Anatomy and Physiology of VSD

Ventricular septal defect (VSD) may be defined simply as a hole in interventricular septum, or as an interventricular communication. In many ways, interventricular communication is a better term, since the hole between the ventricles is not always within the boundaries of the normal ventricular septum. (Baillard et al, 2015)

There is difficulty in determining the plane chosen to represent the defect when there is malalignment between apical and outlet parts of the ventricular septum, or there is overriding of an atrioventricular or arterial valve over the deficient muscular septum. (Baillard et al, 2015)

There are 2 options; the first is the geometric interventricular communication which is the basal continuation of the long axis of the ventricular septum. The second choice is to define the right ventricular boundaries of the entrance to the cone of space between the orifice of overriding valve and crest of muscular septum. This area is rarely planar and is considered a curved surface. This is actually the site closed by patch of surgeon or percutaneously by device. (Anderson et al, 2014)
Figure (1): Different planes of interventricular communication. The yellow arrow shows the continuation of the long axis of the muscular ventricular septum. This area marks the true geometric interventricular communication. The red double-headed arrow shows the margins of the curved surface that would be closed so as to restore septal integrity. *(Spicer et al, 2014)*

**Prevalence:**

Ventricular septal defect (VSD) is one of the most common congenital malformations of the heart, accounting for up to 40% of all cardiac anomalies. VSDs are recognized as being the commonest congenital cardiac malformations after bicuspid aortic valves and mitral valve prolapse. Since many patients can be asymptomatic, and many anomalies close with time, the precise prevalence of ventricular septal defect within populations varies between studies, depending on mode of diagnosis and age of the population. *(Hoffman et al, 2004)*

The defects can exist in isolation, can be complicated by additional intracardiac lesions, or can be part of more complex combinations, such as tetralogy of Fallot, double outlet right ventricle, transposition, or functionally univentricular hearts. *(Spicer et al, 2014)*
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- **Anatomy:**

  **The ventricular septum may be divided into 4 components:**

  The inlet septum is smooth walled and lies beneath the tricuspid valve, extending from the septal attachment of the tricuspid valve to the distal attachment of the tricuspid tensor apparatus.

  The apical trabecular septum is covered with trabecular muscle and lies distally in the septum.

  The infundibular, or outlet septum lies superior to the septal band and makes up the portion of the outflow tracts.

  The membranous septum: the last and the smallest part of the interventricular septum, lies between the anterior and the septal tricuspid leaflets and below the right and the non-coronary cusps of the aortic valve. (*Van Praagh et al, 1989*)

  ![Figure (2): Components of interventricular septum. (*Van Praagh et al, 1989*)](image)

**Embryological Development:**

The atroventricular septum forms from superior and inferior endocardial cushions within the atroventricular canal which grow towards each other and fuse to divide the canal into right and left components.
Growth and trabeculation of the ventricles accounts for formation of the major portion of the muscular septum as the medial walls of the ventricles become opposed and fuse.

While the ventricles enlarge, the AV canal moves rightward, such that the atria communicate with the primitive right ventricle. The conus swellings appear and merge to form the conus septum, separating the conus cordis into the anterolateral and posteromedial portions. The conus septum also separates the interventricular foramen from the AV canal.

Completion of the interventricular septum is accomplished by fusion of the superior portion of the muscular septum, atrioventricular and conotruncal cushions. Later this portion of the septum thins to become the membranous interventricular septum. *(Anderson et al, 2003).*

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**Figure (3):** Representation of the development of the interventricular septum from *Echocardiographic diagnosis of congenital heart disease (An embryologic and anatomic approach)* *(Valdes –Cruz and Cayre, 1999)*

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Defects of the outlet septum are thought to arise from failure of fusion of portions of the conus septum. Inlet defects may be caused by failure of fusion of the right superior endocardial cushion tissue with the muscular septum. Muscular defects, particularly in the trabecular septum, are probably due to excessive excavation of the septum during the growth of the ventricle or inadequate merging of the medial wall of the ventricles. Finally, failure of complete closure of the area that forms the membranous septum, in association with incomplete development of components of the muscular septum, could contribute to perimembranous defect. (Keane and Fyler, 2006)

