Color Doppler Evaluation of Valvular Regurgitation in Normal Subjects

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To determine prospectively the prevalence of mitral, aortic, tricuspid, and pulmonary regurgitation in normal persons, 211 consecutive, apparently healthy volunteers were examined with a color Doppler flow imaging system. The subjects were divided into five age groups (group 1, 6–9 years old; group 2, 10–19 years old, group 3, 20–29 years old, group 4, 30–39 years old, and group 5, 40–49 years old). The prevalence rate of mitral regurgitation in the normal subjects was 38–45% in each group. The mitral regurgitant jets came from the posteromedial commissure in all but two subjects. No aortic regurgitant flow signals were detected in the normal subjects. Tricuspid regurgitation was detected in 15–77% in each group, and pulmonary regurgitation was detected in 28–88%. Regarding the tricuspid and pulmonic valves, the prevalence rate of regurgitation is age dependent (p<0.01) and tends toward the lower rate in groups over the age of 30 years. The tricuspid and pulmonary regurgitant jets came from the center of the coaptation of each valve. The area of the regurgitant jet signals in normal persons was significantly smaller (p<0.001) than that obtained from patients with organic valve disease. Our study shows that in a large proportion of normal persons under the age of 50 years color Doppler echocardiography permits recording of regurgitant signals behind all valves except the aortic. In conclusion, one should be aware of the existence and characteristics of regurgitation in normal persons when evaluating valvular regurgitation by Doppler techniques. (Circulation 1988;78;840–847)

Doppler techniques now permit noninvasive evaluation of intracardiac blood flow and have a widely established record of accuracy in the detection of regurgitation of all four cardiac valves.1–9 Ever since technical improvements have made the detection of even mild regurgitation possible, regurgitant turbulent flow signals have been detected in normal subjects.10–15 The recent development of color Doppler flow imaging, which superimposes color-coded flow patterns on real-time two-dimensional images, has made it possible to map abnormal flow patterns such as those seen in patients with valvular regurgitation.16–18 Being noninvasive, the color Doppler technique is readily applicable to the evaluation of asymptomatic as well as symptomatic patients. Little information is available concerning the characteristics, prevalence, and mechanism of regurgitation in normal subjects. In the present study, the color Doppler technique was chosen to determine the prevalence of valvular regurgitation in a large, consecutive, and prospectively studied series of normal subjects.

Subjects and Methods

 Apparently healthy volunteers without cardiac symptoms were studied. All were healthy persons recruited at random from a mass survey at an elementary school, a junior high school, a university, and from the general community. None had a previous diagnosis of cardiovascular disease. Patients were excluded if they had a pansystolic murmur, late systolic murmur, long ejection systolic murmur, or diastolic murmur. The subjects having abnormal electrocardiographic findings were also excluded. Finally, of the 235 subjects recruited, 24 were excluded because of either abnormal elec-
TABLE 1. Prevalence of Valvular Regurgitation in Each Group

<table>
<thead>
<tr>
<th>Valvular regurgitation</th>
<th>Age (yr)</th>
<th>6–9 (n = 40)</th>
<th>10–19 (n = 47)</th>
<th>20–29 (n = 44)</th>
<th>30–39 (n = 41)</th>
<th>40–49 (n = 39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral regurgitation</td>
<td></td>
<td>18 (45%)</td>
<td>21 (45%)</td>
<td>19 (43%)</td>
<td>17 (41%)</td>
<td>15 (38%)</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td></td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td></td>
<td>31 (78%)</td>
<td>31 (66%)</td>
<td>28 (64%)</td>
<td>14 (34%)</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>Pulmonary regurgitation</td>
<td></td>
<td>35 (88%)</td>
<td>30 (64%)</td>
<td>30 (68%)</td>
<td>14 (34%)</td>
<td>11 (28%)</td>
</tr>
</tbody>
</table>

trocardiograms or examination, which left 211 subjects in our study population. There were 111 females and 100 males, and their age ranged from 6 to 49 years (mean, 29 years). The subjects were divided into five age groups (Table 1) by decades (group 1, 6–9 years; group 2, 10–19 years; group 3, 20–29 years; group 4, 30–39 years; group 5, 40–49 years).

