Relation Between Longitudinal, Circumferential, and Oblique Shortening and Torsional Deformation in the Left Ventricle of the Transplanted Human Heart

Neil B. Ingels Jr., David E. Hansen, George T. Daughters II, Edward B. Stinson, Edwin L. Alderman, and D. Craig Miller

The present study was designed to investigate the anisotropy of systolic chord shortening in the lateral, inferior, septal, and anterior regions of the human left ventricle. At the time of surgery, 12 miniature radiopaque markers were implanted into the left ventricular midwall of the donor heart in 15 cardiac transplant recipients. Postoperative biplane cineradiograms were computer-analyzed to yield the three-dimensional coordinates of these markers at 16.7-msec intervals. In each of the four left ventricular regions, chords were constructed from a central marker to outlying markers, and the percent systolic shortening of each chord was calculated. In each region, chord angles were measured with respect to the circumferential direction (positive angles counterclockwise) and each chord was assigned to one of four angular groups: I. oblique, $-45\pm 22.5^\circ$ or $135\pm 22.5^\circ$; II. circumferential, $0\pm 22.5^\circ$ or $180\pm 22.5^\circ$; III. oblique, $45\pm 22.5^\circ$ or $-135\pm 22.5^\circ$; or IV. longitudinal, $90\pm 22.5^\circ$ or $-90\pm 22.5^\circ$. In the lateral, inferior, and septal regions, respectively, systolic shortening (mean$\pm$SD %) was significantly greater in Group I chords (19$\pm$5%, 17$\pm$5%, and 15$\pm$4%) than those in Group II (15$\pm$5%, 12$\pm$4%, and 11$\pm$4%), Group III (12$\pm$4%, 12$\pm$5%, and 11$\pm$4%), or Group IV (13$\pm$5%, 13$\pm$6%, and 12$\pm$5%). The anterior region was unique in exhibiting equal shortening in both Group I and Group II chords (16$\pm$5%), although the shortening of these chords was significantly greater than that of Group III and Group IV (12$\pm$5%) in this region. A cylindrical mathematical model was developed to relate longitudinal, circumferential, and oblique systolic shortening to torsional deformation about the long axis of the left ventricle. Torsional deformations measured in these 15 hearts were of sufficient magnitude and correct sense to agree with model predictions. These data suggest that torsional deformations of the left ventricle are of fundamental importance in linking the one-dimensional contraction of the helically wound myocytes to the three-dimensional anisotropic systolic shortening encountered in the transplanted human heart. (Circulation Research 1989;64:915–927)

More than two centuries have passed since Senac's first observation that epicardial and endocardial fibers were aligned longitudinally and midwall fibers were aligned circumferentially in the left ventricle of the mammalian heart. Since that time, extensive anatomical studies in both animals and man have provided ample confirmation that fiber angles proceed smoothly from a left-handed helix at the subepicardium to a right-handed helix at the subendocardium.

During the past quarter century, a number of studies have been conducted in animals to determine the functional impact of this intriguing fiber geometry on left ventricular myocardial deformations. Left ventricular shortening has been measured along various axes in canine hearts using a number of measurement techniques. To date, however, the anisotropy of left ventricular shortening in human hearts has not been reported, although the relative dynamics of specific left ventricular
sites (as required for the measurement of such shortening) have been studied in man both during and after cardiac surgery by means of radiopaque clips attached to the epicardium,34-36 strain gauges sutured to the epicardium,37 opacified coronary artery bifurcations,38,39 radiopaque myocardial markers implanted into the midwall40 and sonomicrometers implanted at various transmural depths.41,42

We report here the results of a study investigating the anisotropy of systolic shortening in the inferior, anterior, lateral, and septal regions of the left ventricular midwall of the transplanted heart in awake man. In this study we found that 1) in the inferior, lateral, and septal regions, the direction of maximum systolic shortening is aligned not in the circumferential direction, but obliquely, along the direction of the subepicardial fibers; 2) the anterior region is unique in that the circumferential and oblique subepicardial directions exhibited equal shortening; and 3) oblique (subepicardial fiber direction) and circumferential shortening were significantly lower in the septum than in the lateral free wall.

