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Evolution of Ventricular Septal Defect with Special Reference to Spontaneous Closure Rate, Subaortic Ridge and Aortic Valve Prolapse

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Abstract. The medical records of 685 patients with ventricular septal defect (VSD) were reviewed to determine spontaneous closure, left ventricular-to-right atrial shunt, subaortic ridge, and aortic valve prolapse. Patients had been followed for a mean of 3 ± 2.5 years and median 2.2 years by echocardiography. VSD was perimembranous in 65.7% (450), trabecular muscular in 30.8% (211), muscular outlet in 2.3% (16), muscular inlet in 0.7% (5), and doubly committed subarterial in 0.5% (3). Defect size was classified in 76% (517) as small, in 18% (124) as moderate, and in 6% (44) as large. VSD closed spontaneously in 27% (186 of 685 patients) by ages 40 days to 13.7 years (mean, 2.1 ± 2.2 years; median, 1.3 years). Sixty-six of 450 perimembranous defects (15%) and 120 of 211 trabecular muscular defects (57%) closed spontaneously ($p < 0.001$). Defect size became small in 15% of patients with VSD at mean 2.9 ± 2.3 years (median, 2.3 years). Aneurysmal transformation was detected in 56% (254), left ventricular-to-right atrial shunt in 8.4% (38), subaortic ridge in 5.8% (26), aortic valve prolapse in 11.7% (53), and aortic regurgitation in 7.3% (33) of 450 patients with perimembranous defect. There was no statistical significance between the age at closure and the age of detection of aneurysmal transformation in the patients with perimembranous defect ($p = 0.25$).

Key words: Ventricular septal defect — Spontaneous closure — Left ventricular-to-right atrial shunt — Subaortic ridge — Aortic valve prolapse

The rate of spontaneous closure of ventricular septal defect (VSD) has been reported to be between 11% and 70.8% in various series [1–3, 5, 6, 10, 14–16, 18, 25]. This variation may be due to the study population, criteria for diagnosis, methods of investigation, follow-up period, and the percentage of different types of VSDs. Muscular defects are stated to close more frequently than perimembranous defects [3, 15]. In several studies, it was proposed that ventricular septal aneurysm is an important mechanism of closure and shows a more favorable prognosis in perimembranous defects [7, 17, 20]. In other studies, it was observed that aneurysmal transformation may be particularly likely to develop left ventricular-to-right atrial shunt or subaortic ridge [10, 24]. A left ventricular-to-right atrial shunt may develop through a deformed tricuspid valve [4, 24]. Subaortic ridge may develop and progress to subaortic stenosis after the occurrence of aneurysmal transformation [4, 24]. Aortic valve prolapse may reduce the size of VSD [4]. We reviewed the medical records of 685 patients with VSD who were followed by echocardiography to assess the rate of spontaneous closure, aneurysmal transformation, left ventricular-to-right atrial shunt, subaortic ridge, and aortic valve prolapse.

Materials and Methods

The study population consisted of 685 patients with VSD who had been studied at our institution from 1988 to 1999 and had at least two echocardiographic examinations. Patients with other complex lesions, such as tetralogy of Fallot or double-outlet right ventricle, were excluded. The medical records of 1129 patients with VSD were reviewed. Patients with insufficient medical records (18) were excluded. Patients who had only one echocardiographic examination (426) were not included in the study. Twenty-six of 685 patients had been operated on. The evolution of the defect was studied until the last presurgical echocardiographic examination. Transthoracic echocardiography was performed with a transducer of either 3.5 MHz or 7 MHz interfaced with an Acuson 128/XP 10 ultrasound system. Two-dimensional, M-mode, color-flow Doppler, pulsed Doppler, and continuous-wave Doppler echocardiography were used in all patients. VSDs were classified according to their location and relation to the tricuspid annulus and semilunar valves [16]. Defect size was expressed in terms of the size of the aortic root. Defects approximating the size of the aorta were classified as large, defects one-third to two-thirds the diameter of

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the aorta were classified as moderate, and defects less than one-third the diameter of the aortic root were classified as small [8, 11]. The echocardiograms had been performed during the study period by 5 different examiners only. The original echocardiograms were not reviewed at the time of the study. Data are expressed as mean ± standard deviation. Student's *t*-tests were used to compare variables. The chi-square test was used to assess differences between groups for categorical variables. Statistical significance was inferred at $p < 0.05$.

Results

We followed 685 patients (381 boys and 304 girls) ages 1 day to 26.3 years (mean 2.1 ± 3.3 years, median 6 months) for 1 month to 10.9 years (mean, 3 ± 2.5 years; median, 2.2 years) by echocardiography (1801 patient years). Sixty-three percent of the patients were younger than 1 year old at initial echocardiographic examination (Table 1). Perimembranous defects were the most common defects (Table 2). There were two VSDs in 17 (2.5%) and Swiss cheese VSDs in 5 (0.5%) of the 685 patients. Defect size was classified in 519 (76%) of 685 patients as small, in 123 (18%) as moderate, and in 43 (6%) as large (Table 3).

