Mitral valve prolapse in short-term experimental coronary occlusion: a possible mechanism of ischemic mitral regurgitation

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ABSTRACT  Experimental coronary occlusions were carried out in 12 closed-chest dogs to investigate the functional anatomic characteristics of the mitral valve complex during acute myocardial ischemia. Two-dimensional echocardiography was used to assess left ventricular function, the mitral valve complex, and left atrial size. Presence of mitral regurgitation was assessed by left ventricular contrast echocardiography. Thirty-seven coronary occlusions of up to 10 min in duration were carried out in proximal or distal locations in the left anterior descending and the left circumflex coronary arteries. Mitral regurgitation, which was mild in severity as judged by a small rise in pulmonary artery wedge pressures, was observed in 15 of 37 brief coronary occlusion experiments. Mitral valve prolapse was noted in all 15 experiments, as well as in four additional studies in which mitral regurgitation was not seen. The development of experimental mitral valve prolapse was explained by measurements that demonstrated a relative displacement of the papillary muscle tips toward the mitral orifice. We conclude that mitral valve prolapse is a common sequela of short-term coronary occlusion and is often associated with mild mitral regurgitation. Relative displacement of ischemic papillary muscles toward the mitral orifice appears to be a likely mechanism of acute ischemic mitral valve prolapse.


THE CLINICAL MANIFESTATIONS of papillary muscle dysfunction were first described by Burch et al.1 in 1963. They proposed two major pathophysiologic mechanisms by which ischemic dysfunction may lead to mitral regurgitation and speculated that failure of an ischemic or fibrotic papillary muscle to shorten during ventricular contraction would cause mitral valve leaflet prolapse. Another hypothesis emphasized incomplete valve leaflet coaptation that resulted from abnormal spatial relationships between papillary muscle and mitral cusps caused by aneurysmal left ventricle and displaced papillary muscle accompanying regional myocardial infarction. Divergent conclusions were derived from limited studies of isolated papillary muscle infarction in mongrel dogs that demonstrated no significant mitral regurgitation5-4; other studies showed that papillary muscle dysfunction, acting in concert with abnormal left ventricular wall dynamics or dilatation, could indeed produce mitral regurgitation.5-8 In a review of the functional anatomic characteristics of mitral regurgitation, Perloff and Roberts9 observed that if papillary muscle dysfunction is present, then the chordae tendineae slacken as the ventricular apex moves toward the mitral anulus in systole, causing valve leaflets to prolapse under ventricular pressure into the left atrium. Steelman et al.10 described midsystolic clicks, which may suggest mitral prolapse in the clinical syndrome of papillary muscle dysfunction.

The relationship between mitral regurgitation and short-term myocardial ischemia has not been extensively studied with two-dimensional echocardiography, even though this noninvasive method is suitable for comprehensive assessment of regional wall motions and ventricular function and for systematic de-
scription of altered coaptation of mitral leaflets. Ogawa et al. used two-dimensional echocardiography to define a spectrum of papillary muscle dysfunction, and their data seemed to conform to the mechanisms of mitral regurgitation originally proposed by Burch et al. However, Godley et al. suggested that mitral valve prolapse in patients with ischemic heart disease may merely reflect a random association of two relatively common clinical phenomena.

Thus the pathogenesis of ischemic mitral regurgitation remains unclear, especially in relation to a possible role of mitral valve prolapse. This study was designed to investigate both the frequency and mechanisms of mitral valve regurgitation and prolapse associated with transient acute myocardial ischemia in closed-chest dogs.

