Regional left ventricular rotation and back-rotation in patients with reverse septal curvature hypertrophic cardiomyopathy

Floris Kauer, Bas M. van Dalen, Osama I.I. Soliman, Heleen B. van der Zwaan, Wim B. Vletter, Arend F.L. Schinkel, Folkert J. ten Cate, and Marcel L. Geleijnse*

Department of Cardiology, The Thoraxcenter, Erasmus University Medical Center, Room BA 302, ’s-Gravendijkwal 230, Rotterdam 3015 CE, The Netherlands

Received 28 April 2012; accepted after revision 16 July 2012; online publish-ahead-of-print 16 August 2012

Aims
This study sought to investigate regional left ventricular (LV) rotation in patients with hypertrophic cardiomyopathy (HCM).

Methods and results
The study comprised 44 patients with HCM with a typical reverse septal curvature (age 40±14 years, 33 men) and 44 healthy volunteers (age 39±14 years, 32 men) in whom LV rotation could be assessed at the basal and apical LV level with speckle-tracking echocardiography, using the QLAB Advanced Quantification Software version 6.0 (Philips, Best, The Netherlands). In HCM patients, lower values of initial counter-clockwise rotation at the basal LV level (1.5±1.2 vs. 0.6±0.9°, P<0.001) were seen, in particular in the septal segment (1.7±1.6 vs. 0.4±0.7°, P<0.001). After this period, the direction of rotation changed to clockwise with a peak basal rotation of −4.8±2.0° in controls vs. −6.1±2.5° in HCM patients (P<0.05). Peak basal rotation in HCM patients was in particular higher in the anterior (−6.6±3.0 vs. −4.4±2.4°, P<0.01) and septal (−5.4±2.6 vs. −3.9±1.9°, P<0.05) segments. The normalized (corrected for peak basal rotation) global back-rotation rate was lower in HCM patients (4.1±3.1 vs. 6.3±4.9 s−1, P<0.05), in particular driven by a lower rate in the septal segment (3.8±2.6 vs. 6.4±4.8 s−1, P<0.01). At the apical level, changes in rotation and back-rotation were more homogeneous.

Conclusion
Changes in rotation and back-rotation at the LV basal level in HCM patients are mainly caused by regional changes in the basal septal and anterior segments, the segments mostly involved in the hypertrophic process.

Keywords
Speckle-tracking echocardiography • Regional left ventricular function • Left ventricular rotation • Hypertrophic cardiomyopathy

Introduction
Hypertrophic cardiomyopathy (HCM) is a primary autosomal-dominant disorder of the myocardium caused by mutations in sarcomeric contractile proteins.1 It is well known that HCM patients have not only diastolic dysfunction but also abnormalities in left ventricular (LV) systolic function, in particular in LV longitudinal velocities,2 longitudinal strain,3 radial strain,3 and rotation.4,5 LV rotation is caused by obliquely oriented layers of myocardial tissue in the subendocardium and the subepicardium,6 and can be quantified by speckle-tracking echocardiography (STE).4,7

Since the LV segments in HCM patients are asymmetrically involved in the hypertrophic process,4,8 regional differences in LV rotation may be expected. Therefore, this study sought to investigate regional LV rotation throughout the cardiac cycle in patients with HCM.

Methods

Study participants
The study population consisted of 44 patients with HCM (age 40±14 years, 33 men) and 44 age- and gender-matched, healthy, non-obese
(body mass index <25 kg/m²) volunteers (age 39 ± 14 years, 32 men) in whom complete global and regional rotation could be assessed at both the basal and apical LV level. HCM was characterized morphologically and defined by a hypertrophied, non-dilated LV with a typical reverse septal curvature, in the absence of another systemic or cardiac disease that is capable of producing the magnitude of segment thickening seen. None of the volunteers was known to have hypertension, diabetes, or with a use of medication for cardiovascular disease, and all had a normal 12-lead electrocardiogram, normal left atrial, and LV dimensions, and LV function by transthoracic echocardiography. Informed consent was obtained and the institutional review board approved the study.

