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Clinical features and investigative findings in presence of mitral leaflet prolapse
Study of 85 consecutive patients

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In a 14-month period mitral leaflet prolapse was diagnosed in 85 patients by echocardiography or cine-angiography.

Chest pain alone was the presenting complaint in 30 patients and linked with palpitation, dyspnoea, or syncope in 9. Eleven presented with major neurological disturbances (9 had transient ischaemic attacks), 10 with palpitation, 4 with undue and persistent fatigue, 2 with dyspnoea, and 2 with dizziness. Seventeen were referred not because of symptoms but because of clicks and murmurs.

Overall, chest pain affected 61 patients and unless associated with coronary artery disease was not anginal. Palpitation was admitted by 42 patients; dizziness, lightheadedness, or paraesthesiae by 15, and syncope by 12.

Systolic auscultatory abnormalities were noted in 69: 25 had single clicks, 3 had multiple clicks, 19 had both click(s) and murmur, and 22 had a murmur alone.

Electrocardiography revealed ST segments flat for $>0{\cdot}10$ s in 21, prolonged QT_c in 18, and T wave flattening or inversion in inferior limb and lateral chest leads in 14. The exercise stress test was abnormal in 13 of 27 patients. Mitral valve echograms showed definite mitral leaflet prolapse in 61, 'possible' prolapse in 14, and were normal in 8 patients with angiographic proof of mitral leaflet prolapse. Cardiac catheterization with left ventriculography showed prolapse of posterior mitral leaflet in 36, of both leaflets in 2, and left ventricular wall motion abnormalities in 16 cases. Selective coronary arteriography in 31 cases showed major vessel narrowing of $\geq$ 80 per cent lumen diameter in 4, all with angina.

This consecutive series indicates that the physical event of mitral leaflet prolapse is more common than hitherto appreciated, is prominently associated with non-anginal chest pain, palpitation, and neurological disturbances, and in 90 per cent of cases could be shown echocardiographically.

A rapidly increasing number of reports on the syndrome associated with prolapse of the leaflets of the mitral valve, often suspected because of the presence of systolic clicks and/or murmurs, attests to the fascination and clinical importance of this entity (Reid, 1961; Barlow *et al.*, 1963; Criley *et al.*, 1966; Epstein and Coulshed, 1973; Jeresaty 1973a; Cobbs, 1974).

Features of this syndrome include chest pain which is often unlike 'classical' angina pectoris (Hancock and Cohn, 1966; Jeresaty, 1973a; LeWinter *et al.*, 1974), dyspnoea and fatigue (Hancock and Cohn, 1966; Barlow *et al.*, 1968; Jeresaty, 1973a), and palpitation (Hancock and Cohn, 1966; Jeresaty, 1973a). These symptoms have proved common in our own experience of patients with mitral leaflet prolapse, but we have also encountered a number of cases with neurological problems.

It is the purpose of this report to document symptoms, signs, and investigative findings in patients with mitral leaflet prolapse diagnosed in our unit and thus to help to define the clinical spectrum of this apparently common disorder.

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Subjects and methods

Our data were derived from review of the records of all patients evaluated during a 14-month period in the Cardiac Investigation Unit at University Hospital, London, Ontario, in whom the physical event of mitral leaflet prolapse was demonstrated by echocardiography or contrast cineangiography.

Data on symptoms and physical signs were transcribed from the patients' medical records. Particular care was taken to identify each patient's *presenting* symptoms and to differentiate between these and the symptoms of chest pain, palpitation, dyspnoea, fatigue, lightheadedness, dizziness, or syncope, which we specifically sought in the medical history. Where chest pain was reported, its features were recorded in detail; we accepted it as 'classical' angina pectoris only when it satisfied the criteria of 1) involving at least part of the praecordium, 2) onset related to exercise and subsequent relief with rest, and 3) visceral quality.

Standard non-fasting 12-lead electrocardiograms were recorded at rest. Twenty-seven patients underwent exercise stress testing on a motor driven treadmill according to a standardized procedure (Sheffield, 1972) of graded exercise increments, increasing their heart rate towards an age-related submaximal target rate. Resting and postexercise 12-lead electrocardiograms were recorded in 4 subsets of 3 simultaneous leads by Marquette Series 3000 equipment. Fifteen patients also had 24-hour continuous tape recording of their electrocardiogram by Holter monitor (Bleifer *et al.*, 1974) and 2 were monitored for at least 24 hours in the Coronary Care Unit.

Phonocardiograms were obtained using a piezoelectric crystal contact microphone (Litton-Hellige lightweight heart sound microphone number 217 131 01) and apex cardiograms and carotid pulse tracings with a specially constructed pneumatic system connected to a piezoelectric crystal microphone (Litton-Hellige microphone number 217 133 01). Recordings were made on a Litton Multiscriptor EK 22 5-channel chart recorder with carbon-transfer write-out.

Echocardiography was performed with the patient in the supine or slight left lateral position using a standard Unirad Series C Diagnostic Echoscope System with a 2·5 or 3·5 MHz transducer positioned in the third or fourth left intercostal space. Echocardiograms were recorded by direct photography of the multichannel oscilloscope presentation using Polaroid type 107 film and on Kodak 1895 light-sensitive paper with a 'continuous copy' Honeywell model 1856 Visicorder.

Cardiac catheterization was undertaken in 38 patients. After the measurement of the resting left ventricular end-diastolic pressure, left ventriculograms were obtained sequentially in the 30° right anterior and 45° left anterior oblique projections to assess mitral valve integrity. Additionally the tricuspid valve was assessed by right ventriculography in 8 patients, and in 31 patients selective coronary arteriography was performed.

Results

Patient population (Fig. 1)

Eighty-five patients were seen with a male:female ratio of 36:49 (1:1·4) and a peak incidence among women in the age-group 30 to 39 years. The patients' ages ranged from 15 to 76 years. Only 5 patients gave a history of childhood rheumatic fever. There were no cases of atrial septal defect (McDonald *et al.*, 1971; Betriu *et al.*, 1975).