Materials and methods

The experiments were carried out in 12 closed-chest dogs weighing from 24 to 48 kg that had been anesthetized with 2 mg/kg im morphine and 30 mg/kg iv pentobarbital. The dogs were ventilated with a Harvard respirator and auffed endotracheal tube. A No. 8F catheter was inserted into the right femoral artery and advanced to the ascending aorta, and a pigtail catheter was introduced retrogradely into the left ventricle. A Swan-Ganz No. 7F catheter was placed in the pulmonary artery via the femoral vein. Thus aortic, left ventricular, pulmonary arterial, and pulmonary capillary wedge pressures were measured with fluid-filled catheters and Statham P 23 Db pressure transducers. The intracardiac pressures and a precordial lead electrocardiogram were monitored and recorded on a physiologic multichannel recorder (Model V12; Electronics for Medicine Honeywell) at a paper speed of 25 or 50 mm/sec. Coronary artery occlusions were produced by inflation of a No. 4F balloon catheter inserted through the right carotid artery into a coronary branch. The coronary occlusion was released by balloon deflation within 10 min. Echocardiographic examinations were obtained before, during, and after release of the occlusion. A similar protocol was carried out with proximal and distal occlusions of the left anterior descending and circumflex coronary arteries.

Two-dimensional echocardiographic examination. A commercially available, two-dimensional echocardiographic recorder (ATL Mark III) was used. Echocardiographic examination of the heart was standardized in closed-chest dogs to achieve optimal cross-sectional images, as previously reported. This provided multiple long- and short-axis cross sections of the left ventricle. Multiple short-axis cross sections of the left ventricle were recorded at the level of the mitral valve leaflets, at the papillary muscles, and near the apex. The echocardiograms were recorded on videotape and the images could be replayed in real time, slow motion, or as single frames.

Contrast echocardiograms were obtained by injections of 5 ml of agitated saline or an agitated saline–meglumine diatrizoate (Renografin) mixture into the left ventricle. The criterion for mitral regurgitation observed on the contrast two-dimensional echocardiogram was the appearance of contrast medium in the left atrium during ventricular systole (figure 1).

The diagnosis of mitral valve prolapse on the two-dimensional echocardiogram was made by demonstration of a leaflet bul- lowing into the left atrium, as previously reported. A posterior displacement of mitral leaflet(s) past the annular plane during ventricular systole was considered to be diagnostic of valve prolapse. For its detection, multiple cross-sectional planes and different transducer angulations were used. Two observers analyzed the echo recordings independently to evalu-

FIGURE 1. Two-dimensional left ventricular contrast echocardiogram. A regurgitant jet into the left atrium is noted. LV = left ventricle; LA = left atrium.
Acute mitral regurgitation and/or mitral valve prolapse were produced more often with proximal than with distal occlusions and were more common in the dog with left circumflex artery occlusion than in the dog with left anterior descending artery occlusion. Anterior mitral valve prolapse (figure 3) was more frequent than posterior mitral valve prolapse (figure 4) after short-term coronary occlusion. Although contrast injections into the left ventricle demonstrated presence of mitral regurgitation, quantitative information as to its severity was limited. A quantitative visual analysis of rapid clearance of the contrast agent from the left atrium suggested a mild lesion. Severity of regurgitation was further judged from hemodynamic data on pulmonary capillary wedge pressures, as described below.

We explored several hemodynamic and two-dimensional echocardiographic measurements as possible correlates of the mitral valve prolapse observed during acute experimental ischemia.

(1) Left ventricular end-diastolic pressure and aortic pressure during coronary occlusion were not significantly different between the prolapse and nonprolapse groups, although left ventricular end-diastolic pressure was significantly increased by the coronary occlusion (table 2).

