Abnormal Left Ventricular Contraction Pattern in the Systolic Click-Late Systolic Murmur Syndrome

DETLF G. MATHEY, M.D., PIERRE R. DECOODT, M.D., HOWARD N. ALLEN, M.D., AND H. J. C. SWAN, M.D., PH.D.

SUMMARY A contraction abnormality of the left ventricle has previously been described in patients with systolic click-late systolic murmur syndrome. To determine if the contraction abnormality is present in the preprolapse period, LV dimensions and the instantaneous velocity of circumferential fiber shortening (V<sub>CF</sub>) were studied in 18 patients with mitral valve prolapse and 16 normal subjects using computer analysis of echocardiograms. V<sub>CF</sub> attained its maximum (max V<sub>CF</sub>) during the preprolapse period an average of 94 msec before the mid-systolic click. Max V<sub>CF</sub> was significantly reduced in patients with mitral valve prolapse (2.06 vs 2.55 cm/sec in normal subjects, P < 0.001).

Despite the reduction in max V<sub>CF</sub>, no difference in the extent and percentage of diameter shortening was found between patients and normal subjects. This discrepancy is explained by a sustained rate of mid-to-late systolic diameter shortening in the presence of mitral valve prolapse as manifested by a typical V<sub>CF</sub> profile (P < 0.001) and a longer duration of diameter shortening (353 vs 306 msec in normal subjects, P < 0.01).

The decrease of max V<sub>CF</sub> in patients with mitral valve prolapse suggests a reduction in LV contractility. Since the abnormality is present in the preprolapse period, it is unrelated to a direct mechanical effect of the prolapse itself. Additional fiber shortening in mid-to-late systole indicates that the sudden displacement of the mitral leaflets may have an unloading effect on the left ventricle.

IN ADDITION to the prolapse of the mitral valve, the systolic click-late systolic murmur syndrome is characterized by electrocardiographic, metabolic and contraction abnormalities. Angiographically, the contraction abnormality is manifested as segmental hypo or dyskinesis or diffuse hypokinesis of the left ventricle. In most patients, global left ventricular function remains unaffected. In the subset of symptomatic patients who undergo cardiac catheterization, abnormal hemodynamics at rest or during exercise are frequently noted.

In interpreting angiographic and echocardiographic data in patients with mitral valve prolapse, one must consider that the prolapse may have an unloading effect on the left ventricle. In mid-to-late systole, the mitral valve leaflets are suddenly displaced from the left ventricle into the left atrium causing an abrupt alteration in ventricular geometry. Mitral regurgitation, which may be present during the prolapse period, would contribute additionally to the unloading effect. Unloading of the left ventricle enhances left ventricular wall motion. Angiographic and echocardiographic measurements, which are based on the total dimensional change from end-diastole to end-systole could, therefore, lead to an overestimation of LV performance.

These considerations suggest that myocardial function in this syndrome should be evaluated in the preprolapse period. For this purpose, the instantaneous left ventricular diameter and the instantaneous velocity of circumferential fiber shortening (V<sub>CF</sub>) were measured in patients with mitral valve prolapse and normal subjects using computer analysis of echocardiograms.

Methods

Eighteen patients (mean age 35.5 years, range 25 to 59) with echocardiographic evidence of mitral valve prolapse were studied. Most patients were asymptomatic and were evaluated because of abnormal auscultatory findings. A single mid-to-late systolic click was recorded in all patients. In six patients (3, 4, 10, 14, 17, 18), the click was followed by a late systolic murmur; in two patients (5 and 16), the murmur preceded the click. The early systolic murmur did not coincide with the echocardiographic prolapse which was late-systolic and was preceded by a single click. ECG abnormalities were noted in five of the 18 patients. Nonspecific ST-T abnormalities were seen in patients 4, 10 and 13. Occasional premature ventricular complexes were recorded in patients 5 and 15. A pathologic Q wave in III, aV<sub>F</sub> and V<sub>4</sub> was found in patient 4. Sixteen healthy subjects age 20 to 43 years (mean age 28.4) served as a control group for comparative purposes.

