Atrial Septal Defect, Ventricular Septal Defect

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Abstract

Atrial septal defect (ASD) is the general name for multiple cardiac lesions whose etiology is mainly a congenital defect in the interatrial septum. Atrial septal defects, after bicuspid aortic valve and mitral valve prolapse, are the third most common congenital heart disease. Atrial septal defects are much more frequent in women than men. A long list of assessment methods is used to detect the disease, from noninvasive ones to fully invasive methods. The management depends on both the underlying type of lesion and the general condition of each patient. The outcome is often fair.

Ventricular septal defects (VSDs) are also among the most common congenital heart diseases, being the most common congenital defect at birth up to 40% of all congenital heart diseases. VSDs may involve the interventricular septum (IVS) as an isolated defect, as part of the other congenital disease(s), or as a part of complex congenital heart disease including (but not limited to) the following diseases:

- Conotruncal defects,
- Tetralogy of Fallot,
- Transposition of great arteries,
- Congenitally corrected transposition,
- Double outlet right ventricle,
- Double outlet left ventricle,
- Left-sided obstructive lesions,
- Subaortic stenosis,
- Aortic coarctation,
- Interrupted aortic arc.

Also, there is an important classification of the lesion based on anatomic and embryologic origins. Different diagnostic methods are used to detect the disease. Most small VSDs close spontaneously during the first year of life, while the larger ones or "multiple VSD" cases usually need intervention. If untreated, pulmonary hypertension and systemic desaturation may ensue. Although spontaneous closure is a common phenomenon in infancy and childhood, it occurs much less frequently in adulthood.

Atrial Septal Defect

Introduction

Atrial septal defect (ASD) is the general name for multiple cardiac lesions whose etiology is mainly

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a congenital defect in the interatrial septum. Atrial septal defects, after bicuspid aortic valve and mitral valve prolapse, are the third most common congenital heart disease. Atrial septal defects are much more frequent in women than men (McCarthy et al. 2003; Geva et al. 2014; Menillo et al. 2021).

Embryology

Detailed discussions on the embryology of ASDs can be found in chapter "Cardiovascular System Embryology and Development"— Cardiovascular System Embryology and Its Development; however, a brief discussion is presented here. The septation process is an embryologic stage leading to chamber formation. Interestingly, only the "eutherian mammals" undergo a "two-septal development process" for the creation of the atrial septum, a process that is error-prone, leading to "incomplete closure of the atrial septum" which is known as "probe patency" (Jensen et al. 2019). This process in the common atrium starts at the beginning of the fifth week and includes the following steps (Anderson et al. 2003; McCarthy et al. 2003; Gittenberger-de Groot et al. 2005; Sukernik and Bennett-Guerrero 2007; Geva et al. 2014; Asrress et al. 2015; Calkoen et al. 2016; Kloesel et al. 2016; Jensen et al. 2019):

1. A sickle-formed crest comes down from the roof of the common atrium which makes *septum primum.*
2. The *septum primum* develops caudally towards the endocardial cushion in the atrioventricular canal.
3. Now, *ostium primum* is in the common atrium, allowing interatrial blood flow.
4. Superior parts of the septum primum are fenestrated by apoptosis thereby creating *ostium secundum* allowing the right to left shunt in the fetal circulation; the obliterated superior part of the septum primum will be completed by *septum secundum.*
5. From the common atrial wall roof, a crescent muscular mass grows downward on the right side of the septum primum producing the superior parts of the interatrial septum; it covers the main part of the *ostium secundum* and is called the *septum secundum.*
6. Now, we nearly have the future interatrial septum which is composed of two merging septa: *septum primum* and *septum secundum,*
7. There is a defect in the septum secundum called *fossa ovalis* which is usually compensated by *septum primum*. However, a wide range of defects may affect fossa ovalis and hence, create gaps or deficiencies in the flap valve.
8. Also, there is *foramen ovale*, a defect in the borders of septum primum and septum secundum, which is an obliquely elongated cleft in the interatrial septum—it will be open as long as fetal circulation persists. After birth, due to the transition from fetal circulation to normal circulation, pressure in the left cardiac chambers increases, and foramen ovale is closed; the closure is a physiologic one in the first steps; however, it will be changed to an anatomic closure after a while, anatomically,
9. Pulmonary veins are relocated from the right atrium to the left atrium.
10. *Sinus venosus* is the part of tissue separating right pulmonary veins from the superior vena cava (SVC) posteriorly and also, the inferior aspects of the free right atrium wall. The *coronary sinus septum* is the part of myocardial tissue separating the coronary sinus from the left atrium. Also, the left venous valves and the septum spurium merge with the right side of the septum secundum.

Classification

In this section, the classification of the most common types of ASDs based on the above embryological sequence of events is presented in Table 1. (Kerut et al. 2001; Sukernik et al. 2001; Oliver et al. 2002; McCarthy et al. 2003; Van Praagh et al. 2003; Ashley 2004; Sukernik and Bennett-Guerrero 2007; John et al. 2011; Briggs et al. 2012; Asrress et al. 2015).

