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Ventricular Septal Defect Associated With Aneurysm of the Membranous Septum

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The most common variety of ventricular septal defect, a perimembranous defect, is frequently associated with a so-called aneurysm of the membranous septum. Previous studies have suggested that ventricular septal defects associated with an aneurysm of the membranous septum tend to spontaneously decrease in size or close more than defects without such an aneurysm. To better define the natural history of this entity, clinical and catheterization data from 87 patients with ventricular septal defect and aneurysm of the membranous septum were reviewed. The initial evaluation was made at a median age of 0.3 years (range 0.1 to 11), with the final evaluation at a median age of 10 years (range 1.5 to 20) and a median duration of follow-up of 8.6 years (range 1.2 to 18.8).

Approximately 75% of the ventricular septal defects had a small or no left to right shunt at last evaluation. Overall, 48 patients (55%) had no significant change in the size of the defect, and 39 (45%) showed improvement during the period of observation. Only four patients (5%) had spontaneous closure of the defect. Of the 49 patients who presented with a large left to right shunt, with or without congestive heart failure, 23 (47%) had persistence of a shunt large enough to warrant surgery. When spontaneous improvement occurred, it did so by 6 years of age in all but one patient. Therefore, a continued tendency for a ventricular septal defect associated with an aneurysm of the membranous septum to spontaneously decrease in size or close after this age may be less likely than previously suggested. The actual morphologic substrate of this entity usually consists of tricuspid valve tissue adherent to the edges of the ventricular septal defect.

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Perimembranous ventricular septal defects are the most common type of ventricular defect and consist morphologically of deficiency of the membranous septum and variable portions of the adjacent muscular septum. It has been recognized for years that this variety of ventricular septal defect is frequently associated with septal "aneurysm formation." An aneurysm of the membranous septum has traditionally been defined as an abnormality having the angiographic appearance of a pouch-like structure with distinct margins protruding around the edges of a ventricular defect and bulging into the right ventricle during systole (Fig. 1). There has been considerable controversy about both the anatomic substrate and clinical significance of this entity. Numerous pathologic and clinical studies (1–5) have indicated that the term "aneurysm of the membranous septum" is actually a misnomer in most cases since the tissue making up this structure is usually derived from the tricuspid valve and not from the membranous septum itself.

Another area of uncertainty is the role that "aneurysm formation" plays in the well known tendency for perimembranous ventricular septal defects to spontaneously close or diminish in size. Previous reviews of this subject (2,3,6,7) have suggested that the presence of an aneurysm of the membranous septum associated with a ventricular septal defect may be a marker for a defect that is likely to become smaller or close in the future. We undertook a review of the clinical course of 87 patients with a ventricular septal defect associated with an aneurysm of the membranous septum seen at our institution over the last 22 years in order to further define its natural history.

Methods

Study group. There were 138 angiographically proven cases of ventricular septal defect associated with an aneu-

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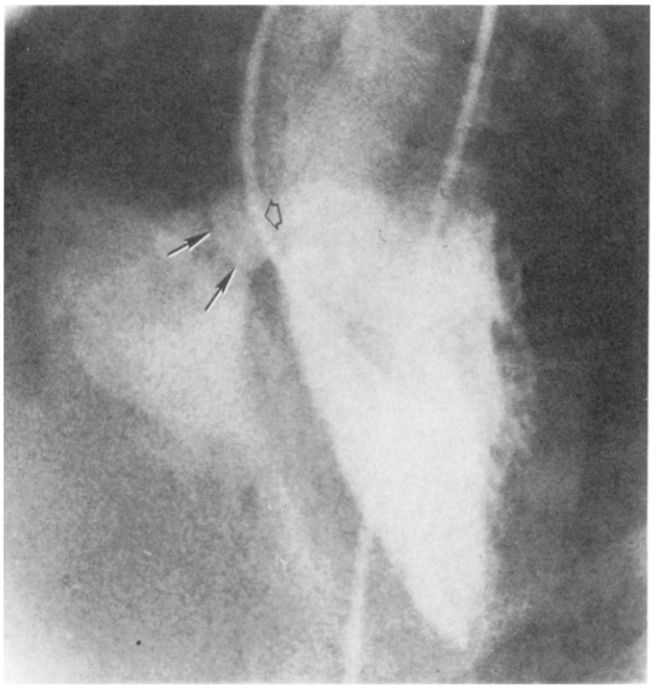

