Regional myocardial work by strain Doppler echocardiography and LV pressure: a new method for quantifying myocardial function

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Urheim, Stig, Stein Inge Rabben, Helge Skulstad, Erik Lyseggen, Halfdan Ihlen, and Otto A. Smiseth. Regional myocardial work by strain Doppler echocardiography and LV pressure: a new method for quantifying myocardial function. Am J Physiol Heart Circ Physiol 288: H2375–H2380, 2005. First published January 6, 2005; doi:10.1152/ajpheart.00946.2004.—There is a need for better methods to quantify regional myocardial function. In the present study, we investigated the feasibility of quantifying regional function in terms of a segmental myocardial work index as derived from strain Doppler echocardiography (SDE) and invasive pressure. In 10 anesthetized dogs, we measured left ventricular (LV) pressure by micromanometer and myocardial longitudinal strains by SDE and sonomicrometry. The regional myocardial work index (RMWI) was calculated as the area of the pressure-strain loop. As a reference method for strain, we used sonomicrometry. By convention, the loop area was assigned a positive sign when the pressure-strain coordinates rotated counterclockwise. Measurements were done at baseline and during volume loading and short anterior descending coronary artery (LAD) occlusion, respectively. There was a good correlation between RMWI calculated from strain by SDE and strain by sonomicrometry (r = 0.73 ± 0.21, r = 0.82, P < 0.01). Volume loading caused an increase in RMWI from 1.3 ± 0.2 to 2.2 ± 0.1 kJ/m³ (P < 0.05) by SDE and from 1.5 ± 0.3 to 2.7 ± 0.3 kJ/m³ (P = 0.066) by sonomicrometry. Short-term ischemia (1 min) caused a decrease in RMWI from 1.3 ± 0.2 to 0.3 ± 0.04 kJ/m³ (P < 0.05) and from 1.3 ± 0.3 to 0.5 ± 0.2 kJ/m³ (P < 0.05) by SDE and sonomicrometry, respectively. In the nonischemic ventricle and during short-term ischemia, the pressure-strain loops rotated counterclockwise, consistent with actively contracting segments. Long-term ischemia (3 h), however, caused the pressure-strain loop to rotate clockwise, consistent with entirely passive segments, and the loop areas became negative, −0.2 ± 0.1 and −0.1 ± 0.03 kJ/m³ (P < 0.05) by SDE and sonomicrometry, respectively. A RMWI can be estimated by SDE in combination with LV pressure. Furthermore, the orientation of the loop can be used to assess whether the segment is active or passive.

Sonomicrometry; pressure-strain loop

Strain Doppler Echocardiography (SDE) has been introduced as a new clinical method to measure regional myocardial function (2, 5, 18). As a measure of systolic function, one may use peak systolic strain, recorded either in the LV long axis as shortening strain or in the short axis as thickening strain. However, peak systolic strain is load dependant and therefore may not reflect systolic function when there are changes in loading conditions (18). This is analogous to the problem with load dependency of LV ejection fraction. In the latter case, one may use LV pressure-volume relations to differentiate between load-induced changes in function and changes in intrinsic myocardial contractility. Assessment of regional pressure-dimension loops, however, has not been feasible in clinical studies. In animal models, however, one may analyze regional function from pressure-segment length loops obtained from micromanometers and implanted sonomicrometric crystals (1, 3, 7, 10, 14, 15, 17). Similar to sonomicrometry, SDE provides a continuous measure of changes in regional dimension, and regional pressure-strain loops may provide information similar to pressure-segment length loops. It remains to be shown, however, that pressure-strain loops recorded by SDE reflect regional myocardial function.

The aim of this study was to investigate if SDE can be used to construct LV pressure-strain loops and if the area of the pressure-strain loop can be used as an index of regional myocardial work (RMW). As a reference method, we used pressure-segment length loops that were constructed from pressure and implanted sonomicrometric crystals.

Methods

Ten dogs of either sex and average body weight of 24.3 kg were given thiopentone (25 mg/kg body wt) and morphine (100 mg iv), followed by an infusion of morphine (50–100 mg/h iv) and pentobarbital (50 mg ev) every hour. The animals were artificially ventilated through a cuffed endotracheal tube using room air with 20–50% oxygen. The ECG was monitored from a limb lead. Jugular and femoral arteries and veins were cannulated. After a median sternotomy, the pericardium was split from the apex to base, and, after the instrumentation, the edges of the pericardial incision were loosely resutured. An inflatable vascular occluder was placed around the left anterior descending coronary artery (LAD), just distal to the first diagonal branch. The dogs were placed in the right supine position during recordings. The animals were euthanized with pentobarbital.

