

# Transcatheter device closure of atrial septal defect and patent foramen ovale in Malta

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## Key words

Cerebrovascular accident/etiology, ischemic attack, transient/etiology, heart septal defects, atrial, heart, catheterization, prostheses and implants, treatment outcome

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## Abstract

Significant atrial septal defects (ASD) are closed, surgically or through a transcatheter device, in order to avoid pulmonary hypertension in late life. A patent foramen ovale (PFO) may need to be closed because of transient shunt reversal resulting in transient ischaemic events or stroke. We report the Maltese experience to date in transcatheter closure of these defects. A total of 46 ASDs and 51 PFOs have been successfully closed at our unit (total 97), with very low complication rates, rates that compare very favourably with results from larger international centres.

## Introduction

### Atrial septal defects

Atrial septal defects (ASDs) account for 10% of all congenital heart disease and are defined as congenital structural deficiencies of the atrial septum.<sup>1</sup> The most common site of the structural deficiency is in the *ostium secundum (fossa ovalis)*. The haemodynamic and pathological consequences of an ASD are dependent on the magnitude and duration of the left to right shunt, and on the resulting response of the pulmonary vascular bed. Large shunts cause right atrial and right ventricular enlargement and the excessive flow into the pulmonary vascular bed may eventually result in fibrotic and vascular occlusive disease with irreversible pulmonary arterial hypertension; this usually occurs in adult life, with increased morbidity and early mortality.<sup>2</sup> Lesions causing significant shunts (defined as a pulmonary to systemic blood flow ratio (Qp/Qs) of > 1.5) are therefore closed in early childhood or whenever a diagnosis is made in later years.

### Patent foramen ovale

*In utero*, the *foramen ovale* serves as a physiologic passage for right-to-left shunting. After birth, increased left atrial flow and pressure result in functional closure of the foramen, and this is usually followed by anatomical closure. However, a probe-patent *foramen ovale* has been shown to persist in up to 25-35% of adults in autopsy series.<sup>3</sup> This can be confirmed *in vivo* by contrast echocardiography, wherein a persistently patent *foramen ovale* (PFO) can be detected in 5-20% of adults.<sup>4</sup> A PFO is usually flap-like potential opening between the atrial septum *primum* and *secundum* in the *fossa ovalis* and not an actual gap in the interatrial septum (Figure 1).

Several studies have confirmed an association between the presence of a PFO and the risk for paradoxical embolism which can result in transient ischaemic episodes (TIA), stroke or peripheral embolisation.<sup>5,6</sup> A retrospective multicenter study demonstrated an annual risk of 1.2% to sustain a recurrent TIA, and of 3.4% to suffer a recurrent stroke or TIA despite medical treatment with oral anticoagulants or antiplatelet drugs in patients with PFO and cryptogenic stroke.<sup>6-8</sup>

PFO and ASD closure has been performed in Malta since 1998, comprising a local team, a visiting cardiologist, and an anaesthetist, with surgical backup.

This paper details the protocol that is followed in patient selection, and subsequent intervention and follow-up for both ASD and PFO. We also outline our results and complications to date.

## Methods

### Protocol

The protocol followed is shown in Figure 2. Patients presenting to the Neurology Department with TIA or stroke are assessed, particularly for risk factors predisposing to cerebrovascular disease. Such factors include increasing age, a history of diabetes mellitus, hypertension, hyperlipidaemia, atherosclerotic disease (including ischaemic heart disease and peripheral vascular disease), valvular heart disease and a history of smoking, alcohol, or use of the oral contraceptive pill.

An ECG is performed to establish whether there is hypertrophy or arrhythmias. Routine blood tests include random blood glucose and a lipid profile. Carotid artery imaging is performed with Doppler ultrasonography or magnetic resonance angiography to exclude carotid artery stenosis. In cases of cryptogenic stroke or TIA, particularly in young patients (< 50 years) with none of the above risk factors identified, further investigations are performed and these include the exclusion of thrombophilic conditions including deficiency of protein C and S, antithrombin III, serum fibrinogen, anti-cardiolipin antibodies, serum homocysteine, genetics for Factor V Leiden deficiency, 660210A mutation in the Coagulation Factor II Gene and MTHFR Genotype C677T mutation.

Echocardiographic assessment is also done as shown in Figure 2. The finding of a PFO where none of the other obvious risk factors are present is considered to be a potential contributor to cerebral ischaemic episodes, and patients are referred for closure.

The methodology followed locally for device closure has already been outlined in a previous paper.<sup>9</sup>

### Patients

All patients who had interventional closure of ASD or PFO were obtained from the Maltese Paediatric Cardiology Database,<sup>10</sup> and from a database maintained by the radiography section at the St. Luke's Catheterization Suite for the period 2002-2007.

