

SPONTANEOUS CLOSURE OF VENTRICULAR SEPTAL DEFECTS IN THE FIRST YEAR OF LIFE

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Background and purpose: The recent increase in the prevalence of ventricular septal defect (VSD) has been ascribed to the improved detection of small defects with echocardiography and the wider use of screening. The aim of this study was to determine the prevalence and timing of spontaneous closure of specific types of VSD in neonates using echocardiographic screening and follow-up.

Methods: Two-dimensional color Doppler echocardiography was performed in 3,472 clinically normal full-term neonates born at Cathay General Hospital to detect isolated VSD. The relative prevalence of muscular versus perimembranous defects and their outcome in the first year of life were evaluated.

Results: VSD was found in 74 neonates (34 male, 40 female), resulting in a prevalence of 21.3/1,000 live births. There were 48 muscular, 25 perimembranous, and one subpulmonic defects. Of the 74 patients, 11 were lost to follow-up. Within the observation period of 12 months, spontaneous closure occurred in 40 patients in the muscular group and in six patients in the perimembranous group. The overall rate of spontaneous closure was 73% by the end of the first year. Only five patients with perimembranous defects received digoxin therapy.

Conclusions: The prevalence of VSD in this series of neonates was 21.3/1,000 live births. The most common location of VSD in the neonatal period was in the region of the muscular septum. Muscular defects were more likely to close spontaneously than perimembranous defects. Most muscular defects underwent spontaneous closure during the 12-month follow-up period.

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Key words:

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neonate
color Doppler echocardiography
spontaneous closure

Ventricular septal defect (VSD) is the most common cardiac abnormality found in children [1-4]. The reported prevalence of VSD has ranged from 1.35 to 6.5/1,000 live births [5-7]. Differences in inclusion criteria may account for the large differences in the reported prevalence of VSD. The prevalence of VSD may also have been underestimated in the past because of the lack of reliable noninvasive diagnostic techniques [8, 9]. The advent of echocardiography with color Doppler flow measurements has made it possible to diagnose VSDs that are asymptomatic, minor, and even without murmur [9-12]. The spontaneous closure rates of various types of VSD have not been well established. We examined 3,472 consecutive full-term neonates with two-dimensional color Doppler echocardiography to determine the relative prevalence of specific types of VSD and their natural course in the first year of life.

Materials and Methods

Subjects

From July 1997 to June 1999, consecutive full-term neonates born at Cathay General Hospital underwent two-dimensional color Doppler echocardiography to detect VSD as a primary cardiac lesion. All examinations were performed at a mean age of 2.2 days (range, 1-5 d). Parental consent was obtained for each neonate prior to screening. Neonates were excluded for the following reasons: prematurity, Down's syndrome, admission to intensive care unit, parents refused scan, early discharge from the hospital. Only patients with isolated VSD or VSD in combination with an open foramen ovale were included in the study. Patients with

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additional structural cardiac abnormalities were excluded.

Echocardiography

The echocardiography examination was performed using an Acuson 128XP/5 (Acuson, Mountain View, CA, USA) with a 5-MHz transducer focused appropriately for the size of the neonate. Two subcostal views, parasternal long- and short-axis, and apical four-chamber views were routinely recorded on videotape and Sony UPP-110 HD paper (Tokyo, Japan). We attempted to visualize the entire ventricular septum using these views. Color Doppler flow mapping was also performed in each view and continuous-wave interrogation of flow velocity was obtained from abnormal jets. A typical systolic color flame crossing the septum and a jet derived from continuous Doppler were considered diagnostic for VSD. Defects were classified as muscular, perimembranous, or subpulmonic according to their location and relation to the tricuspid annulus and semilunar valve [13]. All examinations were reviewed by at least two pediatric cardiologists. The diagnosis of a VSD was established only when the two pediatric cardiologists concurred.

Follow-up

Neonates were followed at approximately 1, 3, 6, and 12 months of age or until spontaneous closure of the defect was confirmed. The VSD was considered spontaneously closed if the characteristic murmur was no longer heard during auscultation or if echocardiogram of the ventricular septum was normal.

