

# Functional Tricuspid Regurgitation Repair at the Time of Left-Sided Valve Surgery: The Impact on the Cardiac Rehabilitation Program

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## Article Info

### Article History:

Received: 11 March, 2021

Accepted: 15 March, 2021

Published: 20 March, 2021

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## Abstract

**Objective:** to compare the early post-operative functional status and the efficacy of the cardiac rehabilitation program (CRP) after isolated left-sided valvular surgery or with concomitant tricuspid valve repair (TVR).

**Methods:** we retrospectively enrolled patients admitted to the Cardiac Rehabilitation Unit of our institution from January 2014 to January 2019, following mitral or aortic valve surgery. In agreement with current guidelines, concomitant tricuspid annuloplasty was added to patients with severe functional tricuspid regurgitation (TR) and in those with mild to moderate TR when annulus dilatation was present. A 6-minute walk test (6mWT) was performed within the second day of admission and repeated pre-discharge. The distances walked on the 6mWT were reported as absolute value and as a percentage of the predicted value, taking into account anthropometric variables. Changes in the 6mWT performance and Barthel index (BI) were assessed to evaluate the impact of CRP on exercise tolerance and functional independence, respectively.

**Results:** of 117 patients, 62 (53%) had isolated left-sided valvular surgery and 55 (47%) had concomitant TVR. There were no significant differences between the two groups in the baseline 6mWT performance and its improvement at the end of CRP. TVR was associated with a worse BI on admission, but with a greater improvement after the CRP and a pre-discharge BI comparable to isolated left-sided surgery. Upon linear regression analysis, diabetes and chronic renal disease were predictors of the baseline 6mWT performance.

**Conclusion:** TVR does not affect the early post-operative functional status and the efficacy of the CRP after valvular surgery.

**Keywords:** Cardiac rehabilitation; Tricuspid regurgitation; Valvular surgery; 6 minute walk test

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## Introduction

Functional tricuspid regurgitation (TR) is often associated with left-sided valvular disease. Although TR might be only mild at the time of surgery, progression of TR severity occurs in nearly 30% of patients after isolated left-sided valve surgery and portends a poor prognosis [1]. Reoperation for late TR is associated with a high perioperative and long-term mortality [2], while performing tricuspid valve repair (TVR) at the time of left-sided valve surgery does not modify the operative risk [3]. Therefore, a more liberal approach in adding TVR at the time of left-sided valve surgery is now advocated by the current ESC and AHA/ACC guidelines on valvular heart disease [4, 5]. Particularly, TVR is recommended as class I in patients with severe functional TR and as class IIa in patients with mild or moderate TR when annulus dilatation is present. However, despite these recommendations, the rates of concomitant TVR are highly variable and suboptimal, possibly due to the persistent fear of perioperative complications [6]. A cardiac

rehabilitation program (CRP) may promote a positive impact in relevant clinical outcomes and is strongly recommended for patients after cardiac surgery, particularly in the elderly because of the high prevalence of frailty and comorbidities [7]. In the setting of cardiac rehabilitation, the 6-minute walk test (6mWT) is frequently used to assess the patient's baseline functional capacity and prescribe exercise training intensity at program entry. Of note, the distance walked on baseline 6mWT is influenced by the type of cardiac surgery, being higher in coronary artery surgery than in the valve and other surgery [8]. Moreover 6mWT is a valuable tool to evaluate the progression in exercise capacity at the end of CRP [9]. Importantly, pre-discharge 6mWT performance has been associated with long-term mortality in patients undergoing a post-cardiac surgery rehabilitation program [10]. Additionally, the Barthel index is a valuable tool for the assessment of the improvement in functional dependence after CRP [11-13]. Despite the large body of evidence regarding the benefit of CRP, comparative data on patients undergoing valve surgery with or without simultaneous TVR are lacking. Therefore, the main purpose of our study was to

compare the early post-operative functional status and the efficacy of the CRP in patients undergoing valve surgery with or without concomitant TVR.

