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Percutaneous atrial septal defect closure: a consensus document of the joint group of experts from the Association of Cardiovascular Interventions and the Grown-Up Congenital Heart Disease Section of the Polish Cardiac Society

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Atrial septal defects (ASD) constitute the most common congenital heart disease lesion in adults. Although ASD closure is recommended in those with right heart enlargement or paradoxical embolism, data informing such indications in adults are quite often limited. This population has many unique issues and needs. Significant progress has been made in recent years in diagnostic modalities, which help proper diagnosis of these patients. However, decision process, especially in selected adult patients population [advanced age, various concomitant diseases, poor left ventricular function (both systolic and diastolic), pulmonary hypertension, concomitant arrhythmias or multiple defects or deficient rims] is still not easy. The data from literature focus predominantly on imaging endpoints and rather short than long-term morbidity and mortality. The evidence-base for outcomes with or without defect closure is scattered among various studies with different observation periods. Moreover, the clinical experience of individual physicians (cardiologists, imaging specialists, operators), but also between small and large experience centers in diagnosing and treating that subgroup of patients is inhomogeneous. In the view of the above facts the joint group of experts from the Association of Cardiovascular Interventions and the Grown-Up Congenital Heart Disease Section of the Polish Cardiac Society developed the following consensus opinion in order to standardize the principles of diagnosis, indications for treatment, methods of performing procedures, and postoperative care in Polish reality.

I. Background information on ASDs

Atrial septal defects is one of the most prevalent congenital heart defects and may frequently remained undiagnosed until adulthood [1-4]. ASD are consequence of various embryological disorders that cause inter-atrial communication. Five types of different anatomic defects are known:
a). *secundum ASD* - 80% to even more than 90% of ASDs in adult population - located in the fossa ovalis region and its surrounding.

b). *primum ASD* - 10% - 15% ASDs; also known as partial atrioventricular septal defect or partial atrioventricular canal - located near the crux of heart, nearly always associated with a cleft in the anterior mitral valve leaflet.

c). *superior sinus venous defect* – up to 5% defects – located near the superior vena cava (SVC) entry and often associated with abnormal connection of right upper pulmonary vein to SVC or right atrium.

d). *inferior sinus venosus defect* – less than 1% defects – located in the inferior portion of the atrial septum, leading to an overriding of inferior vena cava (IVC), often associated with anomalous connection of the right lower pulmonary vein to the IVC.

e). *unroofed coronary sinus defect or coronary sinus septal defect* – less than 1% defects – partially or completely missing roof of coronary sinus with lack of separation from the left atrium - often associated with a persistent left superior vena cava that drains into the coronary sinus.

ASD may from to time to time be diagnosed also together with other congenital cardiac abnormalities like anomalous pulmonary veins drainage, persistent left superior vena cava, pulmonary valve stenosis or mitral valve prolapse. In some of these circumstances, such as in patients with Ebstein anomaly and pulmonary stenosis, the pathophysiology related to the ASD is much more complex, and closure of the defect could cause clinical deterioration [4-6]. Therefore these recommendations address only isolated ASD and not associated with complex cardiac defects.

The shunt volume through ASD depends on defect size, right and left ventricular compliance, and left and right atrial pressures. A simple ASD causes left to right shunt (significant when defect size is relevant – usually more than 10mm) secondary to the higher
compliance of right than left ventricle, and results in right ventricular volume overload and an increased pulmonary flow. This increase results in late right heart failure with diminished functional capacity and fatigue. Atrial enlargement, which develops with time, results in frequent atrial arrhythmias (atrial fibrillation and atrial flutter) and higher risk of thromboembolic complications [6-8]. A clinically significant ASD may lead to late pulmonary hypertension, atrial septal defects, like patent foramen ovale (PFO), may also permit paradoxical embolism resulting in stroke or transient ischemic attack.

Reduction in left ventricular compliance or any conditions (significant ischemic heart disease or hypertension, cardiomyopathies, valve diseases), which are associated with elevation of left atrial pressure, increase left to right shunt. Reduced right ventricular compliance (pulmonary arterial hypertension, right ventricular outflow obstruction (RVOT obstruction), pulmonary arteries stenosis or other right ventricular diseases) or tricuspid valve stenosis and/or regurgitation may decrease left to right shunt or in some cases cause shunt reversal which results in cyanosis.

II. Prevalence and genetics

Although ASDs usually being sporadic, some are inherited as autosomal dominant syndromes and heart lesions could be associated with other congenital defects like as in Holt-Oram syndrome in which pre-axial limb defects are caused by mutations in the TBX5 gene on chromosome 12q24.1. Family forms of ASD with progressive atrio-ventricular blocks may suggest mutations or haploinsufficiency of the Nkx2.5 gene on chromosome 5, while familial ASD without conduction abnormalities may be associated with GATA4 mutations. Also defects in genes responsible for the formation of the atrial septum (e.g., MYH6, TBX20) can
lead to defects of intra-atrial septum. Teratogenes exposure during pregnancy is another potential cause of ASD as observed in fetal alcohol syndrome [9-12].

III. Natural history, clinical presentation and management of un-operated patients

Patients with ASD usually remain asymptomatic until adulthood. Majority of them may develop symptoms beyond the fourth or fifth decade including: shortness of breath, poorer exercise tolerance (dyspnea and fatigue) and supraventricular arrhythmias (atrial fibrillation, atrial flutter, atrial tachycardia or sick sinus syndrome). Sometimes we observe also paradoxical emboli, heart failure or right ventricular failure, and pulmonary vascular disease (5% to 9% of patients).

Studies describing un-operated large ASD patients (before 1980) revealed that nearly 25% of these patients died before 27th year and 90% by their 60th. Life expectancy is still reduced if closure is performed after age 25 years, but survival is much better than previously assumed. Pulmonary artery pressure (PAP) can be normal, but usually increases with age. Severe increase of resistant pulmonary hypertension (PH) is rare (less than 5%) and its development relates to additional multifactorial factors similar to idiopathic PH [13]. After fifth decade the severity of PH and tachyarrhythmias are more common. Symptoms vary widely with age at presentation and shunt volume, what means that symptoms alone cannot guide therapy [1].

The physical examination can reveal systolic silent murmur, a fixed split second heart sound, or a diastolic flow rumble across the tricuspid valve, but the cardiac ultrasonography has enabled early diagnosis. Low mortality rate after surgical repair led to rapid increase of ASD closure procedures over the past 2 decades, but the availability of percutaneous closure procedures facilitated the decision to proceed with intervention
especially in children [13]. Currently only few patients remain treated conservatively without percutaneous or surgical repair due to severe vascular disease leading to irreversible PH and Eisenmenger syndrome.

In patients with atrial fibrillation and/or after thromboembolic event the oral anticoagulation may be considered. There are no data supporting the use of calcium channel-blocking drugs for Eisenmenger syndrome patients. In these patients according to the ESC Guidelines three classes of drugs, targeted to the modification of endothelial dysfunction, have been recently approved for the treatment of PAH: endothelin receptor antagonists (ERAs), phosphodiesterase type-5 inhibitors and prostanoids,. Efficacy and safety of these drugs have been demonstrated in PH associated with congenital heart disease and in Eisenmenger syndrome. Treatment of Eisenmenger syndrome should include also very late complications associated with hyperviscosity symptoms, bleeding and thrombotic diathesis, thrombo-embolic events (paradoxical emboli), microcytosis, iron deficiency, arrhythmias (both supraventricular and ventricular), infectious complications (endocarditis, cerebral abscess, pneumonia) and many others [13].

IV. Non-invasive diagnostics

A). Echocardiography

Echocardiography is main imaging modality in diagnostic of the ASD. It is necessary for both qualification and monitoring of interventional procedures, as well as in follow-up observation with particular emphasis on peri- and postoperative complications [14-17]. Transthoracic echocardiography (TTE) enables not only the recognition of the defect, but also assessment of the hemodynamic significance of the shunt. Transesophageal echocardiography
(TEE) is required in terms of inconclusive TTE or during qualification for percutaneous interventions.

