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Functional Tricuspid Regurgitation After Transcatheter Closure of Atrial Septal Defect in Adult Patients

Long-Term Follow-Up

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ABSTRACT

OBJECTIVES This study aimed to assess the fate of tricuspid regurgitation (TR) after transcatheter atrial septal defect (ASD) closure.

BACKGROUND Although TR frequently occurs in patients with ASD, the change in TR during long-term follow-up after ASD closure remains unknown.

METHODS A total of 419 adult patients who underwent transcatheter ASD closure were enrolled. TR severity was graded by TR jet area on echocardiography.

RESULTS At baseline, 113 patients had severe/moderate TR and 306 patients had mild TR. Among the 113 patients with severe/moderate TR, the TR jet area significantly decreased during a median follow-up of 30 months after the procedure; this decrease was related to the improvement in right ventricular morphology. The severity of TR decreased to mild in 79 (70%) patients. Persistent TR, defined as severe or moderate TR after the procedure, was independently associated with the prevalence of permanent atrial fibrillation. Regarding clinical outcomes, 7 patients with severe/moderate TR and 2 with mild TR were hospitalized because of heart failure. Patients with severe/moderate TR had the worse event-free survival rate than those with mild TR, but more than 90% of them had no cardiovascular events. New York Heart Association functional class and plasma B-type natriuretic peptide levels improved in patients with severe/moderate TR, similar to those with mild TR.

CONCLUSIONS Significant TR decreased during the long-term follow-up period after transcatheter ASD closure. Heart failure symptoms improved in patients with severe/moderate TR. Our findings suggest that transcatheter closure alone can be valuable in patients with ASD complicated with TR. (J Am Coll Cardiol Intv 2017;10:2211–8)

Atrial septal defect (ASD) of secundum-type is a common congenital heart disease in the adult population. Functional tricuspid regurgitation (TR) frequently occurs in adult patients with ASD (1–4). Significant TR has been demonstrated to increase cardiovascular morbidity and mortality (1,5). Although transcatheter closure has been established as an effective treatment for ASD and has become an alternative to surgical closure (6–11), the therapeutic strategy for ASD complicated with significant TR is controversial (2,4,12). A few studies have reported the change in TR immediately after ASD closure (2). However, the change in TR during long-term follow-up remains unknown. Furthermore, little is known about the relationship with clinical outcomes. Understanding the fate of TR after transcatheter ASD closure is important for treatment selection (i.e., transcatheter closure alone vs. surgical closure combined with tricuspid valve [TV] repair). This study aimed to assess the change in TR after

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ABBREVIATIONS AND ACRONYMS

ASD = atrial septal defect

BNP = B-type natriuretic peptide

LV = left ventricular

NYHA = New York Heart Association

RV = right ventricular

TR = tricuspid regurgitation

TV = tricuspid valve

transcatheter ASD closure and its effect on clinical outcomes in adult patients with ASD.

METHODS

STUDY POPULATION. The study population comprised 419 consecutive adult patients (>18 years old) who underwent transcatheter ASD closure from August 2008 to December 2014. Indications for transcatheter ASD closure were a significant left-to-right shunt, right ventricular (RV) volume overload, and/or clinical symptoms of heart failure. The exclusion criterion was pulmonary arterial hypertension with pulmonary vascular resistance >8 Wood units. One patient with Ebstein anomaly was excluded from the study. Transcatheter ASD closure was performed as described previously (13), using the Amplatzer Septal Occluder (St. Jude Medical, St. Paul, Minnesota).

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Before the procedure, pulmonary-to-systemic blood flow ratio and pulmonary arterial pressure were evaluated with cardiac catheterization. All patients received 100 mg/day aspirin at least 48 h before the procedure, and was continued for 6 months after the procedure. Clopidogrel was administered at a dose of 50 to 75 mg/day for 1 month after the procedure. All patients gave written informed consent for the procedure. The study was approved by the ethical committee of our institution.