Strip-chart echocardiograms at 50 mm paper speed were recorded in the supine or left lateral position using an Ecoline 20 ultrasound unit, which was interfaced with an Electronics for Medicine DR 8 recorder. In order to measure left ventricular dimensions, the echo transducer was placed in the 3rd or 4th intercostal space. It was angled in such a manner that the tip of the anterior mitral leaflet or the chordae just below the mitral valve were visualized. At this position, recordings of the motion of the interventricular septum and left ventricular wall were made. In the patient group, a phonocardiogram from the mitral area filtered to display frequencies between 200 and 500 Hz was recorded simultaneously. A lead II ECG was monitored continuously in patients and normal subjects. Only those tracings where a continuous, well-defined endocardium was seen were included in the study.

The tracings were then digitized at a sampling rate of 1000/sec using a hand-controlled articulated cursor. After sampling multiple calibration points, the onset of the QRS complex and the systolic click were sampled with an accuracy of ± 0.5 msec. Then the left ventricular septal and
posterior wall endocardium as well as the ECG and phonocardiogram were outlined by means of the cursor. This information was stored in the core memory of a Sigma 3 computer. By computing the instantaneous distance between the interventricular septum and left ventricular posterior wall, the left ventricular diameter time curve was obtained. Using a least squares differentiation formula (nine point-cubic), the first derivative of this diameter-time curve was calculated and divided by the end-diastolic diameter to obtain instantaneous values for V_{CP}. The diameter time curve, V_{CP}, the phonocardiogram and ECG were graphed on an X-Y plotter (fig. 1). In addition to the plot, all instantaneous values were printed. The following measurements were made automatically by computer:

1) End-diastolic (maximal) diameter (EDD) in cm.
2) End-systolic (minimal) diameter (ESD) in cm.
3) Extent of diameter shortening (EDD-ESD) in cm.
4) Percentage of diameter shortening (\( \frac{EDD-ESD}{EDD} \times 100 \))
5) Duration of diameter shortening (time from EDD to ESD) in msec.
6) Max V_{CP} in circ/sec; beat-to-beat variation of max V_{CP} in six consecutive beats was tested by one way analysis of variance and found to be 11%.
7) Time from onset of QRS to max V_{CP} (T QRS-max V_{CP}) in msec.
8) Time from max V_{CP} to systolic click (T max V_{CP}-X) in msec.

Student's t-test was applied to determine statistical significance between mean values; \( P < 0.05 \) was considered statistically significant. A chi-square evaluation for a \( 2 \times 2 \) contiguous table was performed to test whether or not a statistical difference in the shape of the V_{CP} curve between normal subjects and patients was present. For this purpose, the V_{CP} profiles of normal subjects and patients were mixed randomly. An independent observer was asked to classify them into two groups on the basis of a sharp, V-shaped or sustained, U-shaped V_{CP} profile (fig. 1).

**Results**

The individual data of normal subjects and patients are summarized in tables 1 and 2. Typical echocardiographic recordings and the corresponding computer plots in a normal (\# 12) and a patient with mitral valve prolapse (\#12) are shown in figure 1. Max V_{CP} and percent diameter shortening for all patients and normal subjects are shown in figure 2.

In the patient group, the LV end-diastolic diameter was not significantly different from control (average 5.12 vs 4.80 cm). The percentage of LV diameter shortening throughout systole was identical in both groups (average 42%, fig. 2).

The diameter of diameter shortening, however, was prolonged in patients with mitral valve prolapse averaging 353 vs 306 msec in normal subjects (\( P < 0.01 \)). This longer duration was not related to heart rate, which was 74 in normal subjects and 72 per minute in the patient group.

The principal difference between patients and normal subjects was a lower value of max V_{CP} averaging 2.06 circ/sec in the patient group vs 2.55 circ/sec in the control group (\( P < 0.001 \)) but the individual values showed some overlap (fig. 2). Max V_{CP} occurred an average of 94 msec before the mid-systolic click. Essentially no difference between groups was observed in the timing of max V_{CP} (179 msec after QRS in patients vs 166 msec in normal subjects). In the presence of mitral valve prolapse, a characteristic shape of the V_{CP} curve was seen. In 16 of 18 patients, a broadened, sustained peak of V_{CP} was recognized by a neutral observer, whereas all normal subjects were classified to have a sharp single peak (\( P < 0.001 \)). Examples of the typical configuration of the V_{CP}
curve in patients and normal subjects are given in figure 3.
No difference in blood pressure was noted between the
patient group and the normal subjects.

