CHAPTER 21

Left ventricular rotational mechanics in acute myocardial infarction and in chronic (ischemic and nonischemic) heart failure patients

M Bertini, G Nucifora, N Ajmone Marsan, V Delgado, R J van Bommel, G Boriani, M Biffi, E R Holman, E E Van der Wall, M J Schalij, and J J Bax

Am J Cardiol 2009;103:1506-12.
**ABSTRACT**

**Objectives:** Left ventricular (LV) twist and untwisting rate are emerging as global and thorough parameters for assessment of LV function. This study explored differences of LV twist and untwisting rate in patients with acute myocardial infarction (AMI) and patients with ischemic and nonischemic chronic heart failure (HF).

**Methods:** Fifty patients with AMI, 49 with ischemic HF, and 38 with nonischemic HF were studied. As a control group, 28 subjects without evidence of structural heart disease were included. Speckle-tracking analysis was applied to LV short-axis images at basal and apical levels. LV twist was defined as the net difference of apical and basal rotations at isochronal time points. The first time derivative of LV untwist was defined as the LV untwisting rate.

**Results:** Compared with control subjects, peak LV twist was decreased in patients with AMI and extremely decreased in those with HF (p <0.001, analysis of variance). A strong correlation (r = 0.87, p <0.001) was found between peak LV twist and LV ejection fraction in the overall study population. LV untwisting rate was progressively decreased in patients with AMI and HF compared with control subjects (p <0.001, analysis of variance). A moderate correlation (r = 0.56, p <0.001) was noted between peak LV untwisting rate and grade of diastolic dysfunction in the overall study population.

**Conclusions:** LV twist and untwisting rate are strongly related to LV systolic and diastolic functions, respectively. Impairment of LV function observed in patients with AMI and HF is associated with a decrease of LV twist and untwisting rate.
INTRODUCTION

Recently, a novel speckle-tracking analysis has become available as a simple echocardiographic method to assess left ventricular (LV) twist and untwisting rate. This technique has been validated against sonomicrometry and tagged magnetic resonance imaging, which are currently considered the gold standards for assessment of rotational parameters. Initial studies evaluated LV twist and untwisting rate in patients with myocardial infarction (MI) and heart failure (HF), but thus far, the impact of these different diseases on rotational mechanics has never been systematically evaluated.

The present study assessed differences of LV twist and untwisting rate between patients with acute MI (AMI) and chronic HF.

METHODS

One hundred thirty-seven consecutive patients were enrolled; 50 patients had AMI, 49 had chronic ischemic HF, and 38 had nonischemic HF. Diagnosis of AMI was based on the presence of symptoms consistent with myocardial ischemia lasting ≥30 minutes and ≥2-mm ST-segment elevation in ≥2 contiguous electrocardiographic leads. All patients with AMI underwent urgent coronary angiography, followed by primary percutaneous coronary intervention, and echocardiographic examination was performed within 48 hours after AMI. Cause of HF was considered ischemic in the presence of significant coronary artery disease (>50% stenosis in ≥1 major epicardial coronary artery) on coronary angiogram and/or history of AMI or previous revascularization.

In addition, 28 subjects without evidence of structural heart disease, matched for age and gender, were included as a control group. Clinical echocardiographic analysis included standard 2-dimensional echocardiography to assess LV systolic and diastolic functions. Furthermore, speckle-tracking analysis was applied to assess LV rotational parameters (twist and untwisting rate).

All patients were imaged in the left lateral decubitus position with a commercially available system (Vingmed Vivid 7, General Electric Medical Systems, Milwaukee, Wisconsin) equipped with a 3.5-MHz transducer. Standard 2-dimensional images and Doppler and color Doppler data acquired from parasternal and apical views (2, 3, and 4 chambers) were digitally stored in cine-loop format; analyses were subsequently performed off-line using EchoPac 7.0.0 (General Electric Medical Systems).

LV end-diastolic volume (EDV) and end-systolic volume (ESV) were measured according to the Simpson biplane method and LV ejection fraction (EF) was calculated as ([EDV – ESV]/end-diastolic volume) X 100. Transmitial and pulmonary vein (PV) pulse-wave Doppler tracings, obtained in accordance to recommendations of the American Society of Echocardiography
were used to classify diastolic function as (1) normal, when the E/A ratio was equal to 0.9 to 1.5, deceleration time was equal to 160 to 240 ms, and PV systolic velocity ≥PV diastolic velocity; (2) diastolic dysfunction grade 1 (mild), when the E/A ratio <0.9, deceleration time >240 ms, and PV systolic velocity >> PV diastolic velocity; (3) diastolic dysfunction grade 2 (moderate), when the E/A ratio was equal to 0.9 to 1.5, deceleration time was equal to 160 to 240 ms, and PV systolic velocity was <PV diastolic velocity; (4) diastolic dysfunction grade 3 (severe), when the E/A ratio >2.0, deceleration time <160 ms, and PV systolic velocity was << PV diastolic velocity; or (5) diastolic dysfunction grade 4 (severe), when the E/A ratio >2.5, deceleration time <130 ms, and PV systolic velocity was << PV diastolic velocity.

