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REVIEW ARTICLE

A review of isolated muscular ventricular septal defect

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Abstract

Background Color Doppler echocardiography greatly facilitates the diagnosis of isolated muscular ventricular septal defect with a small shunt.

Data sources Original research articles were collected from database, including PubMed and Google scholar. Relevant articles about muscular ventricular septal defect were included.

Results The frequency of isolated muscular ventricular septal defect is 5.7% in preterm infants and 1.1–5.3% in term infants. Spontaneous closure in muscular ventricular septal defect occurs with higher frequency and earlier than in perimembranous ventricular septal defect. Approximately 80–90% of isolated muscular ventricular septal defect closes spontaneously by 12 months of age. Midventricular muscular ventricular septal defect is spontaneously closed earlier in the short term, but no site difference is found in the long term. The spontaneous closure mechanism is regarded as aposition of the muscle tissue or fibrous tissue formation in the right ventricular side, but in rare cases involves aneurysm formation of the fibrous tissue. Regarding spontaneous closure of isolated muscular ventricular septal defect diagnosed for the fetus, further studies are needed. Chromosomal microarray analysis of fetuses with isolated muscular ventricular septal defect has revealed that it is not a severe risk factor of chromosomal abnormalities.

Conclusions This paper presents a review of the history of the diagnosis and frequency of ventricular septal defect, with discussion of its natural history from the fetal period to after birth in patients with isolated muscular ventricular septal defect.

Keywords Color Doppler echocardiography · Fetus · Infant · Spontaneous closure

Introduction

Fetal echocardiography is useful to detect fetuses with severe congenital heart disease (CHD). In the United States, pregnancy termination has decreased the incidence of severe CHD, although the frequency of isolated patent ductus arteriosus and mild heart disorder has increased [1]. Color Doppler echocardiography [2–4] has facilitated the diagnosis of muscular ventricular septal defect with a small shunt. Its natural history has been elucidated through many studies [5–24]. The aim of this review for isolated muscular ventricular septal defect is to explain the history of diagnosis and the frequency of ventricular septal defect, and its natural history from the fetal period to after birth.

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Classification of muscular ventricular septal defect [25–29]

Various notations of defect sites exist. Table 1 presents the terms of muscular ventricular septal defect in the articles cited herein. The extant nomenclature for ventricular septal defect was reviewed to establish a uniform reporting system. Muscular ventricular septal defects were classified as type 4: outlet, trabecular anterior, trabecular midventricular, trabecular apical, inlet (posterior), multiple, multiple-"Swiss-cheese", and confluent [29].

Frequency of muscular ventricular septal defect

Frequency and prematurity of ventricular septal defect and muscular ventricular septal defect

The frequency of ventricular septal defect diagnosed using two-dimensional and pulsed wave Doppler echocardiography is 7.06 per 1000 in premature infants. It is 1.8 times

higher than that in term infants of 3.85 per 1000 [30]. The frequency of muscular ventricular septal defect in premature infants is also higher than that in mature infants [14, 20]. Reller et al. [31] reported that the respective frequencies of muscular and perimembranous ventricular septal defect are high in infants with low gestational age, low birth weight, high maternal age, and multiple-gestation pregnancy.

Increase of ventricular septal defect frequency and the progress of echocardiography

In the Baltimore–Washington Infant Study conducted during 1981–1984 [32], ventricular septal defect increased from 1.0 per 1000 to 1.6 per 1000. Although the frequency of ventricular septal defect with associated malformations continued to be constant, the frequency of ventricular septal defect diagnosed with pulsed wave, continuous wave, and color Doppler (from 0.3 per 1000 to 0.7 per 1000) increased. There was a 100% increase in the number of membranous ventricular septal defect and a 400% increase in muscular ventricular septal defect. No evidence was found of an epidemic. The increase of prevalence of ventricular septal defect occurred because of improved detection of small, isolated ventricular septal defects using echocardiography [32]. Meberg et al. [33] reported that the frequency of ventricular septal defect increased from 50 to 70.6% of CHD after the induction of echocardiography in 1986 to patients suspicious of CHD.

Prevalence of ventricular septal defect

In the United States (2008), live-birth infants with CHD were 81.4 per 10,000. Those with isolated ventricular septal defect were 41.8 per 10,000. Those with muscular ventricular septal defect were 27.5 per 10,000. Those with perimembranous ventricular septal defect were 10.6 per 10,000. Those with subarterial ventricular septal defect were 0.5 per 10,000 [31]. Including prenatal diagnosis, 82% of CHD were diagnosed within 3 months after birth in Germany (2011). The prevalence of isolated ventricular septal defect was 52.7 per 10,000; that of muscular ventricular septal defect was 27.8% [34]. One report suggests that mild CHD increased in Caucasians and the upper economic class according to the progress of echocardiography apparatus, but severe CHD decreased by pregnancy termination after fetal echocardiography [1].

