Three-Dimensional Left Ventricular Torsion in Patients With Dilated Cardiomyopathy — A Marker of Disease Severity —

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Background: LV twist has a key role in maintaining left ventricular (LV) contractility during exercise. The purpose of this study was to investigate LV torsion instead of twist as a surrogate marker of peak oxygen uptake (peak $\dot{V}O_2$) assessed by cardiopulmonary exercise testing (CPET) in patients with non-ischemic dilated cardiomyopathy (DCM).

Methods and Results: We evaluated 45 outpatients with DCM (50 ± 12 years, 24% females) with 3D speckle-tracking electrocardiography prior to CPET. LV torsion, LV ejection fraction (EF), LV diastolic function, LV global longitudinal (GLS) and circumferential (GCS) strain were quantified. A reduced functional capacity (FC) was defined as a peak $\dot{V}O_2 < 20$ mL/kg/min. LV torsion correlated most strongly with peak $\dot{V}O_2$ ($r=0.76$, $P<0.001$). LV torsion instead of twist was an independent predictor of peak $\dot{V}O_2$ ($B: 0.59$ to 0.71 , $P<0.001$) in multivariable analyses. Impaired LV torsion < 0.61 degrees/cm was able to predict a reduced FC with higher sensitivity and specificity (0.91 and 0.81; area under the curve (AUC): 0.88, $P<0.001$) than LV EF, GLS or GCS (AUC 0.64, 0.63 and 0.66; $P<0.05$ for differences in AUC).

Conclusions: Peak $\dot{V}O_2$ correlated more strongly with LV torsion than with LV diastolic function, LV EF, GLS or GCS. LV torsion had high accuracy in identifying patients with a reduced FC.

Key Words: Dilated cardiomyopathy; Functional capacity; Left ventricle; Three-dimensional speckle-tracking echocardiography; Torsion

Idiopathic non-ischemic dilated cardiomyopathy (DCM) is characterized by progressive left ventricular (LV) dilatation that is accompanied by reduced myocardial contractility. Cardiopulmonary exercise testing (CPET), along with an abnormal peak oxygen uptake (peak $\dot{V}O_2 < 20$ mL/kg/min), is a strong predictor of death and disease progression in these patients.^{1–3} In daily practice, therapy is most commonly assessed echocardiographically by changes in LV ejection fraction (EF). The validity of LV EF in predicting clinical outcome and peak $\dot{V}O_2$ is questionable in chronic systolic heart failure.^{4,5}

LV twist, induced by systolic apical counterclockwise (positive angulation in echocardiography) and basal clockwise rotation, results in a LV wringing motion, which was first described in 1628 by Harvey.⁶ The counterdirectional helical layer architecture of the LV provides the anatomical basis of the twist motion.^{7,8} A normalized twist, called torsion, makes measurements of the LV wringing motion more comparable among differently sized hearts. LV twist/torsion, together with longitudinal and circumferential deformation, indicates an effective LV performance, which is necessary for adequate stroke volume (SV) during incre-

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mental exercise.⁹ Twist motion and apical rotation are sensitive markers for changes in the state of cardiac function and contractility.^{10,11}

However, as with all 2D speckle-tracking techniques used for quantification of the LV, deformation and twist are affected by incorrect acquisition.¹² Cardiac motion is three-dimensional and myocardial speckles move in 3 dimensions. Hence, only a portion of the real myocardial motion can be detected with a 2D method. 3D speckle-tracking echocardiography (STE) is a novel tool to non-invasively quantify myocardial deformation and LV rotation. It has been validated against sonomicrometry, showing agreement with magnetic resonance imaging. 3D-STE allows efficient single-time acquisition of all LV segments in the same 3D data set.^{13–16}

Until now, no systematic studies have been able to elucidate the relationship between peak $\dot{V}O_2$ and LV torsion in patients with DCM. The clinical relevance of LV torsion in treatment guidance for DCM is still unclear. Therefore,

