Evaluation of Left Ventricular Segmental Wall Motion in Hypertrophic Cardiomyopathy With Myocardial Tagging

Stephan E. Maier, MD; Stefan E. Fischer, ME; Graeme C. McKinnon, PhD; Otto M. Hess, MD; Hans-Peter Krayenbuehl, MD; and Peter Boesiger, PhD

Background. Segmental wall motion was assessed noninvasively in eight patients with hypertrophic cardiomyopathy and six healthy volunteers by magnetic resonance myocardial tagging.

Methods and Results. Localization scans were performed for determination of the true short-axis views of the left ventricle (double-angled view). Spatial modulation of magnetization was used to produce a rectangular grid of landmarks. Distortion of the grid was assessed at end diastole, mid systole, and end systole with multiphase gradient echos. Image sets were acquired at three different planes, namely, the base, the equator, and the apex. Quantitative evaluation was carried out by computer-assisted image analysis. Each individual grid crossing point was identified automatically and the displacement calculated. A polar coordinate system with the center of gravity as motion reference point was chosen to assess fractional rotation and radial displacement at the endocardial, midwall, and epicardial layers of the septal, anterior, posterior, and inferior regions. A wringing motion of the left ventricle with a clockwise rotation of $5.0\pm2.4^\circ$ at the base and a counterclockwise rotation of $-9.6\pm2.9^\circ$ at the apex was observed in control subjects. An equal rotation of $5.0\pm2.5^\circ$ at the base and a slightly reduced rotation of $-7.3\pm5.2^\circ$ at the apex was found in patients with hypertrophic cardiomyopathy. A transmural gradient in fractional rotation and radial displacement was observed, with the highest values in the endocardial layer. Rotation in patients with hypertrophic cardiomyopathy was significantly less than in normal volunteers in the posterior region of the equatorial and apical planes. Furthermore, radial displacement was significantly reduced in the septum and inferior wall. In the anterior and posterior wall segments, a reduction of the radial displacement was observed only in the epicardium and midwall layers.

Conclusions. Magnetic resonance myocardial tagging allows the noninvasive assessment of regional wall motion. Both in normal volunteers and in patients with hypertrophic cardiomyopathies, cardiac motion occurs in a complex mode, with the base and the apex rotating in opposite directions and the equatorial plane as a transitional zone (wringing motion). A reduced cardiac rotation can be observed in patients with hypertrophic cardiomyopathy mainly in the posterior region, whereas a reduced radial displacement is found in the inferior septal zone. (Circulation 1992;86:1919–1928)

Key Words • magnetic resonance imaging • cardiac rotation • wall shear • motion, endocardial and epicardial

Chamber dimensions and shortening fractions can be measured by various imaging techniques such as magnetic resonance (MR) imaging, echocardiography, computed tomography, and angiography. The absence of landmarks within the left ventricular wall, even at high image resolution, does not allow discrimination between through-plane and in-plane motion. Myocardial labeling of specific ventricular regions is a precondition to assess the cardiac motion in three dimensions and to differentiate between movements within the various layers of the chamber wall (wall shear). Previously, the three-dimensional movements of the heart have been measured by implantation of radio-opaque\textsuperscript{1,2} or ultrasound\textsuperscript{3} markers and subsequent tracking of their motion under fluoroscopic control or with epicardial echocardiography, respectively. Because of the invasiveness of these modalities, most applications so far have been only experimental and limited to animal models or patients undergoing cardiac surgery. The accuracy of the implantation method is degraded by inflammation, hemorrhage, or fibrosis caused by the insertion of the foreign bodies. Although the general principles of cardiac wall motion have been analyzed by these methods, the limited access for placement of the markers, the relatively small number of markers, and their ill-defined position within the layers of the myocardial wall restrict a general application of these techniques to study cardiac motion in three dimensions.
Myocardial tagging in conjunction with MR imaging is a new method for the noninvasive assessment of cardiac motion in humans. The purpose of the present study was to assess cardiac motion with this technique in different layers of the left ventricle in normal volunteers and patients with hypertrophic cardiomyopathy. To determine cardiac rotation from the base to the apex of the left ventricle, imaging was performed at several anatomic levels. A computer-assisted system was developed for the semiautomatic evaluation of the tagged images.