Discussion

Echocardiographic determination of mean VCF and its
clinical usefulness have been emphasized previously by
several investigators.\textsuperscript{10-12} In order to evaluate the time course
of contraction, VCF has to be measured instantaneously. This
requires high frequency sampling of LV dimensions and
computer assistance for its calculation. Quinones et al.\textsuperscript{12}
constructed a VCF curve by calculating VCF every 20 msec and
fitting a curve through the calculated values. The good cor-
relation between mean angiographic VCF and maximal echo-
cardiographic VCF established by these authors verifies the
value of the echocardiographic method. The method used in
our study resulted in reproducible measurements of VCF as
apparent from figures 1 and 3. Beat-to-beat variation of max
VCF was less than 11%. This variation includes physiologic
beat-to-beat changes as well as the methodical error. The opti-
mized method of calibration, high frequency sampling, con-
tinuous hand-controlled digitization at a high sampling rate of
1000/sec and adequate digital differentiation of the data are the main factors accounting for this degree of repro-
ducibility.

VCF has been shown to be a sensitive parameter of LV con-

\begin{table}
\centering
\caption{Normal Subjects}
\begin{tabular}{|c|c|c|c|c|c|c|c|c|}
\hline
No. & Age & Sex & HR & Arterial blood pressure (mm Hg) & EDD (cm) & LV Diameter shortening & Max VCF (circ/sec) & Sustained peak of Max VCF \\
\hline
1 & 36 & F & 74 & 107/80 & 3.58 & 1.73 & 48 & 248 & 3.11 & 153 & - \\
2 & 23 & F & 82 & 125/78 & 4.41 & 1.89 & 43 & 273 & 2.73 & 118 & - \\
3 & 30 & M & 70 & 132/76 & 3.97 & 1.62 & 41 & 295 & 2.32 & 145 & - \\
4 & 27 & F & 115 & 119/81 & 4.84 & 2.19 & 45 & 277 & 2.46 & 85 & - \\
5 & 24 & M & 66 & 125/84 & 5.19 & 2.17 & 42 & 295 & 2.44 & 210 & - \\
6 & 31 & M & 84 & 135/90 & 6.05 & 2.45 & 40 & 257 & 2.24 & 145 & - \\
7 & 25 & M & 73 & 140/85 & 4.74 & 1.85 & 39 & 363 & 2.37 & 197 & - \\
8 & 26 & M & 72 & 131/90 & 5.43 & 2.24 & 41 & 310 & 2.48 & 110 & - \\
9 & 20 & F & 66 & 110/70 & 4.74 & 1.82 & 38 & 297 & 2.36 & 207 & - \\
10 & 20 & F & 69 & 105/65 & 5.50 & 2.18 & 40 & 270 & 2.16 & 210 & - \\
11 & 39 & F & 51 & 130/70 & 4.61 & 2.16 & 47 & 430 & 2.86 & 190 & - \\
12 & 43 & F & 65 & 123/72 & 4.32 & 2.04 & 47 & 293 & 2.64 & 157 & - \\
13 & 29 & M & 56 & 128/68 & 5.25 & 2.16 & 41 & 353 & 2.61 & 203 & - \\
15 & 26 & M & 83 & 100/65 & 4.40 & 1.87 & 42 & 262 & 2.34 & 165 & - \\
16 & 34 & M & 72 & 100/80 & 5.69 & 2.13 & 37 & 370 & 2.50 & 185 & - \\
Mean & 74 & & & 121/77 & 4.80 & 2.02 & 42 & 306 & 2.55 & 166 & 16/16 \\
\hline
SEM & \pm 4 & \pm 3 & \pm 2 & \pm 1.7 & \pm 0.17 & \pm 0.06 & \pm 1 & \pm 12 & \pm 0.07 & \pm 10 & \\
\hline
\end{tabular}
\end{table}

Abbreviations: EDD = LV end diastolic diameter; Max VCF = maximal velocity of circumferential fiber shortening; TQRS-Max VCF = time from onset of QRS to Max VCF.

