The Syndrome of Systolic Click, Murmur, and Mitral Valve Prolapse—A Cardiomyopathy?

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SUMMARY

Twenty-six patients with systolic clicks, murmurs, and prolapsed mitral valve leaflets were studied because of distressing chest pain or troublesome arrhythmias. Cardiac catheterization revealed normal coronary arteries and a high incidence of left ventricular (LV) dysfunction.

The patients, 20 of whom were women, averaged 41 years of age. Thirteen of the 22 patients experienced chest pain of sufficient severity to warrant hospital admission for suspected acute myocardial infarction. Twenty of 26 had abnormal ECG patterns including sinus bradycardia, 1\(^\text{st}\), 2\(^\text{nd}\), and 3\(^\text{rd}\) block, atrial and ventricular arrhythmias and abnormal ST-T wave vectors. Three had patterns of healed transmural infarctions and five of 16 had positive exercise tests.

LV dysfunction was hemodynamically documented in 20 patients by either elevated LV end diastolic pressure, low resting cardiac index, or inappropriate rise in cardiac index during exercise. In the remaining six, impaired LV dynamics were demonstrated angiographically.

Left ventriculography revealed mitral valve prolapse in all patients, mitral regurgitation in 20, and mild to severe LV hypertrophy in 14 patients. Contractility, determined angiographically, was markedly impaired in 13 patients with marked hypokinesis of the antero-lateral wall of the LV resulting in the appearance of an unusual prominent convexity in this portion of the ventricle in end systole and early diastole. Seven others had similar but less severe impairment of LV contractility.

These results indicate that LV dysfunction, possibly related to a primary myocardial disorder, is a significant component of the syndrome of prolapsed mitral valve leaflet. The findings in the symptomatic patients described in this study cannot be generalized to all patients with this syndrome as our sample excluded patients with mild asymptomatic forms of the disease.

Additional Indexing Words:
Angina pectoris
Anomalous pulmonary venous drainage
Atrial arrhythmias
Coronary arteriography
Hemodynamics
Left ventricular dimensions
Left ventricular dysfunction
Mitrail regurgitation
Subacute bacterial endocarditis
Segmental shortening
Sudden death
Ventricular arrhythmia

Late systolic murmurs with or without nonejection clicks are frequently associated with prolapsed mitral valve leaflets and various degrees of mitral regurgitation.\(^1\)\(^-\)\(^10\) Although the syndrome has been described by many clinical investigators, each has stressed different aspects of the entity. The auscultatory findings, their alteration with vasoactive drugs, the abnormal electrocardiogram, the abnormal mitral valve anatomy and its abnormal function have been emphasized.

Recently, Ehlers et al.,\(^11\) Jeresaty,\(^9\) Gooch et al.\(^12\) and Scampordonis et al.\(^13\) have described an abnormal left ventricular end systolic contour in these patients, suggesting the presence of a myocardial disorder. Liedtke et al.\(^14\) reported reduced contraction of the mitral valve ring and proximal portion of the left ventricle (LV) in nine patients with systolic clicks while Scampordonis et al.\(^13\) demonstrated five abnormal patterns of LV contraction in a large series of patients with proven mitral valve prolapse. These authors conclude that a primary myocardial disorder is present in this syndrome and that it results in asynergistic patterns of ventricular motion. Most of the reported hemodynamic data obtained have been essentially normal, but these studies have been made only in the resting state.
We have recently found\textsuperscript{16} that a high incidence of LV dysfunction is, in fact, present in this syndrome and that it is usually demonstrable during the stress of exercise. This report is an extension of our previous studies and describes 26 symptomatic patients with nonejection clicks, mid to late systolic murmurs, and prolapsed mitral valve leaflets, all of whom were found to have evidence of left ventricular dysfunction.

**Methods and Materials**

Twenty-six patients with nonejection clicks and/or late systolic murmurs were studied because of troublesome arrhythmias or disabling chest pain. All patients were examined by at least two of the authors and all were examined by one of us (SJC). Every patient underwent a complete clinical and electrocardiographic examination. A double Master’s Two Step Test was performed on 16 patients. Cardiac size was evaluated by postero-anterior and lateral chest roentgenograms and individual chamber enlargement was assessed by barium swallow with four cardiac views.\textsuperscript{16}

Phonocardiograms with indirect carotid tracings were recorded in each patient with either a DR-12 Electronics for Medicine physiologic recorder or a 4-channel, direct-writing, Elema-Schonander Mionograph recorder.\textsuperscript{*} Phonocardiograms were recorded in 14 patients during the Valsalva maneuver, and in 13 patients following amyl nitrite inhalation.