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Figure 1. Three-dimensional echocardiography of the left ventricular (LV) chamber (Upper). Apical 4- and 2-chamber views with corresponding basal, mid-level and apical cross-sections of the LV with results of rotation at each level. Exemplary comparison (Lower) of LV twist performance between 2 patients with reduced (Left) and preserved functional capacity (FC) (Right) with LV basal (dotted), apical (dashed) rotation and corresponding “instantaneous” twist curves (solid). Noteworthy between these patients are the accentuated differences in LV rotational mechanics, end-diastolic volume indices (EDV-I) and global circumferential strains (GCS) despite similar LV ejection fraction (EF) and global longitudinal strain (GLS).

the aim of the present study was to analyse LV torsion as a potential marker for disease severity in DCM. 3D-STE may be helpful when CPET is contraindicated, physically impossible or inaccessible, especially in patients with advanced heart failure, and in a clinical or outpatient routine.

Methods

Study Population and Study Design

We prospectively screened consecutive ambulatory outpatients with recently diagnosed (>6 weeks but <3 months) DCM. The patients had a reduced LV EF <50% in the absence of coronary disease, and were receiving the best possible medical treatment according to current heart failure guidelines.¹⁷ All patients were in sinus rhythm, without ventricular pacing or cardiac resynchronization/modulation therapy. Exclusion criteria were as follows: (1) moderate or severe mitral regurgitation (n=7), (2) typical complete left bundle branch block (n=8), (3) inability to undergo CPET (n=3), and (4) poor acoustic window (n=6). All eligible patients underwent CPET with gas exchange

analysis after echocardiography (within 8±5 days) without alteration of medical therapy. The study was approved by the local institutional review board and written informed consent was given by all participants.

3D and 2D Image Acquisition

Apical full 3D data sets of the LV were obtained using a PST-25SX (1–4 MHz) phased-array matrix transducer in the left lateral cubital position at rest (Toshiba Artida 4D System, Japan). Electrocardiogram-gated subvolumes of 4–6 heart cycles were acquired during a breathholding manoeuvre. Elevation tilt, lateral contrast and volume rates (24±3 volumes per second) were adjusted for the best imaging quality. The 2D echocardiography was performed with the same ultrasound system immediately after 3D image acquisition. The pulsed-wave Doppler-derived early transmitral velocity (E) and tissue Doppler-derived lateral mitral annular velocity (E') were obtained from the apical 4-chamber view. The E/E' ratio was calculated to estimate LV filling pressure.¹⁸

Table 1. Demographic, Clinical and Cardiopulmonary Test Data for Study Patients With DCM

Variable	Overall (n=45)	Reduced FC (n=23)	Preserved FC (n=22)	P value
Demographic and clinical data				
Age (years)	50±12	49±9	51±10	0.26
Female sex, n (%)	11 (24)	6 (26)	5 (23)	0.90
Body mass index (kg/m ²)	25±4	25±4	25±4	0.58
Heart rate (beats/min)	73±8	73±6	73±9	0.91
SBP (mmHg)	127±19	126±18	128±19	0.82
DBP (mmHg)	74±15	73±17	75±13	0.91
NT-proBNP (pmol/L)	449 [151–1,471]	532 [155–1,234]	408 [141–944]	0.78
NYHA functional class	1.6±1.2	1.7±1.2	1.5±1.3	0.53
QRS duration (ms)	109±12	117±15	101±13	0.02
Medications				
BB, n (%)	42 (93)	22 (96)	20 (91)	0.61
IAA, n (%)	43 (95)	22 (96)	21 (95)	0.99
Loop, n (%)	30 (66)	15 (65)	15 (68)	0.99
MRA, n (%)	32 (71)	17 (74)	15 (68)	0.74
Cardiopulmonary exercise test data				
Peak workload (Watts)	142±44	123±32	155±45	0.02
Peak heart rate (beats/min)	135±28	134±29	138±26	0.59
Peak SBP (mmHg)	166±33	162±31	171±35	0.59
Peak DBP (mmHg)	86±16	89±18	83±14	0.36
VE/CO ₂ slope	34±6	36±6	31±6	0.04
Blood hemoglobin (mmol/L)	9.3±0.8	9.6±0.8	9.1±0.7	0.91

Data are presented as mean±standard deviation, absolute numbers n with relative frequencies (%) or as median with quantiles [25–75%] for NT-proBNP. P denotes the significance level of an unpaired t-test, χ^2 -test or Yuen's modified t-test for NT-proBNP. BB, β -blockers; DCM, dilated cardiomyopathy; DBP, diastolic blood pressure; FC, functional capacity; IAA, inhibitors of angiotensin-converting enzyme and angiotensin receptor; Loop, loop diuretics; MRA, mineralocorticoid receptor antagonists; NT-proBNP, N-terminal pro B-type natriuretic peptide; NYHA, New York Heart Association; SBP, systolic blood pressure; VE/CO₂, minute ventilation/carbon dioxide production.

