

# Prevalence, Predictors, and Prognostic Value of Residual Tricuspid Regurgitation in Patients With Left Ventricular Assist Device

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**Background**—Although implantation of a left ventricular assist device (LVAD) generally improves tricuspid regurgitation (TR) in short-term follow-up, the clinical significance of residual TR in patients with mid- to long-term LVAD support is unknown. This study aimed to identify the prevalence, predictors, and prognostic value of residual TR in LVAD patients in association with tricuspid valve (TV) deformation.

**Methods and Results**—The study cohort consisted of 127 patients who underwent LVAD implantation without TV procedure and were supported with LVAD at least 1 year. All patients underwent echocardiographic examination preoperatively and 1 year after LVAD implantation. TR was quantitatively assessed by ratio of TR color jet area/right atrial area, and significant residual TR was defined as  $\geq 20\%$  of %TR at follow-up echocardiographic examination. Detailed echocardiographic measurements were also performed, including TV annulus diameter, TV leaflet displacement, and left ventricular and right ventricular systolic function. LVAD implantation significantly improved ratio of TR color jet area/right atrial area as well as left ventricular and right ventricular systolic function and tethering distance (all  $P < 0.05$ ), whereas it enlarged TV annulus diameter ( $P = 0.002$ ). Significant residual TR was observed in 30 (23.6%) patients. Age, preoperative TV annulus diameter, and residual mitral regurgitation were significantly associated with significant residual TR (all  $P < 0.05$ ), whereas TV tethering was not. During a mean follow-up of  $21 \pm 17$  months, patients with residual TR had significantly higher mortality than those without residual TR (log-rank  $P < 0.001$ ).

**Conclusions**—Significant residual TR was observed in  $\approx 25\%$  patients supported with LVAD over 1 year and was associated with unfavorable outcome. (*J Am Heart Assoc.* 2018;7:e008813. DOI: 10.1161/JAHA.118.008813.)

**Key Words:** echocardiography • heart failure • left ventricular assist device • mortality • tricuspid regurgitation

Functional tricuspid regurgitation (TR) is an important complication in patients with advanced heart failure. The etiology of functional TR is annulus enlargement and leaflet tethering secondary to right ventricular (RV) overload, pulmonary hypertension, and left ventricular (LV) dysfunction.<sup>1–3</sup> As annular dilation progresses, mainly in the anterolateral direction, the valve becomes more planar in shape and its dynamic excursion diminishes.<sup>4</sup> Leaflet tethering progresses, as the lower points of the annulus are stretched away from the papillary muscle and displaced.<sup>5</sup>

These tricuspid valve (TV) deformations reduce leaflet coaptation causing TR.<sup>6</sup> The occurrence of TR initiates a vicious cycle of further RV dilatation and dysfunction and, consequently, worsening of TR.<sup>7</sup> TR severity is independently associated with worse survival in heart failure patients<sup>8–11</sup> as well as in patients with isolated TR.<sup>12,13</sup>

Continuous-flow LV assist devices (LVADs) are becoming the standard of care for management of refractory advanced heart failure patients.<sup>14–17</sup> Although implantation of an LVAD leads to mechanical unloading of the LV, may induce ventricular reverse remodeling, and generally improves TR in the short term,<sup>18–20</sup> nonimprovement of significant preoperative TR or TR worsening (namely “residual TR”) is observed in some patients during mid- to long-term LVAD support. However, the frequency and mechanisms of residual TR in LVAD patients are not extensively evaluated. Furthermore, it is also unknown whether patients with residual TR after LVAD implantation have unfavorable outcomes. This study aimed to identify the prevalence, predictors, and prognostic significance of residual TR in patients with over 1 year of LVAD support in association with TV deformation.

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## Clinical Perspective

### What Is New?

- Left ventricular assist device implantation improved the tricuspid regurgitation (TR) and tricuspid valvular tethering, as well as right ventricular and left ventricular systolic function, whereas it worsened annulus dilatation.
- Significant residual TR was observed in  $\approx 25\%$  patients with over 1 year left ventricular assist device support.
- Preoperative tricuspid valvular annulus diameter was significantly associated with residual TR.
- Patients with residual TR had higher mortality compared with those without residual TR.

