Combined Papillary Muscle and Left Ventricular Wall Dysfunction as a Cause of Mitral Regurgitation

An Experimental Study

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SUMMARY
Papillary muscle infarction was produced in 16 mongrel dogs by placing sutures around the base of one of the papillary muscles. In addition, patchy infarction of the adjacent left ventricular wall was produced by placing an Ameroid constrictor around the appropriate coronary artery. Mitral insufficiency developed in 14 of these animals; it was severe in four and mild to moderate in ten. Mitral insufficiency was not produced by isolated infarction of a papillary muscle or by isolated infarction of the left ventricular wall.

It is concluded that papillary muscle infarction alone does not lead to mitral regurgitation, but that papillary muscle dysfunction acts in concert with left ventricular wall dyskinesia or dilatation to produce mitral valve incompetency.

Additional Indexing Words: Cardiac performance Coronary disease Myocardial infarction Valve disease

MITRAL insufficiency due to papillary muscle dysfunction has been widely accepted as a clinical syndrome, but the precise pathophysiologic components involved in this entity have never been clearly defined.

Competency of the mitral valve depends upon the anatomic and functional integrity, not only of the leaflets, but also of the annulus, chordae tendineae, papillary muscles, and left ventricle. Papillary muscle contraction, occurring synchronously with left ventricular contraction, is believed to tauten the chordae tendineae, preventing prolapse of the mitral leaflets into the left atrium.1,2 Loss of this contractile function, resulting from myocardial infarction with subsequent papillary muscle fibrosis or ischemia, has been described by Burch3,4,5 and others6.7 as a cause of mitral insufficiency. This entity has been named “papillary muscle dysfunction.”

A previous study from our laboratory has shown that infarction and later fibrosis of either the anterior or posterior papillary muscle in the canine heart does not lead to mitral regurgitation.8 This observation was confirmed by Tsakiris et al.9

The present study was undertaken to investigate further the role of papillary muscle dysfunction in the production of mitral
insufficiency, on the assumption that it may be at least partly responsible for mitral insufficiency. It was postulated that myocardial infarction or ischemia, producing dyskinesia* or dilatation of the adjacent free wall of the left ventricle, might act in concert with the nonfunctioning or malfunctioning papillary muscle to bring about incompetency of the mitral valve.

Methods

Twenty-six adult mongrel dogs weighing 15–24 kg. formed the basis of this study. This study was initiated in several other animals, but these died before the entire experimental protocol could be completed. The animals were anesthetized with intravenous pentobarbital, 30 mg/kg body weight, an endotracheal tube was introduced, and the lungs were ventilated with a Palmer† respirator. Using sterile technique, a left thoracotomy was performed through the left fifth interspace, the pericardium was opened, and a purse-string suture was placed around the left atrial appendage. After amputating the tip of the appendage, the left index finger was introduced into the left atrium and advanced through the mitral valve in order to palpate the papillary muscle and to guide accurate placement of sutures. Four full-thickness sutures were then placed through the left ventricular wall around the four quadrants of the papillary muscle to be infarcted. Care was taken to avoid the chordae tendineae in the sutures. The sutures were then tied securely on the external surface of the left ventricle, thus infarcting completely the papillary muscle along with a small area of left ventricular wall at the base of the papillary muscle. In 13 dogs an Ameroid‡ constrictor was placed around the proximal portion of the left anterior descending coronary artery, immediately distal to the septal branch. In 10 dogs the Ameroid was placed around the left circumflex coronary artery. The Ameroids were not Vaseline coated and therefore produced rapid arterial constriction in 11 to 26 days.10

The animals were subdivided into four experimental groups. In group I (nine dogs) infarction of the anterior papillary muscle was carried out, and an Ameroid constrictor was placed around the left anterior descending coronary artery, thus producing ischemia and patchy infarction of the anterior free wall of the left ventricle as well (figs. 1 and 2). In group II (seven dogs) infarction of the posterior papillary muscle was carried out, and an Ameroid constrictor was placed around the left circumflex branch to produce posterior-inferior ischemia and patchy infarction.

In group III (seven dogs) only an Ameroid constrictor was placed, in four around the left anterior descending branch, and in three around the circumflex branch. In this group, the papillary muscles were not infarcted. Group IV consisted of three control animals that had only a left thoracotomy.

It should be pointed out that ligation of papillary muscle probably produces a somewhat different pathophysiologic condition than does Ameroid constrictor-induced infarction of the free wall of the ventricle. Following papillary muscle

*In this paper the term “dyskinesia” is used in a general sense to indicate a segment of the left ventricle which contracts less than the remainder of the ventricle (hypokinesia), fails to contract at all (akinesia), or one which bulges paradoxically.
†C. F. Palmer Ltd., Effra Road, London S.W. 2, England.
‡American Plastics Division, Tennoco Chemicals Inc., 300 East 42 Street, New York, New York.

