Incremental value of advanced cardiac imaging modalities for diagnosis and patient management : focus on real-time three-dimensional echocardiography and magnetic resonance imaging

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CHAPTER 22

Effects of cardiac resynchronization therapy on left ventricular twist

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ABSTRACT

Objectives: Left ventricular (LV) twist is emerging as a comprehensive index of LV function. This study explored the effects of cardiac resynchronization therapy (CRT) on LV twist, particularly in relation to LV lead position.

Methods: Eighty heart failure (HF) patients were included. 2D-echocardiography was performed at baseline, immediately after CRT, and at 6 months follow-up. Speckle-tracking analysis was applied to assess LV twist. LV lead was placed preferably in a (postero-)lateral vein and at fluoroscopy, the position was classified as basal, mid-ventricular or apical. Response to CRT was defined as reduction of LV end-systolic volume ≥15% at 6 months follow-up. A control group comprised 30 normal subjects.

Results: Peak LV twist in HF patients was 4.8±2.6° compared to 15.0±3.6° of the controls ($p < 0.001$). At 6 months follow-up, peak LV twist significantly improved only in responders (56%), from 4.3±2.4° to 8.5±3.2° ($p < 0.001$). The strongest predictor of response to CRT was the improvement of peak LV twist immediately after CRT (odds ratio 1.899, 95% confidence intervals 1.334-2.703, $p < 0.001$). Furthermore, LV twist significantly improved in patients with an apical (from 4.3±3.1° to 8.6±3.0°, $p = 0.001$) and mid-ventricular (from 4.8±2.2° to 6.4±3.9°, $p = 0.038$) but not with a basal (5.0±3.3 vs. 4.1±3.2, $p = 0.28$) LV lead position. Similarly LVEF significantly increased in patients with an apical (from 26±7% to 37±7%, $p < 0.001$) and mid-ventricular (from 26±6% to 33±8%, $p < 0.001$) but not with a basal (26±5% vs. 28±8%, $p = 0.30$) LV lead position.

Conclusions: An immediate improvement of LV twist after CRT predicts LV reverse remodeling at 6 months follow-up.

INTRODUCTION

The human heart has a specific helical arrangement of the myofibers with a right-hand orientation from the base towards the apex in the endocardial layers and a left-hand orientation in the epicardial layers. This spiral architecture of the myofibers leads to a left ventricular (LV) systolic wringing motion as a result of an opposite rotation of LV apex and base [1, 2]. The gradient between apex and base in the rotation angle along LV longitudinal axis is called twist and contributes significantly to LV systolic function, in addition to myocardial shortening and thickening [3–5].

In heart failure (HF) patients, LV twist is significantly reduced [6]. Cardiac resynchronization therapy (CRT) is considered a major therapeutic breakthrough for HF patients, and recent large randomized trials have shown that CRT has beneficial effects on HF symptoms, LV systolic function and survival [7, 8]. At present, minimal data are available about the effect of CRT on LV twist [9, 10].

In the current study, the effect of CRT on LV twist was assessed using speckle-tracking echocardiography. Furthermore, the relationship between the change in LV twist and LV reverse remodeling at 6 months follow-up was investigated. Finally, the influence of the LV lead position on the improvement in LV twist and response to CRT was explored.

METHODS

Patient population and protocol

A total of 87 consecutive HF patients scheduled for CRT were prospectively included. According to current guidelines, the inclusion criteria were: New York Heart Association (NYHA) functional class III-IV, sinus rhythm, LV ejection fraction (LVEF) ≤35%, QRS duration ≥120 ms [11]. Etiology of HF was considered ischemic in the presence of significant coronary artery disease (>50% stenosis in ≥1 major epicardial coronary artery) on coronary angiography and/or a history of myocardial infarction or revascularization.

The clinical evaluation consisted of: 1) assessment of clinical status: NYHA functional class, quality of life (using the Minnesota Living with Heart Failure questionnaire) [12] and 6-minute walk distance[13] at baseline and 6 months follow-up; 2) assessment of LV volumes, function, dyssynchrony and twist, using standard echocardiography and speckle-tracking analysis at baseline, within 48 hours (immediately after CRT) and at 6 months follow-up.

In addition, 30 subjects without evidence of structural heart disease, frequency-matched for age, gender and body surface area, were included as a normal control group, selected

from an echocardiographic data base. These subjects were referred for the echocardiographic evaluation because of atypical chest pain, palpitations or syncope without murmur.

Standard echocardiography

All patients were imaged in left lateral decubitus position using a commercially available system (Vingmed Vivid 7, General Electric-Vingmed, Milwakee, Wisconsin, USA). Standard 2-dimensional images were obtained using a 3.5-MHz transducer and digitally stored in cine-loop format; the analysis was performed offline using EchoPAC version 6.0.1 (General Electric-Vingmed).

