increased exercise threshold for angina pectoris after physical conditioning. J Clin Invest 54: 763, 1974

Effect of Acute Ischemia, Nitroglycerin and Nitroprusside on Regional Myocardial Thickening, Stress and Perfusion

Experimental Echocardiographic Studies

RICHARD E. KERBER, M.D., JAMES B. MARTINS, M.D. AND MELVIN L. MARCUS, M.D.

with the technical assistance of Margaret Schrader, Gilbert Koenigsaecker, B.S., and Oscar Lim, M.S.

SUMMARY The purpose of this study was to demonstrate that echocardiography can be used to demonstrate the systolic wall thickening of acutely ischemic myocardium, and to compare the effects of nitroglycerin and nitroprusside on systolic thickening, wall stress and perfusion of ischemic myocardium. In 37 dogs, the ratio of end-systolic-to-end-diastolic posterior wall thickness fell from 1.30 ± 0.02 to 0.88 ± 0.01 (p < 0.001) after circumflex coronary occlusion; perfusions of the area supplied by the occluded artery fell from 98.2 ± 7.5 ml/100 g/min to 36.5 ± 2.9 ml/100 g/min (p < 0.001). Nitroglycerin and nitroprusside were given to lower mean arterial pressure by 7% and 15%. Despite the reduction in coronary perfusion pressure, transmural perfusion, endocardial/epicardial perfusion ratio and systolic thinning remained constant. Both drugs reduced the ischemic "wall stress index" (ventricular pressure × ventricular diameter/wall thickness) by almost 50%. Thus, both nitroglycerin and nitroprusside were equally beneficial in this model of acute myocardial ischemia.

EXPERIMENTAL STUDIES using a variety of techniques\(^1\)\(^\text{--}\)\(^4\) have shown that changes in dynamic wall thickness occur after coronary occlusion. Sassayama et al.,\(^4\) using implanted ultrasonic sonomicrometers, showed that wall thickness changes paralleled the shortening characteristics of adjacent subendocardial segments in response to alterations in heart rate and loading. Thus, wall thickness could be useful for characterizing regional function of ischemic myocardium. Based on these sonomicrometer studies, Ross and Franklin\(^5\) suggested that echocardiography could reveal changes in wall thickness that might be useful for assessing the effects of acute interventions on the regional dysfunction of acutely ischemic myocardium. This suggestion has not yet been validated in an experimental echocardiographic study.

The use of vasodilator agents is one important intervention which might be assessed by echocardiographic evaluation of wall thickness changes.

From the Cardiovascular Division, the Cardiovascular Center, the Department of Internal Medicine, University of Iowa Hospital, Iowa City, Iowa.

Supported by NHLBI grant HL 014388 and by Research Career Development Award HL 00328.

Address for reprints: Richard E. Kerber, M.D., Department of Medicine, University of Iowa Hospital, Iowa City, Iowa 52242.

Received March 16, 1978; revision accepted January 11, 1979.

Circulation 60, No. 1, 1979.
Although arterial pressure manipulations are known to alter myocardial ischemia, there is controversy over the optimal vasodilator agent and the amount of blood pressure lowering that can be safely effected.

The purposes of this study were twofold: 1) to use echocardiography to assess the effect of acute coronary occlusion on the systolic thickening of ventricular myocardium and to compare changes in wall thickness with alterations of coronary blood flow in the ischemic area traversed by the ultrasound beam; 2) to compare the effects of nitroglycerin and nitroprusside, at equivalent mean arterial pressures, on the systolic thinning, perfusion and wall stress of regionally ischemic myocardium.

**Methods**

**Preparation of the Model**

We studied 37 adult mongrel dogs. The dogs were anesthetized with intravenous chloralose-urethane. An endotracheal tube was placed and the dogs were ventilated using a Harvard respirator, room air and supplemental oxygen. Arterial PO$_2$, Pco$_2$, and pH were monitored frequently, and were maintained in a physiologic range by adjusting tidal volume and oxygen. After a midsternal thoracotomy and pericardiotomy, the heart was exposed and suspended in a pericardial sling and heparin (250 units/kg i.v.) was given. The circumflex coronary artery proximal to the posterior descending artery was dissected free and a snare ligature placed around it. We used #8 French polyurethane catheters to record left ventricular and aortic pressures by means of Statham P23 strain gauges at the midchest level. All recordings were made on an Electronics-for-Medicine DR-12 multichannel photographic recorder.