Figure 1. Left ventriculogram in the four chamber view. Note the aneurysmal-like pouch (**solid arrows**) protruding into the right ventricle surrounding a ventricular septal defect (**open arrow**). Contrast medium can be seen entering the right ventricle.

rysm of the membranous septum seen at the Children's Hospital of Pittsburgh between 1960 and 1982. Of these, 51 had the significant associated defects shown in Table 1. These 51 cases were excluded from this study because the associated lesions affected the hemodynamic and clinical evaluation of the severity of the ventricular defect. The remaining 87 patients had either an isolated ventricular defect or an insignificant associated abnormality such as a trivial atrial shunt, a tiny patent ductus arteriosus or subpulmonary stenosis with a gradient across the right ventricular outflow tract of 20 torr or less. The median age at initial evaluation was 0.3 year (range 0.1 to 11), while the median age at final evaluation was 10 years (range 1.5 to 20) and the median duration of follow-up was 8.6 years (range 1.2 to 18.8).

Table 1. Associated Defects in 51 Patients

	No. of Patients
Coarctation of the aorta	14
Subpulmonary stenosis	9
Transposition of the great vessels	7
Atrial septal defect	5
Valvular pulmonary stenosis	4
Corrected transposition of the great vessels	2
Miscellaneous	10

Catheterization data. Hemodynamic data and angiographic studies were reviewed in all patients. Serial cardiac catheterization data were available for analysis in 30 patients with a median interval of 3.9 years (range 1.2 to 12.8) between studies. Clinical data, such as physical examination, chest radiograph and electrocardiogram, were evaluated with particular reference to whether or not patients initially presented with findings of congestive heart failure or a large left to right shunt.

Categorization. Patients were categorized into four groups according to the functional size of the ventricular septal defect. Both catheterization and clinical criteria were used for categorization of the defect. Although all patients in this study had a ventricular septal defect associated with an aneurysm of the membranous septum documented by cardiac catheterization, this invasive study was not always performed early in the patient's course. Therefore, clinical data at the time of presentation were utilized, if necessary, to assess the magnitude of the left to right shunt and determine whether congestive heart failure was present. The combination of cardiomegaly with pulmonary vascular plethora on the chest radiograph, right or left ventricular hypertrophy on the electrocardiogram and an apical mid-diastolic murmur was considered to be the clinical equivalent of a catheterization-documented large left to right shunt (that is, pulmonary to systemic flow ratio [Qp/Qs] $\geq$ 1.8:1). Conversely, a normal chest radiograph and electrocardiogram and absence of an apical diastolic murmur were the clinical criteria for a small left to right shunt (that is, Qp/Qs $<$ 1.8:1). The diagnosis of congestive heart failure was made if tachypnea, tachycardia, hepatomegaly and feeding difficulties with failure to thrive were present.

Operative notes. Although this natural history study was restricted to isolated ventricular septal defects, we also reviewed the operative reports on 25 patients with both isolated and complex ventricular defects (that is, associated with other cardiac abnormalities) who underwent open heart repair. The purpose of this review was to help elucidate the morphologic substrate of an aneurysm of the membranous septum.

Results

Distribution. Group I consisted of those patients who had spontaneous closure of their defect during the study. Because the criteria for admission to this study included documentation of a ventricular shunt, no patients were initially in this category. Group II consisted of patients with a small left to right shunt (defined as a catheterization-documented Qp/Qs $<$ 1.8:1 or its clinical equivalent). Initially there were 38 patients (44%) in this category. Group III consisted of those with a large left to right shunt (Qp/Qs $\geq$ 1.8:1 or its clinical equivalent), but no evidence of congestive heart failure. There were 28 patients (33%) in

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this category at the time of initial evaluation. A Qp/Qs ratio greater than or equal to 1.8:1 was documented by catheterization in 14 patients, while clinical criteria were used in the remaining 14. Finally, Group IV included the 21 patients (24%) who had a large left to right shunt and clinical evidence of congestive heart failure when first seen. Catheterization data during the first year of life were available in 15 of the patients in this group.

