Secundum Atrial Septal Defect and Significant Mitral Regurgitation*
Incidence, Management and Morphologic Basis

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To better understand the association between mitral regurgitation and secundum atrial septal defect and to clarify the evaluation and management of these patients, the records of 235 adult patients with atrial septal defect were reviewed. Ten patients (4 percent) had significant mitral regurgitation defined by clinical, hemodynamic and angiographic criteria. Three patients required mitral valve replacement at the time of closure of the atrial septal defect and four patients had closure alone, one of whom required mitral valve replacement after five years. Three patients did not undergo closure of the atrial septal defect or mitral valve replacement because of severe coexisting medical problems. In six patients, the mitral valves were studied pathologically and all had thick, fibrotic leaflets and short, thick, fibrotic chordae tendineae. Three of these valves also had scattered areas of patchy myxomatous degeneration and three had areas of vascular ingrowth suggestive of rheumatic disease. Although both invasive and noninvasive studies have highlighted the coincidence between atrial septal defect and mitral regurgitation, particularly the frequent association of mitral valve prolapse, our data indicate that this association rarely has clinical significance. Furthermore, the morphologic basis for mitral regurgitation in patients with atrial septal defect consists of leaflet and chordal thickening fibrosis and deformity rather than attenuation and ballooning as would be expected in mitral valve prolapse.

The association between secundum atrial septal defect (ASD) and mitral valve disease has been recognized for many years. Reports have attributed mitral regurgitation (MR) in these patients to disease of the rheumatic valve, congenital valve deformity, and nonspecific valvulitis. In addition, recent noninvasive studies indicate a high incidence of mitral valve prolapse (37-70 percent) in these patients. However, the clinical significance and overall perspective of the association between secundum atrial septal defect and mitral regurgitation has not been fully characterized, nor has the morphology of these valves been defined. This study delineates the incidence, age at onset, management and morphologic basis for significant mitral regurgitation in adult patients with secundum atrial septal defect.

METHODS

The records of 235 adult patients (ages 20-71, mean 41 years) who had secundum atrial septal defects demonstrated

RESULTS

Ten of 235 adult patients with atrial septal defect (4 percent) had significant mitral regurgitation. The pertinent historic and catheterization findings in these ten patients are summarized in Table I. Their ages ranged from 22 to 69 years with a mean of 50 years. At presentation, all patients were symptomatic, all required digitalis and diuretics, and all but one had clinical findings of congestive heart failure.
Table 1—Clinical and Catheterization Findings in Patients with ASD and MR

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/Sex</th>
<th>History of Rheumatic Fever (grade)</th>
<th>NYHA Classification</th>
<th>Mean PA Pressure (mm Hg)</th>
<th>Left Atrial Pressure Peak V wave mean</th>
<th>Right Atrial Pressure Peak V wave mean</th>
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</thead>
<tbody>
<tr>
<td>ASD closure and simultaneous MVR</td>
<td>1</td>
<td>47F +</td>
<td>3</td>
<td>...</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>55M −</td>
<td>3</td>
<td>4.7</td>
<td>50</td>
<td>9</td>
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<tr>
<td></td>
<td>3</td>
<td>66F −</td>
<td>4</td>
<td>4.0</td>
<td>35</td>
<td>12</td>
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<tr>
<td>ASD closure and late MVR</td>
<td>4</td>
<td>39F +</td>
<td>2</td>
<td>4.2</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>ASD closure without MVR</td>
<td>5</td>
<td>44F +</td>
<td>2</td>
<td>3.5</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>47M −</td>
<td>1</td>
<td>8.0</td>
<td>25</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>50F +</td>
<td>2</td>
<td>3.1</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>No surgical intervention</td>
<td>8</td>
<td>65F −</td>
<td>4</td>
<td>2.8</td>
<td>46</td>
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<td>10</td>
<td>22F −</td>
<td>2</td>
<td>3.0</td>
<td>27</td>
<td>13</td>
</tr>
</tbody>
</table>

ASD = atrial septal defect; MR = mitral regurgitation; MVR = mitral valve replacement; NYHA = New York Heart Association; PA = pulmonary artery; Qp/Qs = pulmonary-to-systemic flow ratio.

Seven patients had atrial flutter or fibrillation, although in normal sinus rhythm, all had electrocardiographic evidence of left atrial enlargement. Three patients had left ventricular hypertrophy on their electrocardiogram, and all patients had generalized cardiomegaly (cardiothoracic ratio greater than 0.5) with right ventricular and pulmonary artery prominence on chest x-ray examination. Six patients had radiologic evidence of left atrial enlargement.