**Methods**

**Patient Population**

Six healthy volunteers (five men, one woman; mean age, 31 years; range, 24–38 years) and eight patients with hypertrophic cardiomyopathy (five men, three women; mean age, 50 years; range, 32–70 years) underwent myocardial tagging. All patients had been seen in the outpatient clinic. A clinical examination, an ECG, a chest x-ray, and echocardiography were performed in all patients with hypertrophic cardiomyopathy. Patients with hypertension or concomitant aortic stenosis were excluded from the present analysis. Mean systolic blood pressure was 124 ± 15 mm Hg, and mean diastolic blood pressure was 81 ± 12 mm Hg. No patient had renal failure. The most important clinical and echocardiographic data are summarized in Table 1. Three of the eight patients with hypertrophic cardiomyopathy had outflow tract obstruction with a mean systolic gradient of 56 mm Hg at rest, four showed no obstruction, and one patient had an apical form of hypertrophic cardiomyopathy.

**Image Acquisition**

Labeling of the myocardium is performed before the conventional MR imaging procedure by a localized presaturation of the tissue with a sequence of preparation pulses producing local variations of the z magnetization referred to as tags. The first application with multiple selective excitation resulting in a starlike arrangement of the tags was introduced in 1988 by Zerhouni et al. The spatial modulation of magnetization technique described by Axel and Dougherty produces saturated spins in a pattern of parallel strips and in its bidirectional application of a rectangular grid. The landmarks appear in the final image as hypointense regions superimposed on the normal MR images. In-plane tissue motion occurring after labeling is visible as distortion and displacement of the initial pattern of landmarks. Identification and tracking of corresponding landmarks in a temporal sequence of MR images permits mapping and accurate quantification of cardiac motion. The permanence of the locally perturbed z magnetization is determined by the tissue-specific longitudinal relaxation time $T_1$ and the excitation pulses of the imaging procedure. For heart muscle tissue, where $T_1$ is on the order of 850 msec for a magnetic field of 1.5 T, the recovery of the z magnetization requires a repeated ECG-triggered labeling.

ECG-triggered image acquisition was carried out on a 1.5-T system (Gyrosan HP, release 5.6, Philips, Best, The Netherlands). The imaging angles for the double-angled short-axis views were determined in each patient with spin/echo multislice localization scans using a transverse and an angulated coronal-to-sagittal (right anterior oblique equivalent) view. End diastole was defined as the

**TABLE 1. Clinical and Echocardiographic Data of Patients With Hypertrophic Cardiomyopathy**

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<tr>
<th>Patient</th>
<th>Sex</th>
<th>Form</th>
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<th>CTR</th>
<th>PWC (%)</th>
<th>$\Delta P$ (mm Hg)</th>
<th>SW (mm)</th>
<th>PW (mm)</th>
<th>Sh (%)</th>
<th>$D_{ED}$ (mm)</th>
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NYHA, functional classification according to the New York Heart Association; CTR, cardiothoracic ratio; PWC, physical working capacity in percent of the age-, sex-, and height-corrected normal value; $\Delta P$, systolic pressure gradient assessed by Doppler echocardiography; SW and PW, septal and posterior wall thickness assessed by M-mode echocardiography; Sh, fractional shortening of the left ventricular internal diameter assessed from M-mode echocardiography; $D_{ED}$ and LA, left ventricular end-diastolic and left atrial diameter assessed from M-mode echocardiography; O, obstructive; A, apical; N, nonobstructive.

**FIGURE 1. Timing diagram of the tagging and imaging sequence. Immediately after the R wave, saturation is performed by application of vertical (v) and horizontal (h) spatial modulation of magnetization stripes. Imaging is carried out at three time points during the cardiac systole. The complete image acquisition requires 512 consecutive heart beats. MR, magnetic resonance.**
image closest to the R wave in the ECG (Figure 1). The relatively long delay of 70 msec between the R wave and the first image was given by the application of the tags and the saturation of the neighboring tissue (see below). After the acquisition of gradient echo images covering the entire heart cycle at intervals of 50 msec, end systole was determined by searching the smallest left ventricle contour in a cine loop of the images. Three tagged images were then acquired with time delays selected so that the end-systolic tagged image was acquired at this predetermined time point.

A regular grid of saturated tissue was obtained by a prototype spatial modulation of magnetization sequence with two 1-2-1 binomial radiofrequency pulse trains. The gradient strength between the radiofrequency pulses was adjusted to yield a stripe interval of 10 mm. Smaller stripe intervals were evaluated, but best results (acceptable signal-to-noise ratio and good contrast) were obtained with an interval of 10 mm. Larger stripe intervals were not considered, because the grid distance was too large for an accurate assessment of segmental wall motion. Images were acquired with a conventional gradient echo sequence at a slice thickness of 8 mm and a field of view of 400 mm at a resolution of 128×256 points interpolated to an array of 256×256 points in the final image. The inevitable flow-induced image artifacts were reduced by averaging two acquisitions, saturation of the adjoining planes before each image section excitation, and velocity compensation of the imaging gradients. The gradient echo time was set to 13 msec. Myocardial tagging was performed in the short-axis planes at three or four equidistant anatomic levels between heart base and apex (base, equator, apex, and apical tip) (Figure 2).