Clinical course (Fig. 2). *Of those 21 patients initially in Group IV,* only 1 continued to have congestive heart failure and pulmonary hypertension necessitating early surgical intervention. In 11 patients (52%), the congestive heart failure resolved, but a left to right shunt large enough to warrant operative correction persisted. Diminution of the shunt size to a Qp/Qs ratio less than 1.8:1 occurred in eight patients (38%) and one patient had spontaneous closure of the defect. Serial catheterization data were available in 16 of the 21 patients in this group, and the outcome of this subset was not significantly different from that of the group as a whole. Ten patients (63%) had a persistently large shunt, while the other six (37%) showed a decrease in the size of the shunt.

Of the 28 patients initially in Group III, 11 (39%) had persistence of a large left to right shunt, while the remaining 17 (61%) showed spontaneous improvement. Ten of the patients in Group III had serial catheterizations; in six of these, the findings did not change, while four patients had a spontaneous decrease in shunt size.

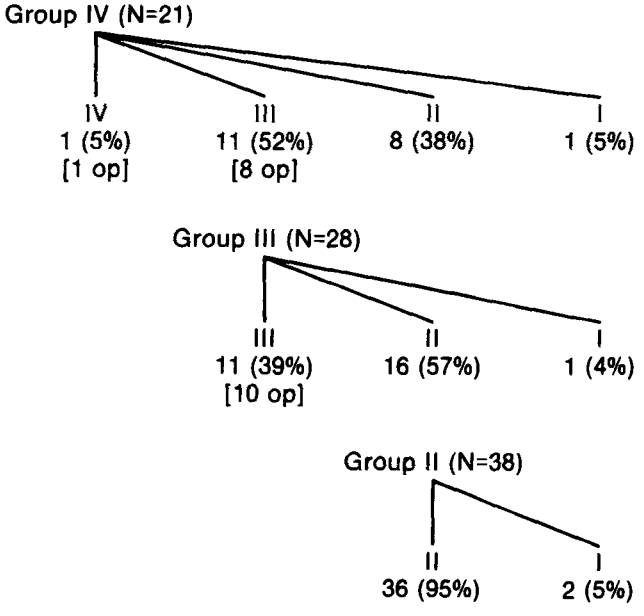
The largest initial group (Group II) consisted of 38 patients with a small left to right shunt. There was a stable clinical course with no significant change in the size of the defect in 36 patients (95%), and only 2 had spontaneous closure. Only four patients in this group had serial catheterizations.

The four patients in the entire study group who had spontaneous closure of the ventricular septal defect were approximately 1.5, 6.5, 13 and 14.5 years of age at the time of closure.

Serial angiography. Serial angiograms were reviewed, and in 16 patients adequate selective left ventriculograms in the oblique views allowed assessment of the size of the defect. Twelve of these patients were initially in Group IV, three in Group III and one in Group II. The median interval between studies was 3.2 years (range 1.3 to 7.9). There was no appreciable change in the size of the ventricular septal defect in eight (50%), while the remaining eight (50%) did have a reduction in the size of the defect.

Overview. The overall results of this study indicated that 64 patients (74%) had a small or no left to right shunt at last evaluation. However, 48 patients (55%) had no significant change in the size of the defect throughout the period of observation, while 39 (45%) showed improvement. Furthermore, there were only four patients (5%) who had spontaneous closure of the defect. Of the 49 patients initially in Groups III and IV who presented with a large left to right shunt (with or without clinical evidence of congestive heart failure), 23 (47%) had persistence of a shunt generally considered large enough to warrant surgery. The mean age at the time of operation or last follow-up evaluation of these patients was 5.3 years, with nine of the patients being 6 years or older. The age at which improvement occurred in the remaining patients initially in Groups III and IV could be determined in 24 cases (Fig. 3). Improvement was defined as spontaneous diminution in the size of the left to right shunt to a Qp/Qs ratio less than 1.8:1 or its clinical equivalent. The mean age was 3.2 years, and all but one of those who showed clinical improvement did so by 6 years of age.

Figure 2. Clinical course of the 87 patients in the study. The outcome of each initial group is shown. See text for details and definition of Groups I, II, III and IV. Op = underwent operation.



