Effect of Alterations of Arterial Blood Pressure and Heart Rate on Segmental Dyskinesis during Acute Myocardial Ischemia and following Coronary Reperfusion

By Richard E. Kerber and Francois M. Abboud

ABSTRACT
The effect of alterations of blood pressure and heart rate on segmental dyskinesis induced by coronary artery ligation and the influence of such manipulations on the magnitude of recovery of the dyskinetic segment during subsequent coronary artery reperfusion were evaluated in 77 open-chest dogs. Wall motion was recorded by ultrasound reflected directly from the ischemic myocardial segment. Acute ischemia produced characteristic regional abnormalities in wall motion: aneurysmal bulging occurred during isometric contraction and wall velocity was markedly reduced during ventricular ejection. During 60 minutes of ischemia, a control group of dogs underwent no interventions and showed no further changes in wall motion. Tachycardia induced by atrial pacing during ischemia had no significant effect. Arterial hypertension during ischemia caused a marked reduction in wall velocity when methoxamine was used: $14 \pm 2$ (SE) mm/sec (ischemia alone) to $6 \pm 1$ mm/sec (ischemia + drug). In contrast, norepinephrine improved wall velocity: $11 \pm 2$ mm/sec (ischemia alone) to $25 \pm 4$ mm/sec (ischemia + drug). Hypertension caused by infusion of phentolamine gave intermediate results, as did hypotension induced by either nitroprusside or hemorrhage during the ischemic period. After 60 minutes the drugs were stopped, the coronary ligation released, and the ischemic myocardium reperfused. The relative order of improvement of wall velocity with reperfusion was $11 \pm 2$ mm/sec (ischemia alone) to $24 \pm 3$ mm/sec (reperfusion) in the group that received norepinephrine, $12 \pm 3$ mm/sec to $20 \pm 1$ mm/sec in the nitroprusside group, $9 \pm 1$ mm/sec to $9 \pm 2$ mm/sec in the phenylephrine group, and $14 \pm 2$ mm/sec to $12 \pm 1$ mm/sec in the methoxamine group. The aneurysmal bulging during isometric contraction also was reduced to a greater degree by reperfusion in the group that received norepinephrine during the ischemic period than it was in the groups undergoing other interventions during ischemia. We conclude that drug-induced elevations in arterial blood pressure can have different effects on the dyskinetic motion of acutely ischemic myocardium and on the degree of recovery following reperfusion depending on the particular agent used. A reduction in blood pressure or an increase in heart rate during the period of ischemia has no significant beneficial effect on the recovery of the dyskinesis toward control levels after reperfusion. However, it remains possible that such manipulations over a broader range of pressure and rate for a longer period of ischemia may have more noticeable effects.

KEY WORDS
- posterior wall velocity
- myocardial infarction
- aneurysm
- ventricular diameter
- aortocoronary bypass graft
- ultrasound
- vasodilator agents
- vasopressor agents
- dogs

Acute coronary artery occlusion produces ischemia in the area of myocardium deprived of its blood supply. In at least a part of this ischemic myocardium, progression to frank infarction can be prevented if the myocardial oxygen supply is increased or the demand reduced (1). Recently, attention has been directed particularly at the size of the experimental myocardial infarction as a useful parameter in assessing the effect of various therapeutic interventions. Using epicardial S-T segment mapping and intramyocardial creatinine phosphokinase assay techniques, it has been shown that increases in coronary perfusion pressure by pharmacologic agents or aortic counterpulsation reduce infarct size and that decreases in coronary perfusion pressure increase infarct size (2, 3). Similarly, coronary artery reperfusion reduces the amount of necrosis produced by coronary artery occlusion (4).
In considering the problem of the salvage of ischemic myocardium, it seems clear that attention must be paid not only to the size of the ultimate infarction but also to the function or the motion of the jeopardized myocardium; the aim of any therapeutic intervention is both to minimize the size of the infarction and simultaneously to preserve or restore normal myocardial function in the ischemic area. Factors that benefit one of these parameters can conceivably have a detrimental effect on the other. Utilizing an ultrasound technique in an experimental canine model, the aim of the present study was to assess the response of the regional wall motion abnormalities of acutely ischemic myocardium to alterations of arterial blood pressure and heart rate during the period of acute ischemia and to determine the effect of such manipulations on the response to subsequent coronary artery reperfusion.

