Dissociation Between Left Ventricular Untwisting and Filling
Accentuation by Catecholamines

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Background. Efficient early diastolic filling is essential for normal cardiac function. Diastolic suction, as evidenced by a decreasing left ventricular pressure during early filling, could result from restoring forces (the release of potential energy stored during systolic deformation) dependent on myofilament relaxation. Although these restoring forces have been envisioned within individual myofibers, recent studies suggest that gross fiber rearrangement involving the connective tissue network occurs early in diastole. This may lead to the release of potential energy stored during systole and suction-aided filling.

Methods and Results. To establish precisely the timing and extent of restoration of the systolic torsional deformation of the left ventricle with respect to early filling at baseline and with enhanced relaxation, we studied untwisting during control conditions and with catecholamine stimulation. Using noninvasive and nondestructive magnetic resonance tagging, torsional deformation of the left ventricle was measured at 20-msec intervals in 10 open-chest, atrially paced dogs, starting at aortic valve closure. Eight equiangular tags intersected the epicardium and endocardium in three short-axis imaging planes (base, mid, and apex). From the intersection points, epicardial and endocardial circumferential chord and arc lengths were measured and angular twist of mid and apical levels with respect to the base (maximal torsion and its reversal, untwisting) was calculated. Echo-Doppler provided timing of aortic valve closure and of mitral valve opening. Zero torsion was defined at end diastole. Torsion at the apical level reversed rapidly between its maximum and the time immediately after mitral valve opening: from 7.0±5.4° to 12.0±8.5° to 6.9±7.8° (mean±SD, both p<0.01) at the epicardium and endocardium, respectively. During the same period, no significant circumferential segment length changes occurred. As expected, after mitral valve opening, filling resulted in significant circumferential segment lengthening, whereas further reversal of torsion was small and nonsignificant. During dobutamine infusion, torsion at end systole was greater and reversal during isovolumic relaxation was much more rapid and greater in extent (p<0.01). Torsion reversed from 11.5±4.3° to 5.7±4.8° and 17.4±6.4° to 6.9±7.7° at epicardium and endocardium.

Conclusions. Untwisting occurs principally during isovolumic relaxation before filling and is markedly enhanced in speed and magnitude by catecholamines. This partial return of the left ventricle to its prejection configuration before mitral valve opening could represent an important mechanism for the release of potential energy stored in elastic elements during the systolic deformation. These myocardial restoring forces would be markedly enhanced by physiological changes consequent to catecholamines such as during exercise, offsetting the concomitant shortening of the filling period. (*Circulation* 1992;85:1572–1581)

KEY WORDS: left ventricular filling • dobutamine • regional function • biomechanics

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ormal left ventricular (LV) filling is dependent on myofilament relaxation, left atrial pressure, atrial contraction, and passive LV compliance.1–3 When one of these functions is impaired or when the filling period is shortened and stroke volume is increased during physiological stress,4,5 maintaining cardiac output is more and more dependent on early rapid filling. Ventricular suction, the intrinsic capability of the left ventricle to create an atrioventricular gradient, is an additional means of achieving efficient early filling.6 Suction is manifested by a decreasing LV pressure during early filling; its existence has been proven in experimental models in which mitral valve opening (MVO) is delayed and negative transmural pressures are observed.7,8 The underlying mechanism for LV suction has not been identified. Restoring forces, providing elastic recoil after ventricular contraction, could

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cause ventricular suction during normal conditions and could be enhanced by catecholamines released during stress, but their exact nature is unclear.9

Torsional deformation of the left ventricle or twist during systole is one possible mechanism by which potential energy could be stored during ejection and then released during diastole to create suction and fast early filling. This could be achieved by straining the intercellular collagen matrix,10 which on relaxation would release its stored energy and restore the diastolic configuration of the ventricle. Although the torsional deformation of the left ventricle during systole has been studied extensively with several techniques,10–19 the timing and extent of the recoil or untwisting has only recently been a focus of attention. Beyar et al.15 measured rotational deformation throughout the cardiac cycle using radiopaque markers implanted in the myocardial midwall and found that a substantial release of torsion occurred during early diastole. In the present study, we measured the reversal of epicardial and endocardial torsion of the canine left ventricle and the changes in circumferential segment length, starting at aortic valve closure, encompassing isovolumic relaxation, MVO, and early filling using nuclear magnetic imaging with tags, noninvasive markers of the myocardium.20 Valve opening and closure were timed by echo-Doppler measurements. To study the effect of a shortened filling period and increased contractility and relaxation, the same measurements were also obtained during dobutamine infusion.

