
Functional Significance of Regional Ischemic Contraction Abnormalities

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SUMMARY To evaluate the progression of segment function following induction of ischemia, the left anterior descending coronary artery was ligated (eight dogs) or cannulated and perfused at various pressures via a bypass-oxygenator (six dogs). Mercury-in-silastic length gauges were sutured to the anterior left ventricle, and pressure was recorded by a catheter-tipped transducer. Segment function was determined from the area of the pressure-length loop by plotting instantaneous left ventricular pressure against segment length and by evaluation of the degree of systolic shortening. Segment function decreased linearly as flow in the left anterior descending artery was decreased in a stepwise fashion by reduction in perfusion pressure from 100 to 20 mm Hg. With both left anterior descending coronary artery ligation and stepwise flow reduction, the pressure-length loop invariably showed four clearly identifiable morphologic patterns which relate conceptually to the specific left ventricular contraction patterns: dyssynchrony, hypokinesis, akinesis, and paradoxical systolic expansion. Re-oxygenation following occlusion invariably revealed return to a normal pattern in reverse order. This study demonstrates that a consistent and predictable progression of segmental contraction abnormalities occurs with ischemia.

SINCE THE CLASSIC DESCRIPTION of ventriculographic contraction abnormalities by Herman et al.,1 qualitative descriptors of segmental contraction patterns such as dyssynchrony, hypokinesis, akinesis, and paradoxical expansion have been generally assumed to reflect, in an unspecified manner, the degree of myocardial ischemia. Recent clinical observations, however, appear to be at variance with this assumption. Dyssynchrony has been described as a normal variant2 and akinesis, which was believed to represent infarction, has been observed to revert to a normal contraction pattern following cardiac stimulation.3, 4 or restoration of perfusion.4 With the capability of altering segmental contraction patterns by both medical and surgical means, a greater understanding of the relationship between the degree of ischemia and the qualitative analysis of segmental contraction patterns is currently needed, particularly as computer-aided methods of rapidly assessing segmental myocardial function become available. Studies correlating wall motion abnormalities with the degree of ischemia are extremely limited. The purpose of this study was first to determine whether there is a specific qualitative pattern of segmental ventricular contraction abnormalities which occurs as the myocardial ischemia progressively increases, and second to relate these observed abnormalities of contraction pattern to the known effects of ischemia upon isolated cardiac muscle function.

Methods

Fourteen mongrel dogs weighing from 17 to 32 kg were anesthetized with intravenous pentobarbital, 30 mg/kg, and respiration maintained with a Harvard ventilator. The left ventricle was exposed through a left lateral thoracotomy and suspended in a pericardial cradle. High-fidelity left ventricular pressure was monitored with a transaortic Biotec catheter-tipped transducer passed from the femoral artery. Aortic pressure was monitored by a 7F femoral catheter attached to a Statham P23Db strain gauge.

For assessment of regional function, methods previously described by this laboratory were employed.5 A 1 cm mercury-in-silastic length gauge (0.31 mm inner diameter; 0.62 mm outer diameter) (Parks Electronics, Beaverton, Oregon) was sutured to the epicardial surface of the left ven-
tricle, parallel to the fibers perfused by the coronary artery to be occluded. The stiffness of this gauge is 1 gram of force per 5% elongation. The length gauge was prestressed for 30 min before each experiment; calibration was performed by attaching the ends of the gauge to the jaws of a vernier caliper and extending the gauge by fixed increments. Resting length of the gauge was 10 mm; when in use this length varied from 10 to 20 mm. Within such a range the calibration of the gauge is linear ± 5%. Technical details concerning gauge placement, calibration, frequency response, etc., have been published in a prior manuscript from this laboratory.5

In six dogs the left anterior descending coronary artery (LAD) was cannulated near its midpoint and perfused with blood withdrawn from the femoral vein of the experimental dog and filtered through a heated disc oxygenator of adjustable height in order to control coronary flow by altering perfusion pressure. Coronary flow at each level of pressure was measured by electromagnetic flowmeter.