Speckle-tracking analysis is based on tracking of natural acoustic markers, or speckles, on standard gray-scale images. This novel technique is angle independent and permits evaluation of myocardial contraction/relaxation along the circumferential, longitudinal, and radial directions.

In the present evaluation, speckle-tracking analysis was applied to determine the LV twist and LV untwisting rate. Parasternal short-axis images were acquired at 2 distinct levels: (1) basal level, identified by the mitral valve, and (2) apical level, defined as the smallest cavity achievable distal to the papillary muscles (moving the probe down and slightly laterally, if needed). The frame rate was 45 to 100 frames/s and 3 cardiac cycles for each parasternal short-axis level were stored in cine-loop format for off-line analysis. The endocardial border was traced at an end-systolic frame and the region of interest was chosen to fit the entire 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 region of interest, if needed. Furthermore, each short-axis image was automatically divided into 6 standard segments, i.e., septal, anteroseptal, anterior, lateral, posterior, and inferior. Subsequently, the speckle-tracking 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. Counter-clockwise rotation was marked as a positive value and clockwise rotation as a negative value when viewed from the LV apex. The software automatically calculated LV twist, defined as the net difference (in degrees) of apical and basal rotations at isochronal time points. The opposite rotation after LV twist was defined as LV untwist and the time derivative of LV untwist was defined as LV untwisting rate (degrees per second; Figure 1).

The following measurements were obtained: (1) peak apical and basal rotations, (2) peak LV twist and peak LV untwisting rate, (3) time to peak apical and basal rotations, and (4) time to peak LV twist and untwisting rate. A pulse-wave Doppler tracing obtained from the LV outflow tract was used to identify timing of aortic valve opening and closure. All timings were expressed as percent systolic phase.

To assess the reproducibility of peak LV twist and peak LV untwisting rate measurements, 20 patients were randomly selected. Bland-Altman analysis was performed to evaluate intra- and inter-observer agreements, repeating the analysis 1 week later by the same ob-
LV rotational mechanics in AMI and HF patients

server and by a second independent observer. Bland-Altman analysis demonstrated good intra-observer and inter-observer agreements, with a small bias not significantly different from 0. Mean differences±2 SDs for peak LV twist and peak LV untwisting rate were 0.05±0.43 and -1.93±15.97°/s for intra-observer agreement and 0.17±1.51 and -3.97±35.63°/s for inter-observer agreement.

Figure 1 Left ventricular twist and untwisting rate in a normal control (Panel A), patient with AMI (Panel B), patient with ischemic HF (Panel C) and a patient with nonischemic HF (Panel D). Apical rotation (upper green line), apical rotation rate (lower green line), basal rotation (upper purple line), basal rotation rate (lower purple line), LV twist/untwist (upper white line), and LV twisting/untwisting rate (lower white line) are displayed.

AVC = aortic valve closure; AVO = aortic valve opening.
Continuous variables are expressed as mean±SD. Categorical data are presented as absolute numbers and percentages. One-way analysis of variance test was used to assess differences in continuous variables across different groups of patients; if the result of the analysis was significant, Bonferroni post hoc test was applied. Differences in categorical variables were analyzed using chi-square tests or Fischer’s exact tests, as appropriate. Linear regression analysis was used to determine relations between peak LV twist and LVEF, between peak LV untwisting rate and grade of diastolic dysfunction, and between peak LV untwisting rate and LVESV. To identify independent determinants of peak LV untwisting rate, a multivariable linear regression analysis was performed including LVESV and grade of diastolic dysfunction as covariates. All statistical tests were 2-sided, and a p-value <0.05 was considered statistically significant. Statistical analysis was performed using SPSS 14.0 (SPSS, Inc., Chicago, Illinois).

RESULTS

Table 1 presents clinical and echocardiographic characteristics of the different patient groups and the control group.

Compared with controls, patients with AMI had significantly lower values of LV apical rotation (9.8±3.0 vs 7.6±3.8°, p = 0.007), LV basal rotation (-6.3±2.4 vs -4.9±2.1°, p = 0.04), and LV twist (15.7±3.1 vs 11.6±3.8°, p <0.001).

