Noninvasive evaluation of pulmonary hypertension by a pulsed Doppler technique

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ABSTRACT We used a pulsed Doppler technique to examine the flow velocity pattern in the right ventricular outflow tract in 33 adults. In the patients with normal pulmonary artery pressure (mean pressure < 20 mm Hg, 16 patients), ejection flow reached a peak level at midsystole (137 ± 24 msec, mean ± SD), producing a domelike contour of the flow velocity pattern during systole. In contrast, the flow velocity pattern in patients with pulmonary hypertension (mean pressure ≥ 20 mm Hg, 17 patients) was demonstrated to accelerate rapidly and to reach a peak level sooner (97 ± 20 msec, p < .01); in 10 of the pulmonary hypertensive patients a secondary slower rise in flow velocity was observed during a deceleration, resulting in the midsystolic notching. The time to peak flow (acceleration time, AcT) and right ventricular ejection time (RVET) were measured from the flow velocity pattern. Either AcT or AcT/RVET decreased with increase in mean pulmonary artery pressure, and a very high correlation (r = .90) was found between AcT/RVET and log_{10} (mean pulmonary artery pressure). The use of this technique permitted the noninvasive estimation of the pulmonary artery pressure.


NONINVASIVE evaluation of pulmonary hypertension has been an important clinical problem for many years. The presence of pulmonary hypertension has been assessed by abnormalities in heart sounds,1 in electrocardiographic tracings, or in chest x-rays,2 but to date, the accurate measurement of the pulmonary artery pressure requires the use of cardiac catheterization procedures. The development of echocardiographic techniques has allowed the investigation of pulmonic valve motion,3 which represents some characteristic abnormalities associated with pulmonary hypertension, such as rapid opening slope in systole,4,5 attenuation or absence of the “a” dip,4,6 prolongation of the ratio of right ventricular prejection period (RPEP) to right ventricular ejection time (RVET),5,7 and midsystolic semiclosure of pulmonic valve.4,6 A recent experimental study8 emphasized that these abnormalities of the pulmonic valve motion were determined by abnormal flow changes in the pulmonary artery. However, flow characteristics with regard to pulmonary artery pressure either in the pulmonary artery or in the right ventricular outflow tract have not been successfully studied in man.

Our objectives were to study the blood flow characteristics in the right ventricular outflow tract in patients with pulmonary hypertension by a puls ed Doppler technique9-11 and to develop an index that would permit quantitative evaluation of pulmonary hypertension by noninvasive methods.

Materials and methods

Patient selection. Thirty-eight patients admitted for diagnostic catheterization were examined by a pulsed Doppler technique. Five patients were excluded in whom Doppler recordings of flow velocity in the right ventricular outflow tract were not satisfactorily obtained because of poor penetration of ultrasound through the chest wall. Doppler examination was performed 18 to 24 hr before cardiac catheterization in 23 patients, within 1 week in four patients, and simultaneously with right-sided pressure recordings in six patients.

The study population comprised 22 female and 11 male subjects, ranging in age from 15 to 66 years (average 44). Eighteen patients had predominant mitral valve disease, seven had atrial septal defect, five had ischemic heart disease, two had primary pulmonary hypertension, and one had predominant aortic valve disease. Twenty patients were in sinus rhythm and the remainder had atrial fibrillation. The mean pulmonary artery pressures (MPAPs) ranged from 6 to 88 mm Hg. Pulmonary hypertension
was defined as MPAP greater than 20 mm Hg. There were 16
patients with MPAP in the 6 to 19 mm Hg range (the
group without pulmonary hypertension), eight in the 20 to 39 mm Hg
range (the group with mild pulmonary hypertension), and nine
in the 40 to 88 mm Hg range (the group with severe pulmonary
hypertension).

**Pulsed Doppler techniques.** The pulsed Doppler examina-
tions were performed with a directional pulsed Doppler flow-
mete11 (Model EUD 5; Hitachi Co., Ltd.) combined with an
electronic beam sector-scanning echocardiograph (Model EUB
10-A; Hitachi Co., Ltd.), which made it possible to locate the
sample site by monitoring simultaneous display of two-dimen-
sional echocardiograms on a cathode ray tube. The pulsed
Doppler flowmeter operated with a carrier frequency of 2.5
MHz and a pulse repetition frequency of either 5 kHz or 10 kHz,
with a disc-shaped sample volume 1 mm in depth with a radius
of 3 mm. The Doppler output was analyzed by a sound spec-
trogram (Lion SG-07). The flow velocity away from the
transducer was displayed above the baseline, and that toward
the transducer was displayed below the baseline on the sound spec-
trogram.

