

Preoperative 6-minute walk test predicts prolonged hospitalization after transcatheter tricuspid valve replacement

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Abstract

The purpose of this study is to determine whether preoperative 6-minute walk test (6MWT) is associated with prolonged postoperative hospitalization in high risk patients with severe tricuspid regurgitation (TR) after transcatheter tricuspid valve replacement (TTVR). Forty-one patients with severe TR who underwent TTVR and discharged between September 2018 and April 2021 were enrolled in this study. Patients were divided into 2 groups according to whether the postoperative hospital stay was >10 days and patients' data were retrospectively collected. 6MWT was performed before operation. Twenty-one patients were in the control group (≤ 10 days) and 20 patients were in the prolonged postoperative stay (PPS) group (>10 days). 6MWT distance was significantly decreased in PPS group (192.70 ± 62.34 vs 274.57 ± 52.09 m, $P < .05$). PPS group had more patients with severe liver disease (50.00% vs 19.05%, $P < .05$), higher systolic pulmonary artery pressure (45.05 ± 9.28 vs 35.57 ± 8.91 mm Hg, $P < .05$) and longer procedure time (159.85 ± 56.61 vs 124.43 ± 31.67 min, $P < .05$). Multivariable logistic regression analysis found 6MWT < 267 m was an independent risk factor with the odds ratio of 10.95 (1.66–72.39, $P < .05$) for prolonged postoperative hospitalization in patients who received TTVR. In the present study, we identified that preoperative decreased 6MWT distance was an independent risk factor for prolonged hospitalization in high risk TR patients after TTVR.

Abbreviations: 6MWT = 6-minute walk test, ICU = intensive care unit, OR = odds ratio, PPS = prolonged postoperative stay, ROC = receiver operating characteristic, sPAP = systolic pulmonary artery pressure, TR = tricuspid regurgitation, TTVR = transcatheter tricuspid valve replacement.

Keywords: 6-minute walk test, postoperative hospitalization, transcatheter tricuspid valve replacement

1. Introduction

Tricuspid regurgitation (TR) is a relatively common heart disease and severe TR is associated with poor long-term prognosis.^[1] Transcatheter tricuspid valve replacement (TTVR) is a novel way for severe TR treatment, especially in TR patients who are at high risk for traditional open surgery.^[2] LuX-Valve (Ningbo Jenscare Biotechnology, Ningbo, China) is a new radial force independent orthotopic TTVR device and it has been implanted in TR patients with satisfactory clinical results.^[3] However, risk factors for prolonged postoperative hospitalization in patients who received TTVR are still unknown.

Six-minute walk test (6MWT) is a simple and reliable tool to evaluate exercise capacity in patients with heart diseases.^[4] Studies have shown decreased 6MWT predicted adverse outcomes in chronic heart failure patients.^[5,6] Besides, it was

reported 6MWT predicted prolonged hospitalization in patients who received transcatheter mitral valve repair.^[7] Based on these findings, it is reasonable to assume that 6MWT distance predicts prolonged postoperative hospitalization in these high risk TR patients who received TTVR.

In the present study, we tried to determine whether preoperative 6MWT is associated with prolonged hospitalization in high risk severe TR patients after TTVR.

2. Methods

2.1. Patients

This is a retrospective study and we identified 41 patients with severe TR undergoing TTVR with LuX-Valve in our center between September 2018 and April 2021. All patients were at

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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high risk for open heart surgery. EuroSCORE II cardiac operative risk model was adopted in this study and the score was calculated from the online calculator.^[8] In this study, patients were planned for examination with echocardiography at postoperative 7 to 10 days and then discharged if the examination was fine and no postoperative complications occurred. Postoperative hospital stay >10 days were defined as prolonged postoperative hospitalization and patients were divided into 2 groups according to whether they had prolonged postoperative hospitalization and patients' data were retrospectively collected from the medical records. Patients who died after surgery were excluded from the study. In the present study, TR was graded in 6 degrees as none, mild, moderate, severe, massive and torrential according to the severity.^[9] Pulmonary artery pressure was obtained by right heart catheterization before operation. This study was approved by the Institutional Review Board of Changhai Hospital and informed consent was adopted from the patients or their direct relatives before operation.

2.2. Procedure details

In brief, a minimally right thoracotomy was made after general anesthesia and double lumen tube intubation. Then the pericardium was suspended and the right atrial was exposed under 1-lung ventilation. Double purse-string sutures were made on the atrial and LuX-Valve was implanted through a 32 F catheter via transatrial approach under the guidance of transesophageal echocardiography and fluoroscopy. Once the device was on position, LuX-Valve was released and adjusted to eliminate the perivalvular leakage. Finally, LuX-Valve was detached from the delivery catheter after carefully adjustment and the catheter was drawn back. Right coronary angiography was performed to help to locate the tricuspid annulus during the procedure. Details of the structure of the LuX-Valve and operation procedures were described in our previous studies.^[3] In this study, procedure success was defined as successful device implantation and retrieval of the delivery system, correct and stable positioning of the valve prosthesis and no severe or life-threatening adverse events occurred during the procedure.

