Pulsed Doppler Echocardiographic Evaluation of Valvular Regurgitation in Patients With Mitral Valve Prolapse: Comparison With Normal Subjects

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Pulsed Doppler echocardiography was used to determine prospectively the prevalence of mitral, aortic, tricuspid and pulmonary regurgitation in 80 consecutive patients with mitral valve prolapse and 85 normal subjects with similar age and sex distribution. Mitral valve prolapse was defined by posterior systolic displacement of the mitral valve on M-mode echocardiography of 3 mm or more (40 patients), the presence of one or more mid- or late systolic clicks (61 patients), or both.

Mitral regurgitation, detected by pulsed Doppler techniques in 53 patients with prolapse, was holosystolic in 24, early to mid-systolic in 6, late systolic in 15 and both holosystolic and late systolic behind different portions of the valve in 8. Definitive M-mode findings were present in only 27 of the 53 patients, and only 21 had mitral regurgitation audible on physical examination. Tricuspid regurgitation was evident by pulsed Doppler echocardiography in 15 patients (holosystolic in 9, early to mid-systolic in 1, late systolic in 4 and both holosystolic and late systolic in 1); 12 of these 15 patients, including all with an isolated late systolic pattern, had an echocardiographic pattern of tricuspid prolapse, but none had audible tricuspid regurgitation. A Doppler pattern compatible with aortic regurgitation was recorded in seven patients, all without echocardiographic aortic valve prolapse and only two with audible aortic insufficiency. A Doppler shift in the right ventricular outflow tract in diastole, suggestive of pulmonary regurgitation, was recorded in 16 of the 78 patients with an adequate Doppler examination; only 1 of the 16 had audible pulmonary insufficiency.

Mitral valve prolapse is a common clinical syndrome, usually recognized by its characteristic auscultatory features and echocardiographic findings (1–9). Pathologic changes, consisting of an increase in the spongiosa component of valve cusps and replacement of variable amounts of the normally dense collagenous fibrosa (10–12), typically in-
volve the mitral valve. Severe myxomatous change of the aortic, tricuspid and pulmonary valves has, however, also been described (10–13). Echocardiographic studies (14–16) also suggest multivalvular involvement in many patients with mitral valve prolapse, with patterns of aortic and tricuspid valve prolapse recorded in 22 to 25% and 21 to 40% of patients, respectively.

Despite the apparent high frequency of mitral prolapse in the general population (8,17,18), the prevalence of valvular regurgitation in this entity has not been defined. Doppler echocardiography permits recognition of regurgitation of all four cardiac valves (19–29). Being noninvasive, it is readily applicable to the evaluation of asymptomatic as well as symptomatic patients. For this reason, Doppler techniques were chosen to determine the prevalence of valvular regurgitation in a large, consecutive and prospectively studied series of patients with mitral valve prolapse. Their findings were compared with those in a similarly studied group of normal subjects without auscultatory or echocardiographic abnormalities.

Methods

Selection and study of patients with mitral valve prolapse. All consecutive patients with a diagnosis of mitral valve prolapse studied in our echocardiographic laboratory between November 1983 and July 1984 underwent physical examination by two trained examiners, phonocardiographic recording, M-mode and two-dimensional echocardiographic imaging and Doppler echocardiography. Criteria for the diagnosis of mitral valve prolapse included either or both of the following:

1. Characteristic auscultatory features. The presence of one or more mid- or late systolic clicks, either in isolation or followed by a systolic murmur extending to or through the aortic component of the second heart sound, was considered diagnostic of mitral valve prolapse. The clicks were confirmed by phonocardiographic study, and their mobility with respiration, sitting, standing and Valsalva maneuver was assessed to further substantiate a mitral valve origin. The presence of an isolated holosystolic or late systolic murmur was not considered sufficient for diagnosis of prolapse.

