Chapter 11

Reduced Left Ventricular Torsion Early After Myocardial Infarction Is Related to Left Ventricular Remodeling

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Circ Cardiovasc Imaging 2010;3:433-442

ABSTRACT

Background. Left ventricular (LV) torsion is emerging as a sensitive parameter of LV systolic myocardial performance. The aim of the present study was to explore the effects of acute myocardial infarction (AMI) on LV torsion and to determine the value of LV torsion early after AMI in predicting LV remodeling at 6-month follow-up.

Methods and Results. A total of 120 patients with a first ST-segment elevation AMI (mean±SD age, 59±10 years; 73% male) were included. All patients underwent primary percutaneous coronary intervention. After 48 hours, speckle-tracking echocardiography was performed to assess LV torsion; infarct size was assessed by myocardial contrast echocardiography. At 6-month follow-up, LV volumes and LV ejection fraction were reassessed to identity patients with LV remodeling (defined as a ≥15% increase in LV end-systolic volume). Compared with control subjects, peak LV torsion in AMI patients was significantly impaired (1.54±0.64° /cm vs 2.07±0.27° /cm, p <0.001). By multivariate analysis, only LV ejection fraction (β = 0.36, p <0.001) and infarct size (β = −0.47, p <0.001) were independently associated with peak LV torsion. At 6-month follow-up, 19 patients showed LV remodeling. By multivariate analysis, only peak LV torsion (odds ratio = 0.77; 95% CI, 0.65–0.92; p = 0.003) and infarct size (odds ratio = 1.04; 95% CI, 1.01–1.07; p = 0.021) were independently related to LV remodeling. Peak LV torsion provided modest but significant incremental value over clinical, echocardiographic, and myocardial contrast echocardiography variables in predicting LV remodeling. By receiver-operating characteristics curve analysis, peak LV torsion ≤1.44° /cm provided the highest sensitivity (95%) and specificity (77%) to predict LV remodeling.

Conclusions. LV torsion is significantly impaired early after AMI. The amount of impairment of LV torsion predicts LV remodeling at 6-month follow-up.

INTRODUCTION

Remodeling of the left ventricle (LV) after acute myocardial infarction (AMI) is associated with the development of heart failure and a poor survival rate.[1,2] Accordingly, identification of patients prone to develop postinfarction LV remodeling represents an important issue in clinical cardiology. These considerations have stimulated research for new parameters able to provide quantitative and objective estimation of post-AMI myocardial damage and to identify patients at risk of LV remodeling.[3] The systolic twisting motion of the LV along its longitudinal axis, resulting from opposite rotation of the LV apex compared with the base, is emerging as an important, sensitive parameter of LV systolic function.[4] Recently, echocardiographic assessment of LV torsional mechanics based on speckle-tracking analysis has been introduced and validated against sonomicrometry and magnetic resonance imaging.[5,6] In the clinical setting, however, not much data on changes in LV torsion after AMI are available,[7,8] and no specific data exist concerning the role of LV torsion in predicting postinfarction LV remodeling. Accordingly, the aim of the present evaluation was 2-fold. *First*, we sought to determine the correlates of LV torsion after AMI, and *second*, we aimed to explore the relation between LV torsion and the development of LV remodeling at 6-month follow-up.

METHODS

Patient Population and Protocol

The population consisted of 146 consecutive patients admitted to the coronary care unit because of a first ST-segment elevation AMI. Diagnosis of AMI was made on the basis of typical ECG changes and/or ischemic chest pain associated with elevation of cardiac biomarkers.[9] All patients underwent immediate coronary angiography and primary percutaneous coronary intervention (PCI). The infarct-related artery was identified

during coronary angiography and by ECG criteria. During PCI, final TIMI (Thrombolysis In Myocardial Infarction) flow was assessed.

Clinical evaluation included 2-dimensional (2D) echocardiography with speckle-tracking analysis to assess LV global longitudinal strain (GLS) and torsion, and myocardial contrast echocardiography (MCE) was performed 48 hours after PCI to assess the extent of perfusion abnormalities and infarct size. At 6-month follow-up, 2D echocardiography was performed to reassess LV volumes and ejection fraction (LVEF). These echocardiographic examinations are part of the routine, comprehensive assessment of AMI patients in our clinics.

In addition, 20 subjects without evidence of structural heart disease and without known risk factors for coronary artery disease, matched for age, sex, and body surface area and who underwent 2D echocardiography, were included as a normal control group. These individuals were derived from the echocardiographic database and were clinically referred for echocardiographic evaluation because of atypical chest pain, palpitations, or syncope without murmur.