3D Image Analysis

Offline analysis of the 3D data set was performed using commercial wall motion tracking software (WMT, Toshiba Medical System, Japan) as previously described¹⁹ (Figure 1). LV end-diastolic and end-systolic volumes as well as LV SV were indexed to body surface-area and used for the calculation of LV EF. The 3D LV sphericity index was calculated by dividing the measured LV end-diastolic volume by the volume of a sphere with a diameter derived from the end-diastolic LV axial length (a perfectly spherical LV would result in a value of 1.0). LV global longitudinal strain (GLS) and global circumferential strain (GCS) were calculated as the means of 16 regional peak systolic strain amplitudes.¹⁸ Rotation of the LV was performed in the same manner. Briefly, short-axis line markers were placed at the basal, mid-, and apical LV level, considering the papillary muscles as anatomic landmarks. The LV basal level was above the mitral annulus, the mid-level was across the papillary muscles, and the apical level was placed beyond the implantation of the papillary muscles. Rotation was computed by the software for each level (i.e., basal, mid- and apical levels) as the mean of the segments. LV twist was calculated as the systolic peak of the “instantaneous” difference between the basal and apical levels (Figure 1).²⁰ Rotation of the LV base and apex was expressed as peak systolic values (degrees). The software measured the distance between the basal and apical levels necessary to calculate LV torsion (twist per level distance=degrees/cm).

Cardiopulmonary Exercise Testing

Patients underwent a symptom-limited bicycle CPET protocol with 3 distinct stages under medical supervision until exhaustion as previously described.²¹ Peak oxygen consumption (peak $\dot{V}O_2$), minute ventilation/carbon dioxide production and the respiratory exchange ratio (RER) were measured or calculated respectively. Patients' blood hemoglobin levels were measured before exercise. Peak RER was considered as a measure of exercise effort. Patients with peak RER ≤ 1.1 were excluded (n=3). Device calibration was performed before each test. Blood pressure values and 12-lead ECG were recorded continuously.

Statistical Analysis

Patients were divided into 2 groups according to the median value of the peak $\dot{V}O_2$ distribution.

A reduced functional capacity (FC) was defined as peak $\dot{V}O_2 < 20$ mL/kg/min.¹ Results are expressed as mean±standard deviation or frequencies and percentages unless otherwise specified. The statistical differences between the groups were assessed using Student's t-test, Wilcoxon's test or Fisher's exact test, as appropriate. The relationships among the echocardiographic and CPET data were evaluated using Pearson's correlation coefficient r. To identify the independent predictors of peak $\dot{V}O_2$, we used multiple linear regression analysis. We tested normality of distributions and heteroscedasticity as proposed.²² Only variables associated with peak $\dot{V}O_2$ in the univariable analyses were included in the multilinear models. Effect sizes were expressed as standardized β estimates (B). Logistic

Table 2. Resting Echocardiographic Data for Study Patients With DCM

Variable	Overall (n=45)	Reduced FC (n=23)	Preserved FC (n=22)	P value
LV geometry				
EDV-index (mL/m ²)	101±27	109±31	92±19	0.03
Sphericity	0.67±0.07	0.70±0.08	0.65±0.07	0.05
ESV-index (mL/m ²)	69±24	78±24	61±17	0.03
LV function				
LV EF (%)	30±8	29±8	31±8	0.34
SV-index (mL/m ²)	32±9	31±10	33±8	0.46
CI (mL/m ² /min)	2.5±0.8	2.5±0.8	2.6±0.5	0.46
E/E' ratio	15±3	16±2	13±2	<0.001

Data are presented as mean±standard deviation. P denotes the significance level of an unpaired t-test. CI, cardiac index; EDV, end-diastolic volume; E/E', ratio of pulsed-wave Doppler-derived early diastolic transmitral flow and tissue Doppler-derived early diastolic velocity from the lateral mitral annulus; EF, ejection fraction; ESV, end-systolic volume; LV, left ventricular; SV, stroke volume. Other abbreviations as in Table 1.