We tested the hypotheses that untwisting occurs principally before filling, when LV cavity size is constrained and suction could develop, and that its extent during isovolumic relaxation is enhanced by dobutamine infusion. Such evidence would support the importance of untwisting as the release mechanism of restoring forces and the likelihood that untwisting plays a critical role in efficient early diastolic filling.

Methods

Nuclear magnetic imaging with tagging was used to mark sites in the myocardium noninvasively and to image the left ventricle at different times during diastole.20 These markers or tags provide the means to calculate torsion and circumferential segment length from the same image acquisition and to measure their changes over time during the cardiac cycle.11,21

Magnetic Resonance Image Myocardial Tagging

The technique of myocardial tagging used in these experiments has been reported in detail in previous studies from this laboratory.11,20 Tags are noninvasive markers that appear as dark stripes on the white myocardium. When placed at end diastole and imaged at other times in the cardiac cycle, they show the displacement and deformation of the myocardium on which they were inscribed. Tagging is achieved by selective radiofrequency saturation of thin planes intersecting the myocardium in a pattern predefined by the operator. In the tagged regions, tissue protons are in a different state of magnetization from those in nontagged regions. This difference in magnetization persists for a time mainly dependent on the longitudinal relaxation time (T1) of the myocardium, which for magnetic field strengths of 0.3–0.6 T is about 400–500 msec. During that time, a standard spin-echo magnetic resonance image acquired orthogonally to the tagging plane will demonstrate a difference in the signal intensity between the tagged and nontagged regions.

Experimental Protocol

Ten adult mongrel dogs (20–22 kg) were studied. The dogs were anesthetized with sodium pentobarbital 25–35 mg/kg and ventilated with a Harvard ventilator. Additional sodium pentobarbital was administered during the study to obtain a steady anesthesia. All dogs had jugular venous lines for fluid administration and a carotid intra-arterial line for pressure monitoring. A left thoracotomy was performed, and the pericardium was opened anteriorly. A pacing lead was sutured to the right atrial appendage, and a Gould heart sound sensor was positioned near the aortic arch with its wires extending through the anterior chest wall to a Gould eight-channel ink recorder system. The heart was replaced in the pericardial sac, which was left open, and the chest wall was approximated. All dogs were atrially paced at an RR interval of 400 msec. Aortic pressure tracings were recorded intermittently between actual image acquisitions to monitor hemodynamic stability.

The dogs were studied under control conditions and during increased contractility and intrinsic relaxation induced by dobutamine infusion. The dose of dobutamine was adjusted to increase mean arterial blood pressure by 10%. This intervention increased intrinsic heart rate by 20–30 beats per minute, and atrial pacing was resumed at least 5–10 beats per minute higher, depending on the variability of the intrinsic rate. A stable and regular heart rate, required for high-quality images, could be obtained only in five of the 10 dogs. In one of the five excluded dogs, this was due to excessive bleeding after dobutamine infusion. The five remaining dogs were paced at heart rates between 190 and 205 beats per minute.

To assure that opening the chest does not alter the overall measurements and conclusions, five additional dogs were studied with a closed-chest preparation using Doppler to time aortic closure and a transvenous pacemaker (repositioned when necessary to continue capturing).

Imaging Protocol

Imaging parameters. Images were acquired on a 0.38-T iron-core resistive magnet (Resonex, RX4000) using a spin-echo sequence modified as above to include tagging, with time to echo (TE)=30 msec, repetition time (TR)=RR interval, using 128 phase and frequency encoding steps and averaging two (or rarely four) excitations. The image slice thickness was 10 mm in all cases. The tag width was 3.5 mm.

Location of imaging planes. After positioning the dog in the magnet, a series of scout images was acquired so that the orientation of the heart in each animal could be assessed and short-axis cardiac images could be obtained. From the axial image that traversed the largest left ventricular cavity area, a new image plane that passed through the left ventricular apex and was parallel to the septum was selected by using visual estimates. This defined a left ventricular long axis. Perpendicular
to this long axis, five parallel short-axis LV planes were selected and imaged using a multislice sequence. From these five short-axis images three were chosen, located at the midventricular level and 15 mm to either side of this middle image. The orientations of four equiangular tag planes, centered at the visual center of the LV cavity on each image plane, were then obtained. One tag plane was chosen to be equivalent to the echocardiographic apical four-chamber projection. As the four tag planes were equiangular, the positions of the other tags were therefore standardized from day to day. After this series of scouts, images of the three LV short-axis planes, with 3.5-mm-wide tags applied at end diastole (the first negative deflection of the R wave of the electrocardiogram), could then be acquired at the specified times (Figure 1).