From the standard apical views (4- and 2-chamber) LV volumes and LVEF were calculated according to the American Society of Echocardiography guidelines [14]. At 6 months follow-up, patients were classified as echocardiographic responders based on a reduction ≥15% of LV end-systolic volume (LVESV) [15].

Segmental wall motion was assessed according to American Society of Echocardiography in order to evaluate the presence of scarred segments within ischemic HF patients [14]. Akinetic and diskinetic segments (wall motion score 3 and 4) were classified as scarred segments [16].

Speckle-tracking analysis

The speckle-tracking software tracks frame-to-frame the movement of natural myocardial acoustic markers, or speckles, on standard gray scale images. Speckles are randomly distributed and each region of the myocardium has a distinguishing pattern, a fingerprint. Furthermore, speckle-tracking analysis is angle independent and allows the evaluation of myocardial contraction/relaxation along the circumferential, longitudinal and radial direction [17, 18].

In the current study, speckle-tracking analysis was applied to evaluate LV dyssynchrony (based on radial strain analysis) and LV twist. Parasternal short-axis images were acquired at 3 distinct levels: 1) basal level, identified by the mitral valve; 2) papillary muscle level; 3) apical level (the smallest cavity achievable distally to the papillary muscles, moving the probe down and slightly laterally, if needed). Frame rate ranged from 45 to 100 frame/s and 3 cardiac cycles for each parasternal short-axis level were stored in cine-loop format for the offline analysis (EchoPAC). The endocardial border was traced at an end-systolic frame and the region of interest (ROI) was chosen to fit the whole myocardium. The software allows the operator to check and validate the tracking quality and to adjust the endocardial border or modify the width of the ROI, if needed. Furthermore, each short-axis image was automatically divided into 6 standard segments: septal, anteroseptal, anterior, lateral, posterior, and inferior.

Aortic valve opening and closure were identified on pulsed-wave Doppler tracings obtained from the LV outflow tract.

LV dyssynchrony analysis

LV dyssynchrony was derived from the radial strain curves obtained from the papillary muscle short-axis view. As previously described, LV dyssynchrony was defined as the time difference of peak radial strain between the anteroseptal and posterior segments [19].

LV twist analysis

The speckle-tracking software calculates LV rotation from the apical and basal short-axis images as the average angular displacement of the 6 standard segments referring to the ventricular centroid, frame by frame. Counterclockwise rotation was marked as positive value and clockwise rotation as negative value when viewed from the LV apex. LV twist was defined as the net difference (in degrees) of apical and basal rotation at isochronal time points. For the calculation of LV twist, averaged apical and basal rotation data were exported to a spreadsheet program (Excel 2003; Microsoft Corporation, Redmond, Washington) (Figure 1) [20, 21]. The following measurements were derived: peak apical and basal rotation, peak LV twist.

Reproducibility

Reproducibility of LV end-diastolic volume (LVEDV), LVESV, LVEF and peak LV twist was assessed on 20 randomly selected HF patients. Bland-Altman analysis was performed to evaluate the intra- and inter-observer agreement repeating the analysis few days later by the same observer and by a second independent observer. The results were expressed as absolute mean difference±2 standard deviation (SD).

The intra-observer agreement for LVEDV, LVESV, LVEF and peak LV twist were 7.4±11.2 ml, 7.0±10.1 ml, 1.9±4.4%, and 0.2±0.3º, respectively.

The inter-observer agreement for LVEDV, LVESV, LVEF and peak LV twist were 12.9±14.7 ml, 11.3±13.9 ml, 2.5±4.9%, and 0.7±0.8º, respectively.