Frequency of neonatal ventricular septal defect and muscular ventricular septal defect (after the induction of color Doppler echocardiography)

The frequency of infants with ventricular septal defect, who were suspected of heart disorder by cardiac murmur and SpO_2 for a newborn period and who were diagnosed using color Doppler echocardiography in all infants, was 0.3–1.35% (Table 2) [19, 24, 35–37]. Table 3 presents the frequency of ventricular septal defect revealed by screening using color Doppler echocardiography for all live infants: 1.8–4.6% in term infants [9, 17, 20] and 5.6% in preterm infants [20]. The frequency of muscular ventricular septal defect is 1.1–5.3% in term infants [6, 7, 9, 11, 17, 21] and 5.7% in preterm infants [13]. The frequency of muscular ventricular septal defect in term infants in Caucasians was higher than in Asians (4.1% to 5.3% vs. 1.1% to 2.3%). Of term newborn infants with muscular ventricular septal defect diagnosed using color Doppler echocardiographic screening, 11–73% had a cardiac murmur. That result demonstrates the frequency difference between cases suspected of heart disorder for a cardiac murmur and cases detected by screening using color Doppler echocardiography. Roguin et al. [11] found that the frequency of muscular ventricular septal defect was 5.7 per 1000 as same as 6.0 per 1000 in that of Kinoshita et al. [19] if excepting infants without a heart murmur. No difference was found between Caucasians and Asians (Table 3). Lin et al. [17] reported that all patients with a perimembranous ventricular septal defect had heart murmur, whereas 46% of patients with a muscular ventricular septal defect had. Infants with a muscular ventricular septal defect frequently have no heart murmur.

Spontaneous closure of muscular ventricular septal defect

Spontaneous closure of infants postnatally

Isolated ventricular septal defect that closed spontaneously during the early neonatal period is regarded as normal

Table 1 Terms of muscular ventricular septal defect in the article cited for this article

Wenink et al. [25]	1979	–	Marginal	Central	–	Posterior	–	–	
Hagler et al. [26]	1985	Anterosuperior	Anterior	–	Apical	Inlet	Multiple anteroapical	–	
Soto et al. [27]	1980	Anterosuperior	Anterior	Midseptal	Apical	Inlet	–	–	
Graham [28]	1989	–	Marginal	Central	Apical	Inlet	Multiple	"Swiss-cheese" septum	
Jacobs et al. [29]	2000	Outlet	Anterior	Midventricular	Apical	Inlet (posterior)	Multiple	Multiple-"Swiss-cheese"	Confluent

Table 2 Newborns with a suspicion of having ventricular septal defect

Author, year	Country	Number of newborn infants	Patients with VSD, %	Patients with m-VSD, %	m-VSD (closed at 12 months), %	Suspicion of CHD
Kinoshita et al. 2004 [19]	Japan	4473	47 (1.1)	27 (0.6)	92	Heart murmur
Kaburagi et al. 2006 [35]	Japan	13,718	113 (0.8)	52 (0.4)	96	Heart murmur
Haraguchi et al. 2013 [36]	Japan	5329	72 (1.4)	–	–	Heart murmur, SpO_2
Hu et al. 2017 [37]	China	167,190	506 (0.3)	–	–	Heart murmur, SpO_2
Cresti et al. 2018 [24]	Italy	31,185	343 (1.0)	289 (1.0)	67	Suspicion of having CHD

CHD congenital heart disease, *m-VSD* muscular ventricular septal defect, *VSD* ventricular septal defect

Table 3 Incidence of patients with muscular ventricular septal defect using color Doppler screening

