Torsional Deformation of the Left Ventricular Midwall in Human Hearts With Intramyocardial Markers: Regional Heterogeneity and Sensitivity to the Inotropic Effects of Ablrupt Rate Changes

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The spiral orientation of left ventricular (LV) fibers suggests that twisting about the ventricular long axis of the apex with respect to the base, i.e., torsional deformation, may be characteristic of LV contraction. To demonstrate this twisting motion, 10 orthotopic human cardiac allograft recipients were studied with biplane cineradiography of tantalum helices implanted within the LV midwall at 12 specific sites. Counterclockwise twisting about the LV long axis (as reviewed from apex to base) accompanied ventricular ejection in all patients. Torsional deformation angles, measured relative to a reference minor axis at the base, were substantially smaller in the anterolateral wall, as compared with counterparts in the apical third of the inferior and lateral walls (anterol = 13.3 ± 6.0°, inferior = 18.7 ± 6.3°, and lateral = 23.4 ± 10.7°). Torsional angles at the midventricular level were roughly half as much and exhibited similar regional variabilities (anterol = 7.3 ± 3.4°, inferior = 10.7 ± 5.2°, and septal = 8.8 ± 3.8°). Comparison of control beats and the initial beat after abrupt cessation of rapid atrial pacing (126 ± 10 beats/min) with return to the control heart rate (96 ± 9 beats/min) permitted the mild positive inotropic effect of tachycardia to be assessed at similar levels of ventricular load. Torsional deformation of the anterolateral and inferoposterior sites increased significantly (p < 0.05) over control values to 15.6 ± 7.5° and 21.2 ± 5.5°, respectively. In contrast, torsional deformation of the lateral wall was essentially unchanged. These data provide direct evidence for torsional deformation of the left ventricle in humans, demonstrate that torsion of the LV chamber is nonuniform, and suggest a dependence of LV torsion upon contractile strength that is attenuated in the lateral wall. (Circulation Research 1988;62:941-952)

Left ventricular (LV) fiber angles vary gradually from the endocardial to the epicardial surface by as much as 160° with the subepicardial and subendocardial fibers oriented obliquely to the ventricular long axis and with fibers in the LV midwall oriented circumferentially. The spiral nature of the myocardial fiber orientation, i.e., twisting about the ventricular long axis of the apex with respect to the base, or torsional deformation, is characteristic of the heart. Consideration of fiber orientation in mathematical models of LV contraction suggests that twisting about the long axis may reduce intramyocardial pressure and equalize transmural differences in sarcomere shortening and end-systolic fiber stress.

LV torsional deformation cannot be studied with conventional imaging techniques or sonomicrometry because precise knowledge of the three-dimensional spatial coordinates of sites fixed within the myocardium is required. In canine studies, deformations of the epicardium have been measured with inductive coils and by imaging markers attached to the epicardial surface with a video camera. The epicardial shear reported in these studies provides direct evidence for torsional deformation of the chamber. Torsion of the LV chamber has also been quantified in dogs as the difference between the angles of rotation of transverse cross-sections at the mitral valve and the low papillary level, with two-dimensional echocardiography and specific anatomic landmarks in these images.

In 1975, while studying the three-dimensional motion of radiopaque intramyocardial markers implanted in the human left ventricle, our group noted that the apical and basal transverse diameters rotated in opposite directions, while the midventricular transverse diameter rotated minimally. More recently, we reported preliminary measurements of systolic torsional deformation and diastolic recoil rates. These initial observations confirmed that twisting about the ventricular long axis occurs in humans and suggested that the myocardial marker technique may be uniquely suited for the study of this phenomenon.

This study describes the regional heterogeneity of LV torsional deformation in humans. A second objective of this study was to demonstrate the influence of the inotropic state upon such deformations. We hypothesized that beats with enhanced contractile strength would be associated with greater torsional
deformation. To test this hypothesis, torsional deformation about a ventricular long axis was measured with biplane cineradiographic images of surgically implanted LV midwall markers in human cardiac allograft recipients, and the inotropic state was altered by abruptly varying the heart rate with an atrial pacing protocol, modified after Mahler et al., which permitted comparison of beats with varying contractile strength at similar loads.  