Methods

Seventy-seven adult mongrel dogs weighing 15-25 kg were anesthetized with sodium pentobarbital (25 mg/kg, iv). Ventilation was maintained with a Harvard respirator via a cuffed endotracheal tube; periodic hyperinflation was performed to prevent atelectasis. The heart was exposed via a midsternal thoracotomy and lifted slightly in a pericardial sling. Systemic anticoagulation was achieved by administering heparin intravenously. Aortic and left ventricular pressures were recorded using no. 8 French polyurethane catheters attached to Statham P23 strain gauges. Left ventricular dP/dt was determined from the left ventricular pressure tracing by a resistance-capacitance differentiating circuit; the catheters were flushed with 5 ml of heparinized saline before each recording. Cardiac output (minus coronary blood flow) was determined with an electromagnetic flow probe placed around the ascending aorta. Recordings were made utilizing an Electronics-for-Medicine DR-12 multichannel photographic recorder that had been modified to display the ultrasound as well as the analogue pressure and electrocardiogram (ECG) signals.

An ultrasound transducer was placed lightly on the exposed anterior surface of the heart, usually resting on the interventricular groove. The ultrasound beam was directed to record the characteristic signal from the left ventricular posterior wall caudad to the mitral valve echo, and it was fixed in place by a stationary arm. Verification of the echo identifications was achieved by rapid injection of 5 ml of normal saline solution through the left ventricular catheter; this maneuver produces a "cloud" of echoes outlining the endocardial-blood interfaces bordering the ventricular cavity.

The echocardiographic registration of the posterior left ventricular wall motion was measured according to the conventions introduced by Kraunz and Kennedy (6) (Fig. 1). Point B, the posterior wall position at end-diastole, is approximately simultaneous with the R wave of the ECG. During isometric contraction, the wall moves slightly posteriorly from point B to point C. The anterior motion from point C to point D is coincident with ventricular ejection, and the motion from point D to point E reflects isometric relaxation. The mean posterior wall velocity (mm/sec) during ejection is the slope of the line drawn from the onset (point C) to the end (point D) of ventricular ejection. Posterior wall excursion (mm) is the amplitude of posterior wall motion measured by the vertical distance from point C to point D. The end-diastolic diameter (mm) is measured as the distance between the interventricular septum and the posterior wall at point B.

Following control hemodynamic and echocardiographic measurements, acute ischemia of the true posterior wall was produced by occlusion of the posterior descending coronary artery and other posterior branches of the circumflex coronary artery. The ultrasound beam then struck the center of the ischemic area.

FIGURE 1

Echocardiographic recordings before and after coronary artery ligation and after 1 hour of reperfusion in a typical dog. Vertical lines show 0.5-second time intervals. IV = interventricular, Ao = aortic, LV = left ventricular, PWV = posterior wall velocity, PWE = posterior wall excursion, and EKG = electrocardiogram. See text for explanation of points B, C, D, and E.

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resulting in a characteristic alteration of the echocardiographic wall motion seen only when the ultrasound beam is reflected off ischemic rather than normal myocardium (7). Further evidence that the beam was actually striking the ischemic area was obtained at the conclusion of the experiment by passing a metal probe through the heart alongside the ultrasound transducer and observing the site of penetration of the left ventricular posterior wall. In all of the dogs in this study, the characteristic motion abnormalities were present on echo recordings after occlusion, and the probe intersected the posterior wall in an area supplied by the occluded coronary artery.

