Muscular subaortic stenosis: the quantitative relationship between systolic anterior motion and the pressure gradient

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ABSTRACT We performed simultaneous echocardiographic and hemodynamic studies in 11 patients with muscular subaortic stenosis to determine whether systolic anterior motion (SAM) of the anterior mitral leaflet and the pressure gradient are related quantitatively. SAM without septal contact was associated with either no gradient or a small impulse gradient of less than 10 mm Hg. SAM with septal contact was always associated with a pressure gradient of more than 10 mm Hg. The size of the pressure gradient correlated inversely with the time periods: (1) onset of SAM to onset of SAM-septal contact \((r = -0.79, p < 0.001)\) and (2) onset of aortic ejection to onset of SAM-septal contact \((r = -0.89, p < 0.001)\). Size also correlated directly with the time period: (3) duration of SAM-septal contact \((r = 0.80, p < 0.001)\). Thus when the time from the onset of SAM to the onset of SAM-septal contact was long, SAM-septal contact developed late in systole, the duration of SAM-septal contact was brief and the pressure gradient was low. When SAM-septal contact developed in early systole, the duration of SAM-septal contact was long and the pressure gradient was high. With the index of time period (3) divided by time period (1), a regression equation was devised to predict the size of the pressure gradient \([\text{pressure gradient (mm Hg)} = 25 \times \text{[ratio]} + 25; r = 0.90, p < 0.001; \text{SE} \pm 15 \text{mm Hg}]\). The echocardiographic time period index was validated prospectively in nine other patients and the significant correlation with the hemodynamically determined gradient persisted \((r = 0.89, p < 0.01)\). We conclude that SAM and the pressure gradient are related quantitatively in muscular subaortic stenosis. These observations have implications regarding the mechanism and significance of the pressure gradient in muscular subaortic stenosis.


SYSTOLIC ANTERIOR MOTION (SAM) of the anterior mitral leaflet was described originally in patients with hypertrophic cardiomyopathy and a coexisting subaortic pressure gradient (muscular subaortic stenosis [MSS]).\(^1\,^2\) In these early reports SAM was suggested as a cause of the pressure gradient, and an index was devised, based on the degree of SAM, to predict the size of the hemodynamically measured gradient.\(^3\) Subsequent reports have demonstrated that SAM is not specific for hypertrophic cardiomyopathy,\(^4\) that it is often unassociated with a pressure gradient,\(^4\,^6\) and that predicted "index gradients" of up to 37 mm Hg can occur without a concomitant gradient at subsequent cardiac catheterization.\(^6\)

In a recent study of 74 patients with hypertrophic cardiomyopathy,\(^4\) all 27 patients with a basal subaortic pressure gradient of more than 30 mm Hg had severe SAM with SAM-septal contact for 30% or more of systole, whereas in the other patients without a significant pressure gradient at rest there was mild-moderate or no SAM. Echocardiographic and hemodynamic events were correlated in another study,\(^7\) in which the temporal relationship between SAM and the pressure gradient was assessed. The time of onset of SAM-septal contact was virtually identical to the time of onset of the pressure gradient, suggesting a cause-and-effect relationship.

The purpose of this study was to examine further the relationship between SAM and the pressure gradient. The objectives were to determine whether there is a quantitative relationship between SAM and the pres-
sure gradient and whether an index based on the degree of SAM could be used to predict the size of the pressure gradient.

Methods

Patients. We studied 11 patients with MSS (eight men, three women, mean age 40 years). The diagnosis was based on established clinical, hemodynamic, and echocardiographic criteria.8

Hemodynamic methods. Hemodynamic investigation was performed as part of the total assessment of symptomatic patients with MSS in consideration of possible operative intervention. Patients underwent both retrograde and transseptal left heart catheterization by the percutaneous Seldinger technique from the right groin. Simultaneous left ventricular inflow and aortic root pressures were recorded with a transseptal catheter advanced through the mitral valve orifice into the left ventricular inflow tract and a retrograde catheter in the aortic root.9, 10 Fluid-filled catheters connected to a Statham 23 Db transducer were used and pressures were recorded on an Electronics for Medicine Recorder.