CLINICAL ASSESSMENT. Clinical assessments were scheduled before and at 1, 3, 6, and 12 months after the procedure, and annually thereafter. New York Heart Association (NYHA) functional class and plasma B-type natriuretic peptide (BNP) levels were assessed. Transthoracic echocardiography (iE33, Philips Medical Systems, Andover, Massachusetts; and Atrida, Toshiba Medical Systems, Tokyo, Japan) was performed. Left ventricular (LV) end-diastolic and end-systolic diameters and RV end-diastolic diameter were measured by 2-dimensional parasternal long-axis views. LV ejection fraction was derived using the biplane Simpson technique. TR was assessed on the basis of the spatial distribution of the central regurgitant jet within the right atrium by color Doppler flow mapping. TR jet area was measured at the time of mid-systole in the apical 4-chamber view using the area trace method. The severity of TR was determined as mild if the jet area was <5 cm^2, moderate if 5 to 10 cm^2, and severe if >10 cm^2 (2,14). TV annular diameter, which was the distance between the septal and lateral annulus, and TV tethering height, which was the distance between the leaflet coaptation and the annular plane, were measured at the time of mid-systole in the apical 4-chamber view using the frame-by-frame technique. Estimated pulmonary arterial systolic pressure was calculated from TV flow velocity using the Bernoulli equation, and right atrial pressure was estimated from respiratory index of the inferior vena cava (15).

STUDY DESIGN. This was a retrospective cohort study. Patients were divided into 2 groups according to the severity of TR at baseline: severe or moderate (severe/moderate) TR, or mild TR. The change in TR after transcatheter ASD closure was assessed. Factors related to the change in TR were evaluated. In addition, predictors of persistent TR, defined as severe or moderate TR at the latest follow-up after the procedure, were identified. Regarding clinical outcomes, the endpoint was defined as cardiovascular mortality and hospitalization for heart failure. Event-free survival rate was assessed in patients with severe/moderate TR and those with mild TR. Patients were followed from the date of the procedure until the date of first documentation of the events or the end of follow-up, whichever occurred first. Follow-up information was obtained by medical records, contact with the patients' physicians, or telephone interview with the patients. NYHA functional class and plasma BNP levels were assessed before and at the latest follow-up after the procedure.

STATISTICAL ANALYSIS. Data are presented as mean ± SD for continuous variables and as number (percentage) for categorical variables. Differences between the 2 groups were analyzed by the Student *t* test and Mann-Whitney *U* test for continuous variables and the chi-square test for categorical variables. Differences between baseline and follow-up in each group were analyzed by the paired Student *t* test and the Wilcoxon signed rank test. Pearson correlation coefficient was calculated to identify the relationship between the change in TR and the change in RV morphology. Univariate and multivariate logistic regression analyses were performed to identify predictors of persistent TR after the procedure. Variables for univariate analysis included age, sex, ASD diameter, pulmonary-to-systemic blood flow ratio, pulmonary arterial pressure, the prevalence of permanent atrial fibrillation, NYHA functional class, plasma BNP levels, LV end-diastolic diameter, RV end-diastolic diameter, RV/LV end-diastolic diameter ratio, TV annular diameter, and TV tethering height. Odds ratios are shown with 95% confidence intervals. The event-free survival rate was estimated by Kaplan-Meier analysis, and the difference was

compared by the log-rank test. Statistical analysis was performed with JMP version 8.0 (SAS Institute Inc., Cary, North Carolina), and significance was defined as a value of $p < 0.05$.

Interobserver and intraobserver differences were analyzed in 20 randomly selected images. TR jet area was measured by 2 blinded observers and by a single observer at 2 different times. Reliability was calculated by Pearson correlation coefficient. Variability was calculated as the percentage error of each measurement and derived as the difference between the 2 measurements divided by the mean value.

RESULTS

BASELINE CLINICAL CHARACTERISTICS. The mean age of all patients was 54 ± 17 years, and 260 (62%) patients were female. The ASD diameter was 18 ± 7 mm, and the device size was 22 ± 7 mm.