**Transthoracic echocardiography**

TTE is the preferred initial diagnostic modality for the detection and diagnosis of ASD. To evaluate properly the size and location of a communication multiple views should be used: different cuts of parasternal and apical but also subxiphoid views are very useful, also in adults with poor acoustic window. A detailed overview of the recommended projections is beyond the scope of this document, but should be consulted in the relevant guidelines [1].

Hemodynamically significant ASD causes dilatation of right ventricle (RV) with paradoxical intraventricular septum movement, right atrium (RA) and pulmonary trunk what can be assessed in TTE [14-16]. Apart from the right ventricular dimension, it is also important to assess its function.

Symptoms of RV overload are one of the indications for closure of the defect. Another parameter evaluated in the TTE is the approximate measurement of systolic or mean pulmonary artery pressure. In case of any doubt, right heart catheterization is required to verify the significance of pulmonary hypertension. TTE is usually efficient enough to determine not only the type of the ASD but also morphology of the septum and the presence of septum aneurysm defined as a redundancy of tissue with the excursion of 10 mm from the atrial septum plane into the RA or left atrium (LA) or 15 mm a combined right and left excursion. TTE should also include evaluation of mitral and tricuspid valve regurgitation as far as ASD may coexist with mitral valve prolapse and dilatation of tricuspid ring, what should be considered during qualification to percutaneous or surgical treatment. It is mandatory to exclude other congenital malformation e.g. ventricular septal defect or pulmonary stenosis.
Another essential issue is the left ventricle systolic and diastolic dysfunction. Closure of ASD may cause left ventricle (LV) overload and acute heart failure with pulmonary edema. It should be emphasized that false positive detection of ASD in TTE may occur as a result of misinterpretation for example of the inflow from inferior vena cava directed towards the atrial septum. Intravenous first-generation contrast infusion or TEE may be conclusive in such condition. Secundum ASD can be misdiagnosed in the presence of a coronary sinus defect - dilated coronary sinus drains to the right atrium and may imitate the lack of continuity of the septum. In this particular condition contrast injection but only through left ulnar vein may confirm diagnosis.

TTE image quality, especially in adult patients, will not always permit a correct and detailed evaluation of the shunt, however the right heart overload should prompt to a thorough search for the its causes, including TEE.

**Transesophageal echocardiography**

TEE examination is performed to confirm the diagnosis of the shunt, define its type and, in the case of ASD II, assess the possibility of performing a percutaneous closure. It is necessary to determine and verify the number, size and shape of defects and their spatial relation to the surrounding structures [14-17]. It is pivotal to evaluate rims, whereas the aortic rim is the only one not obligatory for percutaneous closure. All other rims should be at least 5 mm, although in addition to length, their quality is also important. 3D imaging is critically important for demonstration of the shape, size and spatial relations of especially multifenestrated defects. Further crucial issue is demonstration of drainage of the pulmonary veins to the left atrium and dimension of Eustachian Valve and Chiari network which, in the case of large size or excessive mobility may interfere with catheters. Such comprehensive assessment is possible in 2D imaging, however requires systematic analysis of projections
obtained at different esophagus depths and at different angles. Detailed description of TEE assessment during evaluation and ASD closure procedure (including 3D imaging) can be seen in Supplementary File.

B) Cardiac Magnetic Resonance (CMR)

Echocardiography still remains gold standard in every day routine diagnostic work-up in patients with suspected or otherwise confirmed ASD II. This is further supported by increasing developments in accuracy of the assessment, with wider introduction of real-life 3-dimensional echo. Nevertheless, CMR has recently become increasingly important in the diagnosis and evaluation of different congenital entities in adults, including ASD II [18,19].

In general, three different scenarios for CMR application can be distinguished. First, it can be applied when, for a number of reasons, the quality of echo examinations is not sufficient. In this regard, CMR can provide information in all aspects usually covered in echo including systemic and pulmonary blood flows, however with inferior ability to assess gradients and/or pressures (e.g. pulmonary artery pressure) or accompanying small, mobile tissue structures. Second, when borderline or conflicting results are obtained in echo, CMR can serve as a second-line method that helps to decide on further clinical steps, especially when it comes to volumes and ejection fraction issues. Third, CMR may be considered as a reference imaging modality in areas where it exceeds echo performance. Typically in the suspicion of left-to-right shunt, CMR is considered as ideal modality to delineate pulmonary venous connections, especially anomalous (e.g., innominate or vertical vein) [20,21]. Another area where CMR excels is RV volumes, mass and ejection fraction estimation (RV overload) which can be difficult to accurately assess by echo [22,23]. It is also worth noting that CMR due to lack of ionizing radiation is safe for serial examinations.
C) Cardiac computed tomography (CCT)

In the setting of ASD II CCT indications are similar to CMR [1,24]. CCT is usually more accessible than CMR and is not contraindicated after permanent pacemaker implantation. In terms of diagnostic abilities for adults with congenital heart disease or after surgery/repair due to superior spatial resolution it is best suited for extracardiac vascular anatomy assessment and less useful for ventricular volumes/function or valvular structure/function estimation (compared to echo and CMR). Its major drawback is potentially higher radiation dose, therefore limiting its use for serial applications [25]. When used for cardiac assessment, gating acquisitions with ECG is recommended. Additionally, in older patients (usually >40 years of age) with confirmed ASD type II and referred to either device or surgical closure and with concomitant risk for coronary artery disease, CCTA (coronary computed tomography angiography) might be performed instead of conventional angiography.

D) Exercise test

Adults with congenital heart disease, including ASD, are rather specific group prone to underestimate symptoms and underreport limitations. Moreover, considering life-long duration of disease they may never experienced what is “normal” function. Cardio-pulmonary exercise testing (CPET) with objective assessment of exercise capacity is believed to be useful in both decision-making in unrepaired ASD II and in follow-up after device or surgical closure [1,24]. Usually, in unrepaired ASD one can expect decreased exercise capacity that is demonstrated by maximum oxygen uptake reduction (peak VO$_2$ or VO$_2$ max), especially seen in older patients [26]. It is not well established if this decrease is correlated with hemodynamic parameters at rest (e.g., mean pulmonary arterial pressure, Qp:Qs).

Interestingly, but in agreement with specificity of the population, decreased capacity in CPET can be found in so-called “asymptomatic” patients. Additionally, other parameters that can be affected in baseline CPET are ventilator efficiency (increased VE/VCO$_2$ slope due to RV
dysfunction and/or pulmonary pressure elevation and/or lung disease) and ventilatory anaerobic threshold (decreased due to muscular deconditioning) [26]. Given the objective, reproducible and repeatable assessment and correlation with mortality and morbidity, CPET may play a role in the decision and timing of intervention and afterwards a part of serial follow-up checks after device or surgical closure.

When CPET is not available or patient cannot complete it for different reasons, simple 6-minute walking test can be applied instead, providing more limited data, however with prognostic value still better than relying on medical history alone [24].

**E) Pulse oximetry**

Pulse oximetry is a non-invasive, quick, simple, safe and painless test that measures oxygen saturation (SpO2). It does not require calibration and is able to provide instantaneous data that correlate well with blood gas measurements. Its use has recently been advocated by guidelines in context of screening for group of patients with ASD and accompanying pulmonary vasculopathy [24]. In this subset of patients despite left-to-right shunt present at rest (SpO2>90%) flow mediated dilatation of the pulmonary artery cannot increase appropriately and pulmonary arterial resistances go up during exercise resulting in shunt reversal and subsequent SpO2 drop (<90%). To that end, exercise pulse oximetry can eventually result (e.g. after confirming in CPET) in either the decision of not closing the defect or postponing it with prior preparation and administration of specific pharmacological agents (e.g. sildenafil or bosentan) known to reduce pressures and desaturation [26].