Color Doppler Echocardiography

Color Doppler examinations were performed with a commercially available system (SSH-65A, Toshiba, Tokyo, Japan) and a 2.5- or 3.5-MHz transducer. Pulse repetition frequencies of 4, 6, or 8 kHz were available. A frequency of 4 kHz was routinely used, which allowed measurement of velocities up to 75 cm/sec. The scanning rate used in this study was 12 frames/sec. Flow directed toward the transducer was conventionally coded in red, whereas flow directed away was coded in blue. Variations in velocity are presented by brightness and intensity of color. Because the color Doppler system is based on a pulse mode, the magnitude of flow velocity is limited in all points of the ultrasound sector. If turbulence occurs, green is added to the red or blue underlying color, thus changing the basic color tonality, which results in a mosaic pattern. Doppler color gain was optimized as described previously. Briefly, the gain was first turned down completely and then increased very gradually until the static background noise barely appeared. All images were permanently recorded on a ¾ in. (U-Matic) Sony videotape. Pictures were obtained with a Polaroid camera placed in front of a color television monitor. Color flow mapping was also performed in an M-mode format (superim-

FIGURE 1. Color Doppler echocardiograms from an 18-year-old normal woman. Left panel: Parasternal long-axis view shows bluish green signals (arrow) in the left atrium during systole, which is indicative of mitral regurgitation. Right panel: Short-axis view at the level of the mitral valve shows the regurgitant jet originates from the posteromedial commissure. AO, aorta; LA, left atrium; LV, left ventricle; LVOT, left ventricular outflow tract.
posed on conventional M-mode echocardiographic images) by selective placement of a line cursor on two-dimensional echocardiographic images.

Doppler windows were parasternal long-axis, parasternal short-axis, and apical long-axis views for the aortic valve and parasternal long-axis, parasternal short-axis, and apical four-chamber views for the mitral valve. For the tricuspid valve, the traces were recorded in the right ventricular inflow view and parasternal and apical four-chamber views. For the pulmonic valve, we recorded the traces in the long-axis view of the right ventricular outflow tract and high left parasternal short-axis view. The flow signal was judged as a regurgitation when it was observed as a reversed flow away from the valve by color Doppler echocardiography and when its duration was more than 100 msec by M-mode color flow mapping. Mitral regurgitation was considered to be present if blue, green, or mosaic signals were seen originating from the mitral valve and spreading into the left atrium during systole. Aortic regurgitation was considered to be present if red, yellow, or mosaic signals were seen originating from the aortic valve and spreading into the left ventricle during diastole. Tricuspid regurgitation was judged to be present if blue, green, or mosaic signals were seen originating from the tricuspid valve and spreading into the right atrium during systole. Pulmonary regurgitation was judged to be present if red, yellow, or mosaic signals were seen originating from the pulmonic valve and spreading into the right ventricular outflow tract during diastole.

To compute the maximum area of the regurgitant jet signals with orthogonal planes, videotapes were carefully analyzed frame by frame. By means of a software program already incorporated in the equipment, the outline of the regurgitant jet area was traced with a joystick, and the area was measured by computerized planimetry. The maximum area of the regurgitant jet signals was obtained by measuring the largest jet area of those obtained from orthogonal planes. The regurgitant jet area obtained from normal persons was compared with the regurgitant area obtained from 40 patients with mitral valve disease and compared with that in 40 patients with tricuspid regurgitation in association with left-sided valvular disease confirmed by angiography. The patient population consisted of 23 patients with mitral regurgitation due to ruptured chordae tendineae associated with tricuspid regurgitation and of 17 patients who had rheumatic mitral stenosis and regurgitation combined with tricuspid regurgitation.

Conventional pulsed Doppler echocardiography was also performed by selective placement of a sample volume on the color Doppler echocardiographic regurgitation signals in all subjects. Maximal examination time was limited to 15 minutes for each valve.

Statistical Analysis

Statistical analysis was performed with nonparametric techniques with respect to the prevalence of valvular regurgitation in each age group. A Kruskall-Wallis test was applied to assess the correlation between the prevalence of valvular regurgitation and age groups. A probability value less than 0.01 was considered significant. Observer variability in the subjective assessment of the presence or absence of regurgitation and in the quantitative estimation of
regurgitant jet area in our laboratory has been determined in 40 randomly selected patients. From the accumulated data, there was no interobserver or intraobserver variability in the subjective assessment of the presence or absence of regurgitation. The average intraobserver variability for the quantitative estimation of regurgitant jet area was 2.9% of the mean value, and the average interobserver variability was 4.4% of the mean.