Hemodynamic and echocardiographic recordings were made 5 minutes after coronary artery occlusion and the production of acute ischemia. The dogs were then divided into four groups. The control group (11 dogs) underwent no therapeutic intervention during the ischemic period, which lasted 1 hour. A second group of 10 dogs underwent right atrial pacing during the hour of ischemia to increase heart rate to 125-150% of the postligation rate; the average increase achieved was 50 beats/min (range 32 to 77 beats/min). In a third group, drugs were administered to raise aortic systolic pressure to 125-150% of the postligation level. We attempted to maintain the systolic pressure at this level for the 1 hour of ischemia, although in some dogs the arterial pressure tended to fall somewhat despite increases in the rate of drug infusion. Dogs in this group received either methoxamine (0.25-0.5 mg/min) (12 dogs), phenylephrine (0.1-0.4 mg/min) (9 dogs), or noradrenaline (1-4 mg/min) (12 dogs). In the fourth group of dogs, aortic systolic pressure was lowered during ischemia to 50-75% of the postligation level by either the administration of sodium nitroprusside (0.1-0.2 mg/min) (15 dogs) or the withdrawal of 150-450 ml of blood (8 dogs). After 1 hour of ischemia, the interventions were ended by discontinuing the drug infusions, stopping the atrial pacing, or rapidly reinfusing the warmed blood previously withdrawn. The coronary artery occlusion was then released in all of the dogs, and the ischemic area was thereby reperfused. Dogs that developed ventricular irritability during the period of coronary artery ligation or reperfusion were treated with small amounts of lidocaine administered intravenously. A number of dogs developed ventricular fibrillation during ischemia to 50-75% of the postligation level by either the administration of sodium nitroprusside (0.1-0.2 mg/min) (15 dogs) or the withdrawal of 150-450 ml of blood (8 dogs). After 1 hour of ischemia, the interventions were ended by discontinuing the drug infusions, stopping the atrial pacing, or rapidly reinfusing the warmed blood previously withdrawn. The coronary artery occlusion was then released in all of the dogs, and the ischemic area was thereby reperfused. Dogs that developed ventricular irritability during the period of coronary artery ligation or reperfusion were treated with small amounts of lidocaine administered intravenously. A number of dogs developed ventricular fibrillation, especially after release of the coronary artery ligature; no attempt was made to defibrillate these dogs, and data from them are not included in the results.

Recordings were again made 1 hour after the start of the reperfusion period. The dogs were then killed by an intravenous injection of potassium chloride, and a metal probe was passed through the heart alongside the ultrasound probe to determine the path of the ultrasound beam and verify that the beam was striking the infarcted area. In addition, the coronary artery that had been temporarily occluded during the experiment was opened and inspected to ensure that the arterial lumen was free of clots or intimal damage that might have interfered with reperfusion after release of the ligature.

Statistical analysis was performed with Student's paired t-test, comparing data obtained 5 minutes after ligation (before intervention) with those obtained from the same dog 60 minutes after ligation (at the end of each intervention) and 60 minutes after the initiation of reperfusion. In addition, the data obtained after 60 minutes of reperfusion were compared with control preligation data. In comparing the effects of the different interventions, an unpaired t-test was used.

Results

IMMEDIATE EFFECTS OF CORONARY ARTERY LIGATION

Hemodynamic changes and ultrasound-registered dyskinesis produced by acute ischemia in each of the groups of dogs studied were similar to those previously reported by us (7) (Table 1, Fig. 1). In the control dogs, a significant increase in the B-C amplitude (posterior displacement of the posterior heart wall during isometric contraction) occurred after coronary artery ligation; this increase represents aneurysmal bulging of the ischemic myocardium during isometric contraction. Significant reductions in posterior wall velocity and excursion were also seen. During isometric relaxation, the ischemic myocardium moved abruptly forward (D-E period), indicating recoiling of the stretched and bulging myocardium as the interventricular pressure rapidly fell. The end-diastolic diameter increased significantly with ischemia. These motion abnormalities remained constant during 1 hour of ischemia without further intervention in the control dogs.

EFFECTS OF INTERVENTIONS DURING THE ISCHEMIC PERIOD

Increased Heart Rate.—End-diastolic diameter fell, but there were no other significant ultrasound or hemodynamic changes in response to an increase in heart rate (Table 1).

