Independent effects of preload, afterload, and contractility on left ventricular torsion

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Dong, Sheng-jing, Paul S. Hees, Wen-Mei Huang, Sam A. Buffer, J. R., James L. Weiss, and Edward P. Shapiro. Independent effects of preload, afterload, and contractility on left ventricular torsion. Am. J. Physiol. 277 (Heart Circ. Physiol. 46): H1053–H1060, 1999.—Shortening of oblique left ventricular (LV) fibers results in torsion. A unique relationship between volume and torsion is therefore expected, and the effects of load and contractility on torsion should be predictable. However, volume-independent behavior of torsion has been observed, and the effects of load on this deformation remain controversial. We used magnetic resonance imaging (MRI) with tagging to study the relationships between load and contractility, and torsion. In ten isolated, blood-perfused canine hearts, ejection was controlled by a servopump: end-diastolic volume (EDV) was controlled by manipulating preload parameters and end-systolic volume (ESV) by manipulating afterload using a three-element windkessel model. MRI was obtained at baseline, two levels of preload alteration, two levels of afterload alteration, and dobutamine infusion. An increase in EDV resulted in an increase in torsion at constant ESV (preload effect), whereas an increase in ESV resulted in a decrease in torsion at constant EDV (afterload effect). Dobutamine infusion increased torsion in association with an increase in LV peak-systolic pressure (PSP), even at identical EDV and ESV. Multiple regression showed correlation of torsion with preload (EDV), afterload (ESV), and contractility (PSP; r = 0.67). Furthermore, there was a close linear relationship between torsion and stroke volume (SV) and ejection fraction (EF) during load alteration, but torsion during dobutamine infusion was greater than expected for the extent of ejection. Preload and afterload influence torsion through their effects on SV and EF, and there is an additional direct inotropic effect on torsion that is independent of changes in volume but rather is force dependent. There is therefore potential for the torsion-volume relation to provide a load-independent measure of contractility that could be measured noninvasively.

left ventricle; twist; magnetic resonance imaging

CARDIAC TORSION is the relative rotation of the left ventricular (LV) apex with respect to the base, about LV long axis. During the past decade, this deformation has been widely studied and quantified in both animal and human models with various methods (2–7, 10, 11, 13, 14, 20, 21). Because torsion results from shortening of obliquely oriented myocardial fibers (3, 15), the presence of a unique relation between cavity volume and the extent of torsion is expected and has been reported (2). The effects of load and contractility on torsion should therefore be predictable. However, these remain controversial. Studies in transplanted human hearts (13, 21) suggest that torsion, as measured by radiopaque markers, is not affected by pressure or volume loading, whereas experiments in dog models report that torsion, as measured by markers (2) or an optical device (10, 11), is primarily a function of volume at end diastole and end systole and is preload and afterload dependent. Furthermore, although it has been well demonstrated that torsion is very sensitive to changes in contractility (6, 11, 13, 14, 21) (positive inotropic interventions increase torsion, whereas negative inotropic interventions decrease torsion), it has been difficult to distinguish whether this inotropic effect is mediated through (11) or is independent of (13) changes in volume.

A volume-independent component of torsion has been clearly observed; substantial recoil of torsion is known to occur between the time of aortic valve closure and mitral valve opening, when cavity volume is fixed (10, 11, 23), and systolic torsion has been demonstrated in isolated isovolumic beating hearts (20). Thus under some circumstances, torsion may vary with force, as well as with volume. Because inotropic stimulation enhances pressure (or force) generation at any given end-diastolic volume (EDV) and end-systolic volume (ESV; 17, 18), it may therefore have a direct effect on torsion that is not mediated through changes in volume but through changes in force.

To examine further the individual effects of preload, afterload, and contractility on torsion, we used magnetic resonance imaging (MRI) with tissue tagging (29), which permits the accurate measurement of torsion, to study an isolated, blood-perfused, ejecting heart model that allows independent control of these factors. We hypothesized that 1) preload and afterload, through their effect on volume, affect torsion and 2) there is a further direct inotropic effect on torsion that is independent of changes in volume but rather is force dependent.