**Table 1:** Age by lesion (ASD/PFO) and gender

Age	ASD			PFO		
	All	Female	Male	All	Female	Male
Mean	23	26	15	46	47	46
CL (95%)	5.4	6.9	7.3	4.2	8.1	4.9
Median	14	20	9	49	49	46
SD	18	19	12	15	17	13
Min	4	4	6	7	7	17
Max	66	66	43	71	71	69
n	46	33	13	51	20	31

### Statistics

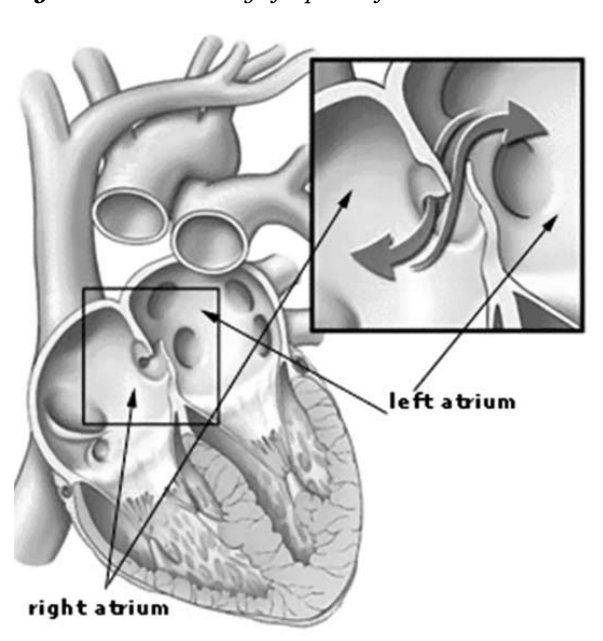
Statistical analysis was performed by Excel (summary statistics and 2-tailed t-tests). A *p* value of less than 0.05 was taken to represent a statistically significant result.

### Results

A total of 46 ASDs and 51 PFOs have been successfully closed at our unit (total 97). A breakdown of lesion by age and gender is given in Table 1. There were no significant differences by age and gender for PFO but the male ASD population was significantly younger than the female ASD population (2-tailed  $t=2.0$ ,  $p=0.013$ ). The PFO population was significantly older than the ASD population (2-tailed  $t=1.9$ ,  $p<0.01$ ).

Five were closed with Helex (Gore, Flagstaff, Arizona) devices and all of the remainder were closed with Amplatzer ASO (atrial septal occluder) devices (AGA, Plymouth, Minnesota).

**Figure 1:** The anatomy of a patent foramen ovale



There were some unusual cases in the series which included the following:

1. Two patients who had ASD closure with Amplatzer devices for residual cyanosis after neonatal treatment for critical pulmonary stenosis.<sup>11</sup>
2. One patient who had two septal defects and in whom closure involved the implantation of two separate Amplatzer devices in the same session.
3. There were two patients with recurrence of neurological events after PFO closure. One of these (who had a Helex device) had a residual shunt documented by echocardiography and had closure of this residual shunt using a Amplatzer cribriform device. No shunt could be documented in the other case and therefore no action was taken.

Complications were few and included:

1. Amplatzer device detachment from the delivery wire while still within the delivery sheath. This was caused by a faulty loader. The sheath and device were removed and the same device was delivered through the same delivery system but using a new loading system.
2. Amplatzer device fully deployed in left atrium in two patients – this was recognized and the device was therefore pulled back into the sheath and redeployed correctly.
3. Amplatzer device everted itself within the sheath – the device was therefore removed and reloaded correctly into the sheath.

4. Four patients with transient atrial fibrillation after PFO closure (3 with Amplatzer devices and 1 with a Helex device) who settled down with medical treatment (cardioversion and/or amiodarone therapy for up to a total duration of 4 months).

