THE CHARACTERISTICS OF HEPATIC VENOUS FLOW VELOCITY PATTERN IN PATIENTS WITH PULMONARY HYPERTENSION BY PULSED DOPPLER ECHOCARDIOGRAPHY

ZHANG-AN, M.D., YOSHIHIRO HIMEURA, M.D., TOSHIAKI KUMADA, M.D.
WATARU HAYASHIDA, M.D., NOBORU ISHIKAWA, M.D., MICHIO NODA, M.D.
FUJIMASA KOHNO, M.D., MASASHI KAMBAYASHI, M.D.
AND CHUCHI KAWAI, M.D.

To determine the characteristic change in the Doppler hepatic venous flow velocity pattern in patients with pulmonary hypertension (PH), 21 patients with PH in sinus rhythm were examined with pulsed Doppler echocardiography. The control group included 13 subjects with chest pain syndrome and normal pulmonary arterial pressure. The hepatic vein Doppler signal was biphasic with one peak during ventricular systole (S wave) and the other in diastole (D wave). A reversed signal was recorded after contraction (A wave). The peak velocity of the A wave (Va), S wave (Vs), and D wave (Vd), the time velocity integral of these waves (Vla, Vls, and Vld), the acceleration time (t-AC), and the slope of acceleration (s-AC) in the S wave were measured. Compared with controls the PH group had a higher value of Va (26.88 ± 10.30 vs 13.41 ± 3.69 cm/sec; p < 0.01), Vla (2.55 ± 1.18 vs 1.20 ± 0.34 cm; p < 0.01), Vla/(Vls + Vld) (0.34 ± 0.22 vs 0.14 ± 0.06; p < 0.01), and s-AC (372 ± 156 vs 203 ± 103 cm/sec²; p < 0.01). They also had a shorter t-AC (101 ± 32 vs 136 ± 27 msec; p < 0.01). There was a weak correlation between the reversed atrial flow and the right heart pressures (r = 0.43 to 0.66). Thus, the hepatic venous flow velocity pattern by Doppler echocardiography is clinically useful in evaluating pulmonary hypertension.

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Third Division, Department of Internal Medicine, Faculty of Medicine, Kyoto University, Japan
Mailing address: Chuichi Kawai, M.D., Third Division, Department of Internal Medicine, Faculty of Medicine, Kyoto University, 54 Shogoin Kawara-cho, Sakyo-ku, Kyoto 606, Japan

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THERE are several useful M-mode echocardiographic and Doppler echocardiographic parameters to evaluate patients with pulmonary hypertension!−5 An absent or diminished A wave!2,6 midsystolic closure or notching in pulmonary valve echocardiogram!7 and an increase in the ratio of the pre-ejection period to the right ventricular ejection time8,9 are all valuable signs in M-mode echocardiographic evaluation of pulmonary hypertension. Doppler echocardiographic studies of the pulmonary arterial flow velocity pattern have demonstrated shortening of the acceleration time as the pulmonary arterial pressure increase.6 Other parameters, such as the ratio of the pre-ejection period to the acceleration time, the ratio of acceleration time to right ventricular ejection time, and the ratio of pre-ejection period to the right ventricular ejection time are also very valuable in Doppler echocardiography.10,11 All of these para-
meters focus on the blood flow in the pulmonary artery itself. However, the relationship between pulmonary hypertension and the hepatic venous flow velocity pattern has rarely been mentioned. We routinely recorded the hepatic venous flow in many patients with various heart diseases in our laboratory, and noticed some interesting findings in patients with pulmonary hypertension.

The purpose of this study was to demonstrate the characteristic changes of the hepatic venous flow velocity pattern in patients with pulmonary hypertension.

