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# Ventricular Septal Defect With Secondary Left Ventricular-to-Right Atrial Shunt Is Associated With a Higher Risk for Infective Endocarditis and a Lower Late Chance of Closure

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## ABSTRACT

**OBJECTIVE.** Although ventricular septal aneurysm may diminish or even close the shunt through the ventricular septal defect (VSD), developing a left ventricular-to-right atrial (LV-RA) shunt may be unfavorable. This study sought to clarify this issue on the basis of an extended observation of such patients.

**METHODS.** Sixty-eight patients (1201 patient-years) who had small perimembranous VSD and LV-RA shunt and were not operated on before 6 years of age were studied.

**RESULTS.** The onset age of LV-RA shunt was  $5.8 \pm 3.3$  years, with clinical improvement later observed in 23 (34%). The murmur disappeared and showed spontaneous closure in 5 (7%). Seven episodes of infective endocarditis occurred in 6 (8.7%, or 58 per 10 000 patient-years), with 2 receiving surgery. Another 4 received surgery during follow-up. With echocardiography, aneurysmal transformation involving the anterior and septal leaflets of tricuspid valve (double sac) was found in 56 (85%), whereas only the septal leaflet (single sac) was involved in 10. Patients with double sac were less likely to show improvement, whereas patients who had superior QRS axis and were female showed clinical improvement more frequently.

**CONCLUSIONS.** VSD with secondary LV-RA shunt is associated with a higher risk for infective endocarditis but still has a low chance for late improvement and even closure.

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### Key Words

ventricular septal defect, left ventricular-to-right atrial shunt

### Abbreviations

VSD—ventricular septal defect  
LV-RA—left ventricular-to-right atrial shunt

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**V**ENTRICULAR SEPTAL DEFECT (VSD) is by far the most common congenital heart disease, and the natural history varies depending on its size, location, and associated anomalies.<sup>1-3</sup> Surgery typically is indicated for patients with a significant left-to-right shunt (a pulmonary-to-systemic flow ratio of  $>2$ ), pulmonary arterial hypertension resulting from increased pulmonary flow, aortic valve prolapse, or right ventricular outflow obstruction.<sup>3</sup> Medical follow-ups are suggested for those with a small left-to-right shunt, particularly in the case of defects involving the membranous portion of the interventricular septum (perimembranous VSD). This type of VSD accounts for the majority (60%–80%) of VSD cases.<sup>3,4</sup> Owing to its proximity to the tricuspid valve, a so-called “aneurysmal transformation” process may emerge, thereby diminishing the shunt or even closing the defect via the adherence of the adjacent tricuspid valve or chordal tissues to the septal crest.<sup>5-7</sup> A Gerbode defect is a septal defect that communicates directly between the left ventricle and the right atrium.<sup>8</sup> Its pathology may be attributed to a congenital defect, be a product of trauma, or may even occur after bacterial endocarditis or aortic valve replacement.<sup>8-11</sup>

What we found, nevertheless, was that patients with perimembranous VSD also might have developed a left ventricular-to-right atrial (LV-RA) shunt after aneurysmal transformation of the VSD.<sup>5,12</sup> A secondary LV-RA shunt after the aneurysmal transformation of the VSD was suggested. An earlier study has also given credence to a close association between the aneurysmal transformation process and an LV-RA shunt in patients with perimembranous VSD.<sup>13</sup> In the presence of a VSD and an LV-RA shunt, surgical repair is often suggested.<sup>14</sup> Given the dearth of relevant long-term data in previous studies, this study used the observations of such patients over an extended period of time to clarify this issue.