Author, year	Country	Number of newborn infants	Gestational age	Patients with VSD, *n* (%)	Patients with m-VSD, *n* (%)	m-VSD with heart murmur, *n* (%)	Closed at 12 months, %
Ono et al. 1990 [6]	Japan	1179	Term	–	15 (1.3)	9 (60)	89
Hiraishi et al. 1992 [7]	Japan	1028	Term	–	21 (2.0)	12 (57)	76
Waki et al. 1993 [9]	Japan	2625	Term	45 (1.8)	30 (1.1)	22 (73)	96
Ooshima et al. 1995 [10]	Japan	502	Preterm 21.1%	10 (2.0)	8 (1.6)	–	86
Roguin et al. 1995 [11]	Israel	1053	Term	–	56 (5.3)	6 (11)	89
Du et al. 1996 [13]	Israel	159	Preterm	–	9 (5.7)	2 (22)	88
Du et al. 1998 [14]	Israel	7696	Preterm 11.3%	103 (1.3)	97 (1.3)	36 (37)	80
Sands et al. 1999 [16]	Northern Ireland	3971	Not described	173 (4.4)	163 (4.1)	–	–
Lin et al. 2001 [17]	Taiwan	3472	Term	74 (2.1)	48 (1.4)	22 (46)	83
Ekici et al. 2008 [20]	Turkey	125	Preterm	7 (5.6)	46 (4.3)	14 (27)	88
		950	Term	44 (4.6)			
Chang et al. 2011 [21]	Taiwan	2891	Term	–	66 (2.3)	–	82
Zhao et al. 2013 [22]	China	5192	Preterm 4.2%	90 (1.7)	55 (1.1)	–	–

m-VSD muscular ventricular septal defect. "–" not described

closure of the ventricular septum [38]. The hypothesis can be presented as follows: (1) the frequency of isolated muscular ventricular septal defect is high in prematurely born infants; (2) no abnormal autopsy finding has been reported for patients with spontaneously closed ventricular septal defect. Color Doppler echocardiographic screening revealed that 76–96% of muscular ventricular septal defect in all term infants closed spontaneously by 12 months of age (Table 3) [6, 7, 9, 11, 17, 21]. Hiraishi et al. [7] reported that initial ventricular septal defect size had no relation to spontaneous closure in muscular ventricular septal defect of mean 3.5 mm (1.1 mm to 6.6 mm). In contrast, Ono et al. [6] reported that the ventricular septal defect tended to close earlier when the defect was not apparent. The apical muscular ventricular septal defect of the size over 4 mm closed slowly [14], although no relation was found between the defect size and age of spontaneous closure [19]. By 12 months of age, 88% of muscular ventricular septal defect in preterm infants had closed spontaneously. No difference was found in the spontaneous closure rate compared to muscular ventricular septal defect in term infants [13].

Course of Swiss-cheese-type or multiple defects

Generally, ventricular septal defects with multiple defects have more shunt than that with a single defect. Du et al. [14] showed that multiple defects close more slowly than solitary defects did. Cresti et al. [24] reported that only 2 of 10 multiple muscular ventricular septal defects had closed spontaneously by 12 months of age, 60% by 2 years of age, and 90% by 6 years of age. The ratio of the left atrium diameter over the aortic diameter was larger for multiple defects than for a solitary defect. The timing of spontaneous closure was later for multiple defects than for a solitary defect. During more than 1 year of tracking, four cases of Swiss-cheese-type apical muscular ventricular septal defect did not close spontaneously [21].

Frequency, spontaneous closure rate, timing of spontaneous closure: comparison among defect positions

In all references, the frequency of midventricular muscular ventricular septal defect was high: midventricular

57%, apical 30%, anterior 11%, and inlet (posterior) 2%. Except for inlet type, which showed high frequency among Caucasians, no difference was found in the frequency of other positions of muscular ventricular septal defect between Caucasians and Asians. Midventricular muscular ventricular septal defect readily closes spontaneously earlier than apical and anterior muscular ventricular septal defect. Meberg et al. [33] explained the tendency as attributable to the weaker mechanical tension of contraction at the apex. Ramaciotti et al. [12] reported that no difference of defect site was found in relation to the ease of spontaneous closure. Ono et al. [6] and Erol et al. [39] also reported no difference between midventricular and apical muscular ventricular septal defect regarding the ease of spontaneous closure. Cresti et al. [24] showed that spontaneous closure rate in muscular ventricular septal defect was higher in central type than in apical or marginal type at the timing of 2 years of age, but no difference was found among all types at 6 years of age (Table 4).