To determine the reduction in LV torsion after AMI, patient data were compared with data from the normal controls. In addition, the independent correlates of LV torsion after AMI were investigated, and the role of LV torsion in predicting LV remodeling (defined as a $\geq$15% increase in LV end-systolic volume [ESV]) at 6-month follow-up was assessed.[1,10]

2D Echocardiography

All AMI patients and control subjects were imaged in the left lateral decubitus position with a commercially available system (Vivid 7 Dimension, GE Healthcare, Horten, Norway) equipped with a 3.5-MHz transducer. Standard 2D images and Doppler and color-Doppler data were acquired from parasternal and apical views (4-, 2-, and 3-chamber views) and digitally stored in cine-loop format; analyses were subsequently performed offline with EchoPAC version 7.0.0 software (GE Healthcare). LV end-diastolic volume (LVEDV) and LVESV were measured according to

Simpson's biplane method, and LVEF was calculated as [(LVEDV−LVESV)/LVEDV]×100.[11]

Qualitative assessment of regional wall motion was performed according to the 16-segment model of the American Society of Echocardiography, and the global wall-motion score index (WMSI) was calculated for each patient.[11] As previously described,[12] transmitral and pulmonary vein pulsed-wave Doppler tracings were used to classify diastolic function as *(1)* normal, *(2)* diastolic dysfunction grade 1 (mild), *(3)* diastolic dysfunction grade 2 (moderate), or *(4)* diastolic dysfunction grade 3 (severe).

Speckle-Tracking Analysis

Longitudinal Strain Analysis

Longitudinal strain analysis of the LV was performed by speckle-tracking imaging (EchoPAC version 7.0.0). Gray-scale 2D apical images of the LV (4-, 2-, and 3-chamber views) were used with a frame rate ranging from 60 to 100 frames per second. From an end-systolic frame, the endocardial border was manually traced, and the software automatically traces 2 more concentric regions of interest (ROIs) to include the entire myocardial wall. Speckle-tracking analysis detects and tracks the unique myocardial ultrasound patterns frame by frame. The in-plane frame-to-frame displacement of each pattern over time is used to derive strain. The software automatically validates the segmental tracking throughout the cardiac cycle and allows the operator further adjustment of the ROI to improve tracking quality. As previously described,[13] mean GLS was calculated, as an index of global LV systolic function, by averaging the GLSs obtained automatically from each apical view.

Torsional Mechanics Analysis

Speckle-tracking analysis was applied to evaluate LV basal and apical rotations, LV twist, and LV torsion. Parasternal short-axis images of the LV were acquired at 2 different levels: *(1)* basal level, identified by the

mitral valve, and *(2)* apical level, as the smallest cavity achievable distally to the papillary muscles (by moving the probe downward and slightly laterally, if needed). Frame rate was 60 to 100 frames per second, and 3 cardiac cycles for each short-axis level were stored in cine-loop format for offline analysis (EchoPAC version 7.0.0). The endocardial border was traced at an end-systolic frame, and the 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. Each short-axis image was automatically divided into 6 standard segments: septal, anteroseptal, anterior, lateral, posterior, and inferior. The software calculated LV rotation from the apical and basal short-axis images as the average angular displacement of the 6 standard segments by referring to the ventricular centroid, frame by frame. Counterclockwise rotations were marked as positive values and clockwise rotations, as negative values when viewed from the LV apex. LV twist was defined as the net difference (in degrees) of apical and basal rotations at isochronal time points. LV torsion was then calculated as the ratio between LV twist (in degrees) and the LV diastolic longitudinal length (in cm) between the LV apex and the mitral plane.[14]

Twenty patients were randomly selected to assess the reproducibility of peak LV twist. Bland-Altman analysis was performed to evaluate intraobserver and interobserver agreement by repeating the analysis 1 month 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 twist was 0.05±0.35°. Interobserver agreement was also good. According to Bland-Altman analysis, the mean difference ±2 SD for peak LV twist was 0.16±1.50°.

Myocardial Contrast Echocardiography

Immediately after 2D echocardiography, MCE was performed to evaluate myocardial perfusion to assess infarct size after AMI. The same ultrasound system was used, and the 3 standard apical views were

acquired with a low-power technique (mechanical index of 0.1 to 0.26). Background gains were set so that minimal tissue signal was seen, and the focus was set at the level of the mitral valve. Luminity (Perflutren, Bristol-Myers Squibb Pharma, Brussels, Belgium) was used as the contrast agent. Each patient received an infusion of 1.3 ml of echo contrast diluted in 50 ml of 0.9% NaCl solution through a 20-gauge intravenous catheter in a proximal forearm vein. Infusion rate was initially set at 4.0 ml/min and then titrated to achieve optimal myocardial enhancement without attenuation artifacts.[15] Machine settings were optimized to obtain the best possible myocardial opacification with minimal attenuation. At least 15 cardiac cycles after high-mechanical-index (1.7) microbubble destruction were stored in cine-loop format for offline analysis (EchoPAC version 7.0.0).[16] The LV was divided according to a standard 16-segment model, and a semiquantitative scoring system was used to assess contrast intensity after microbubble destruction: *(1)* normal/homogenous opacification, *(2)* reduced/patchy opacification, or *(3)* minimal or absent contrast opacification.[11,16] Minimal or absent contrast opacification identifies myocardial segments with a >50% transmural extent of infarction with high accuracy, as previously demonstrated by Janardhanan et al.[17] A myocardial perfusion index (MPI), indicating the extent of infarct size, was derived by adding contrast scores of all segments and dividing by the total number of segments.[16]

Twenty patients were randomly selected to assess the reproducibility of perfusion scoring. A weighted κ test was performed to evaluate intraobserver and interobserver agreement by repeating the analysis 1 month later by the same observer and by a second independent observer. Both intraobserver and interobserver agreements were good (weighted κ = 0.86 and = 0.84, respectively). To avoid measurements bias, all analyses were performed in blinded fashion.