## METHODS

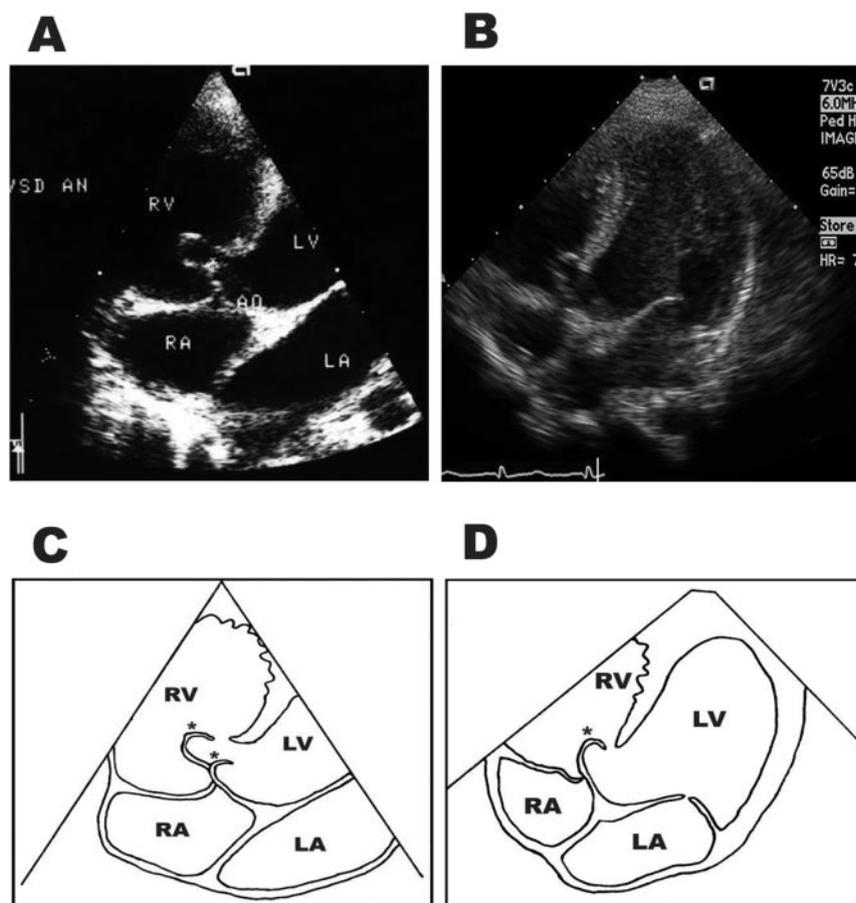
### Patient Cohorts

In 1 of our previous studies, we had characterized the natural evolution of aneurysmal transformation in all patients with perimembranous VSD from the patient database covering 1987–1992 in this institution.<sup>5</sup> Those who had had a small isolated perimembranous VSD (assessed at 6 years of age) with aneurysmal transformation and LV-RA shunt were recruited into the present study and received complete follow-ups in this institution. Patients with possible atrioventricular septal defect or endocardial cushion-type defect were excluded. None of the patient sample had received surgical repair before the age of 6 years. The echocardiographic studies were performed using either Acuson 128 XP or Acuson Sequoia module. The echocardiograms were assessed independently by 2 of the authors.

### Definitions

In this study, the diagnosis of perimembranous VSD was based on previous echocardiographic reports.<sup>15,16</sup> In addition, the diagnostic hallmark for endocardial cushion defect, a left atrioventricular valve with 3 leaflets, could distinguish the endocardial cushion defect from perimembranous VSD. Aneurysmal transformation of perimembranous VSD was defined as echocardiographic evidence of tissue deposition around the margins of the VSD, which then produced a sac-like structure with distinct margins that, with each systole, protruded into the right ventricle and partially occluded the flow through the VSD.<sup>4,5,13</sup> The individual patterns of aneurysmal transformation were determined with echocardiography. On the basis of our previous studies, the echocardiographic pattern of aneurysmal transformation could be described by a double- or single-sac pattern. A double-sac pattern was the result of the aneurysmal transformation process, which incorporated both the septal and the anterior leaflets of the tricuspid valve into a double-sac morphology (Fig 1A and C). The sac produced by the anterior leaflet overlaid the sac of the septal leaflet. An LV-RA shunt then was observed through a widened anteroseptal commissure. As for the single-sac pattern, just the septal leaflet and some chordae of the tricuspid valve were involved, and, thus, only a solitary sac was observed (Fig 1B and D). An LV-RA shunt was defined as the presence of a Doppler demonstration of high-velocity turbulence (with a pressure gradient of  $>50$  mm Hg) moving from the LV, through the VSD, and directly into the RA.<sup>5,13</sup> The pressure gradient of an LV-RA shunt was equivalent to the difference between the systolic LV and RA pressure and could be readily differentiated from tricuspid regurgitation on the basis of the high velocity of the LV-RA shunt in the absence of any elevated right ventricular pressure. From an electrocardiogram, a QRS axis of  $<0$  degrees accompanied by inferior initial activation and large superior terminal activation (ie, an rS pattern in aVF) was defined as a superior QRS axis, or as a left axis deviation.