2. Characteristic M-mode echocardiographic features. Definitive M-mode echocardiographic diagnosis of mitral valve prolapse required posterior systolic displacement of the mitral valve echo by 3 or more mm beyond an imaginary line joining the C and D portions of the mitral valve echo-gram (7). Lesser degrees of posterior systolic movement were also noted, but were considered insufficient for definitive diagnosis. Because inferior angulation of the transducer may produce a false positive pattern of mitral prolapse (4,30,31), special care was taken to record the mitral valve with the transducer placed perpendicularly to the chest wall or oriented superiorly. Patients with a history of rheumatic heart disease or infective endocarditis, evident Marfan’s syndrome, congenital or acquired heart disease other than valvular prolapse or an echocardiographic pattern compatible with a flail or partially flail mitral valve were excluded from the study.

Phonocardiograms were recorded using an Irex System II machine. Medium and high frequency channels were used to optimize detection and timing of nonejection sounds.

Echocardiography. M-mode echocardiograms were performed using an Irex System II, Hoffrel 201A/514 or ATL Mark 600 ultrasonoscope. Mitral prolapse was diagnosed as detailed earlier. The diameter of the aortic root, left atrium and right and left ventricles was measured according to previously published criteria (32).

Two-dimensional echocardiograms were performed using a Hoffrel 201A/514 mechanical sector scanner or an ATL Mark 600 mechanical scanner. Mitral valve prolapse was suspected if there was systolic movement of one or both leaflets above the plane of the mitral anulus in para-sternal long-axis, apical four chamber or subcostal four chamber views (5,6,9). Two-dimensional features, in the absence of a characteristic click or M-mode findings, were not considered sufficient for diagnosis. The decision to exclude patients having only two-dimensional features of prolapse was based on our previous observations that some sagging of one or both mitral leaflets could be observed in most apparently normal individuals when multiple apical views were performed. In this regard, Levine et al. (33) recently suggested that false positive two-dimensional patterns of prolapse may be related to a nonplanar shape of the mitral anulus. Aortic valve prolapse was diagnosed when there was evident inferior diastolic displacement of one or more aortic valve cusps in the parasternal long-axis view (15,16). To avoid a false positive diagnosis related to angulation techniques, the diastolic position of the aortic leaflets was assessed when the clearest parasternal long-axis view of the heart was obtained. Tricuspid valve prolapse was diagnosed when movement of one or more tricuspid leaflets above the tricuspid valve ring, into the right atrium, was evident during systole in the apical four chamber, parasternal short-axis or parasternal right ventricular inflow tract views (14,15,34).

Pulsed Doppler echocardiography. These studies were all performed by the senior investigator (P.C.C.), using an ATL Mark 600 echocardiograph. In the Duplex scanning mode, a radial M-line and Doppler sample volume dot can be superimposed on the real-time two-dimensional image for optimal positioning. By activating a foot switch, the Doppler mode is initiated. In the pulsed Doppler mode, a single transducer pulses along the selected M-line. Only those echoes returning from the sample volume are processed by the flow analyzer. Fast Fourier transform analysis
is used to convert the returning sound waves into their component frequency shifts and amplitudes, for display of spectral information (Y axis and gray scale) over time (X axis). The spectral display can be preserved on hard copy, using a Tektronix recorder, or on video tape. Audio Doppler information, in stereo, is also initiated by foot switch activation of the Doppler mode. In the ATL Mark 600 system, the axial dimension of the sample volume is variable from 1.9 to 9 mm, whereas lateral dimension depends on beam width at the selected sample volume depth. Pulse repetition frequency is automatically optimized for sample volume depth. Flow directed toward the transducer causes spectral information to be displayed above a central zero reference line, whereas flow directed away from the transducer produces information below the line. In the present study, a 3 MHz transducer was used for Doppler interrogation. Sample volume axial dimension was set at 3 or 5 mm, and the wall filter was set at 400 Hz. Gain adjustments were made to maximize the signal to noise ratio of returning signals.

