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Risk factors of recurrent tricuspid regurgitation after valve repair with three-dimensional ring

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Objective: The purpose of this study was to investigate the results of tricuspid valve (TV) repair with three-dimensional ring (3DR) and risk factors of recurrent tricuspid regurgitation (TR).

Methods: We retrospectively investigated 171 patients who underwent TV repair with a 3DR for TR from 2007 to 2016 at our institution. The patients were divided into the non-Recurrence group (<2+ TR) and Recurrence group (≥2+ TR), and compared to identify the cause of recurrent TR. The mean follow-up period was 58±35 months.

Results: The preoperative TR grade was 3.0±0.8. A total of 22 patients had at least ≥2+ TR in the follow-up period. Freedom from ≥2+ TR and re-operation at 5 years were 83.6±3.3% and 97.9±2.1%. Comparison of the non-Recurrence and Recurrence groups revealed significant differences in the preoperative TR grade (2.9±0.8 and 3.4±0.6, p=0.008), proportion of the patients with left ventricular ejection fraction (LVEF) <40% (9% and 32%, p=0.003) and right ventricular end-systolic dimension (RVDs, 22.8±7.1 mm and 31.1±12.3 mm, P=0.001). In the multivariate analysis, LVEF <40% (hazard ratio: 12.65, 95% confidence interval: 2.66–60.18; p=0.002) and RVDs (hazard ratio: 1.08, 95% confidence interval: 1.02–1.14; p=0.02) were identified as risk factors for recurrent TR.

Conclusion: Our results of TV repair with 3DR were of satisfactory. However, patients with preoperative lower LVEF and larger RVDs were identified at risk of recurrent TR. This result suggests the limitation to use of 3DR alone for TV repair and need for additional procedure.

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Key words: Tricuspid regurgitation, Tricuspid valve repair, Three-dimensional ring

Introduction

Effort should be made to control tricuspid regurgitation (TR) because moderate or greater TR is associated with worse survival [1]. Superiority of repair over replacement in long-term survival has been well-known [2]. Regarding repair strategy, ring annuloplasty has been demonstrated superior to suture annuloplasty in survival rate and freedom from recurrence and reoperation [3,4]. Recently, the three-dimensional annuloplasty ring (3DR) was developed based on the three-dimensional (3D) tricuspid annular structure [5,6]. The good results of TV repair with a 3DR were reported [7,8] and 3DR has been widely accepted as a first-line strategy. However, a small but certain number of patients showed recurrent TR after TV repair even with a 3DR. In this study, we investigated the outcomes of TV repair with 3DR and the risk factors of recurrent TR.

Material and Methods

Patients

A total of 178 consecutive patients underwent TV repair with a 3DR for primary and secondary TR from Feburary 2007

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to December 2016 at our institution. Of those, 171 patients were retrospectively investigated, with excluding seven patients who underwent "Spiral suspension technique [9]" which consists papillary muscle approximation and suspension, in addition to the 3DR. TV repair was indicated for ≥2+ TR patients in secondary TR and for symptomatic ≥3+ TR in primary TR. Preoperative patient characteristics, etiology of TR, pre-operative and post-operative echocardiographic evaluation, surgical data, and technique were investigated. The patients were divided into two groups (non-Recurrence group and Recurrence group) to identify risk factors for recurrent TR.

Echocardiographic assessment

Transthoracic echocardiography was performed pre- and postoperatively. Postoperative assessment was performed in the following schedule: 1 week, 6 months, 1 year, and on an annual basis thereafter. The TR grade was semi-quantitatively classified by transthoracic echocardiography as grade 0 (none of trace TR), 1+ (mild), 2+ (mild to moderate), 3+ (moderate to severer) and 4+ (severe). Trans tricuspid pressure gradient (PG) was estimated from peak velocity of TR jet as TRPG. Mid right ventricle (RV) was selected in measuring right ventricular end-diastolic dimension (RVDd) and right ventricular end-systolic dimension (RVDs). TV tethering was defined as the leaflet coaptation point located RV side beyond the annular plane in mid systole. In patients with tethering, tethering height was measured as vertical distance between the coaptation point and annular plane, and tethering area, as enclosed area by annular plane and leaflet. Recurrent TR was defined as ≥2+ TR observed in the follow-up period.

Surgical technique

Two types of 3DR (MC3: Edwards Lifesciences, Irvine, CA, USA: 2007–2013; Contour3D: Medtronic, Minneapolis, MN, USA: 2014–2016) were used for annuloplasty.