The criteria for a small VSD were as follows: (1) from cardiac catheterization, the ratio of pulmonary flow to systemic flow was  $<2$  in the absence of pulmonary arterial hypertension or pulmonary stenosis; or (2) from echocardiography, the z score of the left ventricular end-diastolic diameter was smaller than 2, and no evidence of pulmonary arterial hypertension was found. Because only patients with small perimembranous VSD were included, the change of left ventricular size, pressure gradient, or ratio of pulmonary flow to systemic flow may not be a sensitive index for clinical improvement. Therefore, the clinical improvement was defined as improved heart failure or a decreased intensity in the systolic murmur caused by the VSD (in the absence of pulmonary arterial hypertension) to a grade of less than III with a normal-sized heart on chest radiograph film.



**FIGURE 1**

A and C, Echocardiogram in an apical 4-chamber view (A) and its diagram (C) showing a perimembranous VSD that was covered by an aneurysmal transformation process that incorporated the septal and anterior leaflets of the tricuspid valve into a double-sac morphology. B and D, Echocardiogram in an apical 4-chamber view (B) and its diagram (D) showing a perimembranous VSD that was covered by an aneurysmal transformation process that incorporated only the septal leaflet of the tricuspid valve into a single-sac morphology.

### Statistics

The descriptive data were expressed as the mean  $\pm$  1 SD. Either the  $\chi^2$  test or the Fisher's exact probability test was used to determine the level of significance of each of the events. The event-free curves were estimated by performing a Kaplan-Meier analysis.

### RESULTS

A total of 68 patients (39 female and 29 male) were found to have a perimembranous VSD with aneurysmal transformation and a secondary LV-RA shunt. Their age at initial enrollment into our VSD study ranged from 3 days to 19 years ( $4.7 \pm 4.1$ ; median: 4 years). The total follow-ups amounted to 1201 patient-years, with the mean age at the time of the last follow-up being  $17 \pm 5$  years (6–28 years; median: 16 years). In the 48 patients who first were observed during infancy or who had had adequate echocardiographic evaluation (at least twice) before the development of an LV-RA shunt, the onset age of the LV-RA shunt ranged from 3 months to 12 years ( $5.8 \pm 3.3$  years; median: 5 years). Among them, 5 (7%) had already developed an LV-RA shunt during infancy. By the age of  $\sim$ 52 months, one half of the patients had already developed an LV-RA shunt. Ten patients had heart failure in infancy, which improved

after the development of aneurysmal transformation in all. In 2 of them, the heart failure continued to improve even after the appearance of secondary LV-RA shunt. Electrocardiograms showed the presence of a left superior axis in 11 patients (11 of 68 [16%]).

Clinical improvement after the development of the LV-RA shunt was found in 23 (34%) patients, including improved heart failure in 2 and a decreased intensity in the systolic murmur caused by the VSD (in the absence of pulmonary arterial hypertension) to a grade of less than III with a normal-sized heart on chest radiograph film in 22 patients (1 of whom also had improved heart failure and was also included in the former group). Among the 22 patients, the murmur disappeared in 5 (7%), and among all 5, echocardiography revealed a spontaneous closure of the VSD via aneurysmal transformation. The closure occurred at the individual ages of 9, 12, 13, 17, and 23 years ( $14.8 \pm 5.4$  years). The probability of closure with age is shown in Fig 2A. By the age of 23 years, the probability of spontaneous closure was 17%.