Patients and Methods

Ten patients undergoing orthotopic cardiac transplantation participated in this study. In accordance with the regulations of the Stanford University Medical Committee on the Use of Human Subjects in Research, all patients gave informed consent for insertion of myocardial markers and for the following studies. No complications occurred as a result of these investigations.

Intraoperative Management

During surgery, 12 helices (0.8 x 2.2 mm) of pure tantalum wire were implanted into the LV myocardium of donor hearts at an approximate depth of 5 mm below the epicardial surface as previously described. As illustrated in Figure 1, three markers were evenly spaced from base to apex in the inferior wall along the posterior descending artery; three anterior wall markers were inserted at equidistant sites in close proximity to the left anterior descending artery; and three lateral wall markers were inserted at equidistant points along the lateral margin. An additional marker was inserted into the LV apex, and one or two markers were implanted in the interventricular septum. To mark the approximate position of the aortic valve, two hemostatic clips (1 x 5 mm) were attached to the adventitia of the aorta immediately above the valve commissures. These 12 intramyocardial markers silhouetted the LV cavity in the 30° right anterior oblique (RAO) and 60° left anterior oblique (LAO) projections. Temporary bipolar electrodes were sutured to the right atrium for pacing, and the lead wires were externalized for subsequent use.

Data Acquisition

All studies were performed 3–6 weeks postoperatively at the time of routine right ventricular endomyocardial biopsy for detection of rejection episodes. In two instances in which histological evidence of moderate or severe acute cardiac allograft rejection was present, the study was discarded and repeated after successful treatment of the rejection episode. Six of the 10 patients had a rejection episode before study. In two patients, the temporary pacing wires were removed before study, and atrial pacing was performed with a 6 French bipolar pacing catheter.

Biplane (30° RAO and 60° LAO projections) cinefluoroscopic images were recorded at 60 frames/sec at end-inspiration (with the patient resting comfortably in the supine position) with a General Electric (Milwaukee, Wisconsin) MLX biplane LU-arm system with intensifiers in the 9-inch mode isocentered on the left ventricle. The two x-ray tubes fired in alternating fashion with an 8.3-msec offset because the image quality of the markers is degraded during simultaneous biplane cineradiography. Magnification and distortion factors were determined by imaging a lead grid containing 1-cm squares. Images of three-dimensional
phantoms of known size were obtained with this system and revealed that distance can be measured to within 0.4 mm and that angles can be measured to within less than 1.0°. An analog ECG signal was recorded with a Gould multichannel recorder (Cleveland, Ohio) for determination of the R-R interval. To synchronize the film and paper records, an electronic circuit was used to detect the R-wave peak and to indicate this event on the cinefluoroscopic recordings by means of a light-emitting diode.

The cinefluoroscopic recordings were replayed frame by frame on a specially modified Vanguard projector linked by a vidicon camera to a Hewlett-Packard (Palo Alto, California) 1000 minicomputer with a light pen digitizer. The two-dimensional coordinates \((x, y)\) for the 30° RAO camera and \(y, z\) for the 60° LAO camera) of the center of each marker image were manually digitized with the light pen system, and the marker image coordinates were corrected by the minicomputer automatically for the magnification and distortion of the imaging system. The data from the two corresponding biplane views were transferred to an IBM System/36 minicomputer where three-dimensional coordinates were calculated at 16.7-msec intervals by a parallel ray approximation. The \(y, z\) data from the 60° LAO projection were shifted 8.3 msec to correspond temporally with the data from the orthogonal projection, and the values of the \(y\) coordinates from the two projections were averaged. All subsequent data reduction and analysis were performed with the IBM System/36 computer.

**Data Reduction and Analysis**

Torsional angles were computed at 16.7-msec intervals with an internal cylindrical reference system defined by three of the markers (2, 8, and 5) as illustrated in Figure 2. The line from the apical marker (5) to the midpoint of the line connecting markers 2 and 8 (point M) defined the ventricular long axis. The reference minor axis was defined as the perpendicular to the long axis passing through marker 2. This reference system was redefined on a frame-by-frame basis to distinguish between pure rotation of the heart about the long axis and torsional deformation. On each frame, the \(x, y\), and \(z\) coordinates of each marker were then converted into cylindrical coordinates in which the position of marker \(i\) \((P_i)\) was expressed as the distance \((l)\) from point M to the point of intersection between the long axis and the perpendicular to \(P_i\), radial distance \((r)\) from the long axis to \(P_i\), and angle \((\alpha)\) of the perpendicular from the long axis to \(P_i\) with respect to the reference minor axis. The counterclockwise direction as viewed from apex to base was defined as the positive direction for \(\alpha\). The time-varying torsional deformation angle about the long axis \(\Theta_i(t)\) for a marker at point \(P_i(t)\) at time \(t\) was computed relative to the end-diastolic position \(P_i(ED)\):