Echocardiography

Two-dimensional grey scale harmonic images were obtained in the left lateral decubitus position using a commercially available ultrasound system (IE33, Philips, Best, The Netherlands), equipped with a broadband (1-5 MHz) SS-1. All echocardiographic measurements were averaged from three heartbeats. From the two-dimensional recordings, the following data were acquired: left atrial size, LV end-diastolic and end-systolic dimensions, and end-diastolic segment thickness. The LV mass was assessed with the two-dimensional area–length method [LV Mass = 0.8 x 1.04 (diastolic LV internal dimension + diastolic posterior wall thickness + diastolic septal wall thickness) – (diastolic LV internal dimension)²] + 0.6 g]. The LV ejection fraction was calculated from LV volumes by the modified biplane Simpson rule in accordance with the guidelines. From the mitral-inflow pattern, peak early (E) and active (A) filling velocities, and the E/A ratio were measured. Furthermore, the timing of aortic valve opening and closure, mitral valve opening and closure, the peak and end of the E-wave, and the onset and peak of the A-wave were determined using a pulsed-wave Doppler. In each study, it was verified that the heart rate for the cardiac cycles in which the timing of the different intervals was assessed, was the same as the cardiac cycle used for the analysis of LV rotation parameters.

HCM patients were stratified by the grade of diastolic dysfunction (Grades 1–3): Grade 1, abnormal relaxation: E/A ratio <0.75; Grade 2, pseudo normal filling: 0.75 <E/A ratio <1.5 and E-wave velocity deceleration time >140 ms; and Grade 3, restrictive filling: E/A ratio >1.5 and E-wave velocity deceleration time <140 ms. In addition, all patients with diastolic dysfunction were required to have an E-wave velocity/peak early diastolic wave velocity of the septal mitral annulus ratio (E/Em) of >8. Seven HCM patients (16%) could not perfectly fulfill all of the criteria for a particular diastolic dysfunction group, and were therefore excluded from this part of the analysis.

Speckle-tracking analysis

To optimize STE, images were obtained at a frame rate of 60–80 frames/s. Parasternal short-axis images at the LV basal level (showing the tips of the mitral valve leaflets) with the cross-section as circular as possible were obtained from the standard parasternal position, defined as the long-axis position in which the LV and aorta were most in-line with the mitral valve tips in the middle of the sector. To obtain a short-axis image at the LV apical level (just proximal to the level with end-systolic LV luminal obliteration), the transducer was positioned 1 or 2 intercostal spaces more caudal as previously described by us. From each short-axis image, three consecutive end-expiratory cardiac cycles were acquired and transferred to a QLAB workstation (Philips, Best, The Netherlands) for off-line analysis. Analysis of the data sets was performed using the QLAB Advanced Quantification Software version 6.0 (Philips, Best, The Netherlands), which was recently validated against magnetic resonance imaging for the assessment of LV twist. To assess LV rotation, six tracking points were placed manually (after gain correction) on an end-diastolic frame on the mid-myocardium in each parasternal short-axis image. Tracking points were separated about 60° from each other and placed on 1 (30°, anteroseptal insertion into the LV of the right ventricle), 3 (90°), 5 (150°), 7 (210°), 9 (270°), inferoseptal insertion into the LV of the right ventricle), and 11 (330°) o’clock to fit the total LV circumference.

Rotation is calculated as the change in angle between the regions of interest that are tracked by the software and the LV centre. This LV centre is calculated only in the first frame of the loop. If there is significant intra-thoracic motion of the hearth during the cardiac cycle, this will result in misinterpretation of rotation of the regions of interest because the LV centre is not recalculated in the subsequent frames but remains fixed in position, which will result in rotation even when the regions of interest do not rotate. By the application of motion correction, Qlab will calculate the LV centre on a frame by frame basis and thus correct rotation by filtering out translational cardiac motion. (Figure 1)

Data were exported to a spreadsheet program (Excel, Microsoft Corporation, Redmond, WA, USA) and processed by the use of macros written in Microsoft Virtual Basic to determine global and regional LV peak systolic rotation (Rotmax), and global and regional LV rotation at 25, 50, and 75% of ejection, aorta valve closure, mitral valve opening, E-peak, E-end, A-onset, A-peak, and aorta valve opening. Rotational data were subsequently calculated for the anterior, inferior, lateral (averaging the anterolateral and inferolateral segments), and septal (averaging the anteroseptal and inferoseptal segments) parts of the LV.

