Passive Ventricular Constraint Prevents Transmural Shear Strain Progression in Left Ventricle Remodeling

Allen Cheng, MD; Tom C. Nguyen, MD; Marcin Malinowski, MD; Frank Langer, MD; David Liang, MD, PhD; George T. Daughters, MS; Neil B. Ingels, Jr, PhD; D. Craig Miller, MD

Background—Passive ventricular constraint provides external cardiac support to reduce left ventricular (LV) wall stress and myocardial stretch, which are primary determinants of LV remodeling. Altered wall strain results in cytokine and reactive oxygen species production, which, in turn, stimulates apoptosis and extracellular matrix disruption and could be an important trigger for adverse global LV dilatation and remodeling. The effects of the Acorn cardiac support device (CSD) on regional transmural LV wall strains, however, remain unknown.

Methods and Results—Thirty-three sheep had transmural radiopaque beadsets surgically inserted into the anterior basal and lateral equatorial LV walls, with additional markers silhouetting the left ventricle. Eight animals had CSD implanted (myocardial infarction [MI]+CSD). One week thereafter, the MI+CSD group and 10 animals without CSD (MI) underwent posterior LV infarction by snaring obtuse marginal coronary arteries. Fifteen animals (Sham) had no infarction or CSD. 4D marker dynamics were measured with biplane videofluoroscopy 1 and 8 weeks postoperatively. LV volumes, sphericity index, and transmural circumferential, longitudinal, and radial systolic strains were analyzed. Compared with Sham, infarction (MI) dilated the heart, reduced sphericity index (LV length/width), and increased longitudinal–radial shear strains in the inner half of both the anterior and lateral LV walls. CSD prevented this shear strain perturbation, minimized LV end diastolic volume increase, and augmented the LV sphericity index.

Conclusions—Prophylactic CSD prevented infarct-induced shear strain progression not only in myocardium adjacent to, but also remote from, the infarct. CSD also prevented LV dilatation and sphericization. By attenuating shear strain abnormalities, CSD could prevent the heart from entering into a positive feedback loop of further LV dilatation and exaggeration of LV wall stress and may reduce biochemical triggers portending adverse LV remodeling. (Circulation. 2006;114[suppl I]:I-79–I-86.)

Key Words: myocardial infarction • passive ventricular constraint • CSD • transmural strain • LV remodeling

Left ventricular (LV) remodeling after myocardial infarction (MI) is characterized by a number of important degenerative changes in cardiac structure and function.1–4 Altered LV transmural wall strains have been proposed to cause infarct extension and may have an important role in propagating LV remodeling. Recent laboratory and clinical studies have shown that infarct extension initiates a progressive myopathic process in normally perfused myocardium.2–4 Rodriguez et al5 reported abnormal transmural shear strain patterns adjacent to acutely ischemic myocardium. Cheng et al6 further explored the concept of infarct extension and have shown that transmural shear strains increased not only in myocardium adjacent to, but also remote from, the infarcted region in a chronic ovine model. Altered myocardial strains can result in production of cytokines and reactive oxygen species, which, in turn, stimulate myocyte apoptosis7–9 and extracellular matrix disruption,10–12 important triggers for destructive global LV dilatation and remodeling.2–4

Progressive LV dilatation and chamber shape change (more spherical) can also lead to more myocyte stretch and upregulation of stretch response proteins that can result in the induction of pathological cardiomyocyte hypertrophy.13–16 Subsequently, the heart enters a positive feedback loop of dilatation and further exaggerated wall stress, which leads, ultimately, to progressive global LV dysfunction and heart failure. Reduction of wall stress and myocardial stretching are important means for mitigating this pathophysiological evolution. To interrupt this vicious cycle, various surgical therapies attempting to reduce wall stress/stretch and normalize LV shape have received considerable attention. One of these concepts involves passive external ventricular support, such as the Acorn cardiac support device (CSD), which provides end-diastolic support to reduce LV wall stress and myocardial stretch. A CSD has been shown to halt progressive LV dilatation and improve ejection fraction.17–24 Although multiple

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laboratory and clinical studies have been performed to examine the possible mechanisms of CSD on LV remodeling, its effects on regional 3D myocardial transmural strain adjacent to and remote from an infarct are unknown. This study was designed to test the hypothesis that placement of passive external cardiac constraint would decrease postinfarction LV dilatation and sphericization and prevent abnormal transmural LV wall shear strains.