All patients underwent right and left heart catheterization in the postabsorptive state under mild pentobarbital sedation. The LV was entered retrogradely via the right brachial artery. In three patients the left atrium was entered by manipulating the LV catheter across the mitral valve. Intracardiac and intravascular pressures were measured with P23dB Statham strain gauges and recorded with a DR-12 Electronics for Medicine recorder. Cardiac output was determined by the Fick principle and/or dye dilution technique using indocyanine green dye and a Gilford densitometer. Supine leg bicycle exercise was performed by 18 patients for 8 to 10 min. During the final 2 min of exercise, measurements of intracardiac and intravascular pressures were repeated while oxygen consumption and cardiac output were redetermined. To assess the adequacy of left ventricular response to the stress of exercise, an exercise factor was calculated as the increase in cardiac index per 100 ml/min increase in oxygen consumption per meter squared (\(\dot{V}O_2\)).\textsuperscript{17} An increase in cardiac index equal to or greater than 600 ml/min for each 100 ml/min increase in \(\dot{V}O_2\) was considered normal.

Upon completion of resting and exercise studies, left ventriculography was performed in all patients in a single plane 30\degree right anterior oblique (RAO) projection at 60 frames per second. Five patients were also studied in the left lateral view and one in the left anterior oblique position. Forty cc of contrast material (Renografin-76) were injected into the LV at a rate of 16 cc/sec using a Viamonte-Hobbs power injector. Left ventriculography always preceded selective coronary angiography and when more than one ventriculogram was required, they were spaced at least 15 min apart. Selective coronary cineangiography was performed in 24 patients using the Sones technique.

The ejection fraction (EF) was calculated by measuring the left ventricular volume (LVV) in end systole (ESV) and end diastole (EDV) using the arealength method of Dodge\textsuperscript{18} modified for single-plane calculation.\textsuperscript{19} The 35 mm cine film was viewed on a Tage Arno projector where a normal nonpostextrasystolic beat was selected for volume determinations. The left ventricular end systolic and end diastolic outlines were traced on light paper and the areas measured by planimetry. The respective volumes were calculated from the ellipsoid formula \(V = \frac{\pi LD^2}{6}\). Linear correction factors for LVV determinations were not used since the EF can be calculated from the ratio:

\[
EF = \frac{EDV - ESV}{EDV}
\]

In this expression, the linear correction factors cancel out.

Left ventricular hypertrophy was assessed cineangiographically in the RAO view by measuring the thickness of the LV wall in end diastole at a point midway between the apex and aortic valve. The linear correction factor was derived by comparing the projected diameter of the mid-left ventricular angiographic catheter to the known, previously measured, diameter (2.5 mm) of this catheter. This same measurement of wall thickness, carried out in a control group of 25 patients with no demonstrable heart disease and normal left ventricular dynamics, was found to range from 6.7 to 10 mm. A left ventricular wall thickness of 10 mm or less was, therefore, considered to be normal (grade 0) while a thickness of >10 mm to 14 mm denoted mild hypertrophy (1+), >14 mm to 18 mm, moderate hypertrophy (2+) and >18 mm, severe hypertrophy (3+).

Mitral regurgitation was graded on a scale of increasing severity from 1+ to 4+ using the method of Sellers.\textsuperscript{20} The degree of mitral valve prolapse was arbitrarily graded from 1+ to 4+ with 1+ reflecting mild prolapse while 4+ denoted marked prolapse up to and beyond the aortic valve ring as seen in the RAO view.

In an attempt to assess LV contractility quantitatively, segmental analysis of changing LV geometry during systole was carried out in a method similar to the one described by Lie and Hackett\textsuperscript{14} but modified by using the RAO rather than the lateral view. This projection afforded a much better view of the LV in profile. The longest measured length was designated the long axis (L). The long axis was quadrisected by three diameters drawn perpendicular to it. These lines were designated as the proximal (PD), midventricular (MD) and apical (AD) diameters (fig. 1). Shortening of each diameter was expressed as a percent shortening of its end.
diastolic dimension and helped identify abnormal wall motion if it was present. Similar measurements were made in a group of ten patients with atypical chest pain who had entirely normal resting and exercise hemodynamics, normal coronary angiograms, and normal LV wall motion. Statistical analysis of comparative data was made by means of the Student's t test (table 3).