The degree of diastolic back-rotation was expressed as a percentage of Rotmax: back-rotation = (Rotmax – Rot)/Rotmax × 100%, where Rot is rotation at time t. The back-rotation velocity at a specific interval from t1 to t2 during the cardiac cycle was calculated as (Rot2 – Rot1)/(t2 – t1). Since the back-rotation rate is both dependent on the absolute rotation and intrinsic myocardial properties, also the normalized back-rotation was calculated, defined as the back-rotation rate corrected for absolute rotation. In the Figures, counter-clockwise rotation as viewed from the apex was expressed as a positive value; clockwise rotation was expressed as a negative value. To adjust for intra- and inter-subject differences in the heart rate, the time sequence was normalized to the percentage of systolic duration. End-systole was defined as the point of aortic valve closure.

Statistical analysis

Measurements are presented as mean ± SD. Continuous variables were compared using an independent-samples t-test procedure with a confidence interval of 95% or one-way ANOVA procedure when appropriate and relationships between different parameters were assessed by Pearson’s correlation coefficient using analytics software (SPSS 19, IBM Corporation, New York, USA). A P-value <0.05 was considered statistically significant. Intra-observer and inter-observer variabilities for LV rotation parameters in our centre varies from 2 ± 3 to 10 ± 9%, and 4 ± 4 to 12 ± 8%, respectively.

Results

Echocardiographic dimensions

HCM patients had larger LA dimensions and LV mass (Table 1), in particular because of hypertrophied anterior and septal segments
Regional LV rotation in HCM

Basal LV back-rotation

In control subjects, LV counter-clockwise rotation at the basal LV level from mitral valve closure until 25% ejection was seen. Lower values were seen in HCM patients (1.5 ± 1.2 vs. 0.6 ± 0.9°, P < 0.001). This difference was seen in all basal LV segments (Table 2), but in particular in the septal segment (anterior 2.0 ± 1.6 vs. 0.9 ± 0.8°, P < 0.001, inferior 1.6 ± 1.6 vs. 0.6 ± 0.7°, P < 0.01, lateral 1.4 ± 1.2 vs. 0.6 ± 0.6°, P < 0.01, septal 1.7 ± 1.6 vs. 0.4 ± 0.7°, P < 0.001). After this period, the direction of rotation changed to clockwise with a peak basal rotation of 4.8 ± 2.0° in control subjects vs. −6.1 ± 2.5° in HCM patients (P < 0.05). The peak basal rotation in HCM patients was in particular higher in the anterior (−6.6 ± 3.0 vs. −4.4 ± 2.4°, P < 0.01) and septal (−5.4 ± 2.6 vs. −3.9 ± 1.9°, P < 0.05) segments.

Basal LV re-rotation

In control subjects, but not in HCM patients, a short-lasting change in the direction of basal back-rotation, or re-rotation in a clockwise direction, from E-peak until E-end was seen (−0.4 ± 1.3 vs. 0.4° ± 1.4°, P < 0.005, Figure 3). Regionally this difference in rotation was significant in the hypertrophied anterior (−1.3 ± 2.3 vs. 0.1 ± 1.9°, P < 0.005) and septal (−0.3 ± 1.6 vs. 0.5 ± 2.0°, P < 0.05) segments but not in the inferior (−0.2 ± 2.2 vs. 0.4 ± 2.1°, P = NS) and lateral (0.1 ± 1.9 vs. 0.4 ± 1.9°, P = NS) segments.

