Atrial septal defects in the adult: Management, transcatheter and surgical therapeutic options and outcomes

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ABSTRACT

Patients with simple congenital heart disease such as isolated atrial septal defects (ASDs) are rapidly becoming a relatively large population with a variety of clinical problems that are often missed by pediatric physicians or grown up congenital heart disease specialists, and may involve different adult health professionals such as general cardiologists or internists. Isolated ASDs are common (7% of all cardiac anomalies) and can present at any age, sometimes in conjunction with other genetic disorders such as Down’s syndrome or in a familiar form. The diagnosis is often accidental: Doppler echocardiography and, recently, magnetic resonance imaging are mandatory to assess types and significance of ASDs. Surgical or percutaneous repair should be offered at any age unless associated with pulmonary vascular disease: Percutaneous closure should be preferred in isolated secundum ASD with sufficient rims on trans-esophageal echocardiography, whereas surgery remains the only option for primum and sinus defects. Follow-up of operated patients is based on Holter EKG and echocardiography that should be scheduled every 2 years for secundum and sinus defects and every year for primum defect with valve repair. ASDs in adolescents and adults may be suspected in any physician’s office and doctors should be acquainted with innovative imaging techniques and contemporary therapeutic options in order to deliver proper care to different types of ASDs and assist them after repair with appropriate follow-up strategies.

Key words: Atrial septal defect, catheter-based closure, congenital heart disease, echocardiography

INTRODUCTION

Isolated atrial septal defects (ASD) represent 7% of all cardiac anomalies and can present at any age.[1] Adolescents and adults with simple congenital heart disease such as isolated ASDs are more likely to reach adult age without being diagnosed. There are three major types of interatrial communications: Ostium secundum, ostium primum and sinus venosus defects. Secundum ASD is by far the most common type, occurring in 1/1500 live births, with 65-75% involving females.[2] Adult ASD patients are rapidly becoming a relatively large population with a variety of clinical problems that often go unnoticed by pediatric physicians or grown-up congenital heart disease specialists and may involve different adult health professionals, such as general cardiologists or internists. Both general cardiovascular professionals as well as non-cardiovascular professionals should know the basic concepts underlying proper diagnosis and management of adults with ASDs.

Genetic counseling

Primum defects or atrioventricular septal defects are associated with Down’s syndrome in 40% of cases, and less frequently with Di George syndrome and Ellis-Van Creveld syndrome. ASDs of different types are the most common cardiac abnormalities associated with the Holt-Oram syndrome. Secundum ASD can occur in a familial form, which has been related to GATA4 and NKX2.5 mutations and has a 3% recurrence risk rate in first-degree relatives.[3,4]
Pathophysiology
The ostium secundum ASD is a true defect of the atrial septum that involves the fossa ovalis region, whereas the other two types are defects of the endocardial cushions (ostium primum, Figure 1) or of the junction of the right atrium and the superior/inferior vena cava (sinus venosus Figure 2). Secundum ASDs and, more frequently, sinus venosus defects can be associated with partial anomalous pulmonary venous return.[9] The magnitude of and the direction of flow through an ASD depend on the size of the defect and the relative diastolic filling properties of the left and right ventricles. Conditions that reduce left ventricle compliance and mitral stenosis increase the left-to-right shunt, whereas conditions that reduce right ventricle compliance reduce the left-to-right shunt or cause a right-to-left shunt. A left-to-right shunt is significant when the Qp/Qs ratio is >1.5:1 or when the right chambers are dilated. A significant Qp/Qs ratio is associated with adverse long-term outcomes. Many patients with secundum ASD are free of overt symptoms, although most will become symptomatic at some point in their lives. Often, secundum ASD patients have a mitral valve prolapse. Exercise intolerance is the most common presentation along with atrial fibrillation or flutter due to the atrial dilation and stretching. This usually occurs around 40 years of age.[8] In older patients, decompensate right heart failure may develop and is often associated with pulmonary hypertension caused by excessive pulmonary flow over a long period of time.[9] Significant ASDs cause increased morbidity and mortality if untreated.

Non-invasive diagnosis
Diagnosing a secundum ASD is more often than not incidental because the defect normally causes symptoms late in adult life. Echocardiography and magnetic resonance imaging have completely replaced catheterization in adults with ASD [Table 1].