### What Are the Clinical Implications?

- Evaluation of tricuspid valvular annulus diameter before left ventricular assist device implantation might be useful to identify patients at high risk for significant residual TR.
- Close follow-up should be performed in left ventricular assist device patients with significant residual TR.

## Methods

The data, analytical methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

## Study Population

The records of 423 consecutive patients who underwent continuous-flow LVADs between April 2007 and March 2016 at Columbia University Medical Center were reviewed for this study. Among those, 5 patients with history of TV procedure, 81 who underwent concomitant TV procedure at the time of LVAD implantation, and 20 with in-hospital death were initially excluded. The decision to perform TV procedure was made by the surgeon's discretion on the basis of severity of TR. Of the remaining 317 patients, 147 patients with less than 1 year of LVAD support and 43 with inadequate visualization on echocardiography or without follow-up echocardiographic examination were also excluded. Thus, the final population of this study comprised 127 patients (103 men; mean age,  $58 \pm 15$  years). All clinical data were collected through a review of electronic medical records. These included baseline demographics, laboratory values, and hemodynamic parameters. The study was approved by the Institutional Review Board of Columbia University Medical Center. The requirement of informed consent was waived because of the retrospective nature of the study.

## Distribution of Devices and Postoperative Device Management

Most patients ( $n=108$ ; 85.0%) received the HeartMate II device (Thoratec Corp, Pleasanton, CA). Other LVADs implanted included 14 (11.0%) HeartWare HVADs (HeartWare International, Inc, Framingham, MA), 4 (3.2%) Jarvik 2000 (Jarvik Heart, Inc, New York, NY), and 1 (0.8%) DuraHeart Left Ventricular Assist Systems (Terumo Heart, Ann Arbor, MI). After device implantation, all patients received a standardized heart failure medical regimen including neurohormonal antagonists, diuretics, and antiarrhythmic agents, if needed, on the basis of the individual clinical picture. Heparin was bridged according to the Columbia University Medical Center's protocol. Antithrombotic therapy with aspirin and warfarin was implemented once adequate hemostasis had been achieved. Patients were followed at 1 week after the initial discharge and monthly thereafter unless any issue necessitated more-frequent visits. Clinic visit frequency varied among patients depending on individual medical issues and travel distances.

## 2-Dimensional Echocardiographic Examination

Echocardiographic examination was performed using a commercially available system (iE33 or EPIQ; Philips Healthcare Corp, Andover, MA) by a trained, registered cardiac sonographer before and 1 year (median, 366 days; interquartile range, 337–441) after LVAD implantation. In addition, early postoperative echocardiography ( $<7$  days after LVAD implantation) was also analyzed in 101 (79.5%) patients with adequate image quality. Dimensions of the left cardiac chambers were measured in the standard manner.<sup>21</sup> LV ejection fraction (LVEF) was obtained by using the Simpson's method from apical 4- and 2-chamber views.<sup>21</sup> TR severity was assessed by color Doppler flow mapping of spatial distribution of the regurgitant jet within the right atrium. The TR jet area on color flow mapping and right atrium in the same frame was measured by planimetry, and the ratio of the maximal regurgitant area to right atrium area (%TR) was then obtained. TR severity was graded as follows based on Framingham Heart Study criteria: mild if the %TR was up to 19%; moderate if 20% to 40%; or severe if  $\geq 41\%$ .<sup>10,12,22</sup> Significant TR was defined as moderate or severe TR ( $\geq 20\%$  of %TR). Mitral regurgitation (MR) severity was also assessed by color Doppler flow mapping of spatial distribution of the regurgitant jet within the left atrium in both apical 4-chamber and apical 2-chamber views, and the ratio of the maximal regurgitant area to left atrium area was obtained. Significant MR was defined as moderate or severe MR ( $\geq 20\%$  of the ratio of the maximal regurgitant area to left atrium area).<sup>23,24</sup>