Methods
All of the animals received humane care in compliance with the Principles of Laboratory Animal Care formulated by the National Society for Medical Research and the Guide for Care and Use of Laboratory Animals prepared by the National Academy of Sciences and published by the National Institutes of Health. This study was approved by the Stanford Medical Center Laboratory Research Animal Review Committee and conducted according to Stanford University policy. We had full access to the data and take full responsibility for its integrity. We have read and agree to the article as written.

Surgical Preparation and Marker Data Acquisition
The surgical preparation and marker data acquisition methods for these experiments have been described in detail previously5,25 and are only outlined briefly. Through a left thoracotomy, 33 adult Dorsett-hybrid sheep had 13 subepicardial radiopaque markers surgically implanted to silhouette the LV chamber (Figure 1). Epicardial echocardiography was used to locate and measure the wall depth of a free segment of the midlateral equatorial LV wall between the papillary muscles and a site in the anterior LV wall basal to the insertion of the anterolateral papillary of the left anterior descending coronary artery, with deepest bead placement determined by ED wall thickness measured echocardiography. B, Short-axis echocardiographic image at the anterior basal LV wall; here the transmural beadset was placed basal to the insertion of the anterolateral papillary of the left anterior descending coronary artery, with deepest bead placement determined by ED wall thickness.

Figure 1. Locations of LV epicardial markers and LV lateral equatorial and anterior basal wall transmural beadsets. X1, X2, and X3 are the local circumferential, longitudinal, and radial axes, respectively.

Figure 2. A, Short-axis echocardiographic image at the lateral equatorial LV wall before bead placement. Transmural beadsets were inserted between the papillary muscles (arrow) with deepest bead placement determined by ED wall thickness measured echocardiography. B, Short-axis echocardiographic image at the anterior basal LV wall; here the transmural beadset was placed basal to the insertion of the anterolateral papillary of the left anterior descending coronary artery, with deepest bead placement determined by ED wall thickness.
perfusion coronary angioplasty balloon catheters (GUIDANT Aquila Trac Peripheral Catheter) were placed into the proximal circumflex and left anterior descending coronary arteries. The animals were then euthanized using sodium pentothal (1 gm IV) followed by an intravenous bolus of potassium chloride (80 meq) to arrest the hearts at end diastole (ED). After adjusting LV pressure by blood withdrawal to match the in vivo LV end-diastolic pressure, simultaneous infusions of buffered glutaraldehyde (5%, 300 mL) were infused through both coronary catheters simultaneously with the balloon inflated to fix the hearts in situ. The hearts were then explanted and stored in 10% formalin for histological examination.

Hemodynamics and Cardiac Cycle Timing
See detailed methods reported in Cheng et al.\(^2\) Three consecutive steady-state beats in sinus rhythm were selected for analysis from each study. For each cardiac cycle, ED was defined as the videofluoroscopic frame when LV second derivative of pressure curve, defined by LV derivative of pressure with respect to time (dP/dt\(^2\)) changed sign from minus to plus, a definition that captures the onset of isovolumic relaxation and is consistent with the concept of end systolic elastance.

Finite Cardiac Strains
Placement of the transmural beadset allowed assessment of transmural 3D myocardial deformations (3 normal strains and 3 shear strains) in the lateral equatorial and anterior basal regions of the LV wall. Detailed strain analysis methodology has been described in detail in our previous publication.\(^2\) Strains are reported at 20%, 50%, and 80% depths from the epicardium, with ED as the reference configuration and ES as the deformed configuration.

