Noninvasive Prediction of Transvalvular Pressure Gradient in Patients with Pulmonary Stenosis by Quantitative Two-dimensional Echocardiographic Doppler Studies

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SUMMARY Recent studies suggest that maximal Doppler velocities measured within the jets that form downstream from stenotic valves can be used to predict aortic valve gradients. To test whether the Doppler method would be useful for evaluation and management of pediatric patients with right ventricular outflow obstruction, we evaluated pulmonary artery flow before catheterization in 16 children with pulmonary valve stenosis. We used a 3.5-MHz, quantitative, range-gated, two-dimensional, pulsed, echocardiographic Doppler scanner with fast Fourier transform spectral output and a 2.5-MHz phased array with pulsed or continuous-mode Doppler. Peak systolic pulmonary artery flow velocities in the jet were recorded distal to the domed pulmonary valve leaflets in short-axis parasternal echocardiographic views. The pulsed Doppler scanner, because of its limitations for resolving high velocities, could quantify only the mildest stenoses; but, especially with the continuous Doppler technique, a close correlation was found between maximal velocity recorded in the jet and transpulmonary gradients between 11 and 180 mm Hg. A simplified Bernoulli equation (transvalvular gradient = 4 × [maximal velocity]²) proposed by Hatle and Angelsen could be used to predict the gradients found at catheterization with a high degree of accuracy (r = 0.98, SEE = ± 7 mm Hg). Our study shows that recording of maximal Doppler jet velocities appears to provide a reliable measure of the severity of valvular pulmonary stenosis.

ALTHOUGH the clinical diagnosis of pulmonic stenosis is usually not difficult, mild pulmonic stenosis must occasionally be differentiated from aortic stenosis, ventricular septal aneurysm, or even functional flow murmurs. Additionally, clinical estimation of the severity of pulmonic stenosis can be difficult, especially in postoperative and very young patients.¹

Noninvasive echocardiographic diagnosis of pulmonic stenosis is sometimes difficult. Weyman and associates² reported their experience with M-mode echocardiographic techniques and showed that a deep pulmonary "a" wave occurred in patients with pulmonary stenosis; however, false-negative diagnoses are common and no quantitation of severity has been possible using this observation. Two-dimensional echocardiography images the right ventricular outflow tract and pulmonic valve more completely,³ aiding in the noninvasive detection of significant pulmonic stenosis, especially when severe, but does not appear to allow prediction of the severity of stenosis or the transvalvar gradient.

Doppler echocardiography has been reported as a technique for quantifying the severity of stenotic valvar lesions.⁴ Hatle and co-workers³ suggested that a simplified Bernoulli equation could be used to relate transvalvular aortic gradient to peak Doppler velocity measured at the jet distal to valve orifices. The purpose of this prospective study was to assess the use of two-dimensional echocardiographic Doppler techniques for providing noninvasively derived clinically useful information about the severity of pulmonary stenosis.

Methods

Patients

Sixteen children, ages 1 month to 16 years (mean 4.3 ± 2.5 years) (± SEM), 13 with clinically suspected isolated valvular pulmonic stenosis and three with minor pulmonary valve abnormalities (documented by subsequent angiography) accompanying atrial septal defects, were studied. Two of the 16 patients had undergone valvulotomy (neither of these had significant pulmonary insufficiency), and two patients were studied by Doppler pre- as well as postoperatively. All patients underwent cardiac catheterization within 12 hours of the ultrasonic study. Three patients were studied after premedication for catheterization; three patients were studied in the catheterization laboratory, and pressure and Doppler measurements were performed sequentially. During catheterization, after standard light sedation, pressure gradients were recorded during pullback across the pulmonic valve using an end-hole, fluid-filled catheter (table 1); cardiac output determined at catheterization in six patients was normal.

Ultrasonic Method

Ultrasonic examinations were performed with the patients resting quietly in a supine position. Two commercially available two-dimensional echocardiographic Doppler systems were used in each patient to see if results were in agreement within the velocity ranges over which their capabilities overlap. The first system (Electronics for Medicine/Honeywell) is a 3.5-
MHz mechanical sector scanner with a single-element transducer mechanically oscillated through a 30–75° arc. The transducer could be stopped along any line within the image and a sample volume could be positioned at any depth along that line for range-gated Doppler velocimetry. The size of the sample volume could be adjusted to have an axial length of 2 mm to 2 cm. The Doppler shift was detected only from the region determined by the selected sample volume position. Sample volume width at a depth of 4 cm from the transducer (−6 db from peak) was determined to be ±2 mm in a water tank testing apparatus. Only pulsed Doppler was available with this device. The Doppler signals were sampled at a rate (pulse repetition frequency) of 13,000 samples/sec when the signal was obtained from a depth less than 6 cm, resulting in a maximal nonambiguously detectable velocity of 143 cm/sec, and they were sampled at 7800 samples/sec at a depth of 6–10 cm with a maximal detectable velocity of 85 cm/sec. Doppler output was available as an audio signal as well as a spectral display obtained by fast Fourier transform spectral analysis performed 200 times/sec to provide the quantitative velocity wave forms. The Doppler wave forms, the real-time two-dimensional image, and the simultaneous lead II ECG (fig. 1) were displayed on a monitor and recorded on videotape or on a strip-chart recorder at a paper speed of 50–100 mm/sec.

