Circulation: Cardiovascular Imaging

ORIGINAL ARTICLE

Cardiac Rotational Mechanics As a Predictor of Myocardial Recovery in Heart Failure Patients Undergoing Chronic Mechanical Circulatory Support

A Pilot Study

BACKGROUND: Impaired qualitative and quantitative left ventricular (LV) rotational mechanics predict cardiac remodeling progression and prognosis after myocardial infarction. We investigated whether cardiac rotational mechanics can predict cardiac recovery in chronic advanced cardiomyopathy patients.

METHODS AND RESULTS: Sixty-three patients with advanced and chronic dilated cardiomyopathy undergoing implantation of LV assist device (LVAD) were prospectively investigated using speckle tracking echocardiography. Acute heart failure patients were prospectively excluded. We evaluated LV rotational mechanics (apical and basal LV twist, LV torsion) and deformational mechanics (circumferential and longitudinal strain) before LVAD implantation. Cardiac recovery post-LVAD implantation was defined as (1) final resulting LV ejection fraction ≥40%, (2) relative LV ejection fraction increase ≥50%, (iii) relative LV end-systolic volume decrease ≥50% (all 3 required). Twelve patients fulfilled the criteria for cardiac recovery (Rec Group). The Rec Group had significantly less impaired pre-LVAD peak LV torsion compared with the Non-Rec Group. Notably, both groups had similarly reduced pre-LVAD LV ejection fraction. By receiver operating characteristic curve analysis, pre-LVAD peak LV torsion of 0.35 degrees/cm had a 92% sensitivity and a 73% specificity in predicting cardiac recovery. Peak LV torsion before LVAD implantation was found to be an independent predictor of cardiac recovery after LVAD implantation (odds ratio, 0.65 per 0.1 degrees/cm [0.49–0.87]; *P*=0.014).

CONCLUSIONS: LV rotational mechanics seem to be useful in selecting patients prone to cardiac recovery after mechanical unloading induced by LVADs. Future studies should investigate the utility of these markers in predicting durable cardiac recovery after the explantation of the cardiac assist device.

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CLINICAL PERSPECTIVE

Rotational and deformational parameters of the left ventricular function can provide additional to left ventricular ejection fraction information on the damage of a failing heart. Furthermore, left ventricle rotational mechanics can play the role of prognosticator for myocardial recovery after mechanical unloading with a left ventricular assist device. This piece of information is particularly important in an era characterized by an imbalance between the number of heart donors and recipients. The potential early identification of a patient with heart failure undergoing mechanical unloading with a left ventricular assist device could further maximize his/her antiremodeling medication and make a patient's follow-up monitoring closer as a strategy for left ventricular remodeling identification. Future studies should explore the mechanisms underlying the differences in cardiac rotational and deformational mechanisms in advanced heart failure patients and how these parameters are affected by mechanical unloading in context with myocardial recovery.

Over the last decade, left ventricular assist devices (LVAD) have established their role in improving the quality and length of life in the advanced heart failure (HF) patient.[1,2] An exciting and promising observation of the mechanically unloaded failing heart through LVAD support is the improvement of the cardiac function to the point that some of these advanced HF patients were able to be weaned from the mechanical support.[3–9] Although LV ejection fraction (LVEF) during mechanical unloading is used to identify patients achieving myocardial recovery, it has showed no predictive value before LVAD implantation.[10] The need for measurement of additional quantitative and qualitative indexes of the left ventricle systolic function, beyond EF is a consequence of its complex nature. Myocardial muscle has a helical orientation with the subendocardial fibers after a right-handed orientation and the subepicardial fibers a left-handed orientation. This type of cardiac muscle orientation, during cardiac systole results in a wringing torsional deformation of the left ventricle.[11,12] LV torsion has been found to play a pivotal role in facilitating the homogenous distribution of myocardial forces during systole. Clinical studies in chronic HF patients have associated LV rotational dynamics with the degree of remodeling and the extension of myocardial fibrosis.[13,14] In addition, LV global longitudinal strain (GLS) has been correlated with the extent of myocardial fibrosis in patients with advanced HF.[15,16]

We hypothesized that the extent and type of myocardial dysfunction of patients with advanced chronic HF is heterogeneous and may be predictive of LVAD facilitated myocardial recovery. Specifically, we theorized that the degree and extent of abnormal torsional myocardial mechanics and the degree of the impairment of GLS could predict those patients who were most likely to achieve myocardial recovery during durable mechanical unloading.

METHODS

The data, analytical methods, and study materials will not be made available to other researchers outside the University of Utah Hospital system. Researchers interested in the data, methods, or analysis can contact the corresponding author for more information.

We screened 220 patients with advanced chronic systolic HF who had a clinical indication for LVAD implantation (bridge to transplant/destination therapy/bridge to decision). The study was approved by our institutions' Institutional Review Board and the patients provided the type of informed consent required by this approval. All patients had been diagnosed with chronic and dilated cardiomyopathy and end-stage HF (New York Heart Association IV), despite optimal medical and device therapy. We included patients that fulfilled all the following criteria: (1) chronic HF, (2) adequate quality of 2-dimensional (2D) echocardiographic images that allowed the analysis of rotational mechanics before LVAD implantation, and (3) at least 3 months after LVAD implantation with serial echocardiograms of sufficient quality to assess LVEF. We excluded patients with acute systolic HF or patients with clinical or histological evidence of acute myocarditis. We also excluded patients with atrial fibrillation at the time of echocardiographic analysis, unless the patient was on paced rhythm. Myocardial recovery (Rec Group) post-LVAD implantation was defined as (1) final LVEF ≥40%, (2) relative increase in LVEF ≥50%, and (3) relative LV end-systolic volume index decrease ≥50%. Patients who did not fulfill the above criteria constituted the no recovery group (Non-Rec Group).