However, 7 episodes of infective endocarditis occurred in 6 (8.5%) patients (58 per 10 000 patient-years) at the individual ages of 2, 5, 5, 5, 7, 8, and 12 years, respectively. Two of the 6 with infective endocar-

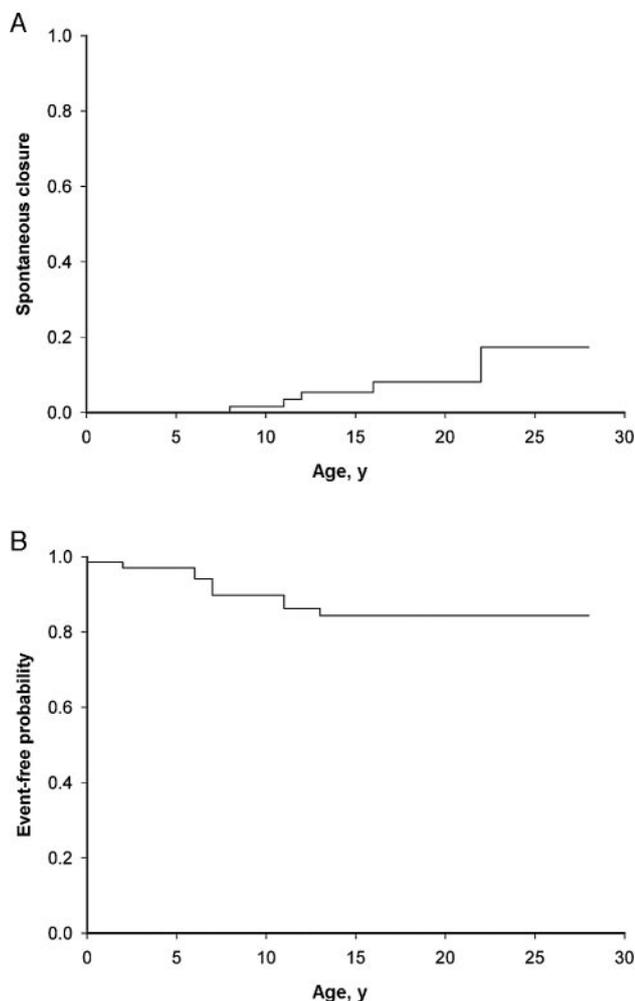


FIGURE 2 A, Probability of spontaneous closure with age in 68 patients who had perimembranous VSD with aneurysmal transformation and a LV-RA shunt. B, Event-free (infective endocarditis or a surgical repair of the defect) curve in the same patient cohort.

ditis received surgery, with 1 being operated on during the acute stage to have vegetation and the periaortic abscess removed, as well as to have the defect repaired. The other received surgical repair of the VSD after completing antibiotic therapy. In both cases, the postoperative course was smooth with no recurrence of infective endocarditis. Another 4 patients received surgical repair of the VSD during the follow-up; 2 had cardiomegaly (at the age of 8 and 12 years); 1 had late-onset subaortic ridge (at the age of 7 years); and 1 patient personally opted for surgery (at the age of 7 years). None experienced exertional dyspnea, palpitation, or arrhythmias. Event-free probability with the endpoints defined as death, endocarditis, or heart surgery is shown in Fig 2B. The event-free probability was 84% by the age of 14 years.

Overall, the echocardiographic features of aneurysmal transformation could be characterized as having either double- or single-sac morphology in 66 patients

but not in 2 in whom the morphology could not be categorized satisfactorily on account of superimposed infective endocarditis. With those 2 (<3%) excluded, 56 (85%) patients had a double-sac whereas 10 (15%) had a single-sac morphology of aneurysmal transformation. Statistical analysis revealed that gender, the presence of a superior QRS axis, and the morphology of aneurysmal transformation all were closely associated with late outcome, including clinical improvement and spontaneous closure (Table 1). Although female patients showed a higher chance of clinical improvement, this was not so for spontaneous closure. The presence of a superior QRS axis in the frontal plane was also more often observed in patients who had shown clinical improvement, but, again, this was not the case for spontaneous closure. Noteworthy is that patients with a double-sac morphology were much less likely to show either clinical improvement or spontaneous closure. Although double-sac morphology was observed more commonly in patients with infective endocarditis or surgical repair, the statistical difference was not significant.

