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Left ventricular twist in clinically stable heart transplantation recipients: A speckle tracking echocardiography study

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ABSTRACT

Background and aim: Cavity twist is an integral part of LV function and its pattern in transplanted hearts is not well known. This study aimed at exploring LV twist in clinically stable heart transplant (HT) recipients with no evidence for rejection.

Methods: We studied 32 HT patients (54 ± 24 months after HT), 34 other cardiac surgery (CS) patients and compared them with 35 health controls using speckle tracking echocardiography, measuring peak twist angle, time-to-peak twist, and untwist rate.

Results: LV twist angle was smaller in the HT group (6.2 ± 3.3°) in comparison with the CS group and controls (13.2 ± 3.5° and 13.1 ± 4.5°, respectively; $p<0.0001$ for all) and untwist rate was reduced (HT group: −74 ± 30°/s; CS group: −118 ± 43°/s; controls: −116 ± 39°/s; $p<0.0001$ for all). Time-to-peak twist was not different between groups. Time after HT was the main independent predictor of both LV twist angle and untwist rate ($\beta = 0.8$, $p<0.0001$).

Conclusion: Though clinically stable, LV twist dynamics are significantly impaired in HT recipients, even in comparison with patients who underwent other cardiac surgery.

1. Introduction

Left ventricular (LV) twist function, defined as the wringing motion of the cavity secondary to the counterdirectional rotation of its apex and base, has an important role for both systolic and diastolic functions [1]. LV twist assists ejection [2,3], whereas rapid untwist secondary to the release of stored elastic energy during early diastole enhances LV suction by augmenting intraventricular pressure gradients [4], and hence allowing ventricular filling at relatively low left atrial pressure [5]. Although assessment of LV twist was initially achieved by magnetic resonance imaging [6], speckle tracking echocardiography (STE) has recently been validated as a reliable alternative method [7–9].

LV twist has been shown to be abnormal in various pathophysiological conditions [10–12] including aortic stenosis and coronary artery disease [13,14], however, there are still limited data on LV twist function in heart transplant (HT) recipients. Early invasive studies [15,16] and a recent preliminary report [17] have suggested that LV twist is abnormal in HT patients with clear evidence for rejection, but the exact status of LV twist in HT non-rejection patients remains unknown.

This study was designed to assess LV twist dynamics of a group of HT clinically stable patients, and to compare them with other cardiac surgical patients and controls, using speckle tracking echocardiography.

2. Methods

2.1. Study population

A total of 32 patients with history of HT and 34 age-matching patients with previous cardiac surgery (coronary artery bypass graft and mitral or aortic valve surgery) and preserved LV ejection fraction, currently followed at our University Hospital in Siena, Italy, were included in this study. All patients were clinically stable at the time of enrolment. Exclusion criteria were: history of diabetes or systemic hypertension; LV systolic dysfunction (EF<55%); atrial fibrillation; atrial flutter or other major arrhythmias; atrioventricular block of any degree; and evidence for rejection, identified by regularly performing right ventricular endomyocardial biopsies, according to the recent recommendations of the International Society for Heart and Lung Transplantation [18]. All HT patients had undergone orthotopic human cardiac allograft transplantation, had received standard postoperative care and were on immunosuppressive therapy. Time after HT was defined as the time between the heart transplantation and the echocardiographic examination. Thirty-five healthy controls matched for the HT recipients' age were also recruited. All subjects gave an informed consent for participation in the study. This project complies with the declaration of Helsinki and was

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performed with the approval by local university ethics committee. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

2.2. Standard echocardiography

Studies were performed using a high-quality echocardiograph (Vivid 7, GE, USA). LV ejection fraction, LV mass and diastolic function were obtained according to the current recommendations of the American Society of Echocardiography [19,20]. Tissue Doppler was used to measure peak systolic, early diastolic, and late diastolic myocardial velocities at the lateral sites of the mitral and tricuspid annuli.