A total of 137 (80%) and 34 (20%) patients underwent median full sternotomy and anterolateral small right thoracotomy, respectively. All operations were performed on cardiopulmonary bypass. After achieving cardiac arrest and total cardiopulmonary perfusion, mattress sutures with 2-0 polyester were placed on the tricuspid annulus from the anterior part of the anteroseptal commissure to the center of the septal annulus via the posterior annulus. The ring size was decided according to the commissural length of the septal leaflet. Twelve patients (11.7%) underwent tricuspid leaflet repair. Leaflet plication was performed in four patients, edge to edge suture in five patients and neochord reconstruction in six patients.

Statistical analysis

Statistical analyses were performed using the JMP software version 15.0 (SAS Institute Inc., Cary, NC, USA). Data were expressed as the mean±standard deviation and independent continuous data were analyzed using the Mann-Whitney U test. All risk factors were analyzed using the chi-squared test or Fisher's exact test. The Kaplan–Meier method was used to calculate the rate of freedom from recurrent TR. Risk factors for time-related events were analyzed using the Cox proportional hazards ratio. Cox proportional hazard regression analyses were performed to identify the predictors of recurrent 2+ or greater TR. P-values <0.05 denoted statistically significant differences.

Results

Preoperative characteristics

Preoperative characteristics is summarized in Table 1. The mean age was 69.8±10.0 years. Of the patients, 74 were males (43%). No significant difference was observed between non-Recurrence and Recurrence group except the etiology of secondary TR. The percentage of cardiomyopathy was larger in Recurrence group compared to non-Recurrence group (p=0.02).

Operative data

Operative data is summarized in Table 2. The most common concomitant procedure was mitral valve repair (n=105, 61%). Isolated TV repair was performed in eight cases (4%). 142 (83%) patients underwent TV repair using a 26mm ring. The mean ring size was 26.4±0.9 mm. No significant difference was observed between non-Recurrence and Recurrence group.

Postoperative outcome

The rate of operative mortality was 2% (n=4). Three patients expired because of heart failure and one patient expired due to non-occlusive mesenteric ischemia perioperatively. At 1 week after surgery, 164 patients (96%) had <2+ TR. The TR grade was 0.7±0.4.

Follow-up rate was 96% completed. The mean duration of the follow-up was 58±35 months. Overall survival rate and cardiac death-free rate at 5 years were 75.0±3.6% and 86.3±2.9%, respectively (Figure 1). 22 patients (13%) had ≥2+ TR in the follow-up period. Of these, 10 patients (6%) developed 3+ or 4+ TR. The rates of freedom from ≥2+ TR and ≥3+ at 5 years were 83.6±3.3% and 93.6±2.0%, respectively (Figure 2). Two patients required re-operation for recurrent severe TR, who underwent TV replacement at 3 years and 5 years after surgery, respectively. The cause of recurrent severe TR was leaflet tethering resulting from RV dilatation in both patients. The rate of freedom from re-operation was 97.9±2.1% (Figure 3).

Echocardiographic assessment

Preoperative data of transthoracic echocardiography are summarized in Table 3. TR grade, percentage of patients with left ventricular ejection fraction (LVEF) lower than 40%, RVDd and RVDs were significantly larger in Recurrence

Table 1. Preoperative characteristics and echocardiographic data

	Total N=171	Non-Recurrence group, N=149	Recurrence group, N=22	P-Value
Age, years	69.8 ± 10.0	69.7 ± 10.0	70.5 ± 10.0	0.8
Male, n (%)	74 (43)	64 (43)	10 (45)	0.8
Atrial fibrillation, n (%)	129 (75)	116 (78)	13 (59)	0.06
Pulmonary hypertension, n (%)	127 (74)	111 (74)	16 (73)	0.9
NYHA ≥ III, n (%)	98 (57)	82 (55)	16 (73)	0.1
Previous cardiac surgery, n (%)	28 (16)	26 (17)	2 (9)	0.5
Etiology of TR, n (%)				
Primary TR	18 (11)	13 (9)	5 (23)	0.05
Secondary TR	153 (89)	136 (91)	17 (77)	
Simple- left-sided valve disease	126 (82)	118 (87)	8 (47)	0.02
Cardiomyopathy	16 (10)	9 (6)	7 (41)	
Left-to-right shunt disease	10 (7)	8 (6)	2 (12)	
Pulmonary valve disease	1 (1)	1 (1)	0 (0)	