- **Genetics And Cause:**

  Most forms of congenital heart disease, including ventricular septal defect, have multifactorial origins. An underlying inherited genetic predisposition could act synergistically with environmental causes to produce cardiac anomalies. Mutations in the transcription factors TBX5 and GATA4 have received particular attention. These factors are expressed in the heart and their interaction is vital for normal cardiac septation. (Maitra et al, 2009) Environmental factors such as teratogens, maternal infections, and untreated maternal metabolic illnesses (e.g., phenylketonuria and pregestational diabetes) have been associated with ventricular septal defect. (Jenkins et al, 2007)

- **Types of VSD:**

  In terms of phenotypic features, all VSDs, whether they are isolated or part of a more complex lesion, can be placed into one of three primary categories when they are viewed from the aspect of the cavity of the right ventricle. (Soto et al, 1980)

  The first category: muscular defects (about 5-20% of VSDs) are located within the trabecular portion of the septum, where they may be single or multiple (Swiss cheese type). These holes have exclusively muscular borders
and may open centrally, apically, anteriorly, or to the right ventricular inlet or outlet components.

**The second category**: perimembranous defects (about 80% of VSDs) lie in the membranous portion of the interventricular septum. Such malformations are characterised by presence of fibrous continuity between leaflets of the tricuspid and aortic valves in the posteroinferior quadrant of the defect. They can extend to open into either the inlet or outlet of the right ventricle. Perimembranous defects are infracristal and adjacent to the aortic valve just beneath the right and noncoronary cusps. The VSD extends caudally to the muscular crest and papillary muscle of the conus (muscle of Lancisi) where the conduction system traverses on the left ventricular side from the atrioventricular node. The defect also borders on the septal leaflet of the tricuspid valve. *(Bailliard et al, 2015)*

**The third category**: Supracristal defects are characterized by the presence of fibrous continuity between the leaflets of the aortic and pulmonary valves in the cranial margin of the defect. Because of the absence of any muscular subpulmonary infundibulum, these defects are doubly committed and directly juxta-arterial. The inferior margin of the defect is muscular and is located within and above the crista supraventricularis. The relationship of the aortic valve to this type is critical, and a leaflet can prolapse through the VSD and cause aortic insufficiency. The conduction system is not in surgical proximity and thus not a risk during surgery. This type accounts for about 5-7% of defects. *(Miller et al, 2006)*
Figure (4): Location of various types of ventricular septal defect. (Left) Location of defects viewed from the right ventricle. (Upper right) Typical doubly committed and juxta-arterial defect. (Lower right) Doubly committed, juxta-arterial, and perimembranous defect. *(Benson et al, 2009)*

Another system used numbers to distinguish between the different types. VSDs are generally classified into 1 of 4 groups depending upon their location in the interventricular septum. Type 1 representing perimembranous defects, Type 2 being muscular, Type 3 being doubly committed, and Type 4 said to represent the inlet defect. *(Moguillansky et al, 2010)*

Inlet VSDs are located posteriorly, immediately subjacent to the tricuspid valve septal leaflet in the inlet portion of the ventricular septum. The conduction system is at risk during repair because of the close proximity of the atroioventricular (A-V) node and conduction bundles that traverse along the inferior margin of the defect on the left ventricular side of the septum. *(Spicer et al, 2013)*
The problem with this approach is that defects opening to the inlet of the right ventricle can be muscular, perimembranous or part of atrioventricular septal defect. It is important to differentiate between the phenotypes of such defects due to the fundamental difference in the location of the atrioventricular conduction axis in each type. Regarding perimembranous defects, the axis lies posteroinferiorly and to the right hand of the surgeon operating through tricuspid valve. On the contrary, with inlet muscular defects, the axis runs in an anterocephaled direction and to the left hand of the surgeon. *(Spicer et al, 2014)*

**Figure (5):** Position of conduction axis in relation to different types of VSD.

(A) Perimembranous VSD  (B) Inlet Muscular VSD *(Spicer et al, 2014).*

- **Pathophysiology of VSD:**

  Several key components determine the pathophysiological response to a ventricular septal defect. Primary factors are the amount and direction of interventricular shunting and the degree of volume loading to the cardiac chambers. Secondary effects include prolapse of the aortic valve and obstruction to the pulmonary or systemic outflow tract. *(Penny and Vick, 2011)*
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Restrictive VSDs are those defects that are small in size with a pressure gradient between the two ventricles, such that the pulmonary artery is protected from the systemic pressure of the contralateral ventricle. While nonrestrictive VSDs are those of large size with no significant pressure gradient between the ventricles. Here, the pulmonary artery is exposed to systemic pressure.

