Obstruction of Inferior Vena Caval Orifice by Giant Left Atrium in Patients With Mitral Stenosis
A Doppler Echocardiographic Study From the Right Parasternal Approach

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Background. To examine whether an extremely enlarged left atrium (giant left atrium) obstructs the venous return from the inferior vena cava (IVC), the velocity of IVC flow was measured at its junction with the right atrium (IVC orifice) in patients with mitral stenosis by use of color and pulsed-wave Doppler echocardiography from a right parasternal longitudinal plane.

Methods and Results: The maximum dimension of the IVC orifice by two-dimensional echocardiography and the maximum IVC orifice flow velocity by pulsed-wave Doppler echocardiography were measured in 74 patients with mitral stenosis and atrial fibrillation (mean age, 59 years). The control population consisted of 16 subjects with atrial fibrillation alone (mean age, 61 years). Flow velocities in the superior vena cava and hepatic vein were also obtained by pulsed-wave Doppler echocardiography from the supravacuclar and subcostal views, respectively. Fifty-one mitral stenosis patients without severe tricuspid regurgitation were divided into two groups according to the left atrial dimension (LAD), which was measured by the standard left parasternal long-axis view (group A: n=33, LAD<65 mm; group B: n=18, LAD≥65 mm). Peak inspiratory and expiratory velocities of IVC orifice flow in diastole averaged over three consecutive inspirations in group B (mean±SD, 93.4±32.0 and 47.6±19.8 cm/sec) were significantly greater (p<0.01) than in the control subjects (67.9±12.8 and 34.5±7.0 cm/sec) and in group A (70.2±18.4 and 38.1±11.5 cm/sec, respectively). However, there were no significant differences in superior vena caval and hepatic vein flow velocities among the three groups. The maximum IVC orifice dimension in group B (11.4±4.4 mm) was significantly smaller than in the control subjects (20.1±2.1 mm) and in group A (18.6±5.4 mm) because of displacement of the atrial septum into the right atrium. There were significant negative correlations between the IVC orifice dimension and the peak IVC orifice flow velocity (r=-0.62, SEE=0.33 cm/sec, n=67, y=e⁻⁰.⁰₁±³, p<0.01) as well as the left atrial dimension (r=-0.71, SEE=0.32 mm, n=67, y=e⁻⁰.⁰₂±³, p<0.01) in these 51 patients and control subjects. In the remaining 23 patients with severe tricuspid regurgitation, the peak inspiratory IVC orifice velocity (n=9, 88.6±30.0 cm/sec) was significantly greater (p<0.05) and the IVC orifice dimension (23.8±9.7 mm) significantly smaller (p<0.05) in patients with a giant left atrium than in those without (n=14, 69.9±15.3 cm/sec and 30.5±9.6 mm, respectively); in the latter, the IVC orifice dimension was significantly (p<0.05) greater than in the controls.

Conclusions. A giant left atrium in patients with mitral stenosis obstructs venous return at the IVC orifice by marked displacement of the atrial septum toward the right atrium. (Circulation 1992;86:214–225)

Key Words • left atrium, giant • mitral stenosis • vena cava, inferior • echocardiography, Doppler

Although pulsed or continuous-wave Doppler echocardiography has permitted the noninvasive quantification of the degree of stenotic valve or obstructive lesions in the cardiac cavity or vessels,¹⁻⁻¹°

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studies of obstruction in the inferior vena cava (IVC) at the junction with the right atrium using Doppler echocardiography have not been reported previously. The transthoracic right parasternal view in the longitudinal plane provides an ideal approach to visualize the right atrium, the atrial septum, the left atrium, and the IVC.¹⁵⁻⁻¹⁷ Similarly, this view allows the direct visualization of IVC flow at its junction with the right atrium (IVC orifice flow). In the course of performing clinical examination of the IVC orifice flow velocities in the right parasternal view with color and pulsed-wave Doppler echocardiography, we have observed some
particular cases of increased flow velocity in patients with mitral stenosis. We hypothesized that extreme enlargement of the left atrium (giant left atrium), which can occur in mitral stenosis, might have affected venous return from the IVC at its orifice into the right atrium by encroachment of the atrial septum into the right atrium. Such encroachment would occur because of asymmetrical enlargement of the left atrium toward the right or in an anteroposterior or superior direction.18–21

The aim of the present study was to examine whether a giant left atrium obstructs the venous return from the IVC in patients with mitral stenosis by measuring flow velocities at the IVC orifice with color and pulsed-wave Doppler echocardiography as well as by measuring IVC orifice dimensions with two-dimensional echocardiography from the right parasternal view.

Methods

Study Population

The initial study population comprised 111 consecutive patients with mitral stenosis diagnosed by two-dimensional echocardiography and continuous-wave and color Doppler echocardiography. Because all the patients with a giant left atrium were in atrial fibrillation, 22 patients in sinus rhythm were excluded from the study. Patients with associated abnormalities that might affect venous return were also excluded. These consisted of five cases with aortic stenosis, five with pericardial effusion, two with left heart failure in New York.