NYHA, New York Heart Association; TR, tricuspid regurgitation

Table 2. Operative data

	Total N=171	Non-Recurrence group, N=149	Recurrence group, N=22	P-Value
Right thoracotomy approach, n (%)	34 (20)	32 (21)	2 (9)	0.3
Cardiopulmonary bypass time, min	176 ± 54	179 ± 53	154 ± 52	0.06
Cross clamp time, min	104 ± 42	106 ± 43	95 ± 37	0.2
Concomitant procedures, n (%)				
Aortic valve replacement	42 (25)	38 (26)	4 (18)	0.6
Mitral valve repair	105 (61)	90 (60)	15 (68)	0.5
Mitral valve replacement	41 (24)	39 (26)	2 (9)	0.1
Coronary artery bypass grafting	18 (11)	18 (12)	0 (0)	0.2
MAZE procedure	46 (27)	42 (28)	4 (18)	0.5
Isolated TV repair, n (%)	8 (4)	6 (4)	2 (9)	0.6
The types of 3DR, n (%)				
MC3 ring	87 (51)	75 (50)	12 (55)	0.7
Contou3D ring	84 (49)	74 (50)	10 (45)	
Ring size, mm	26.4 ± 0.9	26.4 ± 0.9	26.3 ± 0.7	0.6
26 mm, n (%)	142 (83)	123 (83)	19 (86)	
28 mm, n (%)	27 (16)	24 (16)	3 (14)	
30 mm, n (%)	1 (1)	1 (1)	0 (0)	
32 mm, n (%)	1 (1)	1 (1)	0 (0)	

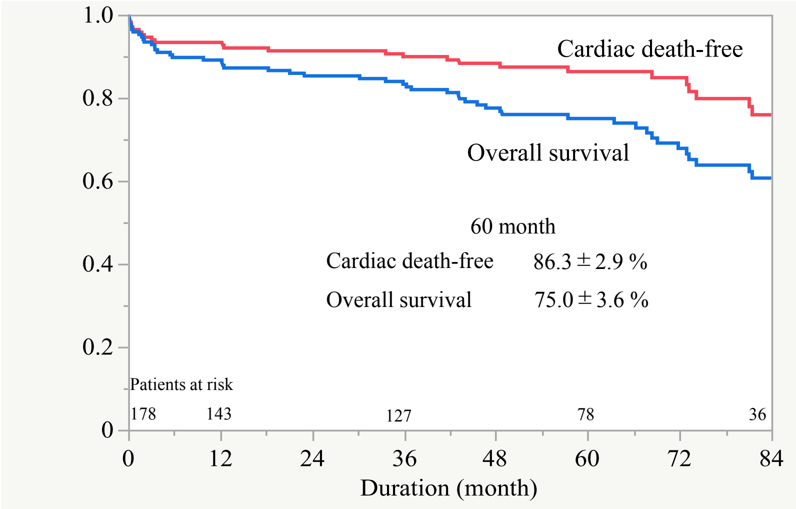

Figure 1. Kaplan–Meier curve of Overall survival rate and Cardiac-death free rate.

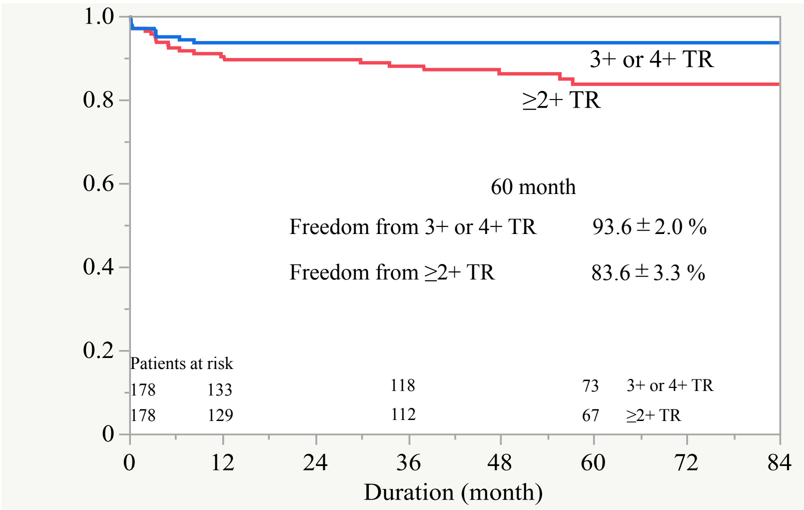

Figure 2. Kaplan–Meier curve of freedom from ≥ 2+ TR and freedom from 3+ or 4+ TR. TR, tricuspid regurgitation