Multiple views were used to assess for regurgitation of the aortic, mitral and tricuspid valves. For the aortic valve, the left ventricular outflow tract immediately below the aortic leaflets was interrogated using parasternal long-axis, apical five chamber and parasternal short-axis views. The latter view is particularly useful for detecting aortic regurgitation, because it permits the left ventricular outflow tract to be examined from its medial to lateral edges. In the case of the mitral valve, the left atrium above both mitral valve leaflets was interrogated using parasternal long-axis and apical long-axis, four chamber and two chamber views. Special care was taken to record Doppler information from all areas above both leaflets, including the angle between the posterior leaflet and the left atrial wall. For the tricuspid valve, the right atrium above the tricuspid leaflets was interrogated using parasternal right ventricular inflow tract, parasternal short-axis and apical four chamber views. Only one view, the parasternal short-axis view, was used to assess for pulmonary insufficiency. The right ventricular outflow tract immediately below the pulmonary valve was interrogated from its medial to lateral edges.

Insufficiency of the aortic and pulmonary valves was diagnosed by the presence of a holodiastolic flow disturbance, recorded on the ventricular side of the respective valve and characterized by marked spectral broadening. Flow disturbance was maximal at the level of the valve. Mitral and tricuspid valve regurgitation were recognized by a systolic flow disturbance, detected on the atrial side of the valve, maximal at valve level and characterized by marked spectral broadening.

Selection and study of normal subjects. Normal volunteers and patients referred to the echocardiographic laboratory for evaluation of an ejection murmur, but found to have no echocardiographic abnormalities, constituted the control group. They were evaluated prospectively, with a protocol identical to that used for study of the patients with prolapse.

Statistical analysis. Equivalence of the patients with prolapse and control subjects with regard to age and sex was determined using appropriate two sample and chi-square tests, respectively. The chi-square test or, where appropriate, Fisher's exact test was used to test for differences between proportions. A probability value of less than 0.05 was considered significant.

Results

Patients With Mitral Valve Prolapse

Demographic characteristics. Eighty consecutive patients with an auscultatory or echocardiographic diagnosis, or both, of mitral valve prolapse were studied. The 55 women and 25 men ranged in age from 18 to 79 years (44 ± 17, mean ± SD). Seventy were outpatients and 10 were inpatients.

Auscultatory abnormalities. Auscultatory abnormalities compatible with prolapse were present in 72 patients (Table 1) and included diagnostic clicks in 61. Eight patients had no audible or recordable click or mitral murmur, either at rest in the supine position or during sitting, standing or performance of the Valsalva maneuver.

Echocardiographic findings. Abnormalities of mitral valve movement considered diagnostic of prolapse were observed on M-mode study in 40 patients (50%). Smaller amplitudes of posterior systolic movement (1.5 to 2.9 mm), considered nondiagnostic, were observed in 26 other patients (33%). Mitral movement abnormalities compatible with prolapse were observed in 74 patients (93%) on two-dimensional examination. Two-dimensional echocardiographic patterns of aortic and tricuspid valve prolapse were detected in 4 (5%) and 20 (25%) patients, respectively. Aortic root enlargement (>3.7 cm) was present in only four patients, whose aortic root diameters ranged from 3.8 to 4.0 cm.

Doppler findings. Left atrial systolic turbulence, compatible with mitral regurgitation, was recorded by Doppler

<table>
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<tr>
<th>Auscultatory finding</th>
<th>No. of patients</th>
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<tr>
<td>Mid- or late systolic click or clicks</td>
<td>61</td>
</tr>
<tr>
<td>Isolated click or clicks</td>
<td>50</td>
</tr>
<tr>
<td>Clicks followed by late systolic murmur</td>
<td>11*</td>
</tr>
<tr>
<td>Isolated late-systolic murmur</td>
<td>4</td>
</tr>
<tr>
<td>Holosystolic murmur</td>
<td>7</td>
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<tr>
<td>No abnormalities</td>
<td>8</td>
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*Includes four patients whose murmur was heard only during standing plus the Valsalva maneuver.
Figure 1. Pulsed Doppler echocardiographic recordings from two patients with mitral valve prolapse. Holosystolic turbulence is detected on the left (black arrows); late systolic turbulence is shown on the right (black arrows). Each horizontal line in each panel indicates a frequency shift of 1 kHz. EKG = electrocardiogram; MV = mitral valve.