Table 3. LV Deformation Parameters in Study Patients With DCM

Variable	Overall (n=45)	Reduced FC (n=23)	Preserved FC (n=22)	P value
LV strain				
GLS (%)	−8.9±3.1	−8.2±3.5	−9.3±2.6	0.18
GCS (%)	−12.8±4.6	−11.6±4.6	−14.1±4.3	0.07
LV twist motion and rotation				
Twist (degrees)	4.3±2.0	3.1±1.4	5.5±1.7	<0.001
Torsion (degrees/cm)	0.61±0.18	0.42±0.17	0.81±0.19	<0.001
Apical rotation (degrees)	1.4±2.1	0.7±2.1	2.1±2.1	0.02
Reverse apical rotation, n (%)	10 (23)	9 (39)	1 (4)	0.001
Basal rotation (degrees)	−3.2±2.0	−2.6±1.6	−3.7±2.2	0.08

Data are presented as mean±standard deviation, absolute numbers n with relative frequencies (%). P denotes the significance level of an unpaired t-test. GCS, global circumferential strain; GLS, global longitudinal strain; reverse apical rotation, <0 degrees. Other abbreviations as in Tables 1,2.

regression analysis was applied for receiver-operating characteristic (ROC) with the area under the curve (AUC) and for calculation of the odds ratio (OR). ROC analysis was used to estimate the cut-off value of LV torsion, which was able to predict a reduced FC with corresponding sensitivity and specificity. Intra- and interobserver agreement was estimated from 21 randomly selected data sets within 1 week by 2 investigators blinded to previous results.²³ Statistical significance was defined as a two-tailed P value <0.05. All analyses were performed with open-source software R (version 3.0.2, 2013, The R Foundation for Statistical Computing, Vienna, Austria).

Results

Demographic and Clinical Characteristics of the Study Population

All 45 outpatients included in this study had clinically stable DCM without clinical signs of cardiac decompensation. Patients' clinical and demographic characteristics and main CPET data are summarized in **Table 1**. None developed severe symptoms during CPET. The echocardiographic characteristics of the studied population are shown in **Table 2**.

Functional Capacity and DCM

Overall peak $\dot{V}O_2$ had a mean of 20.2±5.7 mL/kg/min (median 19.9 mL/kg/min; range 11.9–33.4 mL/kg/min); 23

patients (51 %) had a reduced FC (peak $\dot{V}O_2$ <20 mL/kg/min) with longer QRS duration, lower peak workload (**Table 1**), more dilated LV and a higher degree of diastolic dysfunction (**Table 2**). Patients with a reduced FC had significantly less LV twist motion, often with more reversed apical rotation (<0 degrees) than patients with a preserved FC (**Table 3**). GLS was statistically similar in the 2 groups, although there was a trend of lower GCS in patients with a reduced FC (**Table 3**). GCS and LV spherical dilation were significantly correlated ($r=0.60$, $P<0.001$). Age, sex, LV EF, cardiac index and medical therapy regimens were similar in the 2 groups (**Table 1**). There was a significant correlation between absolute peak $\dot{V}O_2$ and the 2 following clinical demographic variables: N-terminal pro-B-type peptide and QRS duration ($r=-0.33$ and -0.36 , $P<0.05$ for both) (**Table 4**).