**V. Invasive diagnostics – heart catherization**

Right heart catheterization (RHC) is the "gold standard" in the diagnosis of pulmonary hypertension (PH) in patients with ASD, allowing for the correct qualification of patients for
defect closure. To determine detailed hemodynamics for decision-making or to clarify discrepant or inconclusive noninvasive imaging data diagnostic catheterization may be necessary – Figure 1. RHC is necessary to assess the severity of hemodynamic impairment and undertake vasoreactivity testing in selected patients [27].

Qualification to the RHC is based on the results of echocardiography. If peak tricuspid regurgitation velocity (TRV) exceeds 2.9 m/s (or right ventricular systolic pressure – RVSP exceeds 40 mmHg) PH occurrence is highly suspected [27]. RHC should be performed in the expert catheterization laboratory centers in accordance with current guidelines [27-29]. RHC is technically demanding procedure that requires attention to detail to obtain clinically useful information. A great importance has a proper patient hydration before the examination. The procedure is performed from a central vein puncture using a Swan-Ganz catheter terminated with a balloon, to measure the pulmonary capillary wedge pressure (PCWP). Direct measurements of the blood pressures in the right atrium, right ventricle, pulmonary artery, and in some cases also in the left atrium are also performed. Pulmonary hypertension is diagnosed if the mean pulmonary artery pressure (mPAP) is ≥25 mmHg (more than 20 mmHg according to the newest guidelines) and simultaneously pulmonary vascular resistance (PVR) ≥3 Wood’s units (WU) [30]. Determination of cardiac output and pulmonary and systemic flow is performed using the Fick method [27-29]. For this purpose, blood samples for oximetry should be taken from the superior and inferior vena cava (to calculate the oxygen saturation of mixed venous blood in the right atrium), then in the pulmonary artery. Systemic arterial blood oxygen saturation (in the aorta or peripheral artery) should be determined separately. Subsequently calculations using the standard formulas should be performed. Direct oxygen uptake test should be measured before RHC (direct Fick method). This technique is, however, not widely available. It is also possible to estimate oxygen consumption on the basis of the patient’s age, gender and body surface area according to the formula proposed by Bergsta, or
on the basis of body surface area (BSA); BSA × 125 mL/min or BSA × 110 mL/min in elderly patients [31]. Indirect Fick method, which uses estimated values of oxygen consumption, is acceptable (the 20% measurement error is possible) [29]. The minute cardiac output by the Fick method is calculated based on the following formula:

**Cardiac Output** = oxygen consumption (uptake) [ml/min] / arterial oxygen content - venous oxygen content/10 [ml/l]

where:

Arterial oxygen content = 1.36 * hemoglobin concentration [g/dl] * arterial oxygen saturation
Venous oxygen content= 1.36 * hemoglobin concentration [g/dl] * venous oxygen saturation

On this basis, pulmonary flow (Qp), systemic flow (Qs), as well as cardiac index (CI), and pulmonary and systemic vascular resistance values may be calculated. The Qp to Qs ratio exceeding 1.5 in the absence of concomitant, irreversible PH is the indication to closure of the defect.

VI. Classical indications for intervention - catheter/surgical

First surgical ASD repair was reported in 1948 [32], and over the next years, it developed into a procedure with minimal mortality and morbidity. Nowadays, the long-term results of surgical repair of ASD II are excellent, especially in young patients under 25 years of age [13]. Safe methods of minimally invasive surgery improved cosmetic results and shortened recovery [33]. The percutaneous transcatheter closure of ASD II was first published in 1974 [34], and it has become widespread after developing the Amplatzer septal occluder (ASO; AGA Medical), followed by other devices.

ASD closure is indicated in the presence of a substantial left-to-right shunt leading to a significant right heart enlargement due to volume overload [1,24]. The significance of
shunting could be also determined by $Q_p:Q_s$ ratio higher than 1.5, although this index is of secondary importance comparing to the signs of the above mentioned right ventricular remodeling. Such indication is supported by strongest evidence. Presence of pulmonary hypertension, as it has been mentioned before, requires more thorough workup. The right heart catheterization may be useful if the echocardiography is non-conclusive. As the pulmonary arterial hypertension (PAH) is potentially one of the consequences of a L→R shunt the indication for an interventional treatment is additionally constrained by the values of pulmonary artery pressure (PAP) / pulmonary vascular resistance (PVR). ASD closure should not be performed in patients with Eisenmenger physiology, patients with PAH and PVR > 5 WU despite targeted PAH treatment, or desaturation on exercise. New 2020 ESC recommendations for ASD closure are listed in Table I.

**Anatomic factors**

Transcatheter closure has emerged as a leading method of closure in ostium secundum defects. It is now dedicated for patients with feasible morphology (defect diameter ≤ 38mm, sufficient rim of 5mm except towards the aorta - class I. Specific indications for surgical approach include: other than secundum type ASD, insufficient (< 5mm) rim other than towards aorta), need for other cardiosurgical interventions.

The insufficient retro-aortic rim is not an absolute contraindication for transcatheter closure, but was recognized as one of the factors determining the increased risk of device-related aortic or atrial erosion. [35] The qualification for interventional treatment in case of such anatomy should be proceeded within a HeartTeam and the potential risk of a transcatheter approach and a surgical alternative should be carefully discussed with a patient. For transcatheter treatment, the devices without restrictions for the insufficient aortic rim in instruction for use (IFU) should be preferred.
Other types of ASD are usually referred for surgical closure. Patients with borderline anatomy should be discussed within the Heart Team.

**Special populations**

Special populations include patients with small ASD (not fulfilling above criteria) and:

1) history of cerebrovascular or other embolic events that may be explained by right-to-left shunt and paradoxical emboli. Such patients may be considered for ASD closure regardless of the defect size. The hemodynamic significance of L->R shunting is not necessary to be proven in patients with suspicion of paradoxical embolism. In such patients the workup should include opinion of the neurologist (ESC indication IIa, C).

2) patients with orthodeoxia-platypnea syndrome may be considered for transcatheter closure

3) patients with small defects but engaging in professional or recreational activities which can increase the risk of paradoxical embolism (e.g. divers)

4) patients with small ASD planning pregnancy

5) patients with ASD and functional tricuspid regurgitation related to right heart remodeling establish a specific subgroup, not precisely addressed in current guidelines. The results of a prospective registry [36] demonstrated a widespread improvement in TR severity after percutaneous ASD closure, which may support the choice of this treatment over surgical ASD closure with tricuspid repair. The precise identification of TR mechanism remains of critical importance in this setting.
VII. Interventions in special situations:

A) Patients with LV dysfunction and older adults/elderly patients

There are some differences between teenagers/young adults and older or elderly patients with ASD. Elderly patients or older adults (>60 years) with ASD, more frequently present elevated systolic pulmonary artery pressure, significant tricuspid regurgitation and atrial fibrillation. Persistent atrial fibrillation (AF) has been observed in 1/3 of ASD patients older than 60 years. The majority develop symptoms of reduced functional capacity, shortness of breath during exercise and palpitations. Symptoms were observed in 83% of patients older than 60 years [37].

In general, patients with significant shunt and pulmonary vascular resistance <5 WU should undergo ASD closure regardless of symptoms and age [1]. It must be pointed out that elderly patients also benefit from closure [1,37,38]. Patients older than 60 years improved markedly with almost 70% being asymptomatic after intervention when compared with about 16% before [1].

Being significantly less invasive than operation, and associated with fewer complications [39], transcatheter ASD closure became an attractive therapy for the older adults/elderly. Percutaneous closure of ASD can be performed safely and successfully in those patients. Symptoms reduction, improvement of functional exercise capacity, and recovery of both RV and LV functions has been reported [40].

Thus, interventional closure of ASD II with significant left-to-right shunt can be recommended in elderly patients (> 60 years), with good results in the majority of them [41]. In patients of advanced age with ASDs, who are not feasible for device closure, individual surgical risk associated with co-morbidities should be carefully weighed against the potential
benefits of ASD closure. Surgical closure of an ASD should also be considered in patients who are undergoing tricuspid valve repair or replacement [1].

