Effect of Left Ventricular Akinesis on Cardiac Performance

Experimental Study Using a New Model


with the technical assistance of Margaret Gorrilla, R.N. and John Cormack, Research Assistant in Surgery

SUMMARY  The understanding of left ventricular failure and cardiogenic shock after myocardial infarction has been facilitated by a two-component model proposed by Swan et al.1 which views the left ventricle as consisting of a clearly defined infarcted portion and a normally functioning remainder. Although appealing, this model is difficult to substantiate experimentally. We describe a new experimental preparation in which the infarct is simulated by replacing part of the left ventricular wall with an inert patch of Dacron material.

In 18 dogs studied after replacing varying amounts of left ventricular contractile mass with noncontractile patches, the left ventricular end-diastolic pressure rose in proportion to the size of the patch. Contractility was unchanged, and overall left ventricular pump function was normal. These data support the conceptual model. The experimental preparation is applicable to other studies of left ventricular akinesis.

Experimental support for this model has been scarce. Conventional methods of producing akinesis by infarction result in irregular areas of fibrous tissue interspersed with functioning myofibrils, which exhibit varying degrees of contractile function or distention during systole. These problems make accurate evaluation of the conceptual model extremely difficult.

To help clarify this problem, we developed an experimental preparation of left ventricular akinesis with a clearly delineated area that neither contracted nor expanded in ventricular systole. The results of these experiments show close correlation with the predictions of the conceptual model as applied to a noncompliant and noncontracting segment, and offer further insight into the effects of left ventricular akinesis after myocardial infarction. The model is readily applicable to more sophisticated studies of left ventricular function and diastolic compliance.

Materials and Methods

Experimental Model

Mongrel dogs weighing about 20 kg were anesthetized with sodium pentobarbital (Nembutal), 20–30 mg/kg body weight, and were intubated and ventilated. The femoral artery and vein were isolated, and the heart was exposed through a left thoracotomy.
FIGURE 1. Techniques of operation. Three experimental groups: A) ventriculotomy and no muscle resection; B) myomectomy and small patch; and C) myomectomy with larger patch.

Cardiopulmonary bypass was initiated from the right atrium to the femoral artery. The left ventricle was opened through an anteroapical incision, which avoided major coronary branches, and the ventricular incision was closed by direct suture without myomectomy (group A), or was closed with an oval patch of heavy woven Dacron backed with felt after excision of an appropriate segment of myocardium (small patches, group B; large patches, group C — fig. 1). The average weight of muscle removed was 11.3 g and the largest, 19 g; this represented a mean of 13% of the weight of the remaining left ventricle as measured at later autopsy. Twenty-one intact dogs constituted a control group.

Methods of Evaluation

Hemodynamics

Hemodynamic assessment of each animal was undertaken before operation and again 6–8 weeks after operation. For these studies the dogs were anesthetized with Nembutal and instrumented with a high-fidelity left ventricular micromanometer catheter (Millar Instruments, Houston, Texas), a right atrial catheter, an ascending aortic catheter and ECG leads. Recordings were made on an Electronics for Medicine multichannel recorder (Electronics for Medicine DR8, White Plains, New York). Recordings were obtained of right atrial pressure, high-fidelity left ventricular pressure, aortic pressure and left ventricular dp/dt. Cardiac output was determined by the standard dye-dilution technique.

After each set of readings was completed, a solution of isoproterenol was infused until moderate tachycardia was noted (usually 2–4 μg/min), and the studies were repeated.

Radiographic

High-speed cine left ventriculography was performed on six dogs with patches to exclude mitral regurgitation and to confirm absolute akinesis of the patch.

Postmortem

All animals were killed after postoperative hemodynamic evaluation. The heart was removed and the left ventricle dissected free from other structures. The ventricle was weighed and opened so it could be flattened onto a sheet of squared paper. Its outline was carefully recorded and its area accurately measured (fig. 2). The area of the patch was expressed as a percent of the total left ventricular wall area.