Table 1 Classification of atrial septal defect (ASD) lesions

Type of ASD	Mechanism of ASD	Occurrence of the lesion/clinical outcome	Associated lesions
ASD secundum (ASD II)	Failure in pulling-down of septum primum and deficient septum secundum	The most common type of ASD; 70% of all ASDs are ASD II; 65–70% of ASD II are female; about half of them are closed spontaneously; the chance of spontaneous closure is more in smaller size defects and less than 1 year age; increasing age and larger defects less chance for spontaneous closure	Mitral valve prolapse Mitral valve stenosis Pulmonary stenosis
ASD primum (ASD I)	If the ostium primum is not closed by the septum primum an ASD I result; ASD I is located close to the atrioventricular valves and is often associated with an atrioventricular septal defect	50% of ASD I patients are female; usually, surgical treatment is often mandatory for closure of ASD I because there is very little chance for spontaneous closure	Cleft mitral valve (always) Inlet ventricular septal defect Septal aneurysms
Sinus venosus type ASD (SVASD)	SVASD is an unusual type of ASD, with two common locations: If located superiorly, it is near the entry of SVC If located inferiorly, it is near the entry of IVC It is often associated with anomalous attachment of venae cavae and pulmonary veins Often, due to these anatomic locations, it is discussed under partial anomalous pulmonary venous drainage	40–50% of SVASD patients are females There is usually no spontaneous closure—surgical treatment is often mandatory	Partial anomalous venous return Overriding superior vena cava
Coronary sinus septal defect (CSSD)	CSSD occurs if the delicate tissue separating the coronary sinus from the left atrium is not completed; the result is blood shunting through the defect and the orifice of the coronary sinus	An uncommon type of ASD	Unroofed coronary sinus Left superior vena cava persistence Partial/total anomalous venous return
Persistent foramen ovale (PFO)	The pathologic defect is the same as the pathology if fetal circulation persists (Persistence of Fetal Circulation: PFC) which is associated with increased pressure on the right side	PFO, as an independent lesion, is present in as much as 25% of the general population Its occurrence should be considered independently from defects in the interatrial septum	Similar to PFO

Pathophysiology of ASD

Due to ASD, during the early course of the disease, oxygenated blood flows from left to right, leading to the following events (Oliver et al. 2002; Azarbal et al. 2005; Tobis and Azarbal 2005; Warnes et al. 2008; Geva et al. 2014; Zvaigzne et al. 2014; Jensen et al. 2019):

- In nearly all ASD patients, there are varying degrees of the interatrial shunt; if the pressure is higher on one side, the blood would shunt from that side to the other side.
- Often, there is a *left-to-right shunt* in ASD patients; the severity of the shunt and its direction depends on two main factors: the *size of the defect* in the inter-atrial septum and *left*

and right atrial pressures and the relationship between them.

- In ASD secundum, if the defect is less than *10 mm*, the amount of shunt is usually negligible and the severity of right heart overload and pulmonary hypertension is very low.
- If the defect is large enough to induce considerable shunt flow, then, the lungs are overflowed due to the *recirculation of oxygenated blood* to the lungs.
- Increased blood volume load to the lungs often leads to *enlargement of the right heart chambers* (right atrium and ventricle) often associated with impaired function of the right atrium. Also, the pulmonary and right heart vascular systems (both arteries and veins) are enlarged due to pulmonary overflow.
- Over time, pulmonary overflow, pulmonary vascular bed remodeling, ventricular remodeling, and trophic changes in the right and left ventricles lead to *pulmonary hypertension* with different severities. The incidence of right heart failure and pulmonary vascular disease is more prevalent in female patients compared with male patients and also in untreated adults.
- Additionally, decreased blood flow through the left heart leads to shrinkage or compromised growth of the left ventricle and aorta— the final result could be diminished systemic output and finally, *left ventricular systolic dysfunction.*
- If pulmonary hypertension persists and the process of shrinkage in the aorta and left ventricle continues, *Eisenmenger syndrome* may develop. This presents as increased pulmonary pressure over the systemic pressure accompanied by different degrees of right heart failure.
- Often, in the course of the disease, *exercise intolerance* occurs due to impaired hemodynamics, although it is not a common event during the early stages of the disease; however, with advanced age, intolerance increases insidiously,
- Often, enlargement of the right heart, especially the right atrium, is associated with a range of *arrhythmias.*

- For the prevention of disastrous outcomes, *treatment is necessary*. Smaller ASDs impose less burden on the heart and might be closed spontaneously; however, larger ASDs cause a significant burden on the heart leading to unwanted consequences which mandate treatment.
- Some *neurologic complications* might occur during the process of the disease due to particulate or air embolization. For example, paradoxical emboli or rare desaturation episodes may lead to aura, migraine headaches, or even transient ischemic events in the central nervous system.

Diagnosis of ASD

In ASD patients, the process of diagnostic workup should aim mainly at the following:

- Presence of ASD,
- Size of ASD,
- Location of ASD,
- The effect of ASD shunt on left and right ventricular function,
- The effect of ASD shunt on pulmonary circulation,
- Any possible associated lesions.

Diagnosis of ASD

Clinical Presentation and the Course of the Disease

The majority of the patients with ASDs are asymptomatic during neonatal and early childhood. Any of the following findings such as slow weight gain, tachypnea, or recurrent respiratory infections during infancy should raise suspicion of an ASD. Most pediatric patients with ASDs are acyanotic; however, very rarely, mild transient cyanosis may happen in the newborn which is due to a right-to-left shunt. In physical examination, the precordium is hyperdynamic. Fixed splitting of the second heart sound is heard through respiratory cycles; the severity of the pulmonary component of the second heart sound

(P2) corresponds with the severity of pulmonary hypertension only if it is present. The diagnosis in this time domain is usually an incidental finding by echo during routine clinical or paraclinical assessment like looking for the origin of an incidental heart murmur or anything abnormal found in chest X-ray or other studies. Untreated adults have more symptoms and signs, especially related to potential pulmonary hypertension. More explanation regarding adult patients with ASD can be found in chapter "Anesthetic Management of Adults with Congenital Heart Disease"—Anesthetic Management of Adults with Congenital Heart Disease (Andrews et al. 2002; Lammers et al. 2005; Geva et al. 2014; Zvaigzne et al. 2014; Le Gloan et al. 2018; Corno et al. 2021).

In a considerable number of patients with *ASD secundum*, the chance of spontaneous closure is high. The chance of spontaneous closure is higher in those patients with smaller size defects and less than 1 year of age; however, increasing age and larger defects (i.e. more than 10 mm) are not favorable for spontaneous defect closure (Abdelkarim et al. 2016; Behjati-Ardakani et al. 2016). Conversely, *sinus venosus ASD* and *ASD primum* nearly always need surgical treatment and have significant hemodynamic consequences. More than one-fourth of all adult patients with congenital heart defects are ASD cases and among them, about 75% are ASD secundum (Warnes et al. 2008; Vasquez and Lasala 2013).