The technique of examination consisted of placing the trans-
ducer for the Doppler flowmeter in the second or third intercost-
al space along the left sternal border, with the sonar beam
aimed laterally and superiorly. The sample volume was care-
fully positioned just below the pulmonic cusp in the right ventricu-
lar outflow tract on the two-dimensional echocardiograms (fig-
ure 1).

**Analysis of data.** The Doppler flow velocity pattern, ob-
tained by the sound spectrograph, includes various Doppler
frequencies simultaneously, even in a small region such as that
measured in this study. Therefore the envelope of the flow
velocity pattern, i.e., instantaneous maximal velocity, was used
for quantitative analysis. The highest discernible frequencies
were traced by hand. The RVET was defined as the time (msec)
from the onset of ejection to that of zero flow. The time to peak
flow velocity (acceleration time [AcT] in milliseconds) was
defined as the interval between the onset of ejection and peak
flow velocity. The time to peak flow velocity was also ex-
dressed as a ratio to the total duration of the systolic ejection
(time (AcT/RVET)). All measurements from pressure recordings
and flow velocity patterns are presented as the average of five to
11 (mean seven) consecutive cardiac cycles.

AcT and AcT/RVET were determined in seven patients by
one observer on two occasions (intraobserver variability). An-
other observer independently performed the determination for
the same seven patients (interobserver variability). All observ-
ers were blinded to each other's results and to the results of
cardiac catheterization. AcT correlated well between intraob-
server and interobserver determinations, with a correlation co-
efficient of .99 and mean absolute differences between observa-
tions (expressed as a percentage of the first observer's first
observation) of 1.8% (intraobserver) and 6.1% (interobserver).
Good correlations were also obtained for AcT/RVET, with a
 correlation coefficient of .99 and mean absolute differences
between observations of 1.5% (intraobserver) and 6.0% (inter-
observer).

**Cardiac catheterization.** Cardiac catheterization was car-
ried out with a standard technique.12 Right-sided pressure deter-
minations were obtained with use of fluid-filled catheters con-
ected to a P23Db Statham strain gauge. In two patients with
pulmonary hypertension, two catheter-tipped No. 5F micro-
manometers (Model PC-350a; Miller Instruments, Inc.) were
introduced into the pulmonary arterial trunk and the right ventri-
cle to obtain the pulmonary artery and right ventricular pres-
sures and Doppler flow velocity simultaneously.

All values were expressed as mean ± SD. Comparisons
among groups were performed by analysis of variance and Stu-
dent's t test, and linear regression analysis was carried out by
the method of least squares.

**Results**

**Flow velocity patterns in the right ventricular outflow
tract.** A representative recording of flow velocity in the
right ventricular outflow tract obtained in a patient
without pulmonary hypertension is shown in figure 2.
In all 16 patients without pulmonary hypertension,
the pattern of ejection flow velocity exhibited a dome-
like contour with peak velocity in mid systole. In 17

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**FIGURE 1.** Two-dimensional echocardiogram (left) and its schematic (right) showing the direction of ultrasonic Doppler beam
(white broken line in the left panel and black broken line in the right panel) and the sample site (arrows) in the right ventricular
outflow tract just below the pulmonic cusp. RA = right atrium; RV = right ventricle; PA = pulmonary artery; PV = pulmonic
valve.
patients with pulmonary hypertension, the pattern of ejection flow velocity changed in one of two patterns. The first, characterized by a rapid acceleration of flow velocity with an earlier peak than that in the pulmonary normotensives, resembled a triangle in shape (figure 3, *B*). The second consisted of an abnormally rapid rise in flow velocity to a peak level, followed by a rapid deceleration, followed in turn by a secondary slower rise to form a notching (figure 3, *A*). The midsystolic notching was observed in eight of 17 patients with

**FIGURE 2.** Representative flow velocity pattern in the right ventricular outflow tract in a patient without pulmonary hypertension, demonstrating the domelike contour in systole, with a peak level in midsystole.