METHODS

Twenty one patients (12 women and 9 men) with both pulmonary hypertension and sinus rhythm were included in this study (PH group). Their ages ranged from 24 to 68 years (mean 48±14 years). Nine patients had primary pulmonary hypertension, and 12 patients had secondary pulmonary hypertension. Pulmonary hypertension was defined as pulmonary artery systolic and mean pressures exceeding 30 and 20 mmHg, respectively. The diagnosis of primary pulmonary hypertension was established after thorough clinical examination and cardiac catheterization in which no specific cause for pulmonary hypertension was found. The underlying diseases in secondary pulmonary hypertension included dilated cardiomyopathy in 3, mitral or aortic valve disease in 5, coronary artery disease in 2 (old myocardial infarction with left ventricular dysfunction), left atrial myxoma in 1, and post-operation Tetralogy of Fallot in 1. All patients underwent cardiac catheterization for evaluation of hemodynamic data. Fourteen of the 21 patients in the PH group had mild (n=3) or moderate

![Image](image-url)

Fig.1. Schematic representation of the hepatic venous flow velocity pattern in a normal control patient. Identified are biphasic negative signals with one peak during ventricular systole (S wave) and the other in diastole (D wave), with the S wave being dominant. The smaller positive A wave can also be seen just after atrial contraction.

<table>
<thead>
<tr>
<th></th>
<th>Age (y.o.)</th>
<th>PASP (mmHg)</th>
<th>PADP (mmHg)</th>
<th>mPA (mmHg)</th>
<th>RVSP (mmHg)</th>
<th>RVEDP (mmHg)</th>
<th>mRA (mmHg)</th>
<th>PAR (dynes-sec-cm⁻²)</th>
<th>TPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>42±11</td>
<td>21±4</td>
<td>7±3</td>
<td>12±3</td>
<td>24±4</td>
<td>4±1</td>
<td>2±1</td>
<td>80±30</td>
<td>174±38</td>
</tr>
<tr>
<td>PH</td>
<td>48±14</td>
<td>59±23</td>
<td>25±10</td>
<td>37±13</td>
<td>59±23</td>
<td>7±4</td>
<td>5±4</td>
<td>331±292</td>
<td>784±358</td>
</tr>
<tr>
<td>P</td>
<td>NS</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.05</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

PASP=pulmonary artery systolic pressure, PADP=pulmonary artery diastolic pressure, mPA=mean pulmonary artery pressure, RVSP=right ventricular peak systolic pressure, RVEDP=right ventricular end-diastolic pressure, mRA=mean right atrial pressure, PAR=pulmonary arteriolar resistance, TPR=total pulmonary resistance. P=control vs PH.
TABLE II DOPPLER ECHOCARDIOGRAPHIC PARAMETERS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Symbol</th>
<th>Unit</th>
<th>Control</th>
<th>PH (n=11)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>HR</td>
<td>bpm</td>
<td>62.8±0.7</td>
<td>74.7±1.42</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Vs</td>
<td>cm/sec</td>
<td>36.52±2.65</td>
<td>26.89±1.30</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Vd</td>
<td>cm/sec</td>
<td>19.40±0.90</td>
<td>19.43±0.32</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Vla</td>
<td>cm/sec</td>
<td>3.40±0.22</td>
<td>2.35±0.18</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Vla+Vid</td>
<td>cm/sec</td>
<td>0.14±0.06</td>
<td>0.34±0.02</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>s-AC</td>
<td>cm/sec²</td>
<td>103±32</td>
<td>101±32</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>l-AC</td>
<td>msec</td>
<td>136±27</td>
<td>136±27</td>
<td>NS</td>
</tr>
</tbody>
</table>

(n=11) tricuspid regurgitation, and 6 patients had mild pulmonary regurgitation. The control group of thirteen patients (7 women and 6 men), ranging from 27 to 65 years of age (mean 42±11), had normal coronary angiography, normal left ventriculography, and normal left and right heart pressures by cardiac catheterization. They were diagnosed as having atypical chest pain.

Diagnostic right and left heart catheterization was performed through the percutaneous femoral approach in the fasting state, 30 min after oral premedication with 5 mg of diazepam. All other drugs were withheld for at least 24 h before cardiac catheterization. First, right heart pressures and cardiac output by thermodilution were measured with a Swan-Ganz catheter. The zero pressure level was taken at the mid-chest. Routine left heart catheterization was then performed with measurement of aortic pressure, left ventricular pressure, left ventricular cineangiography, and coronary arteriography, in that order.

