PATHOLOGIC STUDIES

Floppy Mitral Valve and Ventricular Septal Defect: An Anatomic Study

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Eighteen percent of heart specimens with isolated ventricular septal defect also had a floppy mitral valve. There was no statistical difference in the incidence of floppy mitral valve in the three age groups considered (< 1 year, 1 to 16 years and 17 to 91 years). In no patient was a floppy mitral valve considered to be the cause of death.

Complications of floppy mitral valve (ruptured chordae tendineae, bacterial endocarditis, mitral regurgitation and fibrin deposits at the mitral valve-left atrial angle) occurred at approximately the same frequency as that reported in autopsy studies of isolated floppy mitral valve. In the specimens with floppy mitral valve and ventricular septal defect, 63% also had floppiness of the tricuspid valve, 16% of the pulmonary valve and 5% of the aortic valve.

The anatomic basis for floppy mitral valve was considered to be spongiosal invasion and disruption of the fibrosa of the valve leaflet. In this study, spongiosal invasion of the fibrosa was fully developed by 3 months of age and there was no evidence that the incidence or severity of spongiosal invasion increased between the ages of 3 months and 88 years. These data suggest that the floppy mitral valve is a congenital lesion that reaches full anatomic expression in infancy. No evidence was found that ventricular septal defect and floppy mitral valve share a common etiology.

In the literature defining mitral valve prolapse and floppy mitral valve, ventricular septal defect is occasionally encountered (1–3). The coexistence of these two lesions was initially considered to be incidental (3). However, recent reports indicate that floppy mitral valve (mitral valve prolapse) and ventricular septal defect occur simultaneously more often than previously reported. Bharati and Lev (4) reported an anatomic study of 36 patients with polyvalvular disease. Grossly and histologically, the defects in all the valves of their patients were comparable with the changes we have reported in floppy mitral valves (5). Five (14%) of their 36 patients had an associated ventricular septal defect. Keck et al. (6) reviewed left ventriculograms of 40 children with ventricular septal defect. Three of these (7.5%) had mitral valve prolapse. More recently, Rippe et al. (7) reviewed echocardiograms of 25 adults with a diagnosis of ventricular septal defect and 10 of these (40%) had mitral valve prolapse. These authors also found an unusually high incidence of mitral valve prolapse among adults with other congenital heart defects. The association of mitral valve prolapse with ventricular septal defect mentioned in these reports prompted us to restudy 112 specimens of heart with an isolated ventricular septal defect from the United Hospitals’ Registry of Cardiac Pathology.

Methods

Source Materials

Among the 112 restudied hearts with isolated ventricular septal defect were 70 (63%) referred from the University of Minnesota and 42 (37%) referred from other cardiac centers. In some of these specimens, a patent ductus arteriosus or a secundum atrial septal defect was also present. Specimens with ventricular septal defect associated with other hemodynamically significant congenital heart anomalies were not included. The specimens were collected during the 30 year period between 1952 and 1981. The age at death ranged from newborn to 91 years.

Eight of the 112 specimens with ventricular septal defect, 1 of which had a floppy mitral valve, could not be adequately evaluated because of previous dissection. The remaining 104 cardiac specimens with ventricular septal defect form the basis of this report. Each of the specimens was restudied...
with particular attention to the size and location of the ventricular septal defect, the presence of other congenital cardiac anomalies and the appearance of each of the four cardiac valves.

**Diagnosis and Quantitation of Severity of the Floppy Mitral Valve**

**Normal mitral valve.** Ranganathan et al. (8) have defined the gross morphology of the normal human mitral valve (Fig. 1). The anterior leaflet is a large, semicircular or triangular structure. In the great majority of subjects, the posterior leaflet is composed of three scallops. Occasionally, more or fewer are present. Each leaflet has a rough zone toward the free edge and a clear zone toward the base. In both leaflets of the normal mitral valve, there are interchordal convexities toward the atrium in the rough zone that vary considerably in height.