2.3. 6MWT

6MWT was performed in a flat and straight corridor with quiet surroundings and 20 m in length. Patients were asked to walk as far as possible along with the corridor mentioned above for 6 minutes without any help. Rest during the test was allowed but patients should get back to walk as soon as possible. Walking distance was recorded after 6 minutes of walking and the test was performed in the same time period within 1 week before the operation. Details of the test in this study was according to the American Thoracic Society guidelines for 6MWT.^[10]

2.4. Statistical analysis

Data were presented as mean \pm standard deviation for continuous variables and number (%) for categorical variables. Statistical comparison in continuous and categorical variables was performed with Student *t* test and Chi-square test, respectively. For continuous variables with statistical differences, receiver operating characteristic (ROC) curve analysis was adopted to address the optimal cutoff value and the area under the curve was obtained to evaluate its efficacy. Independent risk factors for prolonged postoperative hospitalization were determined by univariate and multivariate logistic regression analysis and the risk factors' effect was assessed by odds ratio (OR) and 95% confidence interval. In this study, statistical analysis was performed with Statistical Package for Social Sciences, version 25.0 (SPSS, Chicago, IL).

3. Results

3.1. Patients' information

In this study, mean postoperative in-hospital time was 17.55 ± 18.48 days. Twenty-one patients were divided in the control group (in-hospital time ≤ 10 days) and 20 patients were divided in the prolonged postoperative stay (PPS) group (in-hospital time >10 days). We found 6MWT distance was significantly decreased in PPS group (192.70 ± 62.34 vs 274.57 ± 52.09 m, $P < .05$). More patients have severe liver disease (model for end-stage liver disease-albumin score ≥ 12) in PPS group (50.00% vs 19.05%, $P < .05$). Besides, systolic pulmonary artery pressure (sPAP) was higher in PPS group compared with the control (45.05 ± 9.28 vs 35.57 ± 8.91 mm Hg, $P < .05$). Details of the patients' information was shown in Table 1.

3.2. In-hospital outcomes

In-hospital data of these 2 groups were shown in Table 2. Procedure time was longer in PPS group (159.85 ± 56.61 vs 124.43 ± 31.67 min, $P < .05$). We did not find differences in intraprocedural bleeding, conversion to open surgery and procedure success between 2 groups. One patient in control group had right ventricle wall perforation and this patient was converted to median sternotomy surgery for hemostasis. No heart block occurred during the procedure. But we found postoperative intensive care unit (ICU) and hospital time were longer in PPS group compared with the control (6.05 ± 4.42 vs 2.24 ± 1.09 days, $P < .05$ and 28.05 ± 18.60 vs 7.90 ± 1.26 days, $P < .05$).

3.3. ROC curve analysis

ROC curve analysis was used to determinate the optimal cutoff value of continuous variables which had statistical differences (Fig. 1). We found the optimal cutoff value of 6MWT, sPAP and procedure time were 267 m, 43 mm Hg and 125 minutes with the area under the curve of 0.84 0.76 and 0.71 respectively (Table 3).

3.4. Univariate and multivariable logistic regression analysis

Univariate and multivariable logistic regression analysis were shown in Table 4. Four variables were enrolled in the univariate logistic regression analysis and results showed 6MWT <267 m, sPAP >43 mm Hg, procedure time >125 minutes and severe liver disease were all risk factors for prolonged postoperative hospitalization with the OR of 14.00 (2.97–66.09, $P < .05$), 4.91 (1.09–22.15, $P < .05$), 12.00 (2.20–65.52, $P < .05$) and 4.25 (1.05–17.20, $P < .05$). Then these 4 variables were further analyzed in the multivariable logistic regression analysis and the result showed only 6MWT <267 m was the independent risk factor for prolonged postoperative hospitalization with the OR of 10.95 (1.66–72.39, $P < .05$).

4. Discussion

TR patients in this study were all at very high surgical risk. Traditional medical treatment for these patients had limited benefits and the prognosis was poor.^[11] LuX-Valve was a new developed radial force-independent orthotopic TTVR device and TTVR with LuX-Valve was adopted for TR treatment in high risk patients in our institution with satisfied clinical results.^[3] As a new treatment method, knowledge about the risk factors for postoperative prolonged hospitalization was very limited. 6MWT is a common tool to assess exercise capacity and in this study we found severe TR patients with decreased preoperative

Table 1
Preoperative characteristics.