At baseline, 36 patients had severe TR, 77 had moderate TR, and 306 had mild TR. Comparisons of baseline clinical characteristics between the 113 patients with severe/moderate TR and the 306 with mild TR are shown in Table 1. Patients with severe/moderate TR were older and had larger ASD diameter, higher plasma BNP levels, and larger RV end-diastolic diameter with higher RV/LV end-diastolic diameter ratio than those with mild TR. Patients with severe/moderate TR were more likely to have the prevalence of pulmonary arterial hypertension, defined as mean pulmonary arterial pressure >25 mm Hg, and the permanent atrial fibrillation. Among patients with severe/moderate TR, 27 were in NYHA functional class III and 33 had a history of hospitalization for heart failure.

The median follow-up period after transcatheter ASD closure of all patients was 30 months (range 1 to 104 months).

CHANGE IN TR IN PATIENTS WITH SEVERE/MODERATE TR. Among the 113 patients with severe/moderate TR, the TR jet area significantly decreased (from 9.2 ± 4.0 cm^2 to 4.3 ± 2.9 cm^2; $p < 0.001$) during a median follow-up of 30 months after the procedure (range 1 to 104 months). The change in TR severity is shown in Figure 1. Of the 36 patients with severe TR, the severity of TR decreased to mild in 17 (47%), and to moderate in 13 (36%). Of the 77 patients with moderate TR, the severity of TR decreased to mild in 62 (81%). There were no patients who had the severity of TR increase from moderate to severe. The time course of TR jet area in patients with severe/moderate TR is shown in Figure 2. TR jet area gradually decreased during the follow-up period. There was no further progression of TR.

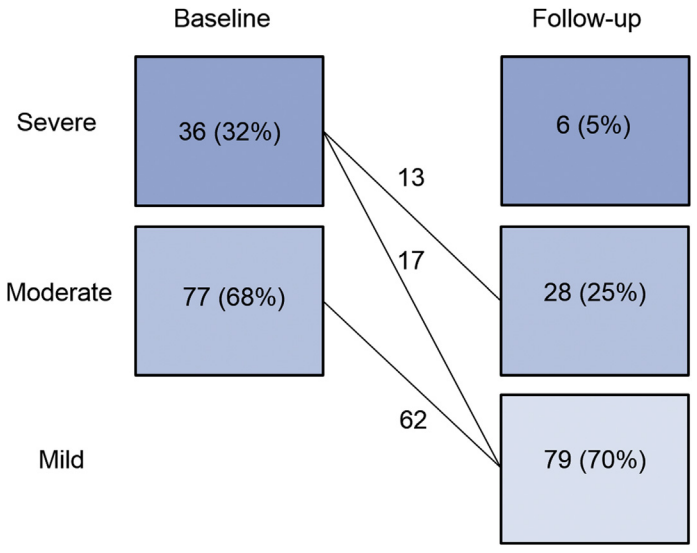
TABLE 1 Baseline Clinical Characteristics

	All (N = 419)	Severe/Moderate TR (n = 113)	Mild TR (n = 306)	p Value
Age, yrs	54 ± 17	64 ± 13	50 ± 17	<0.001
Female	260 (62)	70 (62)	190 (62)	0.979
ASD diameter, mm	18 ± 7	21 ± 8	17 ± 7	<0.001
Device size, mm	22 ± 7	24 ± 7	21 ± 6	<0.001
Pulmonary-to-systemic blood flow ratio	2.5 ± 0.9	2.6 ± 0.9	2.5 ± 0.9	0.276
Pulmonary arterial pressure, mm Hg	17 ± 7	20 ± 7	16 ± 6	<0.001
Pulmonary arterial hypertension	47 (11)	22 (19)	25 (8)	0.001
Permanent atrial fibrillation	44 (11)	35 (31)	9 (3)	<0.001
NYHA functional class I/II	379 (90)	86 (76)	293 (96)	<0.001
NYHA functional class III	40 (10)	27 (24)	13 (4)	
Hospitalization for heart failure	67 (16)	33 (29)	34 (11)	<0.001
B-type natriuretic peptide, pg/ml	107 ± 202	221 ± 268	65 ± 151	<0.001
LV end-diastolic diameter, mm	42 ± 5	41 ± 5	42 ± 5	0.118
LV end-systolic diameter, mm	26 ± 5	26 ± 6	26 ± 4	0.849
LV ejection fraction, %	68 ± 7	68 ± 8	69 ± 7	0.932
RV end-diastolic diameter, mm	36 ± 7	39 ± 6	34 ± 6	<0.001
RV/LV end-diastolic diameter ratio	0.87 ± 0.20	0.97 ± 0.20	0.84 ± 0.19	<0.001

Values are mean ± SD or n (%).