Statistical Analysis

Mean values and standard deviations of all measured variables were calculated for each group. Groups were compared by analysis of variance. In ad-
dition, individual patch sizes were plotted against end-diastolic pressure, and a linear regression calculation was performed.

Results

Eighteen dogs survived long enough to be studied satisfactorily after operation. Each dog was assigned to group A, B or C according to the size of the Dacron patch. The size of the patches, as measured at autopsy, ranged from 9-33 cm², and represented from 9-31% of total left ventricular wall area. No dog survived with a patch larger than 31%, and most with patches larger than 25% died. Dogs who had only ventriculotomy and closure without a patch were assigned to group A (three dogs), those with small patches (less than 17% of left ventricular area) were assigned to group B (seven dogs), and those with large patches (greater than 17%) were assigned to group C (eight dogs).

Average patch size in group B was 12.3 ± 3.4% and in group C, 22.8 ± 6% of total left ventricular wall area. The hemodynamic findings expressed as mean ± SD are listed in Table 1. The results from dogs in group A did not differ significantly from those from intact control dogs in any measured index. Dogs in groups B and C maintained normal heart rates, blood pressure, and cardiac outputs when these were measured 6-8 weeks after operation.

Left ventricular end-diastolic pressure rose progressively with increasing patch size (fig. 3) and averaged 5.9 ± 2.1 mm Hg in normal dogs, 5.3 ± 4.7 mm Hg in group A, 12.4 ± 5.3 mm Hg in group B, and 18.3 ± 8.4 mm Hg in group C (fig. 4). Analysis of variance showed this trend to be significant at the 0.01 level (F = 8.88). Left ventricular contractility, as judged by V max and maximum dp/dt, did not distinguish between dogs with patches and controls (figs. 5 and 6). V max in the controls was 4.3 ± 0.7 circ/sec.

Table 1. Left Ventricular Akinesis: Summary of Hemodynamic Data

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 21)</th>
<th>Group A (n = 3)</th>
<th>Group B (n = 7)</th>
<th>Group C (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>138 ± 15.2</td>
<td>130.7 ± 8.2</td>
<td>138 ± 19.1</td>
<td>127 ± 24.7</td>
</tr>
<tr>
<td>(beats/min)</td>
<td>(192 ± 13.1)</td>
<td>(184 ± 11.4)</td>
<td>(195 ± 30.0)</td>
<td>(176 ± 33.0)</td>
</tr>
<tr>
<td>Peak LVP</td>
<td>155 ± 13.0</td>
<td>139.7 ± 21.2</td>
<td>144 ± 11.6</td>
<td>134 ± 16.0</td>
</tr>
<tr>
<td>(mm Hg)</td>
<td>(142 ± 10.7)</td>
<td>(151.3 ± 5.4)</td>
<td>(150 ± 12.2)</td>
<td>(141 ± 18.5)</td>
</tr>
<tr>
<td>EDP</td>
<td>5.9 ± 2.1</td>
<td>5.3 ± 4.7</td>
<td>12.4 ± 5.3</td>
<td>18.3 ± 8.4</td>
</tr>
<tr>
<td>(mm Hg)</td>
<td>(0.4 ± 1.2)</td>
<td>(2.3 ± 1.7)</td>
<td>(9.6 ± 5.3)</td>
<td>(16.9 ± 12.8)</td>
</tr>
<tr>
<td>AoP</td>
<td>133 ± 13.1</td>
<td>124 ± 14.4</td>
<td>126 ± 7.3</td>
<td>116 ± 18.1</td>
</tr>
<tr>
<td>(mm Hg)</td>
<td>(121 ± 14.2)</td>
<td>(116 ± 9.9)</td>
<td>(120 ± 10.0)</td>
<td>(108 ± 21.3)</td>
</tr>
<tr>
<td>Peak dP/dt</td>
<td>2448 ± 580</td>
<td>2865 ± 713</td>
<td>2804 ± 1004</td>
<td>2467 ± 901</td>
</tr>
<tr>
<td>(mm Hg/sec)</td>
<td>(4800 ± 1318)</td>
<td>(6138 ± 1315)</td>
<td>(5864 ± 1848)</td>
<td>(5919 ± 1472)</td>
</tr>
<tr>
<td>V max</td>
<td>4.26 ± 0.70</td>
<td>3.58 ± 0.26</td>
<td>3.87 ± 1.84</td>
<td>3.67 ± 1.94</td>
</tr>
<tr>
<td>(circ/sec)</td>
<td>(5.79 ± 3.41)</td>
<td>(5.63 ± 1.35)</td>
<td>(5.86 ± 2.47)</td>
<td>(6.16 ± 2.22)</td>
</tr>
<tr>
<td>LVMW</td>
<td>5665 ± 1858</td>
<td>6853 ± 1652</td>
<td>6039 ± 1689</td>
<td>4845 ± 1753</td>
</tr>
<tr>
<td>(g-m)</td>
<td>(8404 ± 2338)</td>
<td>(9694 ± 897)</td>
<td>(10558 ± 2808)</td>
<td>(8397 ± 4363)</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>3.25 ± 0.99</td>
<td>4.20 ± 0.65</td>
<td>4.33 ± 0.77</td>
<td>3.69 ± 0.97</td>
</tr>
<tr>
<td>(l/min)</td>
<td>(5.03 ± 1.32)</td>
<td>(6.17 ± 0.05)</td>
<td>(7.68 ± 1.07)</td>
<td>(6.49 ± 2.24)</td>
</tr>
</tbody>
</table>