**Results**

The clinical, hemodynamic, and angiographic data are summarized in tables 1, 2 and 3. The patients, 20 of whom were female, ranged in age from 19 to 53 years with a mean of 41 years.

**Historical Aspects**

Twenty-two of the 26 patients had disabling subxiphoid or left anterior chest pain which by its character, distribution, and radiation suggested a cardiac origin. In 12 patients the pain was of sufficient severity and duration to warrant admission to a hospital for suspected acute myocardial infarction. In nine of these patients transient ST-T changes occurred with the pain suggesting myocardial ischemia or early infarction (fig. 2 and 3). Eleven of the 12 patients had anterior chest pain with exertion or emotional stress—but only 5 of the 12 patients had relief of pain with sublingual nitroglycerin. Nine other patients with angina or severe disabling chest pain not severe enough to be hospitalized were given nitroglycerin with incon-

**Figure 1**

Schematic representation of left ventricular cavity in end-diastolic, RAO projection. Abbreviations: L = long axis, PD = proximal diameter, MD = midventricular diameter, AD = apical diameter.

**Figure 2**

ECG of patient JS during crushing chest pain. Note VPCs, ST depressions and T inversions.

*Circulation, Volume XLIX, April 1974*

**Figure 3**

ECG, patient JS, 2 days after chest pain. T waves returning to normal.

**Figure 4**

Phonocardiogram (PCG) and carotid tracing, patient IW. There is an early, mid and late systolic click. C = systolic click; 1, 2 = first and second heart sounds.
Table 1

<table>
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<tr>
<th>Pt.</th>
<th>Age</th>
<th>Sex</th>
<th>Hosp.</th>
<th>Angina*</th>
<th>Response to GNT</th>
<th>Resting ECG</th>
<th>Master’s 2-step</th>
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<td>Yes</td>
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</table>

Abbreviations: ALMI = antero-lateral myocardial infarction; Amyl = amyl nitrite inhalation; APC = atrial premature contraction; ASMI = antero-septal myocardial infarction; AT = atrial tachycardia; AVB = atrioventricular block; ESC = early systolic click; ESM = early systolic murmur; IWMI = inferior wall myocardial infarction; LBBB = left bundle branch block; LSC = late systolic click; LSM = late systolic murmur; LVH = left ventricular hypertrophy; M1 = mitral closure; MSC = mid systolic click; MSM = mid systolic murmur; NL = normal; NSR = normal sinus rhythm; GNT = nitroglycerin; PSM = pansystolic murmur; RAD = right axis deviation; RBBB = right bundle branch block; SB = sinus bradycardia; SBE = subacute bacterial endocarditis; ST-T = abnormalities of these segments; VPC = ventricular premature contraction; VT = ventricular tachycardia; AI = aortic insufficiency.

spontaneous variation in the timing of the murmur (fig. 5). Four had the skeletal abnormalities seen in Marfan’s Syndrome, which included pectus deformities, vertebral column deformities, ectopia lentis, high arched palate, and hyperextensible joints.

Roentgenographic Findings

Seven patients (SA, EH, GH, AJ, HR, MSH, M.S.H.)
Mild left ventricular enlargement on postero-anterior and lateral roentgenograms of the chest and all had mild to moderate enlargement of the left atrium on barium swallow. All other patients had normal size cardiac silhouettes with no evidence of individual chamber enlargement.

Electrocardiography

Only six patients had completely normal electrocardiograms at rest. Sinus bradycardia was present in four. Atrial arrhythmias were recorded in eight patients and ranged from atrial premature contractions to atrial tachycardia to atrial fibrillation. Frequent ventricular premature contractions were
### Table 2