\[
\Theta_i(t) = \alpha_i(t) - \alpha_i(ED)
\]

where \(i = 3, 4, 6, 7, 11, 12, \text{ and } 14\) and signifies the site of markers in the middle and apical portions of the left ventricle as defined in Figure 1; \(\Theta_i(t)\) is the corresponding time-varying torsional deformation angle in degrees; \(\alpha_i(t)\) is the angular coordinate in the moving internal reference system at time \(t\) as defined above in degrees; and \(\alpha_i(ED)\) is the value of \(\alpha_i(t)\) in degrees at the time of the peak electrocardiographic R wave (which defined end-diastole). According to this definition, the instantaneous value of \(\Theta_i(t)\) is simply the change in \(\Theta_i(t)\) from its end-diastolic value, and the value of \(\Theta_i(t)\) at end-diastole is set to zero. Neither \(\alpha_i(t)\) nor \(\Theta_i(t)\) has been smoothed because the smoothing algorithm that would best describe the time-varying behavior of these variables is not known. From the unsmoothed values, the peak-to-trough amplitude of \(\Theta_i(t)\) (referred to as \(\Theta\)) was then calculated in degrees.
LV volume was computed on a frame-by-frame basis by a modification of the single plane area-length method, as previously validated by comparison with volume measurements derived simultaneously from standard left ventriculograms. End-diastolic volume ($V_{es}$) and end-systolic volume ($V_{es}$) were computed for each beat as the maximum and minimum LV volumes, respectively. The normalized mean LV circumferential shortening velocity ($V_d$), a commonly used ejection phase measure of LV systolic performance, was computed with a modification of the definition originally proposed by Karlner et al, as previously described by our group.

**Atrial Stimulation Protocol**

The abrupt rate-switch protocol was designed to allow comparison of beats with 1) similar R-R intervals, 2) similar preloads and afterloads, and 3) differing contractile states. The five-stage atrial pacing protocol used (Figure 3) was modeled after Mahler et al and Ricci et al. The important comparisons are: 1) the control ($C_{es}$) beats with the initial post-tachycardia ($PT_{es}$) beat (these beats had matched R-R intervals, preloads, and afterloads, but had enhanced inotropic states in the initial post-tachycardia beat); and 2) the steady-state tachycardia ($T_{es}$) beats with the initial tachycardia ($T_{es}$) beat (these beats had similar R-R intervals, preloads, and afterloads, but had decreased contractility in the initial tachycardia beat). Atrial pacing was performed at twice diastolic threshold (Digital Stimulator, Bloom Associates, Reading, Pennsylvania). After 2 minutes of pacing at a rate (see Figure 3, CONTROL) just above the intrinsic sinus rate, a continuous cinefluoroscopic recording was obtained that included three steady-state beats at the control rate and the first tachycardia beat after an abrupt increase in rate to 133% of control (TACHYCARDIA). Based upon our previous experience with atrial pacing in cardiac transplant patients, this was the maximum range of normally conducted pacing intervals that could be realistically achieved in all individuals given the characteristic resting tachycardia in these patients. After 2 minutes of tachycardia, cinefluoroscopic recordings of another multiple-beat sequence were obtained that included three steady-state tachycardia beats and the initial post-tachycardia beat after an abrupt return to the control rate (POST-TACHYCARDIA). The pacing rate was subsequently changed to 110% of control (INTERMEDIATE) for 2 minutes, and cineangiograms of three or four steady-state ($I_{es}$) beats were recorded at the intermediate rate. At each steady-state heart rate, systolic and diastolic blood pressures were measured with an automated blood pressure cuff (Dinamap 1846P Vital Signs Monitor, Critikon). The accuracy (mean percent error of 1% and 2% for the systolic and diastolic pressures, respectively) of this technique has been verified over a wide range of pressures with simultaneous central aortic pressure measurements. The carotid pulse contour was also recorded and end-systolic pressure was calculated by interpolation to the incisura assigning the systolic and diastolic blood pressures to the peak and nadir of the pulse tracing.