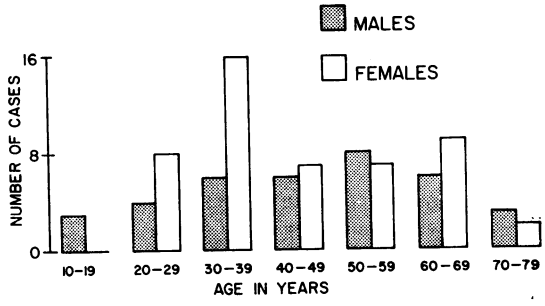

FIG. 1 *Age distribution by decades and sex distribution among 85 patients with mitral leaflet prolapse.*

Mode of presentation (Table 1)

TABLE 1 *Mode of presentation of 85 patients*

Primary presenting complaint	*No. of patients*
(A) *Symptomatic—primary presenting complaint*	
Chest pain alone	30 (35%)
Chest pain with palpitation, or dyspnoea, or syncope	9 (11%)
Palpitation ± syncope	10 (12%)
Dyspnoea	2
Undue and persistent fatigue	4
Major neurological disturbance	11 (13%)
Dizziness	2
(B) *Asymptomatic*	
Referred because click and/or murmur heard	17 (20%)
Total	85 (100%)

Group A were symptomatic with clearly identifiable presenting medical complaints and group B were asymptomatic, a systolic click and/or murmur having been discovered incidentally.

While chest pain alone (35%) or in combination with certain other symptoms (11%) was the most common problem, it is noteworthy that 13 per cent entered hospital because of a *major* neurological disturbance—by which we mean the recent unequivocal occurrence of neurological symptoms, in association with which there was at some stage documented neurological abnormality on physical examination. Among the 11 patients so presenting,

the diagnosis of transient ischaemic attacks was made in 9 and 1 patient had suffered a stroke with hemiparesis; one woman with a past history of rheumatic fever had developed hemichorea, possibly related to oral contraceptives which she had taken for one year (Riddoch, Jefferson, and Bickerstaff, 1971).

Among the 17 patients presenting not because of any symptoms but rather because an auscultatory abnormality had been detected, we found that 11 were truly without significant symptomatology and the remainder admitted noticing occasional chest pain, palpitation, dyspnoea, or dizziness.

Overall incidence of certain symptoms (Table 2)

TABLE 2 *Overall incidence of certain symptoms, which includes both presenting symptoms and symptoms elicited on questioning, among all 85 patients*

Symptoms		*No. of patients*
Chest pain:		61 (72%)
as primary complaint	30 (35%)	
elicited on questioning	31 (36%)	
'classical' angina pectoris	5 (6%)	
nocturnal occurrence	13 (15%)	
Palpitation		42 (49%)
Syncope (one or more episodes)		12 (14%)
Major neurological disturbance:		13 (15%)
as primary complaint	11 (13%)	
Minor neurological disturbance (dizziness, lightheadedness, paraesthesiae)		15 (18%)

This analysis considers presenting symptoms as well as symptoms elicited on questioning. It was evident in assembling this information from all the subgroups identified in 'Mode of Presentation' that many patients did acknowledge additional symptoms in the form of chest pain, palpitation, dyspnoea, fatigue, lightheadedness, dizziness, or syncope.

Although 61 patients in all had suffered chest pain, it was a presenting symptom in only 30 and so 31 patients had to a greater or lesser extent borne it uncomplainingly. In only 5 was it acceptable classical angina. A variety of pains was described in the remainder of this group; 10 patients described their pain as 'sharp' or 'jabbing'; the pain lasted only seconds in a few but more typically lasted minutes, hours, or sometimes even weeks. Thirteen patients reported nocturnal occurrence of pain and this included 3 of the patients with classical angina of effort. One patient had, in her early 30s, experienced two episodes of pain absolutely typical of acute myocardial infarction, each time with transient T wave inversion in leads II, III, aVF, and V5 and V6, and ultimately had normal coronary arteries visualized at selective arteriography. Two men, one in his late 30's and the other in his mid 50's, suffered several episodes of severe chest pain, the features of which suggested myocardial infarction, but subsequently were found to have arteriographically normal coronary arteries.

Palpitation had been experienced by a total of 42 patients, in 7 with definite relation to chest pain, in 6 related to presyncope or syncope, in 1 with chest pain followed by syncope, and in 1 as part of the Wolff-Parkinson-White syndrome.

As well as the 11 presenting with recent major neurological disturbance, there were 2 patients who had developed hemiparesis several years earlier. Twelve had suffered one or more episodes of true syncope. Minor neurological disturbances, taking the form of dizziness, lightheadedness, or peripheral paraesthesiae, affected 15 patients.

Physical examination (Table 3)

TABLE 3 *Features noted on physical examination of 85 patients*

Feature		*No. of patients*
Marfanoid habitus		1
Auscultatory abnormalities:		68 (80%)
Single systolic click	25 (27%)	
Multiple systolic clicks	3	
Systolic click and murmur	19 (22%)	
Systolic murmur, without click	22 (26%)	
No auscultatory abnormality		17 (20%)

In general appearance only 1 patient had a Marfanoid habitus and there were no cases of the true Marfan syndrome. On auscultation a single systolic click was heard in 25 patients, multiple systolic clicks in 3, a systolic click and murmur in 19, while 22 had a systolic murmur alone. Seventeen patients had 'silent' mitral leaflet prolapse, inasmuch as there were no auscultatory abnormalities at any time. The 'silent' group underwent cardiac investigation because of some of the symptoms alluded to earlier.