On microscopic examination, a normal mitral valve leaflet (Fig. 2) is composed of four layers (9–12): 1) the atrialis, a thin layer of collagen and elastic tissue forming the atrial aspect of the leaflet and continuous with the endocardium of the left atrium; 2) the spongiosa, a delicate myxomatous connective tissue between the atrialis and the fibrosa; 3) the fibrosa, which is composed of dense layers of collagen and forms the basic support of the leaflet; and 4) the ventricularis, a thin layer of collagen and elastic tissue that forms the ventricular surface of the mitral valve leaflet and tends to disappear toward the free end of the leaflet. The ventricularis may be considered to be part of the fibrosa (12).

**Floppy mitral valve.** Our methods of diagnosis and quantitation of severity of floppy mitral valve have been reported (5). We require the following features to be present before a gross diagnosis of floppy mitral valve is made (Fig. 3, 4, 8 and 10): 1) Interchordal hooding involving both the rough and clear zones of the involved leaflet or leaflets; 2) height of the interchordal hooding 4 mm or greater; and 3) interchordal hooding involving at least half of the anterior leaflet or at least two-thirds of the posterior leaflet.

Our microscopic criteria for a diagnosis of floppy mitral valve are significant thickening of the spongiosal layer and invasion and disruption of the fibrosa by the spongiosa (Fig. 5 and 9).

Our grading of the severity of the floppy mitral valve is based on the magnitude and the extent of interchordal hooding as follows:

- **Grade I:** Interchordal hooding involving more than half of the anterior leaflet or more than two-thirds of the posterior leaflet (one leaflet involved) (Fig. 8 and 10).

- **Grade II:** Interchordal hooding involving more than half of the anterior leaflet and more than two-thirds of the posterior leaflet (both leaflets involved) (Fig. 3).

- **Grade III:** A significantly greater magnitude of interchordal hooding than that present in grade II (Fig. 4).

**Results**

**Incidence**

**Age.** The patients were arbitrarily divided into three age groups: less than 1 year of age, 1 to 16 years of age and 17 to 91 years of age. The incidence of floppy mitral valve in these three age ranges is depicted in Table 1. The incidence of floppy mitral valve in all ages was 18%. There was no statistical difference in the incidence of floppy mitral valve.
valve in the three age groups. The overall severity of the floppy mitral valve was not greater in older patients with ventricular septal defect (Fig. 4 and 7).

**Sex distribution.** The male/female ratio for patients with ventricular septal defect and floppy mitral valve was 0.90 and was comparable with the ratio of 0.82 in the 104 patients with ventricular septal defect (Table 2).

**Other Mitral Valve Changes**

A thickening of the fibrosa of the proximal one-third of the mitral leaflets was common in patients with ventricular septal defect whether or not a floppy mitral valve was present (Fig. 5 and 6). This change appeared related to increasing age because it occurred in 4 (10%) of 42 in those less than 1 year old, in 7 (21%) of 34 in the 1 to 16 years of age group and in 10 (34%) of 29 in the over 16 years of age group. This fibrous response appeared secondary to the hemodynamic stress imposed on the mitral valve by the flow associated with the ventricular septal defect, and was easily distinguished from the fibrosis present on the atrial and ventricular surfaces of the floppy mitral valve (Fig. 5 and 9).

Six patients had increased spongiosa that did not invade the fibrosa and did not cause hooding (Fig. 6). This change, which was not considered to be diagnostic of floppy mitral valve, was not related to age, occurring in 3 (7%) of 42 in the under 1 year of age group, 1 (3%) of 34 in the 1 to 16 years of age group and 2 (7%) of 29 in the over 16 years of age group. In one patient, a 2 month old girl, the spongiosa invaded and destroyed the fibrosa of the anterolateral scallop of the posterior leaflet (Fig. 6, upper). Because the

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**Figure 2.** Photomicrograph of a normal mitral valve. The thin leaflet is composed of the following layers: atrialis (A), spongiosa (SP) and fibrosa (F). Chordae appear in lower part of illustration. (Elastic tissue stain 20 ×).