The following echocardiographic parameters were also obtained from a modified apical 4-chamber view encompassing the entire RV. First, the RV end-diastolic and end-systolic areas were measured by planimetry, tracing the endocardial outline of RV and the plane of TV. RV fractional area change (RVFAC) was then calculated:  $(RV \text{ end-diastolic area} - RV \text{ end-systolic area}) / RV \text{ end-diastolic area} \times 100$ .<sup>21</sup> RV contractility was also evaluated by using the peak systolic tissue velocity of the RV lateral wall assessed at the tricuspid annulus. Second, measurements of the TV annulus diameter were performed at the time of the maximum TV diastolic opening between the 2 hinge points at the junction between the valvular leaflets and the TV annulus.<sup>25–27</sup> Finally, the distance and area of TV tethering were measured by tracing between the atrial surface of the leaflets and the tricuspid annular plane at the time of maximal systolic closure. All variables were acquired with at least 3 beats and averaged. All measurements were performed blinded to patient clinical information.

## Statistical Analysis

Categorical variables are presented as numbers and percentages and were compared using the chi-square test. Continuous variables are expressed as mean  $\pm$  SD and were compared using a paired/unpaired *t* test or Mann–Whitney *U* test, as appropriate. Univariable and multivariable logistic regression analyses were conducted to identify the variables that were independently associated with residual TR. Related factors with a  $P < 0.05$  in univariable analysis were selected as independent variables for multivariable analysis. Sensitivity and specificity of the cut-off point for the prediction of residual TR were determined using the receiver operating characteristic curve. Univariate and multivariate Cox proportional hazards regression analyses were used to evaluate the association between residual TR and mortality, adjusting for significant potential cofactors (variables with  $P < 0.05$  in the univariate analysis) in the multivariate model. Kaplan–Meier curves were used to represent survival and were compared using the log-rank test.  $P < 0.05$  was considered significant. Statistical analyses were performed using JMP 10 software (version 10; SAS Institute Inc, Cary, NC).

## Results

### Patient Characteristics

Patient characteristics are shown in Table 1. Mean age was  $58 \pm 15$  years, and 103 (81.1%) were men. Etiology of heart failure was ischemic in 51 (40.2%) patients and nonischemic in 76 (59.8%). Treatment strategy was bridge-to-transplant in 69 (54.3%) recipients. Baseline echocardiographic parameters before LVAD implantation are also presented in Table 1. Mean %TR was

$16.5 \pm 10.3\%$ , RVFAC was  $28.0 \pm 9.9\%$ , TV annulus diameter was  $39.4 \pm 4.7$  mm, and tethering distance was  $7.5 \pm 1.8$  mm.

### Alteration of Echocardiographic Parameters

Changes in echocardiographic parameters after LVAD implantation are shown in Table 2. In the entire group, %TR was significantly reduced after LVAD implantation ( $16.5 \pm 10.3 - 12.7 \pm 14.0\%$ ;  $P = 0.013$ ). LVEF ( $14.1 \pm 5.0 - 18.6 \pm 6.8\%$ ;  $P < 0.001$ ), RVFAC ( $28.0 \pm 9.9 - 31.6 \pm 11.3\%$ ;  $P = 0.004$ ), and tethering distance ( $7.5 \pm 1.8 - 6.6 \pm 2.1$  mm;  $P < 0.001$ ) were also improved after LVAD implantation. On the other hand, TV annulus diameter was significantly enlarged at follow-up echocardiographic examination ( $39.4 \pm 4.7 - 41.9 \pm 5.5$  mm;  $P = 0.002$ ), although no significant difference was observed at early postoperative echocardiography ( $39.9 \pm 5.4$  mm;  $P = 0.685$ ).

### Prevalence and Predictors of Residual TR

Significant preoperative TR was observed in 43 (33.9%) patients and 30 (23.6%) patients had significant residual TR, although only 8.9% had significant TR at early postoperative echocardiography. Among the 43 patients with significant TR at baseline, 30 (70.0%) patients experienced improvement of TR at 1 year after LVAD implantation. On the other hand, 17 of 84 patients (20.2%) without significant TR at baseline experienced worsening of TR.