**Wall Thickening (Echocardiography)**

Using a method previously described in detail, we obtained echocardiographic recordings of the interventricular septum, left ventricular cavity and left ventricular posterior wall. Briefly, a 2.25 mHz, 5-cm focused transducer was placed in direct contact with the exposed anterior right ventricular surface, and aimed inferior to the mitral leaflet echoes to record the interventricular septum and left ventricular posterior wall motion. After the circumflex coronary artery was occluded remotely (to avoid altering the position of the echo transducer), the ultrasound beam was reflected from and registered the motion of acutely ischemic posterior myocardium. The transducer was clamped to a rigid bar, thus minimizing transmitted motion from the heart, and providing a fixed reference point for calculation of endocardial motion. The fixed echo transducer and pericardial sling might have constrained cardiac motion somewhat, but this condition was constant throughout the study and should not, therefore, affect the results. The sensitivity of the ultrasonoscope was manipulated to best define the epicardial and endocardial echoes. The thickness of the septum and posterior wall was measured to the nearest millimeter at end-diastole and end-systole. End-diastole was defined as the R wave of the ECG in all recordings. In the control recordings, end-systolic posterior wall thickness was measured 20 msec before the dicrotic notch of the aortic pressure tracing, to correct for the pressure transmission delay in the fluid-filled catheter. After coronary occlusion, end-systolic posterior wall thickness was measured just before the start of the rapid anterior recoiling motion of the ischemic posterior wall, an event which occurs at the end of the phase of systolic ejection. Septal end-systolic thickness was taken at the point of maximum thickening. Figure 1 shows the points of measurement. Endocardial wall velocity and excursion of the posterior wall were measured during systolic ejection, as previously described.

**Myocardial Perfusion**

Our method for determining myocardial perfusion has been previously described in detail. We used 7-10-μ microspheres labeled with $^{141}$Ce, $^{85}$Sr, $^{51}$Cr and $^{41}$Sc. For each perfusion measurement the vial containing the microspheres was mechanically agitated for at least 3 minutes to disperse the spheres adequately. The microspheres were suspended in saline and injected over a 5-second period into the left atrium; the atrial catheter was then flushed with 5 ml of saline. Beginning 1 minute before injection, and continuing for 3 minutes thereafter, blood for reference flow determinations was withdrawn from the right brachial and femoral arteries simultaneously at 2.06 ml/min.

At the end of the experiment, after the echocardiographic recordings were completed, two metal probes were positioned along the ultrasound transducer and passed through the heart in parallel to mark the path of the ultrasound beam. To minimize deformation of the left ventricular wall (and consequent errors in beam localization) we used sharp, #20 needles inserted through the heart while it was still beating. The points of intersection of the probes with the left ventricular posterior endocardium subsequently verified that the specific myocardial segments traversed by the ultrasound beam were among the hypoperfused segments from the area supplied by the ligated coronary artery. If the beam intersected segments subsequently found to be normally perfused, the data from that dog were excluded. The dogs were then killed with an injection of potassium chloride.

The heart was excised and the free walls of the right ventricle, the right and left atria, great vessels, valves, surface vessels and epicardial fat were removed. Using the posterior descending coronary as a reference point, we divided the left ventricle into four equal levels of eight segments each, and each segment was divided into three layers — endocardium, mid-wall and epicardium. Thus, the left ventricle was divided into 96 segments, each about $1.6 \times 1.6 \times 0.3$ cm in size with an average weight of 0.8 g. The relative geometric position of each segment was constant from dog to dog.
Using techniques previously described in detail, we determined the perfusion of each of the 96 small myocardial segments as well as the size of the ischemic area and the endocardium-epicardium perfusion ratio. The perfusion of normal segments is heterogeneous, but only rarely will a single segment's perfusion fall below 2 standard deviations from the mean perfusion of all left ventricular segments. Segments found to have perfusion less than this (seen almost exclusively after coronary ligation) were classified as ischemic.

Statements concerning perfusion of the ischemic area refer to the perfusion of all the segments classified initially as ischemic after coronary occlusion.