Discussion

Incidence. Perimembranous ventricular septal defects are commonly associated with an aneurysm of the membranous septum. In catheterization studies of patients with a ventricular septal defect, Varghese et al. (2) reported a 33% incidence of aneurysm of the membranous septum, while Freedom et al. (7) detected a 57% incidence. The clinical findings of an early systolic ejection sound or an unusual crescendo systolic murmur may suggest the presence of a ventricular septal defect associated with an aneurysm of the membranous septum (7–9). However, the auscultatory, radiographic and electrocardiographic findings of this entity are often indistinguishable from those of a ventricular septal defect without an aneurysm of the membranous septum. Therefore, until the development of two-

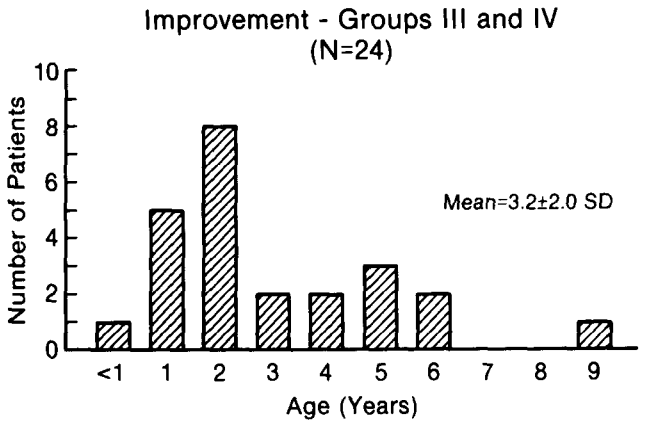


Figure 3. Age at which improvement occurred in patients initially in Groups III and IV (large ventricular septal defect without and with congestive heart failure, respectively). Improvement is defined as diminution in shunt size to a Qp/Qs ratio less than 1.8:1 or its clinical equivalent (see text). SD = standard deviation.

dimensional echocardiography the actual incidence of this abnormality may have been underestimated because of the lack of a reliable noninvasive method of diagnosis. With the recent widespread application of diagnostic ultrasound, the ease of recognition of an aneurysm of the membranous septum has significantly improved (10,11).

Previous studies of natural history. Controversy exists concerning the role of "aneurysm formation" in the spontaneous closure of a ventricular septal defect. The tendency for a ventricular septal defect to close or decrease in size has been recognized for many years, but the actual mechanism for closure remains largely speculative. Numerous studies (2,3,12–20) have shown that between 40 and 60% of all ventricular septal defects spontaneously close. Although closure usually occurs within the first 3 years of life, it may be delayed, with the latest reported closure occurring between 46 and 69 years of age (17). Smaller defects are more likely to close than larger ones, and Alpert et al. (20) reported a 75% incidence of closure of small ventricular septal defects seen within the first 10 years of life. Defects in the muscular septum probably close by physiologic hypertrophy of septal myocardium or by fibrosis around the margins leading to apposition of the edges of the defect (3,12,16).

Varghese et al. (2) concluded from their angiographic studies that aneurysm formation may be an important mechanism of closure of perimembranous ventricular septal defects and suggested that "aneurysmal formation in the membranous septum may occur near the time of closure of the ventricular septal defect." This conclusion was based on two documented cases with spontaneous closure and the finding that an aneurysm of the membranous septum was present more frequently in small defects than in larger ones. In an extensive study of 32 patients with a ventricular septal defect associated with an aneurysm of the membranous septum, Freedom et al. (7) performed serial catheterizations 4 years apart in all patients. Although there were no cases with spontaneous closure, they found that an aneurysm of the membranous septum was more likely to be associated with smaller ventricular septal defects and that visualization of an aneurysm during the second catheterization that had not been seen on the first study was associated with a decrease in the size of the defect in 58% of the cases. These findings suggested that aneurysm formation may be an important mechanism for decreasing the functional size of a ventricular septal defect. In their conclusion, these investigators (7) highlighted the need for extended observations of these patients to better define the natural history.

Current study. The results of our study support the contention that an aneurysm of the membranous septum is not commonly associated with persistently large unrestrictive ventricular septal defects and often is found with defects that have spontaneously decreased in size. Nearly half of the patients showed improvement during the period of observation, and 74% of the overall group had a Qp/Qs ratio less than 1.8:1 at last evaluation. However, 55% of the patients in our series showed no significant change in the size of the defect during follow-up evaluation of a median of 8.6 years (range 1.2 to 18.8). More importantly, 47% of those patients who presented with a large left to right shunt had persistence of a shunt that met standard criteria for elective surgical intervention (that is, Qp/Qs ratio $\geq$ 1.8:1). Therefore, the rate of diminution in size or spontaneous closure is no greater than has been reported for ventricular septal defects in general. In fact, only four patients had spontaneous closure during the extended period of observation in this study. When spontaneous improvement occurred in those patients with a large shunt, with the exception of one case, it did so by 6 years of age. Thus, a continued tendency to improve after this age may be less likely than previously suggested, making this a reasonable age to recommend elective surgery in appropriate cases.