The study was approved by the National Animal Experimentation Board.

Pressure Measurements

A 5-Fr micromanometer-tipped catheter (model MPC-500, Millar Instruments; Houston, TX) was positioned in the LV through a carotid artery. Via the appendage, a 5-Fr micromanometer and a fluid-filled catheter were placed in the left atrium. All pressure transducers were calibrated with a mercury manometer. The pressures were zero referenced against the fluid-filled left atrial catheter. Pressure and ECG data were processed via preamplifiers and were digitized at 200 Hz for further analysis on a personal computer workstation.

Sonomicrometry

One pair of ultrasonic crystals was implanted in the inner half of the anterior LV wall near the apex and aligned parallel with the LV long axis (Fig. 1). The crystals were connected to a sonomicrometer.
strains were calculated in percentage of end-diastolic dimensions. By 18). For the purpose of this study, strain measurements were done only in a personal computer workstation.

The strain recordings were obtained from the same area with a sample length digitized at 200 Hz for further analysis on a personal computer (Sonometrics; London, Ontario, Canada), and the crystal data were converted from mmHg to kJ/m3 (1 mmHg = 133.4 N/m2 = 0.1334 kJ/m3).

By convention, the loop area was assigned a positive sign (i.e., active work) when the pressure-strain coordinates rotated counterclockwise and a negative sign when the rotation was clockwise.

**Experimental Protocol**

In six dogs after baseline recordings, we increased stroke volume by flushing 500 to 1,000 ml saline into a central vein to increase LV end-diastolic pressure by ~10 mmHg. After the return of end-diastolic pressure to baseline values, the LAD was occluded, and recordings were performed 1 min after the onset of occlusion. One baseline recording and one recording during short-term ischemia were not analyzed because of poor quality of the sonomicrometry trace. In four additional dogs, we induced long-term ischemia by occluding the LAD for 180 min.

In each experiment, we confirmed the location of the ultrasonic crystals within the ischemic zone by demonstrating systolic segmental lengthening during LAD occlusion.

Because of interference between sonomicrometry and Doppler echocardiography, we first recorded pressures, ECG, and echocardiographic data during 10 s and then pressures, ECG, and sonomicrometry during the subsequent 10 s. Data were recorded with the respirator off.

**Statistics**

Data are presented as mean ± SE. Differences between groups were analyzed with the Friedman test for related data. Paired data were analyzed with Student’s t-test. The RMW values obtained by the two different methods (sonomicrometry and SDE) were compared by regression analysis using a least-squares method. For all statistical comparisons, \( P < 0.05 \) was considered significant.

**RESULTS**

Hemodynamic variables at baseline and during volume loading and LAD occlusion are presented in Tables 1–3. Figure 2 demonstrates LV pressure-strain loops, using sonomicrometry and SDE at baseline, during volume loading and short-term ischemia. Loop area was used as an index of RMW. During each of these interventions, the loops rotated counterclockwise, consistent with actively contracting segments. The morphology of the loops by SDE resembled that of the loops by sonomicrometry during all interventions. During volume loading, the area of the loops increased, reflecting that more work was performed by the segment. On average, volume loading increased the RMW index from 1.3 ± 0.2 to 2.2 ± 0.1 kJ/m3 (\( P < 0.05 \)) using SDE and from 1.5 ± 0.3 to 2.7 ± 0.3 kJ/m3 (\( P = 0.066 \)) using sonomicrometry. During short-term ischemia, the
RMW index decreased from 1.3 ± 0.2 to 0.3 ± 0.04 kJ/m³ ($P < 0.05$) using SDE and from 1.3 ± 0.3 to 0.5 ± 0.2 kJ/m³ ($P < 0.05$) using sonomicrometry. The orientation of the loops did not change, indicating that the segment was still actively contracting. During long-term ischemia (LAD occlusion 180 min), however, the orientation of the loops turned from counterclockwise to clockwise in all experiments, and the calculated area became negative, $-0.1$ ± 0.03 kJ/m³ ($P < 0.05$ vs. baseline) using sonomicrometry and $-0.2$ ± 0.1 kJ/m³ ($P < 0.05$ vs. baseline) using SDE (Fig. 3). Figure 4 displays individual data and demonstrates good correlation between the RMW index by SDE and sonomicrometry ($y = 0.73x + 0.21$, $r = 0.82$, $P < 0.01$).

