METHODS

Intraoperative Doppler Echocardiography in Hypertrophic Cardiomyopathy: Correlations With the Obstructive Gradient

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Although significant pressure gradients can be recorded across the left ventricular outflow tract in patients with hypertrophic cardiomyopathy, controversy exists regarding the presence or absence of true obstruction. Ten patients with hypertrophic cardiomyopathy were studied at the time of septal myectomy. A sterile continuous wave Doppler transducer was placed on the ascending aorta and directed toward the left ventricular outflow tract to measure velocity simultaneously with invasive gradient measured using solid-state hub transducers by direct puncture of the left ventricle and aorta.

Simultaneous Doppler velocity and invasive gradient measurements (n = 33) were made at rest, before and after myectomy and during interventions with isoproterenol, volume loading and phenylephrine. High velocity flow with a characteristic contour was recorded in patients with a significant gradient. Using the modified Bernoulli equation (gradient = 4 × velocity²), a good correlation was found between the Doppler-derived gradient and the peak instantaneous gradient measured invasively (r = 0.93, y = 0.89x + 12, p = 0.0001). Changes in gradient and velocity due to interventions also correlated well (r = 0.96, y = 0.91x - 3, p = 0.0001).

Continuous wave Doppler echocardiography can accurately estimate the outflow tract gradient. The magnitude, timing and contour of these high velocity flow signals support the hypothesis that true obstruction is present in patients with hypertrophic cardiomyopathy who have a significant gradient.

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licity ($V_{\text{max}}$) across the stenosis measured by continuous wave Doppler echocardiography, using a modification (17) of the Bernoulli equation: Gradient = $4 \times (V_{\text{max}})^2$. Although Doppler methods have been used to assess the flow dynamics in hypertrophic cardiomyopathy (17,22–30), the exact relation between the magnitude of the gradient and the velocity of flow in the outflow tract in hypertrophic cardiomyopathy has not been elucidated.

The purposes of this study were 1) to determine whether Doppler echocardiography can accurately estimate the outflow tract gradient in patients with hypertrophic cardiomyopathy, and 2) to use the pressure and velocity information to determine whether true obstruction does or does not exist in this disorder.

Methods

Study patients. Of 82 patients with hypertrophic cardiomyopathy in whom myectomy has been performed to date at our institution, 10 patients (7 male and 3 female) form the basis of this study. The mean age was 46 years (range 13 to 73).

Nine of the 10 patients had preoperative echocardiograms documenting hypertrophic cardiomyopathy on the basis of previously published diagnostic criteria (15,16,31–36). Systolic anterior motion of the mitral valve was present in all nine patients. No patient had intrinsic stenosis of the aortic valve. Nine of the 10 had previous cardiac catheterization, and a rest left ventricular outflow tract gradient was documented in all. The mean difference at catheterization between rest left ventricular peak systolic pressure and peak aortic pressure was 78 mm Hg (range 27 to 120). In one patient, hypertrophic cardiomyopathy was documented preoperatively by cardiac catheterization without echocardiography, and one patient had echocardiography without catheterization.

All 10 patients had been treated for symptoms referable to hypertrophic cardiomyopathy. In all 10, a clinical decision was made to perform operative myectomy, on the basis of symptoms and hemodynamic findings. The choice of myectomy reflected poor response to medical therapy in 9 of the 10 patients. In one patient, myectomy was recommended after echocardiography showed hypertrophic cardiomyopathy in the presence of symptomatic left main coronary stenosis.

Doppler echocardiography. Intraoperative continuous wave Doppler echocardiographic recordings of maximal left ventricular outflow tract velocity were made using a PEDOF dedicated Doppler transducer with a 2.0 MHz carrier frequency. The Doppler instrument used in six patients was an SD 100 (Vingmed, Inc.), whereas in four patients, a Meridian (Irex Corp.) was utilized. The frequency spectra were displayed in real time and recorded on $\frac{1}{2}$ inch (1.27 cm) videotape for subsequent analysis.

Doppler color flow mapping. Intraoperative two-dimensional Doppler color flow recordings of the spatial distribution of flow in the left ventricular outflow tract were made in two patients using an Aloka 880 instrument (Irex Corp.). A 3.5 MHz phased array imaging transducer was utilized. Images were recorded in real time (30 frames/s) and on $\frac{1}{2}$ inch videotape for subsequent data analysis in slow motion and stop-frame format.

Doppler transducers were sterilized in 100% ethylene oxide at a temperature of 100°F for 6 hours and aerated for 48 hours before use to allow vapors to fully escape.