Exercise Intolerance

An uncommon finding in young ASD patients is the occurrence of exercise intolerance. However, with increasing age, in those who have been untreated, the frequency of exercise intolerance increases surreptitiously due to aggravation of pulmonary vascular function. If ASD secundum remains unrepaired, exercise capacity will decrease as much as 50–60% of the predicted values (Geva et al. 2014; Amedro et al. 2018).

Pulmonary Hypertension

Pulmonary hypertension is not a common finding in neonates and young children, but it may present itself more frequently in untreated adults. Increasing age and female gender are two main predisposing factors for the occurrence of pulmonary hypertension in untreated ASD; Down syndrome, sleep apnea, and pulmonary vascular embolic events are other risk factors. Eisenmenger syndrome is seen in 5–10% of untreated adults (Rosas and Attie 2007; Warnes et al. 2008).

Electrocardiography (ECG)

The main ECG findings for ASD include (Fig. 1):

- Tall P wave due to right atrial enlargement; inverted P waves in inferior leads suggest sinus venosus ASD.
- First degree AV block may be seen.
- Right bundle branch block (usually incomplete form) may be seen especially in untreated adults.
- Right axis deviation; if leftward or left superior QRS axis deviation is seen, one should seek for ASD primum.
- Rhythms other than sinus rhythm are not common; however, atrial fibrillation or flutter may occur in adult patients with prolonged disease leading to right atrium enlargement often occurring after 40 years.
- Hypertrophy of the right ventricle (presented in ECG by RSR′ pattern in right precordial leads) may be seen due to pulmonary hypertension (McCarthy et al. 2003; Webb and Gatzoulis 2006; Lam and Friedman 2011; Geva et al. 2014; Zvaigzne et al. 2014; Kloesel et al. 2016).

Chest X-Ray (CXR)

The chest X-ray is often abnormal in ASD; however, normal CXR does not rule out ASD. The most common findings in CXR of ASD patients include (Webb and Gatzoulis 2006; Geva et al. 2014; Zvaigzne et al. 2014; Behjati-Ardakani et al. 2016; Le Gloan et al. 2018):

- Cardiomegaly which is mainly due to dilation of right-sided chambers is best seen in lateral views. However, in ASD primum, dilation of left-sided chambers may lead to cardiomegaly which may be better seen in lateral views.
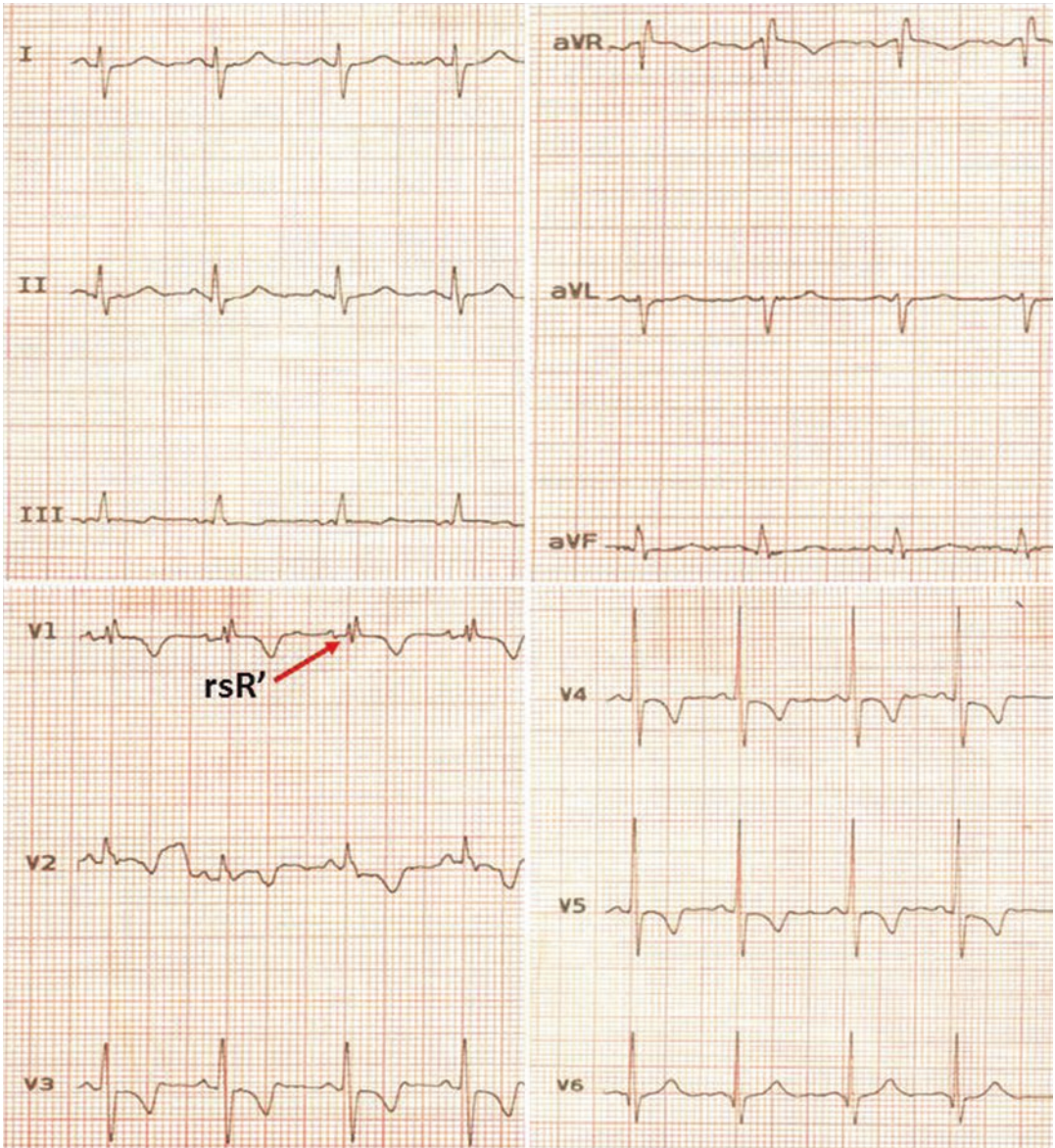
Fig. 1 The rsR′ pattern in lead V1 and right axis deviation are typical characteristics of the atrial septal defect. (Courtesy of Dr. Majid Haghjoo and Dr. Mohammadrafie Khorgami)