Statistical Analysis

Continuous variables are expressed as mean±SD, when normally distributed, and as median and interquartile range, when not normally distributed. Categorical data are presented as absolute numbers and percentages.

Differences in continuous variables between 2 groups were assessed with the Student t test or Mann-Whitney U test, where appropriate. Chi-square test or Fisher's exact test, where appropriate, was computed to assess differences in categorical variables. Differences in continuous variables between >2 groups were assessed by 1-way ANOVA or Kruskal-Wallis test, where appropriate; when the result of the analysis was significant, a post hoc test with Bonferroni's correction was applied.

Univariate and multivariate linear-regression analyses (with an automatic stepwise selection procedure with backward elimination) were performed to evaluate the relation between peak LV torsion among AMI patients and the following variables: age, sex, infarct location (anterior versus nonanterior), multivessel disease, TIMI flow grade 3 after PCI, peak troponin T value, LVEDV, LVESV, LVEF, WMSI, presence of diastolic dysfunction, peak LV GLS, and MPI. Age and sex were entered into the multivariate model independently of their probability value by univariate analysis and were kept fixed throughout the stepwise selection procedure. Regarding the remaining variables, only those with a probability value <0.20 by univariate analysis were entered as covariates in the multivariate model. Linear-regression analyses were performed to evaluate the relation between peak LV torsion at baseline and LVESV at 6-month follow-up, as well as the change in LVESV after 6-month follow-up compared with the baseline value.

Univariate and multivariate logistic-regression analyses (with automatic stepwise selection procedure with backward elimination) were performed to evaluate the relation between the occurrence of LV remodeling at 6-month follow-up and the following baseline variables: age, sex, infarct location (anterior versus nonanterior), multivessel disease, TIMI flow

grade 3 after PCI, peak troponin T value, LVEDV, LVESV, LVEF, WMSI, presence of diastolic dysfunction, peak LV GLS, peak LV torsion, and MPI. Age, sex, and LVESV were entered into the multivariate model independently of their probability value by univariate analysis and were kept fixed throughout the stepwise selection procedure. Regarding the remaining variables, only those with a probability value <0.20 by univariate analysis were entered as covariates in the multivariate model. The incremental predictive value of peak LV torsion over clinical, echocardiographic, and MCE variables was assessed by calculating the global χ^2 values.

Receiver-operator-characteristics curve analysis was performed to determine the accuracy of baseline peak LV torsion to predict LV remodeling at 6-month follow-up in the overall patient population and among anterior and nonanterior AMI patients. A probability value <0.05 was considered statistically significant. Statistical analysis was performed with the SPSS software package (SPSS 15.0, Chicago, Ill).

RESULTS

Reliable speckle-tracking curves for rotation analysis and diagnostic MCE data were obtained in 120 patients; consequently, 26 patients were excluded from further analysis. Of note, no significant difference was observed between included and excluded patients with regard to age (59±10 versus 57±10 years, p = 0.31), male sex (87 [73%] versus 17 [65%], p = 0.47), anterior location of AMI (55 [46%] versus 13 [50%], p = 0.70), and peak value of troponin T (3.04 μg/L [1.65 to 7.03] versus 3.18 μg/L [1.74 to 12.62], p = 0.58). All control subjects had reliable speckle-tracking curves.

Clinical and Echocardiographic Characteristics

Clinical and echocardiographic characteristics of control subjects and AMI patients are listed in Table 1.

Table 1. Baseline clinical and echocardiographic characteristics of control subjects and AMI patients

	Control subjects (n = 20)	AMI patients (n = 120)	p value
Age (years)	56±10	59±10	0.37
Male gender	15 (75%)	87 (73%)	0.82
Diabetes	-	13 (11%)	
Family history of coronary artery disease	-	45 (37%)	
Hypercholesterolemia	-	16 (13%)	
Hypertension	-	43 (36%)	
Current or previous smoking	-	67 (56%)	
Anterior myocardial infarction	-	55 (46%)	
Infarct-related artery			
- left anterior descending	-	55 (46%)	
coronary artery	-	21 (17%)	
- left circumflex coronary artery	-	44 (37%)	
- right coronary artery			
Multi-vessel disease	-	41 (34%)	
TIMI flow grade 3	-	101 (84%)	
Peak troponin T (μg/l)	-	3.04 (1.65-7.03)	
LVEDV (ml)	103±22	104±27	0.91
LVESV (ml)	40±10	55±21	<0.001
LVEF (%)	61±7	48±9	<0.001
LV diastolic longitudinal length (cm)	8.6±0.6	8.3±0.8	0.18
WMSI	-	1.72±0.34	
Diastolic function			<0.001
- grade 0	20 (100%)	47 (39%)	
- grade 1	-	63 (52%)	
- grade 2	-	8 (7%)	
- grade 3	-	2 (2%)	
Peak LV GLS (%)	-19.4±1.7	-14.0±3.8	<0.001
Peak LV basal rotation (°)	-6.8±2.7	-5.1±2.7	0.013
Peak LV apical rotation (°)	11.6±2.8	8.4±4.6	<0.001
Peak LV twist (°)	17.7±2.1	12.7±5.2	<0.001
Peak LV torsion (°/cm)	2.07±0.27	1.54±0.64	<0.001
MPI	-	1.28 (1.08-1.50)	

Abbreviations are as defined in text.

