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Spontaneous resolution of atrial and ventricular septal defects in Malta

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ABSTRACT: Congenital heart disease (CHD) is the commonest congenital malformation, and ventricular septal defect (VSD) and atrial septal defect (ASD) are the commonest forms of CHD. This study was undertaken to determine rates of spontaneous closure of lesions diagnosed at echocardiography after detection of a murmur in Maltese patients born in 1990-94. A significant excess of ASD and VSD was found in Malta, and this was attributed to early echocardiographic diagnosis of small defects, prior to spontaneous closure. A high spontaneous closure rate was found for both ASD and VSD. Rate of closure for both defects was initially high, and tapered off at about 5 to 7 years of age for both lesions. ASDs in excess of 8 mm in diameter at presentation also underwent spontaneous resolution, which is contrary to the known natural history of these defects. Larger VSDs were shown to have a smaller likelihood of closing (p=0.04). Parents and patients can be reassured that spontaneous closure is very likely to occur in the vast majority of these conditions.

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Introduction

Congenital heart disease (CHD) is a label for a heterogeneous group of lesions which comprise the most frequent group of congenital malformations, and are found in 8.8/1000 livebirths[1]. The most common CHD lesions are ventricular septal defect (VSD) and atrial septal defect (ASD), which comprise approximately 30% and 15% of CHD respectively. Both of these lesions cause left to right shunting with cardiac volume overload, and may therefore require closure by open heart surgery or interventional catheterisation. However, the majority of these lesions are relatively small and asymptomatic, and may resolve spontaneously, even if initially associated with heart failure.

Since termination of pregnancy is not available in Malta, the prevalence of CHD at birth is a true reflection of the natural live-birth prevalence of infants with CHD. The true incidence of CHD can only be determined if all livebirths, fetal deaths, and spontaneous and induced abortions are examined, which was not the case in this study. For this reason, the term 'birth prevalence', rather than the 'incidence' of CHD, will be used in this study.

Echocardiography, which has been widely available in Malta since 1988[2], is a very sensitive tool, capable of detecting very minor lesions down to 1 mm in diameter. Indeed, the reported birth prevalence of CHD has increased in all reported studies since the introduction of echocardiography[3].

The aim of this study was to identify all patients with ASD and VSD born in 1990-1994 and diagnosed by 1 year of age, and who had not required surgery, in order to determine rates of spontaneous closure.

Methods

Patients

All diagnosed cases of CHD in Malta are registered in the Maltese Paediatric Cardiology Database, which was the data source for this study. Primary database sources include children being followed up at Children's Outpatients for CHD with or without other problems, copies of all paediatric echocardiogram reports, lists of locally performed elective cardiac catheters and operations, lists of patients sent abroad for urgent cardiac intervention not available in Malta, clinic registers of patients seen at visiting consultant paediatric cardiologist clinics (held 3-4 times a year), and post-mortem reports[2].

All cases of ASD and VSD born in 1990-94 were identified from this database. All of the patients had been initially diagnosed by echocardiography after detection of a murmur. In some patients, spontaneous resolution of the defects had already been documented in the database after resolution of physical signs had prompted a repeat echocardiogram. The remaining patients without echocardiographic follow-up were recalled in January 1997 and a clinical examination along with a full echocardiographic examination consisting of a 2-dimensional scan using standard views, colour Doppler, pulse-wave Doppler and continuous-wave Doppler, were carried out.

Definitions

Atrial septal defect

ASD was defined as a defect in the fossa ovalis allowing blood to flow between the atria. It is not

Table 1 - Birth prevalence of atrial septal defect in Malta compared with earlier studies

Reference	4	7	All ASD in Malta	Operated ASD in Malta
Years studied	1980	1979-88	1990-94	1990-94
N	67	76	64	11
n/1000 live births	0.73	0.37	2.45	0.42
95% CI	(0.57-0.93)	(0.30-0.47)	(1.90-3.15)	(0.22-0.78)

All ASD in Malta vs. references 4 and 7 p<0.0001
Operated ASD in Malta vs. references 4 and 7 p=ns

possible to predict with certainty which defects diagnosed in the neonatal period or in early infancy will close, or become very small so as to be called a patent foramen ovale, or will remain large enough to be called an atrial septal defect. Furthermore, there is no accepted cut-off between the two types of defects. All defects at this site were therefore included.