Echocardiographic methods. All patients underwent standard M mode echocardiographic studies at the level of the mitral valve. Echocardiograms and hemodynamic pressures were displayed simultaneously at 100 mm/sec in most instances. In eight patients the echocardiographic and hemodynamic tracings were recorded on the same paper with an Electronics for Medicine Echocardiograph interfaced into the Electronics for Medicine Console. In three patients the echocardiogram and hemodynamics were examined simultaneously but were recorded on separate tracings. In most of the patients, recordings were performed during manipulation of the pressure gradient by premature beats, respiration, intravenous angiotension, or intravenous isoproterenol.

Quantification of SAM and the pressure gradient. SAM was quantified by measuring (1) the time from onset of SAM (defined as the beginning of the steep ascent of SAM) to the onset of SAM-septal contact, (2) the time from onset of aortic ejection to onset of SAM-septal contact, and (3) duration of SAM-septal contact (figure 1). The pressure gradient was measured from the peak of the left ventricular pressure to peak of the aortic percussion wave. The left ventricular ejection time was measured from the onset of aortic ejection to the dicrotic notch (figure 1).

Sixty-seven cardiac cycles were examined from the 11 patients, chosen because of image clarity (one to 16 cycles per patient), and time periods were corrected for heart rate by dividing by the square root of cycle length. All hemodynamic and echocardiographic measurements were possible in 57 cycles, and the majority of measurements were possible in the other 10 cycles.

Statistical analysis was performed with standard linear regression.

Comparison with “obstruction index.” Representative samples of 15 cardiac cycles from simultaneous echocardiographic and hemodynamic studies in five patients (one to six cycles per patient) were chosen for comparison of the current time period index with the “obstruction index,”13 in which the gradient is calculated from the average mitral-septal distance. Gradients ranged from 4 to 146 mm Hg. Two cardiac cycles with SAM but without SAM-septal contact were included in the comparison.

Prospective validation. Nine patients with MSS (seven men, two women, mean age 44 years) were studied after the retrospective correlation between SAM and the pressure gradient referred to in the original 11 patients. Echocardiography and cardiac catheterization were performed at different times: in seven patients from 1 to 9 days apart and in two patients 3 and 4 months apart. Derivation of echocardiographic data was obtained by averaging time periods from two to five cardiac cycles per patient, and the pressure gradients were derived by averaging three to 10 cardiac cycles per patient. Gradients ranged from 26 to 107 mm Hg.

Results

Both the periods from onset of SAM to onset of SAM-septal contact (figure 2) and onset of aortic ejection to onset of SAM-septal contact correlated inversely with the size of the pressure gradient (r = −.79, r = −.89, respectively, p < .001). The duration of
septal contact correlated directly with the size of the pressure gradient (r = .80, p < .001, figure 3). The time from the onset of aortic ejection to the onset of SAM-septal contact was very close to the time from onset of aortic ejection to the onset of the pressure gradient (r = .84, p < .001). The size of the pressure gradient was directly related to the duration of left ventricular ejection time (r = .73, p < .001).

The correlations between the echocardiographic time periods and the pressure gradient were present within individuals as well as between the patients as a group and were independent of the mode of stimulation of the gradient.

The time from onset of aortic ejection to onset of SAM-septal contact expressed as a percentage of the total left ventricular ejection time was plotted against the pressure gradient and the left ventricular ejection time (figure 4). Early systolic SAM-septal contact was associated with a high pressure gradient and prolonged ejection time. Midsystolic SAM-septal contact was associated with a low pressure gradient and normal or slightly prolonged ejection time.