**FIGURE 2.** Representative images in the short-axis view at different levels from base to apex of a patient with hypertrophic cardiomyopathy. Subimages with a field of view of 200×200 mm. The images on the left represent the end-diastolic, the images in the center the mid-systolic, and those on the right the end-systolic phase. Both rotational and shortening components of the cardiac motion can be observed with the distortion of the grid during systolic contraction. Clockwise rotation is visible in the basal and counter-clockwise rotation in the apical plane.
The radiofrequency pulse flip angles for tagging (135°) and image excitation (30°) were optimized for strong signal and maximal grid contrast. The optimal values were found by theoretical considerations and in vivo examinations. Acquisition of the image profiles of all heart phases during one single scan reduced possible errors caused by patient motion.

Three images were acquired, namely, at end diastole, mid systole, and end systole (Figure 1). The interval times were patient dependent and were usually around 140 msec. Acquisition of later phases was not performed, because the grid pattern of the images becomes very poor in contrast. Representative images of short axis of a patient with hypertrophic cardiomyopathy are presented in Figure 2. Fading of the grid contrast derives mainly from spin relaxation and partial saturation of the spins resulting from the repetitive imaging procedure. Inhomogeneous systolic contraction across the slice thickness distorts the initially upright grid stripes into an oblique position. This is a further cause of grid contrast decay, which occurs only during maximal contraction.

**Image Evaluation**

Although a merely qualitative look at a cine loop of the images may be intriguing (Figure 2), valuable data can be obtained by quantitative evaluation. The numerous grid crossing points were automatically detected by a computerized image analysis (Figure 3). For maximal accuracy, a final manual adjustment of the crossing positions was performed on a high-resolution screen after adequate magnification of the area of interest. Unrecognized grid points in the ventricular cavity were added manually for reconstruction of the grid close to the endocardial border (Figure 3). These points are only hypothetical, however, and they are not used for wall motion analysis. Approximately 20% of all points had to be adjusted manually. Finally, the individual crossing points within the left ventricle were connected by an automatic search algorithm (Figure 3).

A grid point outside the heart was selected for the superposition of all sequential grids from end diastole to end systole. The knowledge of the spatial position of each grid point allowed the quantification of the absolute movements of the cardiac wall. The displacement vectors obtained from three sequential images in a patient with hypertrophic cardiomyopathy are shown in Figure 4.

The center of gravity of the left ventricular segments was used as a reference point, because its translational motion is rather small in comparison to the wall movements (Figure 3). To compute the position, the end-diastolic endocardial and epicardial borders of the ventricle were determined by manual contouring. Four sectors—posterior, anterior, septal, and inferior—were defined by drawing lines from the points where the wall of the right ventricle merges with the left ventricle to the center of gravity. The absolute motion of the left ventricle was described in a polar coordinate system with the center of gravity as reference point. Wall motion was assessed from fractional rotation and radial displacement according to Figure 5. By interpolation of the original grid point positions, it was even possible to describe the motion in the different layers of the heart wall. Regional differences in bulk motion of the wall may obscure local variations in contraction, but the present system seems to be the best available for quantification of regional wall motion at different levels of the heart.

**Statistics**

Comparisons between control subjects and patients with hypertrophic cardiomyopathy were performed with a Student’s t test for unpaired comparisons. In Figures 6 and 7, mean values for the four different regions are given. A value of $p<0.05$ was considered to be significant.

**Results**

A representative series of pictures illustrating myocardial tagging in a patient with hypertrophic cardiomyopathy is shown in Figure 2. For comparison, the mean values of the six healthy volunteers and the eight patients with hypertrophic cardiomyopathy were used. The results are summarized in Table 2 and in Figures 6 and 7.

**Fractional Rotation**

Rotation (Figure 6 and Table 2) was clockwise in the basal plane and counterclockwise in the apical plane (Figure 2). This behavior was observed in both control subjects and patients with hypertrophic cardiomyopathy. The average fractional rotation for the different layers was similar in the two groups (Table 2). Fractional rotation was largest in the endocardium and lowest in the epicardium.