In an attempt to provide a geometrical basis for the features of the shortening anisotropy encountered in this study, a mathematical model was developed (along lines suggested by Arts et al43) to relate longitudinal, circumferential, and oblique systolic shortening to torsional deformation about the long axis of the left ventricle. This model proved capable of accounting for the anisotropic shortening patterns measured in the anterior and lateral free walls but was not as satisfactory in predicting the anisotropy encountered in the septum and inferior aspect of the free wall. The model was used to predict the anisotropic character of left ventricular shortening in small, local ventricular regions (as characterized by most previous studies) and suggested that seemingly negligible torsional deformations (as small as 1°) could give rise to the anisotropic patterns of regional ventricular systolic shortening observed in these studies.

Subjects and Methods

Informed consent was obtained from 15 patients undergoing cardiac transplantation and subsequent radiographic studies in accordance with the requirements of the Committee on the Use of Human Subjects in Research at the Stanford University Medical Center. In a manner described previously,40,44 12 tantalum radiopaque markers, each 0.85 mm in diameter and 2.2 mm in length, were inserted at the time of surgery into the left ventricular myocardium of the donor heart to a depth of 0.5 cm from the outermost left ventricular surface as defined by a preset stop on the insertor tool. Thus, the markers were placed in predominantly circumferential midwall fibers.8 As shown in Figure 1, three of these markers (Nos. 2, 3, and 4) were spaced uniformly in the inferior wall, one (No. 5) was placed near the left ventricular apex, and three (Nos. 6, 7, and 8) in the anterior wall. Three additional markers (Nos. 10, 11, and 12) were then placed in the lateral free wall at positions midway between the anterior and inferior markers, and two septal markers (Nos. 13 and 14) were implanted at basal and midventricular levels via the tricuspid valve. Two radiopaque clips (Nos. 1 and 9, not shown in Figure 1) were attached to the adventitia of the aortic root to approximate the position of the aortic valve. There were no complications due to the implantation of markers or the subsequent radiographic studies.

At an average of 52 days after surgery (range, 6 to 331 days), patients were studied with 60 frame/sec biplane cineradiography by means of two orthogonal, isocentered, alternately pulsed radiographic imaging systems (GE MLX LU-arm biplane unit) in the 30° right anterior oblique (RAO) projection and in the 60° left anterior oblique (LAO) projection. All studies were conducted in awake, supine patients, with respiration held at midexpiration. At least three complete cardiac cycles were imaged during each study.

At the conclusion of each study, a phantom with known dimensions was imaged in each projection. The RAO and LAO cinefilms were then projected by vidicon TV camera onto a computer-linked monitor; the marker and phantom positions were digitized by light pen and the resulting coordinates...
TABLE 1. Left Ventricular Volumetric Parameters for the 15-Patient Group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value ( ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>End diastolic volume (ml)</td>
<td>196±45</td>
</tr>
<tr>
<td>End systolic volume (ml)</td>
<td>125±35</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>71±17</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>37±8</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>95±13</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>6.8±1.6</td>
</tr>
</tbody>
</table>

Values are mean±SD.

stored in computer memory. Coordinates were corrected for distortion and magnification using data from the phantom, and data from the two views were merged to yield the three-dimensional coordinates of each marker at each sampling instant. Accuracy and reproducibility studies demonstrated that segmental lengths between markers could be measured with a mean error of 0.7% and a standard deviation of 3.6% with this system.

As previously validated, coordinates from the RAO view of markers No. 1 through No. 9 were used to estimate left ventricular end-diastolic volume, end-systolic volume, stroke volume, ejection fraction, and cardiac output for each beat in each patient. A summary of these parameters for the 15 patients is given in Table 1. The low ejection fractions observed are typical of those derived from the dynamics of specific myocardial sites, either from midwall markers, as in the present study, or by implanted sonomicrometer crystals in experimental animals. 13

From each sequence, a representative beat was selected for the study of shortening anisotropy in each patient. The dynamics of four left ventricular regions (lateral, inferior, septal, and anterior) were studied. Each region was defined by a central reference marker about which shortening was measured. Marker No. 11 (Figures 1 and 2a) served as the reference for the lateral region, marker No. 3 for the inferior region, marker No. 7 for the anterior region, and marker No. 14 for the septum.