METHODS

Animal Preparation

Ten pairs of mongrel dogs were anesthetized with pentobarbital sodium (25–35 mg/kg iv). The smaller dog of the pair served as the heart donor (mean wt 21.2 ± 1.5 kg) and the larger one as the support dog (mean wt 30.1 ± 1.5 kg). Intravenous heparin (10,000 U), hydrocortisone (250 mg), and indomethacin (25 mg) were administered to the support dog, which was mechanically ventilated (model 613; Harvard Apparatus, South Natick, MA).
The procedures to isolate and support the heart were similar to those previously described (20, 25). Briefly, the femoral arteries and veins of the support dog were cannulated and connected to a perfusion system, which was primed with 1 liter of 50% dextran in saline mixed with the blood of the support dog. The arterial pressure of the support dog was continuously monitored with a fluid-filled catheter placed in the aorta, and serial arterial blood gases were taken and any deficiencies corrected accordingly.

The chest of the donor dog was opened under artificial ventilation. The left subclavian artery was cannulated with the arterial perfusion line and the brachiocephalic artery was cannulated to monitor coronary perfusion pressure. Filtered, warmed (37°C), and oxygenated arterial blood from the femoral arteries of the support dog was supplied to the isolated heart through a pump (model 7518–00; Cole Parmer Instrument, Chicago, IL) under pressure, which was monitored by a fluid-filled catheter and maintained at 80 mmHg by adjusting the speed of the pump. Once the heart was cross-perfused, the azygous vein, superior and inferior vena cavae, descending aorta, and lung hila were ligated, and the heart was removed from the thoracic cavity of the donor dog. The coronary venous blood and any accumulated blood in the left ventricle were drained through veins placed in the respective right and LV apex into a receptacle, and via a second pump it was returned to the femoral veins of the support dog. The left atrium was opened, the chordae tendineae were detached from the mitral valve leaflets, and a plastic ring that holds the isolated heart onto the servopump apparatus was sutured into the mitral valve ring. Electrocardiogram (ECG) leads and atrial pacing leads were sutured onto the heart. The isolated heart was then fixed to the servopump horizontally with a water-filled latex balloon inside the LV cavity. LV pressure was monitored with a fluid-filled catheter placed within the balloon.

**Load Control Via Servopump System**

Load control was carried out by a servopump system (Vivitro Systems, Victoria, Canada), which includes a linear motor, an MRI compatible cylinder pump, a 100-cm long plastic hollow shaft connecting the motor and piston of the cylinder, and a control box. A latex balloon was secured to a plastic tube connected to the fluid port of the cylinder. The cylinder, plastic tube, and balloon were filled with tap water. This servopump system allowed the manipulation of preload via a computer-simulated preload circuit consisting of a filling resistance and pressure source (25), affecting EDV, and the manipulation of afterload via a computer-simulated afterload analog consisting of a characteristic impedance, peripheral arterial resistance, and arterial compliance (3-element windkessel), affecting ESV (12, 26, 27). During the filling phase, the instantaneous LV pressure is compared with the desired left atrial (LA) pressure. The difference between LA and LV pressure is divided by the mitral valve resistance to obtain flow. As long as LV pressure exceeds LA pressure, the flow is zero. If LV pressure is lower than LA pressure, the flow is integrated and a filling volume is obtained. During ejection, LV pressure is compared with simulated aortic pressure. The difference between LV and aortic pressure is divided by the characteristic impedance to obtain flow. This flow is integrated to obtain a volume that is allowed to be ejected from the LV through movement of the pump's piston. The design and implementation details of this servopump system have been reported previously (20, 25).

**Experimental Protocol**

Protocol 1: load alteration. With this experimental preparation, the computer simulation of load may be altered, causing secondary changes in EDV and ESV. In eight hearts, the loading conditions were changed under a constant inotropic status (Fig. 1). We first changed the preload (preload down and preload up) so that EDV during intervention of preload down and ESV during intervention of preload up were arbitrarily maintained at a value that was midway between baseline EDV and ESV. We then changed the afterload, such that the ESV during intervention of afterload down was matched to that during intervention of preload down, and the ESV during intervention of afterload up was matched to that during intervention of preload up, whereas EDV was maintained the same as that of baseline. This combination of volumes was designed to allow assessment of preload effects by comparison of runs with different EDV but identical ESV (i.e., intervention 2 was compared with intervention 4, and intervention 3 to intervention 5). It also allowed determination of afterload effects by comparison of runs with identical EDV but different ESV (i.e., interventions 1, 4, and 5).