In each experiment, immediately following coronary cannulation, perfusion of the distal half of the LAD was continued at a perfusion pressure of approximately 100 mm Hg for at least 20 min. Following this initial stabilization period, perfusion pressure was reduced in a stepwise fashion producing a total of five stages of graded ischemia. Each stage consisted of a reduction in perfusion pressure of approximately 20 mm Hg, which was maintained for a two-minute period to allow for stabilization of hemodynamics under ischemic conditions. This procedure was continued until a range of perfusion pressure from 100 mm Hg down to 20 mm Hg was described. During this period, no additional medications were administered. In all experiments, left ventricular end-diastolic pressure was maintained within a narrow range (5 to 10 mm Hg). In the remaining eight dogs, the perfusion apparatus was replaced by a snare occluder which was placed around either the LAD or its diagonal branch for vessel occlusion, and similar data were recorded. The occlusion was maintained for varying periods of time, from five min to three hours. At the time of release, data was recorded continuously, in the manner described for coronary occlusion.

The output from the length gauge and left ventricular pressure transducer were plotted continuously and simultaneously as an X-Y plot on a memory oscilloscope to obtain a pressure-length loop for the myocardial segment. Left ventricular, aortic, and coronary artery perfusion pressure, myocardial segment length, and the pressure-length loop were then recorded before and after reduction and restoration of coronary perfusion by either graded reduction in flow from the disc oxygenator or direct coronary ligation.

Results

Figure 1 illustrates raw data utilized for construction of the pressure-length loop. The left panel shows epicardial segment length, aortic pressure, and left ventricular pressure. The right panel shows a plot of left ventricular pressure as a function of segmental length throughout the cardiac cycle, which results in a typical normal pressure-length loop. The loop is counterclockwise in orientation and rectangular in morphology. The cyclic pressure-length loop for the myocardial segment is analogous to the pressure-volume loop of the intact heart (fig. 2). Beginning at the lower right-hand corner of the loop, which corresponds to end-diastole, there is a rapid rise in pressure with little change in length during the period of isovolumic systole; during ejection there is a substantial decrease in length with little change in pressure; during isovolumic relaxation there is a rapid fall in pressure with little change in length; and during diastole both pressure and length increase. The integral of pressure with respect to volume during ejection in the intact heart is stroke work. By analogy, the integral of pressure with respect to length during ejection has been utilized as an index of the work performed by the myocardial segment.8 This simultaneous display of pressure and length allows the observer to immediately visualize the performance of the myocardial segment at any instant or in any portion of the cardiac cycle.

![Figure 1](http://circ.ahajournals.org/)

**Figure 1.** Raw data and the pressure-length loop. At the left are typical recordings of (from top to bottom) the electrocardiogram (ECG), aortic flow (AoF), segment length (L), and aortic (AoP) and left ventricular (LV) pressures. At the right is the plot of left ventricular pressure versus segment length throughout one cycle.
Figure 2. The cardiac cycle and the pressure-length loop. Shown above is a schematic version of both the pressure-length loop of the myocardial segment and the pressure-volume loop of the intact heart. Changes in length or volume during segments of the cardiac cycle can be evaluated by knowledge of the ventricular pressure pattern that accompanies the onset of isovolumic contraction, ejection, and isovolumic relaxation. Area within the pressure-volume loop is cardiac work. By analogy, area within the pressure-length loop is an index of segment work.

Figure 3 illustrates the relationship of segmental systolic shortening and pressure-length loop area to regional coronary blood flow in six dogs during gradual ischemia. In all cases there was an approximately linear relationship between segment function and myocardial oxygen supply as measured by these parameters (table 1). Thus, as coronary perfusion was reduced, there was a progressive reduction in regional flow (Q), systolic shortening (ΔL), and loop area (LA).