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Heart Association class IV; two with complete heart block, and one with hyperthyroidism. Thus, 74 patients with mitral stenosis were included. The severity of mitral stenosis in these patients was determined by color and continuous-wave Doppler echocardiography and graded as mild (mitral valve area [MVA], >1.5 cm², n=15), moderate (MVA, 1.0–1.5 cm², n=28), or severe (MVA, <1.0 cm², n=21).22 The severity of associated mitral regurgitation determined by color Doppler echocardiography was graded as mild in 45 patients, moderate in 21, and severe in six according to the method of Miyatake et al.23 Associated mild aortic regurgitation determined by color Doppler echocardiography was observed in eight patients.24 No patient had tricuspid stenosis, constrictive pericarditis, an atriovenous fistula (including patent ductus arteriosus), respiratory disease, or other conditions that could alter venous return such as fever or pregnancy.25 There were 19 men and 55 women (age, 33–80 years; mean, 59±12 years).

The control population consisted of 16 patients (12 men and four women; age, 61±15 years; range, 37–80 years) with atrial fibrillation alone. None of them had any conditions known to influence venous return.

Two-dimensional and Doppler Echocardiographic Examination

Two-dimensional and color and pulsed-wave Doppler echocardiographic examinations were performed in all patients and control subjects. A commercially available system (Toshiba 160-A or 140-A scanner) with a 2.5-MHz phased array transducer was used.

Color Doppler examinations were performed with a 4-kHz pulse-repetition frequency. For each examination, care was taken to use an optimal gain setting. The flow data were color-coded, and the flow toward the transducer was expressed as red and the flow away from the transducer as blue.

Left atrial dimension. The left atrial dimension was obtained in the supine position by the standard left parasternal long-axis view with two-dimensional and M-mode echocardiography.26 The dimension was measured from the M-mode echocardiogram at the time of aortic valve closure and was averaged over three consecutive beats. A left atrial dimension ≥65 mm was regarded as a giant left atrium. The definition of a giant left atrium was decided conventionally in the present study because there were no reports that described distinct criteria for M-mode echocardiography.

The left atrial dimension was 41.6±5.8 mm (mean±SD) in the control group (n=16) and 62.1±14.6 mm in the patients with mitral stenosis. The 74 mitral stenosis patients were divided into two groups according to the presence or absence of a giant left atrium. Patients without a giant left atrium were classified as group A (n=47; left atrial dimension, 53.0±6.9 mm, mean±SD), and those with a giant left atrium were classified as group B (n=27; left atrial dimension, 77.8±10.1 mm) (Table 1). The age, sex, and heart rate in each group are shown in Table 1.

Severity of tricuspid regurgitation. The severity of tricuspid regurgitation was determined in the supine position by color Doppler echocardiography using a left parasternal four-chamber view and was classified by the method of Yoshikawa et al.,27 i.e., mild, a regurgitant jet extending to the proximal one third of the atrium; moderate, regurgitant flow extending two thirds of the atrium; and severe, regurgitant flow extending beyond two thirds of the atrium.

The distribution of severity of tricuspid regurgitation in the control group and groups A and B is shown in Table 1. Mild regurgitation was observed in 14 control patients. In the mitral stenosis patients, mild regurgitation was observed in 26, moderate regurgitation in 23, and severe regurgitation in 23.

Dimension and flow velocity at the inferior vena caval orifice. Two-dimensional and pulsed-wave and color Doppler echocardiography for the IVC orifice were performed from the right parasternal approach in the longitudinal plane by placing the transducer in the third or fourth right intercostal space with the patient in the right lateral position.15,16 After the longitudinal planes of the right atrium, the atrial septum, the left atrium, and the IVC were demonstrated on the two-dimensional echocardiogram, the IVC orifice was visualized by slightly tilting the ultrasound beam downward.

After longitudinal imaging of the IVC orifice, the diastolic maximum dimension between the anterior and posterior walls of the IVC at their junction with the right atrium was measured in inspiration. In the patients with a giant left atrium, because the IVC orifice was extremely narrowed by bulging of the atrial septum into the right atrium beyond the IVC orifice, the dimension of the IVC orifice was measured in the right atrium between the anterior wall of the right atrium and the atrial septum. In these patients, the passage between the bulging atrial septum and the anterior wall of the right atrium actually constituted the narrowest point for IVC orifice flow as it entered the main body of the right
TABLE 1. Clinical Characteristics and Severity of Tricuspid Regurgitation in Control Subjects and Patients With Mitral Stenosis