SAM without septal contact was associated with either no gradient or a small impulse gradient of less than 10 mm Hg\(^1\) (figure 5). When SAM-septal contact was brief, the time from onset of SAM to the onset of SAM-septal contact was long, SAM septal contact occurred late in systole, and the pressure gradient was small. Large gradients were associated with early and prolonged SAM-septal contact (figure 5).

On the basis of these observations an index was devised from the ratio of duration of septal contact to onset of SAM until onset of SAM-septal contact. A significant correlation between the size of the pressure gradient and the size of this index was found (r = .90, p < .001; figure 6). The regression equation to calculate the pressure gradient shown in figure 6 was simplified as shown in figure 7, and the last number was rounded off to 25 from 26 because differences of 1 mm Hg could not be detected with a standard error of 15.
mm Hg, and such differences are clearly not clinically important.

Comparison with obstruction index. The pressure gradient predicted by the obstruction index\(^3\) correlated significantly with the gradient derived from catheterization data \((r = .95, p < .001)\) and with the pressure gradient derived from the current time period index \((r = .91, p < .001)\). In the two cycles with SAM but without SAM-septal contact the hemodynamically derived pressure gradients were 4 and 7 mm Hg, which derived by the obstruction index were 28 and 33 mm Hg. Gradients for this degree of SAM cannot be calculated by the current time period index and they were scored as zero.

Prospective validation. The pressure gradient derived from the current time period index correlated significantly with the gradient derived from catheterization data \((r = .89, p < .01)\).

Discussion

The results of this study demonstrate that SAM and the pressure gradient are related quantitatively in MSS. The quantitative relationship centers on the time of onset and duration of SAM-septal contact. When SAM-septal contact occurs early in systole, the duration of contact is long and the pressure gradient is high. When SAM-septal contact occurs later in systole, contact is brief and the pressure gradient is low.

An index was devised, based on these observations, that can be used to predict the pressure gradient. The advantages of using the index rather than the separate time periods are twofold. First, measurements can be made from the M mode echocardiographic tracing in millimeters without having to calculate the exact number of milliseconds. Second, no correction for heart rate is necessary.

The current time period index differs practically and conceptually from the obstruction index described previously.\(^3\) The obstruction index requires approximately 10 measurements, compared with two required for the current index, and was based on the premise that the gradient would be inversely proportional to the systolic septal-mitral leaflet distance; therefore SAM without septal contact was considered acceptable for
have demonstrated that SAM without septal contact is not associated with a significant pressure gradient. Nevertheless this discrepancy is usually small, and there was a close correlation between the two indexes \( r = .91, p < .001 \).

**Mechanism of the quantitative relationship.** When SAM-septal contact occurs, the left ventricular outflow tract is stenosed and narrowed severely but not obliterated. It seems likely that small areas of the outflow tract must remain patent for flow to keep the aortic valve leaflets open until the end of the systolic ejection period, which hemodynamic,\(^{12}\) echocardiographic,\(^{13}\) and Doppler echocardiographic studies\(^{14}\) have demonstrated as being prolonged when a significant gradient is present.

The pressure gradient across a stenotic orifice, such as that produced by SAM-septal contact, is proportional to the velocity and volume of flow across that orifice.\(^{15}\) When SAM-septal contact occurs in early systole, it is maintained through the majority of systole, the resulting severely narrow subaortic orifice encounters a large proportion of the stroke volume at an initially fast rate of ejection, and the pressure gradient, as determined by the velocity and volume of flow,\(^{16}\) is high. By midsystole the majority of the stroke volume has already been ejected and if SAM-septal contact only then develops, the resulting brief duration of subaortic stenosis will encounter only a small part of the stroke volume at a lower ejection rate; therefore the pressure gradient is low.