## Methods

**Study Population:** We retrospectively enrolled consecutive patients admitted to the Cardiac Rehabilitation Unit of the Fondazione Policlinico Universitario Agostino Gemelli IRCCS (Rome, Italy) from January 2014 to January 2019, following mitral or aortic valve surgery. All patients had been operated in our hospital. Patients were classified in two sub-groups: patients undergoing isolated left-sided valvular surgery and patients undergoing surgery with concomitant tricuspid annuloplasty. TVR was performed in patients with severe functional TR and in those with mild or moderate TR when annulus dilatation was documented ( $>40$  mm or  $> 21$  mm/m<sup>2</sup>) on preoperative 2D echocardiography, according to the current guidelines [4]. Exclusion criteria were primary TR, combined valvular and coronary artery surgery and previous cardiac surgery. The institutional ethical committee approved the study and a written informed consent was obtained from all participants.

**Rehabilitation Program and 6 Min Walk test (6MWT):** All patients underwent an in-hospital rehabilitation program of 14 days. The 6mWT was performed within the second day of admission in the rehabilitation unit and repeated pre-discharge. The patients were instructed to walk as far as possible along a 45-m straight, flat hospital corridor in 6 min (10). Participants were allowed to stop and rest during the test, but were instructed to restart walking when possible. The total distance walked was measured and recorded. Before and immediately after the exercise, the patient's heart rate, blood pressure and oxygen saturation were measured in the sitting position and recorded. Other evaluated parameters included the number and duration of rest periods and symptoms (e.g. angina, severe dyspnea and leg pain). The results of the 6mWT were reported as absolute value in meters and as a percentage of the predicted value, taking into account anthropometric variables (age, sex, weight and height) according to the equation proposed by Enright et al. in healthy subjects [14]. We defined patients as having poor or preserved 6MWT performance if walked distance on admission was, respectively, within or above the lower quartile of percentage of predicted value (predicted cut-off 35%). The effects of the CRP were evaluated as percentage increase in the distance walked

between the two 6MWT. Moreover Barthel index (BI) was calculated at the admission and pre-discharge in all patients. BI evaluates physical and cognitive disability by a score that ranges between 0 and 100 points, where high scores indicate a greater grade of independence [11]. The changes in the BI were assessed in order to evaluate the effects of CRP on the functional independence of patients. Patients underwent a comprehensive rehabilitation, which also included optimization of pharmacological therapy, control of modifiable risk factors and psychological counseling. In relation to the performance on the 6mWT, patients started a tailored exercise program with gradual increase in the intensity and duration. Physical activity included aerobic exercise on a cycle-ergometer or treadmill (targeting 65–75% of the theoretical maximal heart rate), low-level and short-lasting callisthenic exercises and gentle passive stretching involving all major joints. Exercise training was performed twice a day and was supervised by members of the rehabilitation staff.

**Statistical Analysis:** Continuous variables were compared using an unpaired Student's t-test or Mann–Whitney U test, as appropriate, and data were expressed as mean  $\pm$  standard deviation or as median (range). Categorical data were evaluated using the Chi<sup>2</sup> test or Fisher's exact test as appropriate and data expressed as percentages. Linear regression analysis was applied to assess the relation of individual variables with the 6MWT performance. Variables found to be significant at univariate analysis were further analyzed by a multivariate linear regression model in order to identify variables independently associated with 6MWT performance. A two-tailed p value  $<0.05$  was considered statistically significant. All analyses were performed using SPSS V. 20.

## Results

During the study period, 145 patients were admitted to our Rehabilitation Unit for intensive in-hospital rehabilitation following left-sided valvular surgery. Patients unable to perform the 6mWT at the admission (7 patients) or before the discharge (6 patients), in relation to hemodynamic instability or motor function impairment, were excluded. Moreover, 5 patients were excluded because they had combined valvular and coronary surgery performed upon. A final cohort of 117 patients was formed. Of them, 62 (53%) patients had isolated mitral or aortic surgery and 55 (47%) patients had mitral or aortic surgery with tricuspid annuloplasty. Demographic and clinical characteristics of the total population and the two sub-groups are presented in (Table 1).