As shown in Figure 2b, a reference system was defined with origin at the midpoint of the chord joining markers No. 2 and No. 8 and y axis through marker No. 5. The positive z axis is directed out of the plane toward the reader. During the analysis of each region the coordinates of all markers were rotated about the y axis in the maximum volume frame so that the z coordinate of the reference marker was positive and its x coordinate was zero, that is, the reference marker projected onto the y axis. The marker positions in Figure 2b show the

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**FIGURE 2.** Illustration of the definitions of the reference system and the intermarker chords, chord angles and angle groups. (a) Schematic of the left ventricle showing the markers and chords used in the analysis of the lateral region. (b) Projection of three-dimensional lateral region coordinate data at the time of maximum left ventricular volume from one of our patient studies. Tics on x and y axes are 1 cm. The positive z axis is pointing toward the observer. The left ventricular long axis is defined in three-dimensional space from the apical marker (No. 5) to the midpoint of the line (dashed) joining markers No. 2 and 8 which is placed at the origin. A rotation of the marker coordinates about the y axis has placed the projection of the reference marker (No. 11 in the lateral region) onto the y axis. Chords are defined from this reference marker and chord angles are defined (positive counterclockwise) from a normal to the y axis (0° line shown here). For example, the highlighted chord between markers No. 2 and 11 subtends an angle of 31°. (c) Depending on their angle, chords are classified into one of the four angular Groups I-IV shown here. For example, the highlighted chord from No. 11 to No. 2 at 31° is assigned to Group III.
result of this process for the lateral region (with reference marker No. 11) in a patient in this study.

In each region, after such rotation the angular orientation of each chord from the reference marker to the nearest outlying markers (e.g., Nos. 2-8, No. 10, and No. 12 in Figure 2b) was measured relative to a normal to the y axis passing through the reference marker. Each chord was then assigned to one of four angular groups (I-IV) depending on this angle. These groups (Figure 2c) correspond with those employed by Streeter\(^8\) in the study of transmural fiber angles.

The length of each chord in each angular group in each region was calculated from the three-dimensional coordinate data from the maximum volume frame and minimum volume frame. The shortening of each chord in each angle group in each region was then calculated as (length at maximum volume—length at minimum volume)/(length at maximum volume) and expressed as a percentage. The times of maximum and minimum volume were used to standardize measurement of chord shortening because 1) these times can be defined directly from marker coordinate data; 2) they signal the times of maximum and minimum average chord lengths; and 3) they avoid the effects of variations in excitation-contraction times, duration of atrial systole, and asynchrony of chordal contraction. This asynchrony can be seen in Figure 3, which is a representative plot of percent shortening versus time for three chords in the lateral wall.

Torsional deformations about the left ventricular long axis were also determined for each frame in each heart as described previously.\(^4\)\(^\text{—}^6\) The reference axis for torsional deformation was perpendicular to the y axis passing through marker No. 2, and zero torsional deformation was defined during diastasis (as shown in Figure 4). To assess the maximum amount of torsional deformation demonstrated by each heart, the site showing the greatest amplitude of torsional deformation was identified and characterized by its maximum and minimum tor-
Mathematical Model

A cylindrical model was developed to examine the relation between longitudinal, circumferential, and oblique shortening and torsional deformations in the left ventricle. These relations were derived by analysis of 5 sites (A, B, C, D, and E) positioned initially as in Figure 5 on the surface of a cylinder of length 2l and radius r, with zero torsional deformation (θ=0°). Sites B, C, D, and E are at angle Ψ (as measured in the x-z plane, relative to the negative z axis) and marker A is on the positive z axis. The cylinder then contracts to the position of a concentric cylinder of length 2fl (0<l<1) and radius gr (0<g<1) while simultaneously undergoing a torsional deformation of 2θ, which moves sites A, B, C, D, and E to a, b, c, d, and e. Table 2 gives the coordinates of sites A,a, B,b, and E,e on these two cylinders.

The coordinates in Table 2 are used to calculate the chord lengths

\[ L_{AB} = \sqrt{l^2 + 2r^2 (1 + \cos\Psi)} \]  
(1)

\[ L_{AE} = \frac{L_{AB}}{L_{AE}} \]  
(2)

\[ L_{AB} = \sqrt{2g^2 r^2 [1 + \cos(\Psi - \Theta)]} \]  
(3)

and

\[ L_{AE} = \sqrt{\frac{2f^2}{1 + \cos(\Psi + \Theta)}} \]  
(4)

The accompanying shortening values, \( S_{AE} \) and \( S_{AB} \), are then found as

\[ S_{AE} = 100 \times \frac{L_{AE} - L_{AE}}{L_{AE}} \]  
(5)

and

\[ S_{AB} = 100 \times \frac{L_{AB} - L_{AB}}{L_{AB}} \]  
(6)