**Wall Stress**

Left ventricular wall stress is determined by intraventricular pressure, left ventricular internal diameter and left ventricular wall thickness. We used a "wall stress index" relating these parameters as follows: stress index (arbitrary units) = P×D/Th, where P = left ventricular pressure, D = left ventricular internal diameter and Th = left ventricular wall thickness. We made these measurements at the start of systolic ejection (defined by the aortic pulse tracing) and at end-systole. End-systole was defined by either the dicrotic notch of the pulse tracing or by the echocardiogram, as previously discussed.

**Experimental Protocol**

In all 37 dogs, control echocardiographic and hemodynamic recordings and an initial injection of microspheres were made. The circumflex coronary artery ligature was then pulled tight by the remotely controlled snare to occlude the artery. Stabilization for 20 minutes was allowed, after which we performed a second set of echocardiographic and hemodynamic recordings and injected microspheres with a different label.

The initial 23 dogs were then used for other experiments on the effects of afterload increases on systolic thickening of ischemic myocardium. These were reported separately and are not further considered here. In the remaining 14 dogs, we made additional recordings of the effect of intravenous nitroglycerin or nitroprusside. Seven of these dogs received nitroglycerin 0.1–0.5 mg/min i.v. to lower the
postcoronary occlusion mean aortic pressure by 7% and subsequently by 15%. The other seven dogs received sodium nitroprusside 0.5–3.0 μg/min i.v. to the same end points. In each of these dogs, the end point of pressure decrease was maintained for at least 5 minutes while we obtained echocardiographic and hemodynamic recordings and injected microspheres. Measurements during drug infusions were generally made 30–45 minutes after coronary occlusion, and were completed within 60 minutes of the occlusion in all cases.

Statistical analysis of the initial 37 experiments comparing control and coronary occlusion paired data was done using the paired t test. We analyzed the subsequent nitroglycerin/nitroprusside multiple intervention studies using a two-way analysis of variance and, when the F statistic was significant, we used Scheffe’s multiple comparison procedure.

Results

Effect of Circumflex Coronary Occlusion on Systolic Myocardial Thickening and Blood Flow

The result of inducing acute ischemia is shown graphically in figure 2. The preocclusion ratio of end-systolic-to-end-diastolic posterior wall thickness was 1.30 ± 0.02 (SEM) (range 1.10–1.60); after circumflex occlusion this ratio fell to 0.88 ± 0.01 (range 0.61–1.09) \((p < 0.001)\). Transmural perfusion of the ischemic area fell from a control of 98.2 ± 7.5 ml/100 g/min to 36.5 ± 2.9 ml/100 g/min \((p < 0.001)\) after coronary ligation.

Effects of Vasodilators on Ischemic Wall Thickness, Stress and Perfusion

The size of the ischemic area in the seven dogs that subsequently received nitroglycerin was 21 ± 3% of
the left ventricular mass, while in the nitroprusside-treated dogs it was 20 ± 3%. The results of nitroglycerin and nitroprusside administration are shown in tables 1 and 2, and graphically in figures 3–5. By design of the study, both drugs reduced mean aortic pressure by equivalent amounts. Despite the fall in coronary perfusion pressure, transmural perfusion and endocardial-epicardial perfusion ratio of both the ischemic and nonischemic areas remained constant with both drugs. The systolic/diastolic thickness ratios of ischemic posterior myocardium and non-ischemic septal myocardium showed no significant change with either level of blood pressure reduction due to nitroprusside or nitroglycerin.

The posterior wall stress index, both at onset of systolic ejection and at the end of systole, showed large rises after coronary occlusion (fig. 5), due primarily to the increases in ventricular diameter and decreased systolic wall thickness of the ischemic myocardium. During the administration of both nitroglycerin and nitroprusside, large and significant falls occurred in the stress index, which returned to control levels.

Posterior endocardial wall velocity and excursion fell significantly after coronary occlusion. No further changes occurred with either vasodilator agent.