- Pulmonary artery trunk and its perfusion domain are enlarged; however, discordance between the main pulmonary artery body and lung fields, leading to a normal appearance of lung fields in the presence of an enlarged pulmonary artery trunk, may be indicative of pulmonary vascular obstructive lesion.
- Small aortic knuckle due to shrinkage of left heart chambers.

Imaging Techniques in the Diagnosis of Atrial Septal Defects

A definitive diagnosis of ASDs may be confirmed via imaging techniques that demonstrate shunting across the interatrial septal defect. Also, any possible right ventricle overload or associated diseases should be detected and diagnosed. These techniques include mainly echocardiography, cardiac computed tomography, cardiac magnetic resonance, and catheterization (Warnes et al. 2008).

Echocardiography
There is no doubt that two-dimensional transthoracic echocardiography with Doppler is the cornerstone for the evaluation of ASD, although not all ASDs can be visualized with transthoracic echocardiography. Echocardiography is the most common diagnostic modality used for all types of ASD during both the primary assessment of the defect and during follow-up visits (Kharouf et al. 2008). The main elements that should be considered in a comprehensive echocardiographic evaluation for ASD mainly include:

- Visualization of ASD with the characterization of its size and location.
- Determining the direction of interatrial flow.
- Right heart examination.
- Pulmonary artery pressure measurement.
- Assessment and estimation of the pulmonary/systemic flow ratio.
- Pulmonary vein flow.
- Left ventricular function.
- Assessment for any associated abnormalities.
- Assessment of all valves.

Post-Intervention assessment of ASD should focus on the following steps:

1. Any possible residual leak.
2. Right ventricle size/function.
3. Septal motion/curvature.
4. LV size/function.
5. Possible mitral valve prolapse (MVP).
6. Pulmonary valve.
7. Right ventricle systolic pressure.
8. Pulmonary artery pressure.
9. Pericardial effusion.

Common Views for Detection of ASD

- Apical four-chamber view.
- Parasternal short-axis view.
- Subcostal views.
- Also, note that not all ASDs can be detected with transthoracic echocardiography.

Other Imaging Studies

Cardiac Magnetic Resonance (CMR)
Cardiac MR (cardiac magnetic resonance) is used both for anatomic assessments and also, for evaluating the hemodynamic effects of interatrial defects; cardiac MR has a great application in sinus venosus ASD. Also, cardiac MR is considered the gold standard in the assessment of RV volume and function and the pulmonary artery and veins. Cardiac MR is the most accurate and fastest data acquisition modality. However, this technology is not usually used before the treatment of ASD secundum and has a limited application before the treatment of ASD primum (Webb and Gatzoulis 2006; Kharouf et al. 2008; Warnes et al. 2008; Geva et al. 2014).

Cardiac Computed Tomography (CT)
For cardiac CT especially when using high-resolution cardiac CT, many great data could be acquired. However, the data gained from cardiac CT are not significantly more than the data gained from cardiac MR. Cardiac CT also poses a high degree of radiation risk exposure and should be considered if serial examinations are needed.

Cardiac Catheterization

Cardiac catheterization studies are not usually indicated for the evaluation of ASDs, However, cardiac catheterization is useful in the following scenarios (Warnes et al. 2008; Geva et al. 2014):

- ASDs going to be closed with percutaneous devices (i.e., ASD secundum).
- To assess any associated anomaly not diagnosed with other non-invasive imaging modalities,
- For the assessment of the coronary system in adults with ASDs.

Treatment

Regardless of age, ASD closure leads to improvements in the course of the disease, with diminished symptoms and improvement in pulmonary vascular disease, pulmonary arterial pressure, ventricular remodeling, and chamber size. Time of repair depends mainly on the type and size of the defect, age of the patient, associated symptoms, associated anomalies, and several other concomitant factors. However, if treatment is delayed, clinical parameters may become exacerbated; therefore, the sooner treatment is done, the better the general outcome and life expectancy. Surgical closure if performed before 25 years old usually leads to a normal life span. Conversely, if ASD leads to severe irreversible PAH and no evidence of a left-to-right shunt, there is no evidence in favor of ASD closure (Rosas and Attie 2007; Engelfriet et al. 2008; Warnes et al. 2008; Yalonetsky and Lorber 2009; Humenberger et al. 2011; Geva et al. 2014; Sachdeva et al. 2020).

Percutaneous closure of *ASD secundum* with sufficient rims is the preferred approach. Cardiac MR or cardiac catheterization is used for a full assessment of *ASD secundum* and any potentially associated anomaly before repair. However, surgical closure is the main treatment in ASD primum and sinus venosus ASDs. Also, surgical closure of ASD secundum is considered when surgical repair/replacement of a tricuspid valve is planned concomitantly or the anatomy of ASD secundum is not appropriate for deploying a per-

cutaneous device (Warnes et al. 2008). In patients with a diagnosis of ASD primum or sinus venosus ASD (confirmed by echocardiography), no additional imaging studies are needed before surgery (Rigatelli et al. 2007; Kharouf et al. 2008; Warnes et al. 2008; Yalonetsky and Lorber 2009; Humenberger et al. 2011; Geva et al. 2014; Abdelkarim et al. 2016).