Results

Mitral Valve

Regurgitant flow signals were detected in 38–45% in each age group (Table 1). The regurgitant flow signals (Figures 1 and 2) came from the posteromedial commissure in the mitral valve in all but two subjects. Regurgitant flow signals were localized in the vicinity of the mitral valve, and the regurgitant area ranged from 0.03 to 0.88 cm² (mean, 0.26±0.24 cm²).

Aortic Valve

No regurgitant flow signal was detected as originating from the aortic valve in any subject.

Tricuspid Valve

Regurgitant flow signals (Figure 3 and Figure 4) were detected in 15–78% in each group. The prevalence of tricuspid regurgitation decreased in proportion to aging. The tricuspid regurgitant jets originated at the center of coaptation of the tricuspid valve, and the regurgitant area ranged from 0.04 to 1.52 cm² (mean, 0.42±0.40 cm²).

Pulmonic Valve

Regurgitant flow signals (Figure 5) were detected in 28–88% in each group. The prevalence of pulmonary regurgitation decreased in proportion to aging. The regurgitant jets came from the center of the coaptation of the pulmonic valve, and the regurgitant area ranged from 0.03 to 1.04 cm² (mean, 0.28±0.26 cm²).

The mitral regurgitant jet area obtained from 40 patients with mitral valve disease ranged from 0.60 to 17.8 cm² (mean, 5.63±4.15 cm²). The tricuspid regurgitant jet area obtained from 40 patients with tricuspid regurgitation in association with left-sided valvular disease ranged from 0.30 to 16.6 cm² (mean, 5.93±4.24 cm²).

With conventional pulsed Doppler echocardiography, regurgitation signals were detected in all subjects in whom regurgitation signals were detected by color Doppler echocardiography.

Statistical Analysis

No differences were found between men and women in each group. In the tricuspid and pulmonic valves, the prevalence rate of regurgitation depends on the age (p<0.01) with a tendency toward lower rates in the groups over the age of 30 years. The regurgitant jet area (Figure 6) in normal persons was significantly smaller (p<0.001) than the regurgitant area obtained from patients with organic valvular disease.

Discussion

Doppler echocardiography has proven to be a highly accurate and objective noninvasive technique.
for detecting valvular regurgitation. In patients with a variety of cardiovascular diseases necessitating left ventriculography, the sensitivity of pulsed Doppler echocardiography in detecting mitral regurgitation has ranged from 87% to 94%, and the specificity has ranged from 77% to 96%. With aortic regurgitation, pulsed Doppler echocardiography has been reported to have a sensitivity of 94% and a specificity of 82% compared with results of aortography.

In the present study with color Doppler, mitral regurgitation, tricuspid regurgitation, and pulmonary regurgitation were detected in 45–88% of the apparently healthy persons less than 20 years of age. An extremely high prevalence of mitral, tricuspid, and pulmonary regurgitation may indicate that all normal persons may have silent physiological regurgitation. However, the regurgitant flow signals were localized in the vicinity of valve closure, and the regurgitant jet area in normals was significantly smaller than the regurgitant jet area obtained from patients with organic mitral valve disease. Although some investigators have not detected tricuspid or pulmonary regurgitation, others have detected signals suggestive of tricuspid or pulmonary regurgitation in many apparently healthy subjects. Although little information is available concerning the prevalence, characteristics, and mechanisms of these flows in normal subjects, such data appear essential for a Doppler echocardiographic definition of pathological regurgitation. Using continuous wave Doppler echocardiography in 20 normal subjects, Yock et al. reported that the prevalence rates were 95% in the tricuspid valve, 35% in the pulmonic valve, 10% in the mitral valve, and 0% in the aortic valve. In a recent study with pulsed Doppler echocardiography, Kostucki et al. showed prevalence rates of 92% pulmonic, 44% tricuspid, 40% mitral, and 33% aortic regurgitation. In their study, however, the Doppler aortic regurgitant flow signal was always in early diastole. It had no clearly distinguishable audio signal, had very low velocities, and could only be recorded adjacent to the valve. The flow pattern that they have reported was clearly different from that of well-established aortic regurgitant signals, and artifacts cannot be ruled out even when small sample volume and high-pass filters are used.

The recently developed technique of color Doppler flow imaging, which superimposes color-coded flow patterns on real-time two-dimensional images, has made it possible to map abnormal flow patterns such as those seen in patients with valvular regurgitation. The ability to scan the cardiac chamber quickly and thoroughly for abnormal flow signals makes color Doppler examination more comprehensive and less tedious than conventional pulsed Doppler echocardiography.