Typical findings in patients with ASD may include a prominent right ventricular impulse along the left sternal border, a systolic ejection murmur audible along the left upper sternal border caused by the increased flow across the right ventricle outflow tract and a split second heart sound. A diastolic murmur may be heard due to relative tricuspid stenosis. If pulmonary hypertension has developed, the split second heart sound is replaced by a narrowly split S2 with accentuated P2: The patient is usually cyanotic.[3]

A typical EKG shows an axis between 0 and +120 degrees and an RSR’ is often present in V1, especially in significant defects. A radiogram may show enlargement of the right chambers in the lateral view and pulmonary artery dilation: Even significant ASD often has a normal cardiac silhouette and normal pulmonary vascularity.

Echocardiography records the size of the defect, can differentiate (with the transthoracic technique when a good acoustic window is present, otherwise with the transesophageal technique) between secundum, primum and sinus venosus defects and identifies the direction and magnitude of the shunt. The right chambers can be properly estimated by transthoracic echocardiography together with any abnormal paradoxical septal motion that suggests a right chamber volume overload, whereas the pulmonary artery pressure can be calculated from the Doppler velocity of pulmonary or tricuspid regurgitation.[5,7,8] Pulmonary venous return can be evaluated by transthoracic echo and, in difficult cases, should be evaluated by the transesophageal technique. Transthoracic three-dimensional echocardiography enables the ASD location, ASD size and surrounding tissue of the atrial septum to be determined accurately and might replace transesophageal echocardiography (TEE) in patient selection for surgical or transcatheter closure.[9]

Magnetic resonance imaging can give us almost the same information as echocardiography as regards right chambers

Table 1: Indications and available information obtained from different imaging techniques

<table>
<thead>
<tr>
<th>Technique</th>
<th>Indication</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT/TE</td>
<td>Diagnosis of ASD</td>
<td>Type of ASD: Secundum, primum, sinus defect</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>Differential diagnosis</td>
<td>Measurements of ASD</td>
</tr>
<tr>
<td></td>
<td>Evaluation of anatomy</td>
<td>Evaluation of ASD rims</td>
</tr>
<tr>
<td>3-D echocardiography</td>
<td>Difficult ASD sizing/morphology</td>
<td>Visualization of Chiari network, Eustachian</td>
</tr>
<tr>
<td>Computed tomography</td>
<td>Diagnosis of ASD + anomalous venous return</td>
<td>valve, embryonal remnants of early septation</td>
</tr>
<tr>
<td></td>
<td>Coronary angiography in mild age patients with</td>
<td>Evaluation of previous ASD repair</td>
</tr>
<tr>
<td></td>
<td>ASD</td>
<td>Evaluation of rims and ASD size in difficult cases</td>
</tr>
<tr>
<td>Magnetic resonance imaging</td>
<td>Diagnosis of ASD Association with other CHDs</td>
<td>Visualization of anomalous venous return</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Visualization of coronary arteries before any</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ASD interventions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Type of ASD: Secundum, primum, sinus defect</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Measurements of ASD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Evaluation of ASD rims</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Association with venous return</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Evaluation of associated CHDs</td>
</tr>
</tbody>
</table>

ASD: Atrial septal defect, CHD: Congenital heart disease, TT: Transthoracic, TE: Transesophageal
size, defect size, shunt ratio and any associated pulmonary venous return.[10,11]

**Therapeutic options**

Survival rates especially favor patients closed before 25 years of age compared with medically managed patients (85% versus 74% at 10 years), but improved quality of life can also be expected for patients closed over the age of 40 years.[12]

Thus, surgical suture or catheter-based closure is indicated in patients with significant ASD (enlarged right heart chambers) irrespective of age.[13] Catheter-based closure is preferable in patients with secundum ASD and suitable anatomy (Figure 3). Favorable anatomy includes at least 5 mm rims of tissue on TEE, no associated cardiac anomalies such as partial anomalous pulmonary venous drainage and defect size <36-38 mm.[13]

Unfavorable clinical settings for device-based closure include patients with primum ASD or sinus venosus defect, patients with advanced pulmonary hypertension in whom the ASD may be needed to maintain an acceptable quality of life, patients with severe left ventricle dysfunction in whom the ASD works as a pop-off valve, secundum ASD associated with embryonic remnants of atrial septation, whether fenestrated or not, in which device closure may be problematic or impossible or in which more than two devices are required to seal the defect and secundum ASD with diameter over 36 mm in which a very large device would have to be implanted due to the risk of late erosions or thrombosis. Patients with such features should be referred for surgical closure, which, for secundum ASD, usually includes nearly always direct suture and, less frequently, pericardial patch or synthetic patch closure, whereas for primum ASD treatment includes patch closure and repair of the cleft valve. Lastly, a sinus defect requires baffles of the venous return.[14,15]