Protocol 2: contractility alteration. In eight hearts, contractility was increased by dobutamine infusion, whereas EDV and ESV were maintained identical to those of baseline by adjusting the preload and afterload (Fig. 1). Dobutamine was infused through the support dog, and its dosage was adjusted to increase LV peak-systolic pressure (PSP) by at least 30%.

**MRI Acquisition and Analysis**

Image acquisition. MRI was performed on a Resonex 0.38 tesla iron-core resistive magnet (Resonex, RX4000; Sunnyvale, CA) with a receiver-transmitter radio frequency coil that provides enhanced image resolution and signal-to-noise ratios (24). Image acquisition includes a gradient echo sequence modified to include tissue tagging, with temporal resolution of 16 ms, time to echo of 10 ms, flip angle of 30°, and two R-R intervals, 128 phase, and 256 frequency encoding steps, 2–4 averages of excitation, and 20–25 cm field of view. Two (basal and apical) short-axis images, 3.0 cm apart, with eight radial tags, perpendicular to the image planes, were acquired. Tagging and imaging were triggered by the R wave of the ECG; tags were placed at end diastole and 25 images were acquired thereafter. The image slice thickness was 1.0 cm and tag thickness 0.3 cm. Heart rate was kept constant by adjusting the speed of the pump. Once the heart was cross-perfused, the azygous vein, superior and inferior vena cavae, descending aorta, and lung hila were ligated, and the heart was removed from the thoracic cavity of the donor dog. The coronary venous blood and any accumulated blood in the left ventricle were drained through vents placed in the respective right and LV apex into a receptacle, and via a second pump it was returned to the femoral veins of the support dog. The left atrium was opened, the chordae tendineae were detached from the mitral valve leaflets, and a plastic ring that holds the isolated heart onto the servopump apparatus was sutured into the mitral valve ring. Electrocardiogram (ECG) leads and atrial pacing leads were sutured onto the heart. The isolated heart was then fixed to the servopump horizontally with a water-filled latex balloon inside the LV cavity. LV pressure was monitored with a fluid-filled catheter placed within the balloon.

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![Fig. 1. Schematic illustration of volume control during each intervention.](http://ajpheart.physiology.org/)
atrial pacing. Figure 2 shows the end-diastolic and end-systolic basal and apical images.

Image analysis. The files containing the digitized MRI data were transferred through a network to an IBM-compatible personal computer (Gateway 2000 P5–90; North Sioux City, SD), where image processing and data analysis were performed by use of a special software package (Cardiology Image Processing System, Johns Hopkins University).

The tag-endocardium intersection points on both basal and apical short-axis images were identified manually and digitized (8 points per slice). It should be noted that torsion of the endocardial surface, which is larger than that of the epicardial surface, was used in this study. An Akima smoothing algorithm (1) was used to interpolate between the intersection points and to smooth the contour.

Torsion was calculated as an angle between the tag line of apical slice and the projection of the basal tag line on the apical slice (Fig. 3), using a technique that is similar to that previously reported (7). Briefly, the centroid of the intersection points on each image was calculated, and then the slopes of the lines connecting each tag-endocardial intersection point and the corresponding centroid were calculated and expressed as an angle. 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 an intersection point on the basal plane with its centroid and the line connecting the corresponding intersection point to its centroid on the apical plane was calculated, and its arctangent was called the torsion angle (°). This angle is the difference, at each time point, between the position of a basal intersection point and the corresponding apical intersection point, 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 both slices simultaneously, this angle represents the rotation of one point with respect to the other between the time of tag insertion and the time of measurement. Increasing angle (positive sign) indicates counterclockwise rotation of the apex when viewed looking from the apex toward the base (Fig. 3). Mean torsion angles were then calculated as the average of eight values for the eight tag-endocardial intersection points.

Assuming constant arc length change, we related the torsion angle (°) to the short-axis radius of the LV cavity (7). It is necessary to take this into account when comparing torsion at different cavity volumes, as occurs when loads are varied. Circumferential-longitudinal shear (CL shear) is the difference between the systolic position of an apical tag point and the equivalent tag point on the basal slice, expressed as an angle (°, Fig. 3) of which the vertex is the tag point on the basal slice, and calculated as $\gamma = \tan^{-1} \left( \frac{2 \cdot r \cdot \sin(\theta/2)}{h} \right)$ (7), where $r$ is the radius calculated from the area (A) within the endocardial contour, as $r = \left( \frac{A}{\pi} \right)^{1/2}$, and $h$ is the distance between basal and apical slices.