Figure 4 illustrates the typical qualitative alteration of the segmental pressure-length loop following graded ischemia in a single experiment. With progressive reduction in coronary perfusion pressure, the point of onset of morphologic alteration in the pressure-length loop varied; but once begun, an

### Table 1. Relationship Between Regional Perfusion and Function

<table>
<thead>
<tr>
<th>Dog</th>
<th>Q (ml/min)</th>
<th>90–110</th>
<th>70–90</th>
<th>50–70</th>
<th>30–50</th>
<th>10–30</th>
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<tr>
<td>1</td>
<td>20.0</td>
<td>18.0</td>
<td>9.0</td>
<td>3.5</td>
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<td>LA</td>
<td>355</td>
<td>381</td>
<td>266</td>
<td>66</td>
<td>16</td>
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</tr>
<tr>
<td>SS</td>
<td>3.10</td>
<td>3.20</td>
<td>2.25</td>
<td>0.80</td>
<td>0.70</td>
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<td>2</td>
<td>32.5</td>
<td>13.0</td>
<td>4.4</td>
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<td>59.0</td>
<td>47.0</td>
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<td>SS</td>
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<td>49.0</td>
<td>21.5</td>
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<td>LA</td>
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<td>276</td>
<td>90</td>
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<td>LA</td>
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<td>351</td>
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<td>55</td>
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<tr>
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<td>202</td>
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<tr>
<td>SS</td>
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<td>Q</td>
<td>40.9 ± 12.9</td>
<td>31 ± 7.9</td>
<td>18.9 ± 6.4</td>
<td>9.2 ± 4.0</td>
<td>0.1 ± 1.9</td>
<td></td>
</tr>
<tr>
<td>LA</td>
<td>352 ± 24</td>
<td>326 ± 42</td>
<td>231 ± 33</td>
<td>79 ± 23</td>
<td>-9 ± 17</td>
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<tr>
<td>SS</td>
<td>2.9 ± 0.1</td>
<td>2.9 ± 0.1</td>
<td>2.1 ± 0.2</td>
<td>1.20 ± 0.35</td>
<td>0.57 ± 0.10</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: Q = coronary flow (ml/min); LA = pressure-length loop area (mm Hg · mm); SS = regional systolic shortening (mm).
A invariable sequence of morphological changes was uniformly observed. This sequence of changes produced four pressure-length loops of characteristic morphology, defined as follows: The first alteration in the morphology of the pressure-length loop following induction of ischemia was lengthening late in the period of isovolumic relaxation and throughout the period of isovolumic systole, while the amount of systolic shortening remained unchanged (fig. 4B). This initial change in morphology was sometimes of such magnitude that peak length during isovolumic relaxation actually exceeded subsequent end-diastolic length. The effect in this case was to produce a "figure-of-eight" loop.

Second, with further reduction in coronary perfusion, a reduction in shortening during the ejection phase also was observed (fig. 4C). With severe reduction of coronary perfusion pressure, the third characteristic morphology was observed; systolic shortening fell to zero and the pressure-length loop assumed a crescent shape. The area bounded by the loop approached zero in those cases in which isovolumic relaxation length remained less than end-diastolic length (fig. 4D). A shift to the right in the diastolic pressure-length relationship also was observed, presumably in response to repeated passive lengthening during isovolumic systolic lengthening by adjacent contracting muscle. The last morphology, in which the pressure-length loop became clockwise in orientation and systolic expansion was noted, occurred with marked reduction in coronary perfusion pressure (fig. 4E).

In the eight animals in which acute coronary occlusion was performed, an identical sequence of qualitative loop abnormalities was observed in every case (fig. 5). In contrast to the controlled perfusion experiments, in which the morphologic stages remained stable until the next stepwise reduction in pressure, following acute occlusion there was a rapid progression in pressure-length loop morphology over a period of approximately 20 to 200 sec from one stage to the next in a dynamic continuum. The reduction in regional function following complete occlusion is shown quantitatively in figure 6 and table 2.

The pressure-length loop always stabilized at the lowest level of function, Stage E, when the main LAD was ligated. In four experiments in which a diagonal branch, rather than the LAD itself, was ligated, the same morphologic changes appeared. These changes, however, spontaneously partially reversed over a period of several minutes, in which the clockwise pressure-length loop returned to a narrow but counterclockwise orientation.