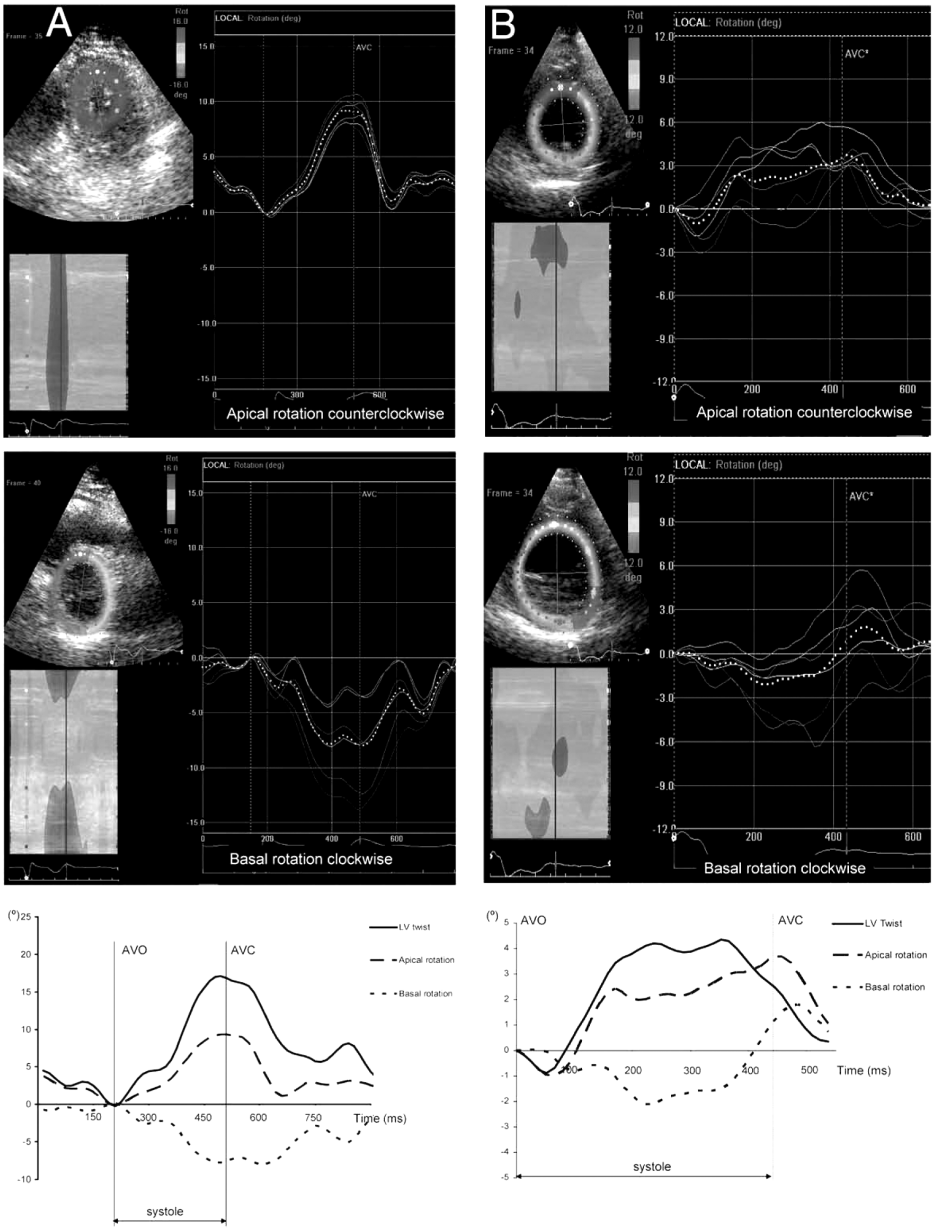

Figure 1 (Assessment of LV twist). Examples of left ventricular (LV) twist in normal control (panel A) and in heart failure patient (panel B). In both panels, the upper parts represent apical and basal rotations and the lower parts represent LV twist calculation after exporting the data to a spreadsheet program (Excel 2003; Microsoft Corporation, Redmond, Washington). AVC: aortic valve closure. AVO: aortic valve opening.

CRT implantation

All patients received a biventricular pacemaker with cardioverter-defibrillator function (Contak Renewal 4RF, Boston Scientific St. Paul, Minnesota; or InSync Sentry, Medtronic Inc. Minneapolis, Minnesota; Lumax 340 HF-T, Biotronik, Berlin). The right atrial and ventricular leads were positioned conventionally. All LV leads were implanted transvenously, and positioned preferably in a (postero)lateral vein. A coronary sinus venogram was obtained using a balloon catheter, followed by the insertion of the LV pacing lead. An 8-F guiding catheter was used to place the LV lead (Easytrak, Boston Scientific, or Attain-SD, Medtronic, or Corox OTW Biotronik) in the coronary sinus.

LV lead position

Target veins were lateral or postero-lateral veins. The LV lead position was determined using biplane fluoroscopy classification [22]. In the right anterior oblique view and/or in the postero-anterior view, the distance between the coronary sinus/mitral plane and the cardiac apex was divided in 3 parts and the LV lead position was classified in 3 groups: basal, mid-ventricular and apical.