There was no significant differences in baseline patient characteristics and laboratory and hemodynamic parameters between patients with and without residual TR except for age, ( $63 \pm 14$  versus  $56 \pm 15$  years;  $P = 0.027$ ), serum blood urea nitrogen level ( $42.2 \pm 20.6$  versus  $32.3 \pm 17.7$  mg/dL;  $P = 0.012$ ), and serum creatinine level ( $1.6 \pm 0.5$  versus  $1.4 \pm 0.5$  mg/dL;  $P = 0.023$ ; Table 1). Patients with residual TR had significantly larger TV annulus diameter at baseline ( $41.7 \pm 4.9$  versus  $38.7 \pm 4.5$  mm;  $P = 0.002$ ), whereas there were no significant differences in LVEF, RV size, and function and TV tethering distance between the 2 residual TR groups. There was no significant difference in prevalence of significant MR between patients with and without residual TR (80.0% versus 78.4%;  $P = 0.847$ ). On the other hand, patients with residual TR had significantly higher prevalence of residual MR compared with those without residual TR (40.0% versus 15.5%;  $P = 0.004$ ). Multivariable logistic regression analysis showed that age (adjusted odds ratio, 1.04;  $P = 0.036$ ), TV annulus diameter (adjusted odds ratio, 1.15;  $P = 0.005$ ), and residual MR (adjusted odds ratio, 4.52;  $P = 0.005$ ) were significantly associated with significant residual TR after LVAD implantation (Table 3). The best cut-off value of the TV annulus diameter for the prediction of residual TR was 42 mm based on the receiver operating characteristic curve analysis (area under the curve = 0.680), providing a sensitivity of 48% and specificity of 84%.

**Table 1.** Baseline Clinical Characteristics and Echocardiographic Parameters Stratified by the Presence of Residual TR

	All Patients (N=127)	Residual TR (N=30)	No Residual TR (N=97)	P Value
Age, y	58±15	63±14	56±15	0.027
Male sex, n (%)	103 (81.1)	22 (73.3)	81 (83.5)	0.214
Hypertension, n (%)	71 (55.9)	15 (50.0)	56 (57.3)	0.456
Diabetes mellitus, n (%)	56 (44.1)	10 (33.3)	46 (47.4)	0.174
Hypercholesterolemia, n (%)	56 (44.1)	13 (43.3)	43 (44.3)	0.924
Body mass index, kg/m <sup>2</sup>	25.7±5.3	24.5±4.3	26.1±5.6	0.148
Ischemic cardiomyopathy	51 (40.2)	16 (53.3)	35 (36.1)	0.092
ICD, n (%)	108 (85.0)	26 (86.7)	82 (84.5)	0.775
Intention to treat				0.586
Bridge to transplant	69 (54.3)	15 (50.0)	54 (55.7)	
Destination therapy	58 (45.7)	15 (50.0)	43 (44.3)	
Preoperative inotrope support	106 (83.5)	25 (83.3)	81 (83.5)	0.982
Hemodynamic parameters				
CVP, mm Hg	9.9±5.4	8.9±5.3	10.3±5.4	0.225
PCWP, mm Hg	23.3±8.5	21.8±7.9	23.7±8.7	0.283
CVP/PCWP ratio	0.45±0.23	0.43±0.27	0.45±0.22	0.620
Mean PAP, mm Hg	35.4±10.4	32.3±8.7	36.3±10.8	0.064
Cardiac index, L/min per m <sup>2</sup>	1.7±0.5	1.7±0.5	1.7±0.5	0.780
PVR, wood units	4.2±2.7	3.9±2.5	4.3±2.7	0.546
Laboratory parameters				
BUN, mg/dL	34.6±18.8	42.2±20.6	32.3±17.7	0.012
Creatinine, mg/dL	1.4±0.5	1.6±0.5	1.4±0.5	0.023
Albumin, g/dL	3.7±0.6	3.7±0.5	3.6±0.5	0.765
Total bilirubin, mg/dL	1.2±0.8	1.1±0.7	1.3±0.9	0.368
Hemoglobin, g/dL	11.9±2.2	11.3±2.0	12.1±2.2	0.106
Echocardiographic parameters				
LV end-diastolic diameter, mm	71.9±10.1	69.1±9.7	72.8±10.1	0.084
LV ejection fraction, %	14.1±5.0	13.3±4.6	14.3±5.1	0.301
LA diameter, mm	49.2±8.0	47.9±8.3	49.6±8.0	0.307
RV end-diastolic area, cm <sup>2</sup>	26.7±8.7	27.1±9.2	26.6±8.6	0.768
RV end-systolic area, cm <sup>2</sup>	19.5±7.8	19.5±7.5	19.6±7.9	0.950
RV fractional area change, %	28.0±9.9	28.9±9.7	27.7±10.0	0.544
RV systolic excursion velocity, cm/sec	8.50±2.78	8.37±3.30	8.54±2.63	0.784
RV systolic pressure, mm Hg	46.5±12.4	48.0±11.2	46.1±12.7	0.464
TV annulus diameter, mm	39.4±4.7	41.7±4.9	38.7±4.5	0.002
TV tethering distance, mm	7.5±1.8	7.3±1.5	7.6±1.9	0.433
TV tethering area, cm <sup>2</sup>	1.2±0.4	1.1±0.4	1.2±0.4	0.461
%TR, %	16.5±10.3	18.6±10.3	15.8±10.2	0.193
%MR, %	35.2±16.1	36.1±17.1	35.0±15.8	0.742
Significant MR, n (%)	100 (78.7)	24 (80.0)	76 (78.4)	0.847