Technique in 53 patients, in at least two different views in each individual. The pattern of turbulent flow was holosystolic in 24, late systolic in 15, and both holosystolic and late systolic behind different parts of the mitral valve in 8 (Fig. 1). Early to mid-systolic turbulence was recorded in six other patients. This was considered to represent mitral regurgitation, albeit atypical, because the recorded flow disturbance was maximal at leaflet level and contained frequency shifts representing high flow velocity. Spurious recognition of left ventricular outflow tract turbulence due to excessive beam width was considered unlikely, because the abnormal spectral Doppler signal disappeared as the sample volume was moved toward both the aortic root and the left ventricular outflow tract. Additionally, the audible Doppler signals from the left ventricular outflow tract and aortic root differed markedly from those recorded in the left atrium. The Doppler pattern of mitral regurgitation was recorded behind the coaptation point alone in 11 patients, behind the coaptation point and the anterior leaflet in 18, behind the coaptation point and portions of both anterior and posterior leaflets in 8 and behind the posterior leaflet alone in 14. Late systolic turbulence was generally best recorded in the angle between the posterior mitral valve leaflet and the left atrial wall, and often required tedious searching for its detection. Of the 53 patients with a Doppler pattern of mitral regurgitation, 27 had definitive M-mode echocardiographic findings of prolapse, whereas 18 had only 1.5 to 2.9 mm displacement and 8 had either no displacement or displacement of less than 1.5 mm. A two-dimensional pattern of prolapse was present in 51 of the 53. Only 21, however, had mitral regurgitation that was audible on physical examination or detectable on phonocardiographic recording at the apex. In four of these, the murmur was audible only during combined maneuvers of sitting or standing plus the Valsalva maneuver, while the positive Doppler findings were detected with the patients at rest in the supine position.

A Doppler pattern of tricuspid regurgitation was detected in 15 patients and could be recorded in at least two views. Nine patients had holosystolic turbulence, one patient had early to mid-systolic turbulence, four patients had late systolic turbulence and one patient had both holosystolic and late systolic turbulence recorded behind different portions of the tricuspid valve (Fig. 2). Twelve of the 15 patients, including all with an isolated pattern of late systolic regurgitation, had an echocardiographic pattern of tricuspid prolapse. None had audible tricuspid regurgitation or jugular venous pulse abnormalities characteristic of tricuspid regurgitation. Flow velocities in all tricuspid regurgitant jets were low, not suggestive of pulmonary hypertension.
A Doppler pattern of aortic regurgitation was detected in seven patients and could be recorded in at least two different echocardiographic views. None of the seven had echocardiographic evidence of aortic valve prolapse, and only two had audible aortic insufficiency. Aortic regurgitation could not be detected by Doppler study in any of the four patients with echocardiographic features of aortic leaflet prolapse.

A pulsed Doppler frequency shift in the right ventricular outflow tract in diastole suggested pulmonary regurgitation in 16 of the 78 patients in whom adequate Doppler examination of the pulmonary valve was possible (Fig. 3). The Doppler flow signal was recorded maximally on the right ventricular side of the pulmonary valve, was holodiastolic and showed marked spectral broadening. No patients had high flow velocity suggestive of pulmonary hypertension. Only two had audible diastolic murmurs (including one with Doppler patterns of both aortic and pulmonary regurgitation).