Elevated Arterial Blood Pressure.—Elevation of blood pressure to approximately equal levels by administration of pharmacologic agents produced variable effects (Table 2). Methoxamine produced large falls in posterior wall velocity and excursion; the B-C amplitude (aneurysmal bulging) was also reduced, and there was a marked increase in end-diastolic diameter. Phenylephrine administration produced significant rises in posterior wall velocity and excursion. End-diastolic diameter fell, but this change was not statistically significant, and there was no change in B-C amplitude. With the norepinephrine infusion, posterior wall velocity and excursion showed striking rises, but end-diastolic diameter declined. An increase in aneurysmal bulging (B-C amplitude) also occurred, but it was not statistically significant.

Reduced Arterial Blood Pressure.—Hypotensive interventions during ischemia also produced variable effects (Table 3). Nitroprusside administration
EFFECTS OF CORONARY ARTERY REPERFUSION

Coronary artery reperfusion was performed after 1 hour of ischemia alone or 1 hour of ischemia plus intervention; measurements were made after 1 hour of reperfusion. In the group of dogs undergoing no intervention during ischemia (Table 1), coronary reperfusion for 1 hour resulted in significant restoration of posterior wall velocity compared with postligation (ischemia) levels (Figs. 1 and 2). The B-C amplitude (aneurysmal bulging during isometric contraction) and the end-diastolic diameter also improved significantly with reperfusion (Fig. 3). Posterior wall velocity did not return to the control preligation levels after 1 hour of reperfusion, although B-C amplitude and end-diastolic diameter did.

After cessation of atrial pacing during ischemia and 1 hour of reperfusion, there was a significant

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CAUSED AS END-DIASTOLIC DIAMETER FELL. ACUTE HEMORRHAGE PRODUCED INITIAL DISEASES IN BLOOD PRESSURE EQUIVALENT TO THOSE RESULTING FROM NITROPRUSSIDE ADMINISTRATION, BUT A COMPENSATORY BLOOD PRESSURE REELEVATED THE PRESSURES; BY THE END OF THE 60-MINUTE ISCHEMIC PERIOD THE NET DECLINES WERE SMALL (TABLE 3). NEVERTHLESS, POSTERIOR WALL VELOCITY SHOWED A SLIGHTLY GREATER INCREASE WITH THIS INTERVENTION. END-DIASTOLIC DIAMETER FELL. RECOVERIES IN ANEURYSMAL BULGING (B-C AMPLITUDE) OCCURRED DURING BOTH HYPOTENSIVE INTERVENTIONS, ALTHOUGH THE DECREASE WAS NOT STATISTICALLY SIGNIFICANT IN EITHER CASE.

Table 4 summarizes the comparative percent recovery (i.e., return toward control levels) for the ultrasound parameters of posterior wall velocity and B-C amplitude in response to alterations of heart rate and blood pressure during ischemia. The percent change in posterior wall velocity during ischemia was calculated for each individual dog as (value at 60 minutes of ischemia - value at beginning of ischemia) / (control value - value at beginning of ischemia). The percent improvement in B-C amplitude during ischemia was calculated for each dog as (value at beginning of ischemia - value at 60 minutes of ischemia) / (value at beginning of ischemia - control value). This table indicates that norepinephrine was the intervention which restored posterior wall velocity most toward control (preischemic levels) and that methoxamine restored it least. Norepinephrine also increased velocity significantly more than did nitroprusside or phenylephrine. Conversely, norepinephrine most exacerbated the aneurysmal bulging during isometric contraction, and methoxamine most reduced it.

All values are means ± se. PWV = posterior wall velocity, PWE = posterior wall excursion, B-C = B-C amplitude (see text), EDD = end-diastolic diameter, and LV = left ventricular.

*P < 0.05, reperfusion vs. ischemia at 5 minutes.
†P < 0.05, reperfusion vs. control.
‡P < 0.05, ischemia at 5 minutes vs. ischemia at 60 minutes or vs. atrial pacing 60 minutes.