We also included 15 subjects without known structural heart disease (control group), who were referred for an echocardiogram for atypical chest pain or palpitations without evidence for myocardial ischemia and other significant arrhythmia. We compared the deformational and rotational echocardiographic parameters of the advanced HF patients, before LVAD implantation, to those of the control group, to determine the degree of the impairment in our HF population. The study was approved by the Institutional Review Board of the participating institutions.

Echocardiography

Study participants were imaged in the left lateral decubitus position with commercially available systems (Phillips and GE machines) coupled with a 3.5 MHz (M4S) transducer and films were digitally stored in cine-loop format; analyses were subsequently performed offline.

Echocardiogram Protocol

Surveillance for functional recovery was undertaken using a protocol developed and tested at the University of Utah.[5] Conventional echocardiograms were performed within 2

weeks before LVAD implantation and 1, 2, 3, 4, 6, 9, and 12 months after implantation. Echocardiographic studies included complete 2D and Doppler examinations. Assessment of LV volumes and LVEF were performed using the apical 4- and 2-chamber views. Right ventricular size was evaluated by means of right ventricular dimension obtained at end-diastole from a right ventricular focused apical 4-chamber view (basal right ventricular end-diastolic dimension). Doppler evaluation included the assessment of mitral inflow velocities. Mitral inflow parameters evaluated included early mitral inflow velocity (E-wave), late or atrial mitral inflow velocity (a-wave), and E-wave deceleration time. The LV sphericity index was calculated by dividing the LV maximal long-axis internal dimension by the maximal short-axis internal dimension at end-diastole. All measurements were performed in accordance with current American Society of Echocardiography guidelines.[17]

LV Rotational Echocardiographic Analysis

Syngo velocity vector imaging technology software (Siemens Medical Solutions, Inc, Mountain View, CA) was used offline to track endomyocardial motion in the pre-LVAD 2D-echocardiogram images. The apical (the smallest cavity achievable distally to the papillary muscles) and basal (identified by the mitral valve) short-axis images were used for velocity vector imaging analysis. After selecting the optimal cardiac cycle, the endomyocardial border was delineated in a click to point approach. After that, the software automatically outlines 6 segments per short-axis view. Images that revealed poor tracking quality were excluded from further analysis. LV rotations at the basal or apical short-axis views were determined as average angular displacement of the 6 myocardial segments. The positive peak of apical LV rotation and negative peak of basal LV rotation were automatically measured. Data points depicting the basal and apical LV rotation were exported to Excel (Microsoft Corporation, Redmond, WA) to calculate LV twist and torsion. Peak LV twist is defined as the maximal instantaneous difference between the apical and basal rotations. Peak LV torsion is defined as the peak LV twist magnitude normalized to LV length. All measurements are the averages derived from 3 cardiac cycles.

Deformational Echocardiographic Analysis

Longitudinal Strain

Gray-scale 2D apical images of the LV (4-, 2-, and 3-chamber views) were obtained, and peak LS analysis of the LV was performed offline by manual tracing of the endomyocardial contour. For each view, LS was calculated as an average of the 6 automatically generated myocardial segments. GLS was calculated as an average of all segments generated by VVI analysis of the 3 apical views.

Circumferential Strain

Circumferential strain (CS) of the mid-LV was calculated using the short-axis view at the level of the papillary muscles. Peak CS was defined as the average CS of all 6 segments (generated as previously described) in the particular short-axis view. For GLS and CS, measurements were derived by the average corresponding values of 3 cardiac cycles. For rotational and deformational analysis, images were acquired at 60 to 80 frames/sec.

Hemodynamics

Patients underwent right heart catheterization within 1 week preceding LVAD implantation, which included measurement of central venous pressure, pulmonary artery pressures, pulmonary capillary wedge pressure, cardiac index.

Intraobserver and Interobserver Variability

Fifteen patients were randomly selected to assess the reproducibility of peak LV apical and basal LV twist. Bland–Altman analysis was performed to evaluate intraobserver and interobserver agreement by repeating the analysis 3 months later by the same observer and by a second independent observer. Intraobserver agreement was excellent. According to Bland–Altman analysis, the mean difference±2 SD for peak LV rotational parameters was 0.09±1.8°, 0.2±3.5% for CS and 0.1±2.2% for LS. Interobserver agreement was also good. According to Bland–Altman analysis, the mean difference±2 SD for LV rotational parameters was 0.2±4.2°, 1.7±4.8% for CS and 1.5±4.1% for LS.

Statistics

Continuous variables are expressed as mean±SD. Categorical variables are expressed as numbers and percentages. Independent sample t test and χ^2 test were used to compare the continuous and noncontinuous characteristics of the HF and

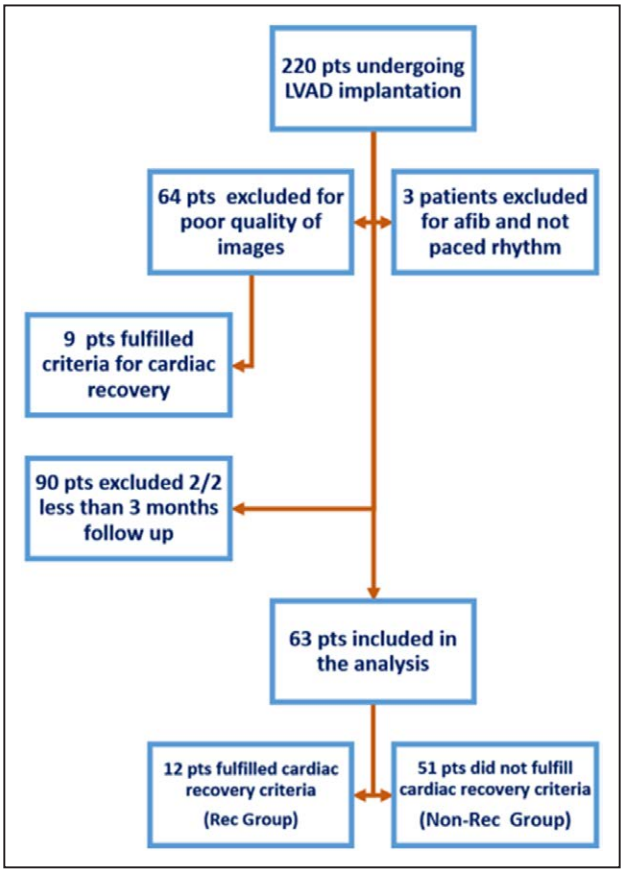

Figure 1. Flow diagram of patients included in the study.
LVAD indicates left ventricular assist device; and pts, patients.