**FIGURE 3.** Flow velocity patterns in the right ventricular outflow tract in pulmonary hypertension. *A*, Flow velocity pattern in a patient with moderate pulmonary hypertension (mean pressure 38 mm Hg). Note the midsystolic notching in flow velocity during ejection. In this case, bidirectional broadening spectrum (arrow) of Doppler frequency during early diastole indicates complication of pulmonary regurgitation, which has been confirmed by pulmonary arteriography. *B*, Flow velocity pattern in a patient with severe pulmonary hypertension (mean pressure 68 mm Hg), showing a rapid acceleration and deceleration without midsystolic notching. It should be noted that both patients show a rapid acceleration and reach a peak level sooner.
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pulmonary hypertension, and the former pattern was observed in seven patients. In the two other patients with pulmonary hypertension and atrial fibrillation, both patterns were observed in the sequence of Doppler recordings. Figure 4 illustrates simultaneous recordings of pulmonary artery and right ventricular pressures and flow velocity in the right ventricular outflow tract during seven consecutive cardiac cycles in one of the patients exhibiting both patterns. The flow velocity pattern varied from beat to beat in the appearance of midsystolic notching and its configuration. There was no significant ejection flow when right ventricular pressure did not exceed pulmonary artery pressure. The flow velocity pattern with midsystolic notching was observed in a beat with a long preceding RR interval, while midsystolic notching was not observed after a shorter RR interval.

Relationships between Doppler indices, AcT and AcT/RVET, and pulmonary artery pressure. The detailed observation of the quantitative analysis are summarized in Table 1. No significant difference in heart rate was observed between the 16 patients without pulmonary hypertension and the 17 patients with pulmonary hypertension (78 ± 22 vs 66 ± 12 beats/min), while normal RVET was shortened in the patients with pulmonary hypertension (269 ± 48 vs 304 ± 38 msec; p < .01). Normal values of AcT (137 ± 24 msec) were greater than 80 ± 23 msec for the 17 patients with pulmonary hypertension (p < .01). The ratio of AcT/RVET was significantly reduced in the patients with pulmonary hypertension compared with that in the patients without pulmonary hypertension (0.30 ± 0.06 vs 0.45 ± 0.05, dimensionless; p < .01).

AcT and the ratio of AcT/RVET were compared with MPAP by means of linear regression analysis, respectively (figure 5, left, and figure 6, left). There

TABLE 1
Summary of findings obtained by cardiac catheterization and pulsed Doppler examination

<table>
<thead>
<tr>
<th>MPAP (mm Hg)</th>
<th>≤19</th>
<th>20–39</th>
<th>≥40</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>16</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>46 ± 15a</td>
<td>48 ± 10</td>
<td>47 ± 9</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>12/4</td>
<td>5/3</td>
<td>5/4</td>
</tr>
<tr>
<td>MPAP (mm Hg)</td>
<td>13 ± 3</td>
<td>27 ± 6b</td>
<td>56 ± 14b</td>
</tr>
<tr>
<td>PASP (mm Hg)</td>
<td>23 ± 6</td>
<td>41 ± 9b</td>
<td>83 ± 21b</td>
</tr>
<tr>
<td>PADP (mm Hg)</td>
<td>8 ± 3</td>
<td>19 ± 5b</td>
<td>38 ± 8b</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>66 ± 12</td>
<td>69 ± 9</td>
<td>86 ± 26</td>
</tr>
<tr>
<td>RVET (msec)</td>
<td>304 ± 38</td>
<td>284 ± 37</td>
<td>256 ± 53c</td>
</tr>
<tr>
<td>AcT (msec)</td>
<td>137 ± 24</td>
<td>97 ± 20b</td>
<td>65 ± 14b</td>
</tr>
<tr>
<td>AcT/RVET</td>
<td>0.45 ± 0.05</td>
<td>0.34 ± 0.05b</td>
<td>0.26 ± 0.02b</td>
</tr>
</tbody>
</table>

PASP = pulmonary arterial systolic pressure; PADP = pulmonary arterial diastolic pressure; HR = heart rate.

aValues are mean ± SD.