The second ultrasound scanner contained a Pedof (Vingmed A/S) Doppler system, which provided both pulsed and continuous-wave Doppler outputs from a 2.5-MHz phased-array along with simultaneous two-dimensional echocardiographic imaging (Irex System 3A). Doppler sampling was performed at an interrogation frequency of 2 MHz. Two-dimensional echocardiographic images and Doppler flow curves were obtained with the same transducer array, but only the central image line could be interrogated for either pulsed or continuous Doppler sampling. In the pulsed mode, to a depth of 6 cm, the maximal unambiguously detectable velocity is 160 cm/sec (pulsed Doppler sample volume size = 7 × 7 mm at 4–6 cm depth), but once located, a stenotic jet could be sampled in continuous Doppler mode with or without simultaneous imaging up to a maximal velocity of 8 m/sec (800 cm/sec). In the continuous mode, no specific depth gate is established, and all velocities along the central line of sight are processed for velocity determination. Doppler outputs from this system were available as an audio signal, a spectral output sampled every 20 msec with spectral analysis performed by a CHIRP Z algorithm and as an analog display of the mean and maximal detected velocities. These analog outputs required manual gain adjustment to maximize the velocities recorded while maintaining a recognizable wave form where both the maximal analog wave form displayed upward and the mean analog wave form displayed downward returned toward each other and close to the zero line in diastole (fig. 2). The analog display, especially, was quite sensitive to the low velocities in turbulent flow, and maximal velocities could be obtained by finding the high-pitched whistling signal of the jet

<table>
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<th>Maximal velocity (cm/sec)</th>
<th>Doppler gradient (mm Hg)</th>
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<td>Restudied after valvotomy: velocity = 217 cm/sec; predicted p/o gradient = 19 mm Hg; intraoperative gradient = 15 mm Hg</td>
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*Study performed in catheterization laboratory in conjunction with pressure measurement.
Abbreviations: ASD = atrial septal defect; H + I = velocities quantifiable and determined with both the Honeywell and the Irex instruments; PI = pulmonary valvular insufficiency; p/o = postoperative.
and then using the 600-Hz filter to minimize the contribution of the lower velocities. If the analog and spectral maximal velocities were within 10% of each other (13 studies), they were averaged. If the difference between the analog and spectral maxima was greater than 10% (three studies), only the spectral velocity was used (fig. 3). In these three patients, despite clear spectral recordings peaking at > 300 cm/sec, the maximal analog velocity trace could not be adjusted to peak at > 250 cm/sec. The two-dimensional image, spectral and analog Doppler outputs, and the simultaneous lead II ECG were recorded on videotape or hard copy at a paper speed of 50–100 mm/sec.

Ultrasonic examinations began with two-dimensional imaging of the right ventricular outflow tract, pulmonic valve, main pulmonary artery, and bifurcation from a parasternal short-axis view. The Doppler range gate was placed in the center of the pulmonary artery distal to the domed pulmonic valve leaflets in line with the apparent orifice. The maximal velocity was found and recorded by changing the position of the sample volume within the main pulmonary artery and changing the position and angulation of the transducer until the highest frequency audio signals were identi-

FIGURE 1. (A) A cursor showing sampling position in the pulmonary artery (pa) distal to a stenotic pulmonic valve. (B) A pulsed Doppler flow curve from a patient with mild pulmonic stenosis (PS) studied retrospectively before the initiation of this study. The patient's record shows mild elevation of pulmonary flow velocities and some spectral broadening. Peak velocity is 115 cm/sec. Ao = aorta; S = sample volume.