Classification by size:

*Based on maximum diameter of VSD when compared to normal size of aortic valve annulus*

- **Small** – less than 1/3 of normal aortic valve annulus diameter.
- **Moderate** – 1/3 to 2/3 of the diameter of the aortic valve annulus.
- **Large** – more than 2/3 of normal aortic valve annulus size.

*Based on amount of pulmonary blood flow (Qp) relative to systemic blood flow (Qs) – Qp:Qs ratio*

- **Small** – Qp:Qs ratio lower than 1.5.
- **Moderate** – Qp:Qs ratio of 1.5 to 2.0
- **Large** – Qp:Qs ratio higher than 2.0 \( (Rolo \ et \ al, \ 2015) \)

Left-to-right shunting might initially be minimal in babies, with fairly large defects due to high pulmonary vascular resistance characteristic of the early neonatal period. As pulmonary vascular resistance falls, left-to-right shunting rises and the patient becomes increasingly symptomatic due to excessive pulmonary blood flow.

In some patients with large ventricular septal defects, pulmonary vascular disease can develop in later childhood or in early adult life. Over time, the symptoms of pulmonary overflow decrease and the patient starts to develop manifestations of low cardiac output due to development of
pulmonary hypertension. Eventually, the direction of shunting might reverse, leading to cyanosis and Eisenmengers syndrome. This result from chronic elevations of pressure associated with functional and structural alterations within the pulmonary vasculature. Presence of relevant longstanding pulmonary hyper-tension could ultimately lead to right-ventricular hypertrophy and dilation. (*Beghetti and Galie, 2009*)

Malformations located near the aortic valve (doubly committed, perimembranous, or muscular) can be complicated by aortic-valve prolapse and regurgitation, which result from generation of venturi forces, in which the high-velocity jet sucks the leaflet of the aortic valve into the restrictive defect. Absence of structural support for leaflets and abnormal commissural suspension may also contribute to this effect. (*Tweddell et al, 2006*)

A double-chambered right ventricle (DCRV) can develop over time and may be a result of the jet lesion of the RV endothelium caused by the high velocity VSD jet. This process results in formation of a proximal high-pressure chamber and a distal low-pressure chamber within the cavity of the right ventricle. (*Telagh et al, 2008*).

**Infective Endocarditis**

Traditionally, antibiotic prophylaxis was recommended routinely in patients with VSD to prevent procedure-associated endocarditis. However, later evidence indicates that endocarditis is most likely to result from chronically poor dental hygiene and daily activities. Recent recommendations suggest that patients with uncomplicated ventricular septal defects do not need antibiotics, but they need primary prevention of dental infections, with meticulous daily dental hygiene. However, antibiotic prophylaxis for dental and other procedures continues to be recommended for 6 months after complete surgical or trans catheter closure of a ventricular septal defect and
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indefinitely when a residual defect is present in relation to patch material. (Wilson et al, 2007)

Clinical scenarios:

1) Symptomatic young infant with pulmonary hypertension

   Infant presenting between 2 to 6 weeks of life with shortness of breath, interrupted feeding, failure to thrive and recurrent chest infections. The physical findings include tachypnea, tachycardia and hepatomegaly.

   The precordial activity is increased with parasternal lift. Auscultation reveals normal first heart sound and narrow split second heart sound with increased intensity of P2. Third heart sound (S3) may be present. A harsh pan systolic murmur best heard at lower left sternal border is present. A low pitched mid diastolic rumble occurring due to increased flow across the mitral valve indicates that the shunt is > 2:1. (Rudolph, 2001)

   In this situation, surgery is recommended within 3 months of birth. While awaiting surgery, medical treatment with low doses of diuretics and angiotensin-converting-enzyme inhibitors is typically used. With adequate monitoring of blood pressure and renal function. (Gantenbein et al, 2008) The early postoperative period can be complicated by pulmonary hypertension, which is usually treated with inhaled nitric oxide. (Bizzarro and Gross, 2005)

2) Asymptomatic patient without pulmonary hypertension but with volume overloaded left heart

   Many centers would recommend closure of ventricular septal defects with the