## DISCUSSION

The pathologic anatomy of LV-RA shunt was summarized in an earlier report by Riemenschneider et al.<sup>9</sup> They provided substantive evidence that most defects are located in or involve parts of the membranous interventricular septum. Such defects often are associated with tricuspid abnormalities, ie, a widened commissure, cleft, perforation, or malformation. Because the features of an aneurysm of the ventricular membranous septum may not always be recognized during surgery or postmortem inspection, not until when angiographic and echocardiographic studies were conducted had the close association between aneurysmal transformation of the VSD and an LV-RA shunt been found.<sup>13,17</sup> Aneurysmal transformation of VSD was, in fact, found in all of those case studies. Furthermore, in the patient cohorts with perimembranous VSD and aneurysmal transformation, an LV-RA shunt may have occurred in as many as 11% of the patients.<sup>5</sup> By the age of 20 years, patients with perimembranous VSD had a 98% probability of developing aneurysmal transformation. Among them, the expected probability of developing an LV-RA shunt was 45%.<sup>5</sup> Hence, it very well may follow that an LV-RA coupled with perimembranous VSD is the most common type of LV-RA shunt. Nonetheless, the long-term prognosis of such patients remains unclear.

The present study clearly demonstrated for the first time that there was a lower, albeit relatively late, chance of clinical improvement for such patients, as compared with those without LV-RA shunts. Also noted was a significantly higher risk for infective endocarditis.

The development of aneurysmal transformation is an important mechanism for the spontaneous closure of perimembranous VSD.<sup>6</sup> In our patients with perimem-

**TABLE 1 Clinical Characteristics and the Long-Term Outcome**

	Follow-ups, y	Gender (M/F)	Onset Age of LV-RA Shunt, y	Superior QRS Axis (Yes/No)	Echocardiographic Features of Aneurysm (Double Sac/Single Sac) <sup>a</sup>
Clinical improvement					
Yes ( <i>n</i> = 23)	18.9 ± 4.6	3/20 <sup>b</sup>	7.0 ± 0.3	7/16 <sup>c</sup>	13/10 <sup>b</sup>
No ( <i>n</i> = 45)	19.1 ± 4.6	16/29	5.0 ± 3.2	4/41	43/0
Spontaneous closure					
Yes ( <i>n</i> = 5)	17.4 ± 4.9	2/3	6.3 ± 1.6	1/4	2/3 <sup>b</sup>
No ( <i>n</i> = 63)	17.2 ± 4.9	27/36	5.7 ± 3.7	10/53	54/7
Infective endocarditis					
Yes ( <i>n</i> = 6)	19.7 ± 3.8	4/2	5.1 ± 1.1	1/5	4/0
No ( <i>n</i> = 62)	17.1 ± 4.9	37/25	6.8 ± 4.1	10/52	52/10
Late surgery					
Yes ( <i>n</i> = 6)	16.5 ± 3.9	3/3	5.1 ± 2.6	1/5	5/0
No ( <i>n</i> = 62)	17.2 ± 5.0	26/36	6.8 ± 4.0	10/52	51/10

<sup>a</sup> Patterns of the echocardiographic features could be categorized in 66 patients but not in 2, in whom the morphology could not be categorized satisfactorily on account of superimposed infective endocarditis.

<sup>b</sup> *P* < .01.

<sup>c</sup> .01 < *P* < .05.

branous VSD and secondary LV-RA shunting after aneurysmal transformation, spontaneous closure was still observed. However, the likelihood of spontaneous closure was much lower than that found in our previous observations of patients without secondary LV-RA shunting after aneurysmal transformation (7% vs 19%).<sup>5</sup> Added to this, the age at spontaneous closure in those with an LV-RA shunt was 14.8 ± 5.4 years, whereas that in those without an LV-RA shunt was an astonishingly low 3.5 ± 3.8 years.<sup>5</sup> As described by Somerville et al,<sup>18</sup> a spontaneous closure of the VSD could still occur in 10 (28%) of 35 adult patients with subtricuspid (perimembranous) VSD after the apposition of tricuspid valve tissue (aneurysmal transformation). However, none of their patients had an LV-RA shunt. In another series of 685 patients with VSD, an LV-RA shunt was found in 8.4%, with spontaneous closure noted in only 1 (2.6%) case.<sup>4</sup>