**DISCUSSION**

The present study demonstrates that RMW can be estimated from combined measurement of LV pressure and myocardial strain by SDE. Over a wide range of strains induced by volume loading and coronary occlusion, the SDE method showed loop areas that correlated well with those measured by sonomicrometry.

**Stress Versus Pressure**

Measurement of RMW requires simultaneous measurement of regional wall stress (force) and dimension, and regional myocardial work index.

**Table 1. Hemodynamic variables (volume loading)**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Volume Loading</th>
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<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>115±9</td>
<td>122±7</td>
</tr>
<tr>
<td>LV peak systolic pressure, mmHg</td>
<td>106±5</td>
<td>130±7*</td>
</tr>
<tr>
<td>LV end-diastolic pressure, mmHg</td>
<td>7±1</td>
<td>22±2*</td>
</tr>
<tr>
<td>LV $dP/dr_{max}$, mmHg</td>
<td>1,924±131</td>
<td>2,515±358</td>
</tr>
<tr>
<td>End-diastolic segment length (LAD region), mm</td>
<td>7.9±0.4</td>
<td>8.7±0.4*</td>
</tr>
<tr>
<td>Peak systolic strain (LAD region) Sonomicrometry, %</td>
<td>$-15±1$</td>
<td>$-19±2$</td>
</tr>
<tr>
<td>SDE, %</td>
<td>$-12±0$</td>
<td>$-19±2$*</td>
</tr>
<tr>
<td>Regional myocardial work index (LAD region) Sonomicrometry, kJ/m³</td>
<td>1.5±0.3</td>
<td>2.7±0.3</td>
</tr>
<tr>
<td>SDE, kJ/m³</td>
<td>1.3±0.2</td>
<td>2.2±0.1*</td>
</tr>
</tbody>
</table>

Values are means ± SE; $n = 5$ dogs. *$P < 0.05$, intervention vs. baseline.

**Table 3. Hemodynamic variables (long-term ischemia)**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Long-Term Ischemia</th>
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<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>110±3</td>
<td>115±17</td>
</tr>
<tr>
<td>LV peak systolic pressure, mmHg</td>
<td>113±9</td>
<td>86±6*</td>
</tr>
<tr>
<td>LV end-diastolic pressure, mmHg</td>
<td>7±1</td>
<td>9±2</td>
</tr>
<tr>
<td>LV $dP/dr_{max}$, mmHg</td>
<td>2,048±275</td>
<td>1,298±61†</td>
</tr>
<tr>
<td>End-diastolic segment length (LAD region), mm</td>
<td>9.7±1.8</td>
<td>11.1±1.9*</td>
</tr>
<tr>
<td>Peak systolic strain (LAD region) Sonomicrometry, %</td>
<td>$-10±1$</td>
<td>9±2*</td>
</tr>
<tr>
<td>SDE, %</td>
<td>$-12±0$</td>
<td>3±1*</td>
</tr>
<tr>
<td>Regional myocardial work index (LAD region) Sonomicrometry, kJ/m³</td>
<td>0.9±0.2</td>
<td>$-0.1±0.03*$</td>
</tr>
<tr>
<td>SDE, kJ/m³</td>
<td>1.4±0.1</td>
<td>$-0.2±0.1*$</td>
</tr>
</tbody>
</table>

Values are means ± SE; $n = 4$ dogs. *$P < 0.05$, intervention vs. baseline; †$P = 0.05$, intervention vs. baseline.

Work equals the product of developed stress and change in dimension or, more accurately, the integral of the stress-dimension loop. Regional myocardial wall stress equals force per unit cross-sectional area and can be calculated from measurements of LV transmural pressure, wall thickness, and local radius of curvature. The measurement of all these variables requires complex methodologies, and one needs to make a number of assumptions regarding local geometry. At present, there are no reliable clinical methods to measure regional ventricular wall stress directly.

In the present study, we used LV intracavitary pressure as a substitute for regional wall stress. Skulstad et al. (16) compared LV pressure-segment length loops to stress-segment length loops in a model similar to that used in the present study. Their interpretations regarding active and passive contributions to regional segmental shortening were qualitatively similar for the two approaches, supporting that the pressure-strain loop reflects regional work. These findings are consistent with the study of Goto et al. (4), which assessed RMW in an experimental model from wall tension-area loops and demonstrated that this measure of regional work was valid also during regional myocardial ischemia.