**Figure 3.** Left, floppy mitral valve (grade II) in a 5 year old girl with ventricular septal defect. The anterolateral (AL) and posteromedial (PM) scallops of the posterior leaflet are thickened and hooded. The anterior leaflet (A) is thickened and hooded but the hooding is somewhat obscured by the tension placed on its chordae when the left ventricle (LV) is held open. Many of the chordae tendineae are thinned. A left ventricular friction lesion is present under the anterolateral scallop. LA = left atrium. Right, floppy mitral valve (grade II) in a 7 month old girl with ventricular septal defect. The anterior leaflet and the scallops of the posterior leaflet are thickened and hooded. The posteroomedial scallop is to the right of the anterior leaflet and the anterolateral scallop to the left.
mitral leaflets were not hooded, we did not classify it as a floppy mitral valve. It is possible that this process is a prodromal stage of the floppy mitral valve.

One patient with ventricular septal defect, a 59 year old woman, had chordal thickening and fusion, fibrosis that obliterated the normal valve layers and no increase in amount of spongiosa. These changes were considered to be caused by rheumatic mitral valve disease.

Causes of Death

The causes of death in patients with ventricular septal defect and floppy mitral valve were not dissimilar from those in patients with ventricular septal defect alone (Table 3). No deaths were considered to be caused by the floppy mitral valve.

Operative intervention was the most frequent cause of death in the two younger groups and was the second most frequent cause of death in the oldest group. Congestive heart failure was a significant cause of death in the under 1 year of age group and a relatively unimportant cause in the two older groups. Pulmonary vascular obstructive disease was an uncommon cause of death and occurred mainly in the over 16 years of age group. Most commonly, the cause of death in the over 16 years of age group was unrelated to the presence of ventricular septal defect.

Secondary Effects

In addition to the primary features of floppy mitral valve just described, additional anatomic changes, termed secondary effects, involve the mitral valve (10, 11). These include: fibrosis of the surfaces of the mitral valve leaflets; thinning or elongation, or both, of the chordae tendineae; and left ventricular friction lesions (Table 4).

Fibrosis of the surfaces of the mitral valve leaflets. In all of the specimens having a floppy mitral valve and a ventricular septal defect, the mitral valve leaflets had fibrosis involving the atrial or ventricular aspects, or both (Fig. 5 and 9). Fibrosis of the atrial surface of the mitral valve was considered to result from abnormal coaptation of one mitral valve unit with its opposite or contiguous member. When the magnitude of mitral valve prolapse was sufficient to allow the base of the posterior leaflet to make contact with

Table 1. Incidence of Floppy Mitral Valve in Patients With Ventricular Septal Defect

<table>
<thead>
<tr>
<th>Age at Death (yr)</th>
<th>Patients With Floppy Mitral Valve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Patients (no.)</td>
</tr>
<tr>
<td>&lt; 1</td>
<td>42</td>
</tr>
<tr>
<td>1 to 16</td>
<td>34</td>
</tr>
<tr>
<td>&gt; 16</td>
<td>29</td>
</tr>
<tr>
<td>Total</td>
<td>104</td>
</tr>
</tbody>
</table>

< 1 year versus 1 to 16 years - \( \chi^2 = 0.52 \) (not statistically different); < 1 year versus > 16 years - \( \chi^2 = 0.50 \) (not statistically different).

Table 2. Male/Female Ratio in Patients With Ventricular Septal Defect and Floppy Mitral Valve

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>&lt; 1 Year</th>
<th>1 to 16 Years</th>
<th>&gt; 16 Years</th>
<th>Total Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients with ventricular septal defect</td>
<td>0.91</td>
<td>0.62</td>
<td>1.0</td>
<td>0.82</td>
</tr>
<tr>
<td>Patients with ventricular septal defect and floppy mitral valve</td>
<td>1.0</td>
<td>0.75</td>
<td>0.5</td>
<td>0.90</td>
</tr>
</tbody>
</table>
Figure 5. Photomicrographs of spongiosal invasion and destruction of the fibrosa of the mitral valve in three children with ventricular septal defect. Upper, the anterolateral scallop of the posterior leaflet of the mitral valve in a 2 month old girl. Spongiosa is increased and has invaded and destroyed the fibrosa between the arrow and free edge. The fibrosa (F) is abnormally thick at the proximal portion of the leaflet. On gross examination, none of the components of the mitral valve were hooded. Thus, despite invasion of the fibrosa by spongiosa, this valve did not meet our criteria for a floppy mitral valve. (Elastic tissue stain 125 ×.) Middle, the anterolateral scallop in a 3 month old girl with grade II floppy mitral valve. The spongiosa is increased and invades and destroys the fibrosa at the central portion of the scallop (arrowhead) as well as at several points more distal. There is a prominent fibrosa in the proximal one-third of the leaflet, typically seen in patients with ventricular septal defect with or without floppy mitral valve. (Elastic tissue stain 125 ×.) Lower, central scallop in a 4 year old girl with grade II floppy mitral valve. The spongiosa (SP) invades and disrupts the fibrosa. There is fibrosis on the atrial aspect (arrow) and fibrosis in the interchordal segments of the ventricular surface of the scallop. LV = left ventricle. (Elastic tissue stain 125 ×.)