**Timing of image acquisition.** Gated images were acquired by entering the desired delay after the electrocardiographic QRS. A Hewlett-Packard 77020A echo-Doppler system with a 2.5-MHz duplex probe was used to determine the time of aortic valve closure and MVO with respect to the QRS by identifying the mitral and aortic flow velocity profiles and valve clicks with continuous-wave Doppler. Control echo-Doppler measurements were obtained at the beginning of each study. During control conditions, imaging commenced at the time of aortic valve closure and was repeated at 20-msec intervals. For the dobutamine intervention, the echo-Doppler was performed at the end of the imaging sequence because removing the dogs from the magnet to use the Doppler between control and dobutamine imaging would have altered the slice orientation. Because the systolic period is shortened by dobutamine, the time of aortic valve closure with respect to the QRS was determined by a phonocardiographically determined second heart sound, which can be done inside the magnet. The value was rounded down to the nearest 10 msec. The exact timing of aortic valve closure and MVO was determined by echo-Doppler after removal of the dog from the magnet.

**Imaging sequences for obtaining 20-msec time resolution.** The total time required for each image frame including radio frequency pulses and gradient generation, was 56 msec. It was therefore impossible to acquire images 20 msec apart in one sequence. To obtain the desired time resolution, three interleaved sequences separated by a 20-msec delay were used, each sequence acquiring three images at 60-msec intervals. Specifically, during any one image acquisition the basal, mid, and apical levels were acquired at times separated by 60 msec. The locations of the three imaging planes were then rotated for the next two acquisitions. This entire sequence was then twice repeated, each time adding an additional 20-msec delay after the QRS. A complete set of images therefore required nine acquisitions.

Because images were acquired during nine acquisitions and each takes 512 cardiac cycles for a total duration of about 40 minutes, constancy of heart rate and hemodynamic stability were obtained by pacing and monitored by arterial pressure readings.

**Analysis**

The three image planes used in this study correspond to three short-axis levels of the left ventricle, i.e., basal, mid, and apical. The four tag planes, perpendicular to these image planes, cross at the center of the left ventricular cavity and form a star pattern on each image level. At a specific image level, tags (being radial lines) intersect with both endocardium and epicardium. These intersection points, eight for both epicardium and endocardium at each image level, were identified as X,Y coordinates on a Dell 310 computer-based contouring system (Cardiology Image Processing System, JHU). Endocardial and epicardial contours were also created with an Akima algorithm, which uses the intersection points of the tag lines with endocardium and epicardium to create smooth contours. These contours were subsequently manually adjusted to fit the actual epicardial and endocardial surfaces optimally. From these data, torsion angles and circumferential segment lengths were calculated.

**Calculation of Torsion Angle**

The technique of analysis used in these experiments is similar to the technique previously described in human studies. Considering the epicardial and endocardial points separately, the centroid of these points was calculated and the slopes of the lines connecting each tag intersection point and the corresponding centroid were calculated and expressed as an angle. This was done for the epicardial and endocardial intersection points of the basal, mid, and apical images at each time point.

To subtract out the effect of rigid body rotation and whole-heart translation, the image of the basal plane at each time point was used as a reference. The difference in the slope of the line connecting a tag point on the basal plane with its centroid and the line connecting the corresponding tag point to its centroid on the more apical plane was calculated, and its arctangent was called the torsion angle (Figure 2). This angle is the difference, at each time point, between the position of a basal tag point and the corresponding tag point on the more apical image level, expressed as an angle of rotation. Because there was no difference in the relative positions of these two points at end diastole (the tags being inserted as a plane in all slices simultaneously), this angle represents the rotation of one point with respect to the other one between end diastole and the time of the measurement. Zero torsion is the reference at end diastole, the time of tag insertion. Increasing angle (positive sign) indicates counterclockwise rotation of a point on a more apical slice when viewed looking from the apex toward the base.

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**Figure 1.** Schematic diagram of tag planes intersecting the long axis of the left ventricle. The relation of only one image plane and two tag planes is depicted (left). At end diastole, the tag planes form a star pattern in each imaging plane; tag planes are seen as radial lines (center). At end systole, the myocardial tags twist and bend, reflecting myocardial deformation (right).
Intraobserver variability was tested by comparing the calculated angles from two analyses by the same observer. The mean differences (±SD) in the angles were 0.77±0.65° and 1.52±1.21° for the epicardium and endocardium, respectively.