The reason why the regurgitant signals were detected easily in younger normal persons may be the superior ultrasonic penetration obtainable in such subjects. The prevalence of tricuspid regurgitation and pulmonary regurgitation decreased in proportion to aging. This may be because ultrasonic penetration becomes poorer in proportion to aging. As a matter of fact, in certain adult individuals, such as those with obesity or emphysema, the ultrasound may be too attenuated to permit adequate detection of Doppler signals from distally located areas. Furthermore, in middle-aged subjects, just as it is sometimes difficult to visualize the
tricuspid valve and pulmonic valve clearly by two-dimensional echocardiography, it is also difficult to detect regurgitant signals by Doppler techniques. However, as the quantification of the quality of the two-dimensional echocardiographic images may be difficult, further investigation is necessary in reference to the question of why the prevalence of regurgitation appears to decrease with age. We have already reported that valvular regurgitation as detected by pulsed Doppler echocardiography increases progressively in proportion to aging in apparently healthy subjects who are 60 years or older and is almost uniformly observed in subjects who are 80 years or older. The high prevalence rate of Doppler-detected regurgitation in the older age groups may represent a true increase in the prevalence of regurgitation. Grossly, the valves become thicker and more opaque with advancing age. The grade of these changes is, in part, genetically determined and, in part, age related. Long-standing mechanical stress also may play a role in producing regurgitation. In our previous study of aged individuals, aortic regurgitation was most frequent, mitral regurgitation was the next most frequent, and right-sided valvular regurgitation was less frequent. The left-sided valves, aortic and mitral, are exposed, of course, to high pressures and may therefore undergo degenerative changes earlier than right-sided valves. No aortic regurgitant signals were detected in young normal subjects in the present study. The reason for the absence of signals of aortic regurgitation in normal persons remains unclear. We believe that this represents a true difference between the prevalence of aortic and both mitral and right-sided regurgitations.

In the last few years, color Doppler flow mapping has been the object of great interest. This new technique, unlike other invasive and noninvasive procedures, provides a dynamic method for studying the spatial distribution of intracavitary flow patterns while observing cardiac structure dynamics in real time. In the present study, the prevalence rate of regurgitation with conventional pulsed Doppler echocardiography was the same as that of color Doppler echocardiography because conventional pulsed wave examinations were performed with the guidance of color Doppler echocardiography. The prevalence rate may become lower if conventional pulsed wave examinations were performed without the aid of color Doppler echocardiography. It is possible to identify unexpected and extremely eccentric or trivial regurgitant flow signals by color Doppler, whereas it is time consuming and often difficult by conventional pulsed Doppler echocardiography. With conventional pulsed Doppler echocardiography, the possibility of false-negative results is very real. Because many regurgitant jets in normal persons are very localized, failure to position the sample volume in the jet may result in failure to detect regurgitation.

Limitations

Because of the nature of the subject population, which was made up of apparently healthy volunteers, cardiac catheterization was not performed. Therefore, we were unable to confirm the presence or absence of valvular regurgitation by angiography. Although color Doppler flow imaging has many advantages, it is possible that false-positive or false-negative diagnoses may have been made. Using conventional, pulsed Doppler echocardiography, previous investigators of the mitral and tricuspid valves have reported negative deflections in early systole in patients without apparent regurgitation. However, as stated by previous investigators, these signals are limited in time and have a typically high-pitched audio signal that can be separated from regurgitant signals. In the present study, signals...
with a duration of less than 100 msec by M-mode color Doppler echocardiography were excluded to avoid such confusion.

Clinical Implications

The principal clinical implication of realizing the possibility of silent Doppler regurgitation is to avoid iatrogenic heart disease. Our study reveals a high prevalence of hemodynamically insignificant degrees of regurgitation from the mitral, tricuspid, and pulmonic valves in normal persons. When valvular regurgitation is recognized by color Doppler echocardiography, other clinical and laboratory evidence of heart disease should be carefully evaluated to avoid overdiagnosis. Furthermore, the characteristics of Doppler-detected valvular regurgitation in normal subjects should be taken into consideration. Whatever the mechanisms of these regurgitant signals, one should be aware of their existence when assessing valvular regurgitation by Doppler techniques.

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References


KEY WORDS • Doppler techniques • normal persons • valvular heart disease
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