corrections for the left atrial wall, fibrosis of the leaflet and the left atrial wall occurred (Fig. 5, middle).

The ventricular surface of the floppy mitral valve exhibited deposits of fibroelastic tissue involving the hooded interchordal segments. This fibrosis appeared to be related to increased stress and tension imposed by prolapse of the interchordal segment. Additionally, thickening of the proximal portion of fibrosa was present in many of these valves, similar to the fibrosal thickening seen in the mitral valve in patients with isolated ventricular septal defect (Fig. 5).

Abnormalities of chordae tendineae. There was a high incidence of thinned chordae in each of the three age groups (Fig. 3 and 10). We did not determine chordal length quantitatively, but on the basis of subjective observations we concluded that the chordae were not elongated in the 19 patients with isolated ventricular septal defect and floppy mitral valve.

Left ventricular friction lesions. These lesions, consisting of fibrous patches on the left ventricular endocardium oriented parallel to contiguous chordae, are considered to result from friction between the chordae and the left ventricular wall (Fig. 3, left) (13). The incidence of left ventricular friction lesions increased with increasing age. In one specimen, from a 43 year old man, the left ventricular friction lesion resulted in entrapment of the chordae (Fig. 8) (13).

Complications of Floppy Mitral Valve

Although complications of the floppy mitral valve are uncommon, they are important because they alter the natural history and clinical expression of the floppy mitral valve. These include ruptured chordae tendineae, bacterial endocarditis, mitral regurgitation and fibrin deposits at the mitral valve-left atrial angle (Table 4).

Primary rupture of chordae. A 48 year old woman with floppy mitral valve and ventricular septal defect had primary rupture of several chordae serving the central scallop. Mitral regurgitation resulted (Fig. 10).

Bacterial endocarditis. One of the 19 patients with ventricular septal defect and floppy mitral valve had bacterial endocarditis. A 5 year old girl who died 5 days after ventricular septal defect closure had active bacterial endocarditis involving the central scallop of the posterior leaflet of
the mitral valve (Fig. 9, lower). There was also a "kissing" lesion of bacterial endocarditis on the left atrial wall opposite the central scallop.

Mitral valve regurgitation. Mitral regurgitation occurred in 5 of the 19 patients with ventricular septal defect and floppy mitral valve (Table 5). In three patients, a 3 month old girl, a 3 month old boy and an 88 year old man (Fig. 4, right), mitral regurgitation was caused by the marked degree of mitral valve leaflet prolapse. In one patient, a 43 year old man, mitral regurgitation was the result of entrapment of chordae in a left ventricular friction lesion (Fig. 8). In a 48 year old woman, mitral regurgitation was caused by chordal rupture (Fig. 10).

Fibrin deposits at mitral valve-left atrial angle. No patients with ventricular septal defect and floppy mitral valve had fibrin deposits at the mitral valve-left atrial angle. The long period of storage for the majority of the hearts in this study would make it unlikely that fibrin deposits would still be identifiable. On the other hand, in four of our patients with ventricular septal defect and floppy mitral valve, a 19 month old boy, a 4 year old girl, a 38 year old woman and a 43 year old man, organized fibrous deposits were present at the mitral valve-left atrial angle (Fig. 9, upper). We believe these represent organized fibrin deposits.