Statistical analysis

All continuous variables had a normal distribution (as evaluated with Kolmogorov-Smirnov tests). Summary statistics for these data are therefore presented as mean±SD. Categorical data are presented as numbers and percentages. Paired T test was used for the comparison between continuous variables at baseline and immediately after CRT and between baseline and at 6 months follow-up. Unpaired T test was performed to compare continuous variables between normal controls and HF patients and between CRT responders and non-responders. Chi-square/Fischer's exact tests were computed to test for differences in categorical variables. Linear regression analysis was performed to determine the relations between LV twist, LVEF and LV dyssynchrony. In order to identify independent determinants of LV twist, a multivariable linear regression analysis using the enter model was performed including as covariates LVEF and LV dyssynchrony. Linear regression analysis was used to assess the relation between the Δ (difference between immediately after CRT and baseline) peak LV twist and Δ LVEF. The differences in peak LV twist during follow-up in responders and non-responders were assessed using ANOVA for repeated measurements. In order to identify variables related to a positive response to CRT, univariable and multivariable logistic regression analysis were performed including clinical (age, gender, etiology, QRS duration at baseline and 6-minute walk

distance at baseline) and echocardiographic (LVESV at baseline, ΔLVESV, LV dyssynchrony at baseline, ΔLV dyssynchrony, peak LV twist at baseline, Δpeak LV twist) characteristics of the patients. Only, significant ($p < 0.05$) univariable predictors were entered as covariates in the multivariable logistic regression analysis which was performed using the enter model. Odds ratio (OR) and 95% confidence intervals (CI) were calculated. Model discrimination was assessed using c-statistic and model calibration was assessed using Hosmer-Lemeshow statistic. The differences in peak LV twist and LVEF between the groups of patients with different LV lead position were assessed by one-way ANOVA. All statistical tests were 2-sided, and a p-value <0.05 was considered significant. A statistical software program SPSS 14.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis.

RESULTS

Patient population

Reliable speckle-tracking for rotation analysis was obtained in all normal controls and in 80 (92%) HF patients. Consequently, 7 (8%) patients were excluded from the study. Of the 80 HF patients enrolled, 9 did not complete the 6 months follow-up; 3 patients died of worsening HF, 1 had LV pacing switched off due to intolerable phrenic stimulation, 1 had CRT device explantation secondary to infection, and 4 were lost to follow-up. Therefore, data at baseline and immediately after CRT were collected for 80 patients and data at 6 month follow-up were collected for 71 patients. Baseline characteristics of normal controls and the HF patients are listed in Table 1.

LV twist baseline

As shown in Table 1, peak apical rotation, peak basal rotation and peak LV twist were severely reduced in HF patients compared to normal controls: 2.4±1.8° vs. 9.4±3.2° ($p < 0.001$), -3.3±2.0° vs. -6.1±2.4° ($p < 0.001$) and 4.8±2.6° vs. 15.0±3.6° ($p < 0.001$), respectively.

A significant relation ($r = 0.53$, $p < 0.001$) was observed between peak LV twist and LVEF in HF patients. This relation was stronger in non-ischemic ($r = 0.60$, $p < 0.001$) than in ischemic HF patients ($r = 0.34$, $p = 0.020$) (Figure 2A). Moreover, a modest relation ($r = -0.33$, $p = 0.003$) was observed between peak LV twist and LV dyssynchrony in HF patients. At multivariable linear regression analysis, LVEF ($\beta = 0.47$, $p < 0.001$) and LV dyssynchrony ($\beta = -0.21$, $p = 0.032$) were independent determinants of LV twist.

Table 1. Baseline characteristics of normal controls and heart failure (HF) patients.

	Normal controls (n = 30)	HF patients (n = 80)	p-value
Age (years)	61±11	64±11	0.091
Gender (male/female)	22/8	61/19	0.46
NYHA class	-	3.0±0.4	-
QoL	-	34±20	-
6-minute walk distance (m)	-	321±109	-
QRS duration (ms)	91±9	148±30	<0.001
Etiology, n (%)			
Ischemic	-	45 (56)	-
Non-ischemic	-	35 (44)	-
Medication, n (%)			
ACE Inhibitors	-	74 (92)	-
ß-blockers	-	69 (86)	-
Diuretics and/or Spironolactone	-	67 (84)	-
LVEDV (ml)	86±26	196±74	<0.001
LVESV (ml)	34±11	146±60	<0.001
LVEF (%)	62±7	26±6	<0.001
LV dyssynchrony (ms)	14±9	146±81	<0.001
Peak apical rotation (°)	9.4±3.2	2.4±1.8	<0.001
Peak basal rotation (°)	-6.1±2.4	-3.3±2.0	<0.001
Peak LV twist (°)	15.0±3.6	4.8±2.6	<0.001

LVEDV: left ventricular end-diastolic volume, LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume, NYHA: New York Heart Association, QoL: Score on the Minnesota Living with Heart Failure Questionnaire