Following reperfusion of the acutely occluded vessel, return of function was found to be variable. Both the rapidity and the magnitude of restoration of function were dependent upon the duration of ischemia and the location of the length gauge relative to the occluded vessel. Recovery of function, however, when observed, followed a rigid sequence which was the reverse of that observed during the induction of ischemia — with one exception: following return of systolic shortening, when restoration of function was nearly complete, a state of isovolumic shortening rather than lengthening was observed during relaxation (fig. 5). Complete reversal of segment function to control levels was observed from all stages, including Stage E, in which the ischemic segment lost all contractile properties (i.e., the pressure-length loop became clockwise and exhibited "paradoxical expansion"), but the three segments which failed to exhibit return of function following reperfusion invariably had exhibited paradoxical expansion prior to reperfusion.
Discussion

This study demonstrates that a consistent and predictable pattern of segmental contraction abnormalities occurs during both the induction of myocardial ischemia (by occlusion or graded flow reduction) and its reversal (following release of occlusion), and that the nature of this qualitative contraction abnormality relates directly to the magnitude of ischemia. These changes are observed within seconds of complete coronary occlusion and exhibit a dynamic progression to a stable state over a period of one to three minutes. From a purely descriptive standpoint, the changes in pressure-length loop morphology can be effectively visualized as a continuum which is not necessarily apparent from multiple illustrations. As shown in figure 7, the progression of shape changes with ischemia can be conceptualized as a force pulling the isovolumic relaxation limb of the loop from left to right until the normal counterclockwise loop becomes clockwise in orientation.

The highly consistent and invariable progression of changes in contraction patterns suggests that these observations reflect an alteration in the fundamental properties of muscle performance with ischemia, which might be recognizable in both papillary muscle and the intact heart. It is the hypothesis of this discussion that the observations in this study are consistent with the known effects of ischemia on isolated papillary muscle function, and as such serve to clarify patterns of segmental wall motion abnormalities in the intact heart, such as those observed during ventricular angiography.

The data from pressure-length loop recordings may be logically extended to understanding of terms such as dysynchrony and regional hypokinesis, akinesis, or systolic expansion, since the vertical axis of the pressure-length loop allows timing of mechanical events in the cardiac cycle and its horizontal axis reflects concomitant length changes in the ischemic segment. The discussion that follows, therefore, will review the spectrum of contraction abnormalities observed in this study, their probable physiologic basis in relation to known effects of ischemia on cardiac muscle, and their predicted observable qualitative manifestations in the intact heart (fig. 8).

Lengthening during Isovolumic Contraction and Relaxation

The major effect of hypoxia on papillary muscle function is to decrease the rate of force development, the duration of contraction, and the magnitude of peak force. When this phenomenon was studied in normal and hypoxic muscles placed in tandem, the earliest effect was found to be dissociation in the time course of contraction of the two

![Figure 5](https://example.com/figure5.png)

**Figure 5.** Progressive alteration in pressure-length loop morphology following acute coronary occlusion. Note the similarity of each loop to the corresponding loop in figure 4.

![Figure 6](https://example.com/figure6.png)

**Figure 6.** Progressive reduction in regional, systolic shortening following acute coronary occlusion in 8 dogs. Data is expressed as a percentage of control ± 1 SEM. Systolic shortening is 20% of control 60 seconds postocclusion.

![Figure 7](https://example.com/figure7.png)

**Figure 7.** Schematic representation of the typical progression of pressure-length loop morphology with progressive myocardial ischemia.
muscles, resulting in paradoxical lengthening of the hypoxic muscle early in the course of tension development. This occurred despite the fact that the hypoxic muscle was able to develop considerable force when allowed to contract isometrically. Since the contraction of the hypoxic muscle was maintained for a shorter period of time than that of the normal muscle, stretching of the relaxing isovolumic muscle also occurred late in the course of the tandem twitch. Applied to the observations in this study, these data serve to provide a physiologic basis for the first detectable change in the contraction pattern of regional ischemic fibers in the intact heart, namely, lengthening in both the isovolumic contraction and relaxation phases. It is hypothesized that the observed lengthening in isovolumic systole was the result of decreased rate of force development in the ischemic muscle, and that lengthening in the isovolumic relaxation phase was the result of diminished duration of contraction. This pattern of lengthening in isovolumic systole and relaxation, with preservation of shortening during ejection, would result in dyssynchrony between ischemic and adjacent normal muscle in the isovolumic periods.