For the most frequent defect, the secundum ASD, percutaneous closure minimizes hospital stay and recovery time, avoids surgical wounds and offers the same benefits as surgery. Successful closure can be obtained in >95% of patients, although small residual shunts that are not hemodynamically significant may be observed in the immediate post-closure echocardiographic study but will usually close within 1 year of the procedure.[16]

Different latest generation devices, mainly made with Nitinol and synthetic tissue, may be used nowadays in order to close secundum ASD including the most widely used Amplatzer septal Occluder (AGA Medical Corp., Plymouth, MN, USA), Gore Septal Occluder Device (W.L. Gore and Associates, Flagstaff, AZ, USA), the Occlutech-
Figulla, (Occlutech GmbH, Jena, Germany) (USA) and others. There are no trials comparing the performance of each device but in general the choice depends on operator experience and preference and on the size of the defect.

Transcatheter closure of ostium secundum ASD has been performed for years using deep sedation or orotracheal intubation, TEE and the sizing balloon technique for size measuring the “stop-flow” diameter of the defect. The procedure includes passing a large compliant balloon inflated with contrast medium across the defect and the computation, via an electronic caliper of the echo or radiological equipment, of the balloon diameter when cessation of left-to-right shunt by color Doppler echocardiography occurs. In most laboratories, intracardiac echocardiography (ICE) is replacing TEE therefore avoiding general anesthesia and related morbidity and increasing patient comfort. The electronic devices with color Doppler capability (Siemens, Philips and St Jude) and the mechanical device (Boston Scientific) with 360° scan can measure the fossa ovalis or the ASD surrounding rims in order to select the proper device size. In particular, the measurement of the aortic rim and of the entire atrial septum length is of paramount importance due to the risk of device impingement on the aortic wall when the aortic rim is too short or the device is oversized.[17] Two orthogonal views are selected to measure the diameters of the fossa ovalis or of the ASD due to the elliptical shape of some defects. ICE has been shown to be equivalent to TEE in resolution and precision.[18] However, ICE has been suggested as the optimal imaging technique to size the defect and for monitoring the device implantation procedure, especially in cases with difficult anatomy.[19,20]

Surgery versus device closure: A brief comparison

Although there are no randomized controlled trials of secundum ASD closure that compare surgical with catheter-based closure, most recent series have demonstrated that percutaneous device-based closure is as safe and effective as surgical closure and decrease the morbidity and mortality of the surgical approach [Tables 2 and 3][12,21-28]. Unfortunately, the series are very different for patient’s age, operative techniques (robotic or standard open chest) and mean follow-up. This heterogeneity makes any comparison insensitive. Nevertheless, the data retrieved from the recent literature suggest that surgery and percutaneous repair are at least similar in success and closure rates. Percutaneous closure is preferable for the less invasiveness, hospital stay duration and immediate complication rate.

Moreover, the recent advancements in mini-invasive surgical techniques for repair of secundum ASD, such

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Pt. sample</th>
<th>Technique</th>
<th>Success rate (%)</th>
<th>Complication rate (%)</th>
<th>Closure rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attie[12] 2002 232 Standard median thoracotomy</td>
<td>100</td>
<td>0</td>
<td>100%</td>
<td>Not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doll[22] 2003 177 Right mini-thoracotomy Standard median sternotomy</td>
<td>100</td>
<td>2.25</td>
<td>98.3%</td>
<td>Not reported</td>
<td></td>
<td></td>
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<tr>
<td>Casselman[23] 2005 74 Endoscopic + TEE Standard median sternotomy</td>
<td>100</td>
<td>14.8</td>
<td>95.9%</td>
<td>Not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liang[24] 2006 53 Right mini-thoracotomy No cardiopulmonary bypass</td>
<td>100</td>
<td>0</td>
<td>98.2%</td>
<td>Not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suchon[25] 2009 52 Standard median thoracotomy</td>
<td>100</td>
<td>19.2</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kutty[26] 2012 207 Standard median thoracotomy</td>
<td>100</td>
<td>2</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costa[27] 2013 105 Standard median thoracotomy</td>
<td>100</td>
<td>68</td>
<td>96%</td>
<td>Not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketowicz[28] 2013 383 Standard median thoracotomy</td>
<td>100</td>
<td>Not reported</td>
<td>Not reported</td>
<td>5.3%</td>
<td></td>
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</tr>
</tbody>
</table>