ASD closure may not be associated with electromechanical improvement in elderly patients despite improvement in ventricular dimensions and symptoms reductions, and appears not to affect the arrhythmias they had before, or frequency of new which develop during follow-up [4,7]. Those patients should be informed about that before intervention.

In patients with angina pectoris or even risk factors for coronary disease, a coronary angiogram is advised before closure [1,42]. Use of CT coronary angiography is reasonable to exclude significant obstructive lesions in patients with a low/intermediate risk of coronary artery disease [24]. Patients with significant stenosis can be treated by percutaneous coronary intervention at the same procedure [42].

In general, the shunt volume depends on RV/LV compliance and defect size. ASD closure with abolishment of left-to-right shunt leads to augmented left ventricular filling by increased left ventricular preload and therefore improved left ventricular stroke volume and increase of functional capacity. In older patients, aging, co-morbidities as hypertension (LV hypertrophy), vascular disease, myocardial infarction, cardiomyopathy may cause decreased left ventricular compliance [43]. A restrictive diastolic ventricular function is generally observed more frequently in older adults, and may lead to secondary pulmonary hypertension and as a consequence to pressure-overload right ventricular failure. In these cases, reduced left ventricular compliance may also increase the left-to-right shunt through the defect, and may secondary lead to volume-overload right ventricular failure and worsening of symptoms [37]. This may justify closure of defects considered to be anatomically borderline.

On the other hand, in patients with impaired LV function (both systolic and diastolic) and increased LV end-diastolic and LA pressures, an ASD can have a decompressive effect on the LV. The abrupt closure of an ASD in this setting may lead to rapid volume and pressure
overload of the left heart, and may result in acute left ventricular failure and pulmonary oedema requiring mechanical ventilation, catecholamines support, and increased doses of diuretics [41]. ASD closure in such situations may also lead to reduced exercise tolerance, supraventricular arrhythmias and biventricular congestive heart failure [37,44].

Patients with evidence of LV dysfunction should undergo careful additional evaluation before ASD closure to establish the optimal treatment [24,43]. Plasma biomarkers (brain natriuretic peptides) may also be helpful in identifying patients with symptoms of subclinical heart failure [45]. If ASD closure is planned in those patients, pre-interventional assessment with echocardiography and evaluation of mitral inflow pattern and ASD balloon occlusion with reassessment of haemodynamics is recommended [37]. The balloon occlusion test consists of temporarily occluding the ASD with a sizing balloon, while maintaining catheters in the left atrium and left ventricle to monitor pressure changes. Special care should be taken not to compromise pulmonary veins and mitral valve inflow with the inflated balloon.

In patients with a left atrial pressure increase of >10 mmHg, or systemic pressure drop, or pulmonary pressure increase (positive balloon occlusion test) the closure has to be postponed [37,46]. Pulsed Doppler measurements of the mitral valve inflow during balloon inflation may also be helpful in estimation of the ASD closure results. The „risky” patients can be recognized if a pathological increase of the E/A ratio of the mitral inflow pattern is observed [37].

Further treatment is requested before defect closure in those patients to reduce the risk of worsening left heart failure symptoms after intervention. Reversible causes of LV dysfunction such as myocardial ischaemia or uncontrolled hypertension should be treated first [46]. If this is not possible, a pharmacological treatment with diuretics, vasodilators, or inotropes is advised. This LV „preconditioning” before ASD closure, applied for 48 hours to four weeks, was successful in all reported high risk patients older than 60 years [47,48].
Self-fenestrated devices (example Amplatzer ASD occluders) have been described to successfully minimise the risk of heart failure and pulmonary oedema following successful device closure. A self-made fenestration of 4 to 6 mm can be made in the occluder to permit residual shunting and can be closed later with a vascular plug if residual shunting is haemodynamically significant and balloon occlusion does not show any significant increase in LV filling pressure [49].

**In summary**, irrespective of the differences with younger patients, the symptomatic older adults/elderly (>60 years) with secundum ASD benefit from transcatheter closure. Coexisting systolic/diastolic left ventricular dysfunction should be taken into account in these patients. The abrupt closure of an ASD in this setting leads to rapid volume and pressure overload of the left heart, and may result in acute left ventricular failure. Patients with evidence of LV dysfunction should undergo additional pre-interventional echocardiographic and catheter evaluation. In some of the patients ASD closure has to be deferred and performed after successful „preconditioning” of the left ventricle.

**B) Patients with pulmonary hypertension**

Pulmonary hypertension (PH), with increased systolic pulmonary arterial pressure (sPAP) ≥40 mmHg, assessed by echocardiography, has been observed in 6% to 35% of patients with ASD II [50]. Moderate to severe PH in ASD is seen in 9–22% cases [51]. PH in ASD patients may be associated with functional capacity limitations, heart failure, atrial tachyarrhythmias and increased mortality. Preprocedural PH remains predictor of heart failure, arrhythmias and mortality even after defect closure [50-52].

If pulmonary hypertension is suspected in echocardiography, RHC should be performed. Pulmonary hypertension is diagnosed if mean pulmonary arterial pressure (mPAP) >20 mmHg and pulmonary vascular resistance (PVR) ≥ 3 Wood units (WU) are found. In
addition, pre-capillary pulmonary hypertension is diagnosed if pulmonary capillary wedge pressure (PCWP) is 15 mmHg or below, and post-capillary pulmonary hypertension is diagnosed if PCWP exceeds 15 mm Hg [30].

PH in the setting of an ASD can be secondary to various etiologies. Post-capillary PH may be secondary to elevated left ventricular (LV) end-diastolic pressure as seen in patients with ischemic heart disease, arterial hypertension, diabetes mellitus and chronic kidney disease or due to mitral valve disease [53]. Pre-capillary PH associated with ASD may be a result of increased blood flow through a large shunt and increased pressure causing pulmonary arteriopathy, but in some cases PH may be disproportionate to the magnitude of shunt. Patients with reversible PH who will clearly benefit from closure of the shunt are at one end of the spectrum. At the other end, however are those with irreversible PH with shunt reversal (Eisenmenger syndrome) in whom closure of ASD is not recommended and will need to be managed pharmacologically (Table 1) [27,53].

The main challenge is how to precisely identify the subgroup of ASD patients with reversible PH who may benefit from shunt closure [53]. A therapeutic strategy in patients with ASD II and significant PH remains controversial due to lack of evidence-based trials. In case of post-capillary PH and left ventricular (LV) dysfunction, ASD closure may precipitate acute LV insufficiency. For this reason, the balloon occlusion test (balloon inflation sealing the defect until the shunt completely disappeared, lasting 10-15 min along with PCWP and PAP monitoring) should be performed. If the PAP decreases by more than 25% with no decrease in systemic pressure and PCWP at the same time, the test is considered positive and closure may be considered [54]. Otherwise, implantation of a fenestrated device may be an option [55].

There is no precise cutoff parameter that would preclude ASD II closure in the presence of pre-capillary PH. Currently, according to the European Society of Cardiology guidelines,
the closure is recommended, if the defect is significant and PVR is less than 5 WU [1].

However, guidelines indicate that PH may be corrected by defect closure when PVR is 5 WU or higher, but the shunt is still left to right, PAP is less than two-thirds of systemic levels, and the ratio of PVR to systemic vascular resistance (SVR) index is below 2/3, without a specific PVR cutoff value. If values exceed 5 WU and PVR to SVR index above 2/3, the decision should be made in an expert center based on a hemodynamic assessment with reversibility test, optimally with nitric oxide usage [1]. According to the American College of Cardiology and American Heart Association 2018 guidelines for management of adults with congenital heart disease closure of an ASD, either percutaneously or surgically, may be considered in the presence of left to right shunting (pulmonary flow – Qp to systemic flow - Qs) is 1.5:1 or greater, systolic PAP (sPAP) is 50% or more of systemic arterial systolic pressure, and/or pulmonary vascular resistance is greater than one third of the systemic resistance [2]. Nevertheless, ASD closure should not be performed in adults with sPAP higher than 2/3 sSAP and, or PVR higher than 2/3 of SVR [2]. On the other hand, Galie considered closure to be contraindicated at a PVR of 4.6 WU or higher (PVR index – PVRI, more than 8 WU*m²), but the recommendation was based on an expert opinion rather than randomized trials [27].