**Table 1:** Demographic and clinical characteristics of the total population and the two subgroups.

Clinical parameters	Total (n = 117)	Isolated surgery (n = 67)	TVR (n = 56)	P value
Age, yrs	67.5 $\pm$ 13.0	69.1 $\pm$ 12.0	67.5 $\pm$ 11.9	0.16
Female sex, n (%)	57 (48.7)	28 (45.2)	29 (52.7)	0.41
Surgery				0.001
Aortic valve surgery, n (%)	46 (39.3)	40 (64.5)	6 (10.9)	
Mitral valve surgery, n (%)	71 (60.7)	22 (35.5)	49 (89.1)	
Hypertension, n (%)	88 (75.2)	48 (77.4)	40 (72.7)	0.62
Diabetes, n (%)	26 (22.2)	13 (21)	13 (23.6)	0.73
Dyslipidemia, n (%)	56 (47.9)	30 (48.3)	26 (47.3)	0.91

Smoking, n (%)	55 (47)	29 (46.8)	26 (47.3)	0.96
CKD, n (%)	9 (7.7)	3 (4.8)	6 (11.1)	0.21
Atrial fibrillation, n (%)	20 (17.1)	9 (14.5)	11 (20.4)	0.4
COPD, n (%)	6 (5.1)	2 (3.2)	4 (7.5)	0.41
Post-operative LVEF, %	56.8 ± 10.9	58.1 ± 11.0	55.3 ± 10.6	0.16
Post-surgical complications, n (%)	10 (8.5)	3 (4.8)	7 (12.7)	0.19

**Legend.:** chronic kidney disease; COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; TVR: tricuspid valve repair.

The rate of post-operative complications was comparable between the two groups. The 6mWT was performed by the second day after rehabilitation admission and within 10 days after cardiac surgery (7±2 days) and repeated at the end of the

CRP. The test was well tolerated by all patients. At baseline, the mean walking distance in the overall population was 202.9±79.7 m, corresponding to 42.9 ±16.4% of the predicted value (Table 2).

**Table 2:** Serial assessment of functional parameters in the total population and the two subgroups.

Functional parameters	Total (n = 123)	Isolated surgery (n = 67)	TVR (n = 56)	P value
Admission 6mWT (m), mean ±SD	202.9 ± 79.7	204.2 ± 77.4	193.6 ± 81.9	0.48
Admission 6mWT (%predicted), mean±SD	42.9 ±16.4	44.3±15.3	41.3±1.75	0.3
Discharge 6mWT (m), mean ±SD	320.1 ± 116.6	309.1 ± 120.4	320.3 ± 102.7	0.61
Discharge 6mWT (%predicted), mean ±SD	64.6 ± 26.6	65.4 ± 27.1	63.7 ± 26.2	0.73
% Improvement 6mWT, mean±SD	88.8 ± 143.4	80.2 ± 94	106.4 ± 201.1	0.39
Admission Barthel index, median (range)	62 (56; 68)	63 (57; 70)	60 (53; 64)	0.008
Discharge Barthel index, median (range)	98 (92; 100)	98 (93; 100)	98 (92; 100)	0.64
Improvement Barthel index, median (range)	34 (28; 40)	31 (24; 38)	36 (29; 42)	0.01

**Legend:** 6mWT: six minute walking test.

The walking distance, expressed both as absolute value and percentage of the predicted value, was similar between patients undergoing surgery with or without concomitant TVR (193.6 ± 81.9, 41.3±1.75 % vs 204.2 ± 77.4 m, 44.3 ±15.3 %, respectively). In the total population, the distance walked increased significantly at the end of the rehabilitation program to 320.1±116.6 m, corresponding to 64.6 ± 26.6% of the predicted value (p < 0.001). The extent of the improvement observed was similar between the two groups. TVR was associated with significantly lower baseline BI score compared

to isolated mitral or aortic surgery (60 [53; 64] vs 63 [57; 70] p=0.01), reflecting a lower autonomy in daily activities at the admission. However patients undergoing TVR had a greater improvement at the end of the CRP (p < 0.001) and the pre-discharge BI scores were comparable between the two groups (98 [92; 100] vs 98 [93; 100]). Regarding univariate linear regression analysis (Table 3) diabetes mellitus (DM) and chronic kidney disease (CKD) were negatively associated with the baseline 6mWT performance (expressed as % of the predicted value).

**Table 3:** Variables associated with baseline 6 WMT performance (expressed as % of the predicted value) by univariate and multivariate linear regression analysis.