Values are mean±SD or n (percentage). BUN indicates blood urea nitrogen; CVP, central venous pressure; ICD, implantable cardioverter defibrillator; LA, left atrium; LV, left ventricle; MR, mitral regurgitation; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RV, right ventricle; TR, tricuspid regurgitation; TV, tricuspid valve.

**Table 2.** Alterations of Echocardiographic Parameters in Patients With and Without Residual TR

	All Patients (N=127)			Residual TR (n=30)			No Residual TR (N=97)		
	Baseline	Follow-up	P Value	Baseline	Follow-up	P Value	Baseline	Follow-up	P Value
LV end-diastolic diameter, mm	71.9±10.1	60.6±12.5	<0.001	69.1±9.7	58.1±11.5	<0.001	72.8±10.1	61.4±12.7	<0.001
LV ejection fraction, %	14.1±5.0	18.6±6.8	<0.001	13.3±4.6	17.2±5.4	<0.001	14.3±5.1	19.1±7.1	<0.001
LA diameter, mm	49.2±8.0	44.3±8.4	<0.001	47.9±8.3	44.8±8.9	0.082	49.6±8.0	44.2±8.3	<0.001
RV fractional area change, %	28.0±9.9	31.6±11.3	0.004	28.9±9.7	30.8±11.2	0.464	27.7±10.0	31.9±11.4	0.004
TV annulus diameter, mm	39.4±4.7	41.9±5.5	0.002	41.7±4.9	44.0±5.3	0.033	38.7±4.5	41.1±5.4	0.017
TV tethering distance, mm	7.5±1.8	6.6±2.1	<0.001	7.3±1.5	7.1±2.2	0.958	7.6±1.9	6.5±2.1	<0.001
TV tethering area, cm <sup>2</sup>	1.2±0.4	1.0±0.5	0.003	1.1±0.4	1.1±0.5	0.711	1.2±0.4	1.0±0.5	<0.001
%TR, %	16.5±10.3	12.7±14.0	0.013	18.6±10.3	34.5±9.6	<0.001	15.8±10.2	5.9±5.9	<0.001
%MR, %	35.2±16.1	12.6±15.8	<0.001	36.1±17.1	21.8±21.1	0.002	35.0±15.8	9.7±12.6	<0.001

Values are mean±SD. LA indicates left atrium; LV, left ventricle; MR, mitral regurgitation; RV, right ventricle; TR, tricuspid regurgitation; TV, tricuspid valve.

Changes in echocardiographic parameters in patients with and without significant residual TR are shown in Table 2. Significant improvement of LV size and LVEF was observed in patients with and without residual TR, whereas RVFAC and tethering distance were improved only in patients without residual TR. TV annulus diameter was enlarged in both groups, although patients with residual TR had significantly larger annulus at the time of follow-up (44.0±5.3 versus 41.1±5.4 mm;  $P=0.017$ ).