**Catheterization Data**

<table>
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<tr>
<th>Pl.</th>
<th>Age/Sex</th>
<th>Rest LVEDP (mm Hg)</th>
<th>PC or LAP (mm Hg)</th>
<th>VO₂ (mL/kg/min)</th>
<th>AV-O₂</th>
<th>CI</th>
<th>Exercise LVEDP (mm Hg)</th>
<th>PC or LAP (mm Hg)</th>
<th>VO₂ (mL/kg/min)</th>
<th>AV-O₂</th>
<th>CI</th>
<th>Exercise factor</th>
<th>MVP*</th>
<th>MVR†</th>
<th>EF</th>
<th>LVH</th>
<th>CA</th>
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<td>149</td>
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<td>2</td>
<td>96</td>
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Abbreviations: AV-O₂ = arterio-venous oxygen difference (Vol. %); CA = coronary angiograms; CI = cardiac index (L/min/m²); EF = ejection fraction; LAP = mean left atrial pressure (mm Hg); LVEDP = left ventricular end diastolic pressure (mm Hg); LVH = left ventricular hypertrophy; MVP = mitral valve prolapse; MVR = mitral regurgitation; PC = mean pulmonary capillary pressure (mm Hg); VO₂ = oxygen consumption index (ml/min/m²).

*Graded from + to ++++ with + reflecting mild prolapse and ++++ marked prolapse up to and beyond aortic valve ring as seen in RAO view.
†Measured according to Sellers et al.²⁵
Table 3

Analysis of Left Ventricular Dimensions and Patterns of Segmental Shortening

<table>
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<tr>
<th>Parameters</th>
<th>Control (n=10)</th>
<th>All patients with PML (n=26)</th>
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Abbreviations: PML = prolapsed mitral valve leaflet; SEM = standard error of the mean.

Phonocardiography

Early systolic clicks (within 80 msec of the first heart sound) were recorded in three patients who had multiple clicks and in two who had isolated clicks. In the remaining patients, the sound was mid to late systolic in timing. The behavior of the clicks following amyl nitrite inhalation and/or during the Valsalva maneuver was assessed in 15 patients. Following amyl nitrite inhalation the nonejection sounds became louder in eight patients, softer in one, and showed no change in four. It occurred earlier in systole (fig. 7) in six patients, later in three, and was unchanged in four.

Systolic murmurs were recorded in 21 patients. Eleven were late systolic in timing, six mid systolic, and four pansystolic. Following amyl nitrite inhalation, the intensity of the murmur increased in eight of ten patients and in four of these patients it occurred earlier. The Valsalva maneuver was performed by 14 patients. In eight, the murmur increased in intensity, in four it decreased, and in two there was no change. An earlier onset of the murmur was noted in two patients (fig. 7).

Hemodynamic Findings

Seventeen patients had completely normal resting

![Figure 5](image)

**Figure 5**

Phonocardiogram (PCG) in patient JS demonstrating marked variability of auscultatory findings from one cycle to another. The click (C) and early systolic murmur (ESM) recorded in the first cycle are not seen in the second. LSM = late systolic murmur.

*Circulation, Volume XLIX, April 1974*

![Figure 6](image)

**Figure 6**

Exercise test in LC showing normal control ECG (upper panel) and 2 minute postexercise tracing demonstrating 1 mm depression of ST segments in V4 and V5.
hemodynamic measurements. The readings at rest on the remaining nine patients demonstrated significant abnormalities which included an elevated left ventricular end diastolic pressure (SA, DB, HR, MSH) or decreased cardiac index (JC, HF, AJ, AQ, HR, SR) (table 2). The resting ejection fraction was reduced (< 0.60) in six of the 24 patients in whom it was measured. Eighteen patients underwent supine leg bicycle exercise. Cardiac indexes in all patients significantly increased, but in nine the increase was not commensurate with the level of exercise attained as judged by the presence of an abnormal exercise factor, i.e., less than 600 ml/min
\[\frac{\text{less than 600 ml/min}}{100 \text{ ml VO}_2/\text{min}}\]

In one patient (AM) an exercise cardiac index was not determined because the patient experienced severe fatigue and could not continue exercising. Nevertheless, during her 90 sec of exercise the left ventricular end diastolic pressures rose slightly to 13 mm Hg. Thus, in 20 of our 26 patients, left ventricular dysfunction was demonstrable at rest or during exercise. In the remaining six, left ventricular dysfunction was detected angiographically. Thus none of our patients had completely normal studies.

**Angiography**

Left ventriculography, performed in a 30° RAO projection, revealed prolapse of the posterior mitral valve leaflet in 25 patients (figs. 8, 9). In patient (AM), the anterior valve leaflet prolapsed and was best seen in the left anterior oblique (LAO) view. The prolapse was mild in seven, moderate in 14, and severe in five. Mitral regurgitation was absent in six patients, mild in 11, moderate in eight, and severe in one. Mild to severe left ventricular hypertrophy was present in 14 patients. None of our patients had features of idiopathic hypertrophic subaortic stenosis. Patient JC had anomalous pulmonary venous drainage of the right lower lobe.