Despite the lack of solid data, acute pulmonary vasodilator testing in reference PH centers is widely recommended in cases with a baseline PVRI of 4–8 WU*m² to assess the residual dilatatory capacity of the pulmonary vascular bed. A decrease of 20% in PVR, and decrease of 20% in PVR to SVR ratio, resulting in a final PVRI <6 WU*m² and a final PVR to SVR ratio of below 1/3 are considered to indicate a favorable outcome after shunt closure [56,57]. Re-evaluation can optionally be made after a short attempt at treatment with specific PH therapy, e.g. endothelin receptor antagonists (bosentan), prostacyclines or phosphodiesterase-5 inhibitors. The major limitation of these recommendations is that they are based on expert opinions or data derived from only from small case series.
C. Patients with multiple defects or deficient rims

*Interventions in patients with multiple defects*

Patients with multiple interatrial defects account for about 10% of all patients with atrial septal defects *secundum* type. There are many challenges to consider when planning percutaneous closure of multiple interatrial defects. One of the basic is to determine accurately the number of defects, the size of individual defects, the distance between them and the topography of the defects among themselves, as well as in relation to the surrounding structures of the heart. It is also important to determine whether the septum structure is stable or aneurismatic, since the latter often have multiple defects.

Meticulous diagnostic imaging is extremely important for the percutaneous closure of multiple interatrial defects. Real-time 3D echocardiography should always be considered in addition to standard transthoracic and transesophageal echocardiography. It facilitates the understanding of spatial relationships and helps to plan the transcatheter procedure reasonably. In addition, which is very important, it allows us to recognize whether the presence of one irregular defect is not incorrectly recognized as multiple defects. In some cases balloon calibration may also be useful when planning the procedure. With its help, we can determine the compliance of the atrial septum tissue, the usefulness of the rims and likelihood of closing the surrounding defects at the same time.

Usually, small defects in the close proximity of large defect can be closed with a single device. This mainly applies if the defects are not located further than 7 mm away from the large defect (the protruding part of the left atrial disc). If a small residual shunt remains close the implant, it usually closes during follow-up due to endothelization process [58]. If it does not happen after 6 months, subsequent device implantation may be considered. Using one device is cost-effective, but most importantly may lead to avoid bulky profiles.
Alternatively, if the defects are close together and the tissue separating them is thin, it is possible to implant an oversized device in the hope that this tissue band will burst creating one larger defect [59].

If the defects are located more than 5-7 mm away from each other, 2 implants should be used. There are various techniques for such implantation. If the defects are far away, the order of release does not matter. However, if the implants interfere with each other, it is best to use the interleaving technique. The implants are released simultaneously in the following order: the left atrial disc of the first implant, then the left and the right atrial disc of the second implant and finally the right atrial disc of the first implant. This ensures the least bulky profile of the atrial septum [60]. Alternatively, occluders can be implanted sequentially, but there is no agreement on this topic in the available literature on which occluder should be implanted first: larger or smaller [59-61].

For multifenestrated large aneurismatic septum, a non-self-centering device placement may be a good option [62]. Sometimes in such cases, in order to close all the defects while stabilizing the floppy septum, one may consider puncturing the central part of the septum with a transseptic needle and implanting through this hole a non-self-centering implant.

Percutaneous closure of multiple (or multifenestrated) interatrial defects is possible and effective, however there are reports of a higher frequency of residual shunts [63].

Interventions in patients with deficient rims

The ideal type of interatrial defect for percutaneous closure is the defect located in the central part of the septum with minimum rims ≥ 5 mm. A deficient rim is defined as <5 mm [64].

The deficient retroaortic rim is present in 36 – 57 % of patients with ASD secundum type [65]. It is recognized that percutaneous closure of ASD with the absent or deficient retroaortic
rim is the cause of an increased risk of erosion, but most leading centers nevertheless treat these patients percutaneously. The deficient retroaortic rim is associated with an increased risk of impingement of the device on the aorta, but this is not associated with aortic regurgitation. More recent studies do not confirm the relationship of the deficient retroaortic rim with an increased risk of erosion or other adverse events [66]. However, in patients with large defects, the absence of the retroaortic rim can cause difficulties in the percutaneous closure of ASD. In this situation the left atrial disc of the implant trends to slip over the anterior wall of the atrium and prolapse into the right atrium. There are a number of technical modifications helpful to close these challenging defects. The most common is the clockwise rotation of the delivery system thus the left disc of the device attempts to position towards the roof of the left atrium before the right disc is implanted. If this technique is ineffective, the left disc of the device can be initially implanted into the right or left upper pulmonary vein. After implantation of the right disk, a gentle tension to introducer sheath is made so the left disk can prolapse from the pulmonary vein into the correct position. Finally, the balloon-assisted closure technique might be considered. By the additional femoral venous sheath, the sizing balloon is introduced to the septum and partly inflated during the device implantation. After the complete implantation of the device, the balloon is deflated and carefully removed. In some cases, the use of steerable introducer sheath or the sets with a more flexible connection between the implant and the insertion cable can also facilitate the closure of a large defect with a deficient retroaortic rim. It must be pointed out that is not recommended to close defects with a deficient or absent retroaortic rim while the lack of superior rim.

The deficient posteroinferior rim occurs in 3.3% of patients with ASD secundum type. Percutaneous closure of this defect is feasible but it is associated with an increased risk of device embolization. Even if the device is well implanted and initially stable, it can slip to the inferior vena cava, what usually takes place a few hours after procedure. In rare situations,
cyanosis can appear after procedure, despite the implant’s stable position. This happens because of the implant’s straddling over the inferior vena cava may lead to a right-to-left shunt to the left atrium. Due to the difficult visualization of posteroinferior rim with the transesophageal echocardiographic guidance, defect assessment and monitoring of the procedure with intracardiac echocardiography is recommended. Since the percentage of complications may be significant, the percutaneous closure of ASD secundum type associated with posteroinferior rim deficiency should rather be avoided [61,67].

In the case of a posterior rim deficiency, the feasibility of percutaneous closure of ASD II depends on the extent of the defect. If it reaches the border with the inferior vena cava, device closure should be avoided due to the significant risk of embolization. It is extremely important to distinguish the deficiency of posteroinferior rim from the deficiency of posterior rim. While there is a significant risk of embolization with the device closure of the former, percutaneous treatment is appropriate for the latter.

The deficient posterosuperior rim rarely accompanies the atrial septal defect. Percutaneous closure of such defect is feasible, but one should be extremely careful, because sometimes it is directed towards the deficient retroaortic rim, and this situation poses a significant risk of atrial wall erosion.

Only secundum type of atrial septal defects should be closed percutaneously, however in recent years, there have been few reports of transcatheter closure of superior sinus venosus type of atrial septal defect using covered stents, however such procedure is still controversial. The use of 3-dimensional reconstruction of the heart with subsequent 3D printing may be extremely helpful in planning such procedure [68].

Some authors believe that finding one deficient rim is generally not a significant problem if the opposing rim is well developed [69]. Although percutaneous closure of ASD II with
deficient rims is feasible in many cases, this technique should not be recommended in most cases except in cases of deficient retroaortic rim.

