The patients in the TR group had more risk factors and poorer cardiac function preoperatively than those in the no-TR group. More bioprostheses were implanted in the TR group than in the no-TR group, probably because of the age difference between the 2 groups. However, mean valve sizes were similar in the 2 groups. The incidence of bicuspid aortic valve and concomitant procedures was similar between the 2 groups. The operative data are summarized in [Table E1](#).

### Clinical Outcomes

No early mortality occurred; however, 18 patients (5.1%) died late. Furthermore, the cardiac-related mortality rate for all study subjects was 3.7% (13 of 354) and was greater in the TR group than in the no-TR group. The incidence of late morbidity was similar between the 2 groups ([Table 2](#)). No reoperation was performed for tricuspid valve disease during the follow-up period.

The overall cumulative survival rate at 10 years was  $87.6\% \pm 3.5\%$ . The freedom from cardiac-related mortality at 10 years was significantly lower in the TR group ( $P = .008$ ), although no intergroup difference was observed at 5 years ([Figure 1](#)). The age-adjusted cardiac death-free survival at 10 years was also lower in the TR group (hazard ratio, 3.9; 95% confidence interval, 1.2-12.2;  $P = .021$ ). No intergroup difference was found for the freedom from cardiovascular events at 10 years ( $85.4\% \pm 3.5\%$  for the TR group vs  $88.9\% \pm 4.8\%$  for the no-TR group;  $P = .298$ ).

Univariate analysis showed that older age ( $P = .050$ ), preoperative hypertension ( $P = .024$ ), and late FTR greater than mild at late follow-up ( $P = .015$ ) were associated with cardiac-related mortality. Subsequent multivariate analysis showed that preoperative hypertension (hazard ratio, 3.9; 95% confidence interval, 1.2-12.4;  $P = .023$ ) and late TR greater than mild (hazard ratio, 4.2; 95% confidence interval, 1.3-13.5;  $P = .014$ ) were independent predictors of cardiac-related mortality. The preoperative NYHA functional class was the only predictor of cardiovascular events (hazard ratio, 2.083; 95% confidence interval, 1.12-3.87;  $P = .020$ ).

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