LV Dimensions and Shape
Instantaneous LV volumes were calculated every 16.7 ms from the 3D coordinates of the epicardial LV markers (Figure 1) by summing the volumes of multiple space-filling tetrahedra. Global LV shape was quantified by a sphericity index defined by LV length divided by LV diameter, where LV length was defined as the distance from the apical marker to the midpoint of the anterior and posterior basal LV markers, and LV diameter was defined as twice the distance from lateral equatorial marker to the midpoint of the anterior and posterior equatorial markers.

Statistical Analysis
Data are reported as mean±1SD. All of the data were compared using 2-way repeated-measures ANOVA with Holm–Sidak pairwise multiple comparisons (Sigmastat 3.1, SPSS, Inc) unless otherwise specified. P<0.05 was considered statistically significant.

Results
Table 1 summarizes the normalized changes in LV ED volume (LVEDV), LV ES volume (LVESV), and LV sphericity index for the 3 groups. Compared with Sham, the postinfarct MI hearts exhibited increased ΔLVEDV and reduced sphericity index (Figure 4a and 4b). The MI+CSD hearts maintained LVEDV values, but the LV sphericity index increased relative to Sham and MI (Figure 4a and 4b). Normalized ΔLVESVs for CSD and MI+CSD were not significantly different from Sham. Changes in LVEDV for Sham, MI, and MI+CSD, respectively, were 7.2±9.6, 26.6±16.0, and 6.7±8.0 mL.

Group mean transmural systolic cardiac strains at 8 weeks in the lateral equatorial LV wall are shown in Table 2 (ED reference configuration and ES deformed configuration). Compared with Sham, the MI group exhibited greater longitudinal-radial shear strain (E\(_{13}\)) in the midwall and subendocardial layer and a larger circumferential-radial shear (E\(_{12}\)) in the subepicardial layer of the LV wall in the lateral equatorial region immediately adjacent to the infarct. The MI+CSD group had no abnormal E\(_{12}\) shear strain in this region; there were no significant differences in normal strains (E\(_{11}\), E\(_{22}\), and E\(_{33}\)) and shear strains (E\(_{23}\), E\(_{13}\), and E\(_{12}\)) when the MI+CSD group was compared with the Sham group.

Group mean transmural systolic cardiac strains in the anterobasal LV wall, remote from the infarct, are shown in Table 3. Relative to Sham, the MI group had greater longitudinal-radial shear strain (E\(_{13}\)) in the midwall and subendocardial layer of the anterobasal region, whereas the MI+CSD group exhibited no abnormal E\(_{12}\) shear strain. There were no significant differences in normal strains (E\(_{11}\), E\(_{22}\), and E\(_{33}\)) and shear strains (E\(_{23}\), E\(_{13}\), and E\(_{12}\)) comparing

### Table 1. LV Size and Shape

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sham</th>
<th>MI</th>
<th>MI+CSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normalized ΔLVEDV</td>
<td>0.97±0.10</td>
<td>1.02±0.10</td>
<td>1.07±0.10</td>
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<tr>
<td>Normalized ΔLVESV</td>
<td>0.93±0.10</td>
<td>1.04±0.10</td>
<td>1.00±0.15</td>
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<tr>
<td>Sphericity index</td>
<td>0.90±0.12</td>
<td>0.95±0.14*</td>
<td>1.28±0.27†</td>
</tr>
</tbody>
</table>

Group mean±1SD data. P values from 2-way repeated-measures ANOVA with Holm–Sidak pairwise multiple comparisons. Normalized ΔLVEDV indicates [(LVEDV\(_\text{week8}\)-LVEDV\(_\text{week1}\))/LVEDV\(_\text{week1}\)+1]; Normalized ΔLVESV, [(LVESV\(_\text{week8}\)-LVESV\(_\text{week1}\))/LVESV\(_\text{week1}\)+1]; Sphericity index, LV length/diameter.