VIII. Short review of the devices available in Poland

Transcatheter occlusion of an atrial septal defect by double umbrella system was first described by King and colleagues in 1974 [34,70]. Various devices have been used in transcatheter occlusion of these defects with different outcomes. The differences in results concerned complication types and rates. Their main problems were low closure efficacy (residual leaks), unstable device position (migrations) and fracture of its elements. A breakthrough came with using nitinol (a superelastic metal alloy of nickel and titanium) to build the skeleton of the Cardio-SEAL device (a modification to the Clamshell device). The next alteration was using a self-centering device (Star-Flex). Thus, transcatheter device retrieval before its release and reposition of the device become possible.

The perfect ASD closure device should be the one that completely closes the defect with minimal risk of complications, the device is easily implantable and can be repositioned and retrieved. As of yet, no device on the market meets all of these criteria. Most of currently available devices show excellent closure efficacy and quite comparable outcomes, however have their own advantages and disadvantages [71-80].

There have been a couple of ASD closure devices available on the Polish market over the past years (described in Table 2 and in details in Supplementary File).

IX. Potential complications of ASD closure

ASD transcatheter closure success rate is reported in about 98% of patients [76,81,82]. The prevalence of residual shunt is decreasing over the time after the procedure, and it is present in majority of patients immediately after device implantation not full closure is
present in only 1 and 2% of patients after 2-years following ASD closure [76,82,83]. Total complication rate vary and it is estimated to be between 2.2 and 8.6% [71, 84-86]. Periprocedural death is reported incidentally, mostly secondary to the other procedure-related major complications.

Complications of percutaneous ASD closure include: device dislodgement, cardiac structure damage or erosion, device impingement on valves, veins or other vessels such as the aorta, new onset atrial arrhythmia, atrioventricular block and thromboembolism arising from thrombosis on the device, air embolism, access site hematoma and bleeding - Table 3. The frequency of complications depends on the experience of the centre, the number of performed procedures, patients selection, and – less importantly - kind of the implanted device.

Device dislodgement

Device dislodgement, with subsequent embolization, occurs usually within 24-48 hours after the procedure with the incidence rate of 0.2 - 1.67% [71,82,84, 86-89]. However, it can also occur sporadically within several months or later after ASD closure [71,89]. The commonest reasons for occluder dislodgement are thin and aneurysmal septum, an inadequate or floppy rim, ellipsoidal shape of the defect, greater defect size (>30 mm), device mobility post-implantation, and operator-related technical issues, especially the use of an undersized ASD device [90]. The most of dislodgements takes place into the main pulmonary artery, left or right atrium, ascending aorta, and right ventricle, however devices can be located also at the left ventricle, descending aorta, abdominal aorta, iliac bifurcation, and iliac arteries [89,91,92]. To prevent, a device embolization, it seems reasonable to use device 1-2 mm greater than „stretched diameter” of the defect provided sufficient rims and the whole dimensions of interatrial septum. Very important in prevention of the occluder embolization is to ensure the proper and stable position of the device by so called a ‘push-pull maneuverer’
(Minnesota manoeuvre) before device detachment. However, if device dislodge (especially to atria, pulmonary artery or aorta), endovascular retrieval is possible using an goose neck snare or loop snare, biopsy forceps or other retrieval dedicated devices. A sheath size at least 2 to 4 F larger than the sheath that was used to deliver the device should be used. In Amplatzer or Amplatzer-like device pulling-out is usually feasible by grabbing a female screw site of the right atrial disc [92]. The primary objective is to bring the device out of the heart into the inferior vena cava and then out from the body through femoral vein. A large, stiff-tip braided sheath, works best [92]. A second venous access may be used to hold the device before snaring the occluder. If the device is in one of the ventricles, especially trapped in the chorda, retrieval may be difficult and it is reasonable to refer the patient to surgery, where both device retrieval and the defect closure could be performed [92]. According to available data, surgical intervention is required in about one fourth of device embolization cases [89]. It must be pointed out, that all operators who perform percutaneous ASD closure should be prepared for percutaneous device retrieval in the event of a device embolization [88].

Cardiac perforation and erosion

Cardiac perforation, which is mostly a catheter-related injury during the procedure, is a very rare complication (0.1%) manifesting usually as cardiac tamponade [88]. It requires immediate heparin neutralisation and decompression by pericardial puncture. If intrapericardial bleeding persists surgical intervention is required. Small, negligible pericardial effusion is sometimes visible during or after the procedure, especially in prolonged implantations. The mechanism is unknown and complete resolution of the effusion is observed within 3 weeks [71].

Cardiac erosion seems to be Amplatzer device specific complication following transcatheter closure of ASD. The rates of erosion ranged from 0.05 to 0.46% [76, 86-88].
Cardiac erosions might appear in less than 24 hours after device implantation, however most of them appeared within 6 months but they could be observed as late as even 9 years after procedure. Cardiac erosion could lead to cardiac tamponade or aortic fistula. It was noticed that 90% of patients with erosions had deficient aortic rims. The motions of the device relative to the aortic root were the main possible mechanisms of cardiac erosion. Avoiding of oversized devices seems to be a crucial factor to prevent cardiac erosions after defect closure [88,92,93].

_Air embolism_

Air embolism may be responsible for transient electrocardiogram changes, including ST segment (ST) depression or ST elevation, accompanied sometimes with chest pain and rhythm disturbances. Usually, it is transient and do not require intervention. In very rare cases with a persistent ST elevation, a coronary angiography may be necessary. Prevention of air embolism requires careful multiple saline flushes of the device, the loading system and the delivery sheath [66,88,93].

_Device impingement_

Device impingement on valves, veins or other vessels should be avoided by careful, attentive inspection by TEE during the implantation [71,88]. In patients with atrioventricular valve rim deficiency, the edge of the device may interfere with the anterior mitral valve leaflet and result in mitral regurgitation. In case of the impingement with cardiac structures, reposition of the device may be helpful or the exchange to a smaller device size (if the size of the defect allows it), otherwise surgical ASD closure should be considered [88,94].

_Arrhythmias and conduction abnormalities_

The reported complications from device closure of ASD include development of atrial tachyarrhythmias or advanced atrioventricular (AV) block. Atrial arrhythmias including extrasystole, supraventricular tachycardia, atrial flutter or atrial fibrillation may occur in up to
5% of procedures [88,92,95]. In majority of cases, they are transient and do not require treatment. In supraventricular tachycardia, atrial flutter or fibrillation a routine management according to guidelines is recommended.

Advanced or complete AV block can occur sporadically (below 1%), as early as at the time of the procedure and device deployment, or hours and days later or even years [86-88, 92,96]. Risk factors include young age and large defect/device size. Generally it’s believed to be caused by compression of the AV node or inflammatory foreign body reaction and scarring at the Koch’s triangle level caused by the device.

Most of the atrio-ventricular blocks are transient. Corticosteroid treatment has been tried but there are no controlled trials for AV block caused by device implantation [92]. Durable or late-onset complete AV blocks require pacemaker implantation [92].

**Thrombus on the device**

Studies showed that the incidence of thrombus on the device is about 1.2% [97]. However, significant differences were noted between different device types. Older generation devices (ASO, Starflex, Cardioseal) have higher incidence of thrombus formation, as compared to more recent devices [93]. The lowest rate of thrombus was reported with the Amplatzer nitinol wire frame filled with polyester fabric and the Helex nitinol wire covered by an ultra-thin membrane of expanded polytetrafluoroethylene [93]. Significant risk factors for thrombus formation were atrial fibrillation and atrial septal aneurysm which had remained after device closure. In most patients, the thrombus resolved under medical therapy with heparin or oral anticoagulants without adverse ischemic events [84,89]. Only few cases required surgical removal of thrombus [88,93]. Although antiplatelet therapy has been recommended for 3-6 months after the procedure, the time frame of thrombus formation ranged from 4 weeks to 7 years after device implantation. Early neurological complications
after transcatheter ASD closure can be resolved by heparin infusion [98]. Late incomplete endothelization of the device with subsequent clinical consequences is also possible [99].