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Figure 1
Photograph showing ligation of anterior papillary muscle (arrow) plus an Ameroid constrictor on the left anterior descending coronary artery.
ligation there is extensive myocardial necrosis and, later, dense fibrosis, so that one would expect total loss of the ability of this structure to contract. By contrast, there is a rather diffuse and patchy infarct and fibrosis after an Ameroid constrictor is placed around one of the coronary arteries, and the extent of left ventricular wall dysfunction is in many cases less marked.

Left atrial pressure measurements were obtained before the animals were operated upon and again obtained on one to several occasions 4 to 30 weeks postoperatively. The animals were anesthetized, bronchoscoped, and the left atrial pressures were measured via a needle passed through the carina into the left atrium. The pressure tracings were recorded on an Electronics for Medicine* multichannel recorder. Selective left ventricular cineangiography was performed in the animals by passing a no. 8 Cournand† catheter retrogradely across the aortic valve into the left ventricle. End-diastolic volumes were obtained using the single-plane cineangiographic technique of Greene and colleagues. The amount of mitral insufficiency was grossly estimated by the degree of left atrial opacification seen following left ventricular cineangiography. Thus, only a small amount of dye seen in the left atrium was considered 1+ mitral insufficiency; 2+ mitral insufficiency was accepted when there was a moderate degree of left atrial opacification; 3+ and 4+ were indicated when fairly dense degrees of opacification of the left atrium occurred, and reflux into the pulmonary veins was seen. In all cases, the cineangiograms were interpreted by two independent observers who were “blind” with respect to the experimental groups.

All of the hemodynamic and cineangiographic studies were performed under comparable physiologic conditions, the dogs having been anesthetized with intravenous pentobarbital, 20–30 mg/kg body weight.

The animals were eventually sacrificed, and both gross and histopathologic studies were performed.

*Electronics for Medicine, Inc., 30 Virginia Road, White Plains, New York.
†United States Catheter and Instrument Co., Box 787, Glens Falls, New York 12801.

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Figure 2

Shows microscopic appearance of free wall of left ventricle. Note the patchy fibrosis.
Table 1

Hemodynamic and Cineangiographic Data*

<table>
<thead>
<tr>
<th>No.</th>
<th>LAP (mm Hg)</th>
<th>V wave (mm Hg)</th>
<th>Mitral regurgitation</th>
<th>LV end-diastolic volume (ml/kg)</th>
<th>LV dyskinesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>8</td>
<td>17</td>
<td>1+</td>
<td>28</td>
<td>0</td>
</tr>
<tr>
<td>2.</td>
<td>22</td>
<td>30</td>
<td>3+</td>
<td>42</td>
<td>ANT</td>
</tr>
<tr>
<td>3.</td>
<td>6</td>
<td>9</td>
<td>0</td>
<td>26</td>
<td>AP</td>
</tr>
<tr>
<td>4.</td>
<td>6</td>
<td>15</td>
<td>2+</td>
<td>30</td>
<td>ANT-AP</td>
</tr>
<tr>
<td>5.</td>
<td>8</td>
<td>12</td>
<td>3+</td>
<td>31</td>
<td>ANT</td>
</tr>
<tr>
<td>6.</td>
<td>11</td>
<td>15</td>
<td>2+</td>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>7.</td>
<td>9</td>
<td>11</td>
<td>0</td>
<td>35</td>
<td>ANT-AP</td>
</tr>
<tr>
<td>8.</td>
<td>12</td>
<td>18</td>
<td>1+</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>9.</td>
<td>8</td>
<td>18</td>
<td>1+</td>
<td>28</td>
<td>ANT</td>
</tr>
</tbody>
</table>

| Group II |             |                |                      |                                 |              |
| 10. | 20          | 28             | 1+                   | 27                             | 0            |
| 11. | 15          | 20             | 4+                   | 36                             | 0            |
| 12. | 9           | 8              | 1+                   | 27                             | INF          |
| 13. | 10          | 20             | 3+                   | 55                             | INF          |
| 14. | 20          | 25             | 1+                   | 44                             | INF          |
| 15. | 13          | 15             | 2+                   | 38                             | 0            |
| 16. | 7           | 15             | 2+                   | 41                             | INF          |

| Group III |             |                |                      |                                 |              |
| 17. | 1           | 3              | 0                    | 37                             | INF          |
| 18. | 7           | 9              | 0                    | 21                             | AP           |
| 19. | 7           | 10             | 0                    | 31                             | 0            |
| 20. | 1           | 8              | 0                    | 26                             | 0            |
| 21. | 9           | 9              | 0                    | 32                             | ANT          |
| 22. | 5           | 10             | 0                    | 24                             | 0            |
| 23. | 7           | 12             | 0                    | 36                             | 0            |

| Group IV |             |                |                      |                                 |              |
| 24. | 2           | 3              | 0                    | 16                             | 0            |
| 25. | 2           | 3              | 0                    | 29                             | 0            |
| 26. | 1           | 3              | 0                    | 30                             | 0            |

*The data presented in this table were those obtained during the final study of the dogs before sacrifice and were obtained 10 to 30 weeks postoperatively.

Abbreviations: LAP = left atrial pressure; LV = left ventricular; ANT = anterior wall; AP = apical; INF = inferior wall. Mitral regurgitation: 0 = none; 1+ = mild; 2+ = moderate; 3+ to 4+ = severe.