Calculation of Segment Length

Regional circumferential shortening was calculated in two ways. First, using the coordinates of the intersections of the tags with epicardium and endocardium, epicardial and endocardial chord lengths were calculated. Second, using the epicardial and endocardial contours, the arc lengths between each adjacent pair of tag intersection points on the epicardial and endocardial surfaces were calculated (Figure 3). Both sets of measurements were then expressed as percent change from the first (end-systolic) time point to every other time point. Zero lengthening is the reference at end systole. Positive lengthening values represent increasing segment lengths with respect to the length at end systole. No significant differences existed between the two methods in these normal ventricles. Arc length changes are reported.

Dissociation of Untwisting and Circumferential Segment Lengthening From Filling

The dissociation of untwisting from filling is expressed as the percentage of untwisting that occurred before the onset of filling, that is, MVO as measured by echo-Doppler. MVO usually did not exactly coincide with an image time; therefore, the linearly interpolated value between the two adjacent imaging time points was used for the percent calculation. The dissociation of untwisting from filling is defined as the peak torsion (at any time) minus the torsion at the time of MVO (interpolated linearly between the two imaged times bracketing MVO) divided by peak torsion. Similarly, the dissociation of segment lengthening from filling is defined as the percentage circumferential segment lengthening at the time of MVO (interpolated linearly between the two times bracketing MVO) minus the smallest or most negative percentage segment lengthening (at any time during isovolumic relaxation). However, actual data points for torsion and segment length given in the “Results” section and in the tables refer to the value of torsion or segment length closest to MVO rather than an interpolation, because the standard errors for interpolations are not meaningful.

Statistical Analysis

The results from each time point were analyzed separately. Epicardial results were analyzed separately from endocardial results. Differences between the time points were tested using an analysis of variance with repeated measures. If a significant difference was found, subgroup analysis using Scheffe and Student-Newman-Keuls techniques was performed. Results are presented in tabular and graphical form as mean torsion angles and percent segment lengths at either epicardium or endocardium at one image level. For control, the results of 10 dogs are reported. For dobutamine, the results of five dogs are presented. Student’s t test for paired observations was used to compare results between the control and dobutamine conditions.

Results

Control Conditions

A consistent dissociation in time was observed between untwisting and filling. Approximately 50% of untwisting occurred before MVO, whereas circumferential segment lengthening occurred nearly entirely after MVO, during filling. This is demonstrated in Figure 4, showing apical epicardial and endocardial
mean torsion angle and segment length changes versus time for 10 control dogs. Apical torsion decreased (untwisting) from 7.0±5.8° to 3.2±5.4° (p<0.01) and 12.0±8.5° to 6.9±7.8° (±SD, p<0.01) at epicardium and endocardium, respectively. This corresponds to 54% and 44% untwisting before MVO, respectively. During the same interval, apical circumferential segment length remained essentially constant (p=NS) from 1.7±1.3% to 2.0±1.5% and −0.3±1.1% to 3.0±2.1% at epicardium and endocardium, a 2.8% and 3.9% length change before MVO, respectively. The segment length change at the endocardium between 200 and 220 msec reached borderline significance (p=0.05). After MVO, torsion at the apex further decreased nonsignificantly (p=0.06) to 2.2° and 3.8° at 340 msec, respectively, whereas segment lengthening occurred at a fast rate to maximum levels (15.2% and 30.5% at epicardium and endocardium, respectively; p<0.01). Values for all time points are reported in Table 1.

At the midventricular level, torsion declined from 3.1±2.9° to 1.5±3.3° (p<0.01) and from 5.8±5.0° to 4.2±5.6° (p<0.01) at epicardium and endocardium, respectively. This corresponds to 52% and 31% untwisting before MVO. Changes in segment length during the same time period were nonsignificant (3.0% and 1.7% at epicardium and endocardium, respectively). After MVO, segment lengthening was significant for epicardium and endocardium (both p<0.01), whereas the torsional change was significant only at the endocardium for the first time interval (260 versus 280 msec, p<0.05) and at 320 msec (versus 300 and 340 msec, p<0.01).

As previously reported, in humans,8 torsion of the apex is larger than torsion of the mid, and endocardial torsion is larger than epicardial torsion at each level. This is related to differences in distance from the basal reference slice (h in Figure 2) and in radius from the cavity centroid.