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caused a moderate increase in posterior wall velocity as end-diastolic diameter fell. Acute hemorrhage produced initial declines in blood pressure equivalent to those resulting from nitroprusside administration, but a compensatory vasoconstriction partially reelevated the pressures; by the end of the 60-minute ischemic period the net declines were small (Table 3). Nevertheless, posterior wall velocity showed a slightly greater increase with this intervention. End-diastolic diameter fell. Reductions in aneurysmal bulging (B-C amplitude) occurred during both hypotensive interventions, although the decrease was not statistically significant in either case.
TABLE 2

Effects of Coronary Reperfusion after Elevation of Arterial Blood Pressure during Ischemia

<table>
<thead>
<tr>
<th></th>
<th>Methoxamine</th>
<th>Phenylephrine</th>
<th>Norepinephrine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(12 dogs)</td>
<td>(9 dogs)</td>
<td>(12 dogs)</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>Ischemia: 5 min</td>
<td>Ischemia: 60 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reperfusion: 60 min</td>
<td>Ischemia: 5 min</td>
</tr>
<tr>
<td>PWV (mm/sec)</td>
<td>29 ± 2</td>
<td>14 ± 2</td>
<td>12 ± 1*</td>
</tr>
<tr>
<td>B–C (mm)</td>
<td>2.0 ± 0.3</td>
<td>4.4 ± 0.5</td>
<td>2.7 ± 0.7*</td>
</tr>
<tr>
<td>PWE (mm)</td>
<td>3.7 ± 0.3</td>
<td>1.8 ± 0.2</td>
<td>1.1 ± 0.1*</td>
</tr>
<tr>
<td>EDD (mm)</td>
<td>16.7 ± 1.3</td>
<td>19.0 ± 1.5</td>
<td>28.8 ± 1.6*</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>175 ± 9</td>
<td>164 ± 9</td>
<td>135 ± 6*</td>
</tr>
<tr>
<td>Aortic systolic pressure (mm Hg)</td>
<td>99 ± 8</td>
<td>94 ± 6</td>
<td>124 ± 8*</td>
</tr>
<tr>
<td>Aortic diastolic pressure (mm Hg)</td>
<td>76 ± 7</td>
<td>76 ± 5</td>
<td>105 ± 7*</td>
</tr>
<tr>
<td>LV end-diastolic pressure (mm Hg)</td>
<td>9 ± 2</td>
<td>8 ± 1</td>
<td>16 ± 2*</td>
</tr>
<tr>
<td>LV dP/dt (mm Hg/sec)</td>
<td>1171 ± 129</td>
<td>1106 ± 115</td>
<td>1056 ± 75</td>
</tr>
<tr>
<td>Cardiac output (liters/min)</td>
<td>2.8 ± 0.2</td>
<td>2.6 ± 0.2</td>
<td>2.2 ± 0.3*</td>
</tr>
</tbody>
</table>

All values are means ± se. Abbreviations are the same as they are in Table 1.

*P < 0.05, ischemia at 5 minutes vs. ischemia + drug at 60 minutes.

†P < 0.05, reperfusion vs. control.

‡P < 0.05, reperfusion vs. ischemia at 5 minutes.
TABLE 3
Effects of Coronary Reperfusion after Reduction of Arterial Blood Pressure during Ischemia

<table>
<thead>
<tr>
<th>Nitroprusside (15 dogs)</th>
<th>Hemorrhage (9 dogs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Ischemia: 5 minutes</td>
</tr>
<tr>
<td>PWV (mm/sec)</td>
<td>29 ± 1</td>
</tr>
<tr>
<td>B-C (mm)</td>
<td>2.3 ± 0.2</td>
</tr>
<tr>
<td>PWE (mm)</td>
<td>3.2 ± 0.2</td>
</tr>
<tr>
<td>EDD (mm)</td>
<td>19.6 ± 1.9</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>169 ± 5</td>
</tr>
<tr>
<td>Aortic systolic pressure (mm Hg)</td>
<td>106 ± 5</td>
</tr>
<tr>
<td>Aortic diastolic pressure (mm Hg)</td>
<td>83 ± 5</td>
</tr>
<tr>
<td>LV end-diastolic pressure (mm Hg)</td>
<td>7 ± 1</td>
</tr>
<tr>
<td>LV dP/dt (mm Hg/sec)</td>
<td>1388 ± 116</td>
</tr>
<tr>
<td>Cardiac output (liter/min)</td>
<td>2.6 ± 0.2</td>
</tr>
</tbody>
</table>