(2) Mean pulmonary capillary wedge pressure was significantly increased during occlusion in both prolapse and nonprolapse groups but was slightly higher in the prolapse group (figure 5). The height of the V wave was $11.3 \pm 4.1$ mm Hg (mean $\pm$ SD) in the prolapse group as compared with $4.8 \pm 2.5$ mm Hg in the nonprolapse group. The highest V wave noted was

Of the 37 coronary occlusions, 15 exhibited mitral regurgitation. All 15, as well as four other occlusions, also resulted in mitral valve prolapse. Thus acute mitral regurgitation was a common sequela of brief coronary artery occlusion in closed-chest dogs and mitral valve prolapse was consistently observed along with mitral regurgitation. Acute mitral regurgitation and/or mitral valve prolapse were produced more often with proximal than with distal occlusions and were more common in the dog with left circumflex artery occlusion than in the dog with left anterior descending artery occlusion. Anterior mitral valve prolapse (figure 3) was more frequent than posterior mitral valve prolapse (figure 4) after short-term coronary occlusion. Although contrast injections into the left ventricle demonstrated presence of mitral regurgitation, quantitative information as to its severity was limited. A quantitative visual analysis of rapid clearance of the contrast agent from the left atrium suggested a mild lesion. Severity of regurgitation was further judged from hemodynamic data on pulmonary capillary wedge pressures, as described below.

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18 mm Hg and did not suggest hemodynamically severe mitral regurgitation.

(3) Left ventricular and left atrial sizes measured by cross-sectional area and mitral annular dimension showed no significant correlation between prolapse and nonprolapse groups (table 2).

(4) Fractional area change of cross sections measured by two-dimensional echocardiography at all three levels of the left ventricle did not differ significantly between prolapse and nonprolapse groups, although it was decreased after coronary occlusion (table 2).

(5) The relative displacement of papillary muscle tips toward the mitral orifice was significantly different in the mitral valve prolapse group (figure 6). Thus, in control images, the amount of the mitral annular movement toward the apex was nearly the same as that of the papillary muscle tip toward the apex so that the relative distance from papillary muscle tip to the mitral orifice was not changed during systole. With coronary occlusion, the mitral annular movement in systole was decreased in the mitral prolapse group; however, there was no significant difference between the prolapse and nonprolapse groups. The apical movement toward the base decreased significantly after coronary occlusion, but, again, there was no significant correlation between prolapse and nonprolapse groups. On the other hand, the papillary muscle tip motion toward the apex, which was significantly less marked after occlusion compared with that of preocclusion control, was further reduced in the presence of mitral valve prolapse. Thus the distance from the tip of the papillary muscle to the mitral annular plane was significantly shorter in the mitral valve prolapse group (20.3 ± 3.3 mm) than that in the nonprolapse group (23.9 ± 4.0 mm) (figure 6).

Discussion

These results suggest that acute mitral regurgitation is a common sequela of brief coronary artery occlusions in dogs and that mitral valve prolapse is consistently observed along with the acute ischemic mitral regurgitation. The degree of ischemia, although not quantitated directly in these studies, was judged by the extent and distribution of asynergy in severe hypokinesia or akinesia and by apparent wall thinning. These wall motion abnormalities were found to be induced after occlusion in all experiments, whether or not they were associated with valve prolapse. We assessed intracoronary balloon occlusion fluoroscopically at meglumine diatrizoate injection into the left main coronary artery, which demonstrated the absence of filling distal to the site of the inflated balloon.

These experimental data differ from those of a clini-
**FIGURE 4.** Posterior mitral valve prolapse (MVP) during left circumflex coronary artery occlusion at the proximal site. Arrow, Billowing of a posterior leaflet into the left atrium. LV = left ventricle; LA = left atrium; Cath = catheter.