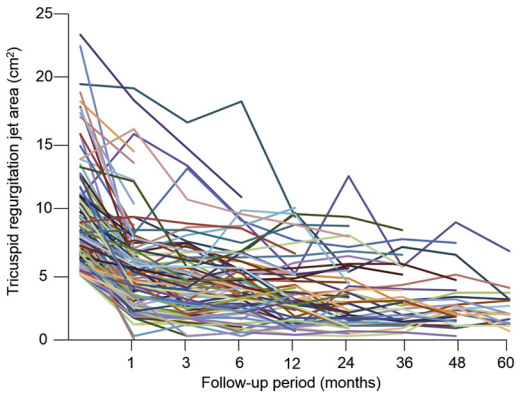
ASD = atrial septal defect; LV = left ventricular; NYHA = New York Heart Association; RV = right ventricular; TR = tricuspid regurgitation.

FIGURE 1 Severity of Tricuspid Regurgitation



Severity of tricuspid regurgitation before and after transcatheter atrial septal defect closure in patients with severe/moderate tricuspid regurgitation.

FIGURE 2 Time Course of Tricuspid Regurgitation Jet Area



Time course of tricuspid regurgitation jet area after transcatheter atrial septal defect closure in patients with severe/moderate tricuspid regurgitation.

Echocardiographic parameters before and at the latest follow-up after the procedure in patients with severe/moderate TR are shown in Table 2. RV end-diastolic diameter, RV/LV end-diastolic diameter ratio, TV annular diameter, and TV tethering height decreased. There was a weak but significant correlation between the decrease in TR jet area and the decrease in RV end-diastolic diameter ($r = 0.34$; $p < 0.001$), RV/LV end-diastolic diameter ratio ($r = 0.37$; $p < 0.001$), TV annular diameter ($r = 0.35$; $p < 0.001$), and TV tethering height ($r = 0.30$; $p = 0.001$).

PREDICTORS OF PERSISTENT TR. Among the 113 patients with severe/moderate TR, persistent TR after the procedure was observed in 34 (30%), including 6 with severe TR and 28 with moderate TR (Figure 1). Univariate analysis showed that persistent TR was associated with age, the prevalence of permanent atrial fibrillation, NYHA functional class, and plasma BNP levels. After multivariate analysis, only the prevalence of permanent atrial fibrillation remained an independent predictor (Table 3).

TABLE 2 Echocardiographic Parameters Before and at the Latest Follow-Up After Transcatheter Atrial Septal Defect Closure in Patients With Severe/Moderate Tricuspid Regurgitation

	Before	Follow-Up	p Value
TR jet area, cm^2	9.2 ± 4.0	4.3 ± 2.9	<0.001
LV end-diastolic diameter, mm	41 ± 5	45 ± 5	<0.001
RV end-diastolic diameter, mm	39 ± 6	33 ± 5	<0.001
RV/LV end-diastolic diameter ratio	0.97 ± 0.20	0.74 ± 0.14	<0.001
TV annular diameter, mm	35 ± 5	30 ± 5	<0.001
TV tethering height, mm	12 ± 3	9 ± 2	<0.001
Estimated pulmonary arterial systolic pressure, mm Hg	42 ± 13	33 ± 9	<0.001

Values are mean ± SD.
Abbreviations as in Table 1.

CLINICAL CHARACTERISTICS OF PATIENTS WITH AND WITHOUT PERMANENT ATRIAL FIBRILLATION. Among patients with severe/moderate TR, comparisons of clinical characteristics between the 35 with permanent atrial fibrillation and the 78 without permanent atrial fibrillation are shown in Table 4. Patients with permanent atrial fibrillation were older and had larger TV annular diameter before the procedure than those without permanent atrial fibrillation. At the latest follow-up after the procedure, patients with permanent atrial fibrillation had larger RV end-diastolic diameter and larger TV annular diameter with higher TV tethering height.