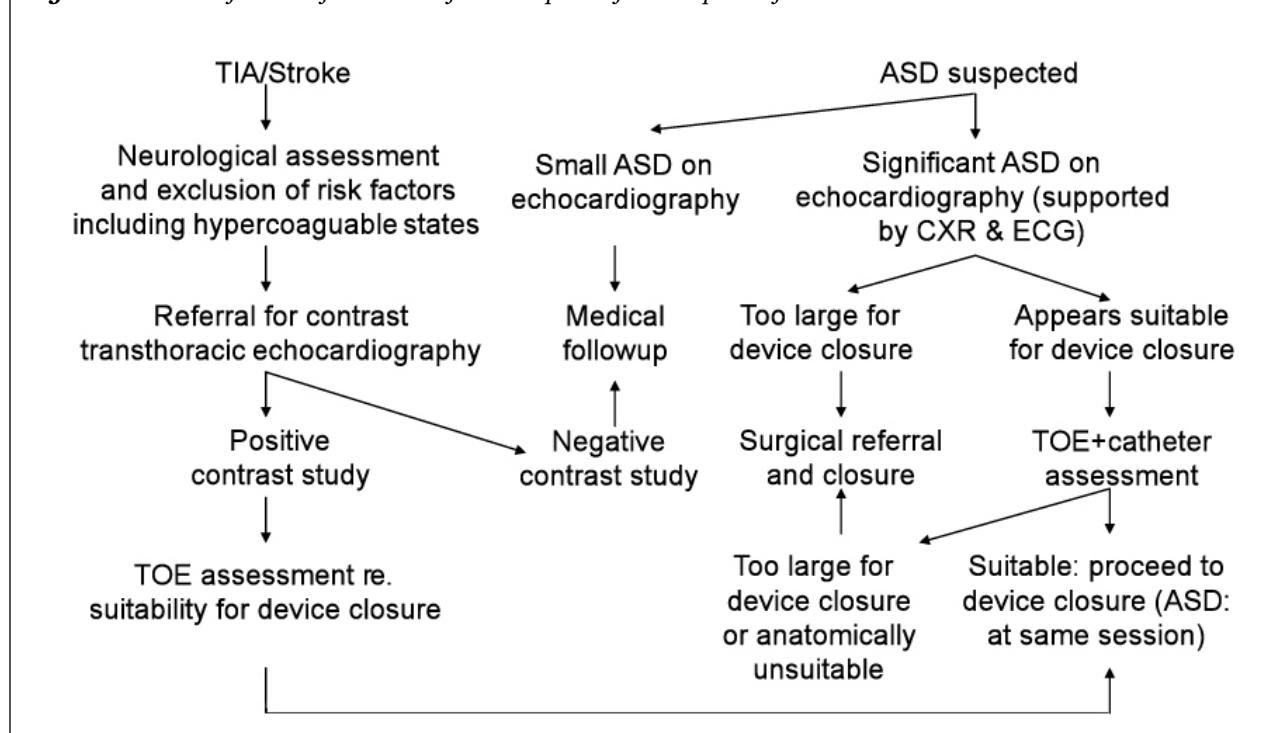
In no patients was an emergency surgical procedure required e.g. for device embolisation or cardiac damage/perforation. There were no pericardial effusions associated with device placement. There was no mortality associated with device placement.

## Discussion

Traditionally, including locally, ASDs, were surgically closed using cardiopulmonary bypass via a right atriotomy.<sup>12</sup> Smaller defects are sutured closed while larger ones are patched with pericardium or synthetic material, with a current mortality of <1%.<sup>12</sup> A wide variety of devices for transcatheter closure of ASDs have been developed in the past two decades and these allow over 80% of ASDs to be closed without open heart surgery, using the same indications as outlined above.<sup>13</sup>

The diagnosis of a PFO is made by contrast echocardiography (e.g. with injection of air agitated saline via the left arm), performing and then releasing a prolonged Valsalva maneuver. A PFO will be revealed by the subsequent transient reversal of the interatrial pressure gradient with contrast crossing from right to left atrium.<sup>14</sup> Ischaemic stroke via paradoxical embolism in the setting of a PFO was first described in 1877,<sup>15</sup> and should be suspected in the absence of a left-sided thromboembolic

**Figure 2:** Protocol followed for closure of atrial septal defect and patent foramen ovale



TOE: transoesophageal echocardiogram

source, the potential for right-to-left shunting or the detection of thrombus in the venous system or right atrium.<sup>16</sup> Transcatheter closure of PFO is also possible by a variety of devices as outlined above for ASD.

We are unable to explain why male ASDs have been closed at a younger age than female ASDs. We can only hypothesise that males may have presented at an earlier age, although this was not supported in a literature search. Indeed, in a previous local publication, no significant gender difference had been shown.<sup>12</sup> ASDs are naturally closed at a younger age than PFO as the latter manifest much later in life with an acute neurological presentation.

Our complication rates have been previously published,<sup>17</sup> and are very low, comparing favourably with larger centres.<sup>18,19</sup>

ASD and PFO closure continue to be successfully undertaken at St. Luke's Hospital to the benefit of the patients and with minimal risk. The advantages of local device placement are that patients benefit by not having to travel to a tertiary centre abroad, with attendant inconvenience, travelling and accommodation costs.

This experience demonstrates the progression of developments in that new techniques and interventions are continually being developed and sooner or later become accepted by the international medical community. Such techniques are then taught to the local medical community by visiting consultants.

Performing the procedure locally adds to the interventional experience of local operators and this familiarity, in turn, further benefits the spectrum of procedures carried out in Malta. For instance, through this experience, we also carry out closure of patent arterial duct and ventricular septal defects.

This is one of the many areas of health care provided in Malta wherein the local service is kept abreast of developments in the international medical community.

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