Relationship Between LV Function Parameters and Functional Capacity

Among the LV function parameters, torsion, twist, diastolic function and apical rotation were the strongest univariate determinants of peak $\dot{V}O_2$ ($r=0.76$, 0.68 , 0.56 and 0.49 , $P<0.001$ for all) (**Figure 2, Table 4**). However, in the multivariable analyses with adjustments for patients' demographic and clinical parameters and LV function, peak LV torsion was an independent predictor of peak $\dot{V}O_2$ ($B=0.59-0.71$, $P<0.001$ for all) (**Table 5**). Moreover, LV apical rotation was more strongly associated with LV tor-

sion ($r=0.61$) than with basal rotation ($r=-0.42$) ($P<0.01$ for both). LV torsion significantly correlated with the E/E' ratio, peak systolic blood pressure, peak workload and QRS duration ($r=-0.57, 0.45, 0.46$ and -0.40 , respectively; $P<0.05$ for all). Furthermore, LV torsion was significantly associated with LV dilation as with LV sphericity and LV end-systolic volume ($r=0.35$ and -0.42 , respectively; $P<0.05$ for both). As anticipated, LV twist (i.e., “unadjusted raw torsion”) was the main determinant of peak $\dot{V}O_2$ ($B=0.50-0.67$, $P<0.01$) with QRS duration, LV end-diastolic volume and LV E/E' ratio as significant covariates ($B=-0.24, -0.33$ and -0.29 , respectively; $P<0.03$ for all) (Table S1). In addition, LV twist and torsion correlated significantly with GCS ($r=-0.45$ and -0.41 , respectively; $P<0.005$ for both), but no associations were found with GLS ($r=-0.27$ and -0.29 , respectively).

Echocardiographic Predictors of Reduced Functional Capacity

Using ROC analysis, LV torsion had a sensitivity of 0.91 and a specificity of 0.81 (AUC=0.88, $P<0.001$) to detect a reduced FC with a best cut-off value of 0.60 degrees/cm (OR=0.05, 95% confidence interval 0.01–0.19, $P<0.001$). Further results of the ROC analysis are depicted in Figure 3.

Intra- and Interobserver Agreement of 3D-STE Parameters

Intra- and interobserver agreements were good for all LV deformation parameters: (a) intra-observer: LV apical rotation 94%; LV basal rotation 94%, LV GLS 96% and LV GCS 93%; (b) interobserver: LV apical rotation 92%; LV basal rotation 93%, LV GLS 94% and LV GCS 93%.

Discussion

The present study evaluated the relationship between LV twist and FC in patients with DCM and tested LV torsion as a surrogate parameter for FC. The major findings of this

Table 4. Relationship Among Peak $\dot{V}O_2$ and the Demographic, Clinical, and Echocardiographic Parameters in the Study Patients With DCM

Variables	r	P value
Demographic and clinical data		
Age	0.07	0.63
Body mass index	-0.02	0.91
NT-proBNP (log)	-0.33	0.04
QRS duration	-0.36	0.01
LV geometry and function		
EDV-index	-0.43	0.003
Sphericity	-0.31	0.05
ESV-index	-0.38	0.009
EF	0.36	0.02
SV-index	0.02	0.87
E/E' ratio	-0.56	<0.001
LV deformation parameters		
GLS	-0.36	0.03
GCS	-0.39	0.01
Twist	0.68	<0.001
Torsion	0.76	<0.001
Apical rotation	0.49	<0.001
Basal rotation	-0.26	0.09

Data are presented as correlation coefficient r with corresponding significance level P value. Peak $\dot{V}O_2$, peak oxygen uptake; NT-proBNP, N-terminal pro brain natriuretic peptide - log transformed. Other abbreviations as in Tables 1–3.

study are as follows. (1) LV twist, torsion and the E/E' ratio were more closely correlated to peak $\dot{V}O_2$ than LV EF or other strain parameters (Figure 2, Table 4). (2) Patients with a reduced FC (peak $\dot{V}O_2 < 20$ mL/kg/min) often had more severely reduced LV twisting motion with reversed apical rotation (Table 3). (3) LV torsion was an important determinant of a reduced FC (Figure 3); a cut-

Figure 2. Strong relationships of left ventricular (LV) torsion with peak oxygen uptake (peak $\dot{V}O_2$) and diastolic dysfunction (E/E' ratio) in the total study population ($n=45$) with regression line (solid), corresponding 95% confidence interval (grey area), correlation coefficient r and corresponding significance level P ; E/E' ratio of pulsed-wave Doppler-derived early diastolic transmitral flow and tissue Doppler-derived early diastolic velocity from the lateral mitral annulus.