The time interval between cardiac catheterization and echocardiographic examination was within 10 days (mean = 5±3 days). Although the time interval between the 2 examinations was rather long, the patients studied remained clinically stable. Two-dimensional echocardiography and pulsed Doppler echocardiographic studies of the hepatic venous flow velocity pattern were performed using a Hewlett Packard 77020 AC system with a transducer frequency of 2.5–3.5 MHz and a screen speed of 50–100 mm/sec. All patients were examined in the supine position with the transducer in the subxyphoid region. Data were taken while the patients held their breath at the end of a smooth expiration to avoid any respiratory influence. The sample volume was positioned at the proximal portion of the hepatic vein, close to the junction with the inferior vena cava, with an angle less than 20 degrees (Fig. 1). As shown in Fig. 1, the Doppler signal from the hepatic vein differed from that of arteries. The velocity curves were biphasic, with one peak during ventricular systole (S wave) and the other in diastole (D wave). The systolic wave was dominant. The hepatic venous flow was away from the transducer in the subxyphoid.
Fig. 2. Hepatic venous flow velocity pattern from a patient with pulmonary hypertension (mean \(PA=71\) mmHg). A marked increase in the reversal flow with right atrial contraction is seen.

Fig. 3. Comparison between the peak velocity of the A wave (Va) in the hepatic venous flow velocity pattern in patients with PH and controls.

View so that S wave and D wave Doppler signals were negative. The smaller positive flow signal was recorded after contraction (A wave).

Videotape was used to record at least 10 consecutive cardiac cycles, and was then evaluated later. Each parameter was analyzed through 5 cardiac cycles. Using the computer in the Hewlett Packard machine, we were easily able to measure the peak velocity of the A wave (Va), S wave (Vs) and D wave (Vd), as well as the time velocity integral of these three waves (Vla, VIs, and VId). The peak frequency was used to measure the peak flow velocity. Because of the thicker dark band of signals in the hepatic venous flow velocity pattern, especially in the A wave, the outer contour line of the Doppler signals was used to measure the time velocity integral. The S wave acceleration time (the time interval between the onset and peak of the systolic phase) and the slope of the acceleration were termed t-AC and s-AC, respectively. The ratio \(Vla/(Vs+VId)\) was also calculated for the purpose of normalization. Interobserver error concerning the measurement of these parameters was found to be small (6.9 percent; \(r=0.98\)).

Statistics
All data were expressed as mean±one
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59±23 mmHg and 37±13 mmHg, respectively, and were significantly higher than those in the control group (Table I). Right ventricular end diastolic pressure and mean right atrial pressure were also significantly higher than those of the control group (7±4 vs 4±1 mmHg; p<0.05, and 5±4 vs 2±1 mmHg; p<0.01, respectively). Pulmonary arterial resistance was significantly increased in the PH group (Table I).

A representative example is shown in Fig. 2. Compared with a control subject (Fig. 1), the hepatic venous flow velocity pattern in the patient with pulmonary hypertension showed a marked increase in reversal flow with the right atrial contraction.

Compared with the control group (Table II, Fig. 3), patients with pulmonary hypertension had higher value of Va (26.88±10.30 cm/sec vs 13.41±3.69 cm/sec; p<0.01), Vla (2.55±1.18 cm vs 1.20±0.34 cm; p<0.01), and Vla/(Vls+Vld) (0.34±0.22 vs 0.14±0.06; p<0.01). In the PH group s-AC was increased (372±156 cm/sec^2 vs 203±103 cm/sec^2; p<0.01) and the t-AC was shorter (101±32 msec vs 136±27 msec; p<0.01) (Table II, Fig.4). There was no significant difference among Vs, Vd, Vls, or VId.

There was a weak, but significant correlation between the atrial flow velocity and right heart pressure for all patients in both groups (Table III). A rough correlation existed between s-AC and mean pulmonary artery pressure (r=0.47), but did not with

TABLE III CORRELATION COEFFICIENT BETWEEN INDEXES OF HEPATIC VENOUS FLOW VELOCITY AND RIGHT HEART PRESSURES (N=34)

<table>
<thead>
<tr>
<th></th>
<th>mPA</th>
<th>RVEDP</th>
<th>mRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Va</td>
<td>0.51*</td>
<td>0.45*</td>
<td>0.62*</td>
</tr>
<tr>
<td>Vla</td>
<td>0.47*</td>
<td>0.43*</td>
<td>0.59*</td>
</tr>
<tr>
<td>Vla/(Vls+Vld)</td>
<td>0.58*</td>
<td>0.45*</td>
<td>0.66*</td>
</tr>
<tr>
<td>s-AC</td>
<td>0.47*</td>
<td>0.34</td>
<td>0.54*</td>
</tr>
<tr>
<td>t-AC</td>
<td>-0.24</td>
<td>-0.33</td>
<td>-0.43</td>
</tr>
</tbody>
</table>

Abbreviations are as in Tables I and II.
*p<0.01, **p<0.001

SD. Statistical analysis of the significance of the difference in the results was performed by means of the unpaired t test. Values of P<0.05 were considered statistically significant. Regression correlation analysis was also used to evaluate the relationship between two parameters.