**TABLE 2**
Hemodynamic data during occlusion

<table>
<thead>
<tr>
<th></th>
<th>Coronary occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (n = 37)</td>
</tr>
<tr>
<td>LV end-diastolic</td>
<td>4.3 ± 2.5</td>
</tr>
<tr>
<td>pressure (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>LV size (cross-sectional areas/cm²)</td>
<td>9.5 ± 2.1</td>
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<tr>
<td></td>
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</tr>
<tr>
<td>Left atrial size</td>
<td>9.8 ± 2.5</td>
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<tr>
<td>(cross-sectional</td>
<td></td>
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<tr>
<td>areas/cm²)</td>
<td></td>
</tr>
<tr>
<td>% FAC of LV short-</td>
<td></td>
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<tr>
<td>axis cross sections</td>
<td></td>
</tr>
<tr>
<td>Mitral leaflet level</td>
<td>35.2 ± 8.8</td>
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<tr>
<td></td>
<td></td>
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<tr>
<td>Midpapillary muscle</td>
<td>42.1 ± 9.7</td>
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<tr>
<td>level</td>
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<tr>
<td>Apex level</td>
<td>44.0 ± 4.9</td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral annular</td>
<td>3.2 ± 0.3</td>
</tr>
<tr>
<td>dimension (cm)</td>
<td></td>
</tr>
</tbody>
</table>

LV = left ventricle; MVP = mitral valve prolapse; FAC = fractional area change; NS = not significant.

Statistical comparisons (vs control): ^p < .05; ^p < .01; ^p < .001.

They failed to observe any instance of mitral valve prolapse in a study of 22 patients with clinical evidence of papillary muscle dysfunction and concluded that incomplete closure of the mitral valve may be the underlying cause of mitral regurgitation accompanying papillary muscle dysfunction. These authors contended...
that mitral valve prolapse develops rarely, if at all, as a direct result of papillary muscle dysfunction. Their patient subsets, however, had mitral regurgitation associated with chronic ischemic damage, and they did not examine acute ischemic episodes. Thus a possible reason for the difference between the results of this clinical study and our data may be related to long-term vs short-term effects of myocardial and papillary muscle ischemia. In a short-term occlusion the left ventricle size increases, but possibly to a smaller extent than in chronic ischemic damage, in which left ventricular dilatation may be pronounced, depending on the extent of left ventricular dysfunction. Moreover, the pathogenesis of mitral regurgitation associated with chronic ischemic dysfunction is likely to be different from that seen in acute ischemia. In another clinical study by Ogawa et al., mitral valve prolapse was observed in three of 14 patients with papillary muscle dysfunction and exhibiting akinetic inferior-posterior wall and papillary muscle fibrosis but with normal cavity size. Nine of the remaining 11 patients had left ventricular dilatation associated with hypokinesis or ventricular aneurysm, and an abnormal tethering of the mitral valve toward the apex was noted. In our study of 37 short-term coronary occlusion experiments we did not observe incomplete systolic mitral leaflet closure arrested within the cavity of the left ventricle as reported by Godley et al., or displacement of mitral valve coaptation toward the apex of the left ventricle as described by Ogawa et al. In this study, anterior mitral leaflet prolapse occurred more frequently than posterior leaflet prolapse. A precise explanation of the observation is difficult, since the left circumflex coronary artery occlusion generally produces a selective infarct of the posteromedial papillary muscle, which one might expect to be primarily associated with posterior leaflet action. However, the chordae tendineae from each papillary muscle are also generally inserted in both leaflets, and involvement of a specific leaflet may be influenced by alteration in ventricular geometry secondary to extensive and profound myocardial ischemia.

The mechanism of mitral valve prolapse during short-term coronary occlusion appears to be related to a failure of papillary muscle shortening or its passive elongation. In either event, the chordae tendineae would slacken during ventricular systole, resulting in prolapse. Although two-dimensional echocardiographic resolution did not permit us to fully quantitate papillary muscle length, we observed a significantly greater decrease in distance from papillary muscle tip to mitral orifice in these instances where mitral valve prolapse occurred.

If these observations in closed-chest dogs have any relevance to human subjects, it is likely that mitral regurgitation associated with acute ischemia (e.g., during an episode of angina) may be related to mitral valve prolapse induced by the transient ischemic episode. The mechanisms of mitral regurgitation complicating myocardial infarction or ischemic left ventricular dilatation (i.e., ischemic cardiomyopathy) are likely to be different and need to be investigated.

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