### Statistical Analysis

Results are expressed as means ± SD. Repeated-measures analysis of variance with the Student-Newman-Keuls correction was used to determine the statistical significance of the interventions. Multiple linear regression was used to determine the effect of EDV, ESV, and dobutamine infusion on torsion, and simple linear regression was used to correlate torsion and stroke volume (SV) and ejection fraction (EF). A P value of <0.05 was considered to be statistically significant.

### RESULTS

Preload alteration changed significantly both EDV and ESV. Compared with baseline, there was no significant difference in EF, although SV decreased during preload down. Afterload alteration changed only ESV, resulting in changes in SV and EF (Table 1). During load alteration, the heart rate was paced at a constant rate (142 ± 3 beats/min). Dobutamine infusion increased PSP, even though EDV and ESV, and thus the SV and EF, were maintained identical to those at baseline condition (Table 1). Because of the chronotropic effect of dobutamine, the heart rate was slightly higher than the baseline pacing rate in four of eight dogs and therefore was paced at this higher rate, but there was no significant difference between baseline and dobutamine infusion (152 ± 12 vs. 163 ± 13 beats/min).
Effect of Preload on Torsion

At constant ESV, the torsion was greater at a higher EDV (Fig. 4). At ESV of 14 ml, torsion was 9.4 ± 3.3° (P < 0.01) at EDV of 26.7 ± 6.4 ml, and 7.1 ± 2.5° (P < 0.0001) at EDV of 32.4 ± 5.2 ml, respectively. Similar results were also found in CL shear: 2.5 ± 0.6 vs. 3.3 ± 0.7° (P < 0.01), and 1.9 ± 1.0 vs. 2.6 ± 0.8° (P < 0.01), respectively.

Effect of Afterload on Torsion

At constant EDV (26.7 ml), the torsion decreased from 12.2 ± 4.0 to 10.7 ± 3.9 to 6.4 ± 5.1° (P < 0.001) as the ESV increased from 14.5 ± 6.4 to 17.1 ± 6.7 to 21.5 ± 7.1 ml, due to the increased afterload (Fig. 5). Similar results were also observed in CL shear, which decreased from 3.3 ± 0.7 to 3.0 ± 0.7 to 1.9 ± 1.0° (P < 0.001).

Inotropic Effect on Torsion

At identical EDV (26 ml) and ESV (17 ml), and therefore identical SV and EF, dobutamine infusion significantly increased torsion (13.3 ± 4.3 vs. 8.7 ± 1.5°, P < 0.05) (Fig. 6) and CL shear (3.4 ± 1.1 vs. 2.5 ± 0.7°, P < 0.05) in association with an increase in LV PSP (160 ± 25 vs. 98 ± 17 mmHg, P < 0.05, Table 1).

Multiple Regression Analysis

To determine further the effect of preload, afterload, and contractility on torsion, we pooled data from all hearts and performed a multiple linear regression analysis using the model

\[ \text{Torsion} = a_0 + a_1 \cdot \text{EDV} + a_2 \cdot \text{ESV} + a_3 \cdot D_i \]

or

\[ \text{CL shear} = a_0 + a_1 \cdot \text{EDV} + a_2 \cdot \text{ESV} + a_3 \cdot D_i \]

where \( D_i \) is a dummy variable to account for inotropic status: \( D_i = 0 \) for baseline inotropic state and \( D_i = 1 \) for dobutamine infusion. We found that there was a significant correlation between torsion and EDV, ESV, and inotropic status (multiple regression: \( r = 0.66, P < 0.0001 \)). As shown in Table 2, EDV was a positive predictor (P < 0.05), i.e., the greater the EDV, the greater the torsion, whereas ESV is a negative predictor (P < 0.0001), i.e., the greater the ESV, the smaller the torsion. Note that the absolute value of the coefficient for ESV is about two-thirds as great as that for EDV, indicating that the effect of EDV on the torsion is about two-thirds as great as that of ESV. The dobutamine infusion also has a significant positive effect on torsion (P < 0.01). Similarly, significant correlation was also found between CL shear and EDV, ESV, and dobutamine infusion (multiple regression: \( r = 0.67, P < 0.0001 \); Table 2).