CHANGE IN TR IN PATIENTS WITH MILD TR. Among the 306 patients with mild TR, the TR deteriorated to moderate in 4 (1%) after the procedure. In these 4 patients, the TR jet area increased from 4.6 to 6.6 cm^2, from 3.2 to 5.4 cm^2, from 4.4 to 6.7 cm^2, and from 4.7 to 5.9 cm^2, respectively.

CLINICAL OUTCOMES. Seven (6%) of the 113 patients with severe/moderate TR and 2 (1%) of the 306 with mild TR were hospitalized because of heart failure during the follow-up period after the procedure. Of the 7 patients with severe/moderate TR, 2 had severe pulmonary arterial hypertension before the procedure and 1 had severe LV systolic dysfunction. The patient with severe LV dysfunction died later. Kaplan-Meier analysis showed that the event-free survival rate was worse in patients with severe/moderate TR than in those with mild TR (log-rank test; $p < 0.001$) (Figure 3). However, more than 90% of patients with severe/moderate TR did not have cardiovascular mortality or hospitalization for heart failure.

Among patients with severe/moderate TR, NYHA functional class improved in 55 (65%) of the 85 with NYHA functional class II or III at baseline (Figure 4). NYHA functional class deteriorated in only 1 patient with severe LV systolic dysfunction. Among patients with mild TR, NYHA functional class improved in 93 (68%) of the 137 patients with NYHA functional class II or III at baseline (Figure 4). Plasma BNP levels significantly improved in patients with severe/moderate TR (from 221 ± 268 pg/ml to 113 ± 146 pg/ml; $p < 0.001$) and those with mild TR (from 65 ± 151 pg/ml to 44 ± 54 pg/ml; $p = 0.023$).

REPRODUCIBILITY. There was good agreement in the measurements of TR jet area between the 2 blinded observers ($r = 0.97$; $p < 0.001$), and those in the

intraobserver ($r = 0.97$; $p < 0.001$). The interobserver and intraobserver variabilities for TR jet area were 5.5% and 6.1%, respectively.

DISCUSSION

The major findings of the present study are as follows: 1) the severity of TR decreased during the long-term follow-up period after transcatheter ASD closure; 2) more than 90% of patients with severe/moderate TR had no cardiovascular events; 3) heart failure symptoms improved in patients with severe/moderate TR; and 4) persistent TR after the procedure was associated with the prevalence of permanent atrial fibrillation. To the best of our knowledge, this is the first study to show the fate of TR during the long-term follow-up period after transcatheter ASD closure, including clinical outcomes.

TR AFTER ASD CLOSURE. Functional TR has been the focus of increasing interest because significant TR is associated with adverse outcomes in terms of heart failure, reduced functional capacity, and mortality (1,5). Although TR frequently occurs in adult patients with ASD (1–4), limited information is available regarding the effects of ASD closure on TR. A few previous studies reported that persistent TR after ASD closure was observed in nearly one-half of patients, suggesting that TV repair should be performed at ASD closure (2,12). However, the sample size was small and the timing of TR assessment after ASD closure was short. One previous study demonstrated that TR decreased with the improvement in functional status at 3 to 6 months after transcatheter ASD closure, but significant TR remained in more than one-half of patients with severe and moderate TR (3). These results were obtained in the mid-term follow-up period and not the long-term follow-up, although the cardiac reverse remodeling process seems to continue (16,17). Therefore, whether significant TR remains unchanged during the long-term follow-up period after transcatheter ASD closure is unclear. There have been no studies to assess the time course of TR during the long-term follow-up period.