<table>
<thead>
<tr>
<th></th>
<th>Control (n=16)</th>
<th>Group A (LAD&lt;65 mm) (n=47)</th>
<th>Group B (LAD≥65 mm) (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61.0±14.0 (30–83)</td>
<td>57.1±10.0 (33–80)</td>
<td>60.2±8.7 (40–72)</td>
</tr>
<tr>
<td>Men:women</td>
<td>13:3</td>
<td>11:36</td>
<td>8:19</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>73.9±14.0 (41–93)</td>
<td>69.5±11.8 (46–93)</td>
<td>72.8±11.6 (53–96)</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>41.6±5.6 (30–49)</td>
<td>53.0±6.9 (42–64)</td>
<td>77.8±10.1 (65–107)*</td>
</tr>
<tr>
<td>Presence of TR</td>
<td>14</td>
<td>47</td>
<td>25</td>
</tr>
<tr>
<td>Severity of TR</td>
<td></td>
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</tr>
<tr>
<td>Mild</td>
<td>14</td>
<td>17</td>
<td>9</td>
</tr>
<tr>
<td>Moderate</td>
<td>0</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>14</td>
<td>9</td>
</tr>
</tbody>
</table>

LAD, left atrial dimension; bpm, beats per minute; TR, tricuspid regurgitation. Values are given as mean±SD (range).

*p<0.01 vs. control and group A.

atrium. This point corresponds functionally but not anatomically to the IVC/right atrial junction. We have therefore referred to the distance between the anterior wall of the right atrium and the bulging atrial septum as the dimension of the IVC orifice in this group of patients.

The flow velocity at the IVC orifice was easily and clearly demonstrated on the color Doppler echocardiogram as a red jet moving toward the transducer from the IVC into the right atrium through the IVC orifice (left upper panel in Figure 1). Pulsed-wave Doppler echocardiographic measurement of the flow velocity at the IVC orifice was performed by placing a sample volume of 2 mm width at the orifice within the color Doppler–imaged flow (right upper panel in Figure 1). As the IVC orifice was extremely narrowed by the bulging atrial septum in the patients with giant left atrium, aliasing of the color Doppler signal from red to blue because of its high velocity was seen in the right atrium beyond the IVC orifice. In these patients, the pulsed-wave Doppler sample volume was placed in the area of the blue Doppler signals. During the examination, the maximum velocity was obtained by finding the high-pitched whistling signal of IVC orifice flow under audio and by color

FIGURE 1. Two-dimensional color and pulsed-wave Doppler echocardiograms obtained in the longitudinal plane from the right parasternum. The inferior vena caval (IVC) orifice flow from the IVC into the right atrium (RA) is demonstrated by color Doppler echocardiography in a patient with mitral stenosis (upper left panel). The upper right panel shows the sampling position used for obtaining pulsed-wave Doppler flow velocities in the IVC orifice. The lower panel shows a pulsed-wave Doppler recording of flow velocities from the IVC orifice in a patient with mitral stenosis. Simultaneous respiratory trace, phonocardiogram, and ECG are displayed. Predominant flow toward the right atrium (above baseline) occurs during diastole and is augmented with inspiration. Small systolic and early diastolic flow reversals that increase with expiration are seen. LA, left atrium.
Doppler echocardiographic guidance. The lowest filter settings were used.

Angle correction was not made in the present study because the correlation of velocities for the angle between the assumed direction of flow and the direction of Doppler sampling was within 15° in both the control subjects and the mitral stenosis patients.

The IVC pulsed-wave Doppler velocities were recorded with a respiratory trace using a heat-sensitive nasal respirometer on videotape and on a strip chart recorder at paper speeds of 25 and 50 mm/sec. Recordings were made during all phases of quiet respiration, avoiding any exaggerated increase caused by deep inspiration. The IVC pulsed-wave Doppler flow velocity in mitral stenosis patients without severe tricuspid regurgitation was recorded as a biphasic flow above the baseline with a predominant diastolic flow velocity and smaller or absent systolic flow velocity. Forward diastolic flow velocity was augmented at the onset of inspiration (lower panel in Figure 1). Small flow velocity reversals in systole or early diastole, which were augmented at the onset of expiration, were observed in patients without severe tricuspid regurgitation below the baseline, and systolic retrograde flow velocity below the baseline was observed during respiration in patients with severe tricuspid regurgitation.

Measurements of IVC orifice flow velocity were accepted only when a series of three consecutive respira-

![Bar graphs of the inferior vena caval (IVC) orifice dimension and IVC orifice flow velocity in the control subjects, group A (mitral stenosis patients without giant left atrium [LA]), and group B (mitral stenosis patients with giant LA). The IVC orifice dimensions in group B are significantly smaller than those in the controls and group A, and the IVC orifice flow velocities in group B are significantly greater than those in the controls and group A.](image1)

![Bar graphs of inferior vena caval (IVC) orifice dimension and IVC orifice flow velocity in the control subjects, mitral stenosis patients without severe tricuspid regurgitation [severe TR(-)], and patients with severe tricuspid regurgitation [severe TR(+)]. The inferior vena caval orifice dimension in mitral stenosis patients with severe tricuspid regurgitation is greater than in the control subjects and the patients without severe tricuspid regurgitation. The IVC orifice flow velocity is not significantly different among the three groups.](image2)
tory cycles were obtained in which the traces were of a similar appearance and shared a similar maximum velocity. The peak and mean velocities of IVC orifice flow in diastole averaged over three consecutive inspirations and expirations were obtained in each subject. Mean velocities were obtained by computerized planimetry of traces using a trackball.