### Prognostic Value of Preoperative and Residual TR

During a mean follow-up period of 21±17 months after follow-up echocardiographic examination, 26 (20.5%) patients died. In the univariate analyses, age (hazard ratio, 1.04; 95% confidence interval, 1.005–1.071;  $P=0.020$ ), serum blood urea nitrogen level (hazard ratio, 1.02, 95% confidence interval, 1.001–1.035;  $P=0.045$ ), and residual TR (hazard ratio, 5.01, 95% confidence interval, 2.30–11.5;  $P<0.001$ ) were associated with mortality, whereas preoperative TR was not. Multivariate Cox proportional hazards regression analyses showed that residual TR was significantly associated with mortality (adjusted hazard ratio, 4.00; 95% confidence interval, 1.78–9.43;  $P<0.001$ ). Kaplan–Meier analysis showed that there was no significant difference in mortality between patients with and without significant preoperative TR (log-rank,  $P=0.844$ ; FigureA), whereas significantly higher mortality was observed in patients with significant residual TR than in those without it (log-rank,  $P<0.001$ ; FigureB).

### Discussion

The main findings of this study include the following: (1) LVAD implantation improved the %TR and TV tethering, as well as RV

and LV systolic function, whereas it worsened annulus dilatation; (2) significant residual TR was observed in ≈25% patients with over 1 year of LVAD support; (3) preoperative TV annulus diameter was significantly associated with residual TR; and (4) patients with residual TR had higher mortality compared with those without residual TR.

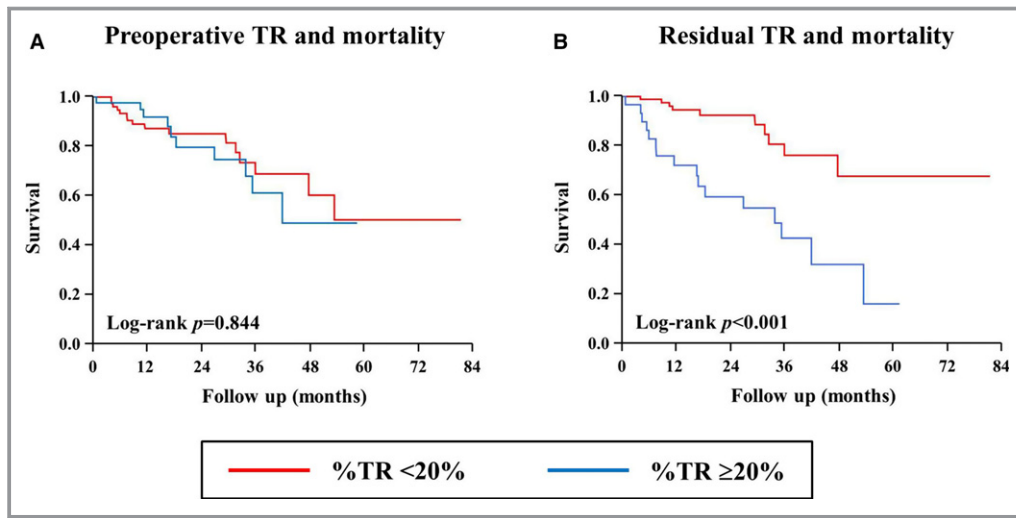
Functional TR in the absence of leaflet abnormalities frequently occurs in patients with heart failure by annulus dilatation and leaflet tethering<sup>1–3</sup> and is associated with unfavorable outcomes.<sup>8–11</sup> Koelling et al demonstrated that severe functional TR was an independent predictor for all-cause mortality in 1421 patients with LVEF <35%.<sup>9</sup> Agricola et al showed that moderate-to-severe functional TR was an independent determinant of overall mortality in 373 patients with heart failure during median follow-up of 32 months.<sup>10</sup> LVAD is an effective therapeutic option for end-stage heart failure. Implantation of a LVAD leads to mechanical unloading of the LV, can induce ventricular reverse remodeling, and generally improves TR in short-term follow-up.<sup>18–20</sup> Morgan et al demonstrated that severity of TR decreased from 11.4% moderate or severe preoperatively to 5% at 1 month after LVAD implantation in 105 patients.<sup>20</sup> However, in the clinical setting, some patients experience nonimprovement of TR or worsening TR (namely “residual TR”) after LVAD implantation during mid- to long-term follow-up. We demonstrated that ≈25% patients had residual TR at 1 year after LVAD implantation. Very interestingly, preoperative TV annulus diameter, but not TV tethering distance, was significantly associated with residual TR, although TV annulus size and tethering distance are not completely independent parameters. The possible mechanisms can be explained as follows. After LVAD implantation, significant improvement of TV tethering distance was observed in our study, which may attenuate the association between leaflet tethering and residual TR. On the other hand, LVAD