We excluded 426 patients from the study because they had only one echocardiographic examination: 136 of these patients underwent surgical repair after the first echocardiographic examination, 284 had perimembraneous defect (38.7% of all perimembraneous defects), 2 had muscular inlet defect (28.6% of all muscular inlet defects), 123 had trabecular muscular defect (36.8% of all trabecular muscular defects), 8 had muscular outlet defect (33.3% of all muscular outlet defects), and 9 had doubly committed subarterial defect (75% of all doubly committed subarterial defects). Of these 426 patients, 250 had small defect (32.6% of all small defects), 56 had moderate-sized defect (31.1% of all moderate-sized defects), and 120 had large defect (73.2% of all large defects).

Table 1. Ages of patients at initial echocardiographic examination

Age group (years)	Number	%
≤ 1	434	63
1.1–5	152	22
5.1–10	68	10
10.1–15	25	4
> 15	6	1
Total	685	100

Table 2. Types of ventricular septal defects

Type of defect	Patients	
	Number	%
Perimembraneous	450	65.7
Muscular		
Inlet	5	0.7
Trabecular	211	30.8
Outlet	16	2.3
Doubly committed subarterial	3	0.5
Total	685	100

Table 3. Incidence of spontaneous closure and reduced size with respect to type and size of defect

Type and size of defect	Total No. of patients	Spontaneous closure	%	Became small	%
Perimembraneous	450	66	15	86	17
Small	308	53	17		
Moderate	106	10	9	66	62
Large	36	3	8	20	56
Muscular inlet	5			2	
Small	2				
Moderate	2			1	
Large	1			1	
Trabecular muscular	211	120	57	11	5
Small	195	115	59		
Moderate	12	4	33	8	
Large	4	1	25	3	
Muscular outlet	16			3	19
Small	12				
Moderate	3			3	
Large	1				
Doubly committed subarterial	3				
Small	2				
Moderate					
Large	1				14
Total	685	186	27	93	14

[a]For small patient groups, the percentage was not calculated

Spontaneous closure of VSD occurred in 27% (186 of 685 patients) by age 40 days to 13.7 years (mean, 2.1 ± 2.2 years; median, 1.3 years). Fifteen percent of perimembranous defects and 57% of trabecular muscular defects closed spontaneously ($p < 0.001$) (Table 3 and Fig. 1). Defect size became smaller in 15% of the patients with ventricular septal defect at a mean 2.9 ± 2.3 years (median, 2.3 years) (Table 3).

Aneurysmal transformation was detected in 152 at initial echocardiographic examination and in 102 developed during follow-up at ages 3 days to 16 years (mean, 3.4 ± 3.8 years; median, 1.6 years) (Table 4).

Left ventricular-to-right atrial shunt was detected in 38 of 450 patients with perimembranous defects (8.4%) at ages 1 month to 14.4 years (mean, 5.4 ± 4.5 years; median, 9 years). In 15 patients in whom left ventricular-to-right atrial shunt was detected at initial echocardiographic examination, the shunt was small in 14 and moderate in 1. These patients were followed 3 months to 5.7 years (mean, 1.7 ± 0.9 years; median, 1.7 years) and the degree of shunt progressed from small to moderate in 1. In 23 patients in whom left ventricular-to-right atrial shunt developed during follow-up (9 months to 10.8 years; mean, 4.8 ± 3.7 years; median, 3.5 years), the shunt was small in 21 and moderate in 2. In only 1 of 38 patients with left ventricular-to-right atrial shunt, did ventricular septal defect close spontaneously.

Subaortic ridge was detected in 26 of 450 perimembranous defects (5.8%) (in 7 at initial echocardiographic examination and in 19 at follow-up) at age 1.2 to 22 years (mean, 5.6 ± 4.3 years; median, 4 years). Mild subaortic stenosis was detected in 3 patients, mild aortic regurgitation in 2, and trivial aortic regurgitation in 2 simultaneously with subaortic ridge. Mild aortic regurgitation developed in 3 of 13 patients who were followed for a median of 1.5 years after the occurrence of a subaortic ridge. No ventricular septal defect with subaortic ridge closed spontaneously.

Aortic valve prolapse was detected in 53 of 450 perimembranous defects (11.7%) (in 22 at initial echocardiographic examination and in 31 at follow-up) at ages 2 months to 19.3 years (mean, 5.2 ± 4.1 years; median, 3.8 years). Aortic regurgitation was detected in 33 (trivial in 15 and mild in 18) of 53 patients with aortic valve prolapse and perimembranous defect. Additionally, aortic valve prolapse was detected in 5 of 16 patients with muscular outlet defects (31%) and in 1 of 3 patients with doubly committed subarterial defects. Mild aortic regurgitation was detected in 2 and slight aortic regurgitation in 2 of 5 patients with muscular outlet defects and aortic valve prolapse. Aortic valve prolapse was detected in 8.6% of all VSDs and aortic regurgitation in 6.4%. No ventricular septal defect with aortic valve prolapse closed spontaneously.