**Nickel Allergy**

Nickel is a contact allergen, and may occur in case of implantation nitinol-containing device. The frequency is not known, however women get sick more often. In case of nickel allergy reaction occurs from 2 days to 1 month after implantation and manifests as headaches, rush/urticaria, difficulty breathing, fewer, palpitations, and rarely pericardial effusion [88,92,100]. Fortunately, all patients respond to medical management by steroids and antiallergenic agents [100-101] and symptoms subside in a few months. In rare cases if medical management is ineffective the device need to be explanted [88,100,101] A nickel skin test is available and may be performed in allergic or “suspected” patients [74]. In case of allergy platinum-coated device may be considered.

**Access-site related complications**

The last, but not least complications are groin hematoma and bleeding episodes following ASD closure. Groin hematoma is reported in up to 5% of patients, more frequently in women. It can be avoided by the ‘Z-shaped’ suture technique of the skin, followed by prolonged local compression on the groin. In cases, of severe bleeding episodes, the patient management should be applied in accordance to guidelines on the management of patients referred to invasive cardiology procedures.

The most frequently used occluder in ASD closure is Amplatzer device. In recent years, several amplatzer-like occluders have been registered and introduced into practice. Recent evaluation of 3 devices (Amplatzer, Figulla, Cera) showed no significant differences in efficacy and safety in short and mid-term follow up [102]. Also other Chinese and Thai nitinol occluders seems to be effective [73,74].
X. Percutaneous ASD closure in children - procedure specifics

The ASD leads to volume overload of the right chambers of the heart and an increased pulmonary blood flow. These changes proceed gradually, making it possible to postpone the decision to operate and choose when best to do it (usually when the child is 3 – 4 years old). Sometimes, however, the symptoms of the defect appear faster, are more severe and the degree of hemodynamic disturbances justifies operating sooner. Atrial septal defects can change as children grow. Small ASDs can close spontaneously. The main predictor of spontaneous closure is the initial ASD diameter of less than 8 mm [103]. On the other hand, the defects can also increase in size as the child grows. McMahon et al.’s study reported a 50% increase in size of ASDs in 2/3 of patients. In some patients the rate of the size increase amounted to up to 0.8 mm per year [104].

It is of extreme importance to monitor the changes in defect size and its hemodynamic consequences. Choosing the best time of qualification for the ASD closure procedure is of particular significance. Treating defects that are not increasing in size as the child grows may be postponed. As time passes, the hemodynamic and anatomical situation becomes increasingly favorable for the safety of the procedure. The decision to close an ASD that increases in size as the child grows should be made without delay. Postponing the decision may cause an increase in the ASD size to child body mass ratio. This may make a percutaneous procedure impossible to conduct. Apart from shortening the heart’s exposition to adverse hemodynamic conditions, the additional benefit of deciding on the procedure sooner is the use of a smaller closure device. The eligibility criteria for ASD treatment in young children are difficult and unclear. It is not fully known when treatment is necessary and what its benefits are.

In the pediatric population, the size of the defect should be assessed in relation to the patient’s body mass when considering the probability of successful device closure. A defect
that can easily be closed percutaneously in an adult may disqualify a child from this treatment method due to small heart size (especially the interatrial septum) and the proximity of the surrounding structures. Petit et al. demonstrated that good outcomes are obtained in patients with a defect to body mass ratio of <1.2 [105]. However, it has been proven to be possible to close much larger defects where the ratio was equal to 2.3 [106].

There is a natural tendency toward closing ASDs in more challenging clinical scenarios and larger defects in smaller patients. Lim et al. conducted an effective percutaneous ASD closure in a 2.8 kg preterm newborn [107]. There are numerous accounts of ASD closure in infants and very small children. Although percutaneous ASD closure is feasible even in very small infants, it requires extensive experience from the interventional team (especially in case of low body mass or large defects) [108]. The treatment of large ASDs in small children has a relatively low procedural success rate and carries a significant risk of procedural and delayed complications [109,110]. Percutaneous defect closure in children is difficult because of the small blood vessel diameter that complicates the procedure. Devices with the smallest size of delivery systems are therefore preferred, as they minimize the risk of damage to the vessels.

Before a small child qualifies for treatment, all risks and benefits must be evaluated. A good echocardiographic visualization of children makes it possible to conduct the procedure under TTE control without the need for TEE. For obvious reasons, however, the procedure always requires general anesthesia.

After closing the defect with the device, the size of the enlarged right heart chambers normalizes quickly. As the child grows there is no problem with the development of heart structures, interatrial septum included. Though the septum is stiffened at the implantation place, it retains its potential to grow in the part not covered by the device.
Long-term follow-up observations of children post percutaneous ASD closure show no difference in the type and number of long-term complications in comparison with the general population [110].

XI. Follow-up recommendations

After percutaneous ASD closure, a transthoracic echocardiography should be performed at 24 h after implantation to ensure that there is no significant pericardial effusion [1,4]. Chest pain or syncope may suggest device erosion or migration and should be evaluated without a delay [71]. After percutaneous defect closure, early (1-3 months) and intermediate (one year) follow-up is recommended with echo examination. Periodic follow-up is required thereafter, during every 2–4 years [1,111,112]. Follow-up evaluation should include transthoracic echocardiography with assessment of a potential residual shunts, right ventricular size and function, tricuspid regurgitation and pulmonary artery pressure (PAP) [97, 113-115]. Patients with residual shunt, elevated PAP or arrhythmias and those repaired at adult age (particularly >40 years) should be followed on a regular basis preferably in specialized centres [1,116,117].

After percutaneous ASD closure careful assessment of arrhythmias by history, ECG and if necessary by Holter monitoring should be carried-out [113,117]. Among late post-operative arrhythmias after ASD closure in younger population (age < 40 years) the most frequent are intra-atrial re-entrant tachycardia or atrial flutter, which can be successfully treated with radiofrequency ablation. In more adult population (age > 40 years) atrial fibrillation becomes more common and may require antiarrhythmic therapy or ablation. Access to the left atrium may be however restricted after device closure. Patients with atrial fibrillation should receive oral anticoagulation. Sick sinus syndrome or heart blocks are less common, but can appear even till 4 years after implantation [1,4,93,96].
Patients successfully repaired under the age of 25 years (no residual shunt, normal PAP, normal right ventricle, no arrhythmias) do not require regular follow-up [1,4,93,117]. However, they should be informed about the possible late occurrence of tachyarrhythmias.

**Medical Therapy**

Dual anti-platelet therapy with acetylsalicylic acid and clopidogrel is recommended for at least 3 months with single anti-platelet drug until at least 6 months after transcatheter closure of ASD [1,2,6,12].

**Infective endocarditis prophylaxis**

Infective endocarditis prophylaxis is recommended for 6 months after ASD device closure [1,4,113,118]. Infective endocarditis can be diagnosed in case of incomplete endothelization even late in follow up [99].

**Exercise/sport**

There are no contraindications or restriction to any kind of sports in asymptomatic patients with ASD without pulmonary hypertension, significant arrhythmias, or RV dysfunction. There is the limitation to the low-intensity recreational sports in patients with pulmonary hypertension. In the case of arrhythmias, the level of effort is limited by the occurrence of symptoms to the level that does not cause symptoms [119].

**Pregnancy and contraception**

In ASD patients without pulmonary hypertension the risk from pregnancy is low. ASD closure performed before pregnancy may prevent worsening of patients clinical status and help to avoid paradoxical embolism. Pregnancy is contraindicated in patients with severe pulmonary hypertension or Eisenmenger syndrome [114-120]. The recurrence rate of congenital heart diseases is 3–10% (excluding familial atrial septal defect and heart–hand syndromes with autosomal dominant inheritance) [120]. There are no contraindications to any type of the contraception in ASD patients [1,119,120].
XII. Recommendations for training physicians to perform ASD closure.

To ensure optimal results ASD closure should be performed in experienced centres that routinely perform other structural heart interventions, like it was advocated in previously published PFO guidelines of the same group [121]. Data from numerous registries regarding ASD and PFO closure procedures show that both individual operators and centres with a small number of procedures performed annually have worse treatment results [122]. Trainee operators should have the theoretical knowledge and technical skills required to safely perform this procedure to ensure the low number of complications.