Twenty-six patients had Doppler findings compatible with insufficiency of valves other than the mitral. Of these, 23 (88%) also had Doppler-detectable mitral regurgitation. Ninety percent of patients with Doppler-detectable tricuspid regurgitation or aortic regurgitation, or both, had detectable mitral regurgitation. Male and female subgroups did not differ significantly with regard to the proportion with regurgitation of the aortic, mitral, tricuspid or pulmonary valve.

Both Doppler echocardiography and assessment of ventricular and atrial cavity sizes suggested that regurgitation was usually mild. Mitral regurgitation could be detected beyond the proximal third of the left atrium (closest to the mitral valve) in only three patients, and tricuspid regurgitation was detected only with sample volume placement in the immediate vicinity of the tricuspid valve. The left ventricle was dilated in diastole (>5.6 cm) in only six patients, and left atrial dimension was greater than 4 cm in only eight patients. Only one patient had right ventricular enlargement (diameter >2.3 cm or 2.6 cm in the supine or left lateral position, respectively), and none had paradoxic septal movement to suggest appreciable right ventricular volume overload.

Normal Subjects

Eighty-five normal subjects were studied. By definition, none had audible clicks or abnormalities on imaging echocardiography. The 51 women and 34 men ranged in age from 17 to 82 years (mean 41 ± 17). Doppler signals compatible with mitral regurgitation (one holosystolic and two early to mid-systolic), tricuspid regurgitation and pulmonary regurgitation were detected in 3, 9 and 15 control subjects, respectively.
Late systolic tricuspid regurgitation was detected only once, in a patient in whom holosystolic tricuspid regurgitation was also evident under another area of the tricuspid valve. No patient had aortic regurgitation. Male and female control subjects did not differ with regard to the proportion with tricuspid or pulmonary regurgitation.

Comparisons between patients with prolapse and normal subjects. The ratio of women to men and the ages of the entire group and of male and female subgroups did not differ significantly in the prolapse and control groups. The prevalence of mitral regurgitation and of aortic insufficiency was higher in the prolapse group than in the normal control group (p < 0.001 and < 0.01, respectively). A pattern of late systolic mitral regurgitation was detected only in the prolapse group. Although tricuspid regurgitation was detected in 19% of patients with prolapse versus 11% of control subjects, this difference did not reach statistical significance. Late systolic tricuspid regurgitation, without accompanying holosystolic turbulence in other views, however, was detected only in those patients with mitral valve prolapse who exhibited additional findings of tricuspid valve prolapse. The prevalence of signals compatible with pulmonary regurgitation was equivalent in both groups.

Discussion

Echocardiography is the technique of choice for evaluation of patients with suspected mitral valve prolapse. It can identify leaflet redundancy and abnormal systolic movement of the mitral valve above the plane of the mitral valve anulus (4–9). It may also detect associated aortic root dilation and tricuspid or aortic valve abnormalities compatible with redundancy and prolapse (6,14–16). Imaging echocardiography is limited, however, in its ability to define valvular regurgitation. While aortic and pulmonary regurgitation may occasionally be recognized by diastolic fluttering of the mitral or tricuspid valve, respectively, frequently no fluttering is apparent. In addition, there are no specific echocardiographic correlates of atioventricular valve regurgitation. Contrast echocardiography may facilitate detection of tricuspid regurgitation, but this technique is invasive, requiring an intravenous injection.
Detection of valvular regurgitation by Doppler echocardiography. Doppler techniques now permit noninvasive assessment of valvular regurgitation. In patients with a variety of cardiovascular disorders necessitating left ventriculography, the sensitivity of pulsed Doppler echocardiography for the diagnosis of mitral regurgitation has ranged from 87 to 94%, and specificity has ranged from 77 to 96% (21,28,29,35,36). Moderate and severe mitral regurgitation is detected more easily than mild mitral regurgitation by Doppler technique (20), and one study has suggested that mitral regurgitation may be more easily detected in patients with rheumatic deformity than in patients with either mitral prolapse or a cleft mitral valve (37). The direction of the regurgitant jet on pulsed Doppler echocardiographic studies correlates well with the direction of the regurgitant jet on angiographic study (38). Indeed, in patients with mitral prolapse, regurgitant flow has been found to be directed posteriorly in those with anterior leaflet prolapse and anteriorly in those with prolapse of the posterior cusp (38). Mapping of the depth and width of the flow disturbance may provide important information with regard to the magnitude of mitral regurgitation (21,39). Left atrial systolic turbulence, suggestive of mitral regurgitation, has not generally been detected in normal individuals (28). Our study confirms the low prevalence of pulsed Doppler signs of mitral regurgitation in apparently normal subjects.