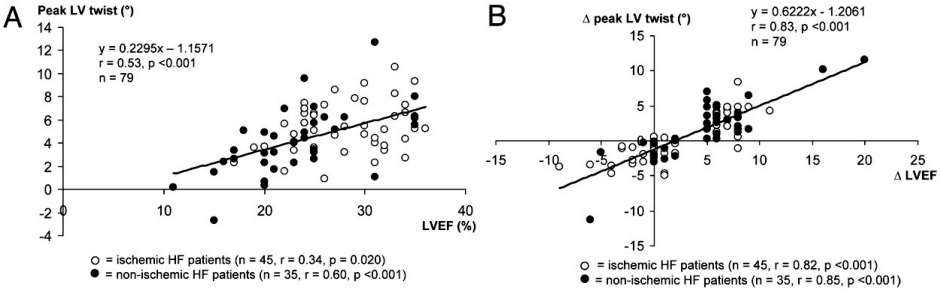

Figure 2 (LV twist and LV systolic function). Panel A: Correlation between baseline peak LV twist and LVEF in heart failure patients (ischemic, white circles, and non-ischemic, black circles). Panel B: Correlation between Δ peak LV twist and Δ LVEF immediately after CRT in heart failure patients (ischemic, white circles, and non-ischemic, black circles).

LV twist after CRT

Immediately after CRT

Immediately after CRT, peak LV twist increased from 4.8±2.6º to 5.9±3.2º (p = 0.007). In particular, Δ peak LV twist was strongly related to Δ LVEF (r = 0.83, p <0.001) and this relation was good in both non-ischemic (r = 0.85, p <0.001) and ischemic HF patients (r = 0.82, p <0.001) (Figure 2B). Furthermore, the relations between Δ peak LV twist and Δ LV dyssynchrony (r = -0.57, p <0.001) and between Δ LV dyssynchrony and Δ LVEF (r = -0.63, p <0.001) were good but less strong than the previous relation between Δ peak LV twist and Δ LVEF.

Six months follow-up

At 6 months follow-up, 40 of 71 (56%) patients were classified as echocardiographic responders to CRT (defined as a decrease in LVESV ≥15%).

No significant differences in the baseline clinical characteristics were found between responders and non-responders (Table 2). At 6 months follow-up, significant improvement in

Table 2. Clinical characteristics of responders vs. non-responders at baseline and 6 months follow-up.

	Responders (n = 40)	Non-responders (n = 31)	p-value
Age (years)	66±10	66±11	0.88
Gender (male/female)	32/8	20/11	0.18
Medication, n (%)			
ACE Inhibitors	37 (92)	29 (93)	0.77
ß-blockers	35 (87)	27 (86)	0.82
Diuretics and/or Spironolactone	34 (84)	26 (84)	0.82
Etiology, n (%)			
Ischemic	20 (50)	18 (58)	
Non-ischemic	20 (50)	13 (42)	0.63
QRS duration (ms)	149±32	149±30	0.97
NYHA class			
Baseline	3.0±0.5	3.0±0.5	0.92
6 months follow-up	2.0±0.7*	2.7±0.6†	<0.001
QoL			
Baseline	35±23	32±15	0.51
6 months follow-up	20±20*	29±19	0.065
6-minute walk distance (m)			
Baseline	306±106	330±107	0.34
6 months follow-up	363±109*	327±110	0.17

* = p <0.001 baseline vs. 6 month follow-up; † = p<0.05 baseline vs. 6 month follow-up. Abbreviations see Table 1.

NYHA class (from 3.0±0.5 to 2.0±0.7, p <0.001), quality of life (from 35±23 to 20±20, p <0.001), and 6-minute walk distance (from 306±106 m to 363±109 m, p <0.001) were observed in CRT responders only (Table 2).

Baseline echocardiographic characteristics were also similar between the 2 groups, except for LV dyssynchrony (Table 3) that was larger in responders compared to non-responders (182±71 ms vs. 116±83 ms, p = 0.003). A trend towards lower values of peak LV twist were noted in responders as compared to non-responders (4.3±2.4° vs. 5.4±2.9°, p = 0.072). At 6 months follow-up, LV dyssynchrony improved in CRT responders (from 182±71 ms to 60±45 ms, p <0.001), whereas in non-responders LV dyssynchrony did not change (116±83 ms vs. 136±89 ms, p = 0.30) (Table 3). Importantly, within ischemic HF patients, CRT responders presented significantly lower number of scarred segments at 2D-echocardiography as compared to non-responders (2.7±0.9 vs. 4.2±2.2, p = 0.016).

Table 3. Standard echocardiographic variables and rotational parameters in responders vs. non-responders at baseline and 6 months follow-up.