By definition, control subjects and AMI patients did not differ in age or sex. Among AMI patients, the infarct-related artery was the left anterior descending coronary artery in 55 (46%) patients; obstructive multivessel disease (ie, >1 vessel with a luminal narrowing ≥70%) was present in 41 (34%) patients. Peak value of troponin T was 3.04 μg/L (1.65 to 7.03 μg/L). Mean LVEF was 48±9%.

Compared with control subjects, AMI patients had significantly reduced peak LV basal rotation (−5.1±2.7° versus −6.8±2.7° , p = 0.013), reduced peak LV apical rotation (8.4±4.6° versus 11.6±2.8° , p <0.001), and consequently decreased peak LV twist (12.7±5.2° versus 17.7±2.1° , p <0.001) and peak LV torsion (1.54±0.64° /cm versus 2.07±0.27° /cm, p <0.001). Among AMI patients, those with an anterior AMI had significantly lower peak LV apical rotation, LV twist, and LV torsion compared with the remaining AMI patients (6.5±4.3° versus 10.1±4.2° , p <0.001; 11.1±5.4° versus 14.0±4.7° , p = 0.002; and 1.35±0.65° /cm versus 1.70±0.58° /cm, p = 0.003, respectively), whereas peak LV basal rotation was not different (−5.4±2.6° versus −4.9±2.8° , p = 0.31). Of note, no significant difference was observed in peak LV basal rotation, apical rotation, LV twist, and LV torsion between patients (n = 37) with anterior AMI due to proximal LAD occlusion versus patients (n = 18) with anterior AMI due to mid or distal LAD occlusion (−5.2±2.5° versus −5.8±2.7° , p = 0.38; 6.9±4.3° versus 5.6±4.2° , p = 0.30; 11.4±5.2° versus 10.7±5.8° , p = 0.67; and 1.36±0.63° /cm versus 1.35±0.72° /cm, p = 0.95, respectively). Examples of LV rotational mechanics curves obtained by speckle-tracking analysis in a control subject and in a patient with AMI are shown in Figure 1.