Table 1. Left ventricular pressure and volume response to intervention

<table>
<thead>
<tr>
<th>EDP, mmHg</th>
<th>PSP, mmHg</th>
<th>EDV, ml</th>
<th>ESV, ml</th>
<th>SV, ml</th>
<th>EF, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>5.5 ± 2.3</td>
<td>104 ± 13</td>
<td>26.7 ± 6.4</td>
<td>17.1 ± 6.7</td>
<td>9.5 ± 1.3</td>
</tr>
<tr>
<td>PL down</td>
<td>3.1 ± 1.4*</td>
<td>89 ± 10*</td>
<td>21.7 ± 6.8*</td>
<td>14.3 ± 6.9*</td>
<td>7.4 ± 1.2*</td>
</tr>
<tr>
<td>PL up</td>
<td>6.5 ± 2.8*</td>
<td>121 ± 13*</td>
<td>32.4 ± 5.2*</td>
<td>21.9 ± 6.5*</td>
<td>10.5 ± 2.7</td>
</tr>
<tr>
<td>AL down</td>
<td>5.3 ± 1.9</td>
<td>84 ± 11*</td>
<td>26.7 ± 6.2</td>
<td>14.5 ± 6.4*</td>
<td>12.2 ± 1.7*</td>
</tr>
<tr>
<td>AL up</td>
<td>5.6 ± 2.0</td>
<td>109 ± 13</td>
<td>26.7 ± 6.4</td>
<td>21.5 ± 7.1*</td>
<td>5.2 ± 1.1*</td>
</tr>
<tr>
<td>Baseline</td>
<td>4.9 ± 2.5</td>
<td>98 ± 17</td>
<td>26.4 ± 5.8</td>
<td>17.0 ± 5.9</td>
<td>9.4 ± 1.0</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>5.9 ± 1.1</td>
<td>160 ± 25*</td>
<td>26.4 ± 5.5</td>
<td>16.7 ± 5.4</td>
<td>9.7 ± 0.6</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 8 dogs. EDP, end-diastolic pressure; PSP, peak systolic pressure; EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; EF, ejection fraction; PL, preload; AL, afterload. *P < 0.05 compared with baseline.

Fig. 4. Effect of preload on torsion at constant ESV. At constant ESV, torsion was greater at higher EDV.

Fig. 5. Effect of afterload on torsion at constant EDV. At constant EDV, torsion decreased as ESV increased.
We also performed similar multiple linear regression analysis using LV PSP instead of coded dummy variable for inotropic status:

\[
\text{Torsion} = b_0 + b_1 \cdot \text{EDV} + b_2 \cdot \text{ESV} + b_3 \cdot \text{PSP}
\]

or

\[
\text{CL shear} = b_0 + b_1 \cdot \text{EDV} + b_2 \cdot \text{ESV} + b_3 \cdot \text{PSP}
\]

Similar results were found and are presented in Table 2.

Relationship Between Torsion and SV and EF

A direct linear relationship between torsion and SV and EF was detected from data of baseline and load alterations (torsion = 3.5 + 0.62·SV, \( r = 0.75 \), and torsion = 1.37 + 0.22·EF, \( r = 0.94 \), Fig. 7, open circles), indicating that the greater the shortening, the greater the torsion. However, data from dobutamine infusion fell upward to and outside of the 95% confidence interval of the relations (Fig. 7, filled circles), indicating that the torsion was greater with dobutamine infusion even at the same SV and EF. Similar relations were found between CL shear and SV and EF (CL shear = 1.04 + 0.18·SV, \( r = 0.90 \) and CL shear = 0.78 + 0.05·EF, \( r = 0.93 \) during load alterations, and data from dobutamine infusion were likewise shifted upward).

**DISCUSSION**

By using MRI tissue tagging and the isolated, blood-perfused, ejecting heart model, we studied the independent effects of preload, afterload, and contractility on mean LV endocardial torsion. We found that 1) preload affects torsion: torsion was greater at higher EDV when ESV was held constant (Fig. 4), 2) afterload affects torsion: torsion decreased at higher ESV when EDV was held constant (Fig. 5), 3) the effect of preload (as assessed by EDV) on torsion is about two-thirds as great as that of afterload (as assessed by ESV) (Table 2), and 4) contractility has a direct volume-independent effect on torsion: dobutamine infusion increased torsion even at identical EDV and ESV (Fig. 6). The independent effect of contractility on torsion was further demonstrated by multiple linear regression analysis.