\(^*\)P<0.05 MI vs Sham. \(^†\)P<0.05 MI+CSD vs MI. \(^\ddagger\)P<0.05 MI vs. MI+CSD. \(^\S\)P<0.05 CSD vs Sham.
### TABLE 2. Transmural Lateral Equatorial LV Wall Systolic Cardiac Strains

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sham (n=10)</th>
<th>MI (n=9)</th>
<th>MI+CSD (n=8)</th>
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<td>20% depth</td>
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<tr>
<td>E_{11}</td>
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<td>-0.04±0.08</td>
<td>-0.03±0.04</td>
</tr>
<tr>
<td>E_{22}</td>
<td>-0.01±0.07</td>
<td>-0.01±0.09</td>
<td>-0.02±0.04</td>
</tr>
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<td>E_{33}</td>
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<td>0.20±0.16</td>
<td>0.17±0.14</td>
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<tr>
<td>E_{12}</td>
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<td>0.04±0.05</td>
<td>0.01±0.03</td>
</tr>
<tr>
<td>E_{23}</td>
<td>0.09±0.08</td>
<td>0.09±0.09</td>
<td>0.09±0.10</td>
</tr>
<tr>
<td>E_{13}</td>
<td>0.02±0.05</td>
<td>0.12±0.10*</td>
<td>0.10±0.09</td>
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<tr>
<td>50% depth</td>
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<td>E_{11}</td>
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<td>-0.00±0.07</td>
</tr>
<tr>
<td>E_{22}</td>
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<td>-0.02±0.11</td>
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<td>E_{33}</td>
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<tr>
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<tr>
<td>E_{23}</td>
<td>0.06±0.07</td>
<td>0.14±0.06*</td>
<td>0.03±0.09†</td>
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<td>E_{13}</td>
<td>0.03±0.05</td>
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<tr>
<td>80% depth</td>
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<td>-0.04±0.08</td>
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<td>E_{22}</td>
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<td>0.00±0.10</td>
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<td>E_{33}</td>
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<td>0.23±0.20</td>
<td>0.20±0.24</td>
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<tr>
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<td>0.03±0.06</td>
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<tr>
<td>E_{23}</td>
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<td>0.20±0.08*</td>
<td>0.03±0.08†</td>
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<tr>
<td>E_{13}</td>
<td>0.06±0.07</td>
<td>0.10±0.12</td>
<td>0.10±0.14</td>
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</tbody>
</table>

Group mean±1 SD) data. ED indicates reference configuration; ES, deformed configuration. Depth was measured as a percentage of the radial distance from the epicardial bead to the most subendocardial bead. E_{11}, circumferential strain; E_{22}, longitudinal strain; E_{33}, radial strain; E_{12}, circumferential-longitudinal shear; E_{23}, longitudinal-radial shear; E_{13}, circumferential-radial shear.

*<p<0.05 MI+CSD vs MI within the same wall depth. †<p<0.05 MI+CSD vs MI within the same wall depth from 2-way repeated-measures ANOVA with Holm–Sidak pairwise multiple comparisons.