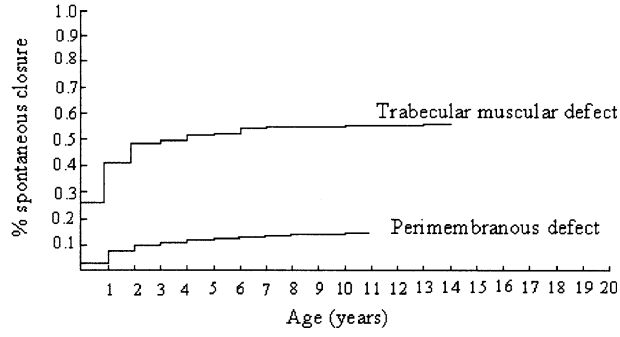

Fig. 1. Actuarial curves show the proportion of spontaneous closure in patients with perimembranous defect and trabecular muscular defect during follow-up of 685 patients with ventricular septal defect.

Table 4. Associated anomalies in 450 perimembraneous ventricular septal defects

Associated anomaly	Number of patients	%
Aneurysmal transformation	254	56
Left ventricular-to-right atrial shunt	38	8.4
Subaortic ridge	26	5.8
Aortic valve prolapse	53	11.7
Aortic regurgitation	33	7.5

There was no significant difference between the age at closure and the age of detection of aneurysmal transformation in patients with perimembranous defects ($p = 0.25$). The age of detection of aneurysmal transformation was younger than the age of detection of left ventricular-to-right atrial shunt, subaortic ridge, and aortic valve prolapse ($p < 0.03$, 0.05, and 0.0007, respectively). The age of detection of left ventricular-to-right atrial shunt did not differ significantly from the age of detection of subaortic ridge and aortic valve prolapse ($p = 0.89$ and 0.92, respectively). There was also no significant difference between the age of detection of subaortic ridge and aortic valve prolapse ($p = 0.73$).

Discussion

In series in which the patients had been followed from birth, muscular septal defects were more common than perimembranous defects [15, 23]. In other series [14, 21], the frequency of perimembranous defect was highest, followed by trabecular muscular, muscular outlet, and muscular inlet defects, respectively, similar to our findings. Our study also showed that the percentage of doubly committed subarterial defect was relatively small (0.4%), although its incidence in Japanese and Chinese was reported to be higher (approximately 30%) [9].

Table 5. Spontaneous closure and associated anomalies in perimembraneous ventricular septal defects in two studies

Associated anomaly	Ramaciotti et al. [19] (%)	Wu et al. [24] (%)
Spontaneous closure	12	8.9
Aneurysmal transformation	76	74
Left ventricular-to-right atrial shunt	15	8.1
Subaortic ridge		3.1
Aortic valve prolapse		0.6
Aortic regurgitation		0.6

The rate of spontaneous closure of VSD has been reported to be between 11% and 70.8% in various[1–3, 5, 6, 10, 14–16, 18, 25]. In our series, the rate of spontaneous closure in all ventricular septal defects was 27%. Spontaneous closure was detected in 15% of perimembranous defects and 57% of trabecular muscular defects. In various series, spontaneous closure was reported in muscular defects to be between 24% and 83% and in perimembranous defects to be between 11% and 37% [2, 3, 14, 20, 24].

Wu et al., [24] reported 74% aneurysmal transformation, 12% spontaneous closure, 8.1% left ventricular-to-right atrial shunt, and 3.1% subaortic ridge in 877 patients (median age, 1 year) with perimembranous defect (Table 5). In this series, median age at initial echocardiographic examination was 6 months. Ramaciotti et al. [20] reported 76% aneurysmal transformation and 8.9% spontaneous closure in 247 patients with perimembranous defect (Table 5). However, in our series, the rate of aneurysural transformation was lower and the rate of spontaneous closure was higher than these studies [10, 12]. This may be due to younger ages in our series. They reported left ventricular-to-right atrial shunt in 10 of 61 patients with perimembranous defect (15%) by echocardiography [20]. The degree of left ventricular-to-right atrial shunt was not reported.

In some cases, aortic valve prolapse reduces the size of VSD [9, 22]. Aortic valve prolapse was reported in 69% and aortic regurgitation in 36% of doubly committed subarterial defects [22]. In this series, aortic valve prolapse was detected in 8.6% of all VSDs and in 11.7% of perimembranous defects. In VSD series, the frequency of aortic regurgitation has been reported to be between 5.5% and 9.4% [12, 13]. Aortic regurgitation was detected in 6.4% of all VSDs and 7.5% of perimembranous defects in this series.

Limitations of the Study

This study is a retrospective review of the medical records. The original echocardiogram examination recordings were not reviewed.

Our patients were not followed from birth, nevertheless, approximately two-thirds were younger than 1 year old and the median age at initial echocardiographic examination was 6 months. Approximately three-fourths of patients with large defect and approximately one-third patients with small or moderate defect had one echocardiographic examination; therefore, they were excluded from the study. Most of the patients with large defects underwent operation after the first echocardiographic examination.

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