Estimation of right heart volume overload, which is a consequence of a haemodynamically significant atrial septal defect, is a subjective measurement, as it is usually very difficult to measure right ventricular cavity size since the anterior free wall of this ventricle lies in contact with the anterior chest wall. 'Eyeball' estimation of right heart volume overload is therefore generally undertaken, and this was deemed too subjective for use in this study.

Atrioventricular septal defects, sinus venosus defects and unroofed coronary sinus defects were excluded. Spontaneous closure was defined as intact atrial septum on 2-dimensional echocardiography with absence of atrial trans-septal flow on Doppler colour-flow mapping and right heart volume overload.

Ventricular septal defect

VSD was defined as a defect in the interventricular septum allowing blood to flow between the ventricles. Atrioventricular septal defects were excluded. Spontaneous closure was defined as intact ventricular septum on 2-dimensional echocardiography with absence of ventricular trans-septal flow on Doppler colour-flow mapping.

Congenital heart disease

It is the established custom in epidemiological studies dealing with CHD to only include cases diagnosed by 1 year of age[4], and this condition was applied. 'Operated' cases of ASD and VSD were defined as those that had previously undergone surgery, or are planned to undergo surgery in the near future. The rest were classified as 'unoperated' defects.

Only cases with a primary diagnosis of ASD or VSD were included in this study. In the Maltese Paediatric Cardiology Database, patients with multiple CHD diagnoses have their individual lesions classified hierarchically. The primary diagnosis is considered that lesion which first necessitates surgical/catheter intervention. In cases where no intervention is necessary, the primary diagnosis is considered to be the lesion which produces the greatest haemodynamic disturbance. In cases where both unoperated ASD and VSD were present, VSD was considered to be the primary diagnosis and the ASD was excluded from further study.

Equipment

All studies were carried out on a Toshiba Sonolayer SSH 65A between January 1990 and April 1996, and with a Hewlett-Packard Sonos 2500 between May 1996 and January 1997, by one of the authors.

Population and statistics

There were 26,117 live births in 1990-1994, with an annual mean of 5223 live births[5]. The data was analysed with Microsoft Excel, SPSS, and Statcalc (EpiInfo), and charted with Statistica on a personal computer. Kruskall-Wallis 1-way analysis of variance was used to test for association between initial defect size and age at spontaneous closure of defects. (χ^2 was used to compare rates of lesions in Malta with those reported in other countries. (χ^2 for trend was used to analyse changes in proportions within this study. 95% confidence intervals for proportions were calculated using the binomial distribution[6]. A p value ≤ 0.05 was taken to represent a statistically significant result.

Results

Atrial septal defect

Sixty four cases of ASD were diagnosed in this period. Fifty three were unoperated, and of these, 3 were lost to follow-up. The birth prevalence of all ASD in Malta overall was significantly higher ($p<0.0001$) than that reported in earlier studies with similar methodologies [4,7], but the birth prevalence of operated ASD in Malta was similar to that reported in these studies (Table 1).

Unoperated atrial septal defect

Three cases were associated with narrow complex tachycardia. The maximum initial recorded ASD diameters for lesions closing and not closing spontaneously ranged from 2-12 mm. No relationship was found between initial size of defect and timing of spontaneous closure (Table 2). Age at echo-recorded closure ranged from 2 months to 7 years (Figure 1). There was no residual right heart volume overload at echocardiography even in those ASDs which had not completely closed. The number of defects not closing was too small to allow comparison between initial size and likelihood of closing.