**Statistics**

Unless specifically indicated, the data are expressed as the mean $\pm$ SD. To demonstrate the nonuniform nature of ventricular torsion, regional torsional deformation angles ($\Theta$) were compared by analysis of variance with one within subjects factor (i.e., the marker site) and two covariates, $r$, and $L/L$. This analysis permitted us to factor out the tendency of $\Theta$ to increase as a function of distance from the reference axis at the base and allowed us to correct for minor errors in $\Theta$, that result from deviations of the LV long axis (as defined by markers 2, 8, and 5) from the actual axis of symmetry. A significant $F$ statistic indicated that the regional variability in $\Theta$ derived from nonuniform torsion of the LV chamber. Analysis of variance for repeated measures was performed to compare results for the five experimental stages. When justified by a significant $F$ statistic, Student’s $t$ test for paired observations was used to determine which of the means differed. Baseline data for the midventricular and
Results

Regional Torsional Deformations

The time course of the regional torsional deformation angles about the LV long axis for the midventricular and apical marker sites of a representative patient are compared in Figure 4. The contours of these curves were generally similar for each marker site, although the amplitudes varied from region to region. In the typical case, \( \Theta(t) \) increased rapidly during the systolic ejection phase, reaching a maximum value near the time of minimum LV volume. After this torsional deformation of the left ventricle during the active phase of contraction, a period of rapid recoil was observed during early diastole.

The values of \( \Theta \) during atrial pacing at the control heart rate are shown in Table 1 for each individual along with the group means. The corresponding radial (\( r \)) and longitudinal (\( l/L \)) coordinates of these markers at end-diastole are provided in Table 2. In patients 5 and 6, the apical marker in the lateral midwall (12) was missing, and in patient 5, the lateral midventricular marker (11) was also missing. Pairwise comparisons of the midventricular and apical markers of the anterior, inferior, and lateral midwalls reveals a significant increase in \( \Theta \) with increasing \( l/L \). In the inferior wall, the mean value of \( \Theta \) increased by 9.7° (\( p = 0.0001 \)) as \( l/L \) increased (\( p < 0.0001 \)) from 0.20 for the midventricular site (3) to 0.54 for the apical site (4). In the lateral wall, a slightly greater increase in \( \Theta \) of 12.7° (\( p = 0.0009 \)) was noted as \( l/L \) increased by a similar amount from 0.27 (site 11) to 0.63 (site 12). This was true even though the "midventricular" and the "apical" markers of the inferior wall were generally closer to the base than were the corresponding lateral wall markers. In the anterior wall, the increase in \( \Theta \) of 6.6° (\( p = 0.0003 \)) was substantially less despite a similar increase in \( l/L \) from 0.53 (site 7) to 0.83 (site 6); however, both markers of the anterior wall were generally closer to the apex than their counterparts in the inferior and lateral walls.

Variability in regional torsional angles (\( \Theta \)) could arise from three sources: nonuniformity of LV torsion, the expected increase in \( \Theta \) as a function of longitudinal distance from the reference minor axis, and errors in \( \Theta \) arising from slight deviations of the torsional axis from the "true" axis of symmetry of the ventricle. For example, consider the hypothetical situation of anterior, inferior, lateral, and septal markers with an equivalent \( l/L \). The axis of symmetry and torsional axis precisely coincide when \( r \) is the same for all four markers, and differences in \( \Theta \) would be attributable to nonuniform LV torsion. Now consider what would happen when the torsional axis is closer to the anterior marker; overestimation of \( \Theta \) would occur for the anterior wall marker, while \( \Theta \) would be artifactually underestimated for the inferior wall marker.