Considering the different segments (Figure 6), regional differences in cardiac rotation were seen. In all three planes, minimal cardiac rotation was observed in the septal region. The clockwise rotation in the basal plane was largest in the posterior and inferior wall. The counterclockwise rotation in the apical plane, however, was largest in the posterior and anterior wall. For the average of all three layers, a significant difference between control subjects and patients with hypertrophic cardiomyopathy was found in the posterior segment of the equatorial plane ($p<0.05$) and apical plane ($p<0.05$).

**Radial Displacement**

Radial displacement (Figure 7 and Table 2) was nearly identical in all planes, with the largest radial displacement in the endocardial layer and the lowest radial displacement in the epicardium in all subjects (Figure 2). Radial displacement in the midwall and epicardial layer of the patients with hypertrophic cardiomyopathy was significantly lower, whereas the radial
displacement in the endocardium was only slightly reduced in comparison to the control subjects. Furthermore, the values of the patients with hypertrophic cardiomyopathy showed a larger variability, which may, at least in part, reflect the variability of the distribution of the hypertrophy in the different subjects.

Regarding regional wall motion, both for the healthy volunteers and the patients with hypertrophic cardiomyopathy, the radial displacement was found to be minimal in the septum throughout all levels (Figure 7). A comparison of the average contraction over all layers showed a significant reduction for the patients with hypertrophic cardiomyopathy in the septum (p<0.05, p<0.02, p<0.01). In the posterior and anterior segments, however, a lower radial displacement was observed only in the epicardial and the midwall layers, whereas the endocardial layers showed a normal contraction.

**Discussion**

**Fractional Rotation and Radial Displacement in Normal Subjects and Patients With Hypertrophic Cardiomyopathy**

The computer-assisted analysis of the images showed a wringing motion of the heart, with a clockwise twist at the heart base and an opposite rotation at the apical level, which also has been reported by Buchalter et al. The equatorial slice acts as a transitional zone between the opposite rotational motions and shows mainly inward motion and wall thickening. Endocardial torsion was detected to be twice as high as in the epicardial layer, indicating a rather strong wall shear. The rotation as well as the contraction in the septum was small throughout all anatomic levels.

Apart from the thickened heart walls of the patients with hypertrophic cardiomyopathy, the motion pattern was not as different as expected from that of the control group with normal left ventricle. Only at the equatorial and apical levels does the hypertrophic ventricle exhibit in the mean a reduced fractional rotation of the posterior segment (Figure 6). Even though the ventricle boundaries were not very well defined in every case, reasonable values for the radial displacement of all
myocardial layers were found. In agreement with the severe structural alterations of the hypertrophied ventricle, radial displacement is smaller in the septum and the inferior segments in all layers at all anatomic levels. In the posterior and anterior segments, radial displacement is reduced in the epicardial layer. The endocardial radial displacement of these segments in patients with hypertrophic cardiomyopathy was normal, however, confirming previous results of a normal-to-supranormal ejection performance\(^1\) (Figure 7 and Table 2). A dissociation between fractional rotation and radial displacement is observed in patients with hypertrophic cardiomyopathy in the inferior septal and posterior region, i.e., a reduction in radial displacement but normal rotation and vice versa. This abnormal cardiac motion is probably directly related to the myopathic process.

A different approach to visualize cardiac motion of a patient is presented in the graphs of Figure 8, where for each position, the absolute radial displacement value is plotted against the absolute rotation value. Thus, regions with little movement appear in the origin of the coordinate system, as can be seen for positions within the septum. This can be explained by the position of the septum as a part of the right and left ventricles. The zone of pure contraction in the equatorial plane with the strongest radial displacement in the posterior wall is represented by values close to the axis of absolute radial displacement. Values with both strong contraction and clockwise rotation are found in the posterior and inferior segments of the basal plane. In the apical plane, the loop of connected values is situated to the left of the displacement axis, indicating a general counterclockwise rotation.

**Comparison With Previous Studies**

A comparison with the results of other authors who used different methods is summarized in Table 3. Buchhalter et al\(^5\) measured the bulk rotation at five levels from the heart base to the apex using the tagging method introduced by Zerhouni et al.\(^4\) The acquisition was restricted to one frame during end systole and allowed only the estimation of rotations relative to an adjacent tagged slice. Buchhalter et al found a counterclockwise twist of the apex relative to the heart base, 19.1\(^\circ\) for the endocardium and 11.2\(^\circ\) for the epicardium. Equivalent values were found in the present study, namely, 18.0\(^\circ\) for the endocardial layers, 14.5\(^\circ\) for the midwall, and 10.6\(^\circ\) for the epicardial layers. In patients with hypertrophic cardiomyopathies, a slightly reduced cardiac rotation was found: 16.3\(^\circ\) for endocardial wall, 12.3\(^\circ\) for the midwall, and 8.6\(^\circ\) for the epicardial wall. Buchhalter et al measured an increase of rotation relative to neighboring slices toward the apex. This is confirmed by the data presented under fractional rotation in Table 2, which show that the rotation relative to the center slice is more marked at the apex than at the heart base.