Table 5. Multilinear Regression of Torsion for Prediction of Peak $\dot{V}O_2$ in Study Patients With DCM			
	B	SE	P value
Model 1: demographic and clinical factors ($r^2=0.56$, $P<0.001$)			
Torsion	0.69	0.10	<0.001
NT-proBNP (log)	−0.16	0.11	0.13
QRS duration	−0.16	0.10	0.12
Model 2: LV geometry ($r^2=0.58$, $P<0.001$)			
Torsion	0.71	0.10	<0.001
EDV-index	−0.18	0.2	0.13
Sphericity	0.11	0.11	0.92
Model 3: LV function and deformation ($r^2=0.58$, $P<0.001$)			
Torsion	0.59	0.13	<0.001
E/E' ratio	−0.22	0.12	0.07
EF	−0.40	0.39	0.31
GCS	−0.42	0.32	0.20
GLS	−0.13	0.20	0.53

B, standardised β -estimate; P, corresponding significance level; r^2 , adjusted regression coefficient of multilinear regression model; SE, standard error of estimate. Other abbreviations as in Tables 1–3.

Figure 3. Receiver-operating characteristic curve analyses showing that left ventricular twist is more accurate than other myocardial strain and functional parameters in identifying patients with a peak $\dot{V}O_2$ of 20 mL/kg/min. *DeLong's test (**Left**): comparison of differences between curves with $P<0.05$. AUC, area under the curve; ESV, end-systolic volume. Other abbreviations as in Figures 1,2.

off value of 0.61 degrees/cm could predict a reduced FC with high sensitivity and specificity in patients with DCM.

LV Torsion and Peak $\dot{V}O_2$

Peak $\dot{V}O_2$ represents peak exercise cardiac output, which in turn relies on an adaptive LV SV. This adaptive mechanism is primarily dependant on the performance of systolic and diastolic coupling of a twist motion during incremental exercise.^{9,24} In the present study, we demonstrated for the first time a strong positive correlation of LV twist and torsion with peak $\dot{V}O_2$ (**Table 4, Figure 2**). The LVs, particularly in DCM, exhibit a progressive spherical dilatation with stretching of the myofibers in a more transverse orientation.²⁵ After an initial phase of reduced LV longitudinal function, LV circumferential strain and the twist motion further deteriorate during progression of heart failure.^{20,26,27} Indeed, we showed a relationship between LV dilation and twist ($r=-0.41$) negatively affecting peak $\dot{V}O_2$ (**Table S1**) in patients with a moderately to severely reduced LV EF. In other words, twist is dependent on the magnitude of LV dilation, which influences global systolic function.²⁸ At first glance, it may appear that LV torsion is independent of LV size for prediction of FC (**Table 5**), but

torsion represents the net twist angle normalized by the LV long-axis length. It anticipates, therefore, the amount of LV dilation in progressive heart failure.

At this stage of the disease, torsional dysfunction is associated with impairment of circumferential strain ($r=-0.41$), but not with longitudinal deformation. Interestingly, Hasselberg and colleagues were able to establish an association between longitudinal strain and peak $\dot{V}O_2$ in heart failure with preserved LV EF, but not in patients with a reduced LV EF.²¹ Recent studies have reported that LV twist in patients with systolic heart failure (overall mean LV EF 31%) is reduced within a range of 4.1–6.1 degrees compared with healthy persons.^{29–33} The present result, 4.3 ± 2.0 degrees of LV twist, is consistent with those reports, irrespective of the imaging method.

LV Torsion and Disease Severity

FC with peak $\dot{V}O_2$ is a strong clinical indicator of disease progression and of survival in heart failure.³ We showed that patients with inappropriate twisting motion, dilated LVs, increased diastolic dysfunction and prolonged QRS duration adapt inadequately during exercise (**Tables 1,3**). Impairment of GLS and LV EF were not related to a

reduced FC (peak $\dot{V}O_2 < 20$ mL/kg/min) (Table 3). In the progression of DCM, mid-myocardial replacement fibrosis disturbs circumferential deformation and twist motion, which results in a “stiffer” LV and leads to deleterious systolic and diastolic ventricular function.³³ This corroborates our finding that LV torsion is more appropriate than longitudinal strain for determining a reduced FC (Figure 3). Furthermore, we demonstrated that LV torsion was strongly associated with the amount of diastolic dysfunction ($r = -0.67$) in DCM patients.