In 12 patients with mitral stenosis, the IVC flow velocity was recorded in both the supine and the right lateral positions, and positional changes were examined by measuring peak and mean inspiratory IVC orifice velocities.

Superior vena caval and hepatic vein Doppler flow velocities. Doppler flow velocities in the superior vena cava were examined with a right supraclavicular view and with the transducer oriented parallel to the superior vena cava. By a method similar to those of previous studies,28,29 the flow velocity of the superior vena cava was identified on the color Doppler echocardiogram, and the pulsed-wave Doppler sample volume was placed in the vessel at 5–7 cm distal to the transducer.

Doppler flow velocities in the hepatic vein were examined in a subcostal view by orienting the transducer parallel to the IVC. By a method similar to that of Pennestri et al., the right superior hepatic vein was identified, and the Doppler sample volume was placed in the vessel at 1–2 cm proximal to its junction with the IVC.

Superior vena caval and hepatic vein flow velocities were recorded with a respiratory trace on videotape and on a strip chart recorder at paper speeds of 25 and 50 mm/sec. Recordings were made during all phases of quiet respiration, avoiding any exaggerated increase caused by deep inspiration. Superior vena caval and hepatic vein flow velocities were recorded as biphasic

flow below the baseline with a predominant diastolic flow velocity and a smaller systolic flow velocity in control subjects and mitral stenosis patients without severe tricuspid regurgitation, whereas systolic retrograde flow velocity above the baseline was observed in the patients with severe tricuspid regurgitation. The peak diastolic velocities of superior vena caval and hepatic vein flow were averaged over three consecutive inspirations in each subject.

Cardiac Catheterization

Cardiac catheterization was performed in 41 patients with mitral stenosis within 48 hours after Doppler echocardiographic study. Peak right ventricular systolic pressure and mean right atrial pressure were obtained by the standard technique with a fluid-filled catheter.

Simultaneous recording of the pressure difference between the right atrium and the IVC was performed in one patient with mitral stenosis having a giant left atrium and a peak IVC orifice Doppler flow velocity of 156 cm/sec with a fluid-filled catheter.

Detection and Measurement of Liver Size

Hepatomegaly was examined by palpation and confirmed by measurement of the distance from the right subcostal margin to the maximum edge of the liver at the midclavicular line in the control subjects and mitral stenosis patients. Three patients were excluded from analysis because of previous hepatitis or liver cyst.

Intraobserver and Interobserver Variation

Intraobserver variability in measurements of the IVC orifice dimension and flow velocity were obtained in 15 randomly selected patients by two independent observers. The average intraobserver variabilities for the quantitative assessment of the dimension and velocity at the IVC orifice were 4.3% and 4.7% of the mean values, respectively, and the average interobserver variabilities were 4.3% and 4.9%, respectively.

Statistical Analysis

The significances of differences of mean values of the IVC dimension, IVC orifice flow, and hepatic vein and superior vena caval flow velocities between groups were assessed by ANOVA. The natural logarithms of the peak flow velocity of the IVC orifice and the left atrial dimension were correlated with IVC orifice dimension by linear regression analysis. The significance of the difference of mean values of the IVC flow velocity in the supine and right lateral positions was assessed in 12 patients with mitral stenosis by Student’s paired t test. Differences in the mean values of the liver size between groups were assessed by ANOVA, and differences in the incidence of hepatomegaly in each group were compared by χ² analysis. Data were expressed as the mean±1 SD. A probability value of less than 0.05 was considered statistically significant.

Results

Inferior Vena Caval Orifice Dimensions and Doppler Flow Velocities

The IVC orifice on the two-dimensional echocardiogram and Doppler signals of the flow velocity at the orifice on the color Doppler echocardiogram were
clearly demonstrated in all 90 subjects, and they all had pulsed-wave Doppler echocardiographic flow velocity tracings that were adequate for analysis.