Spontaneous closure of muscular ventricular septal defect diagnosed using fetal echocardiography (Table 5) [39–48]

Palandini et al. [40] reported extreme difficulty of diagnosing fetal small muscular ventricular septal defect because no difference was found in pressure between right and left ventricles. Perimembranous ventricular septal defects closed easily in the uterus, but only 16.7% of muscular ventricular septal defects closed spontaneously in the uterus. Half of ventricular septal defects of less than 3 mm closed spontaneously in the uterus, which was regarded as the factor of spontaneous closure. Erol et al. [39] reported that 6.8% of ventricular septal defect diagnosed in the fetal period closed spontaneously in the uterus and that only midventricular spontaneously closed in the uterus. Jin et al. [43] reported the frequency of fetal isolated ventricular septal defect as 0.8%, but only two of them (muscular ventricular septal defect 1, perimembranous 1) closed spontaneously in the uterus. All ventricular septal defects of less than 3 mm had closed spontaneously by 3 years of age and 79.5% of those of 3 mm or more. Of them, 42% had muscular ventricular septal defects; also, 54.2% of them had closed spontaneously by 12 months of age and 90.4% by 3 years of age. Li et al. [46] reported that as the factors of spontaneous closure in fetuses with ventricular septal defect, birth weight, and defect diameter were major predictors; they also reported that muscular ventricular septal defect closed spontaneously more easier than perimembranous ventricular septal defect. By contrast, Cho et al. [47] reported the frequency of fetal ventricular septal defect as 1.25%. Intrauterine spontaneous closure occurred in 43.8%. Compared with after birth,

Table 4 Incidence of muscular ventricular septal defect: comparison of defect position

Author, year	Country	Newborn infants	Gestational age	Patients with m-VSD, *n* (%)	Anterior	Midventricular	Apical	Inlet (posterior)	Muscular multiple	Diagnosis
Ono et al. 1990 [6]	Japan	1179	Term	15 (1.3)	5	7	2	0	1	Color Doppler screening
Hiraishi et al. 1992 [7]	Japan	–	Term	39	8	20	11	0	0	Color Doppler screening: 53.8%
Du et al. 1996 [13]	Israel	159	Preterm	9 (5.7)	0	4	3	1	1	Color Doppler screening
Du et al. 1998 [14]	Israel	7696	Preterm 11.3%	97 (1.2)	14	42	21	5	15	Color Doppler screening
Kinoshita et al. 2004 [19]	Japan	4473	Unknown	27 (0.6)	0	16	11	0	0	Auscultation
Chang et al. 2011 [21]	Taiwan	2891	Term	72 (2.5)	5[a]	37[a]	24[a]	0	2[b]	Color Doppler screening
Cresti et al. 2018 [24]	Italy	31,185	Unknown	283 (1.0)	24	164	81	4	10	Color Doppler: 32.6%
Total				542	56	290	153	10		

m-VSD muscular ventricular septal defect. [a]Numbers of patients followed up, [b]2 of 37 patients with midventricular m-VSD

Table 5 Incidence of muscular ventricular septal defect diagnosed by fetal echocardiography and spontaneous closure

Author, year	Country	Total number of fetal echoes	Gestational age at diagnosis (wk)	Fetal isolated VSD	Fetus (m-VSD/p-VSD)	Trabecular m-VSD	Apical m-VSD	Intrauterine spontaneous closure rate in follow-up case, *n*/*N* (%)
Paladini et al. 2000 [40]	Italy	3452	24.8 (17–39)	68[a]	5/23[b]	ND	ND	m-VSD, 1/5 (20.0) p-VSD, 12/23 (52.2)
Axt-Fliedner et al. 2006 [41]	Germany	30,650	23.4 (13–39)	146	131/15	116 (outlet 12, inlet 3)	ND	m-VSD, 29/98 (29.6) p-VSD, 5/10 (50.0)
Bahtiyar et al. 2008 [42]	USA	2410	23.5 ± 4.3 (20–34)	16	16/0	Muscular 10, midmuscular 5	1	m-VSD, 2/16 (12.5)
Jin et al. 2012 [43]	China	14,993	29.3 (24–40)	125	52/14	ND	ND	m-VSD, 1/52 (1.9) p-VSD, 1/14 (7.1)
Erol et al. 2014 [39]	Turkey	23,500	23.1 (19–37)	264	76	63	13	m-VSD, 3/45 (6.7) Trabecular, 3/32 (9.4) Apical, 0/13 (0)
Gómez et al. 2014 [44]	Spain	10,800	Median 30.4 (range 17–41)	248	216/32	Mid muscular 150	66	m-VSD, 4/185 (2.2) p-VSD, 9/26 (34.6)
Yu et al. 2015 [45]	China	ND	26.4 ± 2.9 (23–37)	234	27/152	ND	ND	m-VSD, 9/27 (33.3) p-VSD, 40/152 (26.3)
Li et al. 2016 [46]	China	5855	26.7 ± 1.1 (19–30)	257	20/115	ND	ND	m-VSD, 9/20 (45.0) p-VSD, 30/115 (26.1)
Cho et al. 2017 [47]	South Korea	18,188	22.2 ± 1.5 (24–42)	146	85/61	64	0	m-VSD, 31/85 (36.5) p-VSD, 33/61 (54.1)
Chau et al. 2018 [48]	USA	4090	20.8 ± 4.4 (median 19.1)	153	126/15	ND	ND	m-VSD, 105/126 (83.3) p-VSD,13/15 (86.7)