TEE: Transesophageal echocardiography

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Pt. no</th>
<th>Device</th>
<th>Imaging guidance</th>
<th>Success rate (%)</th>
<th>Complication rate (%)</th>
<th>Follow-up closure rate</th>
<th>Cost analysis (mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim[21] 2002 48 Amplatzer</td>
<td>TEE</td>
<td>100</td>
<td>10.4</td>
<td>95.8% at 12 months</td>
<td>11,541$</td>
<td></td>
<td></td>
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<tr>
<td>Fischer[29] 2003 200 Amplatzer</td>
<td>TEE</td>
<td>100</td>
<td>1</td>
<td>94% at 27 months</td>
<td>Not reported</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Butera[30] 2004 274 Cardioseal/Starflex/Amplatzer</td>
<td>TEE</td>
<td>100</td>
<td>3.6</td>
<td>94% at 24 months</td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang[31] 2004 197 Amplatzer</td>
<td>TEE</td>
<td>97</td>
<td>1.5</td>
<td>96% at 24 months</td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zanchetta[32] 2004 135 Amplatzer</td>
<td>ICE</td>
<td>100</td>
<td>0</td>
<td>98% at 36 months</td>
<td>Not reported</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Masura[33] 2005 151 Amplatzer</td>
<td>TEE</td>
<td>100</td>
<td>0</td>
<td>99.4% at 24 months</td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vidal[34] 2006 83 Amplatzer</td>
<td>TEE</td>
<td>86.7</td>
<td>0</td>
<td>97.2% at 12 months</td>
<td>4,521$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rigatelli[35] 2011 102 Amplatzer</td>
<td>ICE</td>
<td>100</td>
<td>0</td>
<td>95.6% at 10 years</td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aytemir[36] 2012 58 Occlutech-Figulla</td>
<td>TEE</td>
<td>100</td>
<td>2.1</td>
<td>96.5% at 15 months</td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gromann[37] 2014 45 Gore Septal occluder</td>
<td>TEE</td>
<td>100</td>
<td>0</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saritas[38] 2014 185 Cardi-O-Fix septal occluder</td>
<td>—</td>
<td>96</td>
<td>&lt;2</td>
<td>Not reported</td>
<td>4,100$</td>
<td></td>
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</tbody>
</table>

*Children and adults, ICE: Intracardiac echocardiography, TEE: Transesophageal echocardiography
as mini-thoracotomy or endoscopic techniques, make a matched comparison virtually impossible. However, it is likely that such techniques compare more favorably with percutaneous closure due to less invasiveness and reduced hospital stay.

Costs analysis has been performed only by few authors,[21,34] demonstrating a difference in costs of percutaneous devices between developed and developing countries that do not allow clear economic recommendations.

Arrhythmias such as atrial fibrillation, atrial flutter and sick sinus syndrome are very uncommon among patients who undergo ASD closure (either surgical or percutaneous) during early adulthood, but older patients remain at risk for such arrhythmias, although they tend to decrease in the long-term follow-up.[39,40] Functional capacity in patients with ASD improved more widely and faster than that reported in the surgical series: A 15% improvement in peak oxygen uptake at 6 months has been reported after percutaneous closure regardless of defect size and patient’s age.[41] Improved left ventricular filling and systemic output have been reported after percutaneous closure.[42] Effects on cardiac remodeling also seem faster; reduced right cardiac chambers are apparent within 24 h of closure, and the process appears to continue after 1 year, especially for the right ventricle.[43]

Even in the elderly population, closure has been associated with reversibility as in the young (<50 years) patients.[44]

**Unsolved issues**

The degree of acceptable pulmonary hypertension, the need for concomitant atrial antiarrhythmia surgery and the likelihood of symptomatic response, which depends on age at closure, are yet to be resolved. The optimal strategy for patients with secundum ASD >38 mm still needs to be assessed, although an international registry of transcatheter closure has reported acceptable results.[45] Moreover, although catheter-based closure is the first-line treatment for isolated secundum ASD, some practical issues remain unresolved.