Hemodynamic monitoring. Intracardiac pressures were recorded using 18 gauge spinal needles equipped with solid-state hub transducers. The transducers were calibrated to zero by opening the system to air with the transducer at the level from which measurement would be made. For additional calibration, the incoming voltage signal was compared with a reference voltage output corresponding to 100 mm Hg pressure. The pressure waveforms were displayed on real-time oscilloscopic displays. In addition, the analog signals were registered by a digitized system and recorded at 5 ms intervals over one or more 10 second collection periods, using a PDP 11 computer (Digital Equipment Corporation) to provide simultaneous left ventricular and aortic pressure waveforms for measurement of instantaneous gradients.

Intraoperative data collection. The patients were prepared for myectomy in standard fashion. After midline sternotomy and arterial and venous cannulation, but before institution of cardiopulmonary bypass, the Doppler examination shown in Figure 1 was conducted. First, a sterile 2.0 MHz dedicated Doppler transducer was placed against the adventitia of the ascending aorta 1 to 5 cm above the aortic valve. Employing the continuous wave mode, the ultrasound beam was pointed inferiorly toward the left ventricular outflow tract. The transducer location and direction were adjusted to obtain a signal with the highest velocity and the cleanest envelope obtainable, guided by the spectral display and the audio characteristics of the Doppler signal. After noting the location and direction of the optimal transducer position, the transducer was removed.

An 18 gauge spinal needle was then inserted into the ascending aorta by direct puncture. Aortic recordings were verified by observing the quality of the pressure waveform and comparing the systolic and diastolic pressures to a radial artery measurement. A second 18 gauge spinal needle was then inserted into the left ventricle by direct puncture through the anterior wall, taking care to avoid the epicardial coronary arteries. The needle tip was positioned at the midventricular level. The pressure waveform was examined to confirm a left ventricular contour, with a rapid increase in pressure...
coinciding with the aortic upstroke and a rapid decrease in pressure coinciding with the dicrotic notch on the aortic tracing, a pattern that would not be present if the needle tip were intramyocardial.

When optimal pressure waveforms were obtained, the Doppler transducer was again applied and readjusted to obtain the optimal velocity recording from the left ventricular outflow tract. When the velocity and pressure signals were satisfactory, the pressure waveforms and velocity spectrum were recorded simultaneously. Good quality, rest, premyectomy recordings were made successfully in 9 of the 10 patients; in 1 patient, equipment malfunction precluded a basal preoperative measurement.

In addition, in two patients, Doppler color flow mapping recordings were made preoperatively under basal conditions, using a sterile phased array imaging transducer placed on the anterior surface of the heart. The image plane was oriented similarly to the standard long-axis imaging plane to examine the spatial flow dynamics in the left ventricular outflow tract. Color flow mapping was performed approximately 1 to 2 minutes after the rest, premyectomy pressure and continuous wave Doppler recordings, without an obvious interval change in loading conditions.

After the rest premyectomy measurements, in 6 of the 10 patients, an intervention was undertaken before myectomy to record a second set of data points. In three patients whose rest premyectomy gradient was low, isoproterenol was infused to augment the gradient and in three patients, 250 cc of additional blood volume was given for a second premyectomy recording.

In all patients, myectomy was then performed by a transaortic approach, removing a rectangular section of muscle from the hypertrophied septum from just inferior to the aortic valve toward the apex to the most apical extent of the muscular bulge (11,12). After myectomy, weaning from cardiopulmonary bypass and stabilization of the cardiac rhythm and blood pressure, all 10 patients were restudied with simultaneous pressure and velocity measurements at rest. In 7 of the 10 patients, isoproterenol was then infused (to raise the heart rate by 20%) and in 1 patient, phenylephrine was administered, to make a second postmyectomy set of data points during provocation.

Data analysis. Maximal outflow tract velocity was measured from a paper printout of the Doppler velocity spectrum, using the average of three beats. The data selected for analysis were velocity spectra that showed a well-defined envelope, representing clean interrogation of the jet at the smallest flow-limiting orifice along the ultrasound beam. The maximal instantaneous velocity was used to estimate the peak instantaneous gradient by a simplification of the Bernoulli equation. With this method, the effects of viscous friction and flow acceleration are ignored, as is the effect of the relatively low velocity on the left ventricular side of the area of obstruction. Thus, convective acceleration is assumed to be the major contributor to the production of the gradient. The gradient was estimated from four times the square of maximal velocity (17).

Gradients measured by pressure manometers were analyzed using a paper printout of the pressure waveforms, printed on an expanded scale. Three beats were measured and averaged. The instantaneous peak gradient was measured from the maximal left ventricular pressure minus the aortic pressure at that instant.