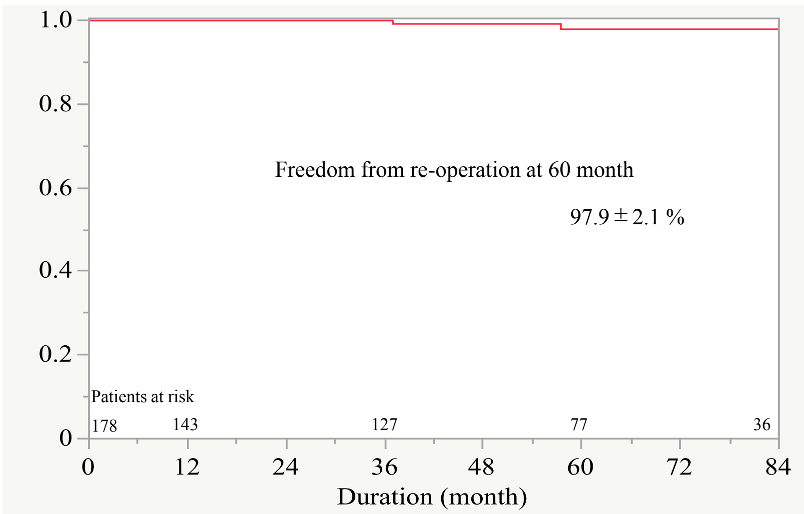

Figure 3. Kaplan–Meier curve of freedom from re-operation.

Table 3. Preoperative echocardiographic data

	Total N=171	Non-Recurrence group, N=149	Recurrence group, N=22	P-Value
TR grade	3.0 ± 0.8	2.9 ± 0.8	3.4 ± 0.6	0.008
LV diastolic dimension, mm	51.3 ± 11.1	50.9 ± 10.6	53.7 ± 14.1	0.5
LV systolic dimension, mm	34.8 ± 11.7	34.4 ± 11.1	38.0 ± 15.6	0.4
Left atrium dimension, mm	52.2 ± 11.6	52.1 ± 11.2	52.7 ± 14.5	0.7
Left ventricular ejection fraction, %	59.8 ± 15.6	60.5 ± 14.7	55.3 ± 21.0	0.6
LVEF < 40%, n (%)	21 (12)	14 (9)	7 (32)	0.003
Right atrium dimension, mm	43.2 ± 7.6	42.0 ± 9.2	50.8 ± 16.7	0.06
RV end-diastolic dimension, mm	32.9 ± 7.6	32.0 ± 6.0	39.6 ± 13.4	0.02
RV end-systolic dimension, mm	24.7 ± 8.2	22.8 ± 7.1	31.1 ± 12.3	0.001
RV end-diastolic area, cm^2	18.7 ± 8.2	17.7 ± 6.1	24.8 ± 14.9	0.2
RV end-systolic area, cm^2	11.6 ± 6.2	11.0 ± 4.9	15.6 ± 11.2	0.3
RV fractional area change, %	38.8 ± 11.9	38.8 ± 12.0	38.6 ± 11.6	0.9
Tricuspid regurgitant pressure gradient, mmHg	41.0 ± 16.3	40.8 ± 16.2	42.4 ± 17.3	0.9
Annular diameter, mm	36.7 ± 6.1	36.4 ± 5.6	38.8 ± 8.4	0.3
Annular diameter/BSA, mm/m^2	25.0 ± 4.4	24.8 ± 4.6	26.0 ± 5.1	0.2
Patients with TV tethering, n (%)	29 (17)	23 (15)	6 (27)	0.1
Tethering height, mm	5.2 ± 2.1	4.6 ± 1.7	7.6 ± 2.1	0.01
Tethering area, cm^2	1.0 ± 0.7	0.8 ± 0.5	1.8 ± 0.9	0.04

TR, tricuspid regurgitation; LV, left ventricle dimension; LVEF, left ventricular ejection fraction; RV, right ventricle; BSA, body surface area

group compared to non-Recurrence group. Right atrial dimension (RAD), RV end-diastolic area (EDA) and RV end-systolic area (ESA) tended to be larger in Recurrence group, but statistically not significant. No differences were observed between two groups in RV fractional area change (FAC), TRPG and annular diameter. In 29 patients who had leaflet tethering, tethering height and tethering area were significantly larger in Recurrence group compared to Non-Recurrence group. Preoperative TR grade, LVEF < 40%, and RVDs were included in the Cox model. LVEF lower than 40% (hazard ratio: 12.65, 95% confidence interval: 2.66–60.18) and RVDs (hazard ratio: 1.08, 95% confidence interval: 1.02–1.14) were the predictor of recurrent ≥2+ TR (Table 4).