This model was used to predict the torsional deformation required in each region to provide a least-squares fit to the experimentally measured oblique shortening (Groups I and III). Input data to the model are Ψ, representative values of l and r, and \( f = l - (\text{Group IV mean shortening}/100) \) and \( g = 1 - (\text{Group II mean shortening}/100) \). Starting at Ψ=0°, Equations 1–6 were solved for successive 0.1° increments in Ψ, and oblique shortening values predicted by the model were computed for angular Groups I and III using Equation 5 for Group I and Equation 6 for Group III. The model torsion (2θ) yielding the least-squares error between experimentally measured mean shortening and model-predicted mean shortening for Groups I and III was calculated for each of the four regions studied, along with the shortening error (the difference between the predicted and measured shortening values) for each group.

Results

Ejection-Phase Shortening Values

Table 3 shows the mean chord shortening from maximum to minimum volume for each angular group in each of the four regions in the 15 transplanted hearts in this study. Group means from Table 3 are also shown graphically for the lateral, inferior, septal, and anterior regions in Figures 6a–d, respectively. Variation in the number of chords in each group and region reflect variations in marker placement. Mean chord lengths at maximum volume are shown for each region in Table 4.

Four findings evident in Table 3 and Figures 6a–d are 1) oblique shortening in line with the subepicardial fiber direction (Group I) was significantly greater than that of Groups II, III, and IV in all regions, with the exception of the anterior region, where Group II shortening was equal to that of anterior Group I; 2) longitudinal shortening (Group IV) was roughly equal to circumferential shortening (Group
II) in the lateral, inferior, and septal regions while the anterior region was unique in exhibiting a significantly greater shortening in the circumferential than longitudinal directions; 3) circumferential (Group II) shortening showed significant heterogeneity, being greatest in the lateral and anterior regions and least in the inferior and septal regions; and 4) both oblique (Group I) and circumferential (Group II) shortening were significantly greater in the lateral than septal regions.

Torsional Deformations

The mean negative torsional deformations (see Figure 4) for the 15 hearts studied (maximally deforming segments) were \(\frac{\text{mean} \pm \text{SD}}{\text{mean}} = -4.6 \pm 1.8^\circ\). Torsional deformations then increased to \(18.0 \pm 4.5^\circ\) at the time of the minimum volume frame.

Model Predictions

For each of the four regions studied, the model was used to predict the torsional deformations required to account for the shortening values measured in that region (see Table 3). Input data to the model were \(l=r=4 \text{ cm} \) (representative values [see Table 4]) and \(\Psi = 90^\circ\).

Taking the lateral region as an example, further input to the model was (from Table 3) \(\frac{\text{mean} \pm \text{SD}}{\text{mean}} = -1.0.13 \pm 0.87\) and \(q = 1.0.15 \pm 0.85\), and the model-predicted torsion to provide a best fit to the Groups I and III data was \(14.4^\circ\) in this region, as shown in Table 5.

Table 5 gives the model-predicted torsions calculated in this manner for each of the four regions studied, along with the measured shortening and predicted shortening for Groups I and III, and the shortening error (i.e., the difference between the predicted and measured shortening values.)

Two features in Table 5 that should be noted 1) given the measured longitudinal and circumferential shortenings, the model predicts both oblique shortening values quite well in the anterior and lateral regions, less well in the septal region, and worst in the inferior region; and 2) the torsions predicted by the model are regionally heterogeneous (consistent with the heterogeneity of measured shortening values), being least in the septal and anterior regions, somewhat larger in the inferior region, and greatest in the lateral region.

Discussion

A principal finding in this study was that, in the inferior, lateral, and septal regions of the transplanted human heart, the direction of maximum systolic shortening of chords defined by midwall markers was aligned, not in the circumferential direction (in line with the midwall fibers\(^9\)) but obliquely, in line with the subepicardial fiber direction. The pattern of shortening in the anterior left ventricular midwall was unique compared with the other regions in that roughly equal (and maximum) shortening was noted in both the Group I and Group II directions (Figure 6d), much as was found by Hattori et al\(^{24}\) in the anterior subepicardium in the dog heart. In previous studies of the anterior midwall region in anesthetized, open-chest dogs, maximum shortening has been found in the Group I direction by a number of investigators,\(^{13,16,19,29}\) although both Fenton et al\(^{14}\) and Freeman et al\(^{15}\) found this maximum in the Group II direction. We also found that circumferential (Group II) shortening was significantly greater than longitudinal (Group IV) shortening in the anterior wall, as did Lew and LeWinter\(^{27}\) in their sonomicrometer studies in dogs.