To elevate these sources of variability in \( \Theta \), analysis of variance with one within subjects factor (i.e., marker number) was applied to our regional torsional data, with \( l/L \) and \( r \) as covariants to take into account the increase in \( \Theta \) as a function of distance from the reference minor axis and to factor out errors in \( \Theta \) arising from our choice of torsional axis. This analysis revealed significant variability among marker sites (\( F = 6.83, p < 0.0001 \)), indicating nonuniformity of LV torsion. Both \( r \) and \( l/L \) were in fact significant.
compared. This regional variation in $\Theta_i$ is also readily
especially apparent when the adjusted mean values are
inferior (3 and 4), and septal walls (14). This is
6) than their counterparts in the lateral (11 and 2),
substantially lower for the anterior wall markers (7 and
TABLE 2. Radial and Longitudinal Coordinates at End-Diastole of Equatorial and Apical Sites During Steady-State Atrial Pacing at Control Rate

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Mean ± SD 3.39 ± 0.49 2.69 ± 0.66 3.32 ± 0.48 2.15 ± 0.74 2.83 ± 0.53 2.44 ± 0.68 3.23 ± 0.44 0.20 ± 0.13 0.54 ± 0.12

$p = 0.0001^*$ $p < 0.0001^*$ $p = 0.0003^*$ $p < 0.0001^*$

Values for the midventricular and apical markers of the inferior (3 and 4), anterior (7 and 6), and lateral (11 and 12) walls were compared by Student's $t$ test for paired observations. $p < 0.05$ denotes a significant difference; $n$, number of observations for the paired comparisons.

Effect of Atrial Pacing

The mean R-R intervals for the group were 633 ± 66 msec for the control beats, 484 ± 44 msec for the first
tachycardia beat, 481 ± 46 msec for the late tachycardia beats, 637 ± 72 msec for the initial post-tachycardia beat, and 565 ± 62 msec for the late intermediate rate beats as shown in Figure 3. On average, the R-R interval of the initial and late tachycardia beats differed minimally (3.5 ± 6.1 msec, \( p = \text{NS} \)); similarly, the R-R interval of the control and initial post-tachycardia beats differed by only 11.7 ± 16 seconds (\( p = \text{NS} \)). Thus, the conditions of the experimental design (close matching of the R-R intervals of the control beats to the initial conditions of the experimental design (close matching = \( \text{NS} \)).

Thus, the differences were not significant.

End-systolic pressure (\( P_{es} \)) was similar (\( p = \text{NS} \)) at all three steady-state pacing rates (Table 3). Shortening of the R-R interval decreased (\( p < 0.05 \)) end-diastolic volume by 7% from control values in the initial and steady-state tachycardia beats. The preload (\( V_{es} \)) of the intermediate steady-state beats was generally less than control and slightly greater than the tachycardia beats, but these differences were not significant.

LV end-diastolic volume was similar for beats with matched R-R intervals (Table 3). Shortening of the R-R interval decreased (\( p < 0.05 \)) end-diastolic volume by 7% from control values in the initial and steady-state tachycardia beats. The preload (\( V_{es} \)) of the intermediate steady-state beats was generally less than control and slightly greater than the tachycardia beats, but these differences were not significant.

End-systolic pressure (\( P_{es} \)) was similar (\( p = \text{NS} \)) at all three steady-state pacing rates (Table 3).

Compared with control, the velocity of circumferential fiber shortening was increased by 25% (\( p < 0.05 \)) in the initial post-tachycardia beat. Since these beats had similar loading conditions, this change reflects a mild increase in inotropic state. Though velocity tended to be greater in the steady-state tachycardia beats than in the initial post-tachycardia beat, the difference was not significant.

LV end-systolic volume of the initial post-tachycardia beats was on average 9 ml less (\( p < 0.05 \)) than control. This suggests a leftward shift in the end-systolic pressure-volume relation, confirming the enhanced contractility of the initial post-tachycardia beats.\(^{26}\) No other significant differences in end-systolic volume were observed; thus, the expected difference in inotropic state between initial and steady-state tachycardia beats could not be demonstrated in terms of an increase in either the extent (\( V_{es} \)) or velocity (\( V_{d} \)) of LV shortening.

Figure 5 illustrates the effect of abrupt rate switches upon torsional deformation and volume in a representative patient. The time-varying torsional deformation curves for marker 6 show greater torsion in the initial post-tachycardia beat than in the steady-state control beat (upper left); the value of \( \Theta_6 \) also is greater in the steady-state tachycardia beat than in the initial tachycardia beat (upper right). The associated volume curves (lower panels) confirm that the end-diastolic volume for these comparisons was closely matched.