According to the "ACC/AHA 2008 Guidelines for the Management of Adults with Congenital Heart Disease," ASD closure in adults (percutaneously or surgically) may be considered if the patient meets the following criteria (*Level of Evidence: C*):

- Net left-to-right shunting,
- Pulmonary artery pressure two-thirds of the systemic pressure or less than that,
- Pulmonary vascular resistance is less than two thirds systemic vascular resistance or it responds to pulmonary vasodilator therapy or test occlusion of the defect (Warnes et al. 2008).

Anesthetic Management During Atrial Septal Defect Repair

Anesthesia for Surgical Treatment

A balanced anesthesia plan is preferred leading to both hemodynamic stability and also, the capacity to perform fast-track extubation. Based upon the patient's condition, arterial and central venous monitoring may be indicated. A pulmonary artery catheter is not recommended and does not derive any additional data that can be obtained with transesophageal echocardiography (TEE). Live time echocardiography is usually performed by an anesthesiologist or cardiologist. Antibiotic prophylaxis should be also considered.

Anesthesia for Interventional Treatment

Although sedation may be used during percutaneous device closure of ASD, anesthesia and tracheal intubation are preferred since transesophageal echocardiography is typically utilized used for

defining the correct deployment of the device and ruling out any residual defect. Sedation may be appropriate if intracardiac echocardiography (i.e., ICE) is utilized.

Ventricular Septal Defect

Ventricular septal defects (VSDs) are among the most common congenital heart diseases. It is the most common congenital defect at birth. If those defects that are part of other complex congenital heart diseases are taken into account, VSDs include up to 40% of all congenital heart diseases (Hoffman 1995; Roguin et al. 1995; Hoffman et al. 2004; Penny and Vick 2011; Jortveit et al. 2016; Dakkak and Oliver 2021). VSDs may involve the interventricular septum (IVS) and is often an isolated defect; however, they might be associated with other congenital disease(s) or as a part of complex congenital heart disease such as the following:

- Conotruncal defects.
  - Tetralogy of Fallot.
  - Transposition of great arteries.
  - Congenitally corrected transposition.
  - Double outlet right ventricle.
  - Double outlet left ventricle.
- Left-sided obstructive lesions.
  - Subaortic stenosis,
  - Aortic coarctation,
  - Interrupted aortic arch.

IVS, which is the main site of the lesion, is composed of two parts:

- The inferior segment which is muscular,
- The superior segment which is membranous.

In the majority of VSDs, blood flows through the left ventricle to the right ventricle, leading to a pulmonary overflow, but systemic desaturation is either absent or minimal. Most small VSDs close spontaneously during the first year of life (Hoffman 1995; Roguin et al. 1995) while the larger ones or "multiple VSD" cases usually need intervention. If they remain untreated, the resultant pulmonary overflow causes a sustained increase in pulmonary vascular resistance (PVR), pulmonary hypertension, and finally, shunt reversal and as a result, systemic desaturation ensues. Although spontaneous closure is a common phenomenon in infancy and childhood, it occurs much less frequently in adulthood.

Embryology and Classification of Ventricular Septal Defects

At the beginning of the fifth week, the primeval ventricles start expanding, leading to the development of the apical parts of the future ventricles from the primary heart tube. This phenomenon has a crucial role in the development of IVS with two main parts:

- *Muscular IVS* develops from the bulboventricular flange; the majority of VSDs are located in this muscular component of IVS.
- *Membranous IVS* connects the upper margin of the bulboventricular flange to the anterior and posterior endocardial cushions. In the "developed" heart, membranous IVS is the smaller part of the septum, at the base of the heart, located between the "inlet" and "outlet" parts of the muscular IVS and beneath the right cusp and the noncoronary cusp of the aortic valve. The membranous septum is divided by the tricuspid valve into two parts known as the pars atrioventricularis and the pars interventricularis. The membranous IVS comprises a small portion of IVS; however, it forms an important boundary between the right-sided chambers and the aortic root (Soto et al. 1980; Minette and Sahn 2006; Anderson et al. 2014).

The development of the IVS is discussed in chapter "Cardiovascular System Embryology and Development"—Cardiovascular System Embryology and Development in detail. However, a brief discussion is presented here:

1. Creation of a median ridge known as the muscular IVS, located near the apex of the ventricular floor; the edge of the muscular IVS is concave and free.
2. Height of IVS is achieved by expansion of the ventricles on each side.
3. IVS myoblasts start active proliferation and increase size.
4. Completion of the conal septum as a result of tissue extension, starting from the inferior part of the endocardial cushion up to the top of muscular IVS—these tissues merge with the neighboring portion of the conus septum.
5. Three sources of tissue take part in the closure of interventricular opening and formation of membranous IVS: the *left* bulbar ridge, the *right* bulbar ridge, and the endocardial cushions.
6. The final step is the closure of the opening above the muscular IVS with the development of the membranous IVS and when the interventricular foramen closes completely.

The *primary ventricular septum* or *primary ventricular fold* is produced following the trabeculation of the ventral part of the muscular IVS. However, there is a smooth part on the dorsal wall of IVS, named the *inlet septum*; this nomenclature is used because it is located nearby the AV canals. The *moderator band* or *septomarginal trabecula* is located on the right wall of muscular IVS, between the primary trabeculated fold and the inlet septum. This structure is a firm connection between the muscular septum and the anterior papillary muscle. When the right ventricular chamber expands, the moderator band is formed nearby the AV canal and dorsal muscular IVS. Eventually, a large part of the mature right ventricular chamber is formed by this expansion. However, if this anatomic area expands incom-

pletely, the developing tricuspid part of the atrioventricular canal remains attached to the interventricular foramen, leading to tricuspid atresia and/or other tricuspid valve anomalies (Lamers and Moorman 2002; Gittenberger-de Groot et al. 2005; Togi et al. 2006; Lin et al. 2012; Spicer et al. 2013, 2014; Poelmann et al. 2014; Laura et al. 2020; Annabi et al. 2021; Dakkak and Oliver 2021).