### TABLE 3. Transmural Anterior Basal LV Wall Systolic Cardiac Strains

<table>
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<th>Variable</th>
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<th>MI (n=6)</th>
<th>MI+CSD (n=6)</th>
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<td>20% depth</td>
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</tr>
<tr>
<td>E_{11}</td>
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<td>-0.07±0.05</td>
<td>-0.02±0.04</td>
</tr>
<tr>
<td>E_{22}</td>
<td>-0.07±0.08</td>
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<td>-0.11±0.05</td>
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<tr>
<td>E_{33}</td>
<td>0.34±0.26</td>
<td>0.33±0.14</td>
<td>0.24±0.19</td>
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<td>-0.01±0.02</td>
<td>0.01±0.03</td>
</tr>
<tr>
<td>E_{23}</td>
<td>0.04±0.07</td>
<td>0.03±0.09</td>
<td>0.11±0.11</td>
</tr>
<tr>
<td>E_{13}</td>
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<td>-0.01±0.11</td>
<td>0.04±0.07</td>
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<tr>
<td>50% depth</td>
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</tr>
<tr>
<td>E_{11}</td>
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<td>-0.09±0.04</td>
<td>-0.06±0.07</td>
</tr>
<tr>
<td>E_{22}</td>
<td>-0.08±0.08</td>
<td>-0.08±0.10</td>
<td>-0.17±0.09</td>
</tr>
<tr>
<td>E_{33}</td>
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<td>0.02±0.03</td>
</tr>
<tr>
<td>E_{23}</td>
<td>0.01±0.05</td>
<td>0.12±0.04*</td>
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</tr>
<tr>
<td>E_{13}</td>
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<td>80% depth</td>
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<tr>
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</tr>
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<td>E_{22}</td>
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<td>0.67±0.32</td>
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<td>E_{12}</td>
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<td>-0.03±0.09</td>
<td>0.06±0.04</td>
</tr>
<tr>
<td>E_{23}</td>
<td>0.04±0.09</td>
<td>0.25±0.20*</td>
<td>0.06±0.11†</td>
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<tr>
<td>E_{13}</td>
<td>0.01±0.23</td>
<td>0.00±0.18</td>
<td>0.09±0.12</td>
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</tbody>
</table>

Group mean±1SD) data of N=8 hearts. ED indicates reference configuration; ES, deformed configuration. Depth measured as a percentage of the radial distance from the epicardial bead to the most subendocardial bead. E_{11}, circumferential strain; E_{22}, longitudinal strain; E_{33}, radial strain; E_{12}, circumferential-longitudinal shear; E_{23}, longitudinal-radial shear; E_{13}, circumferential-radial shear.

*<p<0.05 MI+CSD vs MI within the same wall depth. †<p<0.05 MI+CSD vs MI within the same wall depth from 2-way repeated-measures ANOVA with Holm–Sidak pairwise multiple comparisons.

Discussion

The main findings of this experiment were that passive ventricular constraint attenuated transmural LV wall longitudinal-radial shear strain abnormalities not only in myocardium adjacent to but also remote from the infarction and reduced infarct-induced LV dilatation and sphericalization. Ventricular remodeling is manifested by changes in LV size, shape, structure, and function. These geometric and functional alterations are associated with gene expression and cellular and interstitial changes.1,2,7–11,27 Acute infarct exten-

on is the critical initiating event of this myopathic process in LV remodeling, and altered wall strains have been proposed as a cause of infarct extension and result in production of cytokines and reactive oxygen species, which, in turn, stimulate myocyte apoptosis, disruption of extracellular matrix secondary to activation of matrix metalloproteinases, and fibrosis.7–11 This phenomenon is initially localized to myocardium immediately adjacent to the infarct but then spreads to involve the remainder of the ventricle during the remodeling process to convert normally perfused myocardium into remodeled, hypokinetic myocardium,2,4,28 which ultimately can produce progressive global LV dilatation and systolic dysfunction. Subsequently, the heart enters a positive feedback loop of dilatation and further exaggerated LV wall stress, which eventually can lead to progressive global LV dysfunction and congestive heart failure.