Standard electrocardiography (Table 4)

In only 3 cases was the permanent stable rhythm other than sinus. One 76-year-old man, the oldest person in the study, had atrial fibrillation with a typical mitral insufficiency pansystolic murmur and echocardiographic and radiological evidence of left atrial and ventricular dilatation; though his echocardiogram showed a thin pliable anterior mitral leaflet, mitral calcification was visible fluoroscopically. A 66-year-old woman had atrial flutter, with

TABLE 4 *Commonest abnormalities in 12-lead electrocardiograms in 85 patients*

Abnormality	*No. of patients*
Small septal Q waves (depth < 0·5 mm in at least V5 or V6)	24 (28%)
QTc interval prolonged (Bazett's formula QTc = measured QT/$\sqrt{}$R–R)	18 (21%)
ST segments flat for > 0·10 s:	
a) lateral chest leads only	15 (18%)
b) lateral chest and some limb leads	6 (7%)
T waves flat or inverted in inferior limbs and some chest leads	14 (16%)
Amplitude RV5 or V6 or SV1 or V2 > 25 mm (only 3 with ST—T changes of left ventricular hypertrophy)	11 (13%)

3:1 block and right bundle-branch block: cardiac catheterization revealed a thick-walled left ventricle with normal sized cavity and mitral leaflet prolapse without mitral regurgitation, aortography showed normal patency of the proximal parts of the coronary arteries, and echocardiography showed a pliable prolapsing mitral valve and normal sized left atrium. The third of these cases was a 57-year-old man with the pattern of anteroseptal myocardial infarction of indeterminate age and a low atrial or junctional rhythm with inverted P waves in II, III, and aVF. Four patients manifested ventricular ectopic beats, and in 3 of these the premature beats, when present, produced a bigeminal rhythm.

Two patients had the 'P mitrale' and a prominent P terminal vector in V1, indicative of left atrial enlargement, without any demonstrable mitral regurgitation on left ventriculography. Left anterior hemiblock was noted in 2 subjects. Minor intraventricular conduction defect, manifested by terminal QRS slurring with normal QRS duration, was present in 3 cases. Right bundle-branch block in 2 more cases was the only other intraventricular conduction abnormality. Left ventricular hypertrophy by voltage criteria alone (Lipman, Massie, and Kleiger, 1972) was seen in 8 patients and in 3 further there were additional ST segment and/or T wave changes. Poor R wave progression in V1 to V3 was present in 4 patients without any evidence of hypertrophy or conduction disturbance. Two patients showed the healed anteroseptal myocardial infarction pattern. Prominent Q waves, of depth ≥2 mm, were present in V6 in 2 patients while small (< 0·5 mm deep in I, V5 or V6) or absent septal Q waves featured in 24 and 14 cases, respectively. ST segments, flat for 0·10 s or longer, were noted in 15 patients in lateral chest leads, with an additional similar finding in some of the limb leads in 6; 1 patient had hortizontal ST segments in II, III, and aVF only. Depressed ST segments were

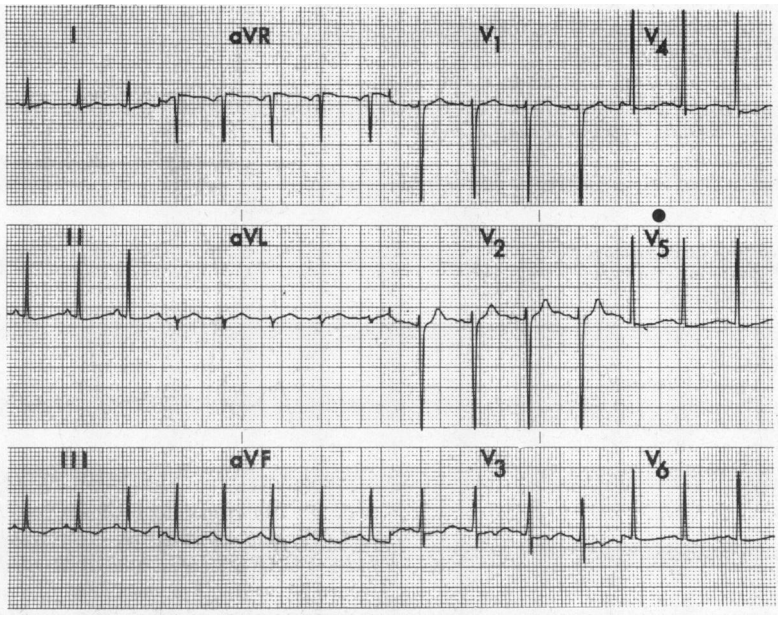

FIG. 2 *Resting electrocardiogram, of standard 1 cm/mV calibration throughout, from a 20-year-old man with mitral leaflet prolapse. The tracing is unequivocally abnormal, with T wave flattening in leads II and V6 plus T wave inversion in leads V3 to V5. The voltage changes of left ventricular hypertrophy are also present ($SV_2 = 27$ mm).*

were present in lateral chest leads in 4 cases, 1 with left ventricular hypertrophy. Excluding the 2 cases of old infarction pattern, flat or inverted T waves were noted in chest leads (usually V4 to V6) and inferior limb leads in 14 patients (Fig. 2); similar T wave abnormality was confined to chest leads in 1 patient, and to II, III, and aVF in 2 patients. Peaked T waves, probably a normal variant, were present in mid and lateral chest leads in 4 cases. Rate-corrected QT interval (QT_c) was prolonged (men >0·42 s; women >0·43 s) in 18 patients. Four patients showed U waves of 40 to 60 per cent of the T wave amplitude.

Electrocardiographic monitoring

Fifteen ambulatory patients were monitored for periods of at least 24 hours with the Holter tape system; 5 manifested arrhythmias and 1 showed periodic ST segment depression. The arrhythmias were 1) many junctional premature beats, 2) periods of sinus tachycardia with frequent junctional premature beats, 3) paroxysms of atrial fibrillation, 4) occasional solitary multifocal ectopic beats plus a few seconds of ventricular tachycardia, and 5) runs of supraventricular tachycardia at rates up to 140 per minute in a 19-year-old man with the Wolff-Parkinson-White abnormality.

Two patients were monitored in bed in our coronary unit for over 24 hours and no abnormality was detected in one while the other manifested frequent ventricular premature beats.