**Table 3.** Univariable and Multivariable Logistic Regression Analysis for the Predictors of Residual TR

	Univariable		Multivariable	
	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value
Age, y	1.04 (1.005–1.07)	0.022	1.04 (1.002–1.08)	0.036
Male sex, n (%)	0.54 (0.21–1.49)	0.227		
Hypertension, n (%)	0.73 (0.32–1.67)	0.457		
Diabetes mellitus, n (%)	0.55 (0.23–1.28)	0.170		
Hypercholesterolemia, n (%)	0.96 (0.41–2.19)	0.923		
Body mass index, kg/m <sup>2</sup>	0.94 (0.86–1.02)	0.136		
Ischemic cardiomyopathy	2.02 (0.89–4.69)	0.095		
ICD, n (%)	1.19 (0.39–4.45)	0.773		
Preoperative inotrope support	0.99 (0.31–2.89)	0.982		
<b>Hemodynamic parameters</b>				
CVP, mm Hg	0.95 (0.87–1.03)	0.214		
CVP/PCWP ratio	0.61 (0.08–3.85)	0.617		
PCWP, mm Hg	0.97 (0.92–1.02)	0.276		
Mean PAP, mm Hg	0.96 (0.92–1.002)	0.063		
Cardiac index, L/min per m <sup>2</sup>	1.12 (0.48–2.42)	0.779		
PVR, wood units	0.95 (0.78–1.12)	0.534		
<b>Laboratory parameters</b>				
BUN, mg/dL	1.03 (1.005–1.05)	0.016	1.01 (0.97–1.04)	0.616
Creatinine, mg/dL	2.36 (1.09–5.45)	0.029	1.69 (0.50–5.78)	0.397
Albumin, g/dL	0.89 (0.42–1.89)	0.763		
Total bilirubin, mg/dL	0.77 (0.41–1.29)	0.345		
Hemoglobin, g/dL	0.85 (0.69–1.03)	0.101		
<b>Echocardiographic parameters</b>				
LV end-diastolic diameter, mm	0.96 (0.92–1.004)	0.080		
LV ejection fraction, %	0.95 (0.87–1.04)	0.289		
LA diameter, mm	0.97 (0.92–1.02)	0.303		
RV end-diastolic area, cm <sup>2</sup>	1.01 (0.96–1.05)	0.768		
RV end-systolic area, cm <sup>2</sup>	1.00 (0.94–1.05)	0.950		
RV fractional area change, %	1.01 (0.97–1.06)	0.541		
RV systolic excursion velocity, cm/sec	0.98 (0.83–1.14)	0.781		
RV systolic pressure, mm Hg	1.01 (0.98–1.05)	0.462		
TV annulus diameter, mm	1.15 (1.05–1.27)	0.003	1.15 (1.04–1.28)	0.005
TV tethering distance, mm	0.91 (0.70–1.14)	0.421		
TV tethering area, cm <sup>2</sup>	0.65 (0.20–1.97)	0.452		
%TR, %	1.03 (0.99–1.07)	0.188		
Preoperative significant MR	1.11 (0.42–3.29)	0.846		
Residual MR	3.64 (1.45–9.16)	0.006	4.52 (1.58–13.4)	0.005

BUN indicates blood urea nitrogen; CI, confidence interval; CVP, central venous pressure; ICD, implantable cardioverter defibrillator; LA, left atrium; LV, left ventricle; MR, mitral regurgitation; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RV, right ventricle; TR, tricuspid regurgitation; TV, tricuspid valve.