Our data revealed that patients with perimembranous VSD and a secondary LV-RA shunt showed a higher risk for infective endocarditis. According to the Second Joint Study on the Natural History of Congenital Heart Defects, the risk for infective endocarditis is estimated at 14.5 per 10 000 patient-years in those with VSD.<sup>19</sup> Contrast this with the estimated risk in this study, which was 58 per 10 000 patient-years, ~4 times higher. Comparing with patients with perimembranous VSD and aneurysmal transformation without LV-RA shunt, the incidence of infective endocarditis in those with perimembranous VSD and aneurysmal transformation with LV-RA shunt was also much higher (8.5% vs 0.3%).<sup>5</sup> The high velocity turbulence of an LV-RA shunt may have been responsible for this increased risk.<sup>20</sup>

From the echocardiographic evaluation in this study, spontaneous closure occurred more frequently in patients with single-sac aneurysmal transformation. Because none of them had been operated on, it can be

deduced only from our previous studies that the echocardiographic features of a single-sac aneurysmal transformation are produced by the attachment of septal leaflet along with some chordae of the tricuspid valve to the septal crest.<sup>12</sup> This is highly indicative that the commissure was only partially incompetent as a result of a relatively spared anterior leaflet from aneurysmal transformation. If the VSD had become smaller with tissue adhesion, then the LV-RA shunt also would have been obliterated. However, when both the anterior and the septal leaflets were incorporated into double-sac aneurysmal transformation, the LV-RA shunt could be observed through the widened anteroseptal commissure. Such morphologic changes have previously been described as relatively common pathologic anatomy for an LV-RA shunt.<sup>9</sup> In our study, such a pattern was the most common type of aneurysmal transformation in perimembranous VSD and LV-RA shunt. Hagler et al<sup>14</sup> previously described 8 patients with perimembranous VSD in whom significant tricuspid regurgitation was produced by the VSD jet's pushing the tricuspid anterior leaflet forward, thereby opening the tricuspid valve orifice. A moderate perimembranous VSD extending slightly below the tricuspid leaflet with only a partial obstruction of the VSD jet was observed in their patients. Their echocardiographic findings were similar to those that have been categorized here as the double-sac type of aneurysmal transformation. In our patients, this double-sac aneurysmal transformation was also associated with a lower chance of clinical improvement, as well as a higher probability of infective endocarditis or surgical repair. Therefore, we suggest that such echocardiographic features with a double-sac aneurysmal transformation in perimembranous VSD may an unfavorable sign.

The present study also demonstrated that the presence of a superior QRS axis might predict a higher pos-

sibility of clinical improvement but not for spontaneous closure. In the study by Tutar et al,<sup>21</sup> a superior QRS axis was found in 20% of their 59 patients with perimembranous VSD and was relatively much more common (but not statistically significant) in those without (50%) than in those with an LV-RA shunt (33%). Electrocardiographic changes of right atrial enlargement and right ventricular hypertrophy were observed in more than half of their patients with an LV-RA shunt. In this study, because only patients with a small VSD were included, it was found that none had any significant right-chamber enlargement. Although the prevalence of a superior QRS axis (16%) was relatively lower, it was still significantly higher than that in normal infants and children (0.4%–1.1%).<sup>21,22</sup> In isolated VSD, Shaw et al<sup>23</sup> identified a superior QRS axis in up to 10% of their patients, and this was more common when the inlet portion of the ventricular septum was involved. An association between a superior QRS axis and aneurysmal transformation of the VSD also has been described in the literature.<sup>24</sup> On these grounds, it is possible that a defect with a superior QRS axis involves the inlet more than it does the trabecular ventricular septum; as a result, the defect may be covered to a greater extent and, hence, shows clinical improvement. However, the possibility of spontaneous closure is still determined by the morphology of aneurysmal transformation.

## CONCLUSION

When a secondary LV-RA shunt develops after aneurysmal transformation, there may still be a chance for perimembranous VSD to show late clinical improvement and even closure. Nevertheless, the likelihood of this is evidently much lower, and the occurrence seems to require a much longer follow-up. Another major concern is an increased risk for infective endocarditis. An echocardiographic characterization of aneurysmal transformation helps to predict the long-term outcome. Surgical repair may be considered in the presence of unfavorable echocardiographic morphology.