The IVC orifice dimensions and flow velocities in groups A and B are shown in Figure 2. The dimension in group B was significantly smaller (p<0.01) than those in the control group and group A. The IVC orifice peak flow velocity during inspiration was significantly greater (p<0.01) in group B than in the control group and group A. On the other hand, the IVC orifice dimension in the mitral stenosis patients with severe tricuspid regurgitation (n=23) was significantly greater (p<0.01) than those in the control subjects and the mitral stenosis patients without severe tricuspid regurgitation (n=51), whereas the IVC flow velocity was not significantly different among the three groups (Figure 3). Therefore, all the mitral stenosis patients in groups A and B were further categorized according to the presence or absence of severe tricuspid regurgitation and were finally divided into four subgroups: mitral stenosis patients with neither severe tricuspid regurgitation nor a giant left atrium (n=33), mitral stenosis patients with a giant left atrium and without severe tricuspid regurgitation (n=18), mitral stenosis patients with severe tricuspid regurgitation and without a giant left atrium (n=14), and mitral stenosis patients with both severe tricuspid regurgitation and a giant left atrium (n=9). Representative views of the IVC orifice obtained by two-dimensional and color Doppler echocardiography and reanalyzed data on the left atrial dimension, IVC orifice dimension, and flow velocity are shown in Figure 4 and Table 2, respectively, for the control subjects and each subgroup. In mitral stenosis patients without severe tricuspid regurgitation, the IVC orifice became narrower as the left atrium became larger, and the atrial septum bulged further into the right atrium (panels a, b, and c in Figure 4). The IVC orifice dimension in the mitral stenosis patients without severe tricuspid regurgitation was still significantly smaller (p<0.05) in the patients with a giant left atrium (11.4±4.4 mm) than those of the control subjects and the patients without a giant left atrium (18.6±5.4 mm). The peak IVC orifice flow velocities in inspiration and expiration were significantly greater (p<0.05) in the mitral stenosis patients with a giant left atrium (93.4±32.0 and 47.6±19.8 cm/sec) than in the patients without a giant left atrium (70.2±18.4 and 38.1±11.5 cm/sec) and the control subjects (67.9±12.8 and 34.5±7.0 cm/sec, respectively). The mean inspiratory IVC orifice flow velocity of the mitral stenosis patients with a giant left atrium (48.3±19.5 cm/sec) was also significantly greater (p<0.05) than those of the patients without a giant left atrium (40.3±11.3 cm/sec) and the control subjects (37.9±7.8 cm/sec). There were no significant differences, however, among these three groups in regard to expiratory mean IVC orifice flow velocity.

In the remaining 23 mitral stenosis patients with severe tricuspid regurgitation, the peak inspiratory IVC orifice velocity was significantly greater (p<0.05) and the IVC orifice dimension was significantly smaller (p<0.05) in patients with the giant left atrium compared with the patients without a giant left atrium, in whom IVC orifice dimensions were significantly greater (p<0.05) than in the control subjects (Figure 4 and Table 2). The peak expiratory IVC orifice flow velocity in the patients with a giant left atrium was significantly greater than in the controls but was not significantly different from that in the patients without a giant left atrium. There were no significant differences among these three groups regarding inspiratory and expiratory mean IVC orifice flow velocity.

**Correlations of IVC Orifice Dimension, Doppler Flow Velocity, and Left Atrial Dimension**

The correlation of the IVC orifice flow velocity with the IVC orifice dimension for the control subjects and for overall mitral stenosis patients was r=−0.31 (n=90). However, there was a significant negative correlation of r=−0.62 (n=67, SEE=0.33 cm/sec, y=e−0.01x+3.8, p<0.01) between the IVC orifice dimension (17.1±5.6 mm) and the peak IVC flow velocity (75.3±24.3 cm/sec) when patients with severe tricuspid regurgitation were excluded from the analysis (left panel in Figure 5).

The correlation of IVC orifice dimension and left atrial dimension for the control subjects and for overall mitral stenosis patients was r=−0.33 (n=90). For the control subjects and the mitral stenosis patients without severe tricuspid regurgitation, however, there was a significant negative correlation of r=−0.71 (n=67, SEE=0.32 mm, y=e−0.68x+3.8, p<0.01) between the IVC orifice dimension and the left atrial dimension (56.9±15.9 mm) (right panel in Figure 5).

**Superior Vena Caval and Hepatic Vein Doppler Flow Velocities**

Doppler signals of the flow velocities were obtained in all subjects in the hepatic vein and in all but two in the superior vena cava. The peak inspiratory flow velocities in the hepatic vein and superior vena cava were not significantly different among the controls and the four patient subgroups (Table 2).

**Examination of Positional Changes of the IVC Orifice Velocity**

In 12 patients with mitral stenosis in whom the IVC orifice velocity could be recorded in two positions, the peak and mean Doppler flow velocity signals did not show any significant changes when the position was altered from supine to right lateral (Table 3).

**Cardiac Catheterization Findings**

**Right-side pressures.** The peak systolic right ventricular and mean right atrial pressures in each subgroup of mitral stenosis patients are shown in Table 4. Although the peak right ventricular systolic pressure in the patients with a giant left atrium and severe tricuspid regurgitation was significantly greater than in the other three subgroups, there were no significant differences between group A and group B without severe tricuspid regurgitation. There were no significant differences of the mean right atrial pressure among the four patient subgroups.