control subjects respectively, and also the baseline characteristics of the recovered and nonrecovered HF patients. Univariate and multivariate linear regression analyses were performed to evaluate the relationship between peak LV torsion in the HF population and the following baseline variables: age, duration of HF symptoms, LVEF, peak CS, GLS, LV end-diastolic diameter (LVEDD), LV end-systolic volume index, and LV end-diastolic volume index. Univariate and multivariate binary regression analyses were performed to evaluate the association of peak LV torsion in the HF population with recovery after adjustment for the following baseline variables: age, duration of HF symptoms, LVEF, CS, GLS, LVEDD, LV end-systolic volume index, and LV end-diastolic volume index. Receiver operator characteristics curve analysis was performed to determine the accuracy of baseline peak LV torsion to predict myocardial recovery after LVAD implantation. A *P* value <0.05 is considered significant.

RESULTS

Out of 220 patients implanted with LVAD, 63 patients met our inclusion criteria, of which 12 fulfilled the criteria of myocardial recovery. Patients excluded from the study group included (Figure 1): 67 patients with inadequate quality of images and 90 patients with <3-month follow-up post-LVAD implantation (which is inadequate period of time to assess the effect of LVAD-induced mechanical unloading on cardiac recovery). We compared the baseline characteristics of the excluded patients to those included in the analysis to address selection biases, and we revealed no significant differences (comparisons were done separately between those with and without myocardial recovery).

Table 1. Baseline Clinical and Echocardiographic Characteristics of Control Subjects and Heart Failure Patients (Before LVAD Implantation)

	Control Subjects (n=15)	Heart Failure Patients (n=63)	*P* Value
Age, y	51±7	52±15	0.72
Males, n (%)	5 (33.3%)	46 (74.0%)	0.28
BSA	2.0±0.2	2.0±0.2	0.76
Weight, kg	91±22	83±18	0.16
Diabetes mellitus, n (%)	1 (6.7%)	9 (14.3%)	0.76
Hypertension, n (%)	2 (13.3%)	15 (23.8%)	0.77
LVEF, %	65±6	18±7	<0.001
LVEDV, mL)	95±17	269±84	<0.001
LVESV, mL	30±9	216±74	<0.001
RVEDD, cm	3.7±0.4	5.0±1.2	0.002
Diastolic filling pattern			<0.001
Normal, %	70	0	
Delayed relaxation, %	30	1	
Pseudonormal, %	0	24	
Restrictive, %	0	75	
Peak LV circumferential strain, %	−24.8±4.9	−4.9±3.5	<0.001
Peak LV longitudinal strain, %	−18.1±2.6	−3.8±3.1	<0.001
Peak LV basal rotation, degree	−7.4±3.0	−1.5±2.9	<0.001
Peak LV apical rotation, degree	8.4±2.9	0.7±2.7	<0.001
Peak LV rotation, degree	15.6±3.0	2.2±3.2	<0.001
Peak LV torsion, degree/cm	1.94±0.45	0.25±0.36	<0.001

BSA indicates body surface area; LV, left ventricle; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; LVEDV, left ventricle end-diastolic volume; LVESV, left ventricle end-systolic volume; and RVEDD, right ventricle end-diastolic diameter.

Clinical and Echocardiographic Characteristics of Normal Controls and HF Patients

Compared with the control subjects, chronic systolic HF patients (before LVAD implantation) had significantly lower LVEF and LV rotational and deformational characteristics (Table 1). Furthermore, HF patients had significantly more impaired GLS and CS parameters (Table 1).

Parameters Affecting Left Ventricle Torsion Before LVAD Implantation

Univariate linear regression analysis revealed significant association of various parameters with peak LV torsion: HF duration, CS, GLS, and LVEDD (Table 2). In linear regression analyses predicting peak LV torsion, a 2-variable model adjusting for peak CS (β=−0.057, *P*=0.001) showed LVEDD was an independent predictor (β=−0.221, *P*=0.002), as did a 2-variable model entering global GLS (β=−0.076, *P*=0.001) and LVEDD (β=−0.181, *P*=0.029). Modeling HF duration, peak CS, and GLS together with LVEDD (Table 2) had a similar result (LVEDD β=−0.164, *P*=0.029).

Table 2. Univariate and Multiple Linear Regression Analysis to Determine the Independent Correlates to Peak Left Ventricular Torsion Before LVAD Implantation

	Univariate		Multivariate	
	B	*P* Value	β	*P* Value
Age	0.01	0.68	…	…
Heart failure symptoms duration	−0.027	0.026	−0.011	0.55
LVEF	0.008	0.23	…	…
Peak LV CS	−0.047	0.010	−0.007	0.72
Peak LV LS	−0.047	0.003	−0.040	0.14
LVEDD	−0.137	0.004	−0.164	0.029
LVESV	0.001	0.20	…	…
LVEDV	0.001	0.11	…	…

CS indicates circumferential strain; LS, longitudinal strain; LV, left ventricle; LVAD, left ventricular assist device; LVEDD, left ventricle end-diastolic diameter; LVEF, left ventricular ejection fraction; LVEDV, left ventricle end-diastolic volume; and LVESV, left ventricle end-systolic volume.