MECHANISM OF TR AFTER TRANSCATHETER ASD CLOSURE. Long-standing left-to-right interatrial shunts cause marked RV dilatation and subsequently result in altered RV configuration (18). RV remodeling, which is characterized by dilatation in the septal-lateral direction, influences TV function as a result of displacement of the papillary muscles attached to both RV free walls and septal walls (19). Such RV and TV morphology at baseline was reportedly related to persistent TR immediately after ASD closure (12,20). However, unlike these previous studies, the present study revealed that these parameters did not predict persistent TR during the long-term follow-up. As a possible explanation for this finding, it can be proposed that the reverse remodeling of RV morphology begins immediately after ASD closure and continues for a

TABLE 3 Predictors of Persistent Tricuspid Regurgitation After Transcatheter Atrial Septal Defect Closure in Patients With Severe/Moderate Tricuspid Regurgitation

	Univariate Analysis		Multivariate Analysis	
	Odds Ratio (95% Confidence Interval)	p Value	Odds Ratio (95% Confidence Interval)	p Value
Age >65 yrs	4.09 (1.71–10.7)	0.001	2.01 (0.70–5.94)	0.193
Female	1.44 (0.63–3.27)	0.386		
ASD diameter >21 mm	0.93 (0.40–2.09)	0.854		
Pulmonary-to-systemic blood flow ratio >2.5	0.59 (0.26–1.31)	0.195		
Mean pulmonary arterial pressure >19 mm Hg	1.54 (0.69–3.50)	0.290		
Permanent atrial fibrillation	7.50 (3.11–19.0)	<0.001	5.09 (1.70–16.8)	0.004
NYHA functional class III	2.87 (1.16–7.14)	0.022	1.58 (0.54–4.44)	0.394
B-type natriuretic peptide >90 pg/ml	3.35 (1.44–8.21)	0.005	0.99 (0.30–3.08)	0.999
LV end-diastolic diameter >40 mm Hg	1.34 (0.59–3.16)	0.484		
RV end-diastolic diameter >38 mm	1.01 (0.45–2.26)	0.983		
RV/LV end-diastolic diameter ratio >1.0	0.95 (0.41–2.19)	0.912		
TV annular diameter >35 mm	1.74 (0.78–3.96)	0.179		
TV tethering height >12 mm	0.84 (0.37–1.88)	0.665		

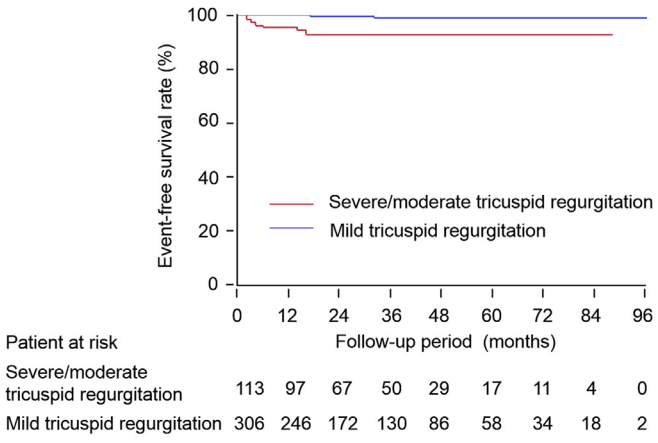
Abbreviations as in Table 1.

TABLE 4 Clinical Characteristics of Patients With Severe/Moderate Tricuspid Regurgitation Complicated With and Without Permanent Atrial Fibrillation

	Permanent Atrial Fibrillation (+) (n = 35)	Permanent Atrial Fibrillation (–) (n = 78)	p Value
Age, yrs	73 ± 8	60 ± 13	<0.001
Female	17 (49)	53 (68)	0.050
ASD diameter, mm	21 ± 9	20 ± 7	0.568
Before the procedure			
LV end-diastolic diameter, mm	42 ± 6	40 ± 4	0.101
RV end-diastolic diameter, mm	41 ± 6	39 ± 6	0.057
TV annular diameter, mm	39 ± 4	34 ± 4	<0.001
TV tethering height, mm	12 ± 3	12 ± 3	0.279
Follow-up after the procedure			
LV end-diastolic diameter, mm	47 ± 5	45 ± 4	0.048
RV end-diastolic diameter, mm	35 ± 4	32 ± 5	0.006
TV annular diameter, mm	34 ± 5	29 ± 4	<0.001
TV tethering height, mm	10 ± 2	9 ± 2	0.043

Values are mean ± SD or n (%).
Abbreviations as in Table 1.