In the case of aortic insufficiency, pulsed Doppler echocardiography has been reported to have a sensitivity of 94% and a specificity of 82%, when compared with results of aortic root angiography (28). Mapping of the level and extent of the Doppler flow disturbance permits grading of the severity of aortic regurgitation in many individuals (19). Similar to our findings in the control group, diastolic turbulence in the left ventricular outflow tract has not been observed in normal individuals (28).

The sensitivity and specificity of Doppler echocardiography in recognition of tricuspid and pulmonary valve regurgitation have been more difficult to assess. The use of right ventricular angiography or of pulmonary arteriography for the diagnosis of tricuspid regurgitation and pulmonary insufficiency, respectively, may produce false positive findings of regurgitation, because of the presence of a catheter across the valve in question. Studies in experimental animals (27) with surgically created tricuspid regurgitation and pulmonary insufficiency, however, suggest that Doppler echocardiography is capable of accurately detecting right-sided regurgitation. In clinical studies, pulsed Doppler echocardiography has been found to have a sensitivity ranging from 87 to 94% and a specificity ranging from 85 to 100% for the diagnosis of tricuspid regurgitation, when compared with invasive diagnoses of tricuspid valve competence made using right ventricular angiography, intracardiac phonocardiography, dye-dilution curves and assessment of the tricuspid valve at the time of surgery (24–27). False negative diagnoses are more common with mild tricuspid regurgitation than with more severe degrees of regurgitation (24,26), and the Doppler signal in patients with mild valvular insufficiency may be less than holosystolic (25). The extent of tricuspid regurgitation, assessed by mapping of turbulence detected using the pulsed Doppler technique, correlates well with the assessment of severity by right ventricular angiography (25). While some investigators (24,27) have not detected right atrial systolic turbulence in normal subjects, others (40) have detected signals suggestive of tricuspid regurgitation in individuals without apparent heart disease, similar to the findings in this study.

Stevenson et al. (23) assessed the sensitivity and specificity of pulsed Doppler echocardiography in the detection of pulmonary insufficiency. To avoid the problem of potential false positive diagnosis of regurgitation, resulting from the presence of a catheter across the pulmonary valve, they studied 40 patients in whom left to right shunts from the aorta to the pulmonary artery allowed contrast medium injected into the aorta to flow back to the pulmonary valve. When compared with detection of contrast in the right ventricular outflow tract, pulsed Doppler echocardiography had a sensitivity of 95% and a specificity of 88% (23). Although Waggoner et al. (27) did not detect diastolic turbulence in the right ventricular outflow tract in normal individuals, other investigators (40,41) have suggested, as does our study, that signals compatible with pulmonary insufficiency may be seen in many otherwise apparently normal subjects. Recusani et al. (42) recently suggested that diastolic signals in the right ventricular outflow tract may represent coronary flow rather than pulmonary insufficiency.