Characteristics of Patients With Myocardial Recovery

Twelve patients (11 with nonischemic and 1 with ischemic cardiomyopathy) fulfilled the criteria for myocardial recovery (Rec Group; Table 3), whereas 51 patients did not fulfill the criteria for myocardial recovery. The baseline characteristics of the Rec and Non-Rec Group are shown in Tables 4, 5, and 6. The Rec Group had significantly shorter duration of HF compared with the Non-Rec group. Additionally, the Rec Group had significantly lower age, higher peak LV torsion, and higher cardiac index values before LVAD implantation (Tables 4 and 6; Figure 2). Because of the small number of cardiac recovery cases, multivariate logistic regression analyses included only up to 2 explanatory variables. In such models, peak LV torsion was associated with recovery when adjusted for HF duration, cardiac index, or age (Table 7). No other variables were associated with recovery in 2-variable models with peak LV torsion, which also was unaffected by those other variables and it remained significant in those models.

In the Rec Group, peak LVEF was achieved within the first 12 months after LVAD implantation, whereas in the Non-Rec Group the LVEF remained stable throughout the follow-up period (Figure 3). Interestingly, LVEF did not differ significantly between the Rec and Non-Rec Group before LVAD implantation. Figure 4 shows the correlation between baseline torsion (before LVAD implantation) with the maximum achieved LVEF under LVAD support. By receiver operator characteristics (Figure 5), peak LV torsion ≥0.35 degree/cm had a sensitivity of 92% and a specificity of 73% to predict myocardial recovery after LVAD implantation.

After LVAD implantation, there were no significant differences in the antiremodeling medical therapy between the Rec Group and Non-Rec Group: b-blocker (83% versus 67%, *P*=0.26), angiotensin-converting enzyme inhibitor/angiotensin II receptor antagonist (83% versus 56%, *P*=0.08) and aldosterone receptor antagonist (62% versus 51%, *P*=0.55) respectively.

Table 3. Characteristics of the Recovery Group of Patients Before and After LVAD Implantation

Patient	1	2	3	4	5	6	7	8	9	10	11	12
Before LVAD implantation												
Age	20	48	68	76	22	16	18	44	44	28	44	30
Sex	M	F	F	M	M	M	M	M	M	F	M	F
Duration HF, y	1.7	0.83	8	1	1	0.08	0.33	0.25	1.2	1.5	2.5	0.5
Etiology HF	Chemo	Chemo	NICM	ICM	chemo	NICM	NICM	NICM	NICM	NICM	NICM	NICM
INTERMACS	2	4	4	6	1	1	2	3	3	3	3	5
B-blocker	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes
ACE-i/ARB	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Inotrope support	No	No	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No
Cr, mg/dL	0.7	2.3	1.5	0.9	1.22	1.64	0.92	1.17	0.97	0.8	1.05	0.92
LVEF, %	13	36	28	38	13	17	12	10	20	22	15	21
LVEDD, mm	53	49	70	54	59	68	68	67	68	69	88	73
MVR (+/4)	1	2	3	0	2	2	1	2	1	3	1	2
CS, %	−6	−8		−20	−4	−3	−2		−4	−6		−3
LS, %	−7.3	−10	−7.4	−8.8	−0.6	−4.4	1.4	−2.7	−2.0	−8.6	−1.3	−8.0
LV torsion, degree/cm)	0.57	1.21	0.35	0.73	0.62	0.47	0.58	0.35	0.56	0.70	0.35	0.32
Post-LVAD implantation												
Follow-up, mo	9	12	12	1	4	12	9	9	6	6	9	9
b-blocker	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
ACE-i/ARB	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
LVEF, %	58	51	55	47	50	60	50	40	42	42	40	45
LVEDD, mm	36	35	28	51	52	47	53	50	47	39	45	44
LVEDV, mL	41	116	55	41	124	98	130	177	90	87	129	106
LVESV, mL	17	40	22	23	50	49	61	117	52	50	68	41
MVR (+/4)	1	1	1	0	1	0	0	0	1	0	0	0

Chemo indicates chemotherapy-induced cardiomyopathy; CS, circumferential strain; Cr, serum creatinine; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LS, longitudinal strain; LVAD, left ventricular assist device; LVEDD, left ventricle end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESV, left ventricle end-systolic volume; LVEDV, left ventricle end-diastolic volume; and MVR, mitral valve regurgitation.

Table 4. Baseline Characteristics of the Recovery and Nonrecovery Groups

	Recovery Group (n=12)	Nonrecovery Group (n=51)	*P* Value
Age, y	38±19	53±16	0.007
Male, n	8	38	0.582
BSA	1.89±0.1	2.00±0.25	0.13
Weight	85±19	78±10	0.26
Duration of HF symptoms, y	1.8±1.0	6.1±4.1	0.03
Cause of HF (ischemic/nonischemic)	1/11	19/32	0.06
Inotropic therapy, %	50	59	0.56
Diabetes mellitus, %	0	19	0.10
Hypertension, %	30	26	0.80
Beta blocker, %	83	77	0.66
ACE-i/ARB, %	67	68	0.93
ICD/CRT	83	92	0.70
LVAD type			0.83
Heartware, %	15	18	
Heartmate, %	75	63	
VentrAssist, %	0	2	
Jarvik, %	10	17	
Indication of LVAD			0.22
Destination therapy, %	8	32	
Bridge to transplant, %	84	57	
Bridge to decision, %	8	11	
Follow-up, mo	7.6±3.8	7.3±3.7	0.85
Creatinine, mg/dL	1.2±0.4	1.3±0.4	0.22
BUN, mg/dL	34±25	23±16	0.79
Hb, g/dL	12.8±2.0	13.1±2.1	0.78
BNP, pg/L	1922±1392	1552±919	0.39
Na, meq/L	133±4	134±6	0.59
T-bilirubin, ng/dL	1.47±0.92	1.42±0.84	0.88
Right heart catheterization parameters			
Systemic systolic BP, mm Hg	97±18	100±8	0.74
Systemic diastolic BP mm Hg	67±11	66±14	0.55
RAP, mm Hg	9±8	10±6	0.67
Mean PAP, mm Hg	37±9	38±8	0.29
PCWP, mm Hg	24±10	25±7	0.76
CI, L per min per m^2	2.24±0.85	1.73±0.40	0.004
PVR, woods	2.00±0.67	4.77±2.94	0.08