Associated conditions. Floppiness of other valves. In this study, we evaluated all the valves in each of the 104 specimens with ventricular septal defect. The incidence of floppiness of other valves in the 19 patients with ventricular septal defect and floppy mitral valve is recorded in Table 6. Floppy tricuspid valve was present in 63% (Fig. 11). Two of the patients with floppy pulmonary valve, a 3 month old male infant and a 4 year old girl, also had a floppy tricuspid valve and thus had a total of three valves involved. In the other patient with a floppy pulmonary valve and in the patient with a floppy aortic valve, the tricuspid valve was not floppy.

Abnormalities of the tricuspid valve are also produced by altered blood flow in patients with ventricular septal
Table 3. Cause of Death in Ventricular Septal Defect and Floppy Mitral Valve

<table>
<thead>
<tr>
<th>Age at Death and Patient Group</th>
<th>Concentric Heart Failure (%)</th>
<th>Operative (%)</th>
<th>Pulmonary Vascular Obstructive Disease (%)</th>
<th>Other (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 year</td>
<td>No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VSD alone</td>
<td>36</td>
<td>39</td>
<td>44</td>
<td>0</td>
</tr>
<tr>
<td>VSD &amp; FMV</td>
<td>6</td>
<td>33</td>
<td>67</td>
<td>0</td>
</tr>
<tr>
<td>1 to 16 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VSD alone</td>
<td>27</td>
<td>7</td>
<td>81</td>
<td>7</td>
</tr>
<tr>
<td>VSD &amp; FMV</td>
<td>7</td>
<td>14</td>
<td>71</td>
<td>0</td>
</tr>
<tr>
<td>&gt; 16 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VSD alone</td>
<td>22</td>
<td>0</td>
<td>23</td>
<td>14</td>
</tr>
<tr>
<td>VSD &amp; FMV</td>
<td>6</td>
<td>17</td>
<td>17</td>
<td>33</td>
</tr>
</tbody>
</table>

FMV = floppy mitral valve; VSD = ventricular septal defect.

defect. When the jet of blood from the ventricular septal defect impinges on the tricuspid valve leaflet, it produces fibrosis of the ventricular surface of the leaflet and localized tricuspid valve prolapse. The spongiosal layer is normal. In the group of 104 specimens with ventricular septal defect, jet lesions of the tricuspid valve occurred in 29% in the under 1 year of age group, in 38% in the 1 to 16 years of age group and in 14% in the over 16 years of age group.

The floppy tricuspid valve was easily distinguished from the jet lesions because it has more generalized prolapse and on microscopic examination there is spongiosal invasion of the fibrosa. In two patients with a ventricular septal defect and a normal mitral valve the tricuspid valve was floppy (a 3 year old boy and a 20 year old man).

Atrial septal defect. In recent years an increased incidence of atrial septal defect in patients with floppy mitral valve has been reported. The significance of this apparent association has been debated. An associated secundum atrial septal defect was present in 3 (16%) of the 19 patients with ventricular septal defect and floppy mitral valve. A secundum atrial septal defect was present in 14 (16%) of the 85 patients with ventricular septal defect and normal mitral valve in this study.

Table 4. Secondary Anatomic Effects in 19 Heart Specimens With Ventricular Septal Defect and Floppy Mitral Valve According to Age at Death

<table>
<thead>
<tr>
<th>Secondary Anatomic Effects</th>
<th>&lt; 1 Year</th>
<th>1 to 16 Years</th>
<th>&gt; 16 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroelastotic lesions of mitral valve leaflets</td>
<td>6 (100%)</td>
<td>7 (100%)</td>
<td>6 (100%)</td>
</tr>
<tr>
<td>Thinned chordae</td>
<td>5 (83%)</td>
<td>5 (71%)</td>
<td>5 (83%)</td>
</tr>
<tr>
<td>Left ventricular friction lesions</td>
<td>1 (17%)</td>
<td>4 (57%)</td>
<td>5 (32%)</td>
</tr>
<tr>
<td>Chordae entrapped in friction lesions</td>
<td>0</td>
<td>0</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>Total</td>
<td>12 (63%)</td>
<td>16 (84%)</td>
<td>17 (90%)</td>
</tr>
</tbody>
</table>

Location and Size of Ventricular Septal Defect

The location and size of the ventricular septal defect in the specimens with and without floppy mitral valve are presented in Table 7. Sixty-seven percent of the specimens had a large defect including the membranous septum. Each of the remaining categories of ventricular septal defect represented 10% or less of the total.

