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

Running title: LV torsion in AMI

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ABSTRACT

Background—Left ventricular (LV) torsion is emerging as a sensitive parameter of LV systolic myocardial performance. 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 first ST-elevation AMI (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 (MCE). At 6-month follow-up, LV volumes and LV ejection fraction (EF) were reassessed, to identify patients with LV remodeling (defined as ≥15% increase in LV end-systolic volume). Compared to control subjects, peak LV torsion in AMI patients was significantly impaired (1.54±0.64º/cm vs. 2.07±0.27º/cm; p<0.001). At multivariate analysis, only LVEF (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. At multivariate analysis, only peak LV torsion (OR=0.77; 95%CI 0.65-0.92; p=0.003) and infarct size (OR=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 MCE variables in predicting LV remodeling. At receiver-operating characteristic curve analysis, peak LV torsion ≤1.44º/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.

KEY WORDS: acute myocardial infarction; infarct size; left ventricular torsion; left ventricular remodeling.
INTRODUCTION

Remodeling of the left ventricle (LV) after acute myocardial infarction (AMI) is associated to the development of heart failure and poor survival rate.\(^1,2\) Accordingly, identification of patients prone to develop post-infarction LV remodeling represents an important issue in clinical cardiology. These considerations have stimulated the research of 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 to 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 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 post-infarction LV remodeling.

Accordingly, the aim of the present evaluation was twofold. First, to determine the correlates of LV torsion after AMI, and second, 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 first ST-segment elevation AMI. Diagnosis of AMI was made on the basis of typical electrocardiographic 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). Infarct-related artery was identified by
the site of coronary occlusion during coronary angiography and electrocardiographic
criteria. During PCI, final TIMI (Thrombolysis In Myocardial Infarction) flow was
assessed.
Clinical evaluation included 2-dimensional echocardiography with speckle-tracking
analysis to assess LV global longitudinal strain (GLS) and torsion, and myocardial
contrast echocardiography (MCE) performed 48 hours after PCI, to assess the extent of
perfusion abnormalities and infarct size. At 6-month follow-up, 2-dimensional
echocardiography was performed to re-assess LV volumes and LV ejection fraction (EF).
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, gender and body surface area,
who underwent 2-dimensional 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
\[ \geq 15\% \text{ increase in LV end-systolic volume [ESV]} \]) at 6-month follow-up was assessed.\textsuperscript{1-10}

**Two-dimensional echocardiography**

All AMI patients and control subjects were imaged in left lateral decubitus position with a
commercially available system (Vivid 7 Dimension, GE Healthcare, Horten, Norway)
equipped with a 3.5-MHz transducer. Standard 2-dimensional images, Doppler and color-
Doppler data were acquired from parasternal and apical views (4-, 2- and 3-chamber) and
digitally stored in cine-loop format; analyses were subsequently performed offline using EchoPAC version 7.0.0 (GE Healthcare, Horten, Norway). LV end-diastolic volume (EDV) and LVESV were measured according to the Simpson’s biplane method and LVEF was calculated as [(EDV-ESV)/EDV] x100.11

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); 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). Grey-scale 2-dimensional apical images of the LV (4-, 2- and 3-chamber views) were used with frame rate ranging from 60 to 100 frames/s. From an end-systolic frame, the endocardial border was manually traced and the software traces automatically two more concentric regions of interest (ROI) 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 validates automatically the segmental tracking along 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 index of global LV systolic function, by averaging the global longitudinal strains 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 (moving the probe down and slightly laterally, if needed). Frame rate was 60-100 frames/s and 3 cardiac cycles for each short-axis level were stored in cine-loop format for the 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 referring to the ventricular centroid, frame by frame. Counterclockwise rotation was marked as positive value and clockwise rotation as negative value when viewed from the LV apex. LV twist was defined as the net difference (in degrees) of apical and basal rotation at isochronal time points. 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 intra- and inter-observer agreement repeating the analysis 1 month later by the same observer and by a second independent observer. Intra-observer agreement was excellent. According to Bland-Altman analysis, the mean difference ± 2 standard deviations (SD) for peak LV twist was 0.05±0.35°. Inter-observer 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 following 2-dimensional echocardiography, MCE was performed to evaluate myocardial perfusion, in order to assess infarct size after AMI. The same ultrasound system was used and the 3 standard apical views were acquired using a low-power technique (0.1-0.26 mechanical index). 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 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. 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). 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; 3) minimal or absent contrast opacification. Minimal or absent contrast opacification identifies myocardial segments with >50% transmural extent of infarction with high accuracy, as previously demonstrated by Janardhanan et al. 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.

Twenty patients were randomly selected to assess the reproducibility of perfusion scoring. Weighted Kappa test was performed to evaluate intra- and inter-observer agreement repeating the analysis 1 month later by the same observer and by a second independent
observer. Both intra- and inter-observer agreements were good (weighted Kappa=0.86 and =0.84, respectively).

In order to avoid measurements bias, all analyses were performed in blinded fashion.