BNP indicates brain natriuretic peptide; BP, blood pressure; BSA, body surface area; BUN, blood urea nitrogen; CI, cardiac index; Hb, hemoglobin; ICD/CRT, implantable cardiac defibrillator/cardiac resynchronization therapy; LVAD, left ventricular assist device; Na, serum sodium; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; and T-bilirubin, total-bilirubin.

DISCUSSION

In patients with chronic advanced systolic HF, LV torsion before LVAD implantation was found to predict myocardial recovery after mechanical unloading with an LVAD (Figure 6). It is noteworthy that patients who experienced myocardial recovery after LVAD implantation had before LVAD implantation LVEF similar to those who did not show post-LVAD myocardial recovery (Figure 6). This is also consistent with prior observations studies (5, 7, 9, and 10).

Previous studies have identified as independent predictors for myocardial recovery the young age and nonischemic cause.[9,18,19] In concordance to those findings, our study also revealed that there was a trend for younger and nonischemic patients to reveal myocardial recovery. Additionally, in our Rec Group of patients, the time from the HF diagnosis to the implantation of the LVAD was significantly shorter compared with the Non-Rec Group of patients. Previous studies also have identified a prognostic role of cardiac deformational and rotational parameters in HF patients undergoing cardiac resynchronization therapy.[20] To our knowledge, this is the first study describing the role of LV torsional mechanics as a predictor for myocardial recovery after mechanical support with an LVAD.

Impact of LV Systolic Dysfunction on LV Torsional and Deformational Parameters in HF Patients

In a normal heart, LV systole is associated with counterclockwise rotation at the apex, whereas the base rotates clockwise (when viewed from the apex), resulting in a twisting motion of the heart.[11] Furthermore, myocardial energy efficiency is thought to be dependent on LV twist by normalizing the fiber shortening of the endomyocardial and epimyocardial layers during contraction.[21,22] Forty percent of the total stroke volume is produced by these twisting forces[23] and not reflected in the LVEF, a relatively crude assessment of LV function.

Clinical studies have shown that in patients with dilated cardiomyopathy, LV twist mechanisms are impaired[24] and predictive of outcome. When we compared the rotational parameters of our HF patients before LVAD implantation to patients without structural heart disease, we observed similar results. The occurrence of progressive LV dilatation with a concomitant increase in LV sphericity index and widening of the LV apex results in the development of a more transverse myocardial fiber direction that ultimately results in impaired LV rotation.[25,26] In our HF study population, both patients who recovered and those that did not experience myocardial recovery had comparable LV sphericity indexes. This finding implies that beyond myocardial architecture disruption and consequent LV remodeling, more extensive myocardial injury as reflected in more abnormal rotational mechanics is more sensitive in predicting post-LVAD recovery. Importantly, LV torsion was related

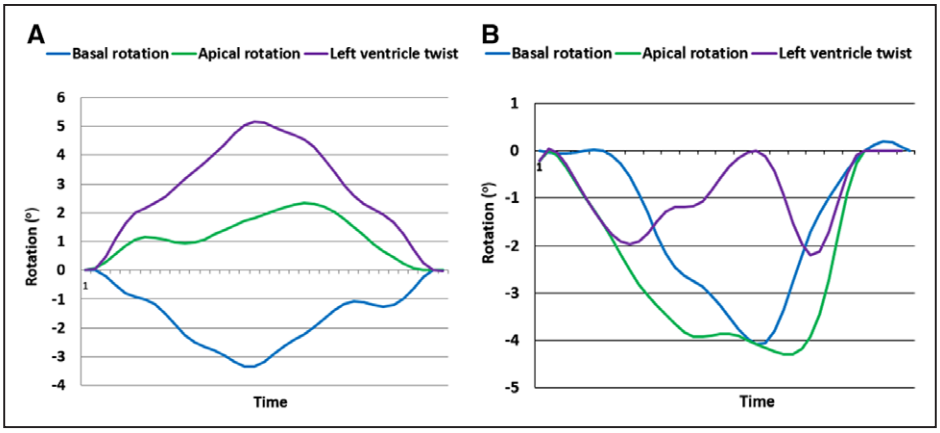

Figure 2. LV twist curves.
LV rotational mechanics curves derived before LVAD implantation from a patient that developed post-LVAD myocardial recovery (**A**) and from a patient that did not develop myocardial recovery (**B**). Patient (**A**) has LV twist of 5.1 degree. Patient (**B**), in contrast to patient A, reveals a clockwise rotation of the apex (the apical rotation is negative instead of positive). This results in both the base and the apex rotating to the same direction during cardiac systole and to practically zero LV twist. LV indicates left ventricle; LVAD, left ventricular assist device; and LVEF, left ventricular ejection fraction.

to the duration of HF which likely also reflects the magnitude and extent of irreversible myocardial injury.

In our pilot study, we were unable to identify a correlation between baseline LVEF and baseline LV rotation parameters. Previous studies in HF patients have identified a correlation between LVEF and LV torsion, and this correlation was weaker in nonischemic compared with ischemic patients.[27] It should be noted that the patient population of our study is characterized by more advanced heart disease as compared with those studies. Half of our patients were inotrope dependent, had lower LVEF, and larger LV chamber volumes compared with the aforementioned clinical studies. LV torsion and LVEF are not identical parameters, and studies have shown that LV torsion can provide additional information about ventricular systolic performance.