LV rotational parameters were not significantly different between patients with ischemic HF and those with nonischemic HF but were significantly impaired compared with patients with AMI; peak apical rotations were 2.5±1.9 and 2.4±1.8°, respectively (p <0.001 compared with patients with AMI) and peak basal rotations were -3.4±2.0 and -2.8±2.2°, respectively (p = 0.003 and p <0.001, respectively, compared with patients with AMI). Consequently, peak LV twists were 5.2±2.2 and 4.0±2.9°, respectively (p <0.001 compared with patients with AMI; Table 1).

Figure 2 shows the progressive decrease of peak LV twist and LVEF among the 4 different groups. In particular, a strong correlation (r = 0.87, p <0.001) was found between peak LV twist and LVEF (Figure 3) and between peak LV apical rotation and LVEF (r = 0.79, p <0.001) in the overall study population; conversely, only a modest relation was found between peak LV basal rotation and LVEF (r = -0.48, p <0.001). Furthermore, time to peak LV twist occurred sooner in patients with AMI, ischemic HF, and nonischemic HF compared with controls (p <0.001, analysis of variance; Table 1).

Peak LV untwisting rate was not significantly different between patients with ischemic HF and those with nonischemic HF, with lower values compared with patients with AMI (-58±34°/s in patients with ischemic HF, p = 0.018; -59±32°/s in patients with nonischemic HF, p = 0.036; Table 1).
Table 1. Clinical, echocardiographic and rotational parameters of controls and patients with acute myocardial infarction, ischemic heart failure (HF) and nonischemic HF.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender male, n (%)</th>
<th>LVEDV (ml)</th>
<th>LVEF (%)</th>
<th>Diastolic function, n (%)</th>
<th>Peak LV twist (°)</th>
<th>Peak LV untwisting rate (°/s)</th>
<th>Time peak LV twist (% systole)</th>
<th>Time peak LV untwisting (% systole)</th>
<th>ANOVA p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal controls (n = 28)</td>
<td>60±11 (75)</td>
<td>21±2.5</td>
<td>67±26*</td>
<td>Grade 0 0 (0)</td>
<td>15.7±3.1†</td>
<td>-108±30*</td>
<td>114±9</td>
<td>116±17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AMI patients (n = 50)</td>
<td>60±11 (76)</td>
<td>38±7.6</td>
<td>103±28*</td>
<td>Grade 1 7 (14)</td>
<td>11.6±3.8*</td>
<td>-75±35*</td>
<td>118±17</td>
<td>116±17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patients with ischemic HF (n = 49)</td>
<td>64±11 (88)</td>
<td>43±8.8</td>
<td>179±67*</td>
<td>Grade 2 12 (24)</td>
<td>5.2±2.2</td>
<td>-58±34</td>
<td>116±17</td>
<td>116±23</td>
<td>0.75</td>
</tr>
<tr>
<td>Patients with nonischemic HF (n = 38)</td>
<td>65±13 (74)</td>
<td>28±7.4</td>
<td>214±71†</td>
<td>Grade 3-4 16 (32)</td>
<td>4.0±2.9</td>
<td>-59±33</td>
<td>116±23</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

* p <0.001; † p <0.01 versus ischemic and nonischemic HF. † p <0.001 versus AMI, ischemic HF, and nonischemic HF.
§ p <0.05 versus AMI.
¶ -58±34 -59±33 <0.001 p-value.
ǁ p <0.05 versus ischemic HF.
‡ p <0.05 versus nonischemic HF.

ANOVA = analysis of variance; AMI = acute myocardial infarction; EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; HF = heart failure; LV = left ventricular.

Figure 2. Peak LV twist (left) and LVEF (right) in controls, patients with AMI, patients with ischemic HF, and patients with nonischemic HF. ANOVA = analysis of variance.
Figure 3. Correlation between LVEF and peak LV twist in the entire study population including controls (white triangles), patients with AMI (black triangles), patients with ischemic HF (white circles), and patients with nonischemic HF (black circles).

Figure 4. (Left) A decreased peak LV untwisting rate is observed in patients with AMI, those with ischemic HF, and those with nonischemic HF compared with controls. (Right) Distribution of normal diastolic function (white bars) and grades 1 (light gray bars), 2 (dark gray bars), and 3 to 4 (black bars) of diastolic dysfunction in controls and patients with AMI, ischemic HF, and nonischemic HF.