**Discussion**

This experimental study proves that systolic thinning or reduction of thickening of ischemic myocardium can be demonstrated by echocardiography, as suggested by Ross and Franklin. Systolic thinning or less-than-normal thickening commonly occurs in patients with acute myocardial infarction, but the perfusion of the area struck by the ultrasound beam has not been previously determined. In this study we determined the perfusion of such areas with labeled microspheres and showed that the echocardiographic recordings were from areas that were grossly hypoper-

**TABLE 1. Dogs Receiving Nitroprusside After Coronary Occlusion (n = 7)**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Coronary occlusion</th>
<th>Nitroprusside 1</th>
<th>Nitroprusside 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hemodynamics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>154 ± 7</td>
<td>149 ± 5</td>
<td>152 ± 8</td>
<td>152 ± 12</td>
</tr>
<tr>
<td>Aortic mean pressure (mm Hg)</td>
<td>87 ± 3</td>
<td>89 ± 4</td>
<td>79 ± 4*†</td>
<td>70 ± 6*†</td>
</tr>
<tr>
<td>Left ventricular systolic pressure (mm Hg)</td>
<td>104 ± 3</td>
<td>106 ± 4</td>
<td>94 ± 4*</td>
<td>83 ± 6*†</td>
</tr>
<tr>
<td>Left ventricular end-diastolic pressure (mm Hg)</td>
<td>5 ± 1</td>
<td>6 ± 1</td>
<td>6 ± 1</td>
<td>5 ± 1</td>
</tr>
<tr>
<td>Left ventricular end-diastolic diameter (mm)</td>
<td>30 ± 2</td>
<td>32 ± 1</td>
<td>30 ± 1</td>
<td>29 ± 1</td>
</tr>
<tr>
<td><strong>Ischemic myocardium</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perfusion (ml/100 g/min)</td>
<td>119 ± 18</td>
<td>43 ± 5†</td>
<td>47 ± 6†</td>
<td>40 ± 8†</td>
</tr>
<tr>
<td>Endo-epi ratio</td>
<td>1.10 ± 0.05</td>
<td>0.79 ± 0.06†</td>
<td>0.78 ± 0.08†</td>
<td>0.87 ± 0.15†</td>
</tr>
<tr>
<td>Posterior wall stress index at end of systolic ejection</td>
<td>168 ± 16</td>
<td>360 ± 48†</td>
<td>252 ± 20*</td>
<td>195 ± 21*</td>
</tr>
<tr>
<td>Posterior wall stress index at onset of systolic ejection</td>
<td>314 ± 46</td>
<td>406 ± 55</td>
<td>302 ± 72</td>
<td>274 ± 85</td>
</tr>
<tr>
<td>End-diastolic posterior wall thickness (mm)</td>
<td>9.6 ± 1.1</td>
<td>8.7 ± 0.8</td>
<td>9.0 ± 0.6</td>
<td>8.7 ± 0.6</td>
</tr>
<tr>
<td>End-systolic posterior wall thickness (mm)</td>
<td>12.8 ± 1.0</td>
<td>8.1 ± 0.7†</td>
<td>8.1 ± 0.5†</td>
<td>8.0 ± 0.6†</td>
</tr>
<tr>
<td>PTs/PTd</td>
<td>1.39 ± 0.09</td>
<td>0.94 ± 0.02†</td>
<td>0.90 ± 0.03†</td>
<td>0.92 ± 0.03†</td>
</tr>
<tr>
<td>Posterior wall velocity (mm/sec)</td>
<td>40 ± 3</td>
<td>18 ± 3†</td>
<td>16 ± 4†</td>
<td>15 ± 4†</td>
</tr>
<tr>
<td>Posterior wall excursion (mm)</td>
<td>5.6 ± 0.4</td>
<td>2.6 ± 0.3†</td>
<td>2.1 ± 0.4†</td>
<td>2.2 ± 0.6†</td>
</tr>
<tr>
<td><strong>Nonischemic myocardium</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perfusion (ml/100 g/min)</td>
<td>111 ± 13</td>
<td>105 ± 7</td>
<td>118 ± 14</td>
<td>100 ± 17</td>
</tr>
<tr>
<td>Endo-epi ratio</td>
<td>0.97 ± 0.04</td>
<td>1.06 ± 0.04</td>
<td>1.04 ± 0.03</td>
<td>0.97 ± 0.03</td>
</tr>
<tr>
<td>End-diastolic septal thickness (mm)</td>
<td>7.5 ± 0.3</td>
<td>6.8 ± 0.2</td>
<td>6.9 ± 0.6</td>
<td>7.7 ± 1.3</td>
</tr>
<tr>
<td>End-systolic septal thickness (mm)</td>
<td>11.0 ± 1.2</td>
<td>10.4 ± 1.6</td>
<td>11.0 ± 2.3</td>
<td>11.1 ± 3.0</td>
</tr>
<tr>
<td>STs/STd</td>
<td>1.45 ± 0.11</td>
<td>1.54 ± 0.26</td>
<td>1.55 ± 0.22</td>
<td>1.41 ± 0.19</td>
</tr>
</tbody>
</table>

All values are mean ± sem.