Three patients required mitral valve replacement at the time of closure of the atrial septal defect (patients 1-3). Two of these patients are now NYHA symptom class 1 after two and six years, and the third patient died postoperatively with severe right and left heart failure.

At the time of initial ASD closure, four patients did not require mitral valve surgery (patients 4-7). In these patients, initial postoperative left atrial pressures were elevated, and all continued to demonstrate significant clinical mitral regurgitation. One patient (patient 4) subsequently required mitral valve replacement after five years. This patient died unexpectedly one year after surgery. Another, (pa-

Table 2—Angiographic and Morphologic Mitral Valve Findings in Patients with ASD and MR

<table>
<thead>
<tr>
<th>Patient</th>
<th>Angiographic Findings</th>
<th>Gross Pathologic and Histologic Findings</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Thickened Valve Leaflets</td>
<td>Prolapse</td>
</tr>
<tr>
<td>ASD closure and simultaneous MVR</td>
<td>1</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>−</td>
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<td></td>
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<tr>
<td>No surgical intervention</td>
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<td>+</td>
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<td>9</td>
<td>−</td>
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ASD = atrial septal defect; MVR = mitral valve replacement.
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Patient 4. Biplane left ventricular angiogram demonstrates significant mitral regurgitation through a thickened prolapsing mitral valve. Anteroposterior view (left), lateral view (right).

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left ventricular angiography was not performed. Six of these patients had mitral valves which were thickened, and six of the valves appeared to prolapse during ventricular systole (Fig 1), including four of the thickened valves. Six mitral valves were studied histologically, including three valves excised at the time of closure of the atrial septal defect, one valve was excised at subsequent mitral valve replacement five years following ASD closure, and two valves were studied post mortem. These valves were all thick and deformed, and had short, thick, and fused chordae tendineae (Fig 2 and 3). Histologic study revealed severe fibrosis in all valves and chordae. In addition, three of these valves had scattered areas of

Figure 2. Patient 10. Post-mortem specimen of the opened heart showing secundum ASD and thickened fibrotic mitral valve (MV) and chordae tendineae. LA = left atrium. LV = left ventricle.

Patient 5), developed grade 2 symptoms with progressive left atrial enlargement over five years. Patients 6 and 7 are grade 1 after one and five years.

The three remaining patients (patients 8-10) had severe mitral regurgitation and left heart failure. Two of these patients died suddenly, one just prior to surgery. In the third patient, symptoms progressed from grade 2 to grade 3 over a three-year interval, but surgery was precluded by advanced age and severe coronary artery disease.

Table 2 delineates the angiographic and morphologic findings of the mitral valve in these patients. The mitral valve was evaluated during left ventriculography in eight patients and in two patients, left ventriculography was not performed. Six of these patients had mitral valves which were thickened, and six of the valves appeared to prolapse during ventricular systole (Fig 1), including four of the thickened valves. Six mitral valves were studied histologically, including three valves excised at the time of closure of the atrial septal defect, one valve was excised at subsequent mitral valve replacement five years following ASD closure, and two valves were studied post mortem. These valves were all thick and deformed, and had short, thick, and fused chordae tendineae (Fig 2 and 3). Histologic study revealed severe fibrosis in all valves and chordae. In addition, three of these valves had scattered areas of

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patchy myxomatous change (Fig 4), two of which appeared to prolapse on angiography. Three valves also demonstrated areas of vascular ingrowth suggestive of old rheumatic valvulitis, although only one of these three patients had a history of rheumatic fever.

Only one patient (patient 6) had the prolapsing mitral valve syndrome, diagnosed clinically, echocardiographically and angiographically. However, because this was a retrospective study which in part predated the widespread use of echocardiography, only one patient with significant mitral regurgitation had an adequate echocardiographic study and in this patient, mitral valve prolapse was present (patient 6). No patient had clinical or morphologic evidence for bacterial endocarditis, and one, (patient 9), had advanced coronary artery disease, with mitral regurgitation presumably related to papillary muscle dysfunction.

**DISCUSSION**

The frequent coexistence of secundum ASD and mitral regurgitation has been well documented, however, the incidence of clinically significant mitral regurgitation, its management and its morphologic basis still warrants delineation.