Apical LV rotation

In control subjects, a brief LV clockwise rotation from the mitral valve closure until the aorta valve opening (isovolumic contraction period) was seen. Lower values were seen in HCM patients (−0.7 ± 0.7 vs. −0.3 ± 0.4°, P < 0.001). This difference was seen in all but the anterior LV segments (anterior −0.5 ± 0.6 vs. −0.5 ± 0.7°, P = NS, inferior −1.1 ± 1.4 vs. −0.3 ± 0.5°, P < 0.001, lateral −1.0 ± 1.1 vs. −0.3 ± 0.5°, P < 0.001, septal −1.0 ± 1.1 vs. −0.5 ± 0.6°, P < 0.01). After this period, the direction of rotation changed to counter-clockwise with a peak rotation of 7.4 ± 2.4° in control subjects vs. 6.9 ± 3.0° in HCM patients (P = NS). In none of the regional LV segments the difference between the peak apical rotation in control subjects vs. HCM patients reached significance.
Apical LV back-rotation

The peak apical rotation was followed by back-rotation in a clockwise direction. The global back-rotation rate at the apical LV level and the normalized (corrected for peak apical rotation) global back-rotation rate at the apical LV level were lower in HCM patients (17.9 ± 13.4 vs. 26.7 ± 16.1 cm/s, P < 0.05 and 3.0 ± 2.0 vs. 4.2 ± 2.6 s⁻¹, P < 0.05). This impairment in the back-rotation rate and the normalized back-rotation rate was seen in all regional LV segments, although only in the lateral segment it reached statistical significance (22.4 ± 18.8 vs. 32.4 ± 18.7 cm/s, P < 0.01; and 3.0 ± 1.8 vs. 5.1 ± 3.5 s⁻¹, P < 0.05).

Relation of back-rotation to diastolic dysfunction and left atrial volumes

Of the 37 analysable HCM patients, 9 patients had normal diastolic function, 2 patients had Grade 1 dysfunction, 19 Grade 2 dysfunction, and 6 Grade 3 dysfunction. The basal septal back-rotation rate was correlated to early diastolic septal mitral annular velocities (r = 0.36, P < 0.05), E/Em (r = −0.31, P < 0.10), and left atrial volume (r = −0.20, P = NS). The normalized basal septal back-rotation rate was correlated to early diastolic septal mitral annular velocities (r = 0.47, P < 0.01), E/Em (r = −0.44, P < 0.01), and the left atrial volume (r = −0.31, P < 0.10).

Discussion

The major findings of this study in HCM patients with a reverse septal curvature are the following, (i) increased peak basal rotation is caused by regional increases in the peak rotation in the anterior and septal segments, (ii) a decreased normalized basal back-rotation rate is in particularly driven by a regional decrease in the septal segment, (iii) at the apical level of the LV global and regional peak rotation rates are not increased, and (iv) the apical back-rotation rate is more homogeneously impaired.
Table 2  Left ventricular rotation parameters in patients with hypertrophic cardiomyopathy and control subjects

<table>
<thead>
<tr>
<th></th>
<th>Control subjects</th>
<th>Patients with hypertrophic cardiomyopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Global</td>
<td>Anterior</td>
</tr>
<tr>
<td><strong>Basal rotation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak systolic</td>
<td>−4.8 ± 2.0</td>
<td>−4.4 ± 2.4</td>
</tr>
<tr>
<td>rotation (°)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apical rotation</td>
<td>7.4 ± 2.4</td>
<td>6.4 ± 3.7</td>
</tr>
<tr>
<td><strong>Basal back-rotation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back-rotation (°)</td>
<td>2.2 ± 1.6</td>
<td>2.6 ± 2.3</td>
</tr>
<tr>
<td>Back-rotation rate</td>
<td>23.5 ± 13.4</td>
<td>35.7 ± 29.9</td>
</tr>
<tr>
<td>(°/s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back-rotation rate</td>
<td>6.3 ± 4.9</td>
<td>8.6 ± 7.5</td>
</tr>
<tr>
<td>normalized (s⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Apical back-rotation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back-rotation (°)</td>
<td>−2.7 ± 1.8</td>
<td>−3.4 ± 2.7</td>
</tr>
<tr>
<td>Back-rotation rate</td>
<td>−26.7 ± 16.1</td>
<td>−28.3 ± 20.5</td>
</tr>
<tr>
<td>(°/s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back-rotation rate</td>
<td>4.2 ± 2.6</td>
<td>5.8 ± 5.6</td>
</tr>
<tr>
<td>normalized (s⁻¹)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Back-rotation rate normalized = back-rotation rate corrected for maximal systolic rotation (back-rotation rate in % of maximal rotation per second).