Metal allergy is one such problem. Currently available devices are made of different materials. The Amplatzer is mainly made of nitinol, whereas GSO and others are made of tissue patch and a small amount of nitinol. Nitinol, a nickel-titanium alloy, is a valuable material in the construction of interventional endoluminal devices because of its biocompatibility, super elasticity, high resiliency and shape memory. The possibility of nickel toxicity has been raised with devices constructed of Nitinol. There is no increase in the concentration of nickel in the blood of patients who have received Amplatzer nitinol devices, suggesting that nickel-titanium is an inert, corrosion-resistant alloy.[46] Nevertheless, nickel seems to be released from the device, causing a systemic rise in serum levels of nickel, possibly until a calcium phosphate layer has formed on the passive oxide film of the device or until endothelialization is complete. Possible biological effects should be considered, particularly in young patients or patients with nickel hypersensitivity. Nickel intolerance or allergy is an issue to be considered in patients to be implanted. However, it is unlikely that skin allergy to nickel will be associated with allergy to an implantable device.

**Post-operative management and follow-up**

In the past, repair of primum defect was associated with a 5% risk of complete heart block, but nowadays this percentage has been considerably reduced by a better knowledge of the atroventricular node.[47] Atrioventricular valve insufficiency and subvalvular aortic stenosis are still possible late consequences of primum ASD repair. Superior vena cava obstruction has been reported after repair of anomalous right pulmonary vein and sinus venous defect. Some complications have been reported with surgical closure of secundum ASD and include pericardial effusion, scar-induced supraventricular arrhythmias and stroke; the risk is very low but is still present. Complications, although rare, may also occur during and after device closure of secundum ASD in less than 1% of patients.[47] Perioperative complications, such as vascular complications, include groin hematomas, bleeding and arteriovenous fistula, but are very rare. Pericardial effusion or tamponade may occur when attempting to cross the ASD or maneuvering the large size sheath during device deployment, in particular in young subjects with small atrial chambers. Rupture of the atrial septum during balloon sizing maneuver has been reported in the past, but seems to have been overcome by new sizing techniques under ICE guidance. Embolization of the device is a rare but potentially life-threatening complication that occurs in less than 1% of cases. To avoid this complication, appropriate sizing is essential and, of course, use of echo guidance to deploy the device.

Following interventional closure of ASDs with Amplatzer Septal occluders, an increased level of cTn-I has been described, which indicates some transient, reversible myocardial membrane instability due to the device or silent coronary embolism during the implantation procedure itself.[48] Careful detection and elimination of air bubbles during the preparation of the device, especially the Amplatzer Occluder, and the loading within the long sheath are mandatory to avoid paradoxical coronary embolisms. Anomalous coronary artery such as anomalous origin of the circumflex coronary artery from the right coronary sinus has been known to cause myocardial ischemia,
especially when the anomalous artery is located between the aortic root and the ASD closing device.

On long-term follow-up, erosions or frame fracture have been described for many devices. Amplatzer ASD Occluder-associated erosions uniquely involve the anterosuperior atrial walls and adjacent aorta. Pathophysiology remains poorly understood. Some of the erosions have presented late after closure. Twenty-five percent may present weeks later (longest, 3 years). Poor posterior rim consistency, aortic rim absense (in multiple views) and absent aortic rim at 0 degree in 100% of the patients and septal mal-alignment and dynamic ASD were present in nearly 50% of the cases. Other complications such as mitral valve dysfunction and obstruction to systemic and pulmonary venous pathways appear to be rare.

Several series have reported different percentages of thrombus formation after ASD device closure. The largest series revealed thrombus formation in 15 of the 593 (2.5%) ASD and patent foramen ovale patients. The thrombus was diagnosed in 14 of 20 patients after 4 weeks and in six of 20 patients later on. The incidence was different for different devices: 7.1% for the CardioSEAL device (NMT Medical, Boston, MA, USA), 5.7% for the StarFLEX device (NMT Medical, USA), 6.6% for the PFO-Star device (Applied Biometrics Inc., Burnsville, MN, USA), 3.6% for the ASDOS device (Dr. Ing, Osypka Corp., Grenzach-Wyhlen, Germany), 0.8% for the Helex device (W.L. Gore and Associates, USA) and 0% for the Amplatzer device (AGA Medical Corp., USA). The difference in thrombus formation between the Amplatzer device on the one hand and the CardioSEAL device, the StarFLEX device and the PFO-Star device on the other was significant. Post-procedure atrial fibrillation and persistent atrial septal aneurysm had been found as significant predictors for thrombus formation.

Follow-up of operated patients should include ASD clinical examination, Holter EKG and echocardiography every 12-18 months, together with bacterial endocarditis prophylaxis for primum, whereas for secundum and sinus defect, physical examination, Holter EKG and echocardiography should be scheduled every 2 years.