FIGURE 2. Continuous-wave Doppler record of patient 15, who had moderately severe pulmonic stenosis (PS). Peak velocity is 340 cm/sec, as shown on both the spectral and the analog maximal velocity traces. In these records, flow away from the transducer is shown as downward, but the maximal velocity in the upper analog trace is always shown upward. The calibration interval for the spectral trace (lower) is 2 m/sec; the calibration for the analog waveforms (upper) is 1 m/sec. Maximal velocity is determined from both the analog as well as spectral records, as discussed in the text.
FIGURE 3. Spectral Doppler record from patient 13, 10 years after valvulotomy performed in infancy, who had severe residual pulmonary stenosis (PS); the tracing is similar to figure 2, except that no analog trace is recorded. Peak systolic velocity is 500 cm/sec. Passage of the pulmonary valve leaflets through the continuous-wave Doppler beam produces opening and closing click artifacts on the record.

fied and the highest maximal systolic velocity was recorded. If this recording position resulted in a sampling angle (the angle between the assumed direction of flow and the Doppler sampling direction) that was not 0°, i.e., not parallel to the apparent direction of flow, then the angle between the direction of sampling and the estimated angle of flow was calculated from a stop-frame image with a protractor, and the correction was applied to the Doppler velocity equation 

\[ V = \frac{\Delta F}{2F_0 \cos \theta} \]

where \( \Delta F \) = Doppler frequency shift (in kHz), \( V \) = the velocity of sound (1540 m/sec), \( F_0 \) = the sampling frequency (3.5 MHz in the Electronics for Medicine/Honeywell, 2 MHz for Doppler in the Irex), and \( \theta \) = the angle between flow and sampling. Angle correction was required in only four patients (all four angles <20°). The angle correction was performed automatically by the Irex system. When an angle cursor was placed, the system automatically readjusted the calibration factors. For Honeywell records, the correction was applied by entering the angle into the same computerized graphics analyzer (Numonics) used to measure the peak velocities. No correction was applied for the angle between sampling and flow in the elevational or azimuthal plane, i.e., obliquity of the jet to the sampling plane, because it could not be assessed and because flow was maximized as well as possible by fine positional changes of the elevational plane. The recorded peak systolic flow velocities from two or three consecutive beats were converted to transvalvular gradients using the simplified Bernoulli equation

\[ VG = 4V^2 \]

where \( VG \) = valvular gradient (mm Hg) and \( V \) = peak Doppler velocity (m/sec). The simplification of the Bernoulli relationship considers only the convective acceleration of blood passing through the stenotic orifice. It neglects flow acceleration as the valve opens and viscous friction, which is minimal in the central lumen of the jet where the velocity profile is flat.

All patients were studied with both instruments. In only three patients, however, were velocities quantifiable without ambiguity using the pulsed Doppler Honeywell device (i.e., velocities <143 cm/sec); in these patients, the two instruments gave estimates within 5% of each other. In the 13 other patients, the Honeywell study verified velocity greater than the Nyquist frequency (equivalent to 143 cm/sec) and the Irex continuous-wave Doppler instrument was used to quantify the maximal velocity.

Control Group

Our previously reported control group of 25 normal children had a mean systolic peak velocity of 72 ± 3.4 cm/sec (± SEM) recorded in the pulmonary artery and a 12-db spectral width of <20 cm/sec when evaluated under similar conditions. Their records provided a comparison to those of the children with pulmonic stenosis.

Statistical Analysis

Maximal velocities were measured by two record readers, each blinded to the results of catheterization. These were always within 10% of each other, and so values were averaged. Correlation coefficients for linear regression analysis were calculated comparing maximal Doppler velocity and derived Doppler valve gradients to actual gradients obtained at cardiac catheterization.

Results

All patients underwent successful Doppler examination for recording of transpulmonic maximal jet velocity. Variable degrees of thickening and abnormal valve motion with doming were detected in all patients by real-time, two-dimensional imaging, but were not quantified. The results are summarized in table 1. All Doppler pulmonary artery flow curves in the pulmonic stenosis patients demonstrated spectral broadening (>30 cm/sec peak systolic spectral width) (fig. 1). Additionally, increased pulmonary artery flow velocities were recorded in all patients (mean peak systolic velocity of 279 ± 38.3 cm/sec compared with normal peak systolic pulmonary artery velocities of 72 ± 3.4 cm/sec in the control group). The three patients whose velocities were quantifiable with both systems had peak velocities within 5% of each other. All other patients had peak velocities beyond the quantification capabilities of the pulsed Doppler system. Peak Doppler flow velocities (r = 0.94, SEM = ± 51 cm/sec), as well as the
derived gradients calculated with the simplified Bernoulli equation \( r = 0.98, \text{ SEE} = \pm 6.5 \text{ mm Hg} \), correlated very well with the gradients measured at cardiac catheterization (figs. 4 and 5).

**Discussion**

Our study indicates that two-dimensional echo Doppler techniques can accurately localize poststenotic transvalvular pulmonary flow jets and estimate the severity of pulmonic stenosis. This capability should be important since gradient determination has previously required cardiac catheterization. Noninvasive techniques, particularly two-dimensional echocardiography and Doppler techniques, have provided some diagnostic information in patients with pulmonic stenosis, but have not allowed quantification of the severity of the lesion. Electrocardiography is still useful for defining children at risk for significant pulmonic stenosis by identifying those with right ventricular hypertrophy, but is of limited value in newborns and in postoperative patients.