Previous Doppler studies in patients with mitral valve prolapse. To our knowledge, there are no prior studies that address the issue of prevalence of regurgitation of all four cardiac valves in patients with mitral valve prolapse. Several previous studies do detail pulsed Doppler echocardiographic findings with regard to the mitral valve (35,36,39,43). One retrospective study (35) of 88 symptomatic patients, admitted to a university hospital for diagnostic evaluation and found to have mitral prolapse on M-mode echocardiographic study, reported a prevalence of 45% for Doppler findings compatible with mitral regurgitation. In the 31 patients undergoing left ventricular angiography, there was excellent correlation between Doppler and angiographic diagnoses of the presence or absence of mitral regurgitation. In another large study (36) of 125 consecutive patients with a mid- to late systolic click, left atrial turbulence was detected in 72%.

The greater prevalence of Doppler findings of mitral regurgitation in that series may relate to the fact that 65% of the 125 patients had a systolic murmur associated with the click. The pattern of systolic left atrial turbulence in patients with prolapse has been described as holosystolic, mid-systolic or late systolic. It is well reported (29,35) that Doppler findings compatible with mitral regurgitation may be present...
in patients without an audible murmur. None of the available studies addresses the prevalence of aortic, tricuspid or pulmonary regurgitation in patients with evident mitral prolapse.

**Observations in this study.** A number of interesting observations emerge from the present study. First, the prevalence of mitral regurgitation, detected by pulsed Doppler echocardiography, is high in patients with mitral prolapse and is frequently detected in the absence of any auscultatory evidence for mitral regurgitation. Second, the occurrence of aortic, tricuspid and pulmonary regurgitation is also far higher than would be expected from physical examination alone. Aortic regurgitation and isolated late systolic tricuspid regurgitation are significantly associated with the mitral valve prolapse syndrome, suggesting that changes in valve structure may be etiologically related not only to mitral regurgitation but also to aortic regurgitation and late systolic tricuspid regurgitation. The prevalence rates of all types of tricuspid regurgitation and of a pattern compatible with mitral valve prolapse or aortic root enlargement. Only one of the seven patients with Doppler signs of aortic regurgitation had an increased aortic root diameter (3.8 cm).

On the basis of our findings, it appears that the Doppler pattern of regurgitation of the atrioventricular valves in patients with mitral valve prolapse is quite variable. Holo-systolic or late systolic turbulence alone may be detected, or both types of turbulence may be detected behind different portions of the atrioventricular valve. Occasional patients have a mid-systolic pattern of left atrial turbulence. This has been thought to represent mitral regurgitation, but alternative possibilities, including artifact due to the width of the sample volume in the far field, cannot be excluded. Left atrial turbulence is often very localized, suggesting a narrow regurgitant jet. Late systolic turbulence is generally detected in only a very narrow region, usually in the angle formed by the junction of the posterior mitral leaflet with the left atrial wall.

**Potential limitations of the study.** Because of the nature of the patient population, which was largely asymptomatic and ambulatory, cardiac catheterization was not performed. Therefore, we were unable to confirm the presence or absence of valvular regurgitation by angiographic techniques. The possibility of false negative studies is very real. Because many regurgitant jets are very localized, failure to position the sample volume in the jet may result in failure to detect regurgitation. In addition, in certain adult patients, such as those with obesity or emphysema, the sound beam may be too attenuated to permit Doppler signals from distally located sample volumes to be adequately detected. It is also possible that false positive diagnoses may have been made. Indeed, several previous Doppler studies of the mitral and tricuspid valves have recognized negative deflections in early systole in patients without apparent regurgitation (20,22,25,37,44). These, however, are generally of short duration, isolated to the period of isovolumetric contraction. They are usually of low kilohertz shift and can be differentiated from the holosystolic and late systolic left atrial turbulence more characteristic of mitral or tricuspid regurgitation. In addition, the possibility that the turbulence detected relates not to regurgitation but to swirling of blood within the prolapsing leaflets cannot be fully excluded (36). In this study, however, the detection of atrial turbulence bore no apparent relation to the magnitude of leaflet prolapse. In addition, other studies (35,39) of patients with prolapse have shown good correlations between angio- graphic and Doppler findings of mitral regurgitation, supporting the thesis that regurgitation is indeed being detected.