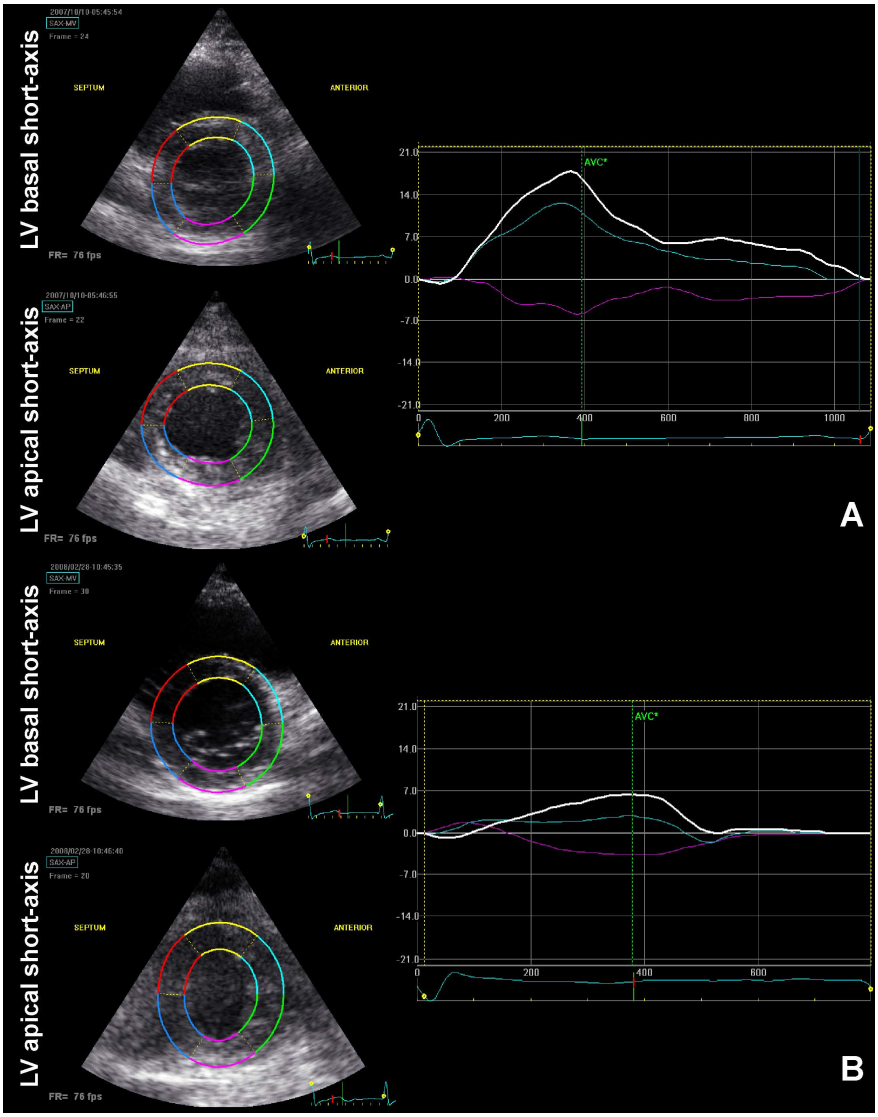


Figure 1. LV rotational mechanics curves of a control subject (**panel A**) and of a patient with anterior AMI (**panel B**). A, Speckle-tracking analysis shows normal peak LV basal (purple line) and apical (green line) rotations and normal peak LV twist (18.4° ; white line). B, Speckle-tracking analysis shows impaired peak LV basal (purple line) and apical (green line) rotations and reduced peak LV twist (6.8° ; white line).

Determinants of LV Torsion Among AMI Patients

Table 2 shows the results of univariate and multivariate linear regression analyses performed to determine the factors related to peak LV torsion among AMI patients. By univariate analysis, several variables were significantly related to peak LV torsion: anterior AMI, TIMI flow grade 3 after PCI, peak troponin T value, LVEDV, LVESV, LVEF, WMSI, presence of diastolic dysfunction, peak LV GLS, and MPI. However, by multivariate analysis, only LVEF (β = 0.36, p <0.001) and MPI (β = -0.47, p <0.001) were independently associated with peak LV torsion. The relation between peak LV torsion and MPI is shown in Figure 2.

Patients without myocardial segments with minimal or absent contrast opacification had higher peak LV torsion compared with patients with ≥1 myocardial segment with minimal or absent contrast opacification (1.84±0.49° /cm versus 1.27±0.63° /cm; p <0.001). In addition, a progressive reduction of peak LV torsion with increasing number of myocardial segments with minimal or absent contrast opacification was observed (Figure 3).

LV Remodeling at 6-Month Follow-Up

Eight of 120 AMI patients included in the initial population did not complete the 6-month follow-up; consequently, data at baseline and at 6-month follow-up were available for 112 patients. At 6-month follow-up, mean LVEDV was 114±37 ml, whereas mean LVESV was 54±29 ml and mean LVEF was 55±10%. A total of 19 patients developed LV remodeling.

Baseline clinical and echocardiographic characteristics of AMI patients with versus without LV remodeling are summarized in Table 3. At baseline, patients who developed LV remodeling had larger LVESVs (p = 0.036), lower LVEFs (p <0.001), and higher MPIs (p <0.001), indicating larger infarct size. Regarding LV rotational mechanics parameters, at baseline patients with LV remodeling had significantly lower peak LV apical rotation (p <0.001), peak LV twist (p <0.001), and peak LV

torsion (p <0.001) compared with patients without LV remodeling; conversely, no difference in peak LV basal rotation was observed between the 2 groups. Patients with more impaired peak LV torsion at baseline had larger LVESVs at 6-month follow-up and a higher change in LVESV in the 6-month follow-up period (Figure 4).

Table 2. Univariate and multivariate linear regression analyses to determine the independent correlates of peak LV torsion in AMI patients

	Univariate		Multivariate	
	β	**p value**	**β**	**p value**
Age	-0.080	0.38	0.057	0.37
Male	-0.048	0.61	-0.046	0.46
Anterior myocardial infarction	-0.27	0.003	-	-
Multi-vessel disease	-0.13	0.17	-	-
TIMI flow grade 3	0.25	0.005	-	-
Peak troponin T	-0.40	<0.001	-	-
LVEDV	-0.25	0.007	-	-
LVESV	-0.51	<0.001	-	-
LVEF	0.65	<0.001	0.36	<0.001
WMSI	-0.66	<0.001	-	-
Presence of diastolic dysfunction	-0.23	0.011	-	-
Peak LV GLS	-0.56	<0.001	-	-
MPI	-0.69	<0.001	-0.47	<0.001

Abbreviations are as defined in text.

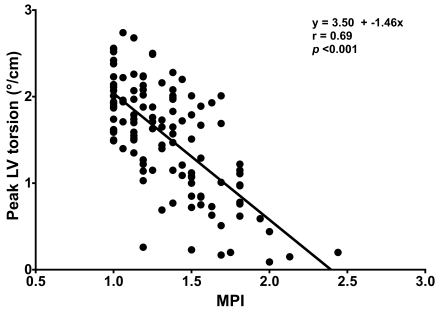


Figure 2. Linear regression analysis illustrating the relation between peak LV torsion and MPI.