Embryologically speaking, a VSD can develop via one of the following mechanisms:

- Incomplete development of the proximal conotruncal swellings,
- Failed fusion of the muscular and membranous ventricular septa,
- Fusion in merging of the ventral and dorsal endocardial cushions (deficiency in atrioventricular septal),
- Deficiency in the development of the interventricular muscular septum.

VSDs may be classified using an anatomic classification system. Table 2 describes the various classification systems; these systems are based on both embryologic development of IVS and anatomic features of VSD (Soto et al. 1989; Van Praagh et al. 1989; Jacobs et al. 2000; Penny and Vick 2011; Morray 2019).

Pathophysiology of Ventricular Septal Defects

The main determinants of the disease and its pathophysiologic course are:

- The *amount* and the *direction* of the interventricular shunt which is determined by VSD size, the severity of the increase in pulmonary vascular resistance (PVR), and the balance between systemic and pulmonary pressure.
- The degree of *volume loading* imposed on each cardiac chamber (Tweddell et al. 2006; Aguilar and Eugenio 2009; Penny and Vick 2011).

Table 2 Classification of ventricular septal defects

Type of VSD	Mechanism of VSD	Occurrence of the lesion/ clinical outcome	Associated lesions
Nonmuscular VSDs include 3 groups: 1. Perimembranous 2. Outlet type 3. Inlet type			
1. Perimembranous VSD (also known as paramembranous VSD, conotruncal VSD)	Involves the membranous part of IVS; lies in the outflow tract of the left ventricle immediately beneath the aortic valve	The most common type of VSD; approximately 80% of all VSDs	Usually extends into the muscular, inlet, or outlet portion of the ventricular septum
1.1 *Superior border perimembranous VSD; also known as conoventricular VSD* Extends until below the aorta or pulmonary artery or both 1.2 *Posterior border perimembranous VSD* Involves tricuspid valve or its annulus 1.3 *Inferior border perimembranous VSD* Passes over the conduction bundle			
2. Outlet type VSD (also known as subpulmonary VSD, juxta arterial VSD, supracristal VSD, infundibular VSD, subarterial VSD, doubly committed)	*Mechanism and location:* the fibrous continuity that is *between aortic and pulmonary valves* borders the VSD; so, the VSD is located immediately below the pulmonary valve, just inferior to the center of the right coronary cusp	*Occurrence:* account for 6% of all VSDs; more common in the oriental population than in western countries (about 30% in oriental compared to 6% in western populations)	*Associated lesions:* risk of aortic valve regurgitation due to the location of defect just below the right coronary cusp The risk of heart block is really low due to the far location from his bundle
3. Inlet type VSD (atrioventricular canal type) VSD	Located just below the septal leaflet of the tricuspid valve	Accounts for 5–8% of all the VSDs	Straddling AV valve chordae
4. Muscular VSDs			
4.1 Apical *muscular*	Located in the apical muscular part of IVS with multiple apparent channels on the right ventricular side and a single defect on the left ventricular side	*ALL MUSCULAR VSDs account for 5–20% of all the VSDs*	
4.2 Mid *muscular* or central *muscular*	Located in the *mid-muscular* segment of IVS with multiple apparent channels on the right ventricular side and a single defect on the left ventricular side		
4.3 High *muscular*	Located in the upper part of the muscular IVS with multiple apparent channels on the right ventricular side and a single defect on the left ventricular side		
4.4 Swiss cheese *muscular*	Multiple defects in muscular IVS		

However, several secondary factors may also affect the pathophysiology of the disease. They are not universal in all VSD patients; however, they occur in some patients and include:

- Presence and degree of prolapse in aortic valve,
- Presence and degree of obstruction in blood flow through the pulmonary outflow tract or systemic outflow tract (Tweddell et al. 2006; Spicer et al. 2014).

During the early days after birth, the degree of the shunt is not severe even in large size VSD since pulmonary vascular resistance is relatively high in the early days of neonatal life. However, after normalization of the pulmonary vascular system and the resulting drop in PVR, the degree of shunt increases, leading to clinical symptoms and signs including those related to pulmonary overflow and left ventricular hypertrophy. In the minority of neonates, PVR does not drop after birth due to VSD leading to sustained neonatal pulmonary pressure, although this is not the typical clinical history of VSD. Typically, PVR remains low until late childhood or early adulthood in most cases. However, the effect of long-term pulmonary overflow would be increased work of the left ventricle, dilation of the left ventricle, and, if untreated, it will lead to left ventricular failure; add to this problem, the chronic effects of pulmonary overflow and the resulting pulmonary hypertension. The final clinical picture is a change in shunt direction from the left-to-right shunt to the usually irreversible right-to-left shunt pattern. If the disease is still ignored, the effects of long-term increased PVR result in right heart failure leading to final stage biventricular failure associated with irreversible pulmonary hypertension (Tweddell et al. 2006; Penny and Vick 2011; Spicer et al. 2013, 2014).