Values are given as mean ± SD; figures in parentheses are values after isoproterenol infusion.
in group A, 3.6 ± 0.3; in group B, 3.9 ± 1.8; and in group C, 3.7 ± 1.9. Maximum dp/dt in the control group was 2448 ± 580 mm Hg/sec; in group A, 2865 ± 713; in group B, 2804 ± 1004; and in group C, 2467 ± 901.

Isoproterenol produced predictable contractility increases as shown in table 1 but did not improve discrimination between the groups. Cardiac output was maintained even in dogs with large patches, and cardiac output increased appropriately with infusion of isoproterenol.

**Discussion**

Myocardial infarction affects left ventricular performance in several ways. Contractile mass is lost, global left ventricular compliance is altered, mechanical function is changed by temporal and three-dimensional contraction inefficiencies, mechanical load may be increased by valve dysfunction (mitral regurgitation), and contractility may be altered. Early attempts to explain these changes were unsatisfactory. Swan et al. proposed a two-component model to explain several aspects of left ventricular function in the presence of an infarcted segment. They distinguished between large and small areas of akinesis, and compliant and noncompliant areas. They recognized the difficulty of defining the contribution of the elastic behavior of the infarcted area to overall ventricular performance, particularly as the compliance of the evolving infarct is time-dependent.

Our model attempts to offer experimental confirmation of the Swan model of a noncompliant, noncontracting segment in an otherwise normal left ventricle. The patches used in this experiment are negligibly dispersible in the physiologic pressure ranges. The area of akinesis can be measured with a high degree of accuracy. A clearly defined segment of akinetic left ventricle is thus produced, with minimal interference with remaining myocardium.

Our results support several of the predictions of Swan et al. Overall left ventricular pump function appears normal even with the stress of isoproterenol infusion. Left ventricular contractility, as assessed by $V_{max}$ and maximum dp/dt, is not different from control at the time of postoperative measurement. We
recognize, however, that the time chosen for our postoperative study may have missed an initial increase in contractility that would enable the animal to survive the early postoperative period. Examples from the clinical situation together with the predictions of the Swan model would suggest that initial compensation may be based on contractility increase, and that this later gives way to alterations in the pressure-volume relationship and a rise in left ventricular end-diastolic pressure. The relationship between akinetic segment area and end-diastolic pressure (fig. 3) from our data is almost identical to that predicted from the model of Swan et al. for a noncompliant infarct.