Individual and group mean data for the apical markers of the inferior (\( \Theta_i \)), anterior (\( \Theta_a \)), and lateral (\( \Theta_l \)) walls are presented in Table 4. The increased contractility of the initial post-tachycardia beat was associated with small but significant increases in both \( \Theta_i \) and \( \Theta_l \) relative to control. A significant difference in \( \Theta_i \) also was demonstrated when the steady-state and initial tachycardia beats were compared; the change is in the same direction as the presumed change in contractility.\(^{13}\)

Interestingly, the apical portion of the lateral wall behaved differently; \( \Theta_3 \) was essentially unchanged by the experimental interventions. This was also true for the four midventricular sites (data not shown). Thus, regional heterogeneity in LV torsion and in its response to small perturbations in LV contractile state was demonstrated.

**Discussion**

The possible functional importance of torsion of the LV chamber has been a subject of interest. Mathematical models of ventricular mechanics,\(^4\) anatomic studies of myocardial fiber orientation,\(^3\) and experimental studies of ventricular mechanics in anesthetized dogs\(^5\) provide evidence for this phenomenon. Torsional deformation can also be inferred from earlier studies by our group.\(^9\) The present investigation uses myocardial marker techniques to confirm that torsional deformation is characteristic of LV mechanics in humans and to demonstrate that the torsional deformation about the long axis of the human left ventricle is nonuniform and sensitive to small alterations in the contractile state of the ventricular myocardium.

Streeter\(^3\) described a gradual change in fiber angle across the LV wall from epicardial to endocardial surfaces. In the human ventricle, left-hand obliquity was observed among subepicardial fibers; a circumferential orientation was predominant among midwall fibers; and right-hand obliquity prevailed among subendocardial fibers. Streeter further demonstrated an imbalance of right- and left-hand oblique modes with a greater number of fibers that assumed the left-hand obliquity (see his Figure 34). He suggested that this imbalance causes a torque in the apex and may be a factor responsible for the twisting motion.
Table 3. Effect of Abrupt Alterations in Heart Rate Upon Hemodynamics

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Mean ± SD 18.7 ± 6.3 17.9 ± 6.0* 19.2 ± 5.0* 21.2 ± 5.5* 19.9 ± 5.4 13.4 ± 6.0 12.7 ± 6.8 † 14.5 ± 7.2 15.6 ± 7.5† 14.5 ± 6.8

F = 5.98  F = 8.03

p = 0.0008  p = 0.0001

*Denotes significant difference (p<0.05) vs. T1 by Student's t test for paired observations; † denotes significant difference (p<0.05) vs. Gl by Student's t test for paired observations.

Table 4. Effect of Abrupt Alterations in Heart Rate Upon Torsional Deformation Amplitude of Apical Sites

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Mean ± SD 18.7 ± 6.3 17.9 ± 6.0* 19.2 ± 5.0* 21.2 ± 5.5* 19.9 ± 5.4 13.4 ± 6.0 12.7 ± 6.8 † 14.5 ± 7.2 15.6 ± 7.5† 14.5 ± 6.8

F = 5.98  F = 8.03

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*Denotes significant difference (p<0.05) vs. T1 by Student's t test for paired observations; † denotes significant difference (p<0.05) vs. Gl by Student's t test for paired observations.

commonly seen at the apex of the beating exposed heart.

In the present study, counterclockwise twisting about the LV long axis of midventricular and apical regions relative to the base (as viewed from apex to base) was observed in all patients. Twisting in this direction suggests that the subepicardial fibers, which spiral with a left-hand screw, influence midwall dynamics of the human left ventricle to a greater extent than do the less numerous subendocardial fibers. This appears to be true for all sites studied, including the septum. The myofibers are imbedded in a complex network of heavily cross-linked collagen; this may provide a functional connection among such fiber layers. Continuity of subepicardial and subendocardial fibers at the LV apex, described by Torrent-Guasp and others, may also be important in the genesis of LV torsion.