Statistical analysis. Comparisons of gradient data obtained from pressure transducers and those estimated from Doppler velocities were made using linear regression by the method of least squares. Correlation coefficients and statistical significance were calculated using RS1 data management software (Bolt, Benerak, and Newman) on a Professional 380 microcomputer (Digital Equipment Corporation).

Results

Simultaneous velocity and pressure data. Figure 2 shows an example of the premyectomy pressure and velocity data. On the top, the spectral display shows that the maximal velocity was 4.9 m/s and the calculated gradient by Doppler
DOPPLER ESTIMATED GRADIENT = 96 mmHg

Figure 2. Velocity and pressure data collected simultaneously in a patient with hypertrophic cardiomyopathy before myectomy. The left ventricular (LV) and aortic (AO) pressure recordings and the Doppler recording were printed on separate paper and superimposed for comparison.

INSTANTANEOUS GRADIENT = 88 mmHg

Figure 3. Outflow gradient correlation between peak instantaneous gradients measured invasively and Doppler-derived gradients (n = 33) for the entire study.

Measurement was 96 mm Hg. On the bottom, a simultaneous pressure recording is shown of left ventricular and aortic pressures. The peak left ventricular pressure is 159 mm Hg and the simultaneous aortic pressure is 71 mm Hg. The maximal instantaneous gradient by the invasive measurement is 88 mm Hg. Note that the high flow velocity is sustained throughout the entire duration of left ventricular ejection. It begins at the crossover of the aortic and left ventricular pressure tracings and ends when the pressures come back together. The shape of the Doppler velocity envelope resembles the shape of the systolic area between the two pressure waveforms. Both show a shoulder or inflection point on the rising phase in early systole.

Correlation between maximal left ventricular outflow tract gradient measured by pressure transducers and that estimated by Doppler recording. Figure 3 shows the overall results from pre- and postmyectomy data, both at rest and during interventions. There were 33 data points in the 10 patients, including 9 rest premyectomy data points, 3 isoproterenol infusion premyectomy data points, 10 rest postmyectomy data points, 7 isoproterenol infusion postmyectomy data points and 1 phenylephrine infusion postmyectomy data point. There was an excellent correlation between Doppler-derived left ventricular outflow tract gradient and peak instantaneous gradient measured invasively using pressure transducers. The line of best fit showed an equation of \( y = 0.89x + 12 \), with a correlation coefficient of 0.93 (\( p = 0.0001 \)).

The majority of the data points on Figure 3 are in the low range because more than half of the data were acquired in the postmyectomy setting. In addition, we did not apply an arbitrary lower cutoff point for application of the Bernoulli equation. Therefore, gradients were calculated from velocities that, in some cases, were too low to indicate significant obstruction. Consequently, the low end of the curve shows many data points clustered along the Y intercept. When we examined only those nine data points that were obtained in the rest premyectomy state, the correlation coefficient was still excellent (\( r = 0.98, p = 0.01 \)).

Comparison of improvements in gradient induced by myectomy. In nine patients, simultaneous hemodynamic data and velocity data were available under rest conditions both preoperatively and postoperatively. In all but one patient, the direction of the change in gradient (namely improvement) was similar between the invasive and the Doppler gradient measurements (Fig. 4). In two patients, both with a high gradient measured at preoperative catheterization, the rest intraoperative premyectomy gradient measured in the operating room was low. In one of these, the isoproterenol-induced premyectomy gradient measured in the operating room by both Doppler and pressure transducer recordings increased by more than 100 mm Hg over the rest value.

Changes in left ventricular outflow gradient induced by interventions. Figure 5 shows data from the interventions we introduced in the operating room in these patients. Data are presented as the differences between the gradient
by a flame-shaped band of color that occurs during the mitral systolic anterior motion and emanates from the point of systolic apposition of the mitral valve against the hypertrophied septum. Color flow mapping depicts high velocity flow disturbances as a mosaic of numerous colors due to aliasing (37,38). In this patient, moments earlier, a significant gradient had been recorded by the pressure transducers and a continuous wave Doppler transducer had recorded the magnitude of the high velocity flow in the outflow tract. Thus, whereas continuous wave Doppler recordings estimate the severity of the obstruction, color flow mapping is useful in documenting that the high velocity flow is located at the point of mitral-septal contact.