**Simultaneous recording of right atrial and inferior vena cava pressure.** The simultaneous right atrial and IVC pressure traces obtained in one patient with an IVC flow velocity of 156 cm/sec demonstrated a positive pressure difference from the IVC to the right atrium throughout the cardiac cycle. Pressure differences of 8 mm Hg during expiration and 13 mm Hg during inspiration were recorded (Figure 6).
TABLE 2. Two-dimensional and Doppler Echocardiographic Findings in the Control and Mitral Stenosis Patients in Four Subgroups

<table>
<thead>
<tr>
<th>Dimensions (mm)</th>
<th>Control (n=16)</th>
<th>Group A (n=33)</th>
<th>Group B (n=18)</th>
<th>p</th>
<th>Group A (n=14)</th>
<th>Group B (n=9)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left atrium</td>
<td>41.6±5.8</td>
<td>53.2±7.4*</td>
<td>78.8±11.2*</td>
<td>&lt;0.05</td>
<td>52.4±6.7†</td>
<td>75.7±5.9†</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>(30-49)</td>
<td>(42-64)</td>
<td>(67-107)</td>
<td></td>
<td>(43-62)</td>
<td>(65-87)</td>
<td></td>
</tr>
<tr>
<td>IVC orifice</td>
<td>20.1±2.1</td>
<td>18.6±5.4</td>
<td>11.4±4.4*</td>
<td>&lt;0.05</td>
<td>30.5±9.2††</td>
<td>23.8±9.7††</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>(16-25)</td>
<td>(8-29)</td>
<td>(3-21)</td>
<td></td>
<td>(16-45)</td>
<td>(8-39)</td>
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</table>

Velocities (cm/sec)

| IVC orifice Peak | Inspiration | 67.9±12.8 | 70.2±18.4 | 93.4±32.0* | <0.05 | 69.9±15.3† | 88.6±30.0†† | <0.05 |
|                 |             | (47-98)   | (33-97)   | (41-156)   |     | (50-110)   | (57-140)    |     |
|                 | Expiration  | 34.5±7.0  | 38.1±11.5 | 47.6±19.8* | <0.05 | 47.1±17.0†  | 50.0±9.6*   | NS   |
|                 |             | (25-52)   | (20-62)   | (20-93)    |     | (29-106)   | (31-67)     |     |
| Mean Inspiration | 37.9±7.8    | 40.3±11.3 | 48.3±19.5* | <0.05 | 41.6±11.1 | 43.8±17.7 | NS   |
| Expiration      | 24.3±5.5    | 22.4±6.9  | 23.4±10.2  | NS         | 27.7±4.4†† | 27.3±11.9 | NS   |
|                 |             | (14-38)   | (13-46)   | (7-41)     |     | (23-40)    | (8-43)      |     |
| SVC Peak, inspiration | 57.6±15.0 | 57.4±19.1 | 58.9±16.8 | NS | 65.4±18.7 | 66.4±9.7 | NS   |
|                 |             | (34-88)   | (25-93)   | (13-82)    |     | (32-99)    | (50-81)     |     |
| HV Peak, inspiration | 54.9±17.1 | 53.9±15.0 | 49.2±15.9 | NS | 53.6±19.0 | 54.4±17.6 | NS   |
|                 |             | (34-94)   | (25-86)   | (30-100)   |     | (33-98)    | (47-95)     |     |

TR, tricuspid regurgitation; IVC, inferior vena cava; SVC, superior vena cava; HV, hepatic vein. Values are expressed as mean±SD (range).

*p<0.05 vs. control.
†p<0.05 vs. group A without severe TR.
‡p<0.05 vs. group B without severe TR.

Incidence of Hepatomegaly

The mean values of the liver size and the incidence of hepatomegaly in each subgroup are shown in Table 5. The mean values of the liver size in patients without severe tricuspid regurgitation was significantly greater (p<0.01) in the patients with the giant left atrium (35.7±9.8 mm) than in those without it (15±0 mm). In patients with severe tricuspid regurgitation, there were no significant differences in the liver size between group A and group B (36.4±8.5 mm versus 36.7±11.5 mm), and neither group was significantly different from group B patients without severe tricuspid regurgitation. Thus, hepatomegaly was present in 33 of 71 mitral stenosis patients (46%). No control patients had hepatomegaly.

The incidence of hepatomegaly in patients without severe tricuspid regurgitation was significantly greater (p<0.001) in group B than in group A (71% versus 10%). In patients with severe tricuspid regurgitation, the incidence of hepatomegaly in both group A and group B patients was significantly more frequent (p<0.001) than for group A patients without severe tricuspid regurgitation (71% and 89% versus 10%). However, neither group was significantly different from group B patients without severe tricuspid regurgitation.