Diagnosis of Ventricular Septal Defects

Clinical Findings

Signs and symptoms are absent in early life; however, they start to appear at 4–8 weeks of age and somewhat earlier in premature neonates. The main clinical findings in VSD patients mainly include the following (Penny and Vick 2011; Spicer et al. 2014):

General Findings
- Growth retardation,
    - Due to several factors including increased blood flow to the pulmonary vascular bed leading to increased breathing work,
    - Decreased oxygen delivery to the systemic organs since larger amounts of blood flow are directed towards the lungs instead of the systemic vascular bed and other organs than the lungs,

Respiratory Findings
- The effects of increased pulmonary vascular blood flow on large airways may be seen as some degrees of pressure on the tracheobronchial tree leading to signs and symptoms of large airway disease,
- Increased pulmonary vascular blood flow in the microvascular system is associated with decreased free space for small airways in the peripheral lung fields,
- Signs and symptoms of smaller airways diseases like tachypnea, wheeze, and respiratory distress; these clinical findings are due to pulmonary vascular occlusive disease that may be seen even as early as 6–12 months of life, especially in patients having unrestrictive VSD,

Cardiovascular Findings

- Left ventricular hypertrophy (if occurs),
  - Associated with cardiac apex lateral displacement,
  - Hyperactive precordium is a common clinical finding in patients with volume or pressure overload,
- Pansystolic murmur—if found is usually inversely related to the size of VSD,
- Eisenmenger syndrome (i.e., severe pulmonary hypertension).
  - The patient may be cyanotic, associated with clubbing,
  - Usually, the pansystolic murmur vanishes and instead, a loud P2 is auscultated due to contraction of the right ventricle against high pressure pulmonary vascular system,
  - The clinical findings related to Eisenmenger syndrome do not develop until the teenage years,
- Irregular pulses,
  - Maybe seen in a minority of patients having underlying arrhythmias.

Chest X-Ray

Some general findings are seen in CXR of VSD patients and mostly include:

- Cardiomegaly,
  - Left ventricle hypertrophy,
  - Right ventricular hypertrophy,
- Increased vascular markings of the lung fields,
  - In patients with Eisenmenger's syndrome, the vascular markings fade off the lungs,
- Hyperaeration of the lung fields in patients with increased pulmonary blood flow and the effect on small airways, leading to hyperinflation of the peripheral lung fields (Minette and Sahn 2006; Penny and Vick 2011; Spicer et al. 2014).

Electrocardiography

No specific electrocardiographic abnormalities are associated with small VSD, especially in early neonates; however, signs of left ventricular hypertrophy may occur later in life. In addition, signs of right axis deviation and right ventricular hypertrophy are seen especially in patients with pulmonary over-circulation or pulmonary hypertension. A minority of VSD patients may have the right bundle branch block (RBBB) (Fig. 2). Complete heart block may be seen in some (Minette and Sahn 2006; Penny and Vick 2011; Bai et al. 2012; Spicer et al. 2014; Morray 2019).

Cardiac Catheterization

The main objective in evaluating VSDs is to assess pressures over the chambers and in vascular beds especially in the pulmonary system since the closure of a VSD in a patient with supra-systemic pulmonary pressure (Eisenmenger's syndrome) leads to deteriorating pulmonary hypertension and very poor outcome. Also, the complexity and number of "defects" could be accurately assessed with cardiac catheterization. In addition, any associated anomalies like concomitant aortic regurgitation can be evaluated, especially in patients with a sub-pulmonary (supracristal) VSD (Minette and Sahn 2006; Tweddell et al. 2006; Warnes et al. 2008; Penny and Vick 2011).

Echocardiography

Echocardiography is considered the cornerstone of all diagnostic modalities both in decision making and in the conduction of treatment. The initial echocardiographic assessment of VSD patients should focus mainly on the following aspects, preferably in the following order of assessment (Cao et al. 2011; Penny and Vick 2011; Spicer et al. 2014).
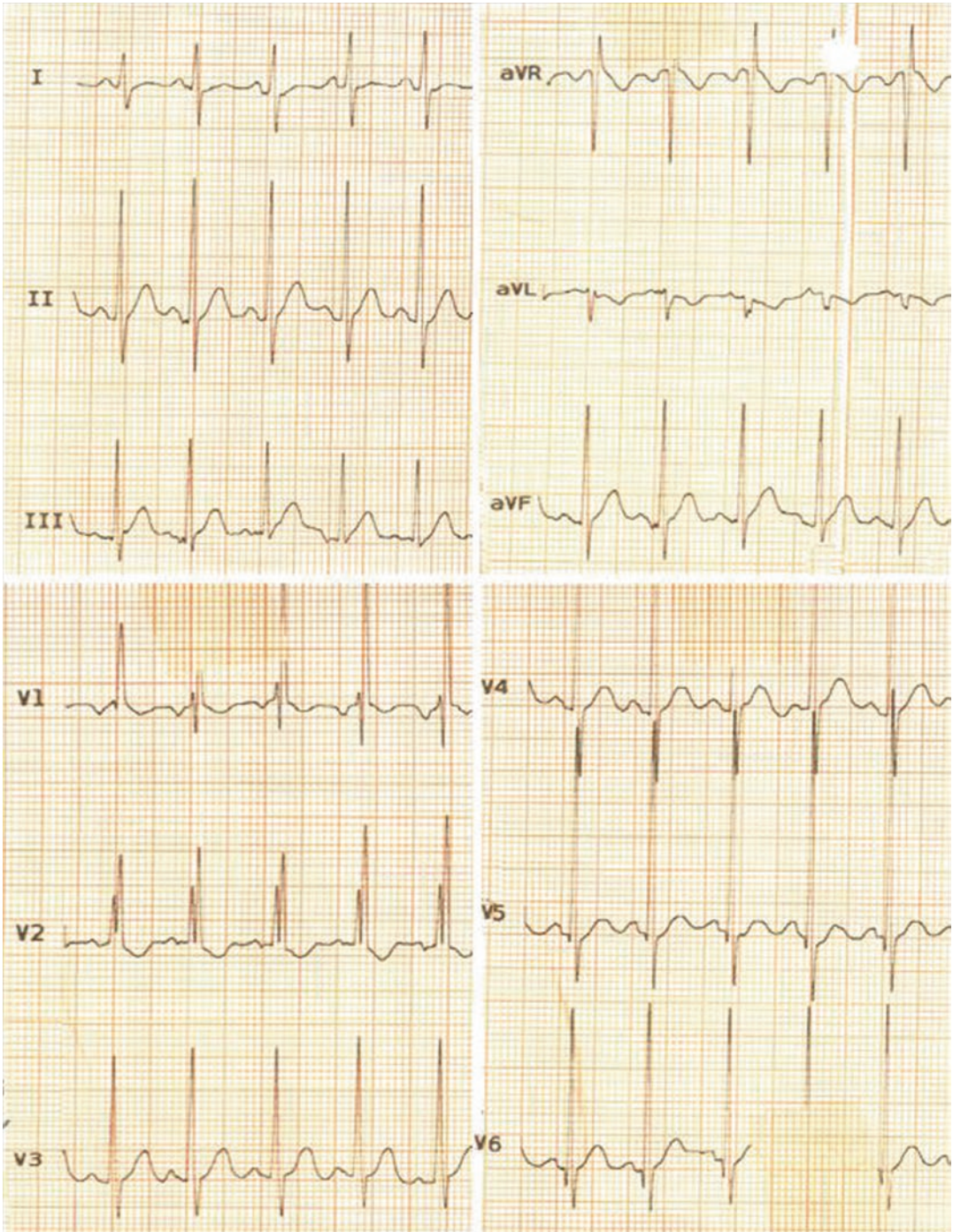
Fig. 2 Ventricular septal defect with pulmonary vascular disease. This ECG shows biventricular hypertrophy and left atrial abnormality. (Courtesy of Dr. Majid Haghjoo and Dr. Mohammadrafie Khorgami)

