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Original article

## Predictors of reversible severe functional tricuspid regurgitation in patients with atrial fibrillation

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### ABSTRACT

**Background:** Atrial remodeling associated with atrial fibrillation (AF) is known to be a risk factor for significant tricuspid regurgitation (TR), but the predictor of reversible TR in patients with severe functional TR and AF has been poorly studied. The aim of this study was to investigate the predictors of reversible TR in patients with severe functional TR and AF.

**Methods:** Among 232 patients with severe TR, a total of 71 patients with severe functional TR and AF were enrolled and divided into 2 groups: reversible TR group ( $n = 16$ ,  $70.1 \pm 15.5$  years, 7 males) vs. non-reversible TR group ( $n = 55$ ,  $72.3 \pm 11.8$  years, 20 males). Improvement of TR to moderate or lesser degree on follow-up (FU) echocardiography was considered as reversible TR in the present study.

**Results:** During  $38.9 \pm 26.7$  months of FU period, reversible TR was observed in 16 patients (22.5%). The presence of left ventricular (LV) systolic dysfunction was significantly prevalent (43.8% vs. 20.0%,  $p = 0.03$ ) and the improvement in LV ejection fraction (EF) more than 10% on FU echocardiography was more significantly frequent (62.5% vs. 23.3%,  $p = 0.003$ ) in the reversible TR group than in the non-reversible TR group. However, the other echocardiographic parameters, including right ventricular function were not different between the groups. In multivariate analysis using Cox proportional hazard model, the improvement of LVEF more than 10% was the only independent predictor of reversible TR (HR = 7.39, 95%CI 1.80–30.28,  $p = 0.005$ ). Nine patients died only in patients with non-reversible TR (12.7%), but the reversibility of TR was not associated with mortality.

**Conclusions:** The improvement of LV systolic function was the only independent predictor of reversible TR. Appropriate medical therapy including management for heart failure should be considered before performing surgery in patients with severe functional TR and AF, especially in patients with LV dysfunction.

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### Introduction

Tricuspid valve (TV) has been regarded as a “forgotten valve” for decades, because tricuspid regurgitation (TR) is usually asymptomatic, not easily detected on physical examination, often

secondary to left-sided heart disease, and controllable by diuretics [1]. However, significant TR is an independent predictor of long-term mortality and increasing severity of TR is associated with poor prognosis regardless of etiology, left ventricular ejection fraction (LVEF), or pulmonary artery pressure [2–4].

Significant TR may develop in the absence of structural abnormalities of the TV and its apparatus, so called functional or secondary TR. TV annular dilatation and/or tricuspid leaflet tethering in association with right ventricular (RV) pressure or volume overload are proposed as pathophysiologic mechanisms of functional TR [5,6]. Functional TR is not uncommon in patients

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with left-sided heart disease or pulmonary hypertension. The incidence of late significant functional TR is reported in up to 40% of the patients who underwent left-sided valve surgery [7]. Atrial fibrillation (AF) is a common arrhythmia in the elderly or patients with structural heart disease. AF usually results in the enlargement of both atria and/or annular dilatation of atrioventricular valves, and these types of atrial remodeling associated with AF are also known to be a risk factor for developing significant functional TR [8,9].

Severe functional TR is associated with poor long-term prognosis, and thus surgery is generally indicated in patients with severe primary or functional TR undergoing left-sided valve surgery in the current guidelines on the management of valvular heart disease [5,6]. Nonetheless, there has been no consensus or established guideline for the timing or indications of surgery for functional TR associated with AF. Because functional TR in association with left-sided valve diseases or various cardiomyopathies may diminish or disappear as the improvement in RV function or underlying causes [10], it would be mandatory to know the natural history or reversibility of severe functional TR associated with AF to avoid the risk of unnecessary valve surgery. However, there has been a lack of data on the natural history or predictors of reversibility of functional TR associated with AF. Therefore, the aim of the present study was to investigate the predictors of reversible TR in patients with severe TR and AF.