Statistical comparisons (with the group without pulmonary hypertension): b p < .01; c p < .05.
FIGURE 5. Time to peak flow velocity (AcT) is plotted against MPAP in all 33 patients studied. **Left.** AcT vs MPAP. The correlation coefficient is −.82, and the relationship between AcT and MPAP appears to be curvilinear. **Right.** AcT plotted against $\log_{10}(\text{MPAP})$ with resultant improvement in the correlation coefficient to −.88. The relation between the variables now appears more linear, and the linear regression equation is $\log_{10}(\text{MPAP}) = -0.0068(\text{AcT}) + 2.1$. TR = tricuspid regurgitation; PH = pulmonary hypertension.

was significant correlation between these values, with a correlation coefficient of −.82 for AcT vs MPAP and −.85 for AcT/RVET vs MPAP, respectively. There was significant deviation from a straight line in the points with higher pulmonary artery pressure, with the curve resembling a logarithmic function. For this reason, when AcT was compared with $\log_{10}(\text{MPAP})$ (figure 5, right) a marked improvement in the correlation coefficient to −.88 was obtained. The regression equation for this relation was

$$\log_{10}(\text{MPAP}) = -0.0068(\text{AcT}) + 2.1$$

and was significant at $p < .0001$. When AcT/RVET was compared with $\log_{10}(\text{MPAP})$ (figure 6, right) the correlation coefficient was −.90. The regression equation was

$$\log_{10}(\text{MPAP}) = -2.8(\text{AcT/RVET}) + 2.4$$

and was also significant at $p < .0001$.

**Discussion**

The purpose of this study was to evaluate pulmonary hypertension from the flow velocity pattern in the right ventricular outflow tract. We preferred the flow in the right ventricular outflow tract to the pulmonary artery flow because the Doppler signals from flow obtained in the latter position often suffered from the mixing of signals caused by systolic fluttering of the pulmonic cusp and/or eddy currents in patients with pulmonary hypertension. We have obtained satisfactory Doppler recordings of right ventricular outflow tract in about 70% of the adults referred to our hospital. Detection rate in patients with pulmonary hypertension was even higher (90%), partly because of pulmonary arterial dilatation and a more parallel orientation of the ultrasonic beam to the blood stream. In clinical use, the pulsed Doppler technique can thus be satisfactorily performed in a high proportion of adults.

Eight of 17 patients with pulmonary hypertension exhibited a characteristic flow velocity pattern with midsystolic notching, which was not observed in any patient with normal pulmonary artery pressure. This characteristic contour of the flow velocity pattern was expected to correspond to midsystolic notching of the pulmonic valve echogram as pointed out in a previous study. In the present study, midsystolic notching of the pulmonic valve echogram was observed in all seven patients who exhibited midsystolic notching in the flow velocity pattern, and the point at midsystolic notching of the flow velocity pattern was temporally coincident with that point in the pulmonic valve echogram (figure 7). Thus this study showed a close correlation between the pulmonic valve motion and flow velocity change in human chronic pulmonary hypertension.

In the previous study in dogs, however, midsystolic notching occurred in only 40% of the animals with elevated pulmonary artery pressure, and in a clinical study, notching occurred in only 38% of the patients with pulmonary hypertension. In the present study, the midsystolic notching was observed in only 53% of the patients with pulmonary hypertension. These findings indicate that midsystolic notching is not always associated with elevated pulmonary artery pressure. In pulmonary hypertension, some factors other than elevated pulmonary artery pressure may be required for production of the midsystolic notching. Therefore midsystol-
FIGURE 6. Ratio of the time to peak velocity (AcT) vs RVET is plotted against MPAP in all 33 patients studied. Left, AcT/RVET vs MPAP. The correlation coefficient is −.85, and the relationship appears to be curvilinear. Right, AcT/RVET is compared with log10(MPAP), with a result that is also more linear. The linear regression equation is log10(MPAP) = −2.8 (AcT/RVET) + 2.4, r = −.90.