RESULTS

All hemodynamic and echocardiographic parameters are listed in Table I and II. There was no significant difference in age between the control and the PH groups. Heart rate was slightly higher in the PH group. In the PH group, pulmonary arterial peak systolic and mean pressures were

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DISCUSSION

The blood flow in the great veins is more difficult to analyse when compared with blood flow in arteries, because many cardiac and noncardiac events can influence venous return. It is quite clear that respiration can significantly influence venous return as can pericardial condition and even body position. All patients were examined in the supine position and held their breath at the end of a smooth expiration in this study. No patient was found to have pericardial disease. Therefore, the influence of these factors was considered to be minimal.

The present study showed that the most obvious change in the hepatic venous flow velocity pattern in patients with pulmonary hypertension was noted in the A wave, as demonstrated by the significant increase in Va, V1a, and V1a/(V1s+V1d) (Table II). This marked retrograde blood flow (the A wave) into the hepatic vein is depicted as a positive wave in the subxyphoid view, immediately after the P wave on the electrocardiogram (Fig. 2). In addition, the S and V1a showed much shorter acceleration time with much steeper slope (Table II). This means pulmonary hypertension does significant effects on the blood flow in the great veins. The venous return and V1a in the great veins are directly related to right atrial actions. Patients with pulmonary hypertension usually have higher right ventricular enddiastolic pressure, as demonstrated in the present study (Table I). Facing the right ventricle with a higher enddiastolic pressure, the right atrium in patients with pulmonary hypertension must contract with greater force to drive blood into the right ventricular chamber. This results in significant increases in right atrial pressure during the active atrial contraction, and also in the mean right atrial pressure (Table I), thus leading to augmentation of the retrograde blood flow into the great veins. This reversed blood flow also exists in normal subjects, but the degree of the reversed flow is much less in normal subjects than in patients with pulmonary hypertension, probably due to a more compliant normal right ventricular chamber. Using color Doppler echocardiography, Nanda showed a very beautiful picture of such reversed flow in a normal subject but in patients with pulmonary hypertension, the reversed blood flow became much conspicuous.

The S wave mainly corresponds to right ventricular systolic phase and is dependent on the effective right ventricular contraction and on a timed right atrial relaxation. During right ventricular systole, the tricuspid valve is closed and the tricuspid annular ring moves downward. The downward movement of the ring produces a “suction effect” just like a pump, and thus enhances venous return from the systemic veins into the right atrium. A timed right atrial relaxation is also important for venous return. Atrial relaxation occurs after completion of the atrial shortening and mainly consists of muscle relaxation and subsequent lengthening of the muscle fibers. The right atrium, which has become narrowest by the active shortening, returns to the pre-shortening cavity size throughout the relaxation period. The extent of the increase in cavity size during this relaxation period depends on the extent of total atrial shortening. Loss of effective atrial contraction, such as in atrial fibrillation and atrioventricular block, results in marked diminution, or even greater, in disappearance of the S wave as well as the A wave. Thus, venous return during atrial relaxation is determined chiefly by the extent of the active atrial shortening, although muscle relaxation should affect the lengthening of the atrial muscle. The mechanism of venous return during right ventricular systole (expressed by the S wave in the present study), therefore, is a complex function of ring motion, atrial active shortening and atrial relaxation. The S wave has both a shorter acceleration time and a steeper slope in patients with pulmonary hypertension (Table II). Although the reason for such S wave changes is unclear at present, there are some possible mechanisms. First, a “seesaw motion effect” (or so-called “to and fro” motion) of blood flow can occur in the great veins. The more the blood flow is driven retrogradely into great veins during the right atrial contraction, the more rapidly venous return will occur during the subsequent right ventricular systolic phase. The second mechanism involves the change in the right
atrial relaxation. As mentioned above, the extent of the increase in right atrial cavity size during the right atrial relaxation is related to the extent of atrial shortening. In patients with pulmonary hypertension, because of the stronger right atrial contraction which is seen as a marked atrial reversed flow (Fig. 2), the increase in the cavity size during the right atrial relaxation becomes much greater. Both of these mechanisms can accelerate the venous return from the great veins during right ventricular systole. Of 21 patients with pulmonary hypertension, 14 patients had tricuspid regurgitation in this study. Comparison of the S wave was made between the patients with and without tricuspid regurgitation. The result showed that there was no significant difference of Vs between 2 groups, while Vs in patient with tricuspid regurgitation tended to be less than that in the patient without tricuspid regurgitation (NS). With tricuspid regurgitation the acceleration of the venous return is interrupted earlier due to the interference of the tricuspid regurgitation flow. Thus, the venous return during the right ventricular systolic phase can not reach a higher velocity, and only exhibits a steeper slope of acceleration and shorter acceleration time. Patients with atrial fibrillation were excluded from this study. In those cases, a reversed S wave induced by tricuspid regurgitation can frequently be recorded in the hepatic venous flow spectrum. However, this type of reversed S wave was not seen in patients with sinus rhythm. With maintenance of sinus rhythm and atrial function, the effective right atrial relaxation may mask the tricuspid regurgitation flow to some degree so that the reversed S wave in the hepatic venous flow spectrum will not appear, unless the tricuspid regurgitation is very severe.