All values are means ± se. Abbreviations are the same as they are in Table 1.
*P < 0.05, ischemia at 5 minutes vs. ischemia + intervention at 60 minutes.
†P < 0.05, reperfusion vs. ischemia at 5 minutes.
‡P < 0.05, reperfusion vs. control.

increase in posterior wall velocity and a fall in end-diastolic diameter compared with ischemic levels. End-diastolic diameter returned to control levels, but posterior wall velocity remained significantly less than control.

Reperfusion after the administration of hypertensive agents produced variable results (Fig. 4). After cessation of methoxamine administration and 1 hour of reperfusion, posterior wall velocity and excursion, which had been very depressed during the drug administration, rose to ischemic levels but remained well below the control preischemic state. The aneurysmal bulging also persisted despite reperfusion (Table 2). The end-diastolic diameter fell but did not return to the levels seen during ischemia alone; it remained much

TABLE 4
Comparative Percent Recovery of Two Ultrasound Parameters in Response to Alterations of Blood Pressure and Heart Rate during Ischemia

<table>
<thead>
<tr>
<th>B-C amplitude (aneurysmal bulging)</th>
<th>Posterior wall velocity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>% Recovery</td>
</tr>
<tr>
<td>Methoxamine</td>
<td>115 ± 43*</td>
</tr>
<tr>
<td>Control (no intervention)</td>
<td>31 ± 29</td>
</tr>
<tr>
<td>Atrial pacing</td>
<td>28 ± 32</td>
</tr>
<tr>
<td>Nitroprusside</td>
<td>-3 ± 35*</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>-11 ± 41</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>-52 ± 49</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>-294 ± 157†</td>
</tr>
</tbody>
</table>

Percent recovery values are means ± se. Interventions are listed in descending order of effectiveness with those above the control value representing a beneficial trend and those below a detrimental trend. See text for method of calculation. The methoxamine-induced reduction of aneurysmal bulging during ischemia reflects the marked dilation of the left ventricle which limited further stretch of the ischemic myocardium during systole.
*P < 0.05 compared with the norepinephrine group.
†P < 0.05 compared with the control group.
Effect of reperfusion alone on posterior wall velocity in individual dogs.

larger than the control value. After phenylephrine administration, reperfusion similarly caused only some improvement in the segmental motion abnormalities; significant dyskinesis remained compared with the control state. End-diastolic diameter returned to control level. After norepinephrine administration, on the other hand, reperfusion improved posterior wall velocity and excursion to a degree exceeding that seen in the dogs undergoing reperfusion after no intervention. End-diastolic diameter showed a small further decline. This improvement in segmental dyskinesis on reperfusion after norepinephrine administration was significantly greater than that on reperfusion after administration of the other two pressor agents (Table 5).

Reperfusion after hypotensive interventions during ischemia showed that the segmental dyskinesis improved to an intermediate degree. After both nitroprusside administration and hemorrhage, posterior wall velocity and excursion improved with reperfusion but remained significantly below control levels; B-C amplitude (aneurysmal bulging) was no longer significantly different from the control state after reperfusion. End-diastolic diameter was below the control levels in both groups after reperfusion.

Table 5 presents comparative intergroup data for the ultrasound parameters of posterior wall velocity and B-C amplitude. The percent recovery of posterior wall velocity after reperfusion was calculated for each individual dog by the following formula: \( \frac{(value \ at \ 60 \ minutes \ of \ reperfusion - ischemic \ value)}{(control \ value - ischemic \ value)} \).