We recorded major rhythm disturbance in 2 other cases. A 23-year-old man had episodes of ventricular tachycardia and of supraventricular tachycardia, unresponsive to pharmacological antiarrhythmic therapy and requiring electrical cardioversion on several occasions, and at other times also manifested continuous ventricular bigeminy. The tracing from this patient between arrhythmic episodes looked normal and is reported as such in Table 4; one 24-hour Holter tape recorded showed no abnormality. A 25-year-old woman developed palpitation while in hospital, and a 12-lead electrocardiogram showed a regular apparently supraventricular rhythm at a rate of 210 per minute.

TABLE 5 *Results of treadmill submaximal exercise stress testing in 27 patients*

Feature		*No. of patients*
Achieved >90 per cent predicted maximum heart rate without significant symptoms		15 (56%)
Exercise terminated prematurely:		12 (44%)
a) chest pain	6	
b) striking fatigue	3	
c) ventricular arrhythmia	2	
d) considerable ST segment depression in V4 to V6	1	
Postexercise ST segment abnormality:		13 (48%)
a) depressed >1 mm for >0·08 s, horizontal or downsloping, during first 6 min	2*	
b) flat for >0·08 s, up to 8 min or beyond	6	
c) flat for >0·08 s, immediately or at 2 min only	2	
d) flat for >0·08 s, only after at least 6 min	2	
e) cupping, or spoon-shaped sagging, up to 10 min	1	

*Both had coronary artery disease with ≥ 80 per cent luminal width narrowing of a major vessel.

Treadmill exercise stress electrocardiography (Table 5)

Twenty-seven subjects underwent our submaximal exercise stress test. Only 15 could complete the test achieving greater than 90 per cent of their predicted maximum heart rate without developing any chest pain or inappropriate dyspnoea. Exercise was terminated in 6 because of onset of chest pain similar to their spontaneous symptoms, 3 were very fatigued, 1 exhibited striking ST segment depression in the V4 to V6 leads during exercise, 1 developed frequent ventricular bigeminy, and 1 developed ventricular tachycardia. ST segment changes were assessed according to the Finnish criteria (Cumming *et al.*, 1973).

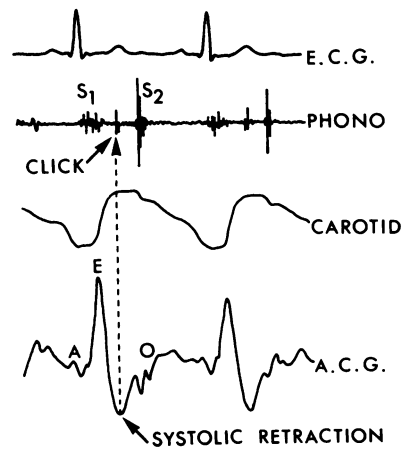

FIG. 3 *Simultaneous recording of electrocardiogram (ECG), phonocardiogram (PHONO), carotid artery pulse (CAROTID), and apex cardiogram (ACG) from a 34-year-old woman. The first heart sound (S_1), second heart sound (S_2), and A, E, and O points of the apex cardiogram are labelled. Systolic retraction of the apex cardiogram is seen to occur precisely coincident with a click just after the midpoint of systole.*

Abnormal postexercise electrocardiograms were noted in 13 patients, including all those with chest pain and with depressed ST segments and bigeminy during exercise. Ten patients developed ST segments horizontal for >0·08 s and 1 developed sagging of the ST segments in leads II and V4 to V6. Only 2 had the classical ischaemic transient flat or downsloping ST segment depression of >1 mm for >0·08 s after exercise (Sheffield and Roitman, 1975) and both had severe coronary artery disease. The changes always occurred in inferior limb and/or mid and lateral chest leads.

Phonocardiograms and apex cardiograms (Table 6)

TABLE 6 *Phonocardiogram results in 44 patients, and apex cardiogram results in 19 patients*

Feature	*No. of patients*
Timing of clicks on phonocardiograms:	
early systole	6
mid systole	16
late systole	6
diastole	none
Systolic retraction on apex cardiograms:	
present	14
absent	5

Forty-four patients had phonocardiograms and as well as confirming the presence of single, or occasionally multiple, systolic clicks this investigation also showed that when a systolic murmur was present its timing could be early systolic or pansystolic but most commonly was mid or late systolic. The timing of the clicks was most often mid systolic, as in 16 patients, but in 6 patients was early systolic and in a further 6 was late systolic. Four patients had multiple clicks.

Systolic retraction was seen in 14 of a total of 19 apex cardiograms. When a click was recorded on a simultaneous phonocardiogram it could be seen to be coincident with the nadir of apex retraction (Fig. 3), as shown by Epstein and Coulshed (1973) and Spencer, Behar, and Orgain (1973).

Echocardiography (Table 7)

Of the 85 patients, 83 were studied echocardiographically and 61 showed abnormalities of the mitral valve closure line considered diagnostic for mitral leaflet prolapse (Shah and Gramiak 1970; Dillon *et al.*, 1971; DeMaria *et al.*, 1974; Popp *et al.*, 1974; Boughner, 1975). Thirty-five showed a deep posterior curvature of the closure line beginning in midsystole (Fig. 4B) and 26 showed a multiecho systolic closure line, concave through-