**Dobutamine Infusion**

This intervention resulted in a decrease of cycle length from 400±3 to 300±26 msec and an increase of

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**TABLE 1. Measurements for Torsion and Segment Length in Control Studies**

<table>
<thead>
<tr>
<th>Control Time (msec)</th>
<th>Mean Torsion (degrees)</th>
<th>Mean Segment Length (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Epi</td>
<td>Endo</td>
</tr>
<tr>
<td>180 AVC</td>
<td>3.1</td>
<td>5.5</td>
</tr>
<tr>
<td>200</td>
<td>2.8</td>
<td>5.8</td>
</tr>
<tr>
<td>220</td>
<td>2.7</td>
<td>5.0</td>
</tr>
<tr>
<td>240 MVO</td>
<td>1.5</td>
<td>4.2</td>
</tr>
<tr>
<td>260</td>
<td>1.4</td>
<td>3.0</td>
</tr>
<tr>
<td>280</td>
<td>1.5</td>
<td>2.1</td>
</tr>
<tr>
<td>300</td>
<td>1.2</td>
<td>1.8</td>
</tr>
<tr>
<td>320</td>
<td>0.9</td>
<td>2.8</td>
</tr>
<tr>
<td>340</td>
<td>0.6</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Time: timing of image acquisition after the peak of QRS. As a reference, occurrence of aortic valve closure (AVC) and mitral valve opening (MVO) are shown. Torsion: torsion expressed in degrees of the epicardium (Epi) and endocardium (Endo) at the mid and apical level, referenced to the basal level. Segment length: circumferential segment length expressed as percent lengthening at each time point with respect to the first (end-systolic) time point. Results for epicardium and endocardium at base, mid, and apex. Values are mean±SD. n=10 dogs.
mean blood pressure from 142±17 to 160±21 mm Hg (both \(p<0.001\)). Because of the increased heart rate, only seven time points were available. The first time point was a mean of 8 msec before aortic valve closure, as measured by Doppler. Mean time of occurrence after the peak of the QRS shifted from 178 to 158 msec for aortic valve closure and from 243 to 195 msec for MVO, shortening the isovolumic period from 65 to 37 msec.

The dissociation between untwisting and filling observed during control conditions is further accentuated by this intervention. Figure 5 shows the results for apical torsion and segment length during dobutamine infusion. All values are reported in Table 2. At the apical level, torsion decreased from 11.5±4.3° to 5.7±4.8° and from 17.4±6.4° to 6.9±7.7° at epicardium and endocardium, respectively, corresponding to a 58% and 67% untwisting before MVO. The reduction in torsion for the midventricular level is from 5.0±1.9° to 1.4±1.5° and from 6.8±2.7° to 2.2±4.1° at epicardium and endocardium, respectively, corresponding to a 73% and 65% untwisting before MVO. No further significant change in torsion angle occurred after MVO. Both the absolute amount of torsion that had dissipated by the onset of filling and the extent of untwisting before MVO were significantly increased after dobutamine stimulation compared with control (\(p<0.01\) for both parameters). By contrast, during isovolumic relaxation, segment lengthening was significant only between 170 and 190 msec at the apical endocardium (2.3% and 11.6% lengthening at epicardium and endocardium, respectively). At the epicardium and endocardium of the mid level, shortening continued until 190 msec and was immediately followed by significant lengthening (10.5% and 16.8%, respectively).

The absolute values of torsion were significantly higher during dobutamine infusion compared with control: Maximal torsion at the apical epicardium and endocardium, dobutamine versus control, was 11.5±4.3° versus 7.0±5.8° and 17.4±6.4° versus 12.0±8.5° (±SD), respectively. As expected, circumferential lengthening increased with dobutamine (\(p<0.01\), paired results); shortening of the base increased more than that of the midventricle or apex during the dobutamine intervention.