FIGURE 3 Event-Free Survival Rate



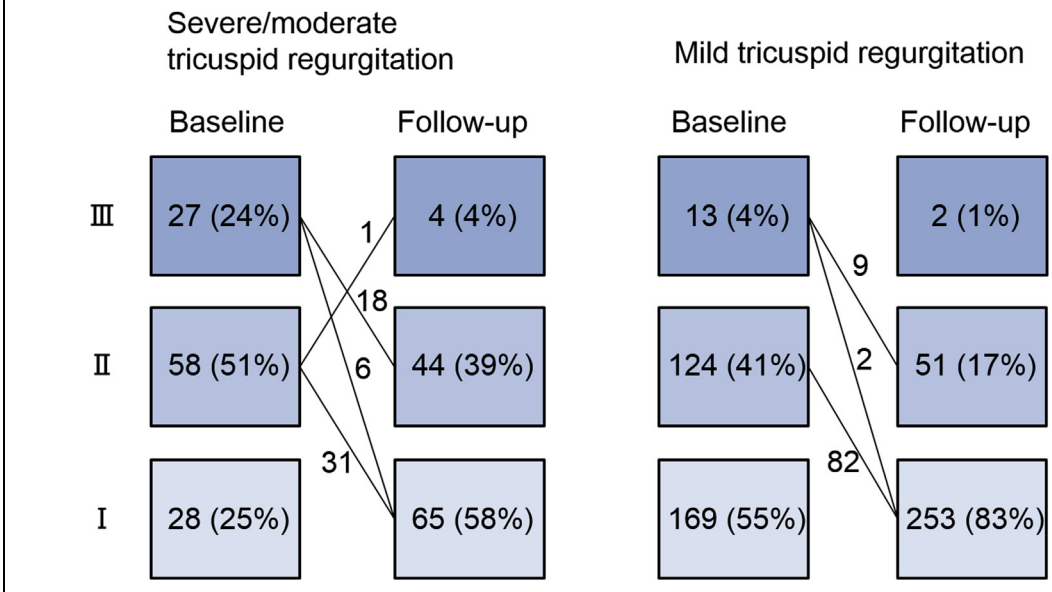
Survival rate without cardiovascular mortality or hospitalization for heart failure after transcatheter atrial septal defect closure in patients with severe/moderate tricuspid regurgitation and those with mild tricuspid regurgitation.

long-term period (16,17). In the present study, the decrease in TR continued after the procedure along with RV reverse remodeling. Thus, persistent TR may be associated with the degree of improvement in RV and TV morphology.

Pulmonary arterial pressure at baseline was also reportedly related to persistent TR after ASD closure in the acute phase (2,21). However, similar to RV reverse remodeling, pulmonary arterial pressure is considered to improve after ASD closure. In the present study, pulmonary arterial systolic pressure was reduced during the follow-up period after the procedure, which might result in no correlation between persistent TR and pulmonary arterial pressure. This finding suggests the possibility that a reduction in pulmonary arterial pressure can improve persistent TR after ASD closure.

The present study found that the prevalence of permanent atrial fibrillation was a predictor of persistent TR. Patients with permanent atrial fibrillation were older and had TV annular dilatation before and after transcatheter ASD closure. Atrial fibrillation is closely related to patient age (3,22,23). Atrial fibrillation in older patients with ASD is the by-product of long-standing right atrial enlargement and stretch and loss of atrial mechanical activity. Right atrial dilatation, leading to TV annular dilatation, is confirmed to be related to functional TR in patients with atrial fibrillation (24,25). Furthermore, the degree of right atrial reverse remodeling is inversely related to patient age at the time of ASD closure (1,26). Thus, the remaining right atrial

FIGURE 4 New York Heart Association Functional Class



New York Heart Association functional class before and after transcatheter atrial septal defect closure in patients with severe/moderate tricuspid regurgitation and those with mild tricuspid regurgitation.

dilatation caused by permanent atrial fibrillation in older patients can be considered as the potential mechanism of persistent TR during the long-term follow-up period after transcatheter ASD closure.