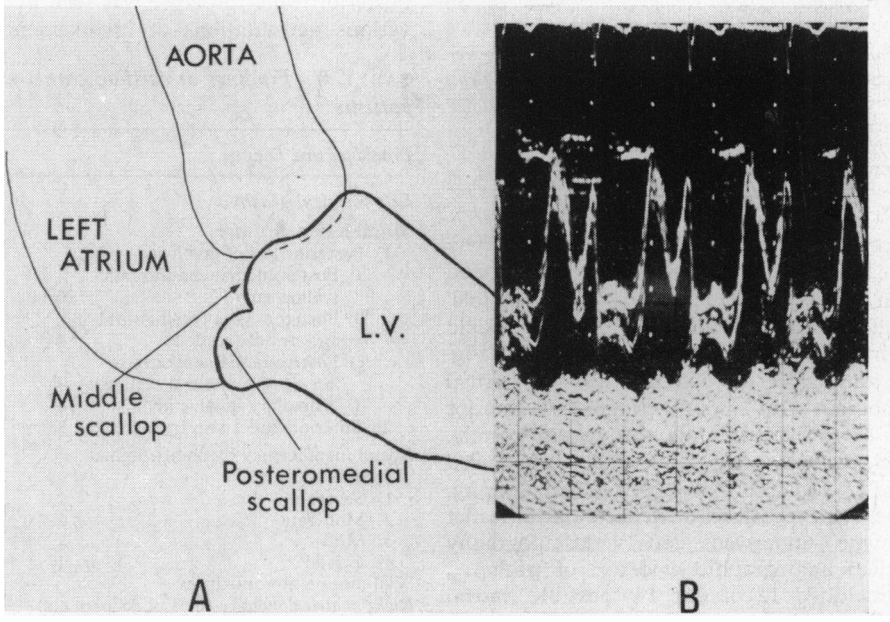

FIG. 4 *Appearances of mitral leaflet prolapse. A) Silhouette of systolic left ventricular (L.V.) angiogram, traced from projection of the 30° right anterior oblique film, with posteromedial commissural and middle scallops of posterior mitral leaflet bulging into left atrium. B) Mitral valve echogram showing deep posterior (i.e. downwards in picture) curvature of multiecho closure line during systole.*

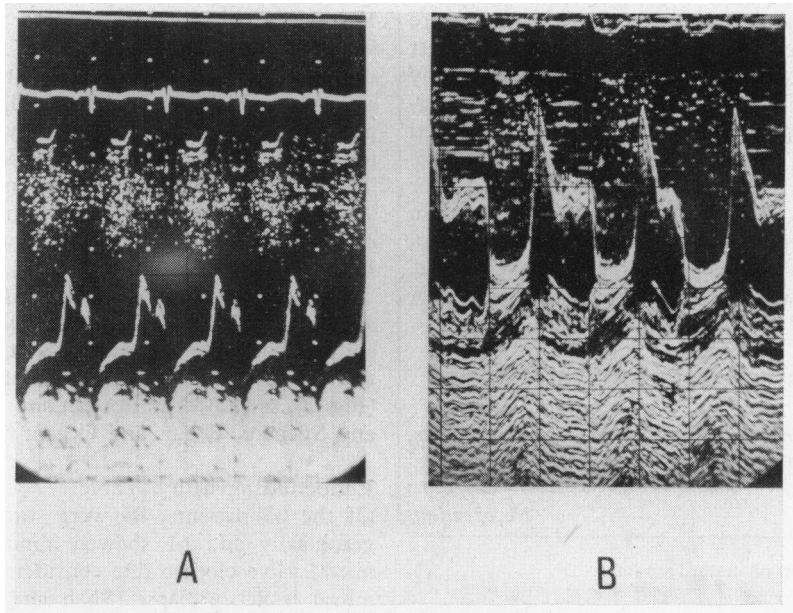

FIG. 5 *Other appearances of mitral echogram in mitral leaflet prolapse (MLP). A) Late systolic minor downturning of closure line in patient with MLP shown on angiography; this pattern we classify as 'possible MLP'. B) Multiecho closure line, concave or sagging throughout systole, indicative of definite MLP.*

TABLE 7 *Mitral valve echogram results in 83 patients*

Interpretation of echogram	*No. of patients*
Definite mitral leaflet prolapse	61 (73%)
'Possible' mitral leaflet prolapse	14 (17%)
Normal mitral systolic closure line	8 (10%)
Total	83 (100%)

out systole (Fig. 5B). Of the remainder, 14 showed a pattern that we classified as 'possible' mitral leaflet prolapse with a minor late systolic downturning of the systolic closure line (Fig. 5A) and the other 8 patients had a normal mitral echogram with smooth, progressive anterior migration of the closure line throughout systole. The 8 patients with normal echograms all showed mitral leaflet prolapse on left ventriculography. All patients with 'possible' or definite mitral leaflet prolapse who underwent left ventriculography showed clear angiographic evidence of prolapse, and this included 12 of our 14 'possible' mitral leaflet prolapse cases.

Cardiac catheterization (Table 8)

The left ventriculograms were assessed for evidence of mitral leaflet prolapse (Criley *et al.*, 1966; Ranganathan *et al.*, 1973; Boughner, 1975). Posterior leaflet prolapse was seen in all cases with various permutations of involvement of postero-

TABLE 8 *Findings at cardiac catheterization in 38 patients*

Procedure and finding		*No. of patients*
Left ventriculography		
Mitral leaflet prolapse		38 (100%)
1) Posterior leaflet involved		
a) Posteromedial commissural scallop only	20	
b) Posteromedial commissural and middle scallops	4	
c) Posteromedial and antero-lateral commissural scallops	4	
d) Triscallop involvement	10	
2) Anterior leaflet also involved	2	
Mitral insufficiency by angiographic appearance		7 (18%)
1) Severe	2	
2) Moderate	2	
3) Mild	2	
4) Trivial	1	
Wall motion abnormalities		16 (42%)
Right ventriculography (in 8 of 38 patients)		
Tricuspid leaflet prolapse		3 of 8 (38%)
Selective coronary arteriography (in 31 of the 38 patients)		
Normal		26 (83%)
Occlusive lesions		5 (16%)
1) >75% narrowing of major vessel	4	
2) 40% narrowing of major vessel	1	