Discussion

Although pulsed or continuous-wave Doppler echocardiography has allowed accurate measurement of flow velocities and prediction of the pressure gradient across a stenotic or obstructive lesion at the optimal portion in the cardiac cavity or vessels,1-14 no previous studies have applied Doppler echocardiography to obstruction at the IVC orifice. This might be related to the difficulty of detecting flow velocities at the IVC orifice with a sufficiently high-quality Doppler shift by standard Doppler techniques.

We have demonstrated in this study the presence of an increased IVC orifice flow velocity associated with narrowing of the orifice caused by bulging of the atrial septum in mitral stenosis patients with giant left atrium. This study reports the first two-dimensional and Doppler echocardiographic description of this condition using a right parasternal approach.

Previous invasive clinical or experimental studies of the IVC in its upper abdominal portion by use of flow manometry have reported a biphasic pattern of flow.30-35 In the present study, flow velocities at the IVC orifice in both control and mitral stenosis patients without severe tricuspid regurgitation, all of whom were in atrial fibrillation, demonstrated a pattern similar to that reported previously with predominant diastolic flow and lesser systolic flow.33 Although the flow velocities recorded showed small variations in magnitude and pattern from beat to beat and with respiration, they were considered to be suitable for quantitative analysis.
because there was an overall constancy of magnitude and pattern and because both the intraobserver and interobserver variation was small.

Advantages of the Right Parasternal Approach

The right parasternal approach was advantageous for several reasons. It allowed the Doppler beam to be virtually parallel to IVC orifice flow, thus providing for high-quality recordings of flow velocity because of the anterior angulation of the IVC at the level of the diaphragm. Accurate detection of IVC orifice flow by this approach appeared possible because the IVC orifice flow velocities exhibited a pattern and respiratory variation similar to those found by direct measurement of flow in the upper abdominal IVC by invasive phasic flowmetry. Additionally, this approach allowed easy differentiation of IVC orifice flow from superior vena cava and coronary sinus flow into the right atrium because of their different origins and directions on color Doppler echocardiography.

Evidence for Localized Obstruction at the Inferior Vena Cava Orifice

Several factors suggest the localized nature of the obstruction of venous return at the IVC orifice by a giant left atrium. An increased flow velocity was observed at the IVC orifice, whereas normal flow velocities were recorded in the same patients within the superior vena cava and hepatic vein. In addition, increased flow velocities were recorded exclusively in those patients with left atrial dimensions ≥65 mm on the standard left parasternal view. Finally, in one patient with a giant left atrium, simultaneous pressure recordings from the right atrium and IVC showed a pressure difference of 13 mm Hg during inspiration. Thus, localized obstruction of venous return at the IVC orifice was confirmed both by Doppler flow velocities and pressure recordings.

Because the IVC orifice dimension was best correlated with the left atrial dimension in patients without severe tricuspid regurgitation (r = -0.71), the narrowed IVC orifice dimension is considered to be a result of the marked encroachment of the atrial septum into the right atrium resulting from left atrial enlargement caused by mitral stenosis. However, it should be pointed out that not all patients with a left atrial dimension >64 mm had increased IVC orifice flow velocities. This suggests that the enlargement of the left atrium may be asymmetrical and that obstruction of flow at the IVC orifice may

![Figure 5. Scatterplots with regression lines showing the correlations between the inferior vena caval (IVC) orifice dimension and the IVC orifice flow velocity (left panel) or the left atrial dimension (right panel) in the control subjects and the mitral stenosis patients without severe tricuspid regurgitation. Significant correlations between the IVC orifice dimension and the peak Doppler flow velocity (left panel, n=67) as well as the IVC orifice dimension and the left atrial dimension (right panel, n=67) are demonstrated by logarithmic function. Numbers of patients do not sum to 67 because one pair has the same value in the left panel and three pairs in the right panel.](image-url)
depend on the direction of enlargement as well as overall left atrial size.\textsuperscript{18-21}

\textbf{Influence of Severe Tricuspid Regurgitation on the IVC Orifice Dimension and Flow Velocity}

In contrast to the narrowed IVC orifice of the patients with giant left atrium, patients with severe tricuspid regurgitation and no giant left atrium had a significantly dilated IVC orifice and no significant increase in the IVC orifice flow velocity. It is easy to suggest that the dilatation of the IVC orifice is a result of IVC and right atrial enlargement caused directly by severe tricuspid regurgitation, as this is well known to cause enlargement of these structures. In mitral stenosis patients with severe tricuspid regurgitation, however, patients with a giant left atrium also showed significantly smaller IVC orifice dimensions and significantly greater IVC orifice flow velocities than those without a giant left atrium. These data suggest that the IVC orifice narrowed by a giant left atrium will be widened by the development of severe tricuspid regurgitation caused by subsequent right atrial enlargement. Thus, the interaction of tricuspid regurgitation and left atrial size in mitral stenosis probably determines the size of the IVC orifice by the degree of the shift of the atrial septum to the left or right, respectively. However, the significance of this combination on the hemodynamics at the IVC orifice in mitral stenosis remains to be investigated.