Role of LV Rotational and Deformational Mechanics in Predicting Myocardial Recovery

In the current study, LV torsion before LVAD implantation was the only independent parameter that correlated with the maximum LVEF after LVAD implantation, predicting myocardial recovery (Tables 4, 5, and 6). Impaired quantitative and qualitative LV rotational parameters in HF patients have been associated with more advanced stages of heart disease.[13,14] In a group of HF patients with

Table 5. Baseline and Post-LVAD Support Conventional Echocardiographic Parameters

	Before LVAD			After LVAD		
	Recovery Group (n=12)	Nonrecovery Group (n=51)	*P* Value	Recovery Group (n=12)	Nonrecovery Group (n=51)	*P* Value
LVEF, %	20±10	17±6	0.19	50±8*	23±8*	0.001
LVEDD, cm	6.5±1.0	6.9±0.9	0.25	4.5±0.8*	6.0±1.3*	0.001
MVR (+/4)	1.5±1.0	1.4±1.0	0.74	0.4±0.5*	0.5±0.7*	0.82
LVEDVi, mL/m^2	128±63	141±43	0.35	56±26*	92±38*	0.002
LVESVi, mL/m^2	103±57	113±39	0.46	27±14*	74±36*	0.001
RVEDD, mm	4.3±0.6	5.0±1.0	0.07	4.3±0.9	4.4±0.9*	0.54
LV sphericity index	1.5±0.2	1.4±0.2	0.86	…	…	…
Diastolic filling pattern						
Normal	0	0		72	28	
Delayed relaxation, %	0	2	0.88	14	24	0.001
Pseudonormal, %	30	27		14	10	
Restrictive, %	70	71		14	38	

LV indicates left ventricle; LVEDD, left ventricle end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESVi, left ventricle end-systolic volume index; LVEDVi, left ventricle end-diastolic volume index; MVR, mitral valve regurgitation; and RVEDD, right ventricle end-diastolic diameter.
*$P<0.05$.

Table 6. Baseline Rotational and Deformational Echocardiographic Parameters

	Recovery Group (n=12)	Nonrecovery Group (n=51)	*P* Value
Apical rotation, degree	1.49±3.3	0.5±2.59	0.27
Basal rotation, degree	−3.44±2.98	−1.05±2.71	0.009
Abnormal rotation direction (base or apex; n)	3	35	0.004
Left ventricle twist, degree	4.87±1.67	1.60±3.16	0.001
Left ventricle torsion, degree/cm	0.56±0.24	0.17±0.34	0.001
Left ventricle longitudinal strain, %	−4.9±3.8	−3.5±2.87	0.14
Left ventricle circumferential strain, %	−6.38±5.44	−4.31±2.70	0.12

nonischemic cardiomyopathy, those with reversed apical rotation correlated with more extensive remodeling and more advanced HF stages.[13] Similarly, in our study, the Non-Rec Group of patients had higher rates of abnormal direction of apical or basal rotation before LVAD implantation. The prognostic role of LV torsion has been studied in HF patients undergoing cardiac resynchronization therapy.[27] Immediately after cardiac resynchronization therapy implantation, patients with improvement in LV torsion predicted LV reverse remodeling 6 months later.

A prognostic role for LV torsion has also been found in patients after an acute myocardial infarction. In that study decreased LV torsion immediately after myocardial infarction predicted adverse LV remodeling after 6 months.[28] A preserved CS in postmyocardial infarction patients has also been found to predict a favorable outcome and consistent with less LV remodeling.[29,30]

In HF patients, deformational LV parameters have also been identified as a prognostic tool. For example, worsening in GLS independently predicted long-term adverse events.[31] In contrast, CS and GLS in our study were not associated with myocardial recovery. However, our patients had likely developed extensive LV remodeling at the time of LV mechanical unloading. This might indicate that as HF and LV remodeling evolves, left ventricle torsion constitutes the last effective contractile mechanism of the failing heart.

Rotational and deformational parameters of LV function could provide significant prognostic information. In an era of imbalance between heart donation and demand, rotational mechanics could be a guidance tool for patient selection with a higher likelihood for myocardial recovery. This could have significant implications more specifically in young patients, where the protentional implantation of the LVAD in earlier stages of HF could enhance the changes for myocardial recovery. These strategies warrant future prospective clinical investigations.

Cardiac Rotational/Deformational Mechanics and Myocardial Recovery in Ischemic Versus Nonischemic Cardiomyopathy

In our study of 20 patients with ischemic cardiomyopathy, only 1 revealed myocardial recovery after LVAD

Table 7. Univariate and Multivariable Logistic Regression Analysis to Determine Independent Predictors of LV Recovery Following LVAD Support

	Univariate		Bivariate	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Heart failure symptoms duration	1.65 (1.13–2.41)	0.010	…	…
Cardiac index	0.20 per L per min per m² (0.06–0.78)	0.020	…	…
Peak LV torsion	0.65 per 0.1 degree/cm (0.49–0.87)	0.014	…	…
Age	1.66 per decade (1.12–2.48)	0.012	…	…
Bivariate models				
Heart failure symptoms duration	…	…	1.67 (1.00–2.49)	0.027
Peak LV torsion	…	…	0.63 per 0.1 degree/cm (0.42–0.94)	0.009
Cardiac index	…	…	0.26 per L per min per m² (0.06–1.14)	0.26
Peak LV torsion	…	…	0.67 per 0.1 degree/cm (0.50–0.91)	0.019
Age	…	…	1.77 per decade (1.13–2.74)	0.013
Peak LV torsion	…	…	0.64 per 0.1 degree/cm (0.50–0.88)	0.005

Odds ratios (OR)>1.0 indicate the odds of not recovering, thus OR<1.0 provides the relative odds of recovery. LV indicates left ventricle.