Although the area of the pressure-strain loop is an index rather than a direct measure of regional work, it has the advantage of being relatively simple to obtain during cardiac catheterization in a clinical setting.

Nakano et al. (12) introduced an alternative clinical method for calculating regional stress-strain loops from the relationship between mean wall stress and the natural logarithm of the reciprocal of wall thickness. In patients with ischemic myocardium, they found that the area of the ischemic loops were reduced (11).

**Potential Applications of Pressure-Strain Analysis**

In the present study, the orientation of the pressure-strain loop was used to differentiate between actively contracting and passive myocardium. A hallmark of actively contracting myocardium is that the segment shortens during systole when LV pressure is rising, whereas passive myocardium lengthens when pressure is rising. Furthermore, passive myocardium shortens during isovolumic relaxation when...
LV pressure is falling. This implies that an active pressure-strain loop rotates counterclockwise. On the other hand, an entirely passive myocardial segment moves essentially up and down along the same curve or, rather, in a clockwise fashion due to slight hysteresis caused by viscoelastic forces. This implies that the direction of rotation of the pressure-strain loop provides information regarding active and passive contributions to regional myocardial deformation and motion. Because the demonstration of active contraction implies viable myocardium, the pressure-strain loop might have potential as a method to differentiate between viable and nonviable myocardium.

In the present study, ischemia resulted in severe myocardial dysfunction with passive systolic lengthening of the segment. Although systolic lengthening implies that the myocardium behaves as a net passive structure, it does not rule out active contributions. The direction of rotation of the loop needs to be taken into account to differentiate between active and passive segments. This principle was demonstrated during short-term ischemia (Fig. 2), which caused the myocardial segment to lengthen during early systole while the pressure-segment length loop rotated counterclockwise, indicating some degree of active contraction. However, during long-term ischemia, the pressure-strain loop (Fig. 3) rotated clockwise and therefore was entirely passive. In a clinical context in patients with coronary artery disease, it is possible that a similar loop analysis may serve as a method to identify viable myocardium. This, however, remains to be determined in clinical studies.

The pressure-strain loop analysis may give us insight into how different therapeutic principles modify myocardial function and how interventions like ventricular pacing changes regional work at the pacing site (13).

Regional contractility calculated as the slope of the end-systolic pressure-segment length relationship (6, 9) has been proposed as a measure of regional myocardial function. Krams et al. (6) reported in an animal study reduction of regional elastance in stunned myocardium. Elastance would be a more direct measure of regional contractility than present methods and, importantly, is expected to be less load dependent. With further refinement of the SDE method, it may be feasible to measure multiple strain loops and LV pressure continuously and thereby calculate regional elastance.

Because the pressure-strain analysis requires invasive pressure, its potential role would be to serve as a supplementary modality during LV catheterization. In principle, however, it may be possible to estimate LV systolic pressure from noninvasive arterial pressure and to estimate regional work as the product of systolic pressure and peak systolic strain. This approach would have several limitations but would have the advantage of being entirely noninvasive.
Limitations

An important limitation of the SDE method is the marked angle dependency (18). Correct orientation of the ultrasound beam relative to the myocardial wall is critical for the application of this imaging modality. The strain curve by Doppler echocardiography was not obtained simultaneously with strain by sonomicrometry and LV pressure. However, the recordings were performed within 20 s with the respirator off, during a stable hemodynamic situation.

The use of LV pressure as a substitute for LV wall stress may lead to errors in ventricles with marked changes in local geometry. However, as demonstrated by others (4, 16), during acute ischemia this does not seem to be a major problem. Another limitation is related to the tendency of strain estimates by SDE to drift throughout one cardiac cycle, and the algorithm that was used to compensate for drifting may introduce errors. However, the most important application of this method would not be the absolute calculated area but relative changes of one region during different interventions and to determine the orientation of the loop as counterclockwise or clockwise.

A fundamental limitation of pressure-strain loops as an approach to define anatomic extension of ischemic dysfunction is related to tethering. Segmental shortening may be markedly impaired in nonischemic myocardium immediately adjacent to the ischemic region, and therefore the size of the ischemic region may be overestimated (8).

In conclusion, an estimate of RMW can be obtained by SDE in combination with LV pressure. The method can discriminate between active and passive segments by taking into account the orientation of the loops. This approach should be tested clinically and could represent a new method for the assessment of myocardial tissue viability during invasive studies.

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GRANTS

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