Ingels et al\(^2\) determined cardiac rotation in a group of patients who had undergone cardiac surgery with implantation of radiopaque markers, which were placed in the midwall of the left ventricular myocardium. The limited number of markers allowed only measurement of midwall rotation of the anteroinferior axis at three equidistant anatomic levels (4.4\(^\circ\) basal, −0.2\(^\circ\) equatorial, and −7.4\(^\circ\) apical). Although different groups of patients were evaluated in the two studies, the accord with midwall data derived from Figure 6 is striking: for the control patients, the findings are 4.6\(^\circ\) rotation at the basal plane, 0.0\(^\circ\) at the equatorial, and −9.2\(^\circ\) at the apical plane, and for the patients with hypertrophic
myocardial tagging is not an established method to measure fractional shortening of the myocardium, the values obtained in the present study appear to be reasonable. McDonald determined fractional shortening of the anteroinferior axis at the level of the heart base with epicardial radiopaque markers. In a group of patients with mitral stenosis but otherwise normal left ventricle, the epicardial fractional shortening was 15.8%. In patients with severe isolated aortic valve disease, the corresponding value was 10.3%. These values agree with the data from the present study (Figure 7), in which the epicardial shortening in the anteroinferior plane was 16.1% for the control group and 9.9% for patients with hypertrophic cardiomyopathy.

Clark et al. assessed regional circumferential shortening by measuring the end-systolic interstripe distance in tagged MR images. The average endocardial circumferential shortening in healthy volunteers was 44% and epicardial shortening 22%. In the present study, radial displacement in the controls amounted to 25% in the endocardium and 17% in the epicardium. But because circumferential shortening and radial displacement are not necessarily the same, these deviations can be explained by differences between radial and circumferential strains. Only directional changes can be compared between the different studies.

Limitations

The current technique allows evaluation of cardiac motion only during systolic contraction, because the grid contrast and signal-to-noise ratio decay rapidly during the multiphase acquisition. Thus, the image quality is insufficient to document the diastolic filling period of the left ventricle. It would be of interest to know whether contraction reaches its maximum in every location during end systole. For this purpose, more frequent sampling at time intervals <100 msec is mandatory. This would also allow the quantification of the velocity of circumferential fiber shortening in the different layers of the myocardium. A grid distance of 5 mm would give more appropriate results in ventricles with normal or even reduced wall thickness. With the present application, however, an improvement of imaging rate and grid resolution is accompanied by a loss in grid contrast and signal-to-noise ratio, to a point where the computerized image analysis procedure inevitably fails.

A modification of the spatial modulation of magnetization sequence promises an improved grid contrast throughout the cardiac cycle even with multiphase imaging. This new method provides at the same time a conventional (untagged) image by a different reconstruction of the original raw data set. This strongly facilitates the determination of the ventricular boundaries and, thus, makes the accurate assessment of fractional shortening for all myocardial layers feasible.

Through-plane motion is another limiting factor that affects to some extent the accuracy of the current methodology. Several authors have investigated the motion of the left ventricle in the direction of the long axis. Ingels et al. showed with radiopaque markers that both the heart base and apex move toward a point 69% of the distance along a line from the anterolateral aortic valve edge to the apex. Rogers et al. found, with MR tissue tagging at the heart base, a movement of 12.8 mm toward the apex. The preliminary results of Moore et al. show that this displacement is not equal in all segments. A three-dimensional acquisition of tagged images would avoid this source of inaccuracy and yield the same results as the planar radiography of radiopaque markers with more accuracy, yet without the drawbacks of an invasive method.

The endocardial and epicardial grid motion can be evaluated accurately in most patients, but some of the differences between normal subjects and patients with hypertrophic cardiomyopathy can be explained by the larger wall thickness rather than a specific effect of the disease.

With improvements of the evolving MR tagging technique, complete mapping of the functional strain components in the human left ventricle can be expected. According to Gallagher et al., the strain components are directly proportional to the fiber orientation. However, fiber orientation is not necessarily tightly correlated with the net strains and, thus, might not be correctly obtained from the tagged images.

References


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