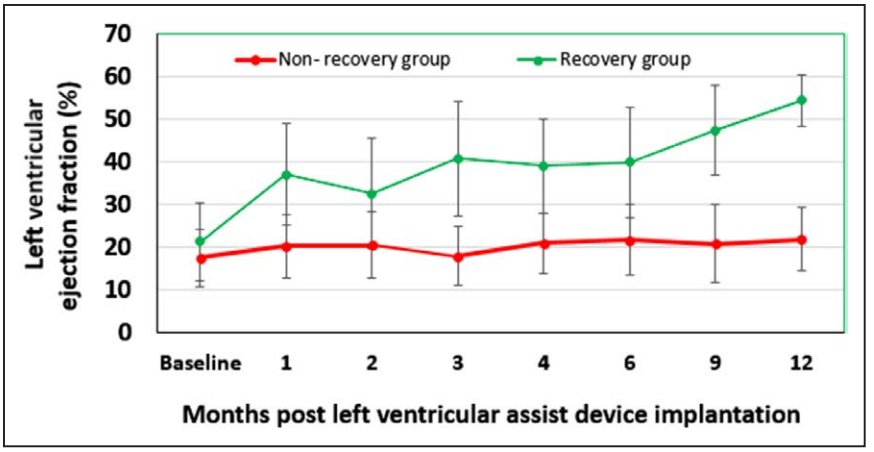

Figure 3. Time course of left ventricular ejection fraction changes following left ventricular assist device (LVAD) implantation. Time course of left ventricular ejection fraction following LVAD implantation in recovery and nonrecovery group of patients.

implantation. This is consistent with our recently reported study which revealed that LVAD-associated unloading resulted in a substantial improvement in myocardial structure, and systolic and diastolic function in 1 in 20 ischemic cardiomyopathy patients and 1 in 5 nonischemic cardiomyopathy patients.[32] Previous studies have also shown that myocardial recovery is significantly less common in patients with ischemic cardiomyopathy compared with the patients with nonischemic cardiomyopathy. In our study, when we compared torsional values of the 19 patients with ischemic cardiomyopathy who had no myocardial recovery with those of patients with nonischemic cardiomyopathy who had no myocardial recovery, we detected no significant difference.

Study Limitations

Because of the well-identified challenges of imaging patients with LVAD devices, there was a large proportion of our patient population with poor quality echo images after LVAD implantation that we were unable to quantify torsional parameters on. For this reason, it is unclear whether the improvement in LVEF in LVAD patients is accompanied by concomitant improvement in torsional parameters. Transesophageal echocardiography could bypass the obstacle of poor imaging quality in LVAD patients with recovered myocardium.[33] Nonetheless, this piece of information could provide additional criteria for potential LVAD explantation and potentially minimizing the risk of HF recurrence. We were, however, able to acquire short-axis basal images (to calculate basal rotation) and short axis images at the midlevel of the LV (for the calculation of the CS) in many of our patients. This data are provided in Table I and Figure I in the Data Supplement. Regardless, the

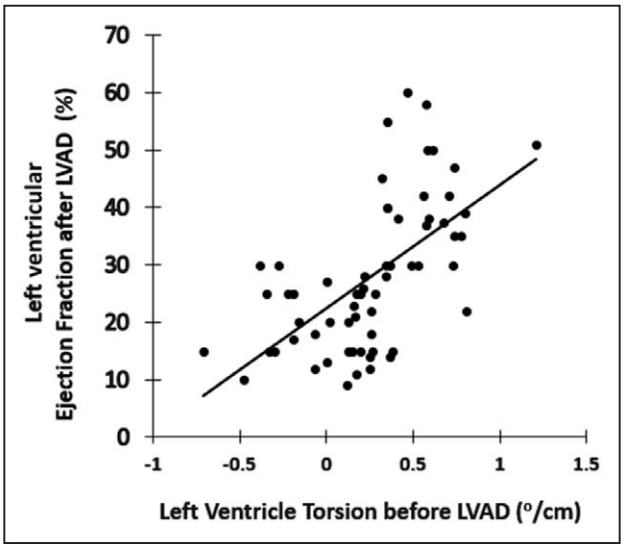

Figure 4. Correlation between peak left ventricle (LV) torsion before left ventricular assist device (LVAD) implantation and end-systolic volume indexed following LVAD implantation (r=0.605, P=001).

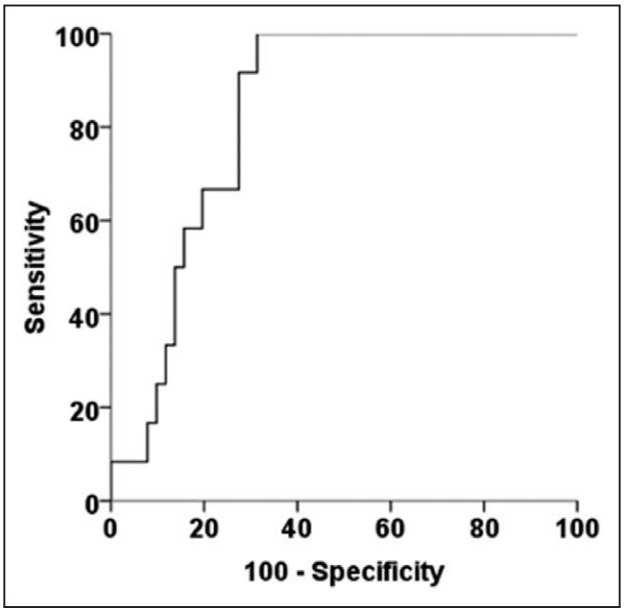

Figure 5. Receiver operator characteristics curve. Receiver operator characteristics curve, testing the accuracy of peak left ventricle (LV) torsion, before left ventricular assist device (LVAD) implantation, to predict myocardial recovery following LVAD support. Peak LV torsion ≥0.35 degree/cm had a 92% sensitivity and a 74% specificity to predict LV myocardial recovery.