Statistical analysis

The Chi-square test was used to compare the difference between prevalence of VSDs in males and females. Actuarial event-free curves were obtained using Kaplan-Meier analysis to compare spontaneous closure rates of muscular and perimembranous VSDs. Log rank analysis was used to examine the significance between the curves for muscular and perimembranous VSD. A *p* value of less than 0.05 was regarded as statistically significant.

in an overall prevalence of 21.3/1,000 live births. The screening population consisted of 1,853 males and 1,619 females with a sex ratio of 1.14:1. The prevalence of VSD in male and female neonates was 18.3/1,000 live births and 24.7/1,000 live births, respectively. Although there was a slightly higher prevalence of both muscular and perimembranous VSDs in females, this difference was not significant (*p* > 0.05). Of the 74 neonates with VSD, 48 had muscular, 25 had perimembranous, and one had subpulmonic defects (Table). The prevalence of muscular defects (13.8/1,000 live births) was higher than that of perimembranous defects (7.2/1,000 live births). All muscular VSDs were either apical or midmuscular; none was of the inlet-septal or 'swiss-cheese' type. One subpulmonic, 22 muscular, and 25 perimembranous VSDs combined with cardiac murmur were identified during physical examination. Other cardiac abnormalities found concomitantly were interatrial communication (2,254), transient patent ductus arteriosus (909), dextrocardia (2), tetralogy of Fallot (2), and coarctation of aorta (1).

Follow-up

Of the 74 neonates with VSD, 63 were followed for 12 months or until the closure of the defect and 11 did not return for follow-up examination. The rates of spontaneous closure for different ages were calculated on the basis of the 63 neonates who completed follow-up. Spontaneous closure had occurred in 46 patients at the end of 1 year, 40 of whom had muscular defects and six of whom had perimembranous defects (Table). A significant difference was found between the curves for muscular and perimembranous VSD by log rank analysis (*p* < 0.001) (Figure). During the observation period, congestive heart failure developed in five patients and digoxin therapy was required. All of these had perimembranous defects. No surgical closure was required in any patient with muscular or perimembranous defect during the first year.

Table. Number of patients with different types of ventricular septal defect (VSD) and timing of spontaneous closure

Type of VSD	n	Sex	Spontaneous closure				
			M/F	1 m/o	3 m/o	6 m/o	12 m/o
Muscular	48	22/26	25	31	35	40	5
Perimembranous	25	11/14	1	3	4	6	6
Subpulmonic	1	1/0	0	0	0	0	0
Total	74	34/40	26	34	39	46	11

m/o = months old; LFU = lost to follow-up.

Results

Prevalence and distribution

Of the 3,472 neonates who underwent echocardiographic scans from July 1997 through June 1999, a primary diagnosis of VSD was made in 74, resulting

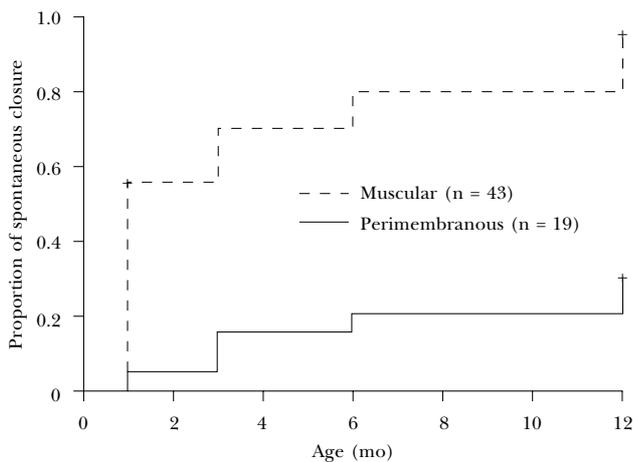


Figure. Kaplan-Meier survival curves comparing spontaneous closure rates of muscular and perimembranous ventricular septal defects.