The D wave occurs in the right ventricular diastolic phase when the tricuspid valve is open. In normal conditions, the amplitude of the D wave and the S wave in the hepatic venous velocity curve are not equal, with the S wave being dominant. In the present study, however, the D wave tended to be reduced but did not have a statistically significant difference between the PH group and the controls. The reason for this is unclear, but may relate to the relatively wide scatter seen in the D values.

Although there were some characteristic changes in the hepatic venous flow velocity pattern in patients with pulmonary hypertension, correlation analysis between indexes for the atrial reversed flow velocity and right heart pressures showed only a weak relationship, as does the s-AC versus the mean pulmonary arterial pressure. The t-AC showed no correlation with them. Many factors in addition to pulmonary arterial pressure can influence these correlations. These include the degree of tricuspid regurgitation, the hepatic vein diameter, the course of the disease (acute, subacute, or chronic), and the overall blood volume. The Eustachian valve, which can be seen in the right atrium at the junction of the inferior vena cava and right atrium, can also influence blood flow in some patients. All of these make the correlation between hepatic venous flow velocity pattern and pulmonary artery pressure more complex.

Pulmonary hypertension is a very important clinical entity in practical cardiology. Many invasive and noninvasive approaches have been used to evaluate pulmonary hypertension. Among them, echocardiography is the most useful noninvasive method. Compared with other echocardiographic approaches, the measurement of the hepatic venous flow velocity pattern has its own advantage. It can provide much information on right atrial performance in pulmonary hypertension, and even more, may reflect right ventricular compliance. Combined with other echocardiographic parameters, observation of the hepatic venous flow velocity pattern is a clinically useful index for evaluation of patients with pulmonary hypertension.

Limitations: We speculate that the reduced right ventricular compliance may play a very important role in the changes in hepatic venous flow velocity pattern in patients with pulmonary hypertension. Recently, analysis of the flow across the tricuspid valve by Doppler echocardiography has been used to study right ventricular diastolic function. A reduction in right ventricular early filling and an increase in right atrial contribution indicate right ventricular dysfunction. Unfortunately, we could not accurately evaluate the right ventricular compliance using Doppler echocardiography in this study.
Many patients with pulmonary hypertension tend to have tricuspid regurgitation, which could pseudonormalize the right ventricular diastolic Doppler inflow pattern. Furthermore, in these patients, heart rate is frequently higher, as seen in the present study. When the heart rate is more than 90/min, the right ventricular diastolic inflow pattern seems to show only one single peak. Therefore, tricuspid regurgitation and higher heart rate make it difficult to evaluate the right ventricular compliance from Doppler echocardiography in patients with pulmonary hypertension. We evaluated the right ventricular diastolic dysfunction from right ventricular pressure and right atrial pressure data derived from catheterization examination, so the information about right ventricular compliance is limited. Finally, the time interval between cardiac catheterization and echocardiographic examination was rather long. Although the patients remained clinically stable, it seems much better to perform these 2 examinations simultaneously.

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