Ventricular septal defect

One hundred and three cases of ventricular septal defect were diagnosed in this period. Eighty one were unoperated. VSD has been found in excess in Malta when compared with earlier studies ($p<0.0001$), and this excess was due to an excess of minor defects[1].

Unoperated ventricular septal defect

Nine cases were associated with a small ASD (≤ 3 mm diameter) and 1 case was associated with very mild pulmonary stenosis (gradient 20 mmHg). Age at echo-recorded closure ranged from 1.9 months to 7 years (Figure 1). No relationship was found between initial

size of defect and timing of spontaneous closure (Table 3). Larger defects had a significantly lesser chance of undergoing spontaneous closure (χ^2 for trend 4.1, p=0.04 - Table 4).

Discussion

Atrial septal defect

The first report of spontaneous closure of a small ASD documented by cardiac catheterisation was in 1966[8]. In the following year, spontaneous closure of defects which had been large and symptomatic was also reported[9]. Diagnosis after 1 year of age was linked to a lesser likelihood of closure and this was unrelated to the initial size at diagnosis[10]. Echocardiography confirmed that large defects causing right heart volume overload can close spontaneously[11]. Different processes of closure were demonstrated, including a valve mechanism at the fossa ovalis[12] and by aneurysm formation of the adjoining septum[13].

Table 4: Ventricular septal defect - initial defect size and likelihood of spontaneous resolution

Initial VSD Size (mm)	Closed spontaneously	Not closed spontaneously
1	16	5
2	31	11
≥3	8	10

χ^2 for trend 4.1, p=0.04

A prospective, echocardiographic study in 1993 on a series of infants diagnosed as having ASD by 3 months of age showed that the strongest predictive factor for closure was initial size at diagnosis. It was reported that ASDs with diameters ≥ 8 mm uniformly failed to close[14]. However, this finding was not borne out in the present study as some defects with sizes at diagnosis in excess of 8 mm underwent spontaneous closure. Our findings suggest a larger cut-off size for lesions which may eventually close spontaneously.

Ventricular septal defect

The clinical diagnosis of a spontaneously closed VSD was first reported in 1918, earlier than ASD as the clinical signs are more obvious, and sudden cessation of a loud murmur is a dramatic finding[15]. Subsequently, closure of VSD was documented by catheter studies[16]. Catheterisation later also showed that defects which were large enough to cause heart failure could also become smaller and even close, thereby avoiding surgery[17]. It also became evident that VSDs could close after infancy, including at school age[18]. Studies dealing with the epidemiology of CHD have shown that approximately 30% of routinely detected VSDs close spontaneously[19].

Table 2 - Atrial septal defect - initial defect size and age at spontaneous resolution

Diameter (mm)	Number closed Spontaneously	Total number of unoperated lesions	Age at documented closure Mean rank (months)
2	2	4	41.50
3	11	22	21.36
4	10	11	22.35
5	6	6	19.42
6	8	9	24.38
7	6	6	23.08
8-12	3	6	29.83
Total	46	64	χ^2=5.2; p=0.5 (6 df)

Kruskall-Wallis 1-way analysis of variance

The advent of echocardiography in the 1970s, a reliable and non-invasive diagnostic technique, facilitated the diagnosis of small defects. This resulted in an apparent doubling in birth prevalence of these defects. However, echocardiography also showed that the rate of spontaneous closure of all minor defects, including those diagnosed in excess due to echocardiography, was higher[3].

Anatomic studies have shown that perimembranous defects tend to be closed by accessory tissue from the adjacent tricuspid valve[20]. Perimembranous defects located in the outlet portion of the ventricular septum may occasionally be closed by prolapse of the right coronary cusp of the aortic valve, producing aortic incompetence[21]. The exact mechanism of closure of muscular defects is uncertain as direct inspection of an intact muscular interventricular septum which formerly contained a VSD does not yield any clues.