The percent recovery of B-C amplitude after reperfusion was calculated for each dog by the following formula: \( \frac{(ischemic \ value - value \ at \ 60 \ minutes \ of \ reperfusion)}{(ischemic \ value - control \ value)} \). This table indicates that for both of the ultrasound parameters, B-C amplitude and posterior wall velocity, dogs that had received norepinephrine showed the most return of ischemia-induced dyskinesis toward normal with reperfusion and that dogs that had received methoxamine showed the least return. Because of the considerable interanimal variation none of the groups subjected to an intervention was significantly different from the group that was not subjected to an intervention for the parameter of B-C amplitude. However, for posterior wall velocity the recovery after methoxamine intervention was significantly less than that of the group that was not subjected to an intervention. Comparison with the norepinephrine-treated group indicated that this group showed significantly greater posterior wall velocity recovery than...
FIGURE 4
Effect of reperfusion on posterior wall velocity after elevations of blood pressure during ischemia with methoxamine (left), phenylephrine (center), and norepinephrine (right).

The various heart rate and blood pressure manipulations performed during the period of ischemia had different effects on the response to subsequent reperfusion. Norepinephrine infusion increased wall velocity while it was being administered during ischemia and also improved the response of the dyskinetic motion to later reperfusion. The other hyper- and hypotensive interventions and atrial pacing depressed to various degrees the response to reperfusion despite the fact that some appeared to have beneficial effects on wall motion when they were given during ischemia. Methoxamine and phenylephrine had particularly deleterious effects on the later recovery of wall velocity. These changes cannot be explained simply by the relatively small and inconstant differences in heart rate and blood pressure between the different groups of dogs.

Especially when considering the deleterious effects of methoxamine on the later response to reperfusion, it might be argued that the beta-receptor blockade this agent induces was affecting regional wall motion abnormalities by virtue of a prolonged generalized depressant effect on generalized cardiac performance (8). However, the heart rate and blood pressure 1 hour after cessation of methoxamine infusion were not significantly different from the predrug (ischemia) values. Moreover, when we administered methoxamine to several additional dogs in whom coronary artery ligation was not performed, heart rate, blood pressure, posterior wall velocities, and end-diastolic diameter returned to control values within 1 hour after the drug was stopped.

Previous investigations have shown that the size of other species with different coronary collaterals cannot be predicted.
of an experimental myocardial infarction is reduced by an elevation in arterial blood pressure and increased by a reduction in arterial blood pressure and also by tachycardia (2). This study indicates that the segmental dyskinesis of an area of ischemic myocardium responds differently to these interventions. Why does this difference exist? Following coronary artery occlusion, one encounters histologically an area of central necrosis surrounded by a zone of ischemic but viable tissue (9). Estimations of infarct size probably measure alterations in the size of this zone of borderline or jeopardized myocardium, which would be significantly affected by the extent of collateral flow and, therefore, by alterations in coronary perfusion pressure (2, 10). However, in the echocardiographic technique used in this study, an ultrasound beam is reflected from the center of the acutely ischemic area, an area which after 1 hour probably consists mainly of "blighted" tissue (1) likely to progress to ultimate necrosis regardless of therapeutic interventions. Elevations in coronary perfusion pressure and collateral flow, although they affect the periphery of the ischemic area, may have less or no effect on the degree of ischemia and dyskinesis in this central region (10). Furthermore, myocardial energy utilization depends on wall tension during systole, which in turn is related to intraventricular pressure and ventricular diameter (11, 12). If the rise in blood pressure is associated with increased ventricular diameter (as it is with methoxamine) (Fig. 5), the central core of the ischemic area may have an increased oxygen demand and energy utilization in addition to a decreased delivery because of mechanical compression of vessels as myocardial wall tension increases. The result would be an imbalance between oxygen demand and delivery which would then be consistent with the observations made in this study, which indicated that administration of methoxamine and phenylephrine during the ischemic period interfered significantly with the subsequent beneficial effects of coronary artery reperfusion on restoring cardiac wall motion from dyskinetic to normal despite the fact that arterial blood pressure was elevated and the size of the ischemic area presumably reduced (2).