Previous studies of the lateral and inferior walls of the left ventricle in the open-chest dog have yielded varied findings. As shown in Figures 6a and 6b, we found that lateral and inferior midwall systolic shortening was greatest in the Group I direction in the transplanted human heart. This finding is in agreement with that of Hattori et al\(^{24}\) and Gallagher et al\(^{23}\) but not with that of Dieudonne,\(^{19}\) who found a Group II maximum direction throughout the entire lateral wall of the dog's left ventricle. Our data in the lateral and inferior regions (Figures 6a and 6b) also support the findings of Lew and LeWinter\(^{27}\) in that midwall circumferential (Group II) shortening and midwall longitudinal (Group IV) shortening were not significantly different in each of these left ventricular regions, but significantly greater circumferential shortening was measured in the anterior than in the inferior regions.

We are not aware of any previous studies of shortening anisotropy in the interventricular septum. Our finding of significantly reduced septal shortening compared with lateral free wall shortening in both the Group I and Group II directions...
FIGURE 6. Group mean percent shortening (scale tics in 1% increments) from maximum to minimum volume by angular group (as in Figure 2c) and left ventricular region. This is a graphical representation of the data in Table 3. The radius of each sector is group mean shortening, and the angle is representative of the chord group shown in Figure 2c. Panel a: Lateral region, centered on reference marker No. 11; Panel b: Inferior region, centered on reference marker No. 3; Panel c: Septal region, centered on reference marker No. 14; Panel d: Anterior region, centered on reference marker No. 7.
Anterior Septal Inferior Lateral Region then followed by a larger counterclockwise deformation later in systole as reported in previous studies. A possible structural basis for this early systolic negative deformation is presented later in this discussion.

It was not immediately apparent to us how to account for the shortening anisotropy encountered in the four left ventricular regions in these transplanted human hearts. If, for example, one assumes that the portion of the left ventricle delineated by the implanted markers from the basal to apical rings (Figure 1) is roughly cylindrical (an assumption with seemingly good predictive value⁴³,⁵⁰,⁵²,⁵³), then it can readily be shown (using the model in Figure 5) that a simple systolic shrinkage of this cylinder in length (i.e., Group IV shortening) and circumference (i.e., Group II shortening) will not yield the shortening anisotropies evident in Groups I and III of Figures 6a–d. As shown in Figure 5 and Table 5, however (and first analyzed by Arts et al⁴⁵), if one introduces an additional torsional deformation, or "twist," of one part of the cylinder with respect to another about the long axis of the cylinder, then shortening anisotropy is generated, or, conversely, if certain shortening anisotropies are generated, the result is a torsional deformation of the cylinder. If, for example, a counterclockwise twist is introduced, as illustrated by angle Θ in Figure 5, then this twist will increase the shortening observed in the Group I direction (e.g., AE, Figure 5) and decrease it in the Group III direction (e.g., AB, Figure 5).

It is of interest that the torsion required by the model to fit the experimental shortening data displays significant regional heterogeneity, with the greatest torsion required in the lateral free wall, next greatest in the inferior wall and least in the septal and anterior walls. These predictions are entirely consistent with our previously reported findings⁴⁴ that the greatest torsional deformation in the human heart is in the lateral free wall, next greatest in the inferior wall and least in the septal and anterior walls. It is thus seen that the contracting left ventricle is not a uniformly deforming, homogeneous structure. Thus, while the present study serves to support the modeling approach of Arts et al⁴³ it also suggests that this approach needs to be refined to take into account these significant regional heterogeneities. While the present study demonstrates that the maximum torsion measured in these 15 hearts is both of the right magnitude and sense to yield the shortening anisotropies observed,

<table>
<thead>
<tr>
<th>Region</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral</td>
<td>14.4°</td>
<td>19</td>
<td>18</td>
<td>-1</td>
</tr>
<tr>
<td>Inferior</td>
<td>10.0°</td>
<td>17</td>
<td>15</td>
<td>-2</td>
</tr>
<tr>
<td>Septal</td>
<td>8.8°</td>
<td>15</td>
<td>13</td>
<td>-2</td>
</tr>
<tr>
<td>Anterior</td>
<td>8.2</td>
<td>16</td>
<td>16</td>
<td>0</td>
</tr>
</tbody>
</table>

All shortening values in percent.
further studies are needed to determine the detailed relation between local shortening anisotropy and local torsional deformations.