\begin{table}
\centering
\caption{Mitrail Valve Prolapse}
\begin{tabular}{|c|c|c|c|c|c|c|c|c|}
\hline
No. & Age & Sex & HR & Arterial blood pressure (mm Hg) & EDD (cm) & LV Diameter shortening & Max VCF (circ/sec) & Sustained peak of Max VCF \\
\hline
1 & 40 & F & 76 & 105/72 & 4.30 & 2.26 & 53 & 338 & 2.16 & 160 & 115 & + \\
2 & 32 & F & 88 & 110/70 & 4.97 & 2.31 & 46 & 365 & 2.49 & 180 & 95 & + \\
3 & 25 & F & 68 & 127/78 & 4.54 & 1.60 & 45 & 380 & 1.78 & 200 & 90 & + \\
4 & 59 & M & 101 & 136/76 & 6.73 & 3.06 & 45 & 380 & 1.78 & 173 & 95 & + \\
5 & 29 & F & 61 & 115/63 & 9.72 & 1.66 & 35 & 308 & 1.74 & 220 & 40 & - \\
6 & 31 & F & 70 & 120/80 & 4.15 & 1.40 & 34 & 385 & 2.27 & 95 & 164 & + \\
7 & 28 & F & 85 & 123/81 & 5.04 & 1.65 & 33 & 327 & 2.00 & 140 & 130 & + \\
8 & 54 & F & 75 & 115/72 & 4.33 & 1.78 & 41 & 355 & 2.42 & 210 & 144 & + \\
9 & 43 & F & 72 & 134/76 & 5.06 & 2.16 & 43 & 360 & 1.72 & 177 & 87 & + \\
10 & 36 & F & 78 & 140/85 & 5.06 & 2.54 & 50 & 330 & 2.31 & 130 & 191 & + \\
11 & 40 & F & 55 & 122/75 & 4.85 & 2.20 & 45 & 430 & 1.77 & 193 & 122 & + \\
12 & 29 & F & 59 & 115/63 & 4.52 & 1.96 & 43 & 318 & 1.99 & 185 & 85 & + \\
13 & 31 & F & 65 & 135/78 & 5.80 & 2.47 & 43 & 315 & 2.07 & 207 & 70 & + \\
14 & 29 & M & 56 & 123/82 & 5.55 & 2.13 & 38 & 360 & 1.73 & 193 & 57 & + \\
15 & 28 & M & 70 & 138/91 & 5.79 & 2.74 & 47 & 395 & 2.18 & 210 & 56 & + \\
16 & 38 & M & 57 & 119/85 & 5.81 & 2.48 & 43 & 440 & 2.35 & 170 & 55 & - \\
17 & 26 & M & 78 & 119/78 & 5.90 & 2.07 & 35 & 420 & 1.96 & 170 & 55 & - \\
18 & 41 & F & 78 & 127/76 & 5.10 & 2.09 & 41 & 315 & 2.29 & 210 & 41 & + \\
\hline
Mean & 72 & & & 123/77 & 5.12 & 2.14 & 42 & 353 & 2.06 & 179 & 94 & 16/18 \\
\hline
SEM & \pm 3 & \pm 2 & \pm 2 & \pm 0.16 & \pm 0.10 & \pm 1 & \pm 11 & \pm 0.06 & \pm 8 & \pm 10 & \\
\hline
\end{tabular}
\end{table}

Abbreviations: EDD = LV end diastolic diameter; Max VCF = maximal velocity of circumferential fiber shortening; TQRS-Max VCF = time from onset of QRS to Max VCF; T max VCF-X = time from Max VCF to systolic click.
tractility responsive to positive\textsuperscript{15, 16} and negative\textsuperscript{16} inotropic stimuli. Recent studies indicate that it may be a better index of contractility than indices derived from analysis of isovolumic contraction.\textsuperscript{15, 16} It appears to be independent of preload,\textsuperscript{17} but, in addition to contractility, it is inversely related to afterload.\textsuperscript{18} During the preprolapse period, a different state of afterload is unlikely between our normal subjects and patients, since no difference in blood pressure values was found. During late systole, the displacement of one or both mitral leaflets in patients with mitral valve prolapse may have an unloading effect on the left ventricle. For these reasons, $V_{CF}$ has to be measured during the preprolapse period.

In previous studies, a close temporal relationship between the onset of mitral valve prolapse and the time of systolic click has been demonstrated.\textsuperscript{19-22} Winkle and co-workers\textsuperscript{9} showed that the onset of echocardiographic prolapse precedes the click by only 30 msec. Since max $V_{CF}$ preceded the click by an average of 94 msec, it was well within the preprolapse period. It may be argued that a “silent” prolapse in other segments of the mitral leaflets could occur earlier than the prolapse coinciding with the click. At present, we feel that the existence of a silent prolapse has not been documented beyond doubt. Most cases of silent prolapse were reported when echocardiographic criteria and techniques were not yet as strictly defined as they are now, and many of these diagnoses may represent echocardiographic artifacts due to improper transducer position. In accordance with the above-mentioned studies, we believe that a single mid-to-late systolic click indicates the onset of a single prolapse.