\textbf{Effect of Posture on the IVC Doppler Flow Velocities}

The inferior vena caval Doppler flow velocities in this study were detected from the right parasternal approach with patients in the right lateral position. We also examined the effect of the right lateral position on IVC flow velocities in both the supine and right lateral positions in 12 patients with mitral stenosis. There were no significant differences in the magnitude of IVC flow between the two positions. Additionally, Higashi et al\textsuperscript{37} investigated the influence of position on IVC hemodynamics by measuring the pressure gradient between the IVC and the right atrium in the supine and right lateral positions in 10 patients with ischemic heart disease having normal right atrial pressures. These authors described a significantly lower pressure gradient in the right lateral position (0.8±0.6 mm Hg) than in the supine position (1.7±0.8 mm Hg). These data also support our findings, because the pressure gradient is related to flow velocity through the modified Bernoulli equation.\textsuperscript{1-7} Thus, the right lateral position does not appear to significantly influence Doppler flow velocities at the IVC orifice.

\textbf{Relation to Venous Congestion}

The results of this study suggest that a localized obstruction at the IVC orifice contributes to venous congestion. Because most patients either were receiving or had recently received diuretics and other medical therapy that may have diminished or alleviated symptoms, the liver size was measured as a clinical marker of venous congestion.\textsuperscript{38}

In our study, a significantly higher incidence of hepatomegaly was observed in patients with a giant left atrium and no severe tricuspid regurgitation. Right atrial pressures in patients with a giant left atrium and no severe tricuspid regurgitation were not significantly elevated or different from those with normal liver size. Thus, localized obstruction at the IVC orifice could contribute to venous congestion in mitral stenosis patients with a giant left atrium in the absence of a significantly elevated right atrial pressure or severe tricuspid regurgitation because severe tricuspid regurgitation and right atrial hypertension are well-documented causes of venous congestion.\textsuperscript{38} In addition, confirmatory hemodynamic evidence for a localized obstruction was found in one patient with a pressure difference from 8 to 13 mm Hg between the IVC and

\begin{table}
\centering
\begin{tabular}{lccc}
\hline
 & \multicolumn{2}{c}{Severe TR (−)} & \multicolumn{2}{c}{Severe TR (+)} \\
 & Group A & Group B & Group A & Group B \\
\hline
Right-sided pressure & & & & \\
RVSP (mm Hg) & 38.9±13.4 (20–57) & 45.3±13.7 (33–55) & NS & 42.6±10.7 (27–52) & 51.8±18.5* (30–66) & <0.05 \\
RAP (mm Hg) & 5.8±1.8 (2–8) & 5.8±1.8 (3–9) & NS & 8.1±4.6* (4–19) & 8±2.6* (6–12) & NS \\
\hline
\end{tabular}
\caption{Right Ventricular Systolic Pressure (Peak) and Mean Right Atrial Pressure of Mitral Stenosis Patients in Four Subgroups}
\end{table}

\begin{table}
\centering
\begin{tabular}{lccc}
\hline
 & \multicolumn{2}{c}{Severe TR (−)} & \multicolumn{2}{c}{Severe TR (+)} \\
 & Group A & Group B & Group A & Group B \\
\hline
Distance from subcostal margin to liver edge (mm) & 15±0 (15–15) & 35.7±9.8 (20–45) & NS & 36.4±8.5* (20–50) & 36.7±11.5* (25–50) & NS \\
Incidence of hepatomegaly & 3/31 (10%) & 12/17 (71%) & <0.001 & 10/14 (71%)* & 8/9 (89%)* & NS \\
\hline
\end{tabular}
\caption{Incidence of Hepatomegaly}
\end{table}

\textsuperscript{*}p<0.05 vs. group A and group B without severe TR.

\textsuperscript{†}p<0.001 vs. group A without severe TR by \textit{X}^2 analysis.
the right atrium. Simultaneous pressure recordings from the IVC and right atrium were not performed in enough patients, however, particularly those with a giant left atrium, for a valid analysis. The relation between localized obstruction at the IVC orifice and venous congestion needs further invasive hemodynamic study for complete elucidation.

Conclusions

The present study is the first to document that mitral stenosis patients with a giant left atrium without severe tricuspid regurgitation have narrowing of the IVC orifice at its junction with the right atrium (IVC orifice) on the two-dimensional echocardiogram. This is associated with a significantly increased flow velocity at the IVC orifice narrowed by extreme rightward displacement of the atrial septum from the gross left atrial enlargement. Furthermore, these patients have significantly higher incidence of hepatomegaly, which may be related to a localized obstruction of flow at the IVC orifice and subsequent venous congestion. These findings suggest that the giant left atrium seen in patients with mitral stenosis may contribute to obstruction of venous return from the IVC and result in venous congestion in the absence of severe tricuspid regurgitation or significant right atrial hypertension.

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