The proposed mechanism for the quantitative relationship is illustrated in figure 8, in which has been plotted the stroke volume curve (derived from the resting aortic flow velocity profile) in the group of patients with nonobstructive hypertrophic cardiomyopathy studied by Murgo et al.\(^{16}\) The pressure gradients and associated ejection times derived from this study are shown for SAM-septal contact occurring at 10% to 50% of the way through systole. When SAM-septal contact develops as early as 10% of the way through systole the resulting subaortic stenosis occurs when 93% of the stroke volume has yet to be ejected. The associated pressure gradient is high at 142 mm Hg, and the left ventricular ejection time is severely prolonged at 425 msec, which is 42% longer than normal (300 msec).
When SAM-septal contact first develops as late as 50% of the way through systole, 95% of the stroke volume will already have been ejected before SAM-septal contact. The resulting pressure gradient is low at 16 mm Hg, and the ejection time is slightly prolonged at 320 msec, which is only 6% longer than normal.

Significance of the quantitative relationship. The hemodynamic significance of the pressure gradient has been questioned by data on aortic flow velocity and cineangiographic studies of left ventricular emptying.

In patients with basal pressure gradients, most of the studies of aortic flow velocity report a rapid early flow velocity in early systole and a sharp decrease in velocity by mid systole. The flow velocity profile in patients with nonobstructive hypertrophic cardiomyopathy has been reported to differ from that in patients with a pressure gradient by some groups. Another group, however, suggests that the similarity of flow velocity profile between the two groups with and without pressure gradients indicates that left ventricular outflow obstruction does not take place in the patients with pressure gradients. However, the mean pressure gradient in the group of patients studied was relatively low at 50 mm Hg (in two patients the gradient was less than 20 mm Hg) and the ejection time was only slightly prolonged. Our results indicate that at a pressure gradient of 50 mm Hg, SAM-septal contact, and the resulting subaortic stenosis would not occur until 40% of the way through the systolic ejection period, by which time 78% of the stroke volume has already been ejected as calculated from the stroke volume curves in the patients with nonobstructive cardiomyopathy (figure 8). Thus SAM-septal contact would encounter only the last 22% of flow in these patients. Analysis of the stroke volume data derived from the resting aortic flow velocity profile is consistent with this interpretation. The time to eject the first 80% of stroke volume was virtually the same in the groups with and without pressure gradients at 125 and 115 msec, respectively, whereas the last 20% of flow took 48% longer in the group with pressure gradients compared with the group without (92 and 62 msec, respectively).

Cineangiographic studies of the left ventricle have shown that left ventricular emptying is rapid, with no clearly apparent difference between patients with or without a pressure gradient. The explanation for these results is that obstruction of the left ventricular outflow tract does not occur. However, left ventricular emptying must be interpreted in light of the associated mitral regurgitation and the timing of SAM-septal contact. In patients with MSS, the presence and severity of the pressure gradient is almost invariably correlated with the presence and severity of mitral regurgitation. The left ventricle ejects rapidly in patients with hypertrophic cardiomyopathy and no pressure gradient. Any tendency to slow down this rapid ejection by the subaortic stenosis resulting from SAM-septal contact is counterbalanced by the accompanying mitral regurgitation, which will facilitate the rapid emptying. The size of the pressure gradient and the timing of SAM-septal contact is also crucial in the interpretation of cineangiographic studies of left ventricular emptying. Thus in the study of Muro et al. describing relatively low pressure gradients, 80% to 90% of left ventricular emptying would have occurred before SAM-septal contact and the associated subaortic stenosis. This is consistent with their findings that the majority of left ventricular emptying was not impeded.

In conclusion, SAM and the pressure gradient are related quantitatively in MSS, and a time period index based on these observations has been devised. The mechanism and significance of this relationship depends on the timing of SAM-septal contact. When SAM septal contact first develops in early systole, the majority of left ventricular stroke volume encounters the resulting subaortic stenosis, the ensuing pressure
gradient is high, and the ejection time is severely prolonged. When SAM-septal contact develops in mid-systole, the majority of left ventricular emptying has occurred before the subaortic stenosis has developed, the ensuing gradient is low, and the ejection time is normal or only barely prolonged.

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