Although the straightforward cylindrical model presented produces an excellent fit to the data in both the lateral and anterior wall regions, this model yields less accurate predictions in the inferior and septal regions (Table 5). One possible reason for this variation could be regional variability in the geometry of the left ventricular wall. In anatomical studies, Hutchins et al. found the septum to be flatter than the free wall and Greenbaum et al. found regions of both positive and negative curvature on the diaphragmatic aspect of the left ventricle. Horowitz et al. also found the left ventricular shape to be irregular, with regions of negative as well as positive curvature. Thus, perhaps the simple cylindrical approximation may be more appropriate in the lateral and anterior regions than in the inferior and septal regions, or perhaps the radii of curvature need to be modified to allow a better prediction of the dynamics of the inferior and septal regions. This area will require considerable future study.

Because the measured anisotropic shortening patterns shown in Figures 6a–d exhibit significant regional heterogeneity and the model calculations (Table 5) suggest that this may imply regional heterogeneity in torsional deformations as well (which has been reported), it is of interest to ask whether structural evidence exists for regional heterogeneity of fiber geometry, which could provide an anatomical basis for these heterogeneous dynamics. There is, indeed, evidence for such anatomical heterogeneity in the human heart. With regard to the circumferential fibers, Greenbaum et al. have found the inferior region of the left ventricle to be composed principally of Group II (circumferential) fibers, while they and others found that only about half of the fibers are so oriented in the lateral, anterior, and septal regions. Since, however, the inferior region in the present study had one of the smaller circumferential shortening values, it would appear that the extent of circumferential shortening and the fraction of circumferential fibers in a given region may not necessarily correlate closely. With regard to the oblique fibers, Streeter suggested that a preponderance of Group I over Group III fibers would cause a torque that would twist the apex. Greenbaum et al. found significantly greater numbers of Group I than Group III fibers in the lateral, inferior, and septal regions (as did Streeter in a pooled free wall sample), which would support the required torsion in these regions, but they found fewer Group I than Group III fibers in the anterior region. Such a fiber imbalance could underlie the unique shortening anisotropy pattern encountered in the anterior region and could generate the small torsional deformation accompanying this anisotropy pattern. Pearlman et al. however, do not corroborate these anatomical findings in that they find roughly equal numbers of Group I and Group

III fibers in the lateral wall of the human left ventricle in their study and significantly more Group III than Group I fibers in the septum, where maximum shortening is still in the Group I direction (Figure 6c).

Assessment of the link between left ventricular anatomy and myocardial torsional dynamics requires consideration of at least the following four factors: 1) from simple geometric considerations, in a cylindrical left ventricular model, if the myocardial fiber density is assumed constant, then up to one-third more fibers will occupy a given epicardial volume shell than an endocardial volume shell of the same thickness. This favors an imbalance in the number of fibers (and hence force) oriented in the subepicardial (Group I) direction; 2) as illustrated in Figure 7, subepicardial fibers are at a greater radius (r,e) than subendocardial fibers (r,i) and this alone would exaggerate the torque from a subepicardial fiber developing the same force at the same helix angle as a subendocardial fiber; 3) the myocardium is not excited simultaneously. McDonald suggested that left ventricular rotational movements may be associated with early activation and contraction of the endocardium and late persistence of contraction in the epicardial layers. Fox and Hutchins and Ohayon and Chadwick have sug-
gested that the subendocardial fibers contract first, and then later the subepicardial fibers contract, "wringing" the ventricle (i.e., producing torsional deformations; 4) local torsional deformation is not expected to reflect only the local fiber geometry but to reflect a global resultant of all torsions generated by all fibers in the myocardium weighted by various factors depending on their coupling to one another and geometric relation to the region under study. The nature, extent, and regional variability of such transmural mechanical coupling ("tethering") between cells in the heart wall is not well understood. Prinzen et al have suggested that two forms of such coupling exist. The first is due to the tight interconnection of neighboring tissue coupled by the weave of blood vessels and collagen bundles that interconnect myocytes. The second is due to global loading as one transmural layer (both actively and passively) loads another. There can be little doubt that this second form of coupling exists, since each myocardial layer is sandwiched between other force-developing layers and must respond to the stresses and strains in these layers that constrain its physical boundary. The data in the present study are consistent with the first form of tethering, as well. Without such tethering, the cylinder outlined by the midwall markers would not respond to the effects of the strains in the oblique fibers, except as the shortening of these fibers contributed to the second form of coupling just described. Thus, in the lateral, inferior, and septal regions, without such coupling, the shortening values in Figures 6a–c would not be expected to show significant variation with angle, and the shortening patterns displayed would therefore be roughly circular. Fairly tight coupling of the first sort, then, allowing the midwall markers to respond to the shortening of oblique fibers would seem to be required to generate the anisotropy patterns noted in Figures 6a–c and the torsional patterns illustrated in Figure 4. Considerably more information is needed concerning both the orientation and coupling of cardiac fibers throughout all regions of the left ventricle before we can hope to understand the complex relations between structure and function in the left ventricular myocardium.