**Effect of Preload on Torsion**

In contrast to the results of this study, it has been previously reported that torsion is insensitive to preload. Hansen et al. (13, 14), using implanted midwall radiopaque markers, did not find change in torsion after volume loading in the transplanted human heart. Similarly, Gibbons Kroeker et al. (10, 11), using an optical apex rotation measuring device, did not observe change in the magnitude of apical rotation either during volume loading with saline or venae cavae occlusion in the dog. However, in these studies of preparations with intact circulation, volume expansion and venae caval occlusion altered afterload as well as preload in the same direction, i.e., volume load increases both preload and afterload (21), while venae caval occlusion decreases both preload and afterload (10, 11). Thus both EDV and ESV increase during volume loading (13), whereas both EDV and ESV decrease during venae caval occlusion (10, 11).
mixed effects account for the unchanged magnitude of torsion in the intact ventricle. The current study demonstrates an important effect of pure preload alteration on torsion.

Effect of Afterload on Torsion

In this study, we found a decrease in torsion in response to increased afterload. This result is consistent with two previous dog studies in which preload was kept constant; MacGowan et al. (20) increased afterload by using an isolated heart model similar to the present study, whereas Gibbons Kroeker et al. (11) increased afterload by single beat aortic constriction in dogs with intact circulation. However, in human transplanted heart studies (13, 21), no change in torsion was observed with methoxamine-induced pressure loading. This observation might result from the fact that a methoxamine-induced increase in afterload could lead to a secondary preload increase as suggested by the increased EDV and end-diastolic pressure (21) and unchanged EF (13, 21) in the patients studied.

The direct linear relationship between torsion and SV and EF is in agreement with the concept that there is a close correlation between torsion and volume, independent of loading conditions, advanced by Arts et al. (2, 3).

From the multiple linear regression analysis, we found that the slope of torsion-EDV relation is about two-thirds as great as that of torsion-ESV relation (the absolute value of regression coefficient is $0.42 \pm 0.18$ vs. $0.73 \pm 0.17$, Table 2), indicating that the effect of preload on torsion is about two-thirds as great as that of afterload. This result is similar to that of an intact dog study that showed that the mean slope of rotation-cavity area relation at end diastole is about one-half as great as that at end systole. (11) This effect is also seen in studies of individual subjects where torsion-volume loops are plotted through the cardiac cycle; during systole the torsion-volume relation is steep, during isovolumic relaxation there is sharp recoil without volume change, and during diastole, the torsion-volume relation is gradual (21).

Effect of Contractility on Torsion

The overall effect of contractility on torsion has been well demonstrated; positive inotropic interventions, such as dobutamine infusion and paired pacing, greatly increase torsion (6, 11, 13, 21), whereas negative inotropic interventions, such as ischemia and rejection reaction of the transplanted heart, markedly decrease torsion (6, 14). In the intact circulation, changes in contractility are accompanied by changes in SV and EF. Therefore, it is difficult to distinguish whether this inotropic effect is mediated through or is independent of changes in volume. We observed here that dobutamine infusion increases torsion, in association with an increase in PSP, even at identical EDV and ESV, indicating that there is a direct inotropic effect on torsion that is not mediated through changes in volume but through changes in force. This effect was not predicted by the modeling studies of Arts et al. (2, 3) and was not observed by Gibbons Kroeker et al. (11) during paired-pacing, a weaker inotropic stimulus.

The dependence of a global myocardial deformation on the force of contraction, independent of changes in volume, is unusual. However, the existence of a volume-independent component of torsion has been well established previously by several investigators. For example, Beyar et al. (5), Rademakers et al. (23), and Moon et al. (21) have shown that during isovolumic relaxation, when cavity volume is fixed, there is a rapid recoil of about 40% of the torsion that has accumulated during systole. In addition, MacGowan et al. (20) observed that considerable torsion persisted in the isovolumic beating heart despite the absence of thickening, or circumferential or longitudinal shortening. Principal strain, to which torsional deformation contributes, also persisted in the isovolumic model.

The mechanism of this volume independence and force dependence of torsion is uncertain. It appears that when increased contractility due to $\beta_1$ stimulation cannot achieve greater cavity volume reduction, the force along the oblique fiber direction is applied toward increased intramyocardial deformation, that is, shear in the CL direction. This interpretation is consistent with the findings of Young et al. (28), who reported that in patients with hypertrophic cardiomyopathy, minimal principal strain magnitude is preserved in association with an increased CL shear, despite decreases in normal circumferential and longitudinal strains and suggested that “the mechanical work is contributing to wall shearing and not to cavity volume reduction.” This shearing is likely to be a manifestation of the further rearrangement of fiber sheets, which slide along “cleavage planes” within the myocardium during systole (19).