Regional Heterogeneity of LV Torsion

In the mathematical model of ventricular mechanics proposed by Arts et al., uniform torsion of a thick-walled cylinder composed of an anisotropic material is assumed. The deformations predicted by this model compare closely with subsequent measurements in canine experiments. Our data strongly suggest, however, that torsional deformation of the transplanted human heart is nonuniform (Table 1). Torsional deformation angles were greatest in the apical portion of the lateral wall, were intermediate in the inferoapical wall, and were smallest in the anteroapical wall. Although marker placement definitely affects these measurements of torsion (i.e., Θ increases with increasing distance from the reference axis), these regional differences remain after these factors are considered. It is interesting that Greenbaum et al. noted considerable variability in LV fiber architecture in humans. Near the apex of the lateral wall, these investigators found a paucity of circumferential fibers; subepicardial fibers with left-hand obliquity were particularly numerous in this region. This unique transmural distribution of fiber angles is probably an important factor contributing to the greater torsion of...
the apical portion of the lateral wall. Anteriorly, the superficial fibers cross the interventricular sulcus at right angles to the ventricular long axis. This circumferential orientation of epicardial fibers in the vicinity of our anterior wall markers may explain, in part, their smaller torsional angles. Asymmetric attachments of the heart to the mitral annulus and aorta may also contribute to such regional variability as well.

**Contractile State Dependence of LV Torsion**

Abrupt shortening of the R-R interval reduces myocardial contractile state in the initial tachycardia beat (which is a "premature" beat), but such rate-related reductions in contractile strength are transient with a "staircase" increase in contractility observed in the beats that follow.\(^1\) Subsequent abrupt lengthening of the R-R interval with return to the control rate further increases the inotropic state in the initial post-tachycardia beat (which is a "postmature" beat); this effect is also transient with contractility waning in successive beats (the "reverse staircase"), eventually returning to control level. The atrial pacing protocol used in the present study was designed to exploit such rate-related changes in the contractile state of the ventricular myocardium.

The relatively narrow range of atrial pacing rates in these transplanted hearts limited the range of inotropic states in the present study. In isolated papillary muscle,\(^2\) in the isolated canine ventricle,\(^2\) and in the isolated canine ventricle,\(^3\) the contractile strength of programmed extrasystoles rises exponentially as the R-R interval immediately preceding the extrasystolic contractions is increased from the shortest coupling interval, reaching a plateau at R-R intervals above 800–1,000 msec. The force-contraction relation described in this manner is shifted "upward and to the left" (i.e., in the direction of enhanced contractile state) when the pacing rate of the steady-state beats preceding the extrasystoles is increased from 60 to 160 beats/min.\(^2\) In our study, the average change in heart rate was only 30 beats/min. Based on the work of Burkoff et al,\(^2\) the change in contractile state associated with an abrupt change in heart rate of this size should be relatively small. Indeed, this appears to be the case as judged by the relatively small changes in LV shortening velocity as summarized in Table 3.

Torsional deformation amplitude, as measured by the anteroapical (\(\Theta_1\)) and inferoapical (\(\Theta_2\)) markers, reflected changes in inotropic strength at least as well as shortening velocity. Comparison of the control and initial post-tachycardia beats revealed that \(\Theta_1\) and \(\Theta_2\) changed significantly and in the same direction as shortening velocity. Comparison of the initial and steady-state tachycardia beats also disclosed significant changes in \(\Theta_1\), that were in the presumed direction of change in contractility; though the mean values of shortening velocity and \(\Theta_1\) were also greater in the steady-state tachycardia beats, the differences were not significant for these two variables.

The response of the apical region of the lateral wall to these alterations in myocardial contractile state was distinctly different. Unlike the anteroapical and inferoapical sites, torsional deformation amplitude of the lateral marker (\(\Theta_1\)) was essentially unchanged by rate-related changes in contractile state. While the reason for this intriguing difference among apical sites is uncertain, the insensitivity of midventricular sites to such changes in contractile state probably reflects reduced signal-to-noise and the low intensity of the contractile stimulus.