The values of gestational age at diagnosis are expressed as mean (range) or mean ± SD (range). *m-VSD* muscular ventricular septal defect, *ND* not described, *p-VSD* perimembranous ventricular septal defect, *VSD* ventricular septal defect. [a]Numbers including fetuses with chromosomal abnormalities, [b]numbers of fetuses without chromosomal abnormalities

the frequency was high. Factors of spontaneous closure in the uterus were perimembranous ventricular septal defect of less than 2 mm in defect and mother's age of less than 35 years. Of fetal ventricular septal defect, 84% closed spontaneously in utero by 26.9 ± 4.5 weeks. Isolated ventricular septal defects closed easily, although ventricular septal defects in fetuses with other malformations or abnormal karyotype did not close. Patients for whom they had not spontaneously closed had other malformations or abnormal karyotypes [48]. All ventricular septal defects of less than 2 mm in the uterus closed spontaneously after birth. The frequencies of spontaneous closure in the uterus varied widely among reports. Which is easier to close spontaneously: perimembranous or muscular ventricular septal defect? That must be judged from future studies of numerous fetuses with ventricular septal defects.

Mechanism of spontaneous closure of muscular ventricular septal defect

Simmons et al. [49] reported five cases with a muscular ventricular septal defect among 1605 autopsy cases. Defect in the center of ventricular septum was closed with a plug of dense fibrous tissue. Sections made through the depression revealed funnel-shaped defect of the muscle in the ventricular septum. The funnel apex was closed by a plug of dense fibrous tissue. Spontaneous closure of muscular ventricular septal defect by fibrous patch [50], ingrowth of fibrous tissue [51], and aposition of myocardium [49] was also found in autopsy. Suzuki [52] observed six adults with a spontaneously closed muscular ventricular septal defect in 600 consecutive autopsies. He suggests that the usual course is muscular encroachment and superimposed primary fibrosis. Nir et al. [53] reported an autopsy case of spontaneous closure of muscular ventricular septal defect of a neonate with double-outlet right ventricle who died 5 hours after birth. Fibrosis, which closed the ventricular septal defect, was mainly found at the right ventricular side. Evidence from pathology [52] and echocardiographic reports [6, 7] indicated that closure occurs from the right ventricular side of the defect. Hiraishi et al. [7] observed spontaneous closure using color Doppler echocardiography and found some defects suggesting that most trabecular septal defects observed in the neonatal period result from incomplete trabecular coalescence of interventricular channels. Cardiac multidetector computed tomography administered to 2725 consecutive patients showed pouches or sacs in the interventricular septum location in 18 patients (0.6%) likely to be spontaneous closure of muscular ventricular septal defect [54].

Specific covering of muscular ventricular septal defect

As seen in membranous ventricular septum [55] or muscular infundibular ventricular septal defect [56], echocardiography showed spontaneous closure attributable to aneurysmal fibrous tissue in inlet or midtrabecular muscular ventricular septal defect [57, 58]. Roldan et al. [59] reported a patient with both atrial and ventricular septal aneurysm and opened muscular ventricular septal defect. Cardiac magnetic resonance imaging showed a spontaneously closed small mid-muscular ventricular septal defect covered by hypertrophied trabeculations on the right ventricular side [60]. Khositseth et al. [61] reported a large apical muscular ventricular septal defect (Swiss-cheese type) with restrictive flow by anomalous muscle bundle, which separated the right ventricle sinus into two parts.

Risk of infective endocarditis of muscular ventricular septal defect

The only risk of ventricular septal defect with small shunt is infective endocarditis [62, 63]. In the Second Natural History Study, its frequency was found to be 14.5 per 10,000 person-years [64]. Reportedly, the defect size was unrelated to the risk of infective endocarditis. The risk before closure is more than twice that after the surgical operation [64]. In 1.8% of adult patients with a ventricular septal defect, infectious endocarditis occurred. All four patients had a perimembranous ventricular septal defect with associated bicuspid aortic valves in one and mitral prolapse with regurgitation in another [63]. Twenty-one patients, all with subvalvular defects, had bacterial endocarditis [62].