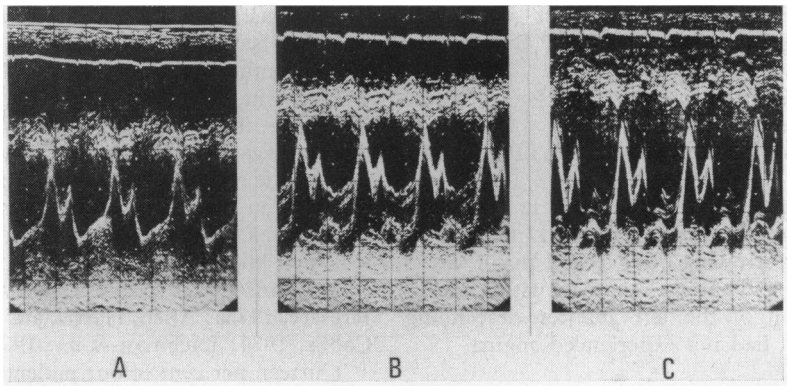

FIG. 6 *Mitral echograms obtained sequentially during same examination of one patient illustrating importance of transducer positioning. A) Apparently normal systolic closure line. B) Multiecho closure line, concave throughout systole, which is indicative of definite prolapse. C) Abrupt downturning of the systolic closure line in early to midsystole, again indicative of definite prolapse.*

medial commissural scallop, middle scallop, or anterolateral commissural scallop. Prolapse of posteromedial commissural scallop alone occurred in 20 patients, of posteromedial commissural scallop and middle scallop in 4 (Fig. 4A), of posteromedial and anterolateral commissural scallops (Fig. 7) in 3, of all 3 scallops in 10, and of anterolateral commissural scallop alone in 1. Two patients also had prolapse of the anterior mitral leaflet. Among 8 patients in whom the tricuspid valve was angiographically assessed, 3 were found to have prolapse of this valve (Gooch *et al.*, 1972a). Mitral regurgtaition was evident in 7 patients and was severe in 2 (both with triscallop posterior leaflet prolapse), moderate in 2 (1 with triscallop and 1 with posteromedial commissural scallop and middle scallop posterior leaflet prolapse), mild in 2 (1 with triscallop and 1 with posteromedial and anterolateral commissural scallop posterior leaflet plus anterior leaflet prolapse), and trivial in 1 (with posteromedial commissural scallop prolapse). Left ventriculograms in 16 of the cases showed ab-

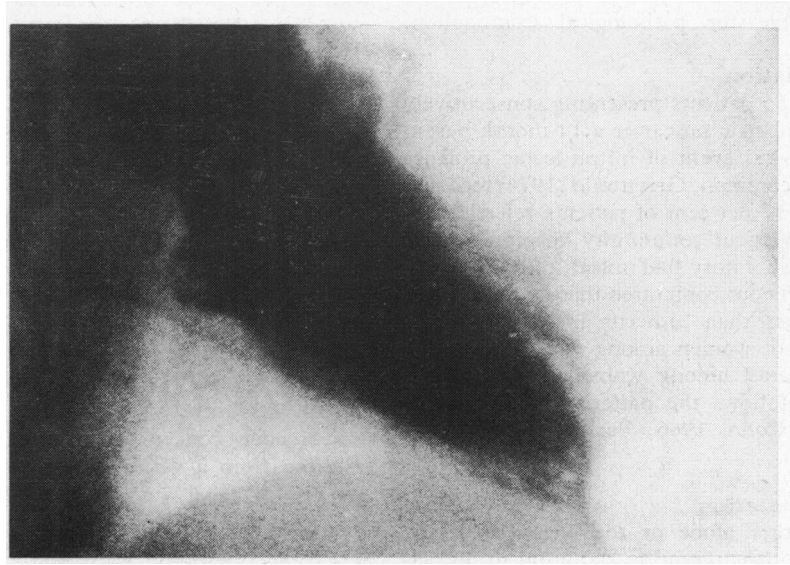

FIG. 7 *Midsystolic frame from left ventriculogram filmed in 30° right anterior oblique projection showing the prominent bulges of anterolateral commissural scallop (upper bulge) and posteromedial commissural scallop (lower bulge) posterior mitral leaflet prolapse.*

normalities of wall motion, most commonly segmental diastolic dyskinesis of the anterolateral left ventricular wall.

Left ventricular end-diastolic pressures before contrast injection were < 12 mmHg (< 1·6 kPa) in 27 subjects and ≥12 mmHg (≥1·6 kPa) in the remaining 11.

Selective coronary arteriography in 31 cases showed occlusive lesions in 5. Four had ≥80 per cent luminal width narrowing of at least 1 major vessel and all of these had angina. Another, with a 40 per cent constriction of the left anterior descending coronary artery, had not experienced angina.

Discussion

We have used the term 'mitral leaflet prolapse' in preference to other designations such as 'mitral valve prolapse' or the 'systolic click—murmur syndrome', for it is a succinct and precise description of the phenomenon which affects the leaflets rather than the whole structure of the mitral valve and it need not be associated with clicks or murmurs (Jeresaty, 1973a; DeMaria *et al.*, 1974). Detailed discussion of the mechanisms responsible for various features associated with mitral leaflet prolapse, many of which are still speculative or controversial, is beyond the scope of this paper and is not attempted; attention is directed to the reviews by Jeresaty (1973a) and Cobbs (1974) which deal with the subject. None of our patients required valve replacement and no mitral valve material has become available for pathological examination.

Patient population

Our sample of 85 patients presenting consecutively in one non-paediatric unit over a 14-month period shows the physical event of mitral leaflet prolapse to be relatively common. Greenwald (1974) reported that more than 12 per cent of patients referred to a Norwalk, Connecticut community hospital's echocardiographic laboratory had mitral leaflet prolapse and this supports our contention that the disorder is much commoner than hitherto appreciated. The preponderance of women among our patients and the peak incidence among women in the fourth decade of life follows the pattern of other series (Hancock and Cohn, 1966; Barlow *et al.*, 1968; Jeresaty, 1973a).

Mode of presentation

Chest pain, either alone or together with other symptoms, was the presenting symptom in 46 per cent of our patients and is the most common presenting complaint in association with mitral leaflet prolapse. Dyspnoea or undue and persistent fatigue brought 6 of the 85 patients to our attention and have been noted by Jeresaty (1973a) often to be the presenting symptoms in mitral leaflet prolapse. One patient, who presented with general malaise, including fatigue, was ultimately felt to have culture-negative endocarditis and had a good therapeutic response to penicillin and streptomycin. We had no cases of culture-positive endocarditis, though as a complication of mitral leaflet prolapse it is well known, and prophylaxis against bacterial endocarditis is advisable (Barlow *et al.*, 1968; Jeresaty, 1973a; Allen, Harris, and Leatham, 1974; Cobbs, 1974; Lachman *et al.*, 1975).