Anatomic substrate. The anatomic substrate that produces the angiographic appearance of a pouch-like structure typical of an aneurysm of the membranous septum has been the subject of many morphologic studies (1,4,5,16). These have clearly shown that the term "aneurysm of the membranous septum" is a misnomer in most cases, since the tissue surrounding the defect is usually derived from the tricuspid valve leaflets rather than from the membranous septum. In a review of 69 specimens with perimembranous ventricular septal defects at our institution, Anderson et al. (5) found that 38% of the specimens showed anatomic evidence of partial or complete closure by tissue arising from the vicinity of the tricuspid valve and membranous septum. The tissue was derived from the tricuspid valve (either accessory tags or adherence of the leaflets) in most cases (84%), and in only two (8%) did the tissue arise from the

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membranous septum itself. The remaining two specimens (8%) showed prolapse of the aortic leaflets reducing the size of the defect.

A review of the intraoperative descriptions of 25 patients who had open heart repair of a ventricular septal defect associated with an aneurysm of the membranous septum at our institution revealed the following findings. In 14 (56%) of the patients, the surgeons could not identify any specific abnormality other than the ventricular defect itself. In the remaining patients, a poorly defined excess of fibrous tissue around the defect, involving either the membranous septum or tricuspid valve leaflets, was described. This supports the contention that an aneurysm of the membranous septum probably most often consists of adherent or abnormal tricuspid valve leaflet tissue that is difficult to characterize or even visualize in the nondistended intraoperative state.

Associated defects. Although we restricted this study to patients with an isolated ventricular septal defect or insignificant associated abnormalities, the entity of a ventricular septal defect with an aneurysm of the membranous septum frequently occurs in the presence of other abnormalities (Table 1). Fifty-one of our patients had associated defects, the most common being coarctation of the aorta, subpulmonary stenosis, large atrial septal defect and valvular pulmonary stenosis. A cause and effect relation between aneurysm of the membranous septum and subpulmonary stenosis has been reported previously (21), but this seems to occur almost exclusively in the setting of corrected transposition of the great vessels. An association with prolapse of aortic cusps or subaortic stenosis has also been suggested (5,22), but there were only two documented cases of significant aortic outflow disease in our series (one with discrete subaortic stenosis and mild aortic regurgitation and one with valvular stenosis).

Terminology. As has been stressed by many, aneurysm of the membranous septum is clearly an inaccurate designation in the vast majority of cases, since morphologically, there is no aneurysm and the structure in question is not the membranous septum. Furthermore, the use of the term "aneurysm" is likely to cause needless concern and confusion among patients who misinterpret this diagnosis in the context of what is commonly understood by the public to be the meaning of this term. Complications generally associated with a true aneurysm, such as rupture leading to a catastrophic cardiac event or unusual susceptibility to endocarditis or thrombosis, do not seem to occur with an aneurysm of the membranous septum. Our long-term follow-up study of more than 750 patient-years, as well as review of the literature, failed to reveal any such documented events other than infrequent reports of bacterial endocarditis. In fact, the only additional connotation that an aneurysm of the membranous septum gives to a ventricular septal defect is a favorable one, since the defect is unlikely to be a large unrestrictive one requiring early operation. Perhaps describing this entity as a "ventricular septal defect associated with restrictive tissue" or a "tricuspid restricted defect" would be more appropriate terminology.

Prospective study. As our study was a retrospective and selective one, requiring angiographic documentation of an aneurysm of the membranous septum, our data do not necessarily reflect the actual distribution of this entity within the spectrum of ventricular septal defects. Even in patients undergoing both studies, the echocardiogram is likely to be more accurate than cineangiography in diagnosis. We recently observed several patients with a large ventricular septal defect whose echocardiogram revealed tissue around the defect's margins that was not apparent on the angiogram. Only with prospective analysis and echocardiographic studies will the true incidence of this common entity be determined.

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