Only qualitative descriptions of Doppler results have been reported for patients with pulmonic stenosis,\(^{10, 11}\) probably because of the nonquantitative nature of older Doppler systems, which only had nonlinear, zero crossing meter-based, time-integral histography as a wave form output. Additionally, accurate and objective determination of pulmonary artery velocities also required pulmonary artery imaging in order to accurately sample the pulmonary artery at a known angle to transvalvular flow. Quantitative information obtained from the Doppler systems used in this study, and particularly the capability of one of the devices to record continuous-wave Doppler from a specific direction determined from within the two-dimensional image, provided a method of quantifying flow within even very high velocity poststenotic jets (e.g., 675 cm/sec).

Pulsed Doppler techniques combined with two-dimensional echocardiographic imaging permit very localized flow sampling, but the pulsing used to achieve range gating, even at relatively high pulse repetition frequencies (10 times those used in M-mode echocardiography) limits its capacity for detecting very high velocities unambiguously. The continuous-mode technique is limited, in that it samples flow throughout the entire depth of the selected image line. However, because the signal is not limited in repetition rate of sampling, it appears capable of detecting the velocities generated even in severe stenotic lesions. In the pulmonary artery sampling technique that we used, even though all backscattered velocity shifts obtained along the direction of sampling were processed, those originating from locations other than the pulmonary artery apparently did not significantly affect the velocity attributed to the flow jet. In our sampling location, lower velocities from the proximal right ventricular outflow tract, and other flows that were lower in velocity and at significant angles to the sampling direction, such as in the descending aorta or left atrium behind the pulmonary artery, were present in the signal but were not added in the peak velocity. The peak detectable velocity was therefore unaltered by the presence of other velocities within the beam.

Although we have not studied any patients with concomitant ventricular septal defect and pulmonic stenosis in whom higher than normal velocities of flow may already exist beneath the pulmonary valve, the gradients in our patients with atrial septal defects and increased flow crossing the valve (all Qp/Qs > 2:1) were not systematically overestimated by the method; in fact, there appeared to be a general underestimation of gradients across the very minimally stenotic valves. Our results are compatible with the work of Holen et al.,\(^{12}\) who showed that the pressure drop was underestimated in mitral stenosis when velocities were low. This probably occurs because when velocities are low, the accelerational and viscus terms in the Bernoulli equation are significant compared with the convective velocities and other investigators have used.\(^{5, 7, 12}\) and both of these accelerational and viscous contributions are neglected when the simplified Bernoulli

**Figure 4.** Linear regression analysis of maximal Doppler velocities and catheterization gradients.

**Figure 5.** Linear regression analysis of Doppler-predicted transvalvular gradients calculated using the simplified Bernoulli equation and gradients obtained at catheterization in the 16 patients with pulmonic stenosis.
equation is used. When the method is used properly, therefore, it is possible to underestimate the transvalvar gradient but difficult to overestimate it unless an inappropriate angle correction were to be applied.

We recently studied six postoperative patients who had significant pulmonary insufficiency. In these patients, the increased volume of flow across the pulmonary valve did not impede our ability to predict the transvalvar gradient if the peak systolic velocity proximal to the valve was close to normal.

Because the Doppler-predicted gradient is a function to the second power of the maximal velocities, one might question whether linear regression analysis is the best technique for evaluating the relationship between maximal velocity and catheterization gradient as shown in figure 4. It would be expected that a curved fit to a power of approximately 0.5 would produce the best correlation of maximal velocity to catheterization gradient. Indeed, when evaluated by a least-squares curved-fitting program, the best curve fit was obtained to a power function of (catheterization gradient)\textsuperscript{0.68}. Fitting the data to the power function did not improve the correlation coefficient, which was still 0.94, but it did reduce the SEE for the regression relationship to ± 48 cm/sec. Similar improvement of the data shown in figure 5, the Doppler-predicted gradient compared with the catheterization gradient, could not be obtained by more sophisticated regression analysis techniques.

In some patients, finding the highest peak velocities within the pulmonary artery was difficult. In these cases, variation in the position of the sample volume, as well as gain manipulation, was necessary until the clearest and highest pitched audible jet was found and the highest velocity spectral record was obtained. Usually, the examination to locate and record the jet took 15–20 minutes.

In conclusion, our study demonstrates that two-dimensional echocardiographic Doppler, especially with continuous Doppler sampling, is a valuable technique for assessing the severity of valvular pulmonic stenosis in children.

References
Noninvasive prediction of transvalvular pressure gradient in patients with pulmonary stenosis by quantitative two-dimensional echocardiographic Doppler studies.

Circulation. 1983;67:866-871
doi: 10.1161/01.CIR.67.4.866

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