Thirteen per cent of our patients presented with recent major neurological disturbances. We are unaware of previous recognition of any relation between mitral leaflet prolapse and transient ischaemic attacks but careful auscultatory and echocardiographic assessment of all patients with evidence of transient cerebral ischaemia now seems warranted. Among those presenting primarily with neurological disturbances, carotid angiography was carried out in 5, showing abnormalities in only 1 (occlusion of the left posterior cerebral artery), and aortic arch angiography in 2 (normal findings in 1 and complete occlusion of the origin of the left common carotid artery in the other).

Overall incidence of certain symptoms

The primacy of chest pain among the symptoms associated with mitral leaflet prolapse is evident, with 72 per cent of our patients so afflicted, a higher prevalence than the 61 per cent found by Jeresaty (1973a) or the 35 per cent found by Hancock and Cohn (1966). The statement (Jeresaty 1973a) that, 'it was usually ill-defined, left precordial, sharp, and either fleeting or lasting several hours' serves well to describe the pain of the majority of our patients.

Our 5 patients with angina underwent coronary arteriography, 4 showing greater than 75 per cent narrowing of at least one coronary artery and the fifth having normal coronaries but left ventricular dilatation and severe mitral regurgitation. This suggests that coronary artery disease be suspected whenever a history of classical angina is elicted in a patient with mitral leaflet prolapse. It fits well with the broader concept of mitral leaflet prolapse resulting from a variety of pathological processes (Roberts, Dangel, and Bulkley, 1973), including papillary muscle ischaemia consequent upon coronary artery disease (Steelman *et al.*, 1971).

Chest pain of dramatic severity, mimicking the pain of myocardial infarction, had occurred in 3 of our patients and all 3 were found to have normal

coronary vessels by selective arteriography. Gulotta *et al.* (1974) have 12 similar cases.

It is probable that the palpitation experienced by 49 per cent of our patients, 48 per cent of Hancock and Cohn's (1966) patients and 46 per cent of Jeresaty's (1973a) patients is the symptomatic declaration of the arrhythmias which are acknowledged frequently to be associated with mitral leaflet prolapse and rarely to be the cause of sudden death therein (Hancock and Cohn, 1966; Pocock and Barlow, 1970; Jeresaty, 1973a; Shappell *et al.*, 1973; Cobbs, 1974). One of our patients, a 47-year-old man, died suddenly 20 months after Holter tape monitoring had revealed a brief run of ventricular tachycardia; he was receiving oral procainamide 500 mg 6-hourly. Syncope, as experienced by 14 per cent of our patients, probably also has an arrhythmic basis.

It is difficult to draw the fine distinction between neurotic symptoms and certain minor symptoms, especially neurological, which may be genuinely and accurately reported by a perceptive patient. Hancock and Cohn (1966) and Jeresaty (1973a) reported symptoms of 'neuropsychiatric' or 'psychiatric' type in 38 per cent and 15 per cent of their patients with mitral leaflet prolapse, respectively. Shappell, Orr, and Gunn (1974) found significant psychopathology in only 1 of 8 symptom-free patients with mitral leaflet prolapse but in 5 of 6 symptomatic patients with mitral leaflet prolapse.

General physical examination

The occurrence of mitral leaflet prolapse in Marfan's syndrome is well documented (Hancock and Cohn, 1966; Pocock and Barlow, 1970; Roberts *et al.*, 1973). It appears unlikely, however, that, in general, mitral leaflet prolapse could be a *forme fruste* of the Marfan syndrome.

Auscultation and phonocardiography

Systolic clicks and murmurs were for many years the key features by which mitral leaflet prolapse could be diagnosed and so determined the cases making up most series before that of Jeresaty (1973a). The increasing availability of echocardiography has led to the recognition of 'silent' mitral leaflet prolapse, as in 20 per cent of our patients and 12 per cent of Jeresaty's (1973a) patients. When a group of 25 patients with angiographically and echographically shown mitral leaflet prolapse had phonocardiograms performed no systolic click or murmur could be shown in 42 per cent of them (DeMaria *et al.*, 1974). Postural changes in the timing and intensity of the systolic clicks and murmurs of mitral leaflet prolapse (Barlow *et al.*, 1968; Epstein and Coulshed, 1973; Fontana *et al.*, 1975) were seen in a number of our patients, and as well as auscultation with the patient standing (Cobbs, 1974) we also commend listening, with the patient sitting forward.

Standard electrocardiography

The range of disturbances of rhythm, T wave polarity and contour, ST segment slope and level, QT_c interval, and U wave prominence revealed in the tracings from our series of patients confirms the pattern of electrocardiographic abnormalities already established (Barlow and Bosman, 1966; Hancock and Cohn, 1966; Engle, 1969; Pocock and Barlow, 1970; Jeresaty, 1973a; Lobstein *et al.*, 1973; Cobbs, 1974).

Voltage criteria for left ventricular hypertrophy, present in 8 of the patients in this series without any concomitant ST segment and/or T wave abnormalities, are insufficient for the diagnosis of left ventricular hypertrophy (Lipman *et al.*, 1972). Poor R wave progression in V1 to V3 and small or absent septal Q waves may be encountered in normal adults, with an incidence comparable to that discovered in this group of patients with mitral leaflet prolapse (Simonson, 1961; Horan and Flowers, 1972).