**Limitations**

Although we can be quite sure that torsional deformation occurs about the LV long axis as defined in this study, we cannot be sure that the torsional axis we have chosen is a favored axis of the ventricle about which maximal torsional deformation occurs. Our choice of the torsional and reference axes was not entirely arbitrary. To relate our findings to myocardial fiber architecture, the LV long axis was chosen to correspond as closely as possible to that used by Streeter\(^2\) in his anatomic studies. For the human cadaver heart, Streeter used the center of each transverse segment to define the \(z\), or LV long, axis. The midpoint between the inferobasal and anterobasal markers should be analogous. These two sites were chosen over the lateral and septal sites at the basal level since epicardial landmarks in the form of the posterior descending and left anterior descending arteries permit more consistent marker placement. The placement of the LV apex marker should also be rather consistent since the apical dimple is usually readily apparent. While there are numerous other ways in which these axes could have been defined, established conventions obviously are nonexistent, and our approach of using well-defined

### Table 4. (Continued)

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\[21.8 \pm 11.7 \quad 20.6 \pm 10.5 \quad 20.7 \pm 11.8 \quad 21.0 \pm 11.4 \quad 21.4 \pm 12.1\]

\[F = 1.23\]

\[p = 0.3158\]
epicardial landmarks should offer the greatest chance of reproducibility.

Although regional heterogeneity of torsional deformation was demonstrated, several potentially important sources of artifact should be mentioned. Among these is the possibility that transmural gradients in torsional deformation of the LV wall influenced our results. This could arise from variability in the depth of insertion or in the relative thickness of transmural fiber layers. To minimize this potentially important factor, a flanged tool that defines the depth of penetration was used to insert the markers. In most instances, the markers should be located among the circumferentially oriented LV midwall fibers at a depth of approximately 5 mm below the epicardial surface, but we cannot verify this in these clinical studies.

The transplanted human left ventricle is subject to injury due to ischemia at the time of transplantation or episodes of acute allograft rejection postoperatively. It has been noted that myocyte necrosis of the transplanted primate heart may be quite severe in certain areas, while other areas are relatively spared; thus, the nonuniformity observed in this study may reflect, in part, regional variability in the contractile performance of the transplanted human heart. We would have expected, however, that regional differences in contractile performance due to these types of myocardial injury would have been randomly distributed. Furthermore, recent studies have shown that the contractility and contractile reserve of the transplanted human left ventricle are normal, and studies from our laboratory demonstrate that the amplitude of LV torsional deformation returns to prerejection values with successful treatment of acute allograft rejection. Patients with acute rejection were specifically excluded from this study.

Much controversy exists regarding the best way to quantify the afterload of the intact, ejecting left ventricle. LV end-systolic pressure and wall stress have been frequently used as measures of afterload; however, philosophical objections to this approach have been raised because the ventricle determines, in part, its own afterload when these variables are used. It may be preferable to consider the load imposed by the arterial tree as the true afterload opposing LV ejection. In our study, end-systolic pressure was unchanged by steady-state changes in contraction frequency, suggesting that LV afterload was similar for
all three steady-state conditions. Though the end-systolic pressure of the initial beat after abrupt rate switches was not measured, we assume that reflex-mediated changes in the arterial load would not occur over this short interval.24 We believe that the rapid rate-switch technique, therefore, permitted us to assess the effect of altered inotropic state on the torsion of the LV chamber independent of both preload and afterload.

In summary, this investigation provides direct evidence for nonuniform torsional deformation of the transplanted human left ventricle. The counterclockwise twisting about the LV long axis we observed, as well as the nonuniformity, can be readily related to the fiber architecture of the human ventricle. Lastly, these data suggest a dependence upon the contractile state of the ventricular myocardium that is attenuated in the lateral wall. While torsional deformation amplitude may prove to be a sensitive index of contractility function, we suspect that certain regions may be more suitable than others in this regard.

Acknowledgments
We would like to thank Margaret D. Allen, MD, Edward B. Stinson, MD, John C. Baldwin, MD, and Philip E. Oyer, MD, from the Department of Cardiovascular Surgery, who inserted the myocardial markers; and Suzanne B. McCarthy and Elaine Moore for help in the preparation of this manuscript. We would also like to thank Geraldine C. Derby, Anne Schwarzkopf, and Carol W. Mead for their contributions. 

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**KEY WORDS** • torsional deformation • ventricular mechanics • inotropic state • tachycardia
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D E Hansen, G T Daughters, 2nd, E L Alderman, N B Ingels, Jr and D C Miller

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