**Discussion**

**Pressure gradient versus high velocity flow.** This study suggests, first, that true obstruction to left ventricular emptying does exist in hypertrophic cardiomyopathy. This is supported by our simultaneous measurement of pressure gradient and high velocity flow. In particular, the peak instantaneous gradient measured invasively correlates well with maximal velocity using four times the square of the velocity derived by Doppler recording. The fact that these variables (pressure and flow) show patterns very similar to the patterns seen in left ventricular outflow obstruction due to valvular aortic stenosis makes it impossible to invoke artifacts such as catheter entrapment or cavity obliteration.

Second, gradient and velocity show parallel changes in response to interventions. Because the relation between pressure and velocity is maintained during maneuvers that change the dynamics, obstruction must be a reality rather than the gradient merely representing an artifact of the pressure recording.

Third, high velocity flow persists throughout the portion of the cardiac cycle in which the gradient occurs. The left ventricle does eject a portion of its contents early in systole. As soon as the mitral valve approaches the interventricular septum, however, the effective cross-sectional area through which blood is flowing is small. In mid- and late systole, a small amount of blood is ejected through a small effective orifice at high velocity across a significant gradient.

**Controversy regarding the presence of obstruction from previous studies.** The controversy surrounding the presence or absence of outflow obstruction in hypertrophic cardiomyopathy has persisted for the past two decades, despite the remarkable number of investigative methods that have been used to study the disorder. Beginning in the early 1960s, numerous investigators (1,2,39-44) demonstrated the presence of an outflow tract gradient by catheterization techniques. One study (45) included intraoperative measurements of pressure and flow (using electromagnetic techniques) in patients with hypertrophic cardiomyopathy. Although the mechanism was only speculative, the gradient...
Figure 6. Doppler color flow image (left) and artist's drawing (right) showing the distribution of the outflow tract jet emanating from the point where the mitral valve contacts the septum in early systole. OT JET = outflow tract jet; MR = mitral regurgitation; SAM = systolic anterior motion of the mitral valve.

was attributed by many to the presence of outflow tract obstruction. However, in 1964, Hernandez et al. (4) hypothesized that the gradient could be an artifact produced by "a virtually empty ventricle contracting on the catheter tip trapped in small, isolated pockets of blood among the trabeculae." In 1965, Criley et al. (5) found support for this concept, using angiographic data to examine the rapidity of left ventricular emptying, suggesting that the gradient was an artifact of cavity obliteration. In other investigations (2,4,46) rapid early systolic ejection has been noted with a variety of investigative techniques. Goodwin (47-49) also believed that the gradient was not due to true obstruction. Murgo and coworkers (3,50) in 1980 used catheters with micromanometer flow meters located in the ascending aorta to demonstrate rapid early ejection. As recently as 1985, it was suggested (51) that the concept of obstruction is erroneous and has hindered our understanding of hypertrophic cardiomyopathy.

Our study supports the mechanism of obstruction suggested by investigations at the National Institutes of Health (27,44,45,52), and summarized in a recent review by Wigle et al. (36). In comparing our results with previously reported studies of hypertrophic cardiomyopathy, it is important to differentiate between measurements of linear velocity (distance/time) and volumetric flow (volume/time). In patients with obstruction, the left ventricle does eject a portion of its contents through the outflow tract early in systole, but this unimpeded flow precedes the onset of obstruction. As soon as the mitral valve abuts against the interventricular septum, the effective cross-sectional area through which blood is flowing becomes quite small. In mid- and late systole after mitral-septal contact, blood is ejected at high velocity under a significant gradient. Thus, obstruction does not exist before mitral-septal contact, but it does exist after mitral-septal contact.

Shabetai (53) suggested that "the systolic pressure gradient, developing mostly after the ventricle has successfully ejected too much of its contents, can hardly be construed as obstruction in the usual sense of the term." That high velocity flow could be recorded in all of our patients with a significant gradient documents the presence of obstruction at those times. That obstruction is present during any portion of the cardiac cycle makes it incorrect to say that obstruction does not exist. In addition, Wigle et al. (54) showed that patients with a higher gradient have a proportionately longer left ventricular ejection time. This suggests that energy is being expended by the left ventricle to overcome obstruction. Furthermore, as the gradient becomes higher, a greater and greater proportion of the stroke volume is ejected after the onset of the gradient (16,34,36,44).