**Decreased Shortening during Ejection**

As ischemia progressed, reduction in the magnitude of shortening during ejection was observed in the pressure-length loop. This phenomenon relates directly to the observation that substantial reduction in force development in both the isolated papillary muscle and in the intact heart follows more profound hypoxia. The predictable correlate of this state would be hypokinesis.

**Absence of Shortening in Systole and Increased Diastolic Length**

With a further increase in the magnitude of ischemia, an increase in the resting end-diastolic length of the ischemic segment was noted in the pressure-length loop. This observation is in contrast to isolated papillary muscles, in which hypoxia is frequently found to result in “ischemic contrac-

![Figure 8](http://circ.ahajournals.org/)

**Figure 8.** Ischemic pressure-length loop morphology and its functional significance. Depicted loops are from a typical experiment following acute occlusion (A = control, B = 5 seconds, C = 10 seconds, D = 60 seconds, E = 120 seconds).
ture”.9 When papillary muscles are subjected to repetitive passive stretch, however, an increase in the tension-length relationship has been observed,6 and early in the course of experimental acute myocardial infarction, an increase in the diastolic pressure-volume relationship has been observed.6 The observed early increase in diastolic segment length of the ischemic segment in our intact heart study, therefore, may reflect the repeated and substantial stretching of the noncontracting ischemic muscle by adjacent normal fibers. The magnitude of change in regional diastolic segment length in acute ischemia is in the range of 5 to 20% and would be difficult to detect clinically, but the absence of contraction in systole would be manifest as akinesis.

Paradoxical Systolic Expansion

The ultimate effect of myocardial ischemia on segmental function in this study was the development of a clockwise pressure-length loop. Profound hypoxia of a papillary muscle results in absence of force development. In the intact heart, the noncontracting ischemic segment is subjected to stretching by adjacent normal fibers. The behavior of the muscle segment is analogous to the response of inert biologic tissue subjected to stretch in which the return to resting length following stretching describes a typical clockwise “hysteresis loop.” This would be expressed as paradoxical systolic expansion in the intact heart.

The failure of regional contraction to return following reperfusion was always characterized by a clockwise pressure-length loop preceding reoxygengation, suggesting that this contraction pattern is the mechanical representation of early loss of viability (which may later be substantially modified by the development of a fibrotic scar). The development of this “hysteresis loop” does not establish non-viability, however, since complete restoration of contraction may occur following postextrasytolic potentiation4,6,10 or with reoxygengation, as observed in this study.

Reoxygengation

Restoration of function following reoxygengation followed a pattern which was the reverse of that observed during induction of ischemia with one exception: when regional function approached control levels, shortening rather than lengthening was observed late in the isovolumic relaxation period. This implies that the force generated by the reoxygengated muscle actually exceeded that generated by adjacent normal fibers. This observation is consistent with the fact that reoxygengated papillary muscles characteristically exhibit prolongation of the duration of contraction,7 and that in tandem papillary muscle studies the reoxygengated muscle stretched the normal muscle late in the course of a simultaneously induced twitch.8

There are clear implications in the foregoing discussion, therefore, that tend to validate the clinical qualitative assessment of segmental wall motion as a semiquantitative marker of ischemia in chronic coronary artery disease. This extension by analogy is less than precise, however, in that the experimental model differs in material ways from the clinical state. First, although the data in this study indicate that increasingly severe ischemia leads to increasingly severe contraction abnormalities, the converse need not necessarily be true. Longstanding ischemia leads to the development of collateral vessels and to known structural alterations of myocardium such as fibrosis. The validity of the analogy between animal and clinical data may suffer both in nature and degree by the presence of such variables, and extrapolation to clinical circumstances must be done with caution. Additionally, the observed epicardial events may not precisely reflect simultaneous endocardial events, since the latter is exquisitely more sensitive to ischemia. In this regard, it is likely that methods which assess endocardial wall motion such as angiography and ultrasound may exhibit an unknown degree of phase-shift in disordered segmental wall motion. These objections notwithstanding, the data suggest that the observable pattern of segmental contraction reflects the magnitude of regional ischemia.

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References

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