Multiple surgical therapies intended to reduce LV wall stress/strain and unload the heart have received considerable attention recently. One such therapy is the Acorn CSD. The rationale for this approach is that limiting the stress and stretching of the myocardium will halt this component of the remodeling process.18–21,29–31
In this experiment, we examined the effects of a prophylactic Acorn CSD on transmural strain patterns in different LV regions to evaluate its potential influence on the prevention of LV wall remodeling. Placement of the transmural beadsets, along with high-speed biplane videofluoroscopy, allowed us to measure regional 3D transmural normal and shear strains throughout the cardiac cycle. The data from the Sham and MI groups revealed that posterolateral MI causes substantial alteration in transmural cardiac shear strains both in myocardium adjacent to and remote from the infarction. In the lateral equatorial wall adjacent to the infarcted myocardium, the MI group exhibited increased circumferential-radial shear strain in the subepicardium and longitudinal-radial shear strain in the midwall and subendocardium. In the anterobasal wall (remote from the infarct), longitudinal-radial shear was increased in the midwall and subendocardium. These altered strain patterns might participate in the pathological cascade, which results in myocyte apoptosis and matrix metalloproteinase activation, although this remains speculative. Passive ventricular constraint placed before the infarction prevented longitudinal-radial shear strain perturbations in both myocardial regions adjacent and remote from the infarction. Minimizing changes in shear strains might attenuate the neurohumoral cascade involved in the LV remodeling process.

In the lateral wall adjacent to the MI, however, CSD did not prevent change in subepicardial circumferential-radial shear strain. Nonetheless, the circumferential-radial shear strains in the MI+CSD group were not statistically different from those in the Sham and MI groups. Interestingly, in-
creased longitudinal-radial shear strain was found only in the inner half of the LV wall in the MI group and not in the subepicardial layer. Future studies are needed to explore these effects more completely, that is, inability of CSD to prevent subepicardial circumferential-radial shear strains in myocardium adjacent to the infarction. Future surgical strategies to reshape the ventricle in patients with heart failure should be designed to reverse or minimize these shear strain abnormalities at all wall depths to prevent the pathological progression from a localized MI to global LV systolic and diastolic dysfunction.

To date, no other study has looked at the CSD effects on regional 3D myocardial strains at different LV wall depths throughout the cardiac cycle. Currently, the spatial and temporal resolution of MRI and ultrasound is not sufficient to make the required measurement directly as reported from this experiment. Several studies, however, have investigated the effects of ventricular constraint on 2D strains and infarct extension in LV remodeling. Pilla et al.32 examined 2D strain with MRI and found that ventricular restraint early after MI improved contractile function of the borderline myocardium and wall thickening dynamics. Blom et al.33 showed that CSD decreased the borderline akinetic area and enhanced myocardial energetics after MI. Moainie et al.34 found significantly smaller short-axis strain in infarcted myocardium when Marlex mesh was placed to stiffen the infarcted LV wall in sheep. Guy et al.35 reported a decrease in end-systolic muscle:cavity area ratio in sheep with Merseline mesh placed over the entire LV wall.

Previous studies of cardiomyoplasty gave rise to the concept of passive ventricular constraint as a potential therapeutic modality for preventing LV dilatation and preserving LV elliptical shape. Kass et al.36 suggested that the benefit of cardiomyoplasty in reversing LV remodeling might have resulted mostly from passive girdling of the heart rather than active augmentation of myocardial contraction. Both human and animal studies have shown that cardiomyoplasty, by preventing further LV dilatation and restoring LV elliptical shape, improves LV function.37,38 In addition to confirming these findings, results from the present study using direct measurement of transmural strains suggests a further importance of passive ventricular containment in potentially preventing infarct extension by attenuating the increase in shear strains both in myocardium adjacent to and remote from the infarct.

Compared with the MI group, CSD prevented LV dilatation and sphericization. These salutary effects might prevent the heart from progressing into the pathological cascade, which culminates in global LV dilatation and congestive heart failure. CSD increased LV sphericity (LV length/diameter) and is consistent with the Acorn CSD compliance properties in both the circumferential and longitudinal axes. For a given load, the CSD allows greater compliance in the longitudinal direction (apex to base) than in the circumferential direction, which allows restoration of the LV elliptical shape.