Previous Doppler studies of hypertrophic cardiomyopathy. Most previous investigations using Doppler echocardiography have used pulsed (range gated) Doppler ultrasound, which has great difficulty recording high velocity jets. Integrating the previously described patterns with the results of this study involves an appreciation of the level at which velocity was interrogated and the time course of both the effective cross-sectional area and the flow velocity at each level. Several investigators (22,27,28) reported on pulsed Doppler recordings of flow velocity in the ascending aorta and described early peak velocities of 1.5 to 2.2 m/s followed by a mid-systolic reduction in velocity. This pro-
vides an understanding of the activity above the level of obstruction where the cross-sectional area of flow is large and changes very little during systole (55). The velocity patterns (distance/time) in the ascending aorta are representative of the time course of the volumetric flow (volume/time) of ventricular ejection. The velocity profiles at this level resemble those of Mugro et al. (3), whose electromagnetic flow manometer was also in the ascending aorta, 9 cm from the catheter tip. Thus, ascending aortic velocity profiles are not the same as the high velocity flow at the level of obstruction that can be recorded with continuous wave Doppler ultrasound.

Hatle and Yock and their coworkers (17,29,30) reported on high velocity profiles recorded with continuous wave Doppler ultrasound from the cardiac apex in ambulatory patients with hypertrophic cardiomyopathy. The shapes of their outflow tract recordings are similar to those in our data, although inverted, with the outflow velocity directed away from the transducer. The envelope of these continuous wave Doppler recordings is representative of events occurring at the limiting orifice, the point of obstruction to left ventricular outflow.

The contribution of the color flow images (Fig. 6) is to document that the location of the high velocity jet is the point of mitral-septal contact. At this level, M mode and two-dimensional echocardiography and angiography demonstrate a rapidly changing outflow tract area as the mitral valve moves anteriorly during early systole. Although the area of the outflow tract in these patients in early systole is small compared with that of normal patients, it is large compared with the effective flow area after mitral-septal contact. Concomitantly, the flow velocity at this level increases steadily and progressively to a peak in mid-systole, followed by a progressive decline in velocity to the end of systole. The contour of this velocity parallels the contour of the difference between left ventricular cavity pressure and ascending aortic pressure (Fig. 2). Both the left ventricular pressure curve and the outflow tract velocity envelope demonstrate an inflection point coinciding with the peak of the aortic percussion wave. This time point represents the onset of obstruction and occurs immediately before mitral-septal contact (16,29,34). The timing and characteristic "dagger" shape of the outflow tract velocity distinguishes it from other signals that can be recorded from the cardiac apex, including mitral regurgitation and midventricular flow at the papillary muscle level (17,29,56).

The potential to measure the outflow tract gradient noninvasively. Despite numerous previous descriptions of Doppler-derived velocity recordings in this condition (17,22–30), no previous author has substantiated a relation between the outflow tract gradient recorded simultaneously with recordings of flow velocity at the point of the obstruction. The reason for this is probably the difficulty in performing good quality Doppler studies in the cardiac catheterization laboratory, in light of the specifics of patient positioning and cooperation that are required for accurate measurement of the outflow tract velocity. The implications of this correlation are substantial regarding the feasibility of noninvasively quantitating the outflow tract gradient in hypertrophic obstructive cardiomyopathy using maximal velocity measurements by continuous wave Doppler echocardiography with the Bernoulli equation.

Several factors should be considered before using Doppler-derived gradients to make decisions that are currently made on the basis of invasive data. In particular, our data illustrate the well known dependence of the outflow tract gradient on loading conditions. The gradient can change markedly from minute to minute. Therefore, nonsimultaneous comparisons are not likely to correlate as well as our data. In addition, there may be difficulty in obtaining quality recordings of left ventricular outflow tract flow velocity in some ambulatory patients, causing underestimation of the true gradient; or confusion with the mitral regurgitation signal recorded from the apex, causing overestimation of the true gradient. Last, in hypertrophic cardiomyopathy, as in other obstructive lesions (18,57), the peak instantaneous gradient may exceed the peak to peak gradient that is reported from a pullback catheter technique. In Figure 2, this represents a discrepancy of 11 mm Hg between the maximal aortic pressure and the mid-systolic aortic pressure.

Conclusion. Continuous wave Doppler echocardiographic measurement of outflow tract velocity in hypertrophic cardiomyopathy can be used to accurately estimate the magnitude of the peak instantaneous outflow tract pressure gradient. This study highlights the dynamic nature of the outflow tract gradient and its dependence on loading conditions. Our data support the hypothesis that true obstruction is present in patients with hypertrophic cardiomyopathy who have a significant outflow tract pressure gradient.

Addendum

Subsequent to initial submission of this manuscript, we have extended this study to include 20 patients, with essentially no change in the results. The overall comparison of 56 Doppler-derived gradients and gradients derived from pressure transducers, equivalent to Figure 3, revealed good correlation (r = 0.94, y = 0.96x + 8, p = 0.00001).

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