Characteristics	Control (n = 21)	PPS (n = 20)	P
Age	67.95 ± 7.80	68.85 ± 7.01	.70
BMI	21.76 ± 2.61	22.07 ± 2.90	.72
EuroSCORE II	9.16 ± 2.91	10.76 ± 3.61	.13
6MWT	274.57 ± 52.09	192.70 ± 62.34	<.05
NYHA IV	14 (66.67)	15 (75.00)	.56
Hypertension	4 (19.05)	2 (10.00)	.71
Diabetes	5 (23.81)	3 (15.00)	.75
Atrial fibrillation	21 (100.00)	19 (95.00)	.49
Coronary artery disease	3 (14.29)	2 (10.00)	1.00
Prior gastrointestinal bleeding	2 (9.52)	4 (20.00)	.61
Anemia	14 (66.67)	11 (55.00)	.44
Pulmonary hypertension	10 (47.62)	15 (75.00)	.07
Renal dysfunction*	11 (52.38)	11 (55.00)	.87
Severe liver disease†	4 (19.05)	10 (50.00)	<.05
Prior stroke	1 (4.76)	2 (10.00)	.97
Previous cardiac surgery	13 (61.91)	15 (75.00)	.37
PPM/ICD	8 (38.10)	6 (30.00)	.59
Severe TR	21 (100.00)	20 (100.00)	1.00
VC	13.55 ± 3.38	12.40 ± 2.39	.22
EROA (mm ²)	108.74 ± 45.13	89.65 ± 33.76	.14
sPAP (mm Hg)	35.57 ± 8.91	45.05 ± 9.28	<.05

Data are presented N (%) or mean ± SD.

6MWT = 6-min walk test, BMI = body mass index, EROA = effective regurgitant orifice area, ICD = implantable cardioverter defibrillator, NYHA = New York Heart Association, PPM = permanent pacemaker, PPS = prolonged postoperative stay, sPAP = systolic pulmonary artery pressure, TR = tricuspid regurgitation, VC = vena contracta.

*Defined as eGFR <60 mL/min.

†Defined as MELD-albumin score >12.

Table 2
In-hospital outcomes.

Characteristics	Control (n = 21)	PPS (n = 20)	P
Intraoperative			
Procedure time (min)	124.43 ± 31.67	159.85 ± 56.61	<.05
Intraprocedural bleeding (mL)	134.76 ± 317.53	138.50 ± 64.50	.96
Conversion to open surgery	1 (4.76)	0 (0.00)	1.00
Procedure success	20 (95.24)	20 (100.00)	1.00
Postoperative			
24 h chest drainage (mL)	179.95 ± 103.98	261.90 ± 187.74	.09
Reoperation for bleeding	2 (9.52)	2 (10.00)	1.00
ICU time (d)	2.24 ± 1.09	6.05 ± 4.42	<.05
Hospital time (d)	7.90 ± 1.26	28.05 ± 18.60	<.05
Gastrointestinal hemorrhage	2 (9.52)	5 (25.00)	.37
Renal failure	1 (4.76)	4 (20.00)	.31
Myocardial infarction	0 (0.00)	1 (5.00)	.49
TR severity ≤mild	18 (85.71)	15 (75.00)	.64
Moderate perivalvular leak	3 (14.29)	4 (20.00)	.94
Moderate central valvular regurgitation	0 (0.00)	1 (5.00)	1.00

Data are presented as N (%) or mean ± SD.

ICU = intensive care unit, PPS = prolonged postoperative stay, TR = tricuspid regurgitation.

6MWT distance had prolonged postoperative in-hospital time after TTVR.

6MWT was widely used to assess preoperative exercise capacity.¹¹⁰ Chen et al found 6MWT was a validated tool to evaluate physical function and associated with postoperative recovery after cardiac surgery.¹¹² It has been reported decreased 6MWT distance was associated with increased postoperative mortality and complications. It was reported decreased preoperative 6MWT predicted poor long-term survival in patients received transcatheter aortic valve replacement procedure.¹¹³ Saji et al reported patients undergoing transcatheter mitral valve repair with short 6MWT distance had longer in-hospital time.¹⁷ De Arenaza et al reported 6MWT predicted postoperative adverse outcomes, postoperative mortality, myocardial infarction and stroke were higher

in patients with decreased preoperative 6MWT undergoing aortic valve replacement.¹¹⁴ These studies indicated that 6MWT was an effective tool to assess patients' physical function in cardiac surgery.