### Table 2. Measurements for Torsion and Segment Length in Dobutamine Studies

<table>
<thead>
<tr>
<th>Time (msec)</th>
<th>Mean torsion (degrees)</th>
<th>Mean segment length (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mid Epi</td>
<td>Endo</td>
</tr>
<tr>
<td>150 AVC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>170</td>
<td>5.0</td>
<td>6.8</td>
</tr>
<tr>
<td></td>
<td>(1.9)</td>
<td>(2.7)</td>
</tr>
<tr>
<td>190 MVO</td>
<td>1.3</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>(2.6)</td>
<td>(4.0)</td>
</tr>
<tr>
<td>210</td>
<td>1.4</td>
<td>2.2</td>
</tr>
<tr>
<td></td>
<td>(1.5)</td>
<td>(4.1)</td>
</tr>
<tr>
<td>230</td>
<td>1.3</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>(4.0)</td>
<td>(7.2)</td>
</tr>
<tr>
<td>250</td>
<td>2.2</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td>(5.7)</td>
<td>(9.5)</td>
</tr>
<tr>
<td>270</td>
<td>2.1</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>(2.6)</td>
<td>(4.3)</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>(3.9)</td>
<td>(5.5)</td>
</tr>
</tbody>
</table>

**Time:** timing of image acquisition after peak of QRS. As a reference, occurrence of aortic valve closure (AVC) and mitral valve opening (MVO) are shown. Torsion: torsion expressed in degrees of the epicardium (Epi) and endocardium (Endo) at the mid and apical level, referenced to the basal level. Segment length: circumferential segment length expressed as percent lengthening at each time point with respect to the first (end-systolic) time point. Results for epicardium and endocardium at base, mid, and apex.

**Values are mean±SD.** \(n=10\) dogs.
Regional Untwisting

Table 3 shows the extent of early untwisting in individual LV regions. The segments labeled in Figure 3 as 1–3 are considered septal, 4–5 inferoposterior, and 6–8 anterior. Torsion is reported from the mid and apical epicardium and endocardium. Only two time points are given: at the time of peak mean torsion and at the point closest to MVO (240 and 190 msec during control and dobutamine, respectively).

During control conditions, the amount of maximal torsion was smallest in the anterior region. However, the percent untwisting at the time of MVO was significantly greater in the anterior region compared with septum and inferoposterior (p<0.01). At the mid and apical anterior epicardium, negative torsion was observed. (In these cases, untwisting is expressed as 100% in Table 3.)

During dobutamine stimulation, maximal torsion became more homogeneous, whereas regional differences in untwisting became accentuated. The extent of untwisting in the anterior wall was greater than that in the inferoposterior wall, which was greater than that in the septum (p<0.01), except at the apical endocardium, in which only anterior was different from septum and inferoposterior.

Comparing control and dobutamine, the extent of septal untwisting at MVO remained unchanged at the endocardium and decreased at the epicardium, whereas inferoposterior early untwisting increased significantly (p<0.01) at the mid epicardium and endocardium and the apical endocardium. Anterior untwisting increased significantly at the mid endocardium.

Regional differences in the extent of early untwisting were present under control conditions and became accentuated with dobutamine stimulation; the regions showing the largest increase of torsion with dobutamine also showed the most complete untwisting by the time of MVO.

Effect of Open-Chest Preparation on Untwisting

Five additional dogs were studied with a closed-chest preparation using Doppler to time aortic closure and a transvenous pacemaker. Apical values of peak torsion and torsion at the time of MVO were 7.7±5.2° and 4.2±5.1° for epicardium and 14.2±7.8° and 8.4±8.1° (±SD) for endocardium. This corresponds to 45% and 41% untwisting at the time of MVO, not significantly different from the open-chest preparation reported above.

Discussion

This study establishes that in the open-chest canine model, untwisting and filling are dissociated in time and
that this dissociation is further accentuated by dobutamine stimulation. Ventricular torsional deformation was examined using noninvasive magnetic resonance imaging and tagging to prevent any interference of the measuring technique with myocardial deformation. Both torsion and circumferential segment length were measured using the same tag intersection points and related to Doppler-derived timing of aortic valve closure and MVO. Untwisting occurred mainly before MVO, whereas circumferential segment lengthening was present mainly during filling. Dobutamine enhanced the extent of untwisting before MVO and further accentuated the dissociation between untwisting and filling. Regional inhomogeneity of untwisting was also further accentuated by dobutamine.

Relevance to Filling

We speculate that the occurrence of untwisting during isovolumic relaxation, when cavity volume is restrained, promotes the development of suction, inducing explosive LV filling after MVO.