**Figure 7**

Phonocardiogram (PCG) in patient AJ. The mid systolic click (CM) occurs earlier with amyl nitrite and during the Valsalva maneuver. With Valsalva, murmur becomes pansystolic (PSM) and increases in intensity. 1, 2 = first and second heart sounds; C = click.

**Figure 8**

Left ventriculography, patient AJ. Left panel: early systolic right anterior oblique (RAO) view. The dotted lines outline the prolapsed posterior mitral valve leaflet and the characteristic convex bulge in the antero-lateral left ventricular wall. Middle panel: Mid systolic. Right panel: Left lateral view, end systolic. Note marked prolapse of mitral valve with moderate regurgitation.

**Figure 9**

but no atrial septal defect. Selective coronary angiography revealed that all patients had entirely normal coronary vessels with a normal distribution (fig. 10).

Analysis of Left Ventricular Contraction

The contractility of the left ventricle was assessed angiographically by first determining qualitatively the strength and uniformity of contraction along several points of the inner surface of the ventricular chamber. The percent shortening of the long axis and the three diameters quadrisectioning the LV cavity were then analyzed and compared with normals (table 3). The extent of shortening of the long axis was 33.4% in normal patients while the proximal, midventricular and apical diameters shortened 54.1, 68.2 and 66.9%, respectively. In our patients with prolapsing mitral leaflets the extent of shortening was significantly impaired in all dimensions averaging 13.2% for the long axis (P < 0.001) and 41.4 (P < 0.005), 41.6 (P < 0.001) and 49.2% (P < 0.005) for the proximal, midventricular and apical diameters, respectively. The data suggest that there is generalized hypokinesis or impaired contractility of the left ventricle but that it is most marked in the midventricular segment.

In only six patients (SA, JC, LI, AM, SM, MS) was contractility, or the pattern of contraction, judged to be entirely normal. Thirteen patients (SC, HF, EG, EH, AJ, FL, JM, AQ, SR, JS, MSH, IW, MW) had marked hypokinesis of the midportion of the antero-lateral wall of the left ventricle resulting in the appearance of an unusual prominent bulge in this portion of the ventricle in end systole (figs. 8, 9). Seven other patients (DB, GH, LG, AK, IK, KL, HR) demonstrated a similar, but less prominent, abnormal end systolic configuration.

Interestingly, relaxation of the bulging portion of the LV occurred earlier than in the rest of the chamber so that the convexity was accentuated in early diastole. The significance of asynergic relaxation is not known. Patients IW and KL, in addition to prolapsed mitral valve leaflets, had marked bulging of the postero-inferior left ventricular wall into the cavity during systole of the type previously described by Ehlers et al.11 and Gooc'h et al. and Scampordonis et al.12, 13 In none of our cases was there evidence of dyskinesis or asynergy.

Clinical Course

Follow-up periods ranged from 12 to 38 months with a mean of 28 months. Patient DB, who had Marfan's disease, died in acute pulmonary edema not related to her prolapsed mitral valve but to newly acquired acute severe aortic insufficiency probably related to her connective tissue disorder. She had only a minimal amount of aortic regurgitation when she was studied.

Patient JS died suddenly at home while engaged in a telephone conversation.

Patient SR had several episodes of syncope presumed, but not proven, to be due to complete heart block. Bundle of His studies were entirely normal but within three weeks, she developed right bundle branch block, then second degree block, and finally, complete heart block with Stokes Adams attacks necessitating implantation of a permanent transvenous pacemaker. The etiology of her complete heart block is unknown. Patient FL had bundle of His studies performed which showed prolonged A–H intervals and periods of intermittent second degree block with the block occurring proximal to the His bundle. Because of recurrent syncope, this patient, too, had a permanent transvenous pacemaker implanted.

One patient (SA) developed enterococcal subacute bacterial endocarditis which responded well to parenteral penicillin and streptomycin therapy. Twelve patients (SA, SC, HF, LG, LI, AJ, FL, AM, JM, AQ, MS, IW) are still severely incapacitated by their anginal syndromes or recurrent arrhythmias despite the use of coronary dilators, propranolol, and other antiarrhythmic agents. Medical treatment for this pain syndrome has been rather ineffective and the control of arrhythmias has also been less than optimal. Although the majority complain of dyspnea on exertion and excessive fatigue, none has been in overt congestive heart failure.