2.3. Speckle tracking echocardiography

For the assessment of twist function, LV short-axis planes were obtained at basal and apical levels with adequate frame rates (range 60–90 f/s). The basal plane was defined as that allowing visualization of the mitral valve, whereas the apical plane was acquired distal to the papillary muscles. Particular care was taken to obtain LV cross-sections as circular as possible. Three consecutive cardiac cycles were recorded during a quiet breath hold, and stored in digital cine-loop format for subsequent off-line analysis. STE analysis was performed using a dedicated software (EchoPac, GE, USA). After manual demarcation of LV endocardial border using a point-and-click approach, a circular region of interest including the whole short-axis LV myocardial area was depicted by the software. The software then divided each region of interest in 6 radial segments and tracked myocardial speckles frame-to-frame within each segment, with the possibility of manual adjustment to optimize individual segment tracking quality. LV rotation curves for each segment and two mean curves representing basal rotation and apical rotation were obtained. All curves were calculated as the average of three consecutive cardiac cycles. By convention, clockwise rotation as viewed from the apex was expressed as a negative angle and counter-clockwise rotation as a positive angle. LV twist was calculated as the instantaneous net difference in mean rotation between the apical and basal levels. Peak LV twist angle was defined as the maximum systolic value reached by the LV twist curve. LV untwist rate was calculated as the early diastolic peak time derivative of the time–twist angle curve. Time-to-peak LV twist was measured and expressed as a percentage of RR interval [21]. LV global longitudinal strain (GLS) was calculated as the averaging values of all myocardial segments in the apical 2, 3 and 4-chamber views. Radial and circumferential strains were measured from the parasternal short-axis views at the basal and apical levels, as previously described [22]. Global circumferential strain (GCS) was obtained as the averaging values of all myocardial segments in the short-axis views at the basal and apical levels.

2.4. Reproducibility

To assess the reproducibility of LV twist angle and untwist rate, 20 patients were randomly selected: Bland–Altman analysis was performed to evaluate the intra- and interobserver agreement by repeating the analysis 1 week later by the same observer and a second independent observer. Bland–Altman analysis demonstrated good intra- and interobserver agreement, with small bias not significantly different from zero. Mean differences ± 2 standard deviations of LV twist angle were 0.4 ± 1.6% and 0.6 ± 2.1%, and for the LV untwist rate 5.9 ± 2.6% and 6.4 ± 3.2% for intra- and inter-observer agreement, respectively.

2.5. Statistical analysis

Data are shown as mean ± SD. ANOVA followed by the Scheffé's post-hoc multiple comparison test was used to compare normal variables between groups. Pearson's correlation coefficients were calculated to assess the relationships between continuous variables. Stepwise multivariate regression was used to identify independent predictors of LV twist indices. To determine the predictors of LV twist and untwist rate, age, gender, body mass index, body surface area, heart rate, systolic and diastolic blood pressure, absolute and indexed end-diastolic and end-systolic LV volumes, LV mass, indexed LV mass, LV ejection fraction, diastolic LV inflow indices, tissue Doppler mitral and tricuspid annulus velocities, E/e′, donor age, graft ischemic time, and pre-transplant mean pulmonary artery pressure were tested in a multivariate analysis model. A p value < 0.05 was considered statistically significant. Analyses were performed using the SPSS (Statistical Package for the Social Sciences, Chicago, Illinois) software Release 11.5.

3. Results

3.1. General characteristics

Table 1 shows the main characteristics of the study population. Body weight and BMI were higher in the HT and CS groups compared with controls. The CS group had higher LV mass and indexed LV mass than the other two groups. The rest of the conventional measurements were not different between the three groups.

Table 1
Main characteristics of the study groups. LV = left ventricular; S′ = peak systolic mitral annulus velocity; E′ = peak early diastolic mitral annulus velocity; A′ = peak late diastolic mitral annulus velocity; CABG = coronary artery bypass graft; mPAP = mean pulmonary artery pressure.