The opposite beneficial results of norepinephrine infusion may also be explained by these considerations. Unlike methoxamine and phenylephrine, norepinephrine has significant positive inotropic effects which resulted in the observed sharp increase in posterior wall velocity and the significant reduction in end-diastolic ventricular diameter during the infusion of this agent. The reduction in ventricular diameter would tend to lower myocardial oxygen requirements in the ischemic area and minimize the compression of coronary vessels and thereby diminish the amount of necrosis by reducing the imbalance between oxygen supply and demand (13). Subsequent reperfusion would then be more successful in restoring cardiac wall motion toward normal. To some degree the beneficial effects of the reduction in ventricular diameter and wall tension probably are counterbalanced by the increase in oxygen requirements associated with norepinephrine-induced augmentation of cardiac contractility; isoproterenol, ouabain, and glucagon have all been shown to increase the severity and the extent of ischemic injury, presumably via this mechanism (2).

The effect of atrial pacing, nitroprusside, and hemorrhage on the response to subsequent reperfusion also probably depends on the balance of a number of variables. With all of these interventions, ventricular diameter fell; the resultant decrease in wall tension would tend to reduce myocardial oxygen requirements in the ischemic area. Counterbalancing this beneficial effect would be the hypotension and the tachycardia seen during these interventions, which would increase oxygen requirements and reduce coronary perfusion and collateral flow (2). The net result of all of these...
interventions was to moderately depress the recovery of the dyskinetic area.

The response to coronary artery reperfusion showed interanimal variation. In a minority of the dogs, reperfusion accentuated the dyskinesis produced originally by acute ischemia (Fig. 6). These dogs presumably sustained a more severe or a larger myocardial insult after the original coronary artery ligation. Other investigators have found that after prolonged coronary artery occlusion revascularization may be followed by decreases in strain gauge–measured tension of both central and border zones of ischemia (14) and by myocardial hemorrhage (15). Postmortem gross inspection often revealed extensive epicardial hemorrhage in this subgroup of dogs, a finding we seldom encountered in the dogs that showed improvement in dyskinesis after reperfusion.

Ludbrook et al. (16) have shown that echocardiographically measured posterior wall velocity does not correlate well with other accepted indexes of total left ventricular performance. Throughout this discussion we have taken the ultrasound parameters of aneurysmal bulging during isometric contraction and wall velocity during ventricular ejection to reflect localized wall motion abnormalities of the ischemic area. Some of the observed changes in these parameters during the various interventions may conceivably evolve from alterations in contractility and motion in surrounding nonischemic myocardium, resulting in passive changes in the dyskinesis of the central ischemic zone. However, because of the globular shape of the ventricle the surrounding nonischemic myocardium should move more or less perpendicularly to the ultrasound beam. Only net motion directly toward or away from the transducer is registered, thereby minimizing such effects on the motion of the ischemic area. Additional support for the concept that the observed aneurysmal bulging and wall velocity changes primarily reflect localized ischemic wall motion changes comes from current studies in our laboratory relating these ultrasound measurements to myocardial perfusion determined by a labeled (radioactive) microsphere technique; preliminary data indicate that changes in the echo parameter correlate well with alterations in myocardial perfusion in the ischemic area.

We conclude that elevation of arterial blood pressure, which reduces the size of an experimental myocardial infarction, may simultaneously worsen the segmental dyskinesis of the ischemic myocardium and have deleterious effects on the subsequent response to reperfusion depending on the pressor agent used. Reduction of arterial blood pressure and tachycardia have some beneficial effects on ischemic wall velocity, but they are not maintained after later reperfusion. In particular, this study suggests that if elevation of arterial blood pressure is contemplated in an effort to increase coronary or systemic perfusion, norepinephrine may have a substantial advantage over other pressor agents such as phenylephrine or methoxamine in that it increases wall velocity during ischemia and improves the subsequent response of the ischemic area to reperfusion.

![Figure 6](image_url)

_Echocardiographic recordings before and after coronary ligation and after 1 hour of reperfusion. Segmental dyskinesis is worsened by reperfusion. Compare with Figure 1; abbreviations are the same as they are in Figure 1._

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References

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Effect of alterations of arterial blood pressure and heart rate on segmental dyskinesis during acute myocardial ischemia and following coronary reperfusion.

R E Kerber and F M Abboud

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