FIGURE 7. Comparison of the flow velocity pattern (top) in the right ventricular outflow tract with the pulmonic valve echogram (bottom). The flow velocity pattern shows a typical midsystolic notching, and the pulmonic valve echogram shows a midsystolic semiclosure with reopening. Note that the point at midsystolic notching of the flow velocity pattern is coincident with that of the pulmonic valve echogram, as indicated by vertical line on the second beat.
ie notching would not be the most accurate means of estimating pulmonary artery pressure level. This is supported by our result that the appearance of the midsystolic notching was not related to the pulmonary artery pressure in the patient who exhibited both patterns, with and without midsystolic notching (figure 4), and by the report\textsuperscript{13} that the midsystolic notching is observed in the absence of pulmonary hypertension. Bauman et al.\textsuperscript{13} studied this phenomenon in a patient with idiopathic dilatation of the pulmonary artery and proposed two other hypotheses to explain the mechanism: that the reflection of the pressure wave front reaches the pulmonic valve prematurely and that there are eddy currents around the valve in the enlarged main pulmonary artery. Our results demonstrated that the flow velocity pattern varied from beat to beat in a patient with atrial fibrillation and that midsystolic notching was observed when stroke volume was large, while it was absent in a beat when stroke volume was small (figure 4). We could not define how stroke volume affects the flow velocity pattern; however, stroke volume as well as pulmonary artery pressure appear to contribute to the production of midsystolic notching.

This study demonstrated another abnormal characteristic of the flow velocity pattern in the right ventricular outflow tract in the patients with pulmonary hypertension. As pulmonary artery pressure increased, a peak in flow velocity was achieved sooner and AcT and AcT/RVET became shorter. Above a MPAP of 40 mm Hg there was deviation from a linear correlation, and this may reflect the effects of other hemodynamic variables on AcT at this high level of MPAP. However, the excellent correlation of $\log_{10}(\text{MPAP})$ with either AcT or AcT/RVET was believed to be good enough to predict MPAP.

In nine of 11 patients with mild or moderate tricuspid regurgitation, actual MPAPs were distributed below the regression line. The alternate ejection route through the tricuspid valve might well cause earlier peak in flow velocity, analogous to the similar flow pattern demonstrable in mitral regurgitation.\textsuperscript{14} However, there was no significant difference between the regression line of AcT vs MPAP relation obtained from 11 patients with tricuspid regurgitation and that from our 33 patients. Thus the good correlation between the Doppler index and MPAP stands regardless of underlying tricuspid regurgitation.

Furthermore, these Doppler indices reflected the beat-to-beat changes in pulmonary artery pressure in the patient with pulmonary hypertension and atrial fibrillation (figure 4). The correlation coefficient between beat-to-beat peak pulmonary artery pressure and AcT/RVET was $-0.87$, which indicated that AcT/RVET as well as MPAP might predict beat-to-beat change in pulmonary artery pressure.

The clinical usefulness of echocardiography as a noninvasive method of estimating pulmonary artery pressure has been described by several investigators.\textsuperscript{4, 5, 7, 15-17} In the echocardiographic examination of the pulmonic valve, the inferiorly directed beam from higher positioning of the transducer induces a hypertensive pattern even in the normotensive subjects, and the diagnostic importance of echocardiogram of the pulmonic valve should be carefully evaluated in light of the spatial relationship of the echo beam and the valve.\textsuperscript{18} However, the Doppler index, either AcT or AcT/RVET, measured from the velocity pattern is thought to be independent of beam direction, since the vector of ejection flow hardly changes during systole in the right ventricular outflow tract.

Quantitative evaluation of severity of pulmonary hypertension by a pulsed Doppler technique has potential advantages. It can be used to perform repeated examinations without any side effects; it can also be used to follow stages in the development of pulmonary hypertension complicating certain disease processes to evaluate the effects of therapeutic agents and to determine the timing of corrective surgery.

Our results indicate that the pulsed Doppler technique is useful not only in the analysis of the flow dynamics but also in the diagnosis and evaluation of pulmonary hypertension. In addition to differentiating patients with elevated pulmonary artery pressures from those with normal pulmonary artery pressures, this method provides an estimate of the pulmonary artery pressure. The use of this technique in the evaluation of pulmonary hypertension represents another extension of its capabilities.

We gratefully acknowledge the important contribution made by Dr. Hirohide Matsuo, professor at Kagawa Medical School, Japan.

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Noninvasive evaluation of pulmonary hypertension by a pulsed Doppler technique.
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Circulation. 1983;68:302-309
doi: 10.1161/01.CIR.68.2.302
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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