The torsion that occurs during ejection is counterclockwise, that is, in the direction of the epicardial fibers and perpendicular to the endocardial fibers. Ingels et al.\(^ {13}\) have postulated that epicardial contraction dominates the direction of torsion because these fibers are at larger radii and therefore produce greater torque than do those in the inner layers. The process can be viewed as a spring between the epicardium and endocardium that is stretched during systolic thickening as the epicardium twists and moves inward but the endocardium moves further inward. As epicardial fibers relax and begin to lengthen along their fiber direction during isovolumic relaxation,\(^ {24}\) they dominate the direction of untwisting, and the epicardium starts to move outward as it unwinds. The spring is stretched further at its epicardial side and part of the force that stretched it at its endocardial side is released; therefore a pulling force on the endocardium develops but cannot displace it because the intracavitary volume is constant during isovolumic relaxation. This could, however, contribute to a faster pressure decay in the cavity and therefore decrease the time constant of pressure fall. The more torsion reversal that has occurred by the time of MVO, the more rapid the release of potential energy will be in the form of a negative transmural pressure creating an atrioventricular gradient for filling. Although almost no circumferential segment lengthening was observed in this study during isovolumic relaxation, this does not preclude fiber lengthening because fibers run at an approximate 45° angle,\(^ {23}\) and a change in fiber length without a change in circumferential length can occur with a shear deformation only.

Elastic recoil and restoring forces have recently received attention as possible factors in early diastolic phenomena.\(^ {6,9,25,26}\) As summarized by Robinson et al.,\(^ {9}\) restoring forces can be subdivided into cardiac and extracardiac forces. The latter are the result of the stretching of the great elastic vessels and the connective tissue, holding the heart in place. The former can be subdivided into internal and external restoring forces. Internal restoring forces are dependent on bending or double overlap of filaments within each cardiac myocyte; external restoring forces are related to the elastic collagen matrix surrounding the myocytes.\(^ {27-29}\) Thickening of the individual muscle fibers can stretch the net ham-

mock-like endomysial fibers, and slippage of fiber layers secondary to torsional deformation during systole could deform the coiled perimysial fibers, which might release their energy during early diastole.

Dobutamine

During some circumstances, such as exercise, the same or a larger amount of blood must enter the LV cavity during a shorter filling period. An enhancement of the mechanism proposed here could provide the increased atrioventricular gradient needed to accomplish this. Because the amount of untwisting that has occurred by the time of MVO could be one of the determinants of the degree of suction, the results of this study, showing a further dissociation in time between untwisting and filling during dobutamine infusion, support this theory. The mechanism for this further dissociation may be the increased intrinsic relaxation rate during catecholamine stimulation. When the epicardial fibers relax faster, untwisting proceeds faster and the spring effect on the endocardium is more pronounced. The higher paced heart rate, present in this study during dobutamine, could also contribute to faster fiber relaxation or changed relations in the sequence of epicardial to endocardial activation and inactivation through a positive inotropic effect.

Using transient mitral orifice occlusion, Hori et al.\(^ {6}\) have shown that the pressure in the left ventricle does indeed fall below zero early in diastole and that infusion of calcium increased this suction. Suga et al.\(^ {7}\) used a completely different model: the excised, immersed dog heart in which the mitral valve was replaced by a wide-open ring with a flow probe. They showed a substantial flow across this ring toward the ventricular cavity during diastole. This suction flow increased with inotropic stimulation. The mechanism for this dependence of suction on inotropic state remained unclear, although a relation with some restoring forces was invoked. We suggest that restoring forces, generated by the increased deformation of the collagen matrix of the left ventricle during systole and released by nearly complete untwisting occurring during isovolumic relaxation, are responsible for the observed enhancement in filling characteristics.

Regional Untwisting

Although untwisting starts before MVO in all LV locations, significant regional differences in untwisting exist. The anterior wall, showing the least torsion in control conditions and the largest increase in torsion during dobutamine, invariably displays the most untwisting at the time of MVO. As torsion at any site is the end result of opposing forces of the different fiber layers interacting through the cardiac wall,\(^ {13}\) a similar interaction may govern untwisting as well. Because inactivation progresses from epicardium to endocardium, untwisting initiated by inactivation and lengthening of counterclockwise epicardial fibers could be promoted by continued shortening of clockwise endocardial fibers.\(^ {30}\) The regional variability in untwisting may reflect local differences in the fiber orientation of the layers of the LV wall or in the relative strength of these layers. For example, the fibers in the anterior wall endocardium may be more numerous or oriented in a way that more
The addition, phenomenon of phase augmentation of untwisting during early diastole. Differences in wall curvature could also be responsible for regional differences in the amount of twist and untwisting. The importance of these regional differences for global diastolic function during normal conditions and enhanced relaxation during catecholamine stimulation remains to be established.