Significant mitral regurgitation was present in 4 percent of 235 patients with secundum ASD. This infrequent occurrence of clinically significant mitral regurgitation contrasts with the incidence of mitral valve prolapse demonstrated echocardiographically or angiographically, which ranges from 37-70 percent.12-14 It is possible that with advancing age, the incidence of significant mitral regurgitation in ASD may increase, since there was a significant difference in the mean age of our 235 patients with atrial septal defect (41 years), and those with associated mitral regurgitation (mean 50 years), P < .05. Others
have also reported the infrequent occurrence of mitral regurgitation in secundum atrial septal defect in the young,22,23 in contrast to older patients with atrial septal defect.8,9,10,19-21

The clinical course of mitral regurgitation is altered by the presence of an atrial septal defect. Some patients with severe mitral regurgitation may not manifest symptoms of mitral regurgitation because the atrial septal defect “unloads” the left atrium. This complicates the management of patients with atrial septal defect who are generally felt to be operable candidates regardless of symptoms. If residual mitral regurgitation is significant following atrial septal defect closure, increased left atrial and pulmonary venous pressures develop and may produce or increase symptoms, as occurred in two of our patients.11,21,28 However, the decision to replace the mitral valve at the time of closure of the atrial septal defect must be weighed against the unknown longterm risk of prosthetic mitral valve replacement. This decision necessitates adequate assessment of the severity of mitral regurgitation, which may be difficult. Left atrial pressures at catheterization may not correlate with the degree of mitral regurgitation, in these patients, but tend to more closely reflect right ventricular filling pressures.29,30 Left ventricular angiography also may not accurately quantitate mitral regurgitation in these patients, because of left-to-right “run-off” through the atrial septal defect, as well as the dilutional effects of the large volume of unopacified pulmonary venous drainage. For these reasons, the decision to replace the mitral valve at the time of closure of the atrial septal defect, may depend upon intraoperative inspection and palpation of the mitral valve during ASD repair, as well as intraoperative maneuvers to unmask significant mitral regurgitation, such as increasing afterload by partial occlusion of the ascending aorta, or by volume loading. When mitral regurgitation is severe, mitral valve replacement at the time of closure of the atrial is indicated, as in patients 1-3. When mitral regurgitation is less severe, closure of the ASD alone may suffice, although some of these patients who might not require early mitral valve replacement, may require it subsequently.11,21 For this reason, in patients with atrial septal defect and mitral regurgitation, we generally delay closure until symptoms occur, at which time correction of both lesions may be necessary.

The morphologic basis for significant mitral regurgitation and secundum atrial septal defect is still unclear. Although the high coincidence of mitral valve prolapse has been noted,12-14 our data indicate that the classic morphology associated with clinical mitral valve prolapse, ie—long, thin, chordae tendineae, and thin billowing, redundant myxomatous valve leaflets,29 is, in fact, rarely present in these patients. Instead, our patients had severe mitral valve fibrosis, and short, thick fibrotic chordae tendineae more suggestive of chronic rheumatic valve disease. Three patients had vascular ingrowth also suggestive of chronic rheumatic valvulitis18 and four patients actually had a history of rheumatic fever. While the findings of fibrosis and mitral valve thickening are consistent with rheumatic heart disease, these findings may also be entirely nonspecific.19 Furthermore, a rheumatic etiology in these patients is inconsistent with the rarity in our experience with associated mitral stenosis, which was present in only one of 235 patients with secundum atrial septal defect, yet would be expected to be more frequent than mitral regurgitation, if the etiology of the mitral regurgitation were indeed rheumatic.

Although angiographic evidence for mitral valve prolapse (patients 3, 4, 7, 8), has been noted by others,29 histology confirmed the coexistence of both fibrosis and myxomatous change in some of the same valve leaflets (patients 1, 4, 8), a finding noted by others in isolated mitral regurgitation.10,30 It is possible that valve thickening and fibrosis are secondary to the chronic hemodynamic stress related to the left-to-right shunt.10,30 Of interest is a recent study which attributed a decrease or loss of echocardiographic mitral valve prolapse in patients following repair of atrial septal defect alone to altered postoperative left ventricular geometry.31 These findings are consistent with our observations that in association with atrial septal defect, the etiology for mitral regurgitation is different from that of classic isolated mitral valve prolapse as evidenced by our histologic findings. An alternative possibility, however, is that mitral valve fibrosis and thickening as seen in our patients represents the end-stage of classic mitral valve prolapse.10,30

In summary, despite a reported high incidence of mitral valve prolapse in atrial septal defect, clinically significant mitral regurgitation is uncommon and when present is generally found in the older patient. These mitral valves are usually thick and fibrotic, suggesting either a rheumatic or chronic degenerative process rather than the anticipated progressive billowing and attenuation seen in classic valve prolapse.

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