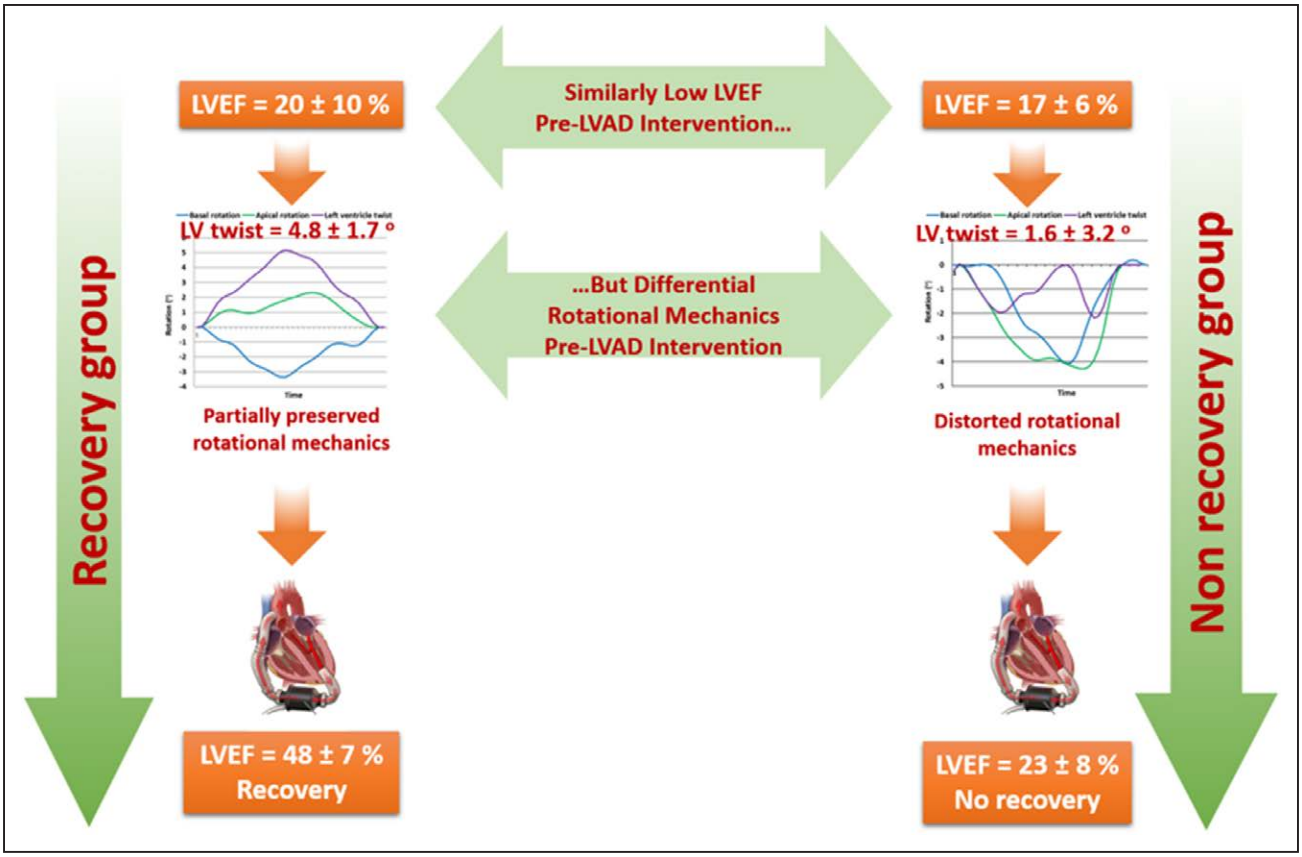

Figure 6. Role of cardiac rotational mechanics in predicting myocardial recovery following LVAD-induced mechanical unloading.
Two groups of advanced HF patients presenting with similarly low LVEF had differential left ventricular rotational mechanics at the pre-LVAD implantation time point. Only the group with partially preserved rotational mechanics responded favorably following LVAD-induced mechanical unloading with a significant increase in its LVEF. Left ventricular rotational mechanics can provide prognostic insights and improve patient selection for cardiac recovery before LVAD implantation. HF indicates heart failure; LV, left ventricle; LVAD, left ventricular assist device; and LVEF, left ventricular ejection fraction.

lack of this information does not invalidate the role of LV torsion as a predictor of myocardial recovery after LV mechanical unloading.

Additionally, the number of patients that fulfilled the criteria for myocardial recovery is relatively small. However, in the 2-variable model, LV torsion was still the parameter associated with myocardial recovery. Future prospective studies with larger samples are needed aiming to identify the role of cardiac mechanics in myocardial recovery and provide mechanistic insights, after cardiac unloading with an LVAD.

Conclusions

The interesting observation of myocardial recovery in a subset of mechanically unloaded advanced heart population is desirable and should be further pursued as a therapeutic strategy. The application of criteria for early identification, before LVAD implantation, of the population prone to a favorable response could result in enhancement of myocardial recovery by intensifying the antiremodeling medication regimen and also to closely monitor the cardiac function with serial imaging. In the current pilot study, cardiac rotational mechanics before LVAD implantation identified a population prone to myocardial recovery after cardiac mechanical support. Notably, the recovered group of patients compared with the nonrecovered group had similarly reduced pre-LVAD LVEF. Further study of cardiac rotational mechanics in LVAD supported HF patients are needed to confirm the results of the present study and potentially provide an additional guiding tool for LVAD explantation in patients with recovered myocardial function.

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Disclosures

None.

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