	Responders (n = 40)	Non-responders (n = 31)	p-value (responders vs. non-responders)
LVESV (ml)			
Baseline	144±58	153±67	0.56
6 months follow-up	110±43*	164±72‡	0.001
LVEF (%)			
Baseline	26±6	26±6	0.91
6 months follow-up	37±7*	26±6	<0.001
LV dyssynchrony (ms)			
Baseline	182±71	116±83	0.003
6 months follow-up	60±45*	136±89	<0.001
Peak apical rotation (°)			
Baseline	2.3±1.7	2.8±2.1	0.32
6 months follow-up	5.0±3.0*	2.1±2.3	<0.001
Peak basal rotation (°)			
Baseline	-3.2±2.2	-3.5±1.7	0.51
6 months follow-up	-4.3±1.9†	-2.1±2.2†	<0.001
Peak LV twist (°)			
Baseline	4.3±2.4	5.4±2.9	0.072
6 months follow-up	8.5±3.2*	3.3±2.2*	<0.001

* = p <0.001 baseline vs. 6 month follow-up; † = p <0.01 baseline vs. 6 month follow-up; ‡ = p<0.05 baseline vs. 6 month follow-up.
Abbreviations see Table 1.

Concerning the rotational parameters, in responders peak LV twist progressively improved during follow-up (ANOVA p-value <0.001), whereas in non-responders a progressive deterioration of peak LV twist was noted (ANOVA p-value <0.001) (Figure 3). Particularly, both apical and basal rotation significantly improved in responders (from 2.3±1.7° to 5.0±3.0°, p <0.001 and from -3.2±2.2° to -4.3±1.9°, p = 0.006), whereas only basal rotation significantly deteriorated in non-responders (from -3.5±1.7 to -2.1±2.2, p = 0.001) (Table 3).

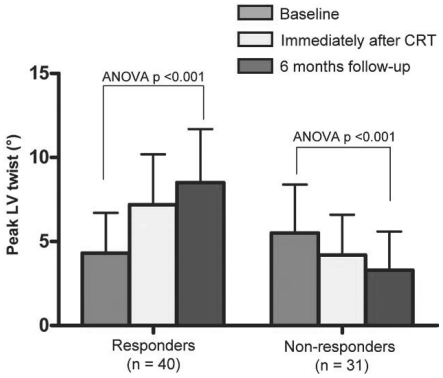

Figure 3 (LV twist in responders and non-responders). Peak LV twist in responders and non-responders at baseline, immediately after CRT and at 6 months follow-up.

Prediction of LV reverse remodeling

At univariable logistic regression, LV dyssynchrony at baseline, Δ LV dyssynchrony, Δ LVESV and Δ peak LV twist were significantly related to LV reverse remodeling at 6 months follow-up (Table 4). At multivariable logistic regression analysis, Δ peak LV twist was the strongest predictor of response to CRT at 6 months follow-up (OR = 1.899, 95%CI = 1.334-2.703, p <0.001) (Table 4).

Table 4. Univariable and multivariable logistic regression analysis for prediction of response to CRT (defined as reduction in LVESV ≥15%).

Dependent variable:	**Univariable analysis**		**Multivariable analysis**	
Response to CRT at 6 months follow-up	OR (95% CI)	p-value	OR (95% CI)	p-value
Independent variables				
Age	1.003 (0.958-1.050)	0.90		
Female gender	2.198 (0.756-6.404)	0.15		
Ischemic etiology	0.722 (0.281-1.858)	0.50		
QRS width at baseline	1.000 (0.985-1.016)	0.97		
6 minutes walking test at baseline	0.998 (0.993-1.002)	0.34		
LVESV at baseline	0.998 (0.990-1.005)	0.56		
Δ LVESV immediately after CRT	0.949 (0.915-0.984)	0.005	0.998 (0.950-1.049)	0.94
LV dyssynchrony at baseline	1.013 (1.005-1.021)	0.002	1.011 (1.001-1.022)	0.037
Δ LV dyssynchrony immediately after CRT	0.992 (0.986-0.998)	0.010	1.007 (0.996-1.017)	0.21
Peak LV twist at baseline	0.844 (0.698-1.019)	0.078		
Δ peak LV twist immediately after CRT	1.837 (1.378-2.449)	<0.001	1.899 (1.334-2.703)	<0.001

c-statistic: 0.885

CI: confidence intervals; CRT: cardiac resynchronization therapy; LV: left ventricular; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; OR: odds ratio.