**Finally, the etiology of the valvular regurgitation is not clear,** because there are no available pathologic correlations. The significantly higher prevalence of aortic and mitral regurgitation in patients with prolapse than in control subjects and the association of late systolic tricuspid regurgitation with tricuspid valve prolapse, however, suggest that valvular changes in prolapse are etiologically important in mitral and aortic regurgitation and in late systolic tricuspid regurgitation. Doppler findings of right-sided valvular regurgitation have been observed previously in many otherwise apparently normal individuals, consistent with the findings in our control group (40,41). Therefore, the signals compatible with holosystolic tricuspid regurgitation and with pulmonary regurgitation observed in our patients may well be unrelated to myxomatous valve change. Also, it is known that Doppler patterns of tricuspid and pulmonary regurgitation are not uncommonly associated with pulmonary hypertension (27). Because cardiac catheterization was not performed in our patients, we cannot exclude the possibility that pulmonary hypertension was responsible for right-sided valvular regurgitation. However, none of our patients had signs or symptoms of right heart failure, right ventricular enlargement on echocardiographic study or increased flow velocities in the tricuspid or pulmonary regurgitant signals. Only 6 of the 23 with tricuspid or pulmonary regurgitation, or both, had one or more of the following echocardiographic signs suggestive of more than mild mitral regurgitation: left ventricular end-diastolic diameter greater than 5.6 cm; left atrial diameter greater than 4.0 cm; or detection of left atrial systolic turbulence more than one-third of the way toward the back wall of the left atrium. We consider it unlikely, therefore, that severe mitral regurgitation, producing pulmonary hypertension, was responsible for right-sided valvular regurgitation in our patients.

**Clinical implications.** More complete characterization of valvular abnormalities, possible when pulsed Doppler echocardiography is added to routine imaging echocardi-
ography, should enable better assessment of the natural history of the mitral prolapse syndrome. In particular, it may permit better separation of patients into groups at higher and lower risk of complications such as infective endocarditis, progressive valvular regurgitation and arrhythmias, including sudden death. One clinical follow-up study (4) of patients with a click or late systolic murmur, or both, documented a mean of 13.7 years earlier, revealed that complications of prolapse were more likely to occur in patients with a documented murmur. Another study (46) has found an increased prevalence of complex ventricular arrhythmias in patients with mitral regurgitation complicating mitral valve prolapse. Because our current study suggests that Doppler echocardiography is capable of detecting signs of valvular regurgitation in many patients without clinically apparent valvular insufficiency, Doppler echocardiography may provide a more powerful tool for risk stratification. Indeed, one retrospective study (35), using pulsed Doppler echocardiography to evaluate symptomatic patients with prolapse, revealed that patients with mitral regurgitation had a higher prevalence of ventricular arrhythmias than did patients without mitral regurgitation. The usefulness of Doppler techniques in identifying patients with prolapse and a higher incidence of complications remains to be determined. Such analysis will require a large, prospectively studied series of patients.

In conjunction with M-mode and two-dimensional echocardiography, pulsed Doppler techniques may improve the sensitivity of echocardiography for the detection of valvular abnormalities. In this series, Doppler findings of mitral regurgitation were apparent in 26 individuals in whom M-mode echocardiography was either negative or inconclusive for the diagnosis of prolapse and in 2 patients without apparent prolapse on two-dimensional examination. The additive role of Doppler echocardiography is supported by a previous study of 125 patients with characteristic mid- to late systolic clicks, 65% of whom also had a late systolic murmur (36). While M-mode and two-dimensional echocardiographic studies revealed signs of prolapse in 50 and 68% of patients, respectively, pulsed Doppler abnormalities were noted in 72%, and 93% of all patients had abnormalities detected on at least one of the three examinations.

References