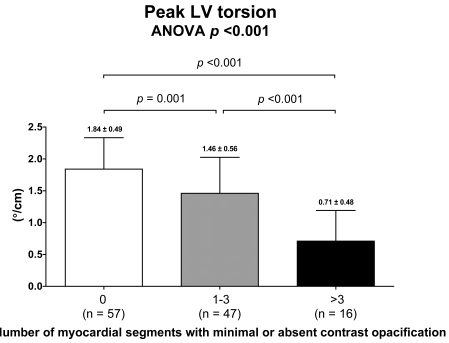


Figure 3. Relation between peak LV torsion and number of myocardial segments with minimal or absent contrast opacification.

Table 4 shows the results of univariate and multivariate logistic regression analyses performed to determine the relation between clinical and echocardiographic characteristics at baseline and LV remodeling at 6-month follow-up. By univariate analysis, several variables were significantly related to LV remodeling: anterior AMI, peak troponin T value, LVESV, LVEF, WMSI, presence of diastolic dysfunction, peak LV GLS, peak LV torsion, and MPI. However, by multivariate analysis, only peak LV torsion (odds ratio = 0.77; 95% CI, 0.65 to 0.92; p = 0.003) and MPI (odds ratio = 1.04; 95% CI, 1.01 to 1.07; p = 0.021) were independently related to the development of LV remodeling. Furthermore, peak LV torsion provided modest but significant incremental value over clinical, echocardiographic, and MCE variables in predicting LV remodeling (Figure 5).

By receiver-operator-characteristics curve analysis (Figure 6), peak LV torsion $\leq$1.44° /cm provided the highest sensitivity (95%) and specificity (77%) to predict LV remodeling; diagnostic accuracy was high in both anterior and nonanterior AMI patients (Figure 6).

Table 3. Baseline clinical and echocardiographic characteristics of AMI patients without vs with LV remodeling

	No LV remodeling (n = 93)	LV remodeling (n = 19)	p value
Age (years)	58±10	61±9	0.20
Male gender	66 (71%)	15 (79%)	0.48
Diabetes	9 (10%)	2 (11%)	0.91
Family history of coronary artery disease	36 (39%)	7 (37%)	0.88
Hypercholesterolemia	13 (14%)	2 (11%)	0.74
Hypertension	34 (37%)	6 (32%)	0.68
Current or previous smoking	54 (58%)	9 (47%)	0.39
Anterior myocardial infarction	35 (38%)	13 (68%)	0.013
Multi-vessel disease	29 (31%)	9 (47%)	0.18
TIMI flow grade 3	81 (87%)	14 (74%)	0.16
Peak troponin T (μg/l)	2.54 (1.29-5.25)	9.63 (4.96-12.51)	<0.001
LVEDV (ml)	101±23	106±34	0.59
LVESV (ml)	51±15	63±24	0.036
LVEF (%)	50±8	40±8	<0.001
LV diastolic longitudinal length (cm)	8.2±0.7	8.3±0.6	0.76
WMSI	1.63±0.30	2.05±0.21	<0.001
Presence of diastolic dysfunction	52 (56%)	16 (84%)	0.021
Peak LV GLS (%)	-15.0±3.3	-11.1±3.3	<0.001
Peak LV basal rotation (°)	-5.4±2.6	-4.6±2.5	0.20
Peak LV apical rotation (°)	9.7±4.1	3.5±3.0	<0.001
Peak LV twist (°)	14.4±4.3	6.6±3.5	<0.001
Peak LV torsion (°/cm)	1.75±0.51	0.80±0.44	<0.001
MPI	1.19 (1.00-1.41)	1.75 (1.38-1.81)	<0.001
Medical therapy at discharge			
- Antiplatelets	93 (100%)	19 (100%)	1.00
- Angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers	93 (100%)	19 (100%)	1.00
- Beta-blockers	89 (96%)	18 (95%)	1.00
- Statins	93 (100%)	19 (100%)	

Abbreviations are as defined in text.

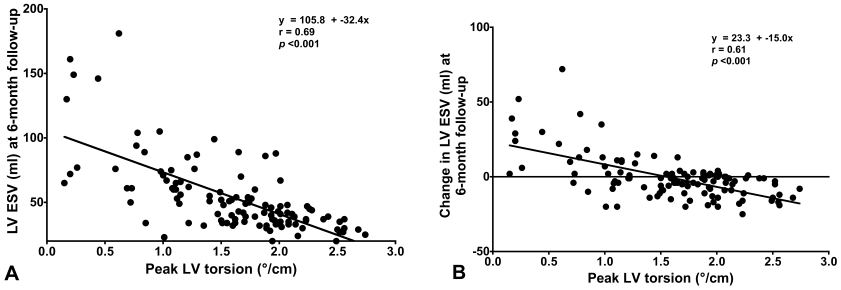
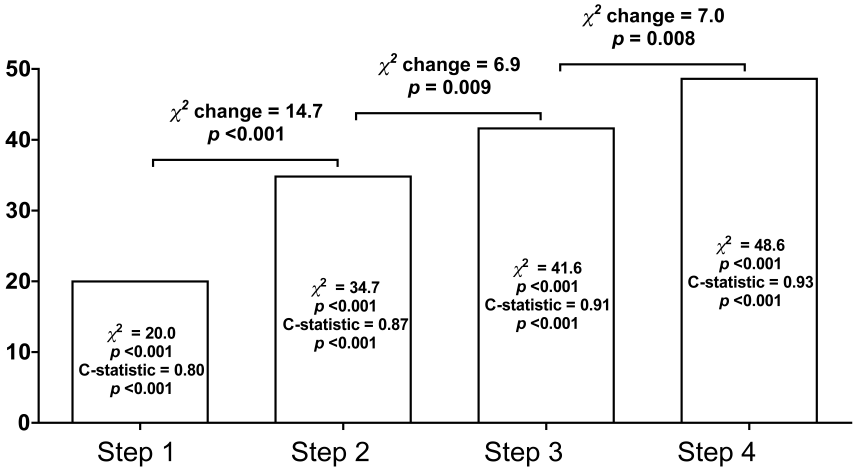