Discussion

The syndrome of mid systolic or nonejection
click, mid to late systolic murmur, and prolapsed mitral valve leaflet is now well recognized.1-12 The past nine decades has seen a slow accumulation of isolated data relative to this entity. Only recently has it been possible to bring together a composite description of this syndrome which includes clinical, radiologic, auscultatory, phonocardiographic, electrocardiographic, anatomic, hemodynamic, angiographic, familial, and genetic aspects of the disease.

Mid systolic sounds were first described by Coffer and Barbillon in 1887.21 Systolic "gallop rhythms" were later described by Thompson and Levine,22 Johnston,23 and Luisada and Alimurung.24 They believed systolic clicks were benign, were not associated with rheumatic heart disease, and that their main importance was that they could be mistaken for diastolic gallop sounds. It is interesting that a significant number of patients studied by these authors had abnormal electrocardiograms and complained of anterior chest pain and frequent palpitations.

Originally, the systolic sounds were thought to be extracardiac in origin and were related to pleuropericardial adhesions. This concept was based largely on the work of Gallavardin,25,26 who described pleuropericardial adhesions in four autopsied cases in whom systolic clicks had been heard, and on the observations of Johnson,23 who found that mid systolic clicks and murmurs changed markedly with changes in position and respiration.

Barlow et al.,27 and later, Segal and Likoff,28 utilizing left ventricular cineangangiography, clearly demonstrated that patients with mid to late systolic clicks and late systolic murmurs did in fact have mild mitral incompetence and that the regurgitation occurred during the latter part of systole.

Using transeptal intracardiac phonodiagnostic, Ronan et al.,29 Leighton et al.,5 and Leon et al.30 convincingly disproved the long held notion that all murmurs due to mitral incompetence were pansystolic and that murmurs confined to late systole were likely to be entirely innocent.30 These investigators found that late systolic murmurs arose from the mitral valve complex and radiated into the left atrium, corroborating their regurgitant nature. Their intracardiac sound recordings clearly pointed to the mitral valve or its supporting structures as the source for mid systolic clicks.

The patients described in the earlier reports all had mild mitral incompetence so that it was generally assumed that all patients with these auscultatory findings had insignificant mitral regurgitation. Criley et al.1 and Linhart and Taylor2 dispelled this notion when they reported similar cases with moderate to severe mitral regurgitation and left ventricular hypertrophy. These authors also called attention to the fact that these patients had an unusual anatomic deformity of the mitral valve which was characterized by billowing or prolapsing of the posterior mitral valve leaflet into the left atrium during ventricular systole. A number of other studies have confirmed the association of the nonejection clicks, late systolic murmurs, and the mitral regurgitation with prolapse of the posterior leaflet of the mitral valve.3,4,7,10

Upon reviewing the numerous underlying conditions producing the mitral valve deformity, it becomes readily apparent that this entity cannot be encompassed in a single homogeneous group. The various associated conditions include Marfan's syndrome,1,10,31,32,38 myxomatous degeneration of the cardiac valves (floppy valve syndrome),34,35 trauma,1,32 rheumatic valvulitis,29,29,29 and arteriosclerotic heart disease.36 In the great majority of cases no specific etiology could be found, but several studies suggested that a familial or a genetic factor plays a role.2,6,7,37,38 That some of the mitral lesions encountered might be congenital may be inferred from the detection of a murmur during early childhood11 and by their frequent occurrence with other congenital heart defects, notably, atrial septal defect.5,9,38

Prominent and troublesome features of this syndrome have been atrial and ventricular arrhythmias, symptoms of angina pectoris or atypical chest pain ranging from mild to severe, and abnormal electrocardiograms which frequently connote ischemia and/or infarction of the inferior wall. There is, as yet, no adequate explanation for these abnormalities but they are reminiscent of those seen in patients with cardiomyopathy.

Several investigators1,2,3,4,29 have reported on the resting hemodynamics in this syndrome, and having noted little or no hemodynamic derangement at rest, they concluded that left ventricular function was normal. No one has systematically studied left ventricular function during stress and only Gooch et al.12 performed a significant number of selective coronary studies in these patients all of whom were found to have normal coronary arteries.