The initial echocardiographic assessment of the VSD should include the following items:

- Morphology of the defect,
- Malalignment of the defect considering the IVS,
- Size and number of the defect(s),
- Location(s) of the defect(s),
- Gradient across the defect.

Additionally, due to the possible impact of the VSD, the tricuspid valve should be assessed with special focus on the following items:

- Morphology of the tricuspid valve,
- Redundant/aneurysmal tissue in the tricuspid valve,
- Possibility of tricuspid regurgitation.

Right ventricular outflow tract (RVOT) impact from the VSD warrants assessment of the following:

- Hypertrophy of the right ventricle,
- Pulmonary stenosis (PS).

Left ventricular outflow tract (LVOT) should also be assessed due to concerns regarding the following:

- Subaortic ridge.
- Prolapse of the coronary cusps.
- Aortic stenosis/aortic insufficiency.

Mitral valve with special concerns regarding:

- Supra-mitral ring.
- Mitral stenosis/mitral regurgitation.

Also, the following aspects should be assessed:

- Left ventricular size/function.
- Left atrial size.
- Checking for the presence of patent ductus arteriosus.
- Checking for the presence of aortic coarctation.
- Right ventricular systolic pressure and pulmonary artery pressure should be assessed.

In postoperative/post-bypass echocardiographic assessment, it is imperative to assess any possible residual VSD or any possible VSD patch leak. Any residual deficits may require a further surgical reassessment of the defect for successful closure. Also, the function of the left and right sides of the heart and their adaptation to the new post-correction condition should be examined. Post-surgical or intervention, a complete and thorough echocardiographic assessment should be performed (Roberson et al. 1991; Minette and Sahn 2006; Cao et al. 2011; Penny and Vick 2011; Bai et al. 2012; Spicer et al. 2014).

Treatment of Ventricular Septal Defects

The main approach in treatment is *surgical patch closure* of the defect using the atrioventricular

valve approach or semilunar valve approach; ventriculotomy is rarely recommended due to its major sequelae. For muscular defects, especially those that are apical, *transcatheter closure* is used more than other types of VSD due to a very difficult surgical approach. Currently, transcatheter closure is not a routine practice for perimembranous VSDs since there is a considerable chance of heart blocks due to atrioventricular dissociation and some degree of impairments in adjacent valves may occur. With the invention of softer devices and lower profile delivery systems, this method may be used in the future with more frequency for perimembranous defects. Also, in some of the smaller patients with very "difficult" apical VSDs, there is still room for using pulmonary artery banding to prevent irreversible pulmonary hypertension in hope of future corrective surgery. The difficulties in closing muscular apical defects have led some centers to use a hybrid approach by inserting a device in the operating room after surgical exposure of the lesion through a sternotomy (Spicer et al. 2013, 2014; Santhanam et al. 2018; Morray 2019; Aboulhosn and Hijazi 2020; Brown et al. 2021; Cen et al. 2021; Chambault et al. 2021).

Anesthetic Management

A balanced anesthetic with the use of volatile agents and intravenous anesthetics is considered optimal; no conclusive data has been shown to favor any one agent or technique. The use of a pulmonary artery catheter is not indicated as routine monitoring; however, an invasive arterial catheter and the central venous catheter are both commonly used in these patients based on patient condition and co-morbidities. Pulmonary vascular resistance (PVR) should be managed to prevent and increase or decrease blood pressure; increased PVR leads to right-to-left shunting and desaturation; decreased PVR leads to pulmonary over-circulation and increased left-to-right shunting. On-table extubation is used in many centers with attention to PVR and pulmonary arterial pressure; in patients with prolonged defects (especially the adults) or those with associated mixed anomalies more sophisticated

assessment should be done before early extubation, especially ruling out any residual defect. Also, RV function, LV function, and pulmonary artery pressure should be assessed after bypass using TEE. Appropriate postoperative pain management is a key issue to address. In patients with a previous history of PA banding, care should be given to control hemostasis in redo corrective surgeries. In patients undergoing device closure, general anesthesia is often the preferred approach, especially when using TEE for the detection of residual defects (Takeuchi et al. 2000; Galante 2011; Twite and Friesen 2014).

Outcome

The overall outcome of children with VSDs is favorable. Jortveit et al. studied 3495 children with VSDs; their overall mortality and/or morbidity rate was very low coupled with a low incidence of arrhythmias (4.6%), aortic regurgitation (3.4%), endocarditis (3.4%), and pulmonary hypertension (0.3%) (Jortveit et al. 2016).

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