Figure 4. Relation between peak LV torsion at baseline and LVESV at 6-month follow-up (**panel A**) and the change in LVESV after 6-month follow-up compared with baseline value (**panel B**).

Table 4. Univariate and multivariate logistic regression analyses to determine the independent predictors of LV remodeling at 6-month follow-up

	Univariate		Multivariate	
	OR (95%CI)	p value	OR (95%CI)	p value
Age	1.03 (0.98-1.09)	0.20	1.00 (0.93-1.08)	0.94
Male	1.53 (0.47-5.04)	0.48	3.62 (0.66-19.8)	0.14
Anterior myocardial infarction	3.59 (1.25-10.3)	0.017	-	-
Multi-vessel disease	1.99 (0.73-5.40)	0.18	-	-
TIMI flow grade 3	0.42 (0.13-1.36)	0.15	-	-
Peak troponin T	1.23 (1.11-1.36)	<0.001	-	-
LVEDV	1.01 (0.99-1.03)	0.47		
LVESV	1.04 (1.01-1.07)	0.006	0.99 (0.94-1.04)	0.77
LVEF	0.85 (0.78-0.92)	<0.001	-	-
WMSI*	1.73 (1.34-2.24)	<0.001	-	-
Presence of diastolic dysfunction	4.21 (1.15-15.4)	0.030	-	-
Peak LV GLS	1.43 (1.19-1.71)	<0.001	-	-
Peak LV torsion*	0.72 (0.62-0.82)	<0.001	0.77 (0.65-0.92)	0.003
MPI*	1.79 (1.39-2.31)	<0.001	1.04 (1.01-1.07)	0.021

*: OR and 95%CI are intended for 0.1 unit increase. Abbreviations are as defined in text. OR indicates odds ratio. C-statistic = 0.93.



Step 1 included clinical variables (i.e. age, male gender, anterior myocardial infarction, multi-vessel disease, TIMI flow grade 3 and peak troponin T).
Step 2 included clinical and echocardiographic variables (i.e. left ventricular end-systolic volume, left ventricular ejection fraction, wall motion score index, presence of diastolic dysfunction and peak left ventricular global longitudinal strain).
Step 3 included clinical and echocardiographic variables and myocardial contrast echocardiography estimated infarct size (i.e. myocardial perfusion index).
Step 4 included clinical, echocardiographic and myocardial contrast echocardiography variables, and peak LV torsion.

Figure 5. Incremental value of peak LV torsion over clinical, echocardiographic, and MCE variables in predicting LV remodeling at 6-month follow-up.

DISCUSSION

The results of the present evaluation show that LV torsion is significantly impaired early after AMI, owing to a reduction of both basal and apical rotations. Infarct size (assessed by MCE) was independently related to LV torsion. In addition, LV torsion early after AMI was significantly and independently related to the occurrence of LV remodeling at 6-month follow-up.

Impact of AMI on LV Rotational Mechanics

Previous experimental and clinical studies have consistently shown an impairment of LV torsional deformation in the setting of acute and chronic MI.[7,8,18–21] In addition, LV torsion was related to global LV systolic

function and the extent of wall-motion abnormalities.[7,8,21] The present evaluation confirms and extends these previous observations. LV systolic function was indeed significantly related to LV torsion. More important, an independent correlation between infarct size (assessed by MCE and expressed as MPI) and LV torsion was noted on multivariate analysis. The larger damage of the LV subepicardial myofibers and the greater disarrangement of the typical architecture of LV myofibers secondary to larger infarcts may explain the observed relation between infarct size and LV torsion.