Our data suggest that this altered configuration can occur entirely intramyocardially, independently of inward endocardial wall motion, and that it may contribute importantly to force development. It is possible that such deformation may occur in association with greater systolic compression of myocardium due to further extrusion of blood from the intramyocardial vessels. That is, myocardial volume may be reduced in systole to a greater extent with inotropic stimulation, allowing more wall deformation to occur. The absolute reduction in myocardial volume during systole is small, less than 4% at baseline (16), and has been difficult to detect by MRI methods.

Another possible mechanism for altered wall deformation without an overall cavity volume change, might be a change in LV cavity shape during inotropic stimulation. Altered shape might result in a redistribution of myocardial mass, such that increased torsion could occur. A shape analysis could not be performed in this study since long-axis images were not obtained, due to time constraints imposed by the fragile isolated heart preparation. Olsen et al. (22) measured both short- and long-axis diameters using implanted ultrasound crystals and reported that inotropic stimulation did not alter the relationship between LV eccentricity and volume; however, eccentricity does not fully describe LV
shape. Future MRI study of torsion should include long axis imaging and detailed shape analysis, so that the interrelationships among shape, volume, and torsion can be evaluated.

Finally, torsion results from a balance of opposing effects of shortening of epicardial counterclockwise fibers and endocardial clockwise fibers, with epicardial fibers dominating. Relative endocardial ischemia due to inotropic stimulation might lead to alteration in this endocardial-epicardial force balance, and increased torsion. Similarly, if inotropic stimulation were to result in a larger absolute force increment in the epicardial compared with endocardial fibers, the balance would shift and torsion would increase. The mechanisms of this force-dependent increase in torsion require further study.

**Limitations**

The combined use of MRI tagging and the isolated heart model is unique. Torsion can be measured nondestructively, unlike with implanted beads, and factors such as preload, afterload, and contractility can be controlled independently, compared with the model with intact circulation. However, there exist some limitations. Currently, MRI acquisition requires a steady state, and therefore rapid beat-by-beat variation of torsional dynamics during an intervention cannot be measured. Secondly, the isolated heart model has some nonphysiological aspects. Most importantly, the heart rates of these isolated hearts were high; the presence of incomplete relaxation or rate-related changes in contractility might make the results differ from those observed at lower heart rates. Also, the mitral ring is fixed and the chordae tendineae are severed; DeAnda et al. (8) reported reduced torsion in dogs with mitral valve replacement. However, when expressed in similar units, the magnitude of torsion under baseline conditions of the present study is quite similar to those reported by Buchalter et al. (6) and Beyar et al. (5) in intact dogs and is greater than that reported by DeAnda et al. (8) in dogs with mitral valve replacement, suggesting that the extent of twist was not greatly disturbed in this model. Third, in this experiment we varied a computer simulation of preload and afterload, which changed end-diastolic and end-systolic volumes. Our model only approximates the true afterload seen by the LV myocardium because it does not consider longitudinal and circumferential radius of curvature, wall thickness, etc. However, the secondary volume changes were precisely controllable and easily measurable and therefore the volumes (in ml) rather than loads are reported here. Fourth, we attribute the inotropic-related change in torsion at constant volume to differences in force development; we cannot exclude the possibility that other effects of dobutamine that were not measured here, such as velocity of shortening and ejection, may also have contributed. Finally, although it has been demonstrated that there is a regional variation in torsion (6, 7, 13, 14, 20), we used global values in this study.

In conclusion, MRI tagging allowed us to measure systolic torsion nondestructively in the isolated, blood-perfused, ejecting heart model in dogs, enabling study of the individual effects of preload, afterload, and contractility on torsion while maintaining other factors constant. Changes in load (preload or afterload) result in changes in systolic torsion, which are mediated through alteration in SV and EF. Dobutamine infusion increases systolic torsion associated with an increase in PSP even when volumes are identical to those at control, indicating that there is an inotropic effect on cardiac torsion that is independent of, rather than mediated through, changes in volume, but is force dependent. These relationships may have clinical implications. We speculate that the torsion-volume relationship might provide a load-independent measure of contractility that could be measured noninvasively. This potential application requires further study.

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