LV twist in relation to LV lead position

Considering the 71 patients with 6 months follow-up, 68 patients had the LV lead placed in a (postero-)lateral vein and 3 in an anterior vein. The 3 patients with the LV lead positioned in an anterior vein were non-responders at 6 months follow-up. Of the remaining 68 patients, the LV lead position was classified (from the right anterior oblique/postero-anterior view on fluoroscopy) as basal in 17 (25%), mid-ventricular in 34 (50%), and apical in 17 (25%) patients. At baseline, peak LV twist was not significantly different between patients with apical, mid-ventricular and basal LV lead position, (ANOVA p-value = 0.68). However, at 6 months follow-up, peak LV twist showed a significant improvement in patients with apical (from 4.3±3.1° to 8.6±3.0°, p = 0.001) and mid-ventricular (from 4.8±2.2° to 6.4±3.9°, p = 0.038) LV lead position, whereas in patients with a basal LV lead position, peak LV twist did not change significantly (5.0±3.3° vs. 4.1±3.2°, p = 0.28) (Figure 4A). Similarly, LVEF increased significantly in patients with an apical (from 26±7% to 37±7%, p <0.001) and mid-ventricular (from 26±6% to 33±8%, p <0.001) but not with a basal (26±5% vs. 28±8%, p = 0.30) LV lead position (Figure 4B). Figure 5 shows an example of responder with the LV lead placed in an apical position of a postero-lateral vein and significant improvement in peak LV twist and LVEF after CRT (both immediately after CRT implantation and at 6 months follow-up).

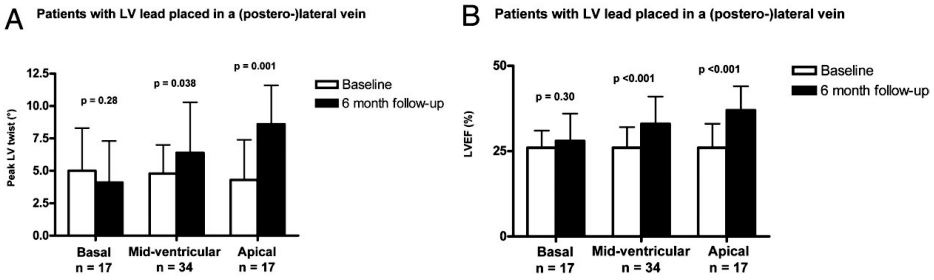

Figure 4 (LV twist and LVEF in relation to LV lead position). Panel A. Peak LV twist at baseline and 6 months follow-up in patients with basal, mid-ventricular and apical LV lead position. Significant improvement was observed in patients with an apical or mid-ventricular LV lead position but not in patients with basal LV lead position. Panel B. LVEF at baseline and 6 months follow-up in patients with basal, mid-ventricular and apical LV lead position. Significant improvement was observed in patients with an apical or mid-ventricular LV lead position but not in patients with basal LV lead position.
LV: left ventricular; LVEF: left ventricular ejection fraction

DISCUSSION

The current study evaluated the effects of CRT on LV twist and provides new insights on the relationship between LV rotational mechanics, CRT response and LV lead position. The main findings can be summarized as follows: 1) LV twist was significantly reduced in HF patients;

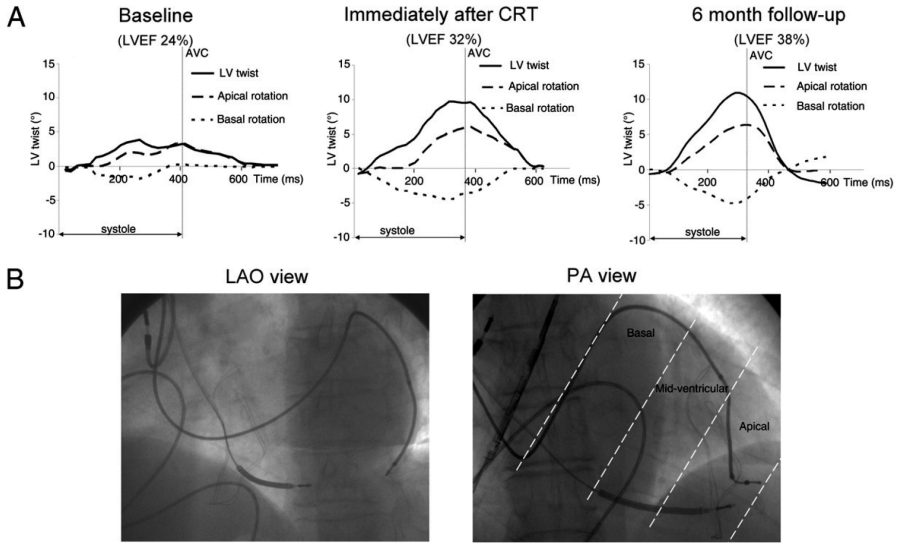

Figure 5. Example of a CRT responder with LV lead in an apical position. Panel A. Peak LV twist improved from 3.9º at baseline to 9.7º immediately after CRT implantation. Peak LV twist further improved at 6 months follow-up (peak LV twist 10.9º). AVC: aortic valve closure. Panel B. Biplane fluoroscopy: the left anterior oblique (LAO) view shows the LV lead in a posterolateral cardiac vein; in the postero-anterior (PA) view the distance between the coronary sinus/mitral plane and the cardiac apex was divided (dotted lines) in 3 parts (basal, mid-ventricular and apical).