Floppy mitral valve was associated with the following categories of ventricular septal defect: large infracristal, large muscular, combination of large infracristal and large muscular, and small muscular. The incidence of floppy mitral valve in each of these categories was roughly comparable.

Figure 8. Entrapment of chordae tendineae in a left ventricular friction lesion (arrows) in a 43 year old man with grade I floppy mitral valve. There is prolapse of the anterolateral scallop of the posterior leaflet (AL) of the mitral valve while the anterior leaflet (A) is normal. LA = left atrium; LV = left ventricle.
Floppy mitral valve did not occur in the specimens with supracristal ventricular septal defect or in specimens with aneurysm of the membranous septum with a small ventricular septal defect, but the number of these cases was small.

Two of the patients with a large membranous ventricular septal defect had spontaneous closure of the defect by means of adherence of the tricuspid valve to the defect. One of these had a floppy mitral valve and the other did not. Four patients with a small muscular ventricular septal defect, all over 16 years of age, had had recent spontaneous closure of the defect. None of these had a floppy mitral valve.

**Discussion**

**Anatomic basis of floppy mitral valve.** In our experience, based in part on a review of 179 autopsy specimens...
Figure 11. A floppy tricuspid valve in a 7 month old girl with ventricular septal defect and grade II floppy mitral valve. The right atrium (RA) and right ventricle have been opened. There is pronounced interchordal hooiding of all leaflets of the tricuspid valve.

Table 6. Floppiness in Other Valves in 19 Heart Specimens With Ventricular Septal Defect and Floppy Mitral Valve

<table>
<thead>
<tr>
<th>Age at Death (yr)</th>
<th>No. With Ventricular Septal Defect and Floppy Mitral Valve</th>
<th>Floppy Tricuspid Valve</th>
<th>Floppy Pulmonary Valve</th>
<th>Floppy Aortic Valve</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>6</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1 to 16</td>
<td>7</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>&gt;16</td>
<td>6</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>All ages</td>
<td>19</td>
<td>12 (65%)</td>
<td>3 (16%)</td>
<td>1 (5%)</td>
</tr>
</tbody>
</table>

of floppy mitral valve (5) and this current study, the critical feature defining the floppy mitral valve is spongiosal invasion and disruption of the fibrosa. This process destroys the functional integrity of the mitral valve leaflet and allows stretching and interchordal hooiding of the leaflet. In our previous study (5), there was no evidence that incidence or severity of spongiosal invasion of the fibrosa was age-related. In this current series, spongiosal invasion of the fibrosa was fully developed and resulted in interchordal hooiding of the mitral leaflet by 3 months of age. There was no evidence that the incidence or severity of spongiosal invasion of the fibrosa increased between the ages of 3 months and 88 years. Pomerance (14) also observed in an adult autopsy series that significant mitral leaflet ballooning did not progress with increasing age.

There is considerable variation in the amount of spongiosa in the normal mitral valve leaflet (15). Of the patients with ventricular septal defect in this study, 6% had increase

of spongiosa of the mitral valve leaflets that did not invade the spongiosa. In these patients, there was no interchordal hooiding and we considered the mitral valve to be normal.

Abnormalities of the chordae tendineae have been suggested as the cause for floppiness of the mitral valve. We observed thinning of the chordae in 89% of the specimens with floppy mitral valve (5) and in 79% of the specimens with floppy mitral valve and ventricular septal defect. However, floppiness of the mitral valve occurred in patients who did not have chordal thinning. Lengthening of the chordae tendineae has also been suggested as the basic cause of the floppy mitral valve. Chordal lengthening was present in less than 25% of the specimens from adults with floppy mitral valve we previously reviewed (5) and was not present in this current series.