LV diastolic function plays an important role in LV contractility through effective coupling of ventricular blood suction and ejection.³⁴ In contrast, we demonstrated clearly that LV torsion is an independent predictor of peak $\dot{V}O_2$ in DCM patients with moderately to severely reduced LV EF (Table 5). Our results suggested that LV torsion not only epitomizes solely systolic LV function, but also represents a link to diastolic function in DCM. However, the eventual mechanism linking fibrosis and disease progression needs further exploration. Popescu and colleagues demonstrated that DCM patients with a reversed apical rotation and blunted twist motion exhibit severe LV remodelling compared with those with normally directed apical rotation.³⁵ In line with these observations, we found that patients with a reduced FC often had a more reversed LV apical rotation (i.e., negative angulation) (Figure 2, Table 2) with prolonged QRS duration (Table 3). A prolonged QRS duration is indicative of a higher degree of electrical dyssynchrony. Indeed, left intraventricular dyssynchrony triggers unfavourable twist mechanics and negatively affects functional capacity.³⁶ The amplitude of LV twist motion and peak $\dot{V}O_2$ are inversely related to QRS duration even in the absence of a left bundle branch block as demonstrated in our study. Recent studies underpinned the use of cardiac resynchronization therapy on LV twist and on LV reverse remodelling in systolic heart failure patients.^{30,31}

Clinical Implications

The results of the present study demonstrated a clear relationship between LV torsion and functional capacity, suggesting that LV torsion may have strong prognostic relevance in DCM patients. Echocardiography represents the basic examination for initial diagnosis and follow-up of patients with heart failure. The results of this study support the idea that twist assessment should be more prominent in first-line and follow-up examinations of heart failure patients, avoiding repeated CPET in unstable or physically disabled persons. STE might be a valuable, easily accessible and non-invasive tool in the diagnostic work-up of DCM patients to monitor subtle changes in disease progression and therapy. Nevertheless, more studies are needed to elucidate the clinical effect of LV twist in DCM.

Study Limitations

Our study was designed to test whether LV torsion can function as a surrogate parameter of peak $\dot{V}O_2$ in DCM patients. The limited number of patients did not allow us to provide a definitive statement about the clinical outcome. The degree of torsion is age-dependent, which might limit the generalisability of our study results to a broader population of heart failure patients. The prognostic value of peak $\dot{V}O_2$ between 15 and 20 mL/kg/min is debatable. However, we used an absolute peak $\dot{V}O_2$ value of

20 mL/kg/min in our study as recommended to assess heart failure severity and prognosis. 3D echocardiography is limited by its relatively low volume rate, which decreases its ability to capture events occurring in the fast phases of the cardiac cycle, such as isovolumetric relaxation. Hence, we have not assessed LV untwist, which measures the diastolic LV reverse rotation during isovolumetric relaxation time. However, we demonstrated good agreement of the speckle-tracking system in measuring systolic rotation. The fact that we demonstrated a relationship between functional capacity and resting myocardial function strengthens the clinical importance of the twist motion. Nevertheless, we had no echocardiographic information during exercise. Our findings should be confirmed in a larger population of patients to provide a direct comparison between 3D echocardiographic measures, exercise capacity and clinical outcome.

Conclusions

Our study has provided novel data showing that LV torsion was highly correlated to functional capacity and LV function. Furthermore, LV torsion was superior to LV EF in identifying patients with reduced FC. A threshold of 0.61 degrees/cm in LV torsion was highly sensitive and specific in predicting impaired cardiopulmonary fitness. Considering the strong relationship between FC and cardiac prognosis, LV torsion derived from 3D echocardiography may have the potential to identify and follow-up patients with a poorer prognosis and may open the potential for a new clinical routine in heart failure patients.

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Disclosures

The authors declare no conflicts of interest.

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Supplementary Files

Supplementary File 1

Table S1. Multilinear regression analysis of twist for prediction of peak VO₂ in study patients with DCM

Please find supplementary file(s);
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