Follow-up of muscular ventricular septal defect

No clear consensus exists about the value of follow-up for small muscular ventricular septal defect [66]. In the survey regarding the follow-up of hemodynamically non-significant muscular ventricular septal defect in the United Kingdom, if growth is good and no pulmonary hypertension occurs, 67% of pediatric cardiologists follow-up every 3 years, and 15% every year [67].

Genetics of muscular ventricular septal defect and counseling

In recent years, amniocentesis has been performed for chromosome examination when a heart disorder is found from fetal echocardiography. Using chromosome microarray analysis, Svirsky et al. [68] investigated 30 cases of isolated muscular ventricular septal defect diagnosed as fetal echocardiography and reported that muscular ventricular septal defect was not a significant risk factor for chromosomal abnormalities and that it has a favorable clinical outcome. He described that delayed closure of the ventricular septum is a normal variant. In some normal cases, the closure is not limited solely to the fourth and fifth post-conception weeks. This event is not a malformation. Lin et al. [17] stated that muscular ventricular septal defect might result from delayed physiologic development rather than from disease. Newman [69] reported that ventricular septal defects often occur as random errors in development at a frequency that is determined largely by the complexity of normal cardiac morphogenesis. This hypothesis has two major implications: many ventricular septal defects are not preventable and parents need not feel responsible for ventricular septal defects in their children. To

avoid unnecessary anxiety, parents should be informed of this benign muscular ventricular septal defect whether it is identified by echocardiography intentionally or accidentally [11]. However, a rare report describes a study of autosomal dominant familial muscular ventricular septal defect [70].

Environmental factors to muscular ventricular septal defect

Sands et al. [16] reported seasonal variation of birth date in patients with a ventricular septal defect. Summer birth confers some protection from ventricular septal defect. This result implies that it can be advantageous to conceive in September and November because cardiac septation would then occur during autumn or early winter. Sands et al. [16] quoted a report by Clark [71]: "It has been suggested that muscular ventricular septal defects arise from cell death within an already formed ventricular septum, while perimembranous defects may be the result of failed fusion secondary to transient interruption of the blood supply to the developing septum." Botto et al. [72] indicated the relation between maternal fever and ventricular septal defect. By contrast, Oster et al. [73] did not find that relation. Shi et al. [74] showed maternal fever of the first trimester as a risk factor of congenital heart disease through a meta-analysis. They inferred that it was a risk factor of ventricular septal defect and right obstructive defect. The mechanism of spontaneous closure between muscular and perimembranous ventricular septal defect differs. Therefore, further investigation is needed in future studies.

Conclusions

Color Doppler echocardiography greatly facilitates the diagnosis of isolated muscular ventricular septal defect with a small shunt. The frequency of infants with ventricular septal defect, who were suspected of heart disorder by cardiac murmur and SpO_2 for a newborn period and who were diagnosed using color Doppler echocardiography in all infants, was 0.3–1.35%. The frequency of ventricular septal defect revealed by screening using color Doppler echocardiography for all live infants: 1.8–4.6% in term infants and 5.6% in preterm infants. The frequency of isolated muscular ventricular septal defect is 1.1–5.3% in term infants and 5.7% in preterm infants. Infants with a muscular ventricular septal defect frequently have no heart murmur. Spontaneous closure in muscular ventricular septal defect occurs with higher frequency and earlier than in perimembranous ventricular septal defect. Approximately 80–90% of isolated muscular ventricular septal defect closes spontaneously by 12 months of age. The timing of spontaneous closure was later for multiple defects than for a solitary defect. The frequency of midventricular muscular ventricular septal defect was high: midventricular 57%, apical 30%, anterior 11%, and inlet (posterior) 2%. Midventricular muscular ventricular septal defect is spontaneously closed earlier in the short term, but no site difference is found in the long term. The frequencies of spontaneous closure in the uterus varied widely among reports. Regarding spontaneous closure of isolated muscular ventricular septal defect diagnosed for the fetus, further studies are needed. The spontaneous closure mechanism is regarded as aposition of the muscle tissue or fibrous tissue formation in the right ventricular side, but in rare cases involves aneurysm formation of the fibrous tissue. Chromosomal microarray analysis of fetuses with isolated muscular ventricular septal defect has revealed that it is not a severe risk factor of chromosomal abnormalities.

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Compliance with ethical standards

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