**Figure.** Kaplan–Meier survival curves after follow-up echocardiographic examination, according to the preoperative TR (A) and residual TR (B). TR indicates tricuspid regurgitation.

implantation causes chronic leftward displacement of the interventricular septum, which may lead to deterioration of preexisting TV annulus enlargement and gradually increase functional TR with subsequent further RV preload increases. Indeed, we showed significant TV annulus enlargement after LVAD implantation in patients with and without significant residual TR, and that annulus enlargement was not observed in early postoperative echocardiography. Kukucka et al recently showed that preoperative TV annulus dilatation was associated with survival after LVAD implantation in 122 patients without severe TR.<sup>28</sup> Residual TR may play a key role in the association of enlarged TV annulus with increased mortality risk. RVFAC also did not predict residual TR in this study. Significant improvement of RVFAC after LVAD implantation may attenuate the association between RVFAC and residual TR. Furthermore, RVFAC emerged as a poor parameter for the determination of RV contractility in recent studies,<sup>29,30</sup> suggesting that, in the presence of TR, estimates of radial contraction may misdiagnose the presence of RV dysfunction because of the decrease in RV afterload caused by the leaking valve, just as the LVEF assessment is limited by MR.<sup>13</sup> Tricuspid annular plane systolic excursion, RV index of myocardial performance and/or assessment using 3-dimensional echocardiography may provide additional information of RV contractility and its association with residual TR.<sup>30,31</sup> Hemodynamic parameters were not independently associated with residual TR in this study. Because recent studies showed that preoperative pulmonary artery pulsatility index<sup>32,33</sup> and RV stroke work index<sup>34,35</sup> are associated with early right heart failure after LVAD implantation, future studies are needed whether these parameters predict the residual TR in patients with mid- to long-term LVAD support. In addition, ischemic cardiomyopathy tended to have more residual TR in this study, although previous work showed

that nonischemic cardiomyopathy is a risk factor for early right heart failure.<sup>34</sup> This might be partially explained by the small number of patients, as well as difference of study population and follow-up period.

We also demonstrated that patients with significant residual TR had worse survival compared with those without residual TR. On the other hand, there was no significant survival difference between patients with and without preoperative significant TR. Residual TR after LVAD implantation may serve as a surrogate for adverse outcomes post-LVAD implantation during long-term follow-up. In addition, evaluation of TV annulus diameter before LVAD implantation might be useful to identify patients at high risk for residual TR and associated outcomes. Patients with dilated TV annulus may benefit from certain modifications in surgical procedure technique and/or pharmacological intervention. In addition, because residual MR was also significantly associated with residual TR, therapeutic interventions to reduce the MR might have beneficial effect on residual TR. Those concepts, however, require testing in prospective, large, controlled trials. Furthermore, the progression of underlying RV myopathy should be kept in mind for the management of LVAD patients, which might attenuate the effect of TV intervention for reduction of residual TR in LVAD patients. Our study encourages further investigations for the management of residual TR in LVAD patients.

### Study Limitations

This study is a retrospective observational analysis of a single center's experience and included LVAD patients without concomitant TV surgical procedure, which might not allow generalization of the results to LVAD patients with severe TR. In addition, residual TR was observed only in 30

patients, which might be insufficient to conclude the observed association. Future prospective study should be performed to confirm the results of this study and to evaluate the time course of TR after LVAD implantation in a larger population. TR is a dynamic parameter that is highly dependent on RV volume/pressure loading characteristics. Therefore, when echocardiographic examinations were performed, stable hemodynamic conditions were carefully confirmed during transthoracic echocardiographic examination. Moreover, RV size and geometry are technically difficult to determine accurately with 2-dimensional echocardiography because of its anatomic complexity. Although the 3-dimensional echocardiography now offers an accurate and real-time assessment of the size and shape of RV and the TV deformation,<sup>30,36</sup> high feasibility, and reproducibility of TV annulus diameter using 2-dimensional echocardiography in apical 4-chamber view has been reported when compared with 3-dimensional echocardiography.<sup>26</sup>

## Conclusions

Significant residual TR was observed in  $\approx 25\%$  patients supported with LVAD for 1 year and was associated with unfavorable outcome. Evaluation of TV annulus diameter before LVAD implantation might be useful to identify patients at high risk for significant residual TR. Furthermore, close follow-up should be performed in patients with significant residual TR.

## Disclosures

None.

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