Spontaneous resolution of atrial and ventricular septal defects in Malta
Victor Grech,* Mark Bailey,* Victor Mercieca**

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. 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, 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.

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 catheterisations 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.

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

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

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

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. The data was analysed using 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. (χ²) was used to compare rates of lesions in Malta with those reported in other countries. (χ² for trend) was used to analyse changes in proportions within this study. 95% confidence intervals for proportions were calculated using the binomial distribution. 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. 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 diameter 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 echocardiography was found to be related to age 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

VSD was defined as a defect in the interventricular septum allowing blood to flow between the ventricles. All 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 to be the lesion which produces the greatest haemodynamic disturbance.
size of defect and timing of spontaneous closure (Table 3). Larger defects had a significantly lesser chance of undergoing spontaneous closure ($\chi^2$ 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 2 - Atrial septal defect - initial defect size and age at spontaneous resolution

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>Number closed spontaneously</th>
<th>Total number of unoperated lesions</th>
<th>Age at documented closure Mean rank (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>2</td>
<td>4</td>
<td>41.50</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>22</td>
<td>21.36</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>11</td>
<td>22.35</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>6</td>
<td>19.42</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>9</td>
<td>24.38</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>6</td>
<td>23.08</td>
</tr>
<tr>
<td>8-12</td>
<td>3</td>
<td>6</td>
<td>29.83</td>
</tr>
</tbody>
</table>

Total 46 64 $\chi^2=5.2$; $p=0.5$ (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 performed.

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

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>Number closed Spontaneously</th>
<th>Total number of unoperated lesions</th>
<th>Age at documented closure Mean rank (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15</td>
<td>20</td>
<td>27.33</td>
</tr>
<tr>
<td>2</td>
<td>31</td>
<td>42</td>
<td>28.03</td>
</tr>
<tr>
<td>3-5</td>
<td>8</td>
<td>19</td>
<td>25.75</td>
</tr>
</tbody>
</table>

Total 55 81 $\chi^2=0.1$; $p=0.9$ (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. 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.

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