The group of experts from the Association of Cardiovascular Interventions and the Grown-Up Congenital Heart Disease Section of the Polish Cardiac Society recommends that the training physician should acquire theoretical knowledge regarding the indications for procedure, patient preparation, practical experience with the equipment, proper selection of the device size, conduction of the procedure, and peri- and post-procedural pharmacotherapy. It is also necessary to get the knowledge about the possible complications of the procedure, their prevention and treatment. After theoretical and practical training in a centre with extensive experience (at least 3 sessions), the training operator should perform a minimum of 20 ASD closure procedures independently but under the supervision of an experienced operator (proctor) [123,124]. However, based on experts opinion, the presence of cardiac surgery on-site is not required in centers who want to start ASD/PFO closure procedures programme.
References:


resonance in adults with congenital heart disease from the respective working groups of the European Society of Cardiology. Eur Heart J. 2010; 31: 794–805.


results: endorsed by the Society for Cardiovascular Angiography and Interventions.

Table 1. Classical recommendations for atrial septal defect closure according to the new 2020 European Society of Cardiology guidelines for the management of adult congenital heart disease

<table>
<thead>
<tr>
<th>Indications for atrial septal defect closure</th>
<th>Class</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with ASD and evidence of right ventricle volume over-load and no pulmonary hypertension or left ventricular disease.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Balloon testing is recommended before the decision to close in patients with ASD and left ventricle disease.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Patients with suspicion of paradoxical embolism regardless of size of the defect.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Patients with elevated PVR (3-5 WU) when significant left to right shunt is present (Qp:Qs &gt;1.5).</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Fenestrated ASD closure may be considered in patients with PVR &gt;_5 WU, when significant L-R shunt (Qp:Qs &gt;1.5) is present and PVR falls below 5 WU after PH treatment.</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

**ASD** – atrial septal defect  
**WU** - Wood Units  
**PVR** – pulmonary vascular resistance
### Table 2. Comparison of commonly used devices for atrial septal defect closure available in Poland

<table>
<thead>
<tr>
<th>Device</th>
<th>Company</th>
<th>Construction</th>
<th>Connection system</th>
<th>Available sizes</th>
<th>Delivery system</th>
<th>Number of sizes</th>
<th>comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amplatzer Septal Occluder</td>
<td>Abbott (USA)</td>
<td>Nitinol double discs</td>
<td>Micro thread</td>
<td>4-38 mm.</td>
<td>6-12 F</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Figulla Flex II</td>
<td>Occlutech GmbH German</td>
<td>Nitinol double discs</td>
<td>Unique flexible ball connection</td>
<td>4-40 mm.</td>
<td>7-12 F</td>
<td>20</td>
<td>Titanium oxide-covered nitinol</td>
</tr>
<tr>
<td>Cera, CeraFlex*</td>
<td>LifeTech Scientific Co - China</td>
<td>Nitinol double discs</td>
<td>Micro thread/premounted flexible connection*</td>
<td>6-42 mm.</td>
<td>7-14 F</td>
<td>19</td>
<td>Titanium nitride-coated nitinol wire.</td>
</tr>
<tr>
<td>Cocoon Septal Occluder</td>
<td>Vascular Innovations Co - Thailand</td>
<td>Nitinol double discs</td>
<td>Micro thread</td>
<td>8-40 mm.</td>
<td>7-14 F</td>
<td>17</td>
<td>Nitinol wire nanocoated with platinum</td>
</tr>
<tr>
<td>Hyperion</td>
<td>Shanghai Shape Memory Alloy Co, - China</td>
<td>Nitinol double discs</td>
<td>Micro thread</td>
<td>6-42 mm.</td>
<td>8 to 14 F</td>
<td>19</td>
<td>pre-oxidized nitinol wires</td>
</tr>
<tr>
<td>Memopart ASO</td>
<td>Lepu Medical Co - China</td>
<td>Nitinol double discs</td>
<td>Micro thread</td>
<td>6-42 mm.</td>
<td>8 to 14 F</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Nit-Occlud ASD-R</td>
<td>PFM Medical – Germany</td>
<td>double-disc “reverse configuration” of the single-nitinol-layer on the LA disc</td>
<td>“snare-like” central locking wire and a pusher with a distal wire nose. Premounted</td>
<td>8-30 mm.</td>
<td>8 to 14 F</td>
<td>12</td>
<td>one piece of nitinol wire without any connecting elements</td>
</tr>
<tr>
<td>Ultrasound II ASD Occluder</td>
<td>Cardia Minneapolis – USA.</td>
<td>nitinol wire frame forms two sails with a self-centering mechanism.</td>
<td>Flexible biotom-like connection</td>
<td>6-34 mm.</td>
<td>9 to 11 F</td>
<td>15</td>
<td>covered by a polyvinyl alcohol membrane</td>
</tr>
</tbody>
</table>
Table 3. Complications of the transcatheter atrial septal defect closure procedures

<table>
<thead>
<tr>
<th>Complication</th>
<th>Incidence (%)</th>
<th>Onset</th>
<th>Clinical significance</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Device-related cardiac perforation</strong></td>
<td>0.1</td>
<td>mostly within 24-48h, the potential for late occurrence (up to 3 y)</td>
<td>potentially lethal cardiac tamponade, hemopericardium</td>
<td>Heparin neutralization, pericardial effusion drainage, surgical intervention if required</td>
</tr>
<tr>
<td>cardiac erosion</td>
<td>0.05 - 0.46</td>
<td>majority within 96 h, probable during the first 6-8 m, incidentally up to 9 y</td>
<td>potentially lethal cardiac tamponade, hemopericardium, aortic fistula</td>
<td>pericardiocentesis for pericardial effusion and tamponade, surgical intervention</td>
</tr>
<tr>
<td>device embolization</td>
<td>0.2 - 1.67</td>
<td>mostly within 24-48h, sporadically within several months</td>
<td>depends on place of dislodgement</td>
<td>anticoagulation, percutaneous device retrieval, surgical retrieval if required</td>
</tr>
<tr>
<td>device impingement</td>
<td>extremely rare</td>
<td>up to several weeks, usually due to device shift or wire fracture</td>
<td>severe mitral valve regurgitation, pulmonary edema</td>
<td>replacement of the device with a smaller device if possible, surgical intervention</td>
</tr>
<tr>
<td>device thrombus</td>
<td>1.2</td>
<td>mostly during 1-6 m</td>
<td>cardiovascular embolic events</td>
<td>anticoagulation, in rare cases surgical intervention</td>
</tr>
<tr>
<td><strong>Atrial tachyarrhythmias</strong></td>
<td>1.3-5.0</td>
<td>increased in a periprocedural period, then subsides over time</td>
<td>hemodynamic compromise, thromboembolic events</td>
<td>according to event specific guidelines</td>
</tr>
<tr>
<td><strong>Conduction abnormalities</strong></td>
<td>Below 1</td>
<td>typically in the first 24h, or hours and days later than resolve over time</td>
<td>hemodynamic compromise</td>
<td>in case of durable advanced block device removal (early phase), pacemaker placement if late-onset advanced heart block</td>
</tr>
<tr>
<td>Advanced heart block</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Access-site complications</strong></td>
<td>1-3</td>
<td>up to 24h after the procedure</td>
<td>anemia, local pain</td>
<td>usually conservative</td>
</tr>
<tr>
<td>groin hematoma, bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nickel allergy</strong></td>
<td>unknown</td>
<td>24h – 1 m</td>
<td>headache, rush/urticaria, fewer, palpitations, difficulty breathing</td>
<td>medical therapy with steroids, anti-allergic agents, in rare cases device explanation</td>
</tr>
</tbody>
</table>

h – hour(s), m – month(s), y. – year(s)
Figure 1. A diagnostic algorithm for patients with atrial septal defect and pulmonary hypertension.