* *p < 0.05 vs coronary occlusion.
† †p < 0.05 vs control.

Abbreviations: endo-epi = endocardial-epicardial; PTs/PTd = systolic/diastolic posterior wall thickness ratio; STs/STd = systolic/diastolic septal thickness ratio.
TABLE 2. Dogs Receiving Nitroglycerin After Coronary Occlusion (n = 7)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Coronary occlusion</th>
<th>Nitroglycerin 1</th>
<th>Nitroglycerin 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>160 ± 9</td>
<td>150 ± 10</td>
<td>144 ± 10</td>
<td>145 ± 9</td>
</tr>
<tr>
<td>Aortic mean pressure (mm Hg)</td>
<td>96 ± 10</td>
<td>95 ± 7</td>
<td>88 ± 7</td>
<td>80 = 7†</td>
</tr>
<tr>
<td>Left ventricular systolic pressure (mm Hg)</td>
<td>118 ± 10</td>
<td>114 ± 8</td>
<td>105 ± 8</td>
<td>95 ± 8*</td>
</tr>
<tr>
<td>Left ventricular end-diastolic pressure (mm Hg)</td>
<td>7 ± 2</td>
<td>11 ± 2</td>
<td>9 ± 1</td>
<td>8 ± 2</td>
</tr>
<tr>
<td>Left ventricular end-diastolic diameter (mm)</td>
<td>29 ± 2</td>
<td>35 ± 3†</td>
<td>35 ± 3†</td>
<td>33 = 3</td>
</tr>
<tr>
<td>Ischemic myocardium</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perfusion (ml/100 g/min)</td>
<td>134 ± 22</td>
<td>39 ± 11†</td>
<td>42 ± 14†</td>
<td>37 = 14†</td>
</tr>
<tr>
<td>Endo-epi ratio</td>
<td>1.05 ± 0.06</td>
<td>0.76 ± 0.03†</td>
<td>0.71 ± 0.04†</td>
<td>0.71 = 10†</td>
</tr>
<tr>
<td>Posterior wall stress index at end of systolic ejection</td>
<td>244 ± 51</td>
<td>446 ± 60†</td>
<td>395 ± 64</td>
<td>273 = 40*</td>
</tr>
<tr>
<td>Posterior wall stress index at onset of systolic ejection</td>
<td>325 ± 77</td>
<td>482 ± 57†</td>
<td>433 ± 57</td>
<td>344 = 54*</td>
</tr>
<tr>
<td>End-diastolic posterior wall thickness (mm)</td>
<td>8.6 ± 1.0</td>
<td>7.6 ± 0.4</td>
<td>7.0 ± 0.3</td>
<td>7.5 ± 0.2</td>
</tr>
<tr>
<td>End-systolic posterior wall thickness (mm)</td>
<td>10.5 ± 1.0</td>
<td>6.7 ± 0.5†</td>
<td>7.1 ± 0.5†</td>
<td>7.5 ± 0.4†</td>
</tr>
<tr>
<td>PTs/PTd</td>
<td>1.25 ± 0.06</td>
<td>0.88 ± 0.03†</td>
<td>1.00 ± 0.04†</td>
<td>0.96 = 0.03†</td>
</tr>
<tr>
<td>Posterior wall velocity (mm/sec)</td>
<td>34 ± 4</td>
<td>18 ± 3†</td>
<td>18 ± 2†</td>
<td>18 = 2†</td>
</tr>
<tr>
<td>Posterior wall excursion (mm)</td>
<td>4.2 ± 0.5</td>
<td>2.7 ± 0.6†</td>
<td>2.5 ± 0.4†</td>
<td>2.9 ± 0.3†</td>
</tr>
<tr>
<td>Non-ischemic myocardium</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perfusion (ml/100 g/min)</td>
<td>136 ± 20</td>
<td>121 ± 22</td>
<td>143 ± 40</td>
<td>130 ± 44</td>
</tr>
<tr>
<td>Endo-epi ratio</td>
<td>1.00 ± 0.05</td>
<td>1.02 ± 0.03</td>
<td>1.04 ± 0.04</td>
<td>1.03 ± 0.05</td>
</tr>
<tr>
<td>End-diastolic septal thickness (mm)</td>
<td>6.9 ± 0.5</td>
<td>5.9 ± 0.6</td>
<td>6.7 ± 0.6</td>
<td>6.5 ± 0.5</td>
</tr>
<tr>
<td>End-systolic septal thickness (mm)</td>
<td>9.9 ± 1.2</td>
<td>8.3 ± 0.8</td>
<td>9.3 ± 0.9</td>
<td>9.0 ± 0.6</td>
</tr>
<tr>
<td>STs/STd</td>
<td>1.45 ± 0.15</td>
<td>1.47 ± 0.23</td>
<td>1.30 ± 0.07</td>
<td>1.39 = 0.09</td>
</tr>
</tbody>
</table>