Variable	Univariate analysis β (95% C.I.)	P value	Multivariate analysis β (95% C.I.)	P value
Diabetes	-0.27 (-0.15; -0.03)	0.003	-0.18 (-0.15; -0.02)	0.02
CKD	-0.12 (-0.2; -0.03)	0.01	-0.2 (-0.22; -0.01)	0.03

At the multivariate regression analysis both DM (β -0.18, [95%CI -0.15; -0.02], P=0.02) and CKD (β -0.2, [95%CI -0.22; -0.01], P=0.03) confirmed their predictive value on 6MWT performance. No significant associated was found between the distance walked and the type of surgery or the post-operative left ventricular ejection fraction (LVEF %), evaluated

both as continuous and dichotomous (LVEF more or less than 35%) variable. Patients with a low initial functional capacity (<35% walking distance predicted) demonstrated a greater improvement in the functional capacity after training compared with patients with preserved performance (+153% vs +53%, p < 0.001). Moreover

there were not significant differences in the extent of improvement regarding to sex, age, comorbidities, type of surgery and LVEF%.

## Discussion

This study was performed on a cohort of patients entering a cardiac rehabilitation program early after valvular surgery. The results showed that patients undergoing valvular surgery with additional TVR had a similar benefit in exercise tolerance, but a larger improvement in functional independence at the end of CRP. Moreover comorbidities, particularly diabetes and CKD, were independently associated with the baseline 6mWT performance, while no correlation was found between the distance walked and the type of surgery. To the best of our knowledge, there are no published reports on the effects of performing simultaneous TVR on the functional recovery during rehabilitation after valvular surgery. In the present study, TVR was more frequently performed in patient's undergoing mitral surgery compared to aortic surgery. Functional TR occurs in patients with left-sided valvular disease as a result of increased left atrial pressure, that leads to pulmonary hypertension and a subsequent rise in right ventricle pressure with progressive right ventricle dysfunction and annulus dilatation, which create the anatomic substrate for functional TR [15]. Consequently, the early increase in left atrial pressure in patients with mitral valve disease could explain the more frequent association with functional TR compared to patients with aortic valve disease. TVR provides a reverse remodeling of the right ventricle, lower recurrence of TR and improvement of long-term functional status, even in the absence of significant TR, when annulus dilatation is present [16, 17]. Therefore, a more liberal approach in performing TVR at the time of left-sided valve surgery is now recommended by the ESC and AHA/ACC guidelines on valvular heart disease [4, 5]. However the rates of concomitant TVR are still suboptimal, maybe because of the fear of increased risks for this additional procedure [18]. Of importance is that current evidence supports the fact that concomitant TVR does not significantly increase the perioperative mortality and morbidity when correcting left-sided valve disease, despite requiring longer surgical time [3, 18]. In this context, our results showed that simultaneous tricuspid valve repair does not affect the early post-operative functional capacity and the efficacy of the CRP in these patients, adding evidence to the safety of this procedure. In our population, TVR was associated with a greater disability after cardiac surgery, demonstrated by the lower baseline BI score, but with a larger functional improvement at the end of the CRP. The disability observed at baseline in the TVR group could be explained by either the longer surgical procedure or a pre-existing poor functional status, related to the more advanced cardiopathy. However, the pre-discharge BI scores were comparable between the two groups, reflecting the complete recovery of functional independence in patients which had

surgery with TVR. As previously reported [8, 19] we confirm that the distance walked before the rehabilitation program is significantly related, besides gender and age, to the presence of at least one comorbidity, particularly diabetes or CKD. On the other hand, chronic obstructive pulmonary disease (COPD) did not emerge as predictor of the 6mWT in our population, probably because of the small proportion of patients affected. Conflicting data have been reported on the effect of postoperative LVEF on the 6mWT performance before the rehabilitation program. In agreement with Fiorina [8] we did not find a significant correlation between LVEF and the distance walked. In contrast, other smaller-sized studies reported that a poor LV systolic function negatively affected the 6mWT performance [20, 21], possibly as a consequence of physical deconditioning in patients with LV systolic dysfunction. Our study has some limitation. Firstly, this is a retrospective analysis of a relatively small cohort of patients followed in a single institution. Moreover, even if the indication to performing TA was given in agreement with current guidelines, the comparison of the two sub-groups could be hampered by a surgical selection bias.

## Conclusion

TVR does not affect the post-operative functional status and the efficacy of the CRP after valvular surgery. Our data support the safety of performing simultaneous TVR in conjunction with left-sided valvular surgery, when significant TR or annulus dilatation are present.

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