Echocardiography screening of asymptomatic neonates soon after birth has shown an even higher birth prevalence of muscular VSD of 200-530/1000 live births[22,23]. These additional defects are not only asymptomatic, but clinically undetectable. The spontaneous closure rate found in these studies of approximately 75% was also higher than that reported for spontaneous closure of routinely detected defects[22,23]. This study demonstrates a high birth prevalence of ASD and VSD due to the diagnosis of minor defects which would otherwise have gone undetected and resolved spontaneously.

The present study was not prospective. However, patients were systematically reviewed in the Children's Outpatients, and echocardiography was routinely

Table 3 - Ventricular septal defect - initial defect size and age at spontaneous resolution

Diameter (mm)	Number closed Spontaneously	Total number of unoperated lesions	Age at documented closure Mean rank (months)
1	15	20	27.33
2	31	42	28.03
3-5	8	19	25.75
Total	55	81	χ^2=0.1; p=0.9 (2 df)

Kruskall-Wallis 1-way analysis of variance

requested, particularly after cessation of physical signs. This allows age at spontaneous closure to be defined within a reasonably narrow span of time.

A prospective study regarding the natural history of ASD and VSD is currently being undertaken by the authors. This study will include structured follow up at echocardiography with standardised measurements of chamber sizes and flow until intervention/spontaneous resolution.

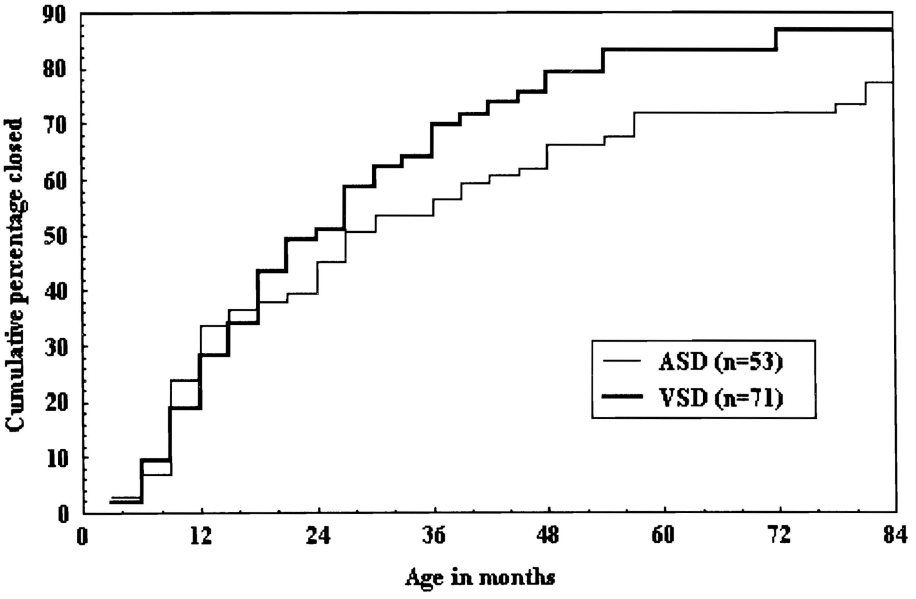
Conclusions

Many ASDs diagnosed by 1 year of age are a variant of the norm and have a very high closure rate. The child's parents should be reassured and given follow-up appointments for repeat echocardiography in order to document closure. In the event of non-closure or partial closure with significant residual right heart volume overload, surgery/interventional catheterisation can be undertaken electively. Small VSDs may also be considered to be a variant of the norm, and follow-up appointments for repeat echocardiography should be given in order to document closure. Until this happens, antibiotic prophylaxis is mandatory[24]. The local detection rate of these defects is high due to easy access to echocardiography.

Moderate VSDs should also be treated conservatively, as even these may actually become smaller or even close spontaneously.

Unfortunately, a diagnosis of a 'hole in the heart', irrespective of the size, always generates severe parental anxiety. Parents therefore should be reassured by the high rate of spontaneous resolution.

Fig. 1 - Cumulative number of closing atrial and ventricular septal defects with time



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