Discussion

The results of TV repair with a 3DR were satisfactory with freedom from 3+ or 4+ TR of 93.6±2.0% at 5 years and only two patients required re-operation. Our result also showed that LVEF lower than 40% and larger RVDs were predictors of recurrent ≥2+ TR.

Previous studies have reported prevalence of recurrent 3+ or 4+ TR for DeVega procedure at 5years was 24% or 28%, and for a classic ring annuloplasty, 10% or 17% [3, 10]. Compared these reports, our result of TV repair with a 3DR showed a better result on prevalence of postoperative 3+ or 4+ TR. Similarly to our results, Choi et al. reported a good results of TV repair with a 3DR "MC^3" [11] with the ratio of

Table 4. Cox regression analysis

Cox	Hazard ratio	95% confidence interval	p-value
LVEF < 40%	12.65	2.66-60.18	0.002
RV systolic dimension	1.08	1.02-1.14	0.02
TR grade	2.37	0.85-7.49	0.2

LVEF, left ventricular ejection fraction; RV, right ventricle; TR, tricuspid regurgitation freedom from ≥ 2+ TR at 10 years of 92%. In their report, however, primary TR was not included and preoperative ≥ 2+ TR was 47% of the study patients, which were differences with our study.

It is known that recurrent TR associated with severe LV dysfunction. LV dysfunction causes pressure and/or volume overload, resulting in LV dilatation. In addition, elliptically change in shape is frequently encountered in patients with severe LV dysfunction. These geometric LV abnormalities affect RV geometry and function directly through the interventricular septum, or indirectly contributing to pulmonary hypertension [12]. Our present study also included a patient who had cardiomyopathy with dilated LV and developed TR after surgery. Bonis et al documented that there were few cases of developing TR in patients who obtained reverse LV remodeling after mitral valve repair in dilated cardiomyopathy [13]. It suggests it is important to control left-sided valve disease and achieve reverse LV remodeling for patients who had TR associated with left-sided valve disease and LV dysfunction.

Our study showed that larger RVDs was a risk factor after TV repair with a 3DR. Previous studies of 3DR showed TV annular size, severe TR grade or atrial fibrillation as a risk factor of recurrent TR, however RVDs was not evaluated in these reports [11, 14]. Calafiore et al. reported that RV dilatation was a risk factor of recurrent TR after tricuspid annuloplasty, including the result of TV repair with a classic ring or flexible ring [15]. RV dilatation causes free wall dilatation and extends length between papillary muscles [16], resulting in TR. Although tethering was not identified as a risk factor for recurrent TR with univariate analysis because small number of our study patients, tethering height and tethering area were significantly greater in Recurrence-group compared to non-Recurrence group. Previously, Fukuda et al. reported that tethered leaflets were associated with recurrent TR [17]. Amedi et al showed that TV annuloplasty with a MC3 ring for functional TR did not improve leaflet tethering in vivo model [18]. Including our result, those reports indicate the limitation of 3DR for severe tethered TV and need for additional procedure to repair the leaflet tethering. Some methods for the repair of TR due to leaflet tethering (e.g., leaflet augmentation, clover technique, right ventricular reduction and right ventricular papillary muscle approximation) have been reported [19–22]. The "spiral suspension technique" was developed in our constitution and has been performing for the cases with leaflet tethering since 2015 [9]. This technique approximates and suspends the pupillary muscles toward mid septal annulus. In this study, seven patients were excluded, but six patients of these, TR well controlled with reduction of RV size. The long-term outcomes will be determined in the future.

Limitation

Small sample size was one of study limitation. Other limitations include the retrospective manner of this study. Echocardiographic 4 chamber views properly visualize leaflet tethering and tethering was retrospectively evaluated in this study, but real time on cart two-dimensional measurement or offline analysis with three-dimensional approach may enable more accurate quantification of leaflet tethering.

Conclusion

The long-term results of TV repair with a 3DR were acceptable. LVEF lower than 40% and increased RVDs were identified as risk factors of recurrent TR. These factors are directly or indirectly associated with dislocation of papillary muscle and therefor leaflet tethering. Leaflet tethering may be augmented by annuloplasty, contributing to recurrent TR. For the durable repair, therefore, additional or alternative procedure to TV repair with a 3DR may be necessary in patients with reduction of LVEF or enlargement of RVDs.

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