2) LV twist improved in responders and worsened in non-responders to CRT; 3) the strongest predictor of LV reverse remodeling at 6 months follow-up was Δ peak LV twist (immediate change in LV twist after CRT); 4) an LV lead placed in a (postero-)lateral vein with apical or mid-ventricular position was associated with the greatest improvement of LV twist after CRT and with the highest response rate to CRT.

Relationship between LV twist and LV function

Several techniques have been applied for the assessment and quantification of LV twist. For this purpose, tagged cardiac magnetic resonance imaging and sonomicrometry are considered the gold standard, but the most recent speckle-tracking echocardiographic technique, used in the present study, demonstrated a good agreement with these imaging modalities [20, 21]. Previous studies, using both tagged cardiac magnetic resonance imaging and speckle-tracking analysis, suggested an important relation between LV twist and LVEF [4, 9]. Similarly, in the current study the relation between LV twist and LV systolic function was good ($r = 0.53$, $p < 0.001$), illustrating the potential role of LV twist as comprehensive index of LV systolic function. Furthermore, the results of the present study highlight that the relation between LV

systolic function and LV twist was stronger in non-ischemic patients as compared to ischemic patients. A possible reason may be the presence of regional myocardial damage in ischemic patients, involving specifically the apex or the base with a different effect on LV twist [23].

Finally, LV twist was modestly related to LV dyssynchrony ($r = -0.33$, $p < 0.001$), but at multivariable linear regression analysis, LV dyssynchrony was still independently related to LV twist. This finding points out that LV twist not only is a sensitive and thorough parameter of LV function, but also it may reflect the extent of LV (dys)synchrony.

Relationship between LV twist and CRT response

The effects of CRT on torsional mechanics were different in responders and non-responders. A trend towards more reduced LV twist at baseline in responders as compared to non-responders was observed. In the present study, a significant improvement of LV twist was observed in CRT responders and a significant worsening in non-responders. In contrast, a previous study of Zhang et al. did not show any significant increase of LV twist in responders to CRT [10]. The different results may be related to sample size and population characteristics.

In the multivariable model, baseline LV dyssynchrony and an immediate improvement in LV twist after CRT were the only predictors of LV reverse remodeling at 6 months follow-up. The predictive value of LV dyssynchrony has been shown already in previous studies [19, 24]. The novelty of the present study is that CRT may (partially) restore LV twist, possibly by providing a more physiologic electrical depolarization and mechanical contraction of the myofibers. Specifically, CRT partially restored LV torsional behavior in responders, by not only improving apical rotation but also basal rotation. In non-responders, the deterioration of LV twist was mainly due to worsening of the basal rotation underscoring the influence of the basal level on LV twist [25].

Relationship between LV twist and LV lead position

Previous studies showed that HF patients treated with CRT showed the best hemodynamic improvement when the LV pacing lead was positioned in (postero) lateral veins [26]. In the current study, 3 patients had the LV lead placed in an anterior vein, and none of them responded to CRT. The remaining 68 patients had the LV lead positioned in the (postero-)lateral vein. In these patients, the optimal position of LV lead inside the target vein was explored. Patients with a mid-ventricular or apical position had the largest systolic improvement, and showed a significant increase in LV twist, whereas patients with a basal LV lead position did not improve systolic function and decreased in LV twist, confirming that pacing site may influence torsional behavior of the LV [27]. Similarly, a recent study by Helm et al.[28] reported

that the optimal site of stimulation (although in a canine model of HF) was the LV free wall centered over the mid-apical part. This finding may be related to the fact that normal cardiac depolarization is directed from the apex towards the base [29], and an earlier activation of the LV basal region, altering the normal contraction pattern of the myofibers, may lead to a significant deterioration of LV twist. Another explanation for the findings may be related to the fact that the myocardial wall is thinner towards the apex [30, 31]; therefore, the epicardial LV lead in this position is closer to the Purkinje network. Consequently, pacing from this position may generate a cardiac pulse which spreads faster to the entire myocardium with a more physiological activation [32–34.]

CONCLUSIONS

LV twist is reduced in HF patients and improves in patients who respond to CRT. Particularly, the change in LV twist immediately after CRT predicts LV reverse remodeling at 6 months follow-up.

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