Myocardial fibers which are aligned purely in the circumferential or longitudinal directions are not capable of twisting the ventricle about its long axis. Thus, the oblique fibers which spiral about the long axis of the thick-walled left ventricular chamber are likely to be the origin of the torsional deformations which have been both proposed on anatomical grounds and measured experimentally. It is not clear, however, how these oblique strains are coupled to yield the resulting torsional deformations since, as depicted schematically in Figure 7, these oblique fibers twist in a left-handed helix in the subepicardium and a right-handed helix in the subendocardium, and, further, the relative proportions of these right and left-handed oblique fibers have been shown to vary by region in the human heart. To a first approximation, at any given time during systole in a cylindrical left ventricular model, the torque about the long axis contributed by a given fiber at a given radius (e.g., \( r \) or \( r_0 \) in Figure 7) depends on the product of this radius and the circumferential component of the force developed by that fiber at that instant. This circumferential component, in turn, depends on sarcomere lengths, the time after stimulation, and the helix angles at that instant. Taking into account the appropriate viscoelastic couplings between fibers, the total left ventricular torque at a given point in the left ventricular wall is then the vector sum of all such torques from all such fibers, which clearly depends strongly on the transmural distribution of the number of fibers at each helix angle throughout the left ventricular wall.

With this as background, we propose the following description of the manner in which myocardial fibers interact during left ventricular systole. 1) At the onset of excitation, the papillary and subendocardial fibers are first to be excited. Thus, as shown in Figure 4, the torsional deformation becomes negative at this time because subendocardial fibers are wrapped in a right-handed helix (Figure 7) and the subepicardial fibers have not yet begun to develop their counter-rotating force. This early force development in the papillary muscles, trabeculations, and subendocardial fibers initiates shortening, stiffens the left ventricle in the longitudinal direction, begins the development of left ventricular pressure, and simultaneously develops tension in the chordae to prevent eversion of the mitral valve. 2) The midwall fibers are then excited and constric the chamber without contributing much to torsion because they are oriented primarily in the Group II (circumferential) direction. This circumferential force development continues to build the chamber pressure. 3) Very soon thereafter the subepicardial fibers are excited, and they begin to develop a counter-rotating torque to the subendocardial fiber torque. This torque quickly dominates the subendocardial torque because the subepicardial fibers are at larger radii (i.e., \( r_0 \) versus \( r \) in Figure 7), and, even if subendocardial forces exceed subepicardial forces, the larger subepicardial lever arms produce sufficient torque to drive the torsional deformation toward positive angles (as in Figure 4). This large subepicardial torque is coupled transmurally to the midwall and subendocardium and results in global positive left ventricular torsional deformation, which enhances strains in the Group I direction and reduces those in the Group III direction. In the subepicardium, this torsion aids contraction in the principal fiber direction and reduces it at right angles to the fiber direction. In the midwall, this torque couples to enhance shortening in the circumferential (principal fiber) direction. In the subendocardium, this torsion causes fiber rearrangement such that the apparent shortening is greater at right angles to the principal fiber direction than along the principal fiber direc-
tion itself. This is consistent with previous studies,\textsuperscript{15-17,19,66} which have shown that although fiber direction and principal strain direction are not substantially different in the subepicardium, they are nearly perpendicular in the subendocardium. Our present findings suggest torsion as a possible mechanism underlying this behavior.

4) As systole progresses, with its concomitant and complex wall thickness increase,\textsuperscript{22,26,31,32,43,67,68} due only in part to the constant volume property of contracting muscle cells,\textsuperscript{53-65} this difference between $r_2$ and $r_1$ increases still further, giving an ever-increasing torque advantage to the subepicardial fibers. This advantage is compounded as the force in the subendocardial fibers begins to decay.