The correct follow-up of patients who received devices is more problematic as there is no consensus as to what defines appropriate follow-up after ASD closure. Most centers around the world follow the patients for at least 1 year after device implantation, and yearly thereafter: TEE was initially scheduled at 1 month and 1 year post-implantation; however, thanks to the wide experience gained with the device, we believe transthoracic echocardiography should be sufficient. Twenty-four-hour EKG monitoring at 1-6 months seems advisable to monitor the presence of asymptomatic atrial fibrillation or flutter. Long-term therapy after closure with antiplatelets is a debated issue. Aspirin alone or in combination with Clopidogrel or Aspirin plus Prasugrel have been used by different operators based on no particular scientific evidence. However, we believe that after 6 months, one can discontinue such medication if the closure is complete. Endocarditis prophylaxis is also given for a period of 6-months, after which if the defect is completely closed, one should not prescribe the antibiotics.

**Pregnancy, activities and insurance remarks**

Operated ASDs theoretically have no restrictions in any field of social and active life, including pregnancy and sport. Specifically, following the guidelines of grown-up congenital heart disease, patients with secundum or sinus ASD with no pulmonary vascular disease have no contraindications for pregnancy or restrictions regarding oral contraceptives. Moreover, they have no physical restrictions and are in class I for insurance companies if closed early. Patients with ostium primum or atrioventricular defects with no pulmonary vascular disease have no restrictions to physical activity and pregnancy if closure was uncomplicated, and they do not suffer from arrhythmias — They are in class II for insurance, if properly closed.

Because of the small risk of paradoxical embolus, arrhythmias or heart failure, a cardiological consultation is always necessary during pregnancy but the only contraindication is once again the presence of severe pulmonary arterial hypertension.

**Pulmonary arterial hypertension**

Pulmonary vascular disease may occur in up to 5-10% of patients with untreated ASDs, especially in females. In rare occasions, probably also due to recurrent embolic phenomena, high pulmonary resistance causes right-to-left shunting at the atrial level, leading to the Eisenmenger syndrome that occurs when the ASD in not restrictive and when there is rest cyanosis. Sudden death, heart failure and hemoptysis are the main cause of death in such patients. Surgery may include heart-pulmonary transplantation and pulmonary transplantation, but is of very limited importance due to high mortality and poor number of donators. Moreover, there are no studies about patients with previous ASD. Transcatheter-based techniques now include the use in elderly people with decompensated right ventricle and pulmonary hypertension and the use of an homemade fenestrated device that has been suggested to offer a good option in the challenging subset of patients. Although there is no trial in the pipeline for a new vasodilator in untreated ASD patients, latest generation
vasodilators such as bosentan and epoprostenol have been reported to effectively manage such patients.\textsuperscript{[60,61]} In particular, a timed closure after targeted medical therapy has been suggested to be effective.\textsuperscript{[62]}

**CONCLUSIONS**

Adults with isolated ASDs are more likely to reach adult age without being diagnosed. This diagnosis should be kept in mind in the presence of symptoms and signs of pulmonary overload. This review article shows that all the diagnostic and therapeutic advancements developed in the last 6 years have made the diagnosis and treatment simpler and faster even in most complex cases. Standard echocardiography is the first-line imaging modality to confirm suspicion of such defects. Three-dimensional echocardiography and magnetic resonance imaging are the most modern and more promising techniques in case of difficult diagnosis. Although the poor number of comparative studies and the lack of randomized trials comparing surgical with percutaneous closure in uncomplicated secundum ASD does not allow any clear recommendations in respect of complications and economic cost, some indications can be retrieved from the literature. Percutaneous device-based closure or conventional or mini-invasive surgery should be proposed on the basis of types of defects (secundum, primum or sinus defects). In case of secundum ASD, decision about surgery or device-based closure should be made on the basis of anatomical characteristics of the defect. At the moment, percutaneous closure seems to be the first choice in uncomplicated defects with sufficient rims, whereas mini-invasive surgery seems to be indicated in case of difficult anatomy, poor rims or defects larger than 40 mm.

Meticulous patients selection and judicious follow-up appear to be mandatory in order to deliver proper care to different types of ASDs and assist them after repair with modern follow-up strategies.

**REFERENCES**

Rigatelli, et al.: ASD management

48. 32nd Bethesda Conference. Care of Adult with Congenital Heart Disease October 2-3 2000.
53. 52nd Bethesda Conference. Care of Adult with Congenital Heart Disease October 2-3 2000.