Physical capacity is an important factor for prognosis in TR patients after surgery intervention. Besler et al found patients with postoperative longer 6MWT distance had improved nutritional status, decreased N-terminal pro-brain natriuretic peptide levels, cholinesterase levels and renal function after transcatheter tricuspid repair.¹¹⁵ Benedetto et al found TR less than moderate patients received concomitant tricuspid annuloplasty during mitral valve surgery had improved 6MWT distance accompanying with improved right ventricular remodeling and TR progression.¹¹⁶ These findings indicated that TR correction had benefits for physical capacity improvement.

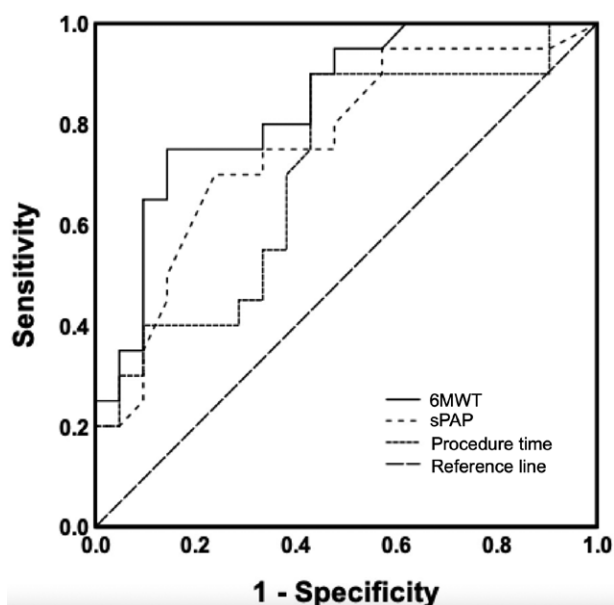


Figure 1. ROC analysis based on 6MWT, sPAP and procedure time. Area under the curve were 0.84 for 6MWT, 0.76 for sPAP and 0.71 for procedure time. 6MWT = 6-minute walk test, ROC = receiver operating characteristic, sPAP = systolic pulmonary artery pressure.

Table 3
ROC curve analysis.

	AUC	P	Cutoff value
6MWT (m)	0.84	<.05	267
sPAP (mm Hg)	0.76	<.05	43
Procedure time (min)	0.71	<.05	125

6MWT = 6-min walk test, AUC = area under the curve, ROC = receiver operating characteristic, sPAP = systolic pulmonary artery pressure.

However, the role of physical capacity in predicting outcomes in high risk TR patients received TTVR was less well known and our study found decreased preoperative 6MWT distance indicated prolonged postoperative hospitalization in such population.

Patients included in this study were all at very high risk for traditional surgical procedure and previous studies showed a poor perioperative prognosis, especially for patients with decreased 6MWT.^[17] Patients with decreased 6MWT distance in this study had prolonged postoperative hospitalization and ICU time. Considering postoperative prolonged ICU time was risk factor for poor long-term survival,^[18] further study on the relationship between 6MWT and the long-term prognosis is

needed and TTVR in patients with decreased 6MWT should be carefully considered.

We compared patients' information between control group and PPS group and found more patients in PPS group had severe liver disease, increased sPAP and longer procedure time. Previous study found severe liver disease was a risk factor for decreased postoperative survival in patients undergoing transcatheter aortic valve replacement.^[19] Increased systolic pulmonary artery pressure was also reported associated with postoperative adverse events in patients received heart transplantation.^[20] In this study, although severe liver disease, increased sPAP and longer procedure time were also risk factors for postoperative prolonged hospitalization in univariate logistic regression analysis, multivariate analysis showed only decreased 6MWT distance was an independent risk factor for postoperative prolonged hospitalization.

The present study had some limitations. First, this study was a retrospective small sample study and the results might have some biases, especially in the cutoff value of 6MWT distance. Second, TTVR with LuX-Valve was a new treatment method for TR patients and the prognosis of patients were affected by the operator's learning curve, which also affected the study results. Based on the above, a randomized perspective large sample study is needed to further investigate the role of physical function in predicting postoperative prolonged hospitalization in TR patients received TTVR.

5. Conclusions

In the present study, we identified that preoperative decreased 6MWT distance was an independent risk factor for prolonged hospitalization in high risk TR patients after TTVR.

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Table 4
Logistic regression analysis.

Variables	Univariate			Multivariate		
	OR	95% CI	P	OR	95% CI	P
6MWT <267 m	14.00	2.97–66.09	<.05	10.95	1.66–72.39	<.05
sPAP >43 mm Hg	4.91	1.09–22.15	<.05	5.34	0.76–37.64	.09
Procedure time >125 min	12.00	2.20–65.52	<.05	4.27	0.50–36.27	.18
Severe liver disease	4.25	1.05–17.20	<.05	4.55	0.75–27.77	.10

6MWT = 6-min walk test, CI = confidence interval, OR = odds ratio, sPAP = systolic pulmonary artery pressure.

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