*P < 0.05, **P < 0.01 compared with healthy controls.

***P < 0.05, ****P < 0.01 compared with opposite LV wall.
**Rotation and back-rotation at the LV basal level**

LV rotation originates from the dynamic interaction between oppositely wound subepicardial and subendocardial myocardial fibre helices. The direction of LV rotation is governed by the epicardial fibres, most likely because of their longer arm of movement. In healthy controls, initially a counter-clockwise rotation was seen at the LV basal level, most likely due to the predominant mechanical activity that develops along the right-handed subendocardial helix of myocardial fibres during isovolumic contraction. This phenomenon was less clearly visible in HCM patients, despite more basal clockwise rotation seen later in systole. Impaired subendocardial myocardial fibre function, evidenced in this study by lower longitudinal velocities of the mitral annulus, provides a rational explanation for this finding and is most likely caused by endocardial ischaemia due to microvascular dysfunction, as was previously shown by our group. Although decreased counter-clockwise rotation at the basal level during isovolumic contraction was seen in all LV segments in HCM patients, it was mostly decreased in the septal segment, the segment mostly involved in the hypertrophic process. After the isovolumic contraction period, increased peak basal clockwise rotation was seen in HCM patients. This finding may also be explained by a dysfunction of subendocardial fibre helix since this helix in systole normally tries to rotate the LV in the opposite, counter-clockwise direction. Also, larger radius differences in hypertrophic muscle between the subepicardium and the subendocardium may increase the dominant action of the subepicardial fibres and increase the peak basal clockwise rotation. In control subjects regional peak basal clockwise rotation was lower in the anterior and septal segments. In HCM patients, it was due to a marked increase in the peak basal rotation in these specific segments that global peak basal rotation in HCM was increased, although the peak basal rotation in the septal segment was still lower compared with the lateral segment. Again, as seen in this study, these are the LV segments mostly involved in the hypertrophic process.

After the peak basal rotation, back-rotation started. During the isovolumic relaxation period, rotated fibres at the basal and apical level act like a compressed coil that springs open while abruptly releasing potential energy. In a healthy heart this process may be actively supported by still depolarized subendocardial fibres that are, in contrast to the systolic period, now not opposed by active contraction of the subepicardial fibres. In control subjects, there were no significant differences in regional absolute and normalized back-rotation rates at the basal LV level. In HCM patients, global normalized back-rotation rate was lower, equalling less percentual back-rotation at any time point in the isovolumic relaxation period, as was previously reported by our group. In all regional LV segments lower absolute and normalized back-rotation rates were seen, although statistical significance was again only seen for the septal segment, the segment mostly involved in the hypertrophic process with most likely impaired compliance and impaired subendocardial myocardial fibre function.

![Figure 3](https://academic.oup.com/ehjcimaging/article-abstract/14/5/435/2947814)
Apical rotation and back-rotation
In healthy controls, initially a clockwise rotation was seen at the LV apical level, most likely because of the aforementioned predominant mechanical activity that develops along the right-handed subendocardial helix of myocardial fibres during isovolumic contraction. Similarly as at the basal LV level, this phenomenon was less clearly visible in HCM patients, again most likely related to impaired subendocardial myocardial fibre function in HCM patients.2,5,19 After the isovolumic contraction period counter-clockwise rotation was seen in both control subjects and HCM patients, with comparable peak values. Also, in both groups peak systolic rotation was lowest in the anterior segment, consistent with the presence of less oblique myocardial fibres in the anterior LV segments.6 Several reasons may account for a non-increased peak systolic rotation. In HCM patients with a reverse septal curvature there is a gradient in the LV mass thickness from the basal to the apical myocardium.8 So, the aforementioned mechanisms that may increase LV rotation (larger radius differences in hypertrophic muscle between the subepicardium and the subendocardium, dysfunctional subendocardial fibre helix) will play a less important role at the LV apical level. In addition, the helical fibre configuration may not be optimal because of the distorted apical morphology,4,20 and the effectiveness of LV segment contraction depends on its curvature: the more convex towards the LV cavity the segment is, the less it contracts.21 Similarly, regional absolute and normalized back-rotation rates were quite homogeneously lower, although statistical significance was only seen for the lateral segment.