	HT group (n = 32)	CS group (n = 34)	Control group (n = 35)	p value
Age (years)	61.2 ± 5.0	63.1 ± 4.2	59.0 ± 6.5	0.31
Gender (% of females)	45.4	46.0	55.0	0.24
Height (cm)	170 ± 8	169 ± 8	168 ± 7	0.38
Weight (kg)	75 ± 12*	75 ± 14*	67 ± 10	0.015
Body mass index (kg/m^2)	26.0 ± 4.1*	25.3 ± 3.5*	23.7 ± 3.1	0.038
Systolic blood pressure (mm Hg)	128 ± 14	124 ± 11	123 ± 13	0.22
Diastolic blood pressure (mm Hg)	80 ± 7	79 ± 7	78 ± 6	0.48
Heart rate (bpm)	79 ± 11	79 ± 15	76 ± 14	0.49
LV mass (g)	139 ± 44	163 ± 46†	136 ± 28	0.019
Indexed LV mass (g/m^2)	75 ± 22	90 ± 26†	76 ± 15	0.014
LV ejection fraction (%)	59 ± 4	58 ± 7	59 ± 5	0.72
Mitral E/A ratio	1.2 ± 0.4	1.1 ± 0.4	1.2 ± 0.3	0.66
S′ (cm/s)	9.3 ± 2.4	8.5 ± 1.7	9.2 ± 1.5	0.071
E′ (cm/s)	12.5 ± 4.6	11.2 ± 4.0	12.1 ± 4.2	0.39
A′ (cm/s)	10.0 ± 3.1	10.9 ± 3.8	10.9 ± 3.5	0.52
E′/A′ (cm/s)	1.4 ± 0.8	1.2 ± 0.6	1.2 ± 0.5	0.37
E/E′ (cm/s)	6.5 ± 3.4	6.8 ± 3.3	6.5 ± 2.7	0.91
Time after surgery (months)	54 [31–78]	47 [44–57]	–	0.23
Type of surgery				
CABG	–	10 (29%)	–	
Mitral valve surgery	–	11 (32%)	–	
Aortic valve surgery	–	13 (38%)	–	
Additional transplantation data				
Age of donor (years)	28.2 ± 5.1	–	–	
Graft ischemic time (min)	218 ± 99	–	–	
Pre-transplant mPAP (mm Hg)	24.9 ± 12.3	–	–	

* p < 0.05 vs control group.
† p < 0.05 vs HT group and control group.

3.2. LV longitudinal, circumferential and radial deformation (Table 2)

HT patient myocardial deformation measurements were not different from controls but CS patients had lower values of GLS than controls (p = 0.012).

3.3. LV twist function (Fig. 1, 2 and Table 2)

LV basal rotation (p < 0.0001) and apical (p < 0.0001) rotation were both reduced in HT patients and the twist angle was significantly lower in the HT group in comparison with the CS group (p < 0.0001) and controls (p < 0.0001). Likewise, LV untwist rate was lower in the HT group compared with the CS group (p < 0.0001) and controls (p < 0.0001). The time-to-peak LV twist was not different between groups (p = 0.17).

3.4. Correlates of LV twist in the HT group

In HT patients, among all clinical and echocardiographic variables, LV twist angle significantly correlated with time from HT (R = 0.84, p < 0.0001) (Fig. 3), E/A ratio (R = 0.36, p = 0.04), and tricuspid S′ (R = −0.46, p = 0.009). Untwist rate significantly correlated with time from HT (R = −0.59, p = 0.0002) and heart rate (R = −0.37, p = 0.003). In a stepwise multivariate regression analysis, only time from HT (β = 0.8, p < 0.0001) and tricuspid S′ (β = −0.2, p = 0.04) remained independently associated with LV twist angle (overall model p < 0.0001). Time from HT (β = −0.54, p = 0.0007) and heart rate (β = −0.32, p = 0.03) were independent predictors of LV untwist rate. The models explained 77.5% and 44.2% of the variability in LV twist and untwist rate, respectively. Time from HT was largely the principal determinant, accounting for 96.4% and 79.6% of the