EFFECT OF TRANSCATHETER ASD CLOSURE ON CLINICAL OUTCOMES. As expected, the event-free survival rate was worse in patients with severe/moderate TR than in those with mild TR. However, the cause of hospitalization for heart failure in patients with severe/moderate TR included complicated diseases, such as pulmonary arterial hypertension and severe LV systolic dysfunction. Although patients with severe/moderate TR had worse condition of heart failure, such as NYHA functional class, plasma BNP levels, the prevalence of atrial fibrillation, and a history of hospitalization for heart failure, most of them had no cardiovascular events during the follow-up period. Heart failure symptoms improved in patients with severe/moderate TR, leading to an improvement in quality of life. On the basis of clinical outcomes, transcatheter ASD closure may be effective in patients with significant TR.

CLINICAL IMPLICATIONS. The present study showed that TR gradually decreased during the long-term follow-up period after transcatheter ASD closure, in parallel with RV reverse remodeling. Persistent TR was observed in approximately 30% of patients with severe/moderate TR, but less frequently than in previous studies (2,3,12). The event-free survival rate in patients with severe/moderate TR was not worse. The improvement in heart failure symptoms was equivalent to that in patients with mild TR. Surgical closure of ASD has a low risk but has the potential for complications and causes prolonged hospital stay and psychological trauma (10). Age contributes to an increased risk of complications. Although the effectiveness of robotic technology for surgical closure, including improved quality of life and reduced postoperative pain, has been demonstrated (27,28), adult patients tend to refuse or hesitate to undergo surgical closure. Compared with surgical closure, transcatheter closure has therapeutic advantages, such as less invasiveness, fewer complications, and shorter hospital stay (8–10). Transcatheter closure has become an alternative to surgical closure in recent years. Thus, adult patients may prefer transcatheter closure even with significant TR. However, despite the lack of evidence, surgery is considered to be selected in patients with ASD complicated with TR (2,12). In the present study, transcatheter closure resolved TR incompletely in patients with severe/moderate TR but resulted in good clinical courses. These findings suggest that transcatheter closure alone can be recommended for adult patients with ASD complicated with significant TR.

The present study also showed that the prevalence of permanent atrial fibrillation was a key predictive factor for persistent TR. Because the prevalence of atrial fibrillation increases with age (3,22,23), transcatheter closure in the early phase may play an important role in preventing persistent TR. In addition, radiofrequency catheter ablation is beneficial for atrial fibrillation to maintain sinus rhythm. Therefore, the therapeutic strategy of combining radiofrequency catheter ablation and subsequent transcatheter closure may be effective for the prevention of persistent TR.

STUDY LIMITATIONS. There are some limitations in the present study. First, this was a retrospective cohort study that lacked a control group. Large prospective studies are required to confirm our findings. Second, there was selection bias because only patients undergoing transcatheter closure were selected. Third, the severity of TR was not estimated by quantitative evaluation. However, the distribution of TR jet area was reportedly correlated with the severity of TR measured invasively (29). Finally, RV function was not evaluated. TV structures were not assessed by 3-dimensional echocardiography. Further studies are required to clarify these details.

CONCLUSIONS

Significant TR decreased during the long-term follow-up period after transcatheter ASD closure. Heart failure symptoms improved in patients with severe/moderate TR. Our findings suggest that transcatheter closure alone can be valuable in adult patients with ASD complicated with significant TR.

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PERSPECTIVES

WHAT IS KNOWN? Functional TR frequently occurs in patients with ASD. However, the fate of TR after ASD closure remains unknown. Thus, the therapeutic strategy for ASD complicated with significant TR is controversial (i.e., transcatheter closure alone vs. surgical closure combined with tricuspid valve repair).

WHAT IS NEW? TR gradually decreased during the long-term follow-up period after transcatheter ASD closure, in parallel with right ventricular reverse remodeling. Transcatheter closure resulted in good clinical courses in patients with significant TR. Our findings suggest that transcatheter closure alone can be valuable in adult patients with ASD complicated with significant TR.

WHAT IS NEXT? Large prospective studies are required for a better understanding of the effects of transcatheter closure on significant TR and its influence on clinical outcomes in patients with ASD.

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