All values are mean ± SEM.
*<p < 0.05 vs coronary occlusion.
†<p < 0.05 vs control.
Abbreviations: endo-epi = endocardial-epicardial; PTs/PTd = systolic/diastolic posterior wall thickness ratio; STs/STd = systolic/diastolic septal thickness ratio.

Fused after coronary ligation. Thus, loss of systolic wall thickening, which can be shown by echocardiography, commonly accompanies acute hypoperfusion. This validates the clinical inference of Corya et al., who suggested that systolic wall thinning by echocardiography indicates acute myocardial ischemia.

The second objective of this study was to assess the effects of nitroglycerin and nitroprusside on ischemic myocardial function, perfusion and wall stress. We compared the two agents by inducing equivalent declines in mean aortic pressure. In assessing the functional response of ischemic myocardium, we found that despite the lowering of arterial pressure, the systolic thinning of ischemic myocardium was not exacerbated. Other parameters of regional function — systolic endocardial velocity and excursion — also remained unchanged with both drugs. Ischemic region transmural myocardial perfusion and endocardial-epicardial perfusion ratios also did not fall, despite reduced coronary perfusion pressure, indicating coronary vasodilator effects of both agents. Previous studies by us using this model have shown modest rises in ischemic myocardial perfusion, but no change in endocardial motion of ischemic myocardium if no intervention is undertaken within 5–60 minutes after coronary occlusion. Thus, neither nitroglycerin nor nitroprusside had any major effect on ischemic motion or perfusion, compared with the effect of time alone.

Wall stress is a major determinant of myocardial oxygen requirements, but the effect of vasodilators on ischemic wall stress has not been studied. Various formulas to measure wall stress have been proposed. Ratshin et al. measured circumferential wall stress and showed a significant correlation between ultrasound and angiographic measurements. This measurement, however, requires the assumption that the ventricular minor axis is equal to half the major axis. To avoid this assumption, Brodie et al. measured meridional wall stress (stress acting at the midplane of the heart in the direction of the apex-to-base axis), and also showed a good agreement between ultrasonic and angiographic methods. This still requires the theoretical assumption that the shape of the left ventricle can be approximated by a prolate ellipse,
and a ventricle with dysynergy cannot be so approximated. Wall stress calculations using either the traditional angiographic methods or the hemodynamic-ultrasonic methods have not been validated in ventricular dysynergy. The wall stress formula we used is the most simplified relationship of the three parameters that determine wall stress — ventricular pressure, diameter and thickness. It avoids all unvalidated geometric assumptions concerning the shape of dysynergic ventricles. It is not intended as an exact measurement of true stress, but as an index to demonstrate the directional effect of the different interventions on the stress of the small left ventricular wall area sampled.

Using this formula for wall stress, we found that the posterior wall stress index nearly doubled after cor-

![Graph](image)

**Figure 3.** Effect of nitroprusside and nitroglycerin on transmural perfusion and endocardial/epicardial perfusion ratio of normal and ischemic myocardium. The figures “7%” and “15%” indicate the amount of drug-induced reduction of mean aortic pressure from the level after coronary occlusion. No significant changes in perfusion occurred in response to either drug.