Discussion

In the present study, the overall prevalence of 21.3 VSDs per 1,000 live births is much higher than previously reported [4–7, 9, 14]. Recent studies found a very high frequency of isolated VSDs when term neonates were routinely investigated using two-dimensional color Doppler echocardiography [14–16]. The case-identifying method probably contributed to the unexpectedly high prevalence [15]. By using color Doppler echocardiographic screening in consecutive live-birth neonates, many asymptomatic neonates and neonates with undetected murmurs or defects that could only be seen by color Doppler would not be missed [15]. When VSDs were screened in non-selected populations using echocardiography, muscular defects were most common [7, 12, 17]. We also found that the vast majority of VSDs were small and located in the muscular septum. Thus, the high prevalence of muscular defects may be a reason for the observed total increase in the prevalence of VSD.

Muscular VSDs close more frequently than perimembranous defects [9, 12, 18]. Trowitzsch et al found a spontaneous closure rate of 37.9% for muscular defects and 4.7% for perimembranous defects within the first 13 months of life [12]. Wu et al found the expected probability of developing spontaneous closure in isolated perimembranous VSD was 35% [19]. Shirali et al studied 156 cases for a mean of 28 months and found a significantly higher spontaneous closure rate for muscular defects [18]. However, Moe and Guntheroth reviewed the charts of 222 patients and

found no significant difference in rates of spontaneous closure between perimembranous and muscular defects [20]. The spontaneous closure rate of specific types of VSD in our study was comparable to those of other series [12, 18, 20]. The total spontaneous closure rate was significantly higher for muscular than for perimembranous defects at the end of 1 year (93% and 31.6%, respectively). The findings of both high prevalence and spontaneous closure rate in small muscular defects suggest that the high prevalence of VSD was not caused by an actual increase in prevalence, but by improved diagnostic methods and strategies for finding such defects.

The concept of endothelial roughening leading to spontaneous closure, whether incrementally in small muscular defects and by aneurysmal membranous formation or by adhesion of the tricuspid valve leaflets, accounts for all accepted mechanisms of spontaneous closure in VSD [5, 19–21]. However, Mitchell et al proposed that the time of ventricular septal closure may not be limited to the fourth and fifth postconceptive weeks but rather may extend throughout pregnancy and into the postpartum period [22]. Meburg et al suggested that small muscular defects with spontaneous closure in early life may represent the tail of a normal developmental process and not defects in the sense of malformation [7]. Our finding that most of the muscular defects underwent spontaneous closure supports the hypothesis that these defects may result from delayed physiologic development rather than from disease.

Sands et al studied risk factors for VSD in low-risk neonates and found that gender and season of birth affected the prevalence [14]. They suggested that both genetic and environmental factors may be involved in the etiology of VSD [14]. Roguin et al speculated that environmental factors or unknown teratogens may have been responsible for the high prevalence of small muscular VSDs [15]. However, Newman found no difference in prevalence among races, seasons, maternal age, birth order, sex, and socioeconomic status [23], and suggested that VSD often occurs as a random error in development and many VSDs are not preventable. Therefore, to avoid unnecessary anxiety, parents should be informed of this benign muscular VSD whether it is identified by echocardiography intentionally or accidentally [15]. Many would argue that small muscular VSDs are of limited importance and, as such, do not merit diagnosis. However, such a perspective may have practical clinical implications on how to inform parents, and in deciding which VSDs should be included in studies to examine genetic or teratogenous factors contributing to this type of congenital heart disease [23].

Perimembranous VSDs usually account for most moderate and large defects that require medical or

surgical treatment [17, 24]. In our study, five patients with perimembranous defects exhibited signs of heart failure and required digoxin therapy during the 12-month follow-up period. In contrast, no patient with a muscular defect developed symptoms of heart failure or required management. Our data on the development of congestive heart failure and the percentage of patients requiring medical treatment in the first year suggests that the overall prognosis in muscular defects is much better than that in perimembranous defects.

In conclusion, the overall prevalence of 21.3 VSDs per 1,000 live births in this study was much higher than in previous studies. This may be attributable to early echocardiographic screening in neonates that allowed even very small muscular defects to be discovered. The rate of spontaneous closure was higher in muscular defects than in perimembranous defects. Most muscular defects underwent complete or substantial spontaneous closure during the 12-month follow-up period. Color Doppler echocardiography is a useful technique for establishing the natural course of VSD in neonates.

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