In this view, then, the crucial role of the subendocardial fibers is to develop tension, shortening and longitudinal stiffness early in systole. Later, when the midwall and epicardial fibers are excited, these outer fibers increasingly dominate the systolic deformations, leaving the subendocardial fibers with a diminishing contractile role as they are crushed and rearranged by contraction of the outer layers. These concepts need to be tested.

The findings in the present study may have important clinical implications. They suggest that torsional deformation is a fundamental component of left ventricular wall motion that should be considered in assessing left ventricular function and that clinical conditions (such as hypertrophy, fibrosis, dilatation, ischemia, infarction, or rejection) that might affect such torsional deformations may profoundly affect left ventricular function by altering the distribution of left ventricular wall stresses and therefore torsionally influenced myocardial strains. Previous studies\textsuperscript{28,43,50,69} have suggested that torsion may serve to equalize transmural sarcomere shortening, despite greater circumferential shortening in the subepicardium than subendocardium\textsuperscript{15,19,21-23,25} and that this, in turn, may reduce transmural gradients of oxygen utilization, wall stress, and contractile work during the ejection phase.\textsuperscript{69} Beyar and Sideman\textsuperscript{69} have speculated that reductions in torsional deformations accompanying hypertrophy and fibrosis could increase the gradient of sarcomere work and oxygen utilization across the myocardium and thus accelerate the development of subendocardial fibrosis.

Considerable caution, however, must be exercised in extrapolating the results of this present study to the left ventricular dynamics of the normal human heart. Although transplanted hearts are typically from young donors, they are initially free of significant myocardial and coronary artery disease, and demonstrate normal contractile characteristics and reserve,\textsuperscript{70} such hearts have undergone an obligatory ischemic interval and reperfusion, are denervated, do not have an intact pericardium, and may have suffered myocyte necrosis, which accompanies episodes of rejection.\textsuperscript{71} Further, although none of the patients in this study had overt obstructive coro-

nary lesions, coronary artery disease is accelerated in these hearts,\textsuperscript{72} and both right and left heart filling pressures are typically elevated into the upper normal range.\textsuperscript{73}

In this study, we found agreement between the large-scale three-dimensional chord dynamics measured in the transplanted human heart and the large-scale three-dimensional chord dynamics predicted by our cylindrical model, provided that torsional deformation was included. It is also of interest that the large-scale shortening anisotropy patterns we measured are quite similar to the strain patterns found in previous studies using closely spaced sites in well-defined local regions in the left ventricle of the dog.\textsuperscript{14-16,19,20,23-25,27-29,66} While it remains to be demonstrated experimentally that this large-scale/local relation indeed exists in the human heart, the following calculation suggests that this may well be the case. Using the model (Figure 5), with $r=4$ cm, $L=0.5$ cm, $f_g=0.85$, $\Psi=173^\circ$ to simulate a roughly $1 \times 1$ cm study-region in the left ventricular free wall, we calculate that a model torsion ($\Theta$) of only $1.2^\circ$ in this small lateral region would yield a Group I shortening of $19\%$ and Group III shortening of $12\%$, both being very close to the large-scale anisotropy values given in Table 3 for the lateral region. This calculation suggests, then, that large strain anisotropies in small, local regions can be generated by very small local torsional deformations which can arise, in turn, from their coupling to large-scale left ventricular torsional deformations. If future studies demonstrate the validity of this relation, then analyses of both local and regional left ventricular strains need to take such torsional deformations into account.

In summary, we have documented, for the first time, the anisotropy of systolic shortening in the left ventricle of the human heart, and 1) developed a mathematical model that suggests that torsional deformations about the long axis of the left ventricle could be the basis of this anisotropy; 2) shown that global left ventricular torsional deformations could change sign during systole; 3) linked the helical geometry of myocardial cells to these torsional deformations; 4) suggested a sequence of systolic myocardial events that could generate these deformations; and 5) shown that global shortening anisotropy is regionally heterogeneous and that this correlates with the previously reported heterogeneity of regional torsional deformations. Further studies will be required to determine whether these global relations between longitudinal, circumferential, and oblique shortening and torsional deformations will also apply in local left ventricular regions under a variety of physiological conditions.

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Relation between longitudinal, circumferential, and oblique shortening and torsional deformation in the left ventricle of the transplanted human heart.

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