## Materials and methods

### Patient population

Between 2005 and 2012, a total of 232 patients ( $67.4 \pm 14.1$  years, 80 males) who were first diagnosed as having severe TR on echocardiography were identified. Among these, 156 patients were excluded and the reasons for exclusion were as follows: no follow-up (FU) echocardiography or inappropriate echocardiographic images for analysis ( $n = 82$ ), prior valve surgery ( $n = 64$ ), intracardiac device implantation ( $n = 14$ ), congenital heart disease ( $n = 9$ ), intrinsic disease of tricuspid valve apparatus such as prolapse or chordae rupture ( $n = 1$ ), acute or chronic cor pulmonale ( $n = 3$ ), thyrotoxicosis ( $n = 1$ ), and rhythms other than AF ( $n = 44$ ). A total of 71 patients with AF with FU echocardiography were finally

enrolled and divided into 2 groups: reversible TR group ( $n = 16$ , 7 males,  $70.1 \pm 15.5$  years) vs. non-reversible TR group ( $n = 55$ , 20 males,  $72.3 \pm 11.8$  years) (Fig. 1). Improvement in TR to moderate or lesser degree on FU echocardiography was considered as reversible TR in the present study. Improvement in LVEF in the present study was defined as more than 10% increase of EF compared to previous examination. No patient spontaneously converted to sinus rhythm during the follow-up period.

### Echocardiographic measurements

Echocardiographic examinations were performed at initial presentation and during FU period. Images were taken while patients were in the left lateral decubitus position. Conventional echocardiographic studies including Doppler studies were performed according to the recommendations of the American Society of Echocardiography (ASE) [11]. Left ventricular end-systolic and end-diastolic dimensions, interventricular septal and posterior wall thicknesses, and left atrial anteroposterior diameter were determined from two-dimensional images. Ejection fraction was calculated using the conventional Teicholz's and biplane Simpson's method. Doppler echocardiograms were recorded on a strip chart recorder with a sweep speed of 100 mm/s. Early transmitral velocity ( $E$  wave) was measured by pulsed-wave Doppler from the apical four-chamber view, with the sample volume located at the tip of the mitral leaflets. Early diastolic ( $e'$ ), late diastolic ( $a'$ ), and systolic ( $s'$ ) velocities at the septal mitral annulus were obtained in this view by tissue Doppler imaging. The  $E$  wave deceleration time (DT) was measured as the time between the peak early diastolic velocity and the point at which the steepest deceleration slope was extrapolated to the zero line.

A severe TR was defined as a TR with a distal jet area  $\geq 10$  cm<sup>2</sup>, vena contracta width greater than 0.7 cm, and systolic flow reversal in hepatic veins according to the current guideline of ASE [12]. Pulmonary artery systolic pressure was assessed by the maximal velocity of the TR jet using a modified version of Bernoulli's equation [13]. Right atrial pressure was estimated as 5 mmHg if the inferior vena cava (IVC) was not dilated ( $< 1.7$  cm) and there was a 50% decrease in the diameter during inspiration, 10 mmHg if the IVC was dilated with normal inspiratory collapse, and 15 mmHg if the IVC was dilated and did not collapse with

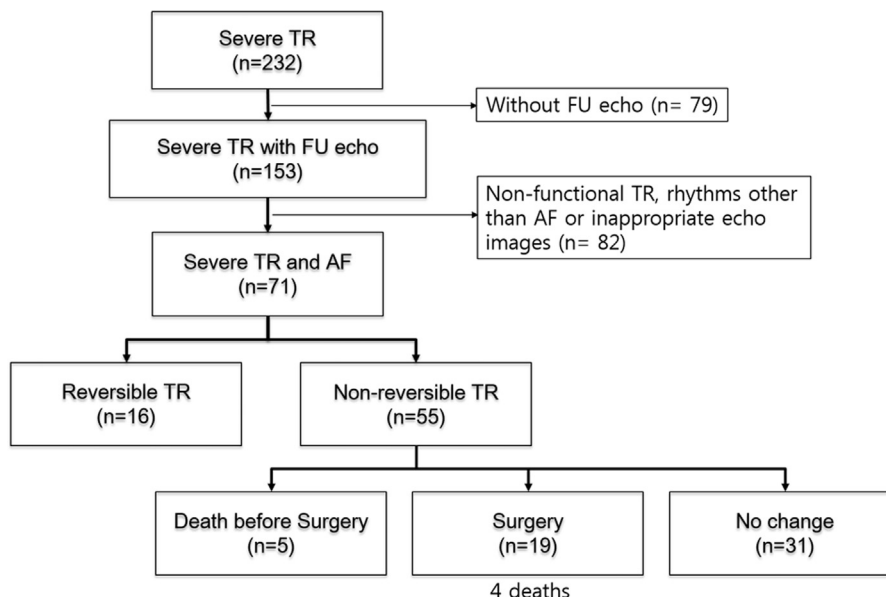


Fig. 1. Study flow and clinical outcomes of the studied patients. TR, tricuspid regurgitation; FU, follow-up; AF, atrial fibrillation.

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