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## REFERENCES

1. Hoffman JI, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol.* 2002;39:1890–1900
2. Helmcke F, de Souza A, Nanda NC, et al. Two-dimensional and color Doppler assessment of ventricular septal defect of congenital origin. *Am J Cardiol.* 1989;63:1112–1116
3. McDaniel NL, Gutgesell HP. Ventricular septal defect. In: Allen HD, Gutgesell HP, Clark EB, Driscoll DJ, eds. *Moss and Adam's Heart Disease in Infants, Children and Adolescents.* 6th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2001:636–651

4. Eroglu AG, Oztunc F, Saltik L, et al. Evolution of ventricular septal defect with special reference to spontaneous closure rate, subaortic ridge and aortic valve prolapse. *Pediatr Cardiol.* 2003; 24:31–35
5. Wu MH, Wu JM, Chang CI, et al. Implication of aneurysmal transformation in isolated perimembranous ventricular septal defect. *Am J Cardiol.* 1993;72:596–601
6. Anderson RH, Lenox CC, Zuberbuhler JR. Mechanisms of closure of perimembranous ventricular septal defect. *Am J Cardiol.* 1983;52:341–345
7. Beerman LB, Park SC, Fischer DR, et al. Ventricular septal defect associated with aneurysm of the membranous septum. *J Am Coll Cardiol.* 1985;5:118–123
8. Gerbode F, Hultgren H, Melrose D, et al. Syndrome of left ventricular-right atrial shunt successful surgical repair of defect in five cases, with observation of bradycardia on closure. *Ann Surg.* 1958;148:433–446
9. Riemenschneider TA, Moss AJ. Left ventricular-right atrial communication. *Am J Cardiol.* 1967;19:710–718
10. Velebit V, Schoneberger A, Ciaroni S, et al. "Acquired" left ventricular-to-right atrial shunt (Gerbode defect) after bacterial endocarditis. *Tex Heart Inst J.* 1995;22:100–102
11. Winslow TM, Friar DA, Larson AW, et al. A rare complication of aortic valve endocarditis: diagnosis with transesophageal echocardiography. *J Am Soc Echocardiogr.* 1995;8:546–550
12. Wu MH, Chang CI, Wang JK, et al. Characterization of aneurysmal transformation in perimembranous ventricular septal defects: an adhered anterior leaflet of tricuspid valve predisposes to the development of left ventricular-to-right atrial shunt. *Int J Cardiol.* 1994;47:117–125
13. Leung MP, Mok CK, Lo RNS, et al. An echocardiographic study of perimembranous ventricular septal defect with left ventricular-to-right atrial shunting. *Br Heart J.* 1986;55:45–52
14. Hagler DJ, Squarcia U, Cabalka AK, et al. Mechanism of tricuspid regurgitation in paramembranous ventricular septal defect. *J Am Soc Echocardiogr.* 2002;15:364–368
15. Soto B, Becker AE, Lie JT, et al. Classification of ventricular septal defects. *Br Heart J.* 1980;43:332–343
16. Sutherland GR, Godman MJ, Smallhorn JF. Ventricular septal defects: two-dimensional echocardiographic and morphologic correlations. *Br Heart J.* 1982;47:316–328
17. Burrows PE, Fellows KE, Keane JF. Cineangiography of the perimembranous ventricular septal defect with left ventricular-right atrial shunt. *J Am Coll Cardiol.* 1983;1:1129–1134
18. Neumayer U, Stone S, Somerville J. Small ventricular septal defects in adults. *Eur Heart J.* 1998;19:1573–1582
19. Gersony WM, Hayes CJ, Driscoll DJ, et al. Bacterial endocarditis in patients with aortic stenosis, pulmonary stenosis or ventricular septal defects. *Circulation.* 1993;87(suppl 1):1121–1126
20. Citak M, Rees A, Mavroudis C. Surgical management of infective endocarditis in children. *Ann Thorac Surg.* 1992;72: 755–760
21. Calcaterra G, Puglisi R. Left axis deviation in healthy infants and children. *Int J Cardiol.* 1989;24:236–238
22. Pearl W, Stafford EM. Left axis deviation in children. *Int J Cardiol.* 1992;34:119
23. Shaw NJ, Godman MJ, Hayes A, et al. Superior QRS axis in ventricular septal defect. *Br Heart J.* 1989;62:281–283
24. Farru-Albohaire O, Arcil G, Hernandez I. An association between left axis deviation and an aneurysmal defect in children with a perimembranous ventricular septal defect. *Br Heart J.* 1990;64:146–150

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