Peak LV untwisting rate and grade of diastolic dysfunction among the 4 groups are shown in Figure 4. A moderate correlation (r = 0.56, p < 0.001) was noted between peak LV untwisting rate and grade of diastolic dysfunction in the overall study population (Figure 5). Furthermore, peak LV untwisting rate was significantly related to LVESV (r = 0.42, p < 0.001). At multivariable linear regression analysis LVESV (beta 0.16, p = 0.047) and grade of diastolic dysfunction (beta 0.47, p < 0.001) were independently related to peak LV untwisting rate.

No significant differences were found among the different groups for time to peak LV untwisting rate (Table 1).
DISCUSSION

The present study comprehensively evaluated differences in LV twist and untwisting rate in patients with AMI, ischemic HF, and nonischemic HF, providing new insight in the relation between LV rotational mechanics and LV function. The main findings can be summarized as follows: (1) LV twist is strongly related to LV systolic function and LV untwisting rate is modestly, but significantly, related to diastolic function; (2) impairment of LV function is associated not only with a decrease of LV twist and untwisting rate but also with an earlier peak of LV twist during systole.

As previously demonstrated in a mathematical model, LV twist distributes equally LV fiber stress and shortening across the LV wall. Accordingly, LV twist increases the efficiency of sarcomere shortening and improves myocardial deformation during LV ejection. In the present study, a significant impairment of LV twist was observed in patients with AMI and HF compared with controls. Moreover, a strong relation between degree of impairment of LV twist and observed impairment of LVEF was noted, confirming previous findings demonstrating a relation between LV twist and LVEF. The strong correlation found between LV apical

Figure 5. Correlation between grades of diastolic dysfunction (see definition in text) and peak LV untwisting rate in controls (white triangles), patients with AMI (black triangles), patients with ischemic HF (white circles), and patients with nonischemic HF (black circles).
rotation and LVEF is not surprising, because LV apical rotation contributes more to LV twist than LV basal rotation. The different effects of AMI and long-term LV remodeling (in HF) on LV twist were also explored. LV twist was more decreased in patients with chronic HF compared with AMI. These findings may be explained by different mechanisms underlying a decrease in LV twist. In patients with HF, LV twist impairment is probably the result of a long-lasting process, with a rearrangement of LV myofibers with a consequent loss of the specific LV architecture responsible for the wringing motion. Conversely, in patients with AMI the decrease of LV twist may result from an acute impairment in rotation of the LV region involved in the infarction. Severity of this impairment appears related to transmurality of the infarction and to extent of dysfunctional myocardial segments.

Intriguingly, time to peak LV twist occurred sooner in patients with AMI and those with HF compared with controls. The impaired LV rotational mechanics observed in AMI and HF most likely explains this finding; less time is needed to reach peak LV twist because of the decreased contraction and rotation of LV myofibers. In addition, diseased LV myofibers are not able to fully counteract systolic ventricular pressure, preventing further myocardial shortening and, consequently, leading to sooner peak LV twist.

LV systolic twist consists of a deformation of the interstitial matrix resulting in storage of potential energy; the rapid release of potential energy stored during systole in isovolumic relaxation time leads to LV untwisting. In turn LV untwisting generates an intraventricular pressure gradient facilitating diastolic LV filling. Indeed, LV untwisting rate is emerging as an index of diastolic function. In particular, LV untwisting rate was related to the time constant of LV pressure decay (tau) and the intraventricular pressure gradient. In the present study, a good relation between LV untwisting rate and global diastolic function was observed. The relation was not perfect, probably because LV untwisting rate is a marker of diastolic suction rather than global diastolic function. LV untwisting rate was also independently related to LVESV; however, on multivariable linear regression analysis, grade of diastolic dysfunction was the strongest determinant of LV untwisting rate.

A significant impairment of LV untwisting rate was observed in patients with AMI and HF compared with control subjects. In patients with AMI, impairment in LV untwisting rate may be related to increased ventricular stiffness and consequent diastolic dysfunction due to recent acute ischemia and infarction. In patients with HF, LV untwisting rate was even more decreased compared with patients with AMI. This observation may be explained by the presence of extensive, diffuse LV fibrosis as encountered in patients with HF, which is not (yet) present soon after AMI.

Although groups of patients with different grades of diastolic dysfunction were studied, no significant differences in time to peak LV untwisting rate were noted. This finding is in line with previous experimental and clinical studies in which only peak of untwisting rate but not time to peak untwisting rate was affected by grade of diastolic dysfunction.
As limitations, acquisition of LV apical short-axis images (highly dependent on the acoustic window) and through-plane motion, particularly at the basal level, could have affected the accuracy of the measurement of LV rotational parameters.
REFERENCES


7. Lang RM, Bierig M, Devereux RB et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18:1440 –1463.