Temporal dispersion in basal and apical back-rotation and basal re-rotation
In control subjects a temporal dispersion in back-rotation between the basal and apical LV level was seen during diastole. It was previously suggested that the base-to-apex relaxation facilitates active restoration of the LV cavity in early diastole.22,23 In addition, a short-lasting change in the direction of basal back-rotation, or re-rotation, from the E-peak until the E-end was seen in contrast to continuous back-rotation at the LV apical level. This re-rotation may be related to the sudden appearance of the rotational forces of the endocardial fibres, at the moment of complete cardiac polarization. These differences at the apical and basal LV level in normal subjects may have an important role in the development and maintenance of the LV intraventricular pressure gradient24 and the vortex pattern,22 which ensure that suction and expulsion forces are generated in the most energy-efficient way. In HCM patients the hypertrophic geometry, regional cardiac dysfunction, and asynchronous conduction25 distort the timing and efficiency of the loading and expulsion dynamics of the hypertrophic LV. This was already shown by Notomi et al.24,26 who studied in control subjects and a small number of HCM patients the mechano-haemodynamic causality of three successive echocardiographic phenomena in early diastole: pressure decay during isovolumic relaxation, peak untwist rate, and peak inter ventricular pressure gradient. The regional and global changes in rotational parameters found in this study may attribute to diastolic dysfunction in HCM patients and their inability to raise the intraventricular pressure gradient with exercise without increasing the left atrial pressure.26,27 This has been clinically related to maximal oxygen consumption.28–30

Limitations
In the current study, only patients with good echocardiographic image quality that allowed for the complete segmental assessment of LV rotation at both the basal and apical LV levels were included. In our centre this represents about three-fourths of the patients. Obviously, this limitation may hamper the clinical implementation of LV rotation parameters. In addition, there still may have been some influence of the tracking ability, in particular in the problematic anterior wall,7 on measured values.

Conclusion
Changes in rotation and back-rotation at the LV basal level in HCM patients with a typical reverse septal curvature are mainly caused by regional changes in the basal septal and anterior segments, the LV segments mostly involved in the hypertrophic process. At the apical level changes in rotation and back-rotation are more homogeneous.

Conflict of interest: none declared.

References
10. Lang RM, Biering M, Devereux R, Flachskaamp F, Foster E, Pelikka PA 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: 1440–63.
Pacemaker lead extraction complicated by a ‘free floating’ infected mass in the right atrium with embolization to the lung

Senthil Kirubakaran* and Christopher Aldo Rinaldi

Guy’s and St Thomas’ NHS Trust, Westminster Bridge Road, London SE16EH, UK
*Corresponding author. Tel: +44 1962881573; Fax: +44 2071881011; Email: senthilk1uk@yahoo.co.uk

An 81-year-old man with ischaemic cardiomyopathy and a biventricular pacemaker and defibrillator was referred for system extraction due to infection. A transoesophageal echocardiogram (TOE) demonstrated a large mass/thrombus on the right atrial pacing lead (Panel 1). Surgical extraction was felt to be a high risk, therefore under general anaesthesia and using TOE, the left ventricular and right atrial leads were removed by manual traction and the defibrillator lead using a laser system (Spectranetics Excimer Laser System). Following extraction, the mass which was previously attached to the right atrial lead, was ‘free-floating’ within the right atrium (Panel 1, see Supplementary data online, Movie 1). After 1 min, this disappeared with likely embolization to the pulmonary circulation.

This case illustrates the rare finding of leaving residual infected masses following transvenous pacemaker lead extractions and highlights the potential complication of embolization to the lungs. Transoesophageal echocardiography has been shown to be useful in these cases for determining the presence and evaluating the size of infected masses on pacing leads. When considering a surgical approach, factors such as mass friability, the presence of a patent foramen ovale or ASD and other surgical indications should be assessed.

Supplementary data are available at European Heart Journal – Cardiovascular Imaging online.