**Statistical analysis**

Continuous variables are expressed as mean and 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 two groups were assessed using Student t test or Mann-Whitney U test, if appropriate. Chi-square test or Fisher exact test, if appropriate, were computed to assess differences in categorical variables.

Differences in continuous variables between more than 2 groups were assessed using one-way ANOVA test or Kruskal-Wallis test, if appropriate; if the result of analysis was significant, post-hoc test with Bonferroni’s correction was applied.

Univariate and multivariate linear regression analysis (using automatic stepwise selection procedure with backward elimination) were performed to evaluate the relationship between peak LV torsion among AMI patients and the following variables: age, gender, infarct location (anterior vs. non-anterior), multi-vessel disease, TIMI flow grade 3 after PCI, peak troponin T, LVEDV, LVESV, LVEF, WMSI, presence of diastolic dysfunction, peak LV GLS, and MPI. Age and gender were entered in the multivariate model independently from their p value at univariate analysis and were kept fixed throughout the stepwise selection procedure. Regarding the remaining variables, only those with p value <0.20 at 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 analysis (using automatic stepwise selection procedure with backward elimination) were performed to evaluate the relationship between the occurrence of LV remodeling at 6-month follow-up and the following baseline variables: age, gender, infarct location (anterior vs. non-anterior), multi-vessel disease, TIMI flow grade 3 after PCI, peak troponin T, LVEDV, LVESV, LVEF, WMSI, presence of diastolic dysfunction, peak LV GLS, peak LV torsion and MPI. Age, gender and LVESV were entered in the multivariate model independently from their p value at univariate analysis and were kept fixed throughout the stepwise selection procedure. Regarding the remaining variables, only those with p value <0.20 at 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 $\chi^2$ values.

Receiver operator characteristic (ROC) 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 non-anterior AMI patients.

A $p$ value $<$0.05 was considered statistically significant. Statistical analysis was performed using the SPSS software package (SPSS 15.0, Chicago, Illinois).

**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 as
regard to age (59±10 vs. 57±10, \( p=0.31 \)), male gender (87 [73\%] vs. 17 [65\%], \( p=0.47 \)),
anterior location of AMI (55 [46\%] vs. 13 [50\%], \( p=0.70 \)) and peak value of troponin T
(3.04 \( \mu \text{g/l} \) [1.65-7.03] vs. 3.18 \( \mu \text{g/l} \) [1.74-12.62], \( p=0.58 \)). 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. By definition, control subjects and AMI patients did not differ in age or
gender.

Among AMI patients, the infarct-related artery was left anterior descending coronary
artery in 55 (46\%) patients; obstructive multi-vessel disease (i.e. more than 1 vessel with a
luminal narrowing \( \geq 70\% \)) was present in 41 (34\%) patients. Peak value of troponin T was
3.04 \( \mu \text{g/l} \)). Mean LVEF was 48±9\%.

Compared to control subjects, AMI patients had significantly reduced peak LV basal
rotation (-5.1±2.7° vs. -6.8±2.7°, \( p=0.013 \)), reduced peak LV apical rotation (8.4±4.6° vs.
11.6±2.8°, \( p<0.001 \)), and consequently decreased peak LV twist (12.7±5.2° vs. 17.7±2.1°,
\( p<0.001 \)) and peak LV torsion (1.54±0.64°/cm vs. 2.07±0.27°/cm, \( p<0.001 \)).

Among AMI patients, those with anterior AMI had significantly lower peak LV apical
rotation, LV twist and LV torsion, compared to the remaining AMI patients (6.5±4.3° vs.
10.1±4.2°, \( p<0.001 \), 11.1±5.4° vs. 14.0±4.7°, \( p=0.002 \) and 1.35±0.65°/cm vs.
1.70±0.58°/cm, \( p=0.003 \), respectively), whereas peak LV basal rotation was not different
(-5.4±2.6° vs. -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 vs. patients (\( n=18 \)) with anterior AMI due
to mid or distal LAD occlusion (-5.2±2.5° vs. -5.8±2.7°, \( p=0.38 \); 6.9±4.3° vs. 5.6±4.2°,
\( p=0.38 \).
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.

Determinants of LV torsion among AMI patients

Table 2 shows the results of univariate and multivariate linear regression analysis performed to determine the factors related to peak LV torsion among AMI patients. At univariate analysis, several variables were significantly related to peak LV torsion: anterior AMI, TIMI flow grade 3 after PCI, peak troponin T, LVEDV, LVESV, LVEF, WMSI, presence of diastolic dysfunction, peak LV GLS and MPI. However, at multivariate analysis, only LVEF ($\beta=0.36$, $p<0.001$) and MPI ($\beta=-0.47$, $p<0.001$) 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 to patients with ≥1 myocardial segment with minimal or absent contrast opacification (1.84±0.49/°/cm vs. 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 out 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; 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 LVESV (p=0.036), lower LVEF (p<0.001), and higher MPI (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 to 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 LVESV at 6-month follow-up and a higher change in LVESV in the 6-month follow-up period (Figure 4). Table 4 shows the results of univariate and multivariate logistic regression analysis performed to determine the relationship between clinical and echocardiographic characteristics at baseline and LV remodeling at 6-month follow-up. At univariate analysis, several variables were significantly related to LV remodeling: anterior AMI, peak troponin T, LVESV, LVEF, WMSI, presence of diastolic dysfunction, peak LV GLS, peak LV torsion and MPI. However, at multivariate analysis, only peak LV torsion (OR=0.77; 95%CI 0.65-0.92; p= 0.003) and MPI (OR=1.04; 95%CI 1.01-1.07; 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).