The significant reduction of max $V_{CF}$ in patients with mid-systolic click late-systolic murmur syndrome suggests diminished contractility in those areas of the left ventricle that were visualized by echocardiography. Additional abnormalities in other segments of the left ventricle cannot be excluded by this technique. Our finding confirms previous angiographic reports\textsuperscript{4-8} and, in particular, the study by Liedtke and co-workers,\textsuperscript{9} who used the lateral projection to evaluate left ventricular wall motion. The lateral projection most likely includes those areas of the left ventricle that are visualized by echocardiography. These authors found that the left ventricular inflow tract was hypokinetic in their patients with mitral valve prolapse. Although diffuse hypokinesis of the left ventricle has been described as well, in most patients the contraction abnormality was found to be localized. This could explain the finding that a serious reduction in max $V_{CF}$ was found in only 10 of our 18 patients, although in no patient did max $V_{CF}$ exceed the average of the normals. The study also demonstrates that the impairment of left ventricular contractility is present in the preprolapse period and, therefore, obviously unrelated to any direct mechanical effect of the prolapse itself. The eight patients with normal $V_{CF}$ values may have had a normal left ventricle or segmental contraction abnormalities in areas that were not examined by our technique. Angiocardiography, which was not justified in these mostly asymptomatic patients, might have failed to detect the contraction abnormality, since sampling rate (1000 Hz in echocardiography vs 60–120 Hz in angiocardiography) and spatial resolution of the left ventricular contour are not sufficient to obtain reproducible $V_{CF}$ curves.

Despite the reduction in max $V_{CF}$, extent and percentage of diameter shortening were normal in patients with mitral valve prolapse. This is explained by the sustained rate of diameter shortening during mid-to-late systole as manifested by a typical $V_{CF}$ profile and a longer duration of diameter shortening. Both findings suggest LV unloading secondary to the prolapse.

\textbf{References}

Effect of Increased Free Fatty Acids on Myocardial Oxygen Extraction and Angina Threshold during Atrial Pacing

GILLES R. DAGENAIS, M.D., AND BERNARD JALBERT, M.D.

SUMMARY To evaluate whether elevated arterial free fatty acids (FFA) increase myocardial oxygen demand and ischemia, 15 fasting patients with coronary artery disease underwent a standardized atrial pacing test before (PT1) and during (PT2) heparin infusion. The patients were monitored for clinical and electrocardiographic (ECG) manifestations of ischemia. Myocardial extraction of lactate, inorganic phosphate, oxygen and FFA was measured before and during each PT. The control arterial FFA was 0.65 ± 0.03 μmole/ml and rose to 1.83 ± 0.16 μmole/ml during heparin infusion. Myocardial oxygen extraction at rest and during PT was not affected by the increase in arterial FFA. Seven patients asymptomatic during PT1 did not develop ischemic manifestations during PT2. In eight patients with angina during both PTs, increased arterial FFA concentration did not modify the severity of anginal pain, the amount of ST-segment depression and the myocardial balance of lactate or inorganic phosphate. Elevation of arterial FFA by heparin neither increased myocardial oxygen extraction at rest or during pacing nor accentuated ischemic manifestations during PT.

MYOCARDIAL OXYGEN EXTRACTION of the isolated rat heart and the anesthetized dog heart is augmented, with no change in mechanical work, when free fatty acid (FFA) delivery to the myocardium is increased. Furthermore, elevated arterial FFA increase myocardial ischemia in anesthetized dogs. From these observations, it might be expected that pharmacological agents such as heparin or catecholamines, which increase arterial FFA, would prove hazardous in patients with ischemic heart disease. The present study was undertaken to determine whether a heparin induced elevation of arterial FFA increases myocardial oxygen extraction and ischemic manifestations at rest and during a standardized atrial pacing test in patients with angiographically documented coronary artery disease.

Patients and Methods

Fourteen males and one female, aged between 35 and 56 years, hospitalized because of chest pain for coronary
Abnormal left ventricular contraction pattern in the systolic click-late systolic murmur syndrome.
D G Mathey, P R Decoodt, H N Allen and H J Swan

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