The QT_c interval was 0·43 s or longer in 73 per cent of Hancock and Cohn's (1966) patients and was 0·45 s in a 27-year-old woman with recurrent and eventually fatal ventricular fibrillation (Shappell *et al.*, 1973). Gooch *et al.* (1972b) had 7 cases with mitral leaflet prolapse with QT interval prolongation, but 3 of these were taking quinidine. Moderate prolongation of the QT_c is considered to be a standard electrocardiographic feature of mitral leaflet prolapse by Cobbs (1974). A long QT interval, which represents delayed ventricular repolarization and so prolongation of the vulnerable period for ventricular arrhythmia, is associated with syncope and ventricular fibrillation in certain inherited disorders (Vincent, Abildskov, and Burgess, 1974; Schwartz, Periti, and Malliani, 1975). Beta-adrenergic blocking agents and stellate ganglionectomy have abbreviated the QT interval in these syndromes with partial or complete suppression of ventricular arrhythmias. Intravenous propranolol did not alter the prolonged QT_c of one patient with mitral leaflet prolapse (Shappell *et al.*, 1973). We found no correlation between QT_c prolongation and arrhythmias in individual patients. Propranolol has relieved the symptoms of chest pain and palpitation in some of our patients and is recommended antiarrhythmic therapy by Pocock and Barlow (1970), Jeresaty (1973a), and Cobbs (1974). However, Cobbs (1974) denies its efficacy in the chest pain of mitral leaflet prolapse.

Treadmill exercise stress electrocardiography

The provocation of ventricular arrhythmias in patients with mitral leaflet prolapse subjected to exercise testing is well known (Pocock and Barlow, 1970; Del Rio *et al.*, 1971; Gooch *et al.*, 1972b; Sloman, Wong, and Walker, 1972; Jeresaty, 1973a), but in our series was less frequent than expected. Our 48 per cent incidence of ST segment abnormalities after exercise accords with the experience of Del Rio *et al.* (1971), Sloman *et al.* (1972), and Jeresaty (1973a). The long-lasting, evanescent, or delayed postexercise ST segment change evident in 11 of our patients not known to have coronary insufficiency (Table 5) is highly unusual in patients with angina pectoris caused by coronary artery narrowing (Wood *et al.*, 1950; Sheffield and Roitman, 1975).

Echocardiography

The utility of mitral valve echography in the diagnosis of mitral leaflet prolapse is well established (Feigenbaum, 1973; Cobbs, 1974; DeMaria *et al.*, 1974; Joyner, 1974; Popp *et al.*, 1974). Feigenbaum (1973) states that the echocardiographic findings are quite specific and that cardiac catheterization is unnecessary to confirm a diagnosis. We agree with the specificity of a positive test but found 10 per cent false negative mitral echograms and a further 15 per cent showing only minor abnormalities of the systolic closure line. Normal mitral echograms in confirmed mitral leaflet prolapse cases have been noted previously (Kerber *et al.*, 1971; DeMaria *et al.*, 1974), and the importance of careful transducer positioning and scanning is illustrated in Fig. 6. We have shown (Boughner, 1975) that the accuracy of the mitral echogram depends to a considerable extent on the amount of posterior leaflet involvement. The echogram readily detects biscallop or triscallop posterior leaflet prolapse, but single scallop posterior leaflet prolapse may be difficult to detect and can be missed.

Cardiac catheterization

Since mitral leaflet prolapse could be shown angiographically in every patient in whom the mitral echogram had the definite or 'possible' mitral leaflet prolapse pattern, the merit of this direct approach to visualizing the deformity and malfunction of the valve is confirmed. We were convinced of anterior leaflet prolapse in only 2 of our patients, but it is acknowledged that overlap of the mitral leaflets creates difficulties in identifying anterior leaflet prolapse in left ventriculograms (Kittredge *et al.*, 1970; Jeresaty, 1971). Gooch *et al.* (1972b) did not report it in any of their 23 patients studied angiographically and others have not attempted the differentiation in single plane (Popp *et al.*, 1974) or biplane studies (DeMaria *et al.*, 1974).

Mitral regurgitation among our patients appeared severe in only 2 cases, and in total only 7 had any evidence of mitral regurgitation. This illustrates that in at least one sense our group of patients had a milder form of the mitral leaflet prolapse disease complex. Among Jeresaty's (1973a) 39 patients studied angiographically, 20 had mitral insufficiency, 8 being severe and 5 mild, and Gooch *et al.* (1972b) reported angiographically demonstrable mitral insufficiency in 21 of 23 patients with mitral leaflet prolapse.

The 11 patients (29%) with LVEDP $\geq$12 mmHg (1·6 kPa) were not predominantly those with mitral regurgitation or significant coronary artery narrowing—perhaps a reflection of the myocardial dysfunction reported in some cases of mitral leaflet prolapse (Gooch *et al.*, 1972b; Gulotta *et al.*, 1974).

Left ventricular wall motion abnormalities in 42 per cent of our patients catheterized resemble closely those described by Gooch *et al.* (1972b) in 17 of their 23 subjects. Most characteristic has been the early diastolic dyskinetic bulging of the middle portion of the anterolateral left ventricular wall, but dysynergy of the posteroinferior wall during systole has also been observed.

Unless classical angina is present it appears that fully patent major coronary arteries are a standard finding in mitral leaflet prolapse, as in 9 of 10 cases (Gooch *et al.*, 1972b), 26 of 27 cases (Jeresaty, 1973b), 5 of 5 cases (Lobstein *et al.*, 1973) and 26 of 26 cases (Gulotta *et al.*, 1974). Nevertheless mitral leaflet prolapse may coexist with the common primary condition of atheromatous coronary artery narrowing.

Conclusion

Mitral leaflet prolapse is a disturbance of coaptation of the mitral leaflets during ventricular systole, with prolapse of the posterior or, more rarely, both leaflets into the left atrium; in the majority of cases it can be shown by echocardiography, without false positive results. We have found that the physical event of mitral leaflet prolapse occurs commonly and is not always associated with clicks or murmurs. A predilection for certain symptoms, inlcuding chest pain, palpitation, dizziness, syncopc, and other transient neurological disturbances, is evident in those with mitral leaflet prolapse. The varied pathogenesis (Roberts *et al.*, 1973; Cobbs, 1974) must cleary be a mrjor determinant of prognosis but in most of our cases we find ourselves ignorant of the precise nature of the mitral abnormality, let

alone the mechanism of production of the various symptoms. For most patients with mitral leaflet prolapse the prognosis appears good (Allen *et al.*, 1974), but this is tempered by knowledge of the few who die suddenly with arrhythmias, have worsening mitral regurgitation, develop endocarditis, or, as we have shown, suffer neurological disturbances.

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