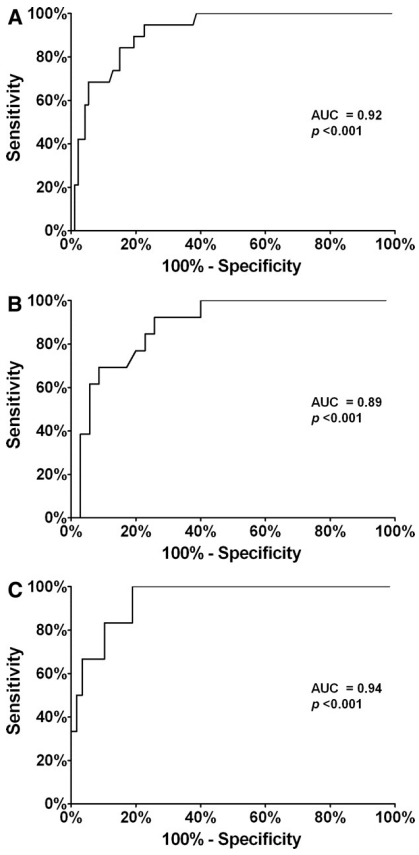


Figure 6. Receiver-operator-characteristics curve, testing the accuracy of peak LV torsion to predict LV remodeling at 6-month follow-up. **Panel A**. In the overall patient population, peak LV torsion ≤1.44° /cm provided the highest sensitivity (95%) and specificity (77%) to predict LV remodeling. **Panel B.** Among patients with anterior AMI, peak LV torsion ≤1.29° /cm provided the highest sensitivity (92%) and specificity (74%) to predict LV remodeling. **Panel C.** Among patients with nonanterior AMI, peak LV torsion ≤1.44° /cm provided the highest sensitivity (100%) and specificity (81%) to predict LV remodeling. AUC indicates area under the curve.

Epicardial myofibers are indeed extremely important to maintain LV torsional deformation.[4] Epicardial myofibers (compared with endocardial fibers) produce larger torque (related to the larger radius) and determine the overall direction of rotation.[4] Damage to epicardial fibers therefore appears mandatory for an impairment of LV torsional mechanics. Indeed, the present evaluation underscores that larger infarcts (as indicated by higher MPI values), leading to more extensive, transmural damage (spreading to epicardial myofibers),[17] result in a larger impairment of LV torsion. Previous experimental studies in an occlusion-reperfusion model provide evidence for this hypothesis by showing that LV torsion was impaired in the presence of transmural ischemia, whereas LV torsion was preserved in the presence of subendocardial ischemia only.[22,23] In addition, LV myofibers have a typical spiral architecture that is also extremely important in determining the LV systolic wringing motion. Large infarcts may be associated with extensive distortion of the typical architecture of LV myofibers, altering their obliquity and eventually impairing LV torsion.[24]

Role of LV Torsion in Predicting LV Remodeling

Besides being strictly related to the myocardial damage after AMI, LV torsion at baseline was found to be a strong predictor of LV remodeling at 6-month follow-up; interestingly, this relation remained even after adjustment for other univariate predictors of LV remodeling, including infarct size (expressed as MPI). Peculiar properties of the LV systolic twisting motion may explain this finding.

LV torsion indeed is not simply an index of global LV systolic function; previous mathematical models revealed the essential role of LV torsion in optimizing LV oxygen demand and the efficiency of LV systolic thickening by uniformly distributing myofiber stress across the myocardial wall.[25] A significant impairment of LV torsion after AMI will therefore result in increased myofiber stress and oxygen demand of the remaining noninfarcted myocardium. This low-efficiency state would further impair

myocardial contractility, possibly representing the initial step of a vicious circle of progressive LV dilatation and decline in LV systolic function.[18,24]

Clinical Implications

The present evaluation underscores the value of LV torsion as a sensitive global parameter of LV systolic myocardial performance. Its impairment early after AMI is strictly related to the extent of myocardial damage and possibly plays an important role in the development of LV remodeling. Indeed, peak LV torsion provided modest but significant incremental value over clinical, echocardiographic, and MCE variables in predicting LV remodeling. Accordingly, this parameter may be used in clinical practice as an early marker for risk stratification. Early assessment of LV torsion after AMI by speckle tracking echocardiography could identify patients (with reduced LV torsion) who may benefit from aggressive medical therapy to prevent LV remodeling, heart failure, and poor outcome.

Limitations

Some limitations should be acknowledged. First, only patients with ST-segment elevation AMI were included; consequently, the results cannot be extrapolated to patients with non–ST-segment elevation AMI. Another important limitation concerns the acquisition of short-axis images. The acquisition of true LV apical short-axis images is indeed dependent on the acoustic window (more than the basal short-axis view) and may be technically difficult to acquire in some patients. In addition, transducer position has a strong impact on the assessment of apical rotation by speckle-tracking echocardiography. It should, however, be emphasized that the most caudal transducer position was used to acquire the parasternal short-axis apical view; moreover, all patients without true LV apical short-axis images were not included in the present evaluation. Furthermore, motion throughout the planes at the basal level may reduce the accuracy of measurement of LV basal rotation. Finally, the impairment of LV torsion observed early after AMI may be partially related to the

presence of myocardial stunning; further studies are needed to assess the evolution of LV torsion after the acute phase of AMI.

CONCLUSIONS

LV torsion is significantly impaired early after AMI. The amount of impairment of LV torsion is related to infarct size. In addition, LV torsion at baseline predicts the occurrence of LV remodeling at 6-month follow-up, with modest but significant incremental value over clinical, echocardiographic, and MCE variables.

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