![Graph](image)

**Figure 4.** Effect of circumflex occlusion, nitroprusside and nitroglycerin on the posterior wall systolic/diastolic thickness ratio. After coronary occlusion the ratio fell to < 1 (systolic thinning). No further significant changes occurred with either nitroglycerin or nitroprusside.
These coronary occlusions, but was then substantially lowered to control levels by both nitroglycerin and nitroprusside, while perfusion of ischemic areas was maintained. These effects should be beneficial, because the lowering of wall stress and the resultant reduction of myocardial oxygen demand is a major mechanism for reduction of myocardial injury after coronary artery occlusion. This helps to explain the results of DaLuz et al., who showed that myocardial lactate production decreased with nitroprusside, indicating an improved supply-demand ratio.

In the systemic circulation, nitroglycerin is generally held to act primarily on the capacitance vessels, while nitroprusside has a more balanced action, affecting both capacitance and resistance vessels. In the coronary circulation, nitroglycerin dilates large vessels and collateral channels, but has relatively little effect on small resistance vessels independent of its effects on cardiac metabolism. The effects of nitroprusside on the various segments of the coronary bed have not been entirely clarified. In our study, both agents caused coronary vasodilation and nonsignificant reductions in left ventricular filling pressure. Differences between the two drugs may have been minimized by administering them to equal degrees of blood pressure lowering in dogs not in congestive heart failure.

Previous studies have shown both beneficial and deleterious effects with nitroglycerin and nitroprusside. Several causes for such reports of variable effects are possible. First, the degree of blood pressure lowering achieved in the different studies is important. Lang et al. found that no improvement in regional dyskinesis occurred with nitroglycerin when systolic blood pressure fell 9%, while Theroux et al. showed improvement in shortening of ischemic segments when nitroglycerin lowered systolic blood pressure by about 20%. Miller et al. found that nitroprusside initially maintained coronary blood flow constant and reduced preexistent ischemia; but when the blood pressure was reduced below 87 mm Hg, coronary blood flow declined, with a resultant increase in ischemia. In preliminary studies we also found that when mean arterial pressure was decreased by 30–40% with either drug, myocardial perfusion fell significantly. According to our results, when pressure declines are limited to 7% and 15% of the pretreatment mean arterial pressure, myocardial perfusion is maintained.

Second, the parameter of drug effectiveness evaluated has also influenced the conclusions of previous studies. Capurro et al. and Chiariello et al. emphasized coronary flow and found that nitroprusside was deleterious or, at best, caused limited improvement. However, studies concentrating on myocardial function or contractility have found nitroprusside to be effective in improving function. DaLuz et al. and Banka et al. using mercury-in-silastic length gauges and Walton-Brodie strain gauges, showed increased contraction in ischemic, border and normal zones with this drug.
Echocardiographically measured thickness changes may not be as sensitive as these other methods, since we did not show improvement in thickening with either agent at either pressure level.

A third important variable concerns the experimental conditions under which the studies were done. We studied anesthetized, open-chest dogs. In two studies by using the same segmental sonomicrometer technique, the same investigators showed that nitroglycerin partially restored contraction of ischemic areas in open-chest dogs, but failed to do so in closed-chest, conscious dogs.

In conclusion, we found that echocardiography can detect changes in wall thickening secondary to acute ischemia. Using this technique to assess the effect of acute interventions on regional ischemic myocardial function, we found that both nitroglycerin and nitroprusside reduced the wall stress of acutely ischemic myocardium while maintaining coronary perfusion and wall thickening. These findings are derived from open-chest, anesthetized dogs subjected to acute coronary occlusion, and may not necessarily be applicable to a closed-chest, conscious human with chronic coronary artery disease.

References
2. Goldstein S, DeFong JW: Changes in left ventricular wall dimensions during regional myocardial ischemia. Am J Cardiol 34: 56, 1974
Effect of acute ischemia, nitroglycerin and nitroprusside on regional myocardial thickening, stress and perfusion. Experimental echocardiographic studies.
R E Kerber, J B Martins and M L Marcus

Circulation. 1979;60:121-129
doi: 10.1161/01.CIR.60.1.121
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1979 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/60/1/121

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/