It is important in this respect that Gibson et al. have shown that wall thinning can be dissociated from filling and that its timing and extent are important determinants of normal diastolic function. Regional wall thinning variability could be related to timing differences of untwisting, as areas that are still contracting and moving inward permit endocardial outward displacement to accompany torsion recoil in other regions during isovolumic relaxation. It is conceivable that segmental ischemia and other abnormal conditions might further increase the regional inhomogeneity of untwisting; these effects await further study. The phenomenon of intracardiac flow toward the apex during isovolumic relaxation in hypertrophied ventricles could represent another expression of regional inhomogeneity of untwisting.

Previous Studies

Systolic shear deformation was studied by Prinzen et al. using epicardial suction coils and by Osakada et al. and Feigl and Fry. Using implanted radiopaque beads and spirals, Ingels et al. and Waldman et al. have studied torsional deformation in humans and dogs. Those investigations have established the importance of torsion for anisotropic shortening and proposed its role in augmenting systolic LV wall thickening. Although the early diastolic phase is not commented on in most of these studies, the figures contain information about the entire cardiac cycle. In most cases, rapid recoil of torsional deformation is seen in early diastole. Using radiopaque markers, Beyar et al. have shown the dependence of twist–radial shortening relations on the phase of the cardiac cycle. Although twist and shortening were related during systole, torsion reversal occurred during early diastole without a concomitant change in radial length. Yun et al. recently measured rapid untwisting in early diastole in human transplant recipients by using implanted beads and noted a reduction during transplant rejection.

The results of our study define the timing of untwisting with respect to isovolumic relaxation and its relation to circumferential segment lengthening by using a noninvasive technique, but more importantly, the relevance of this phenomenon for LV filling dynamics is emphasized by its augmentation with catecholamine stimulation.

Potential Limitations

Magnetic resonance images were reconstructed from signals obtained from repeated tissue excitation and relaxation gated to the electrocardiogram and therefore represent an average over multiple cardiac cycles. In addition, information from nine acquisitions was used to derive the required temporal resolution, spanning a period of 30 minutes. During this time, a steady state was desired, so steps were taken to assure this insofar as possible. The RR interval was held constant by atrial pacing. Additional doses of anesthesia were not given during a set of acquisitions. After the appropriate dose of dobutamine was established, a constant infusion was maintained, and imaging was then delayed for 30 minutes to allow equilibration. Arterial blood pressure was monitored after every acquisition (about every 5 minutes) and never varied more than 5 mm Hg during the scan or 10 mm Hg during the whole series of nine scans. Inconstant hemodynamic state is therefore unlikely to have confounded our results.

The width of the tags (3.5 mm) could introduce variability in measurement of their position, which is taken as the center of the tag. However, the variability in determination of tag position is much smaller than the changes observed in this study.

Shortening or lengthening along the LV long axis during isovolumic relaxation would change the level of the myocardium that is imaged at the different time points because the image planes are fixed in absolute space. In this study, long-axis measurements were not performed, but data available from other studies from this laboratory show that total long-axis shortening of the canine heart during systole is 5%; during isovolumic relaxation, the long axis shortens only 1–2%. This small long-axis dimension change would not materially affect the measured torsion and would have only a minor effect on circumferential segment length.

Although magnetic resonance is a noninvasive method that does not require the use of an open-chest preparation, thoracotomy with pericardiotomy were performed in this protocol to allow epicardial atrial pacing (to assure constancy of the RR interval) and intrathoracic phonocardiography (to assure accurate timing of aortic closure after dobutamine administration). To ascertain that opening the chest does not alter the overall measurements and conclusions, five additional dogs were studied with a closed-chest preparation using Doppler to time aortic closure and a transvenous pacemaker (repositioned when necessary to continue capturing). The results for peak torsion and torsion at the time of MVO were essentially the same as in the open-chest preparation, suggesting that the dissociation of untwisting from filling was not influenced by the thoracotomies performed in this study.

Conclusions

The recoil of the systolic torsional deformation of the left ventricle is dissociated from filling in the canine model. This dissociation is further accentuated by inotropic stimulation with dobutamine infusion. Regional inhomogeneity of untwisting is present in control conditions and is accentuated by catecholamines. This supports the hypothesis that torsion reversal is an important mechanism for rapid early filling and could form the physiological basis of external restoring forces, generating suction at normal ventricular volumes and promoting both pressure decay and filling. Also, the increase in extent of torsion reversal during dobutamine infusion offers a possible explanation for the needed enhancement of diastolic function during conditions with shortened filling periods.

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