It has been suggested that mitral valve anulus dilation and increased size of the mitral valve leaflets may be characteristic of the floppy mitral valve. In a study of 50 normal adult mitral valves, Rustad et al. (16) found the range of mitral valve anulus circumference to be 7.5 to 11 cm. They measured the anterior mitral valve leaflet at its midpoint from base to free edge. The range of this measurement was 1.6 to 2.9 cm. Because the range of anular circumference and leaflet size in normal mitral valves is so great, we do not feel these measurements are a reliable index of the floppy mitral valve. Moreover, Isner and Roberts (17) found mitral valve leaflet surface areas to be comparable in 10 specimens with floppy mitral valve and 67 control specimens.

Relation of floppy mitral valve to mitral valve prolapse. The floppy mitral valve, as we have defined it anatomically, has a high incidence (7.5%) in an adult autopsy population and a high incidence (18%) in an autopsy population of infants, children and adults with ventricular septal defect. In our series, interchordal hooiding and spongiosal invasion did not increase in severity or in incidence with increasing age. Moreover, in the great majority of patients, the presence of the floppy mitral valve had not adversely influenced their health. For these reasons, we suggest that the floppy mitral valve we have defined may be comparable with primary mitral valve prolapse as defined by Barlow and Pocock (18). Because most of the patients in our current study died before the time when floppy mitral valve, mitral valve prolapse or the click-murmur syndrome, alone or in combination was generally recognized, clinical, laboratory and pathologic correlations were not possible.

Bias. The fact that most of the cardiac specimens were obtained before the general appreciation of floppy mitral valve makes it unlikely that a heart found its way into our collection because of the coexistence of these two lesions. Moreover, the comparable incidence of floppy mitral valve in large membranous infracristal septal defects, large muscular ventricular septal defects, the combination of these two defects, and small muscular ventricular septal defects suggests that the incidence of floppy mitral valve in this
Table 7. Location and Size of Ventricular Septal Defect in Subjects With and Without Associated Floppy Mitral Valve

<table>
<thead>
<tr>
<th>Patient Groups and Ages at Death (yr)</th>
<th>Large Infracristal</th>
<th>Large Muscular</th>
<th>Large Infracristal and Large Muscular</th>
<th>Small Muscular</th>
<th>Aneurysm of Membranous Septum and Small Ventricular Septal Defect</th>
<th>Supr막al</th>
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<tbody>
<tr>
<td>Ventricular septal defect</td>
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<tr>
<td>and floppy mitral valve</td>
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</tr>
<tr>
<td>&lt;1</td>
<td>5</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1 to 16</td>
<td>7*</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&gt;16</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0</td>
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<tr>
<td>Ventricular septal defect</td>
<td></td>
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<td>and normal mitral valve</td>
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<td></td>
<td></td>
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<tr>
<td>&lt;1</td>
<td>29</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>1 to 16</td>
<td>18*</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>&gt;16</td>
<td>8</td>
<td>2</td>
<td>0</td>
<td>5*</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

*1 large infracristal ventricular septal defect spontaneously closed by tricuspid valve, 14 spontaneously closed recently.

series of specimens with ventricular septal defect may approximate that in the general population of patients with ventricular septal defect.

Comparison with an adult autopsy series of floppy mitral valve. It is instructive to relate this study of floppy mitral valve and ventricular septal defect to our recently reported series of 102 specimens of floppy mitral valve in an adult autopsy group of 1,376 specimens (5). The incidence of floppy mitral valve in the adult autopsy group was 7.5% whereas the incidence of floppy mitral valve in patients with ventricular septal defect was 18%. Because the incidence of mitral valve prolapse in “normal” patient groups has ranged as high as 17% (19), it is not possible to state that the incidence of floppy mitral valve in patients with ventricular septal defect is higher than that in the normal population.

The male/female (M/F) ratio in patients with floppy mitral valve and ventricular septal defect was 0.9. The ratio in the 104 patients with ventricular septal defect in this series was 0.82 and the reported ratio in patients with ventricular septal defect is 1.0 (20). These appear to be comparable values. In our adult autopsy series, we reported a male/female ratio of 1.5. Some clinical studies of mitral valve prolapse have a preponderance of females.

The incidence of the secondary effects fibrosis of the surfaces of the mitral leaflets and thinned chordae was comparable in this series and the adult autopsy group.