Results

Seven of the nine animals from group I developed left atrial pressures greater than normal,* and in eight there was a tall V wave with rapid Y descent, compatible with mitral insufficiency (table 1). Six of the seven animals from group II had elevated left atrial pressures; all of these six had prominent V waves (fig. 3). All eight of the animals serially studied from groups I and II had higher left atrial pressures 4 to 15 weeks postoperatively. The pressure then fell to the level noted in table 1 in the ensuing weeks. The average fall in pressure was 6 mm Hg (range, 3–17 mm Hg) over the 8–15 week period (fig. 3). This phenomenon was probably related to an improvement in heart failure and changes in atrial and ventricular compliance.12

The left atrial pressure was slightly elevated in four of the seven dogs from group III and was normal in the three control animals in group IV.

*The left atrial pressure in an anesthetized normal dog with an intact thoracic cage is below 6 mm Hg (unpublished observations).

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Table 1 and figure 4 show the cineangiographic findings. Seven of the nine animals from group I and all from group II demonstrated mitral regurgitation. This was severe in four and mild to moderate in ten of the 16 animals with combined papillary muscle and free left ventricular wall infarction (fig. 4). None of the control animals and none of those with only an Ameroid constrictor around the coronary artery had mitral regurgitation. There was no difference between the incidence or severity of mitral insufficiency between group I, those with anterior wall and papillary muscle infarction, and group II, those with posterior wall and papillary muscle infarction.

Areas of akinesia or dyskinesia were seen in 13 animals, six of these from group I, four from group II, and three from group III. These abnormalities were associated with severe mitral regurgitation in three animals, moderate mitral regurgitation in two animals, and mild insufficiency in three. Five animals with no demonstrable mitral insufficiency had ventricular dysskinetic segments. Three of the four dogs with severe mitral regurgitation (3+ to 4+) had large left ventricular end-diastolic volumes. In the animals in which the mitral regurgitation was either mild or absent, the left ventricular end-diastolic volumes ranged from normal to increased (table 1). Thus, both left ventricular dilatation and/or dyskinesia may develop without producing mitral regurgitation.

**Pathologic Studies**

Twelve hearts from groups I and II were examined at autopsy. Ten had moderate to severe fibrosis and atrophy of the infarcted papillary muscle. The other two had less marked fibrosis. In three animals the contralateral papillary muscle had become markedly hypertrophied and dilated (fig. 5). In all but two of the hearts examined from groups I and II, the left ventricle was both hypertrophied and dilated. The left ventricular myocardium, in the area supplied by the stenosed or

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**Figure 3**

Left atrial pressures in one of the animals from group II.

**Figure 4**

Group II animal with 3+ mitral insufficiency. Note retrograde filling of the pulmonary veins. Arrow points to the Ameroid constrictor around the circumflex coronary artery. LV = left ventricle; LA = left atrium; PV = pulmonary vein.

**Figure 5**

Left arrow points to atrophied anterior papillary muscle (group I). The arrow to the right points to the posterior papillary muscle which is hypertrophied.
occluded coronary artery, showed varying degrees of patchy and diffuse fibrosis. The degree of stenosis of the coronary artery constricted by the Ameroid ranged from 80 to 100%.

Discussion

Two mechanisms have been hypothesized to account for mitral insufficiency due to "papillary muscle dysfunction": (1) there may be absent or ineffective papillary muscle contraction due to infarction or ischemia, so that during ventricular systole, as the left ventricular apex moves toward the mitral annulus, the chordae slacken with resultant prolapse of the mitral leaflets into the left atrium; (2) a shortened, fibrotic papillary muscle may develop which, when displaced by ventricular dilatation, aneurysm, or muscle hypertrophy, works at a mechanical disadvantage. The chordae then pull upon the valve leaflets in a more oblique direction than normal, and valvular incompetency may occur.

Initial studies from this laboratory have shown quite clearly that selective paresis of a papillary muscle does not affect the competence of the mitral valve. The extension of these studies, reported here, indicates that localized areas of dyskinesia of the free wall of the left ventricle, or ventricular dilatation, appear to act in combination with the papillary muscle dysfunction to produce mitral insufficiency. This concept was also suggested by Tsarkiris et al. in their study on experimental papillary muscle damage. They found mild mitral incompetence during control hemodynamic conditions and during periods of increased aortic pressure induced by angiotensin administration in two of 11 animals in which, in addition to papillary muscle infarction, there were damaged areas of left ventricle adjacent to the bases of the papillary muscle. The infarcting agent in their experiment was 1.0 to 1.5 ml of 10% formalin injected directly into the papillary muscle. Dilatation or dyskinesia most likely produces a malignment of or a faulty foundation for the papillary muscles, thus contributing to their malfunction.

Our findings are in accord with clinical observations of Brody and Criley and of Shelburne et al. Both groups noted dilated, poorly contracting, dyskinetic left ventricles in their patients with presumed papillary muscle dysfunction. We have made similar observations in several patients studied with mitral insufficiency related to coronary artery disease.

References

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