At ROC curve analysis (Figure 6), peak LV torsion ≤1.44°/cm provided the highest sensitivity (95%) and specificity (77%) to predict LV remodeling; diagnostic accuracy was high in both anterior and non-anterior AMI patients (Figure 6).

**DISCUSSION**
The results of the present evaluation show that LV torsion is significantly impaired early after AMI, due to a reduction of both basal and apical rotation. Infarct size (assessed using 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 consistently showed an impairment of LV torsional deformation in the setting of acute and chronic myocardial infarction.\(^7;8;18-21\) 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 importantly, an independent correlation between infarct size (assessed using MCE and expressed as MPI) and LV torsion was noted at 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.

Epicardial myofibers are indeed extremely important to maintain LV torsional deformation.\(^4\) Epicardial myofibers (compared to endocardial fibers) produce larger torque (related to the larger radius), and determine the overall direction of rotation.\(^4\)

Damage of epicardial fibers appears therefore 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 using an occlusion-reperfusion model provided evidence
for this hypothesis, by showing that LV torsion was impaired in the presence of transmural ischemia, while LV torsion was preserved in the presence of subendocardial ischemia only.\textsuperscript{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.\textsuperscript{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.\textsuperscript{25} A significant impairment of LV torsion after AMI will therefore result in increased myofiber stress and oxygen demand of remaining non-infarcted 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.\textsuperscript{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 using 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-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 acoustic window (more than 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 be however underlined 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 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.

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

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

EF: ejection fraction; EDV: end-diastolic volume; ESV: end-systolic volume; GLS: global longitudinal strain; LV: left ventricular; MPI: myocardial perfusion index; WMSI: wall motion score index.
Table 2. Univariate and multivariate linear regression analyses to determine the independent correlates of peak LV torsion in AMI patients.

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

Abbreviations as in Table 1.
Table 3. Baseline clinical and echocardiographic characteristics of AMI patients without versus with LV remodeling.

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

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

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

C-statistic=0.93

*: OR and 95%CI are intended for 0.1 unit increase.

Abbreviations as in Table 1.
FIGURE LEGENDS

**Figure 1.** Left ventricular (LV) rotational mechanics curves of a control subject (panel A) and of a patient with anterior acute myocardial infarction (panel B). Panel 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). Panel 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).

**Figure 2.** Linear regression analysis illustrating the relation between peak left ventricular (LV) torsion and myocardial perfusion index (MPI).

**Figure 3.** Relation between peak left ventricular (LV) torsion and number of myocardial segments with minimal or absent contrast opacification.

**Figure 4.** Relation between peak left ventricular (LV) torsion at baseline and LV end-systolic volume (ESV) at 6-month follow-up (Panel A) and the change in LVESV after 6-month follow-up compared with baseline value (Panel B).

**Figure 5.** Incremental value of peak left ventricular (LV) torsion over clinical, echocardiographic and myocardial contrast echocardiography variables in predicting LV remodeling at 6-month follow-up.

**Figure 6.** Receiver-operator characteristic curve, testing the accuracy of peak left ventricular (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 acute myocardial infarction (AMI), peak LV torsion ≤1.29°/cm provided the highest sensitivity (92%) and specificity (74%) to predict LV remodeling. **Panel C.** Among patients with non-anterior AMI, peak LV torsion ≤1.44°/cm provided the highest sensitivity (100%) and specificity (81%) to predict LV remodeling. AUC: area under the curve.
Figure 1a
Figure 2

The graph shows the relationship between Peak LV torsion (°/cm) and MPI. The equation for the line of best fit is:

\[ y = 3.50 + (-1.46)x \]

Where:
- \( y \) is Peak LV torsion (°/cm)
- \( x \) is MPI
- \( r = 0.69 \)
- \( p < 0.001 \)
Peak LV torsion
ANOVA $p < 0.001$

$p < 0.001$

$p = 0.001$

$p < 0.001$

Number of myocardial segments with minimal or absent contrast opacification
Figure 4a

A

\[ y = 105.8 + -32.4x \]

\[ r = 0.69 \]

\[ p < 0.001 \]
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 6a

AUC = 0.92

p < 0.001
Figure 6b

AUC = 0.89

p < 0.001
Figure 6c

AUC = 0.94

p < 0.001
Reduced Left Ventricular Torsion Early After Myocardial Infarction is Related to Left Ventricular Remodeling

Gaetano Nucifora, Nina Ajmone Marsan, Matteo Bertini, Victoria Delgado, Hans-Marc J. Siebelink, Jacob M. van Werkhoven, Arthur J. Scholte, Martin J. Schalij, Ernst E. van der Wall, Eduard R. Holman and Jeroen J. Bax

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