The incidence of the left ventricular friction lesion appeared to be age-related. Left ventricular friction lesions were present in 75% of the adult autopsy series (mean age at death 69 years). In the patients with floppy mitral valve and ventricular septal defect, the incidence was 82% in patients dying over 16 years of age (mean age at death 37), 57% in the 1 to 16 years of age group and 17% in the under 1 year of age specimens.

The incidence of the complications of floppy mitral valve—primary rupture of chordae, bacterial endocarditis, mitral valve regurgitation and fibrin deposits at the mitral valve-left atrial junction—was comparable in the two autopsy groups.

The incidence of floppiness of the tricuspid valve was comparable in the two autopsy series (40 and 63%). In clinical studies of mitral valve prolapse, tricuspid valve prolapse has occurred in the following frequencies: Werner et al. (21), 11 (48%) of 23; Morganroth et al. (22), 31 (48%) of 64; and Maranhao et al. (23), 32 (52%) of 61.

The anatomic basis of floppy tricuspid valve is fibrosal destruction by the spongiosa. The common anatomic basis of floppy mitral valve and floppy tricuspid valve and their frequent coexistence suggest a common etiology based on fundamental anatomy, rather than lesions produced by acquired stress.

The incidence of floppy pulmonary valve and of floppy aortic valve was comparable in the two autopsy studies. The anatomic cause of floppiness of the semilunar valves was spongiosal invasion of the fibrosa.

Floppy mitral valve in children. Bisset et al. (24) identified 118 children with the characteristic auscultatory features of mitral valve prolapse. The youngest child was 2-1/2 years of age and the mean age was 9.9 years. Echocardiograms were performed in 92 of these patients; 91% had the features of mitral valve prolapse. These authors recognized only one patient who did not have the auscultatory features of mitral valve prolapse. On the other hand, Brown (25) reported on 23 patients in whom the diagnosis of mitral valve prolapse had been made with echocardiography. The mean age of these patients was 8.1 years and the youngest was 8-1/2 months. Eight of the 23 patients with mitral valve prolapse did not have the typical auscultatory findings usually associated with this syndrome. Pickoff et al. (26) reported on 51 children who presented with premature ventricular complexes. Six of these patients (12%)
had echocardiographic evidence of mitral valve prolapse. None had the auscultatory features of mid-systolic click or late systolic murmur. These studies neither define the incidence nor shed light on the anatomic basis of floppy mitral valve in children.

The anatomic development of floppy mitral valve is fully achieved in infants as young as 3 months. The amount of spongiosa did not increase with increasing age. The magnitude of fibroal destruction and the degree of interchordal hooding did not increase throughout the 9 decades represented in this study. These findings are consistent with the theory that the floppy mitral valve is a congenital lesion. Moreover, neither the incidence nor the severity of floppy mitral valve is influenced by the size or location of the ventricular septal defect. These facts make it unlikely that the floppy mitral valve is an acquired lesion resulting from the hemodynamic stress imposed on the mitral valve by the ventricular septal defect.

We did not uncover any evidence that ventricular septal defect and floppy mitral valve share a common congenital etiology. On the contrary, two lines of reasoning suggest that these two conditions occur independently. First, the incidence of floppy mitral valve is comparable in different types of ventricular septal defect (infracristal, small muscular, large muscular) that appear to have different embryologic bases. Second, the basic anatomy, incidence of secondary effects and complications and natural history of floppy mitral valve seem no different in groups with and without ventricular septal defect.

Conclusions. If, as these observations suggest, floppy mitral valve and ventricular septal defect are unrelated occurrences, several tentative conclusions are warranted. 1) The incidence of floppy mitral valve is comparable in all ages. 2) The anatomic basis of floppy mitral valve is the same for infants, children and adults. 3) The severity of floppy mitral valve is defined at birth and the severity does not change with age. 4) The amount of surface fibrosis on the leaflets and the incidence of left ventricular friction lesions increase with age, but have no apparent deleterious effects. The incidence of chordal entrapment in friction lesions and of primary rupture of chordae increases with age and both of these result in mitral regurgitation. 5) Floppy mitral valve is underdiagnosed in the pediatric population. This is of concern because bacterial endocarditis occurs in children with floppy mitral valve, and optimal management of the patients with floppy mitral valve includes prophylaxis against bacterial endocarditis.

References
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