Asymmetric disordered patterns of ventricular contraction have been observed by several investigators11,12,13,14 in the systolic click-prolapsed mitral valve leaflet syndrome. Ehlers et al.11 was among the first to recognize and point out an
unusual left ventricular contour in six young females with the syndrome. They noted a marked postero-inferior bulging which encroached on the left ventricular cavity during systole. Gooch et al. and Scamparodinis et al.12, 13 described similar findings in a number of their patients. In addition, they noted that 27 of their 87 patients had asynergistic contractions or relaxations of the left ventricle producing a convex bulge of its anterolateral wall in end systole or early diastole. Liedtke et al.14 analyzed segmental contraction of the left ventricle in nine patients with the systolic click syndrome (only two of whom had demonstrable prolapse of the mitral leaflets) and found that there was a significant reduction in the extent and velocity of shortening in the region of the mitral valve ring and in the inflow tract area of the left ventricle. In this group of patients, and in a small group with papillary muscle dysfunction secondary to arteriosclerotic heart disease and previous myocardial infarctions, the inferior papillary muscle head failed to contract appropriately and its spatial orientation was not in the mid ventricle but toward the mitral valve ring during systole. Ostensibly, this results in loss of support of the posterior mitral valve leaflet and produces mitral valve incompetence. Whether this is sufficient to go on to produce mitral valve prolapse is not known.

Most of the emphasis has been on the abnormal ballooning of the mitral valve and the abnormal patterns of LV contraction while little attention has been paid to the performance characteristics of the left ventricle during the stress of exercise.

In our series, resting or exercise hemodynamics were abnormal in 20 of our patients and in the remaining six, left ventricular dysfunction was recognized by angiographic techniques. In addition, by utilizing segmental analysis to assess LV contractility in this group of patients, we were able to demonstrate generalized impairment of contractility along the four axes that were measured. Decreased shortening was most prominent in the mid ventricular segment and is probably responsible for the convex systolic bulging seen in so many of these patients. In this respect, our findings differed from those of Liedtke et al.14 who found that the extent of segmental shortening was decreased in the region of the mitral valve ring and LV inflow. This disparity probably results from our use of RAO rather than the lateral projection of the left ventriculogram. Twenty-four patients had entirely normal coronary arteriographic studies. Thus, every one of our patients had evidence of myocardial disease which was completely unrelated to major coronary arterial disease.

These data, and those of others,11, 12, 13, 14 coupled with the fact that 85% of our patients had disabling chest pain and the majority had significant ST depression, striking T wave inversion, or serious ventricular arrhythmias at some point in their clinical course, support the contention that the syndrome of prolapsed mitral leaflet has a significant component of left ventricular disease, the exact nature of which is not yet fully understood. Although the etiology of the myocardial disease is not known, it is difficult to believe that the mitral valve prolapse, per se, could be responsible for the impaired ventricular contractility. Similarly, the abnormal left ventricular performance cannot be ascribed to the presence of mitral incompetence since the majority of the patients had minimal or mild mitral regurgitation. On the other hand, it is quite possible that the left ventricular dysfunction is responsible, in some unknown fashion, for both the mitral valve prolapse and the mid systolic timing of the mitral regurgitation.

Our cases do not constitute a representative sample of patients with the prolapsed mitral leaflet syndrome since the sample excludes patients with mild asymptomatic forms of the disease. (We do not believe extensive investigation with invasive technique is justifiable in this latter group of patients.) The patients in this series—most of whom had disabling chest pain or arrhythmias and many of whom had left ventricular hypertrophy—probably represent an advanced form of the disease.

As the observations in this syndrome continue to accumulate, these will contribute to our understanding of this disease and perhaps to our finding rational therapies for some of the disabling features of this syndrome.

Acknowledgment

The authors wish to thank Randolph Kramer, Maureen Horan RN, and Pat Bruce for their valuable technical and professional assistance.

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Circulation, Volume XLIX, April 1974
The Syndrome of Systolic Click, Murmur, and Mitral Valve Prolapse-A Cardiomyopathy?
STEPHEN J. GULOTTA, LOUIS GULCO, VELLORE PADMANABHAN and STUART MILLER

_Circulation_. 1974;49:717-728
doi: 10.1161/01.CIR.49.4.717

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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