Although left ventriculography was performed on a small number of dogs with patches, it was not part of our initial protocol, and not enough data are available to draw conclusions about volume or compliance changes. It may be assumed that left ventricular compliance will decrease in this model and that this will have contributed to the survival of the study animals. The degree of acute left ventricular dilatation is restricted to fairly narrow limits by ventricular compliance, though by the time of these studies, some increase in the size of the left ventricle must be assumed. Future experiments may define the extent of these volume and compliance changes. Nevertheless, the effect will be to move the functioning myocardium to a more effective point on the Starling curve, thereby compensating for the akinetic area.

We did not attempt to vary the site of the akinetic area, and therefore no conclusions may be drawn about the possibly different effect of anteroapical compared with basal or posterior infarcted segments. Attempts were made to minimize interference with papillary muscle function, and no evidence of mitral valve dysfunction was noted in dogs having ventriculography.

The conceptual model offers theoretical limitations to the area of left ventricular myocardium that can be rendered akinetic. If the infarct approaches 40% of left ventricular area, restoration of adequate stroke volume would be predicted to require an end-diastolic volume that would not be attainable within the range of physiologic end-diastolic pressures. This figure is reasonably close to the maximum predicted by Klein et al. in their clinical study of left ventricular aneurysm in which they stated that akinetic areas larger than 25% require ventricular dilatation for compensation. Without dilatation, the degree of shortening required of the myofibril to maintain stroke volume would exceed physiologic limits. Most of our dogs receiving patches larger than 25% of total left ventricular wall area died in acute pulmonary edema, although one survived with a patch of 31%. With ventricular dilatation, the area of akinesis becomes relatively smaller and adaptation is possible, but, as indicated earlier, there are limits to the degree of acute dilatation possible.

**Conclusion**

The two-component conceptual model of left ventricular akinesis proposed by Swan et al. is supported by our experimental model of a noncompliant akinetic segment in an otherwise normally functioning canine heart. Compensation for loss of contractile mass, increase in compliance, and loss of mechanical efficiency is achieved by a rise in end-diastolic pressure and movement to a more favorable point on the Starling curve. Increases in contractility played no part in the compensatory mechanism in this model at the time of the study.

Some predictions of the conceptual model are confirmed. The suggestion that akinetic areas larger than 40% of left ventricular area would not be consistent with survival was supported; and end-diastolic pressures necessary to produce adequate ejection volumes under these circumstances are unattainable.

Further work is needed to extend this study to examine akinetic areas of defined compliance and to document the volume changes that occur, and thus confirm or reject other aspects of the conceptual model. Our experimental preparation appears to be ideally suited to this.
A Mathematical Model of the Dynamic Geometry of the Intact Left Ventricle and Its Application to Clinical Data

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SUMMARY In this paper we examine the relations that may exist between the geometric variables most frequently used to describe left ventricular contraction. The left ventricle is represented by a thick-walled cylinder contracting both radially and longitudinally. For this model, wall thickening, mid-wall radius shortening and longitudinal axis shortening can be shown to be uniquely related during contraction, whereas it can be demonstrated that internal radius shortening is not uniquely related to these variables, but is also determined by the specific geometry of the cylinder, expressed in terms of the mid-wall radius-to-wall thickness (R/h) ratio of the cylinder. Detailed analysis of the same variables in 44 normal subjects, 32 patients with aortic stenosis and 54 patients with valvular regurgitation (33 aortic and 21 mitral), strongly suggests that the same relations are also clinically applicable. For instance, ventricular longitudinal axis shortening can be estimated with some accuracy from the standard M-mode echocardiogram. Also, wall thickening can be viewed as the direct reflection of the shortening that occurs in the circumferential and longitudinal directions, whereas internal radius shortening is significantly influenced by the R/h ratio of the ventricle, a consideration which becomes important when analyzing results in patients with left ventricular hypertrophy.

Acknowledgment

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References

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MYOCARDIAL PERFORMANCE in the intact left ventricle has been evaluated in terms of extent and velocity of shortening with respect to the meridional and equatorial dimensions of the ventricle. More recently, the extent and rate of left ventricular wall thickening during systole have also been shown to be sensitive parameters of changes in ventricular function.1-5 Gould et al.6 particularly underlined the importance of wall thickening as a component of ventricular contraction, and attempted to describe the separate contributions of longitudinal shortening, circumferen-

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