These findings of LV size and shape are consistent with multiple previous ventricular constraint studies. Pilla et al.32 and Blom et al.33 reported a 39% and 42% reduction in LVEDV, respectively, in sheep with CSD placed after anterior wall infarction. Chaudhry et al.17 reported smaller LV volumes and greater sphericity index in CSD-treated dogs. Enomoto et al.39 demonstrated the LVEDV and LV sphericity were better preserved in animals with ventricular constraints.

Furthermore, recent clinical findings from the Acorn CorCap CSD randomized trial29,40 demonstrated that CSD can normalize LV size and shape over time, improve quality of life, and enhance freedom from major cardiac procedures. Moreover, the recent Acorn CorCap surgical report by Mann et al.40 demonstrated that CSD enhances reverse LV remodeling when CSD was added to mitral ring annuloplasty or mitral valve replacement in patients with nonischemic CHF and functional mitral regurgitation. This emphasizes the importance of a ventricular approach to a ventricular disease, which directly reduces myocardial stress and strain.

In summary, this study allowed direct examination of the effects of prophylactic Acorn CSD on regional transmural shear strains in myocardium in 2 separate LV regions. Prophylactic CSD prevented infarct-induced abnormal longitudinal-radial shear strains not only in myocardium adjacent to, but also remote from, the infarction site and prevented infarct-induced LV dilatation and sphericization. By attenuating these shear strain abnormalities, CSD may reduce biochemical triggers portending progressive LV remodeling. A better understanding of regional strain perturbations will be important for the future development of surgical and catheter interventional treatments (passive ventricular constraint, Coapsys, Surgical Anterior Ventricular Restoration (SAVR), Dor, Fontan stitch, papillary muscle sling, Menicanti tri-level LV repair, coronary sinus cerclage, etc) aimed at reversing deleterious LV remodeling. Surgical strategies designed to reverse shear strain abnormalities (both direction and magnitude) may be a new paradigm for preventing the progression of localized MI to global LV systolic and diastolic dysfunction, but a better understanding of LV transmural wall deformations (normal strains and shear strains) is needed.

Limitations
Considerable caution must be exercised in extrapolating the result of this experiment in sheep hearts to the human heart. Because a second operation is not allowed per Stanford Medical Center Animal Research Protocol, a prophylactic model was used in this study. Such a prophylactic surgical intervention is not a clinical reality and would be associated with adverse effects, for example, obliteration of all epicardial anatomy precluding future consideration of coronary bypass grafting. Furthermore, although results from this study could be interpreted to suggest that early application of CSD could be beneficial, the appropriate timing for CSD implantation remains controversial and needs considerable future investigation.

Passive ventricular constraint prevented the increase in regional transmural (midwall and subendocardium) longitudinal-radial shear strains after posterior wall MI but not subepicardial circumferential-radial shear strains in myocardium adjacent to the infarct. These results have spawned our current investigation, using quantitative histological tech-
niques and transmural fiber-sheet strain analytical methods to better understand the underlying basis of these findings at a more fundamental level and to examine the CSD effects on the LV microstructure (ie, myocardial fiber and sheet) architecture and dynamics. The need for immediate glutaraldehyde fixation for quantitative histological microstructural measurement precluded assessment of tissue perfusion using dye or microsphere injection and infarct size measurements. The present study is highly invasive and, clearly, MRI will ultimately be the best method for this type of study, because MRI studies are noninvasive and allow assessment of the entire LV, rather than just a few specific regions. However, the current spatial resolution of MRI is not sufficient to make the required measurements directly for this study. Most MRI studies have reported average strain contributions over the entire transmural thickness at each LV site or used model assumptions for each LV wall depth. If the transmural thickness of the LV wall is ~10 mm, and one wants to resolve the strains of one third of the wall (~3 mm) within 0.05, this requires a spatial resolution of 0.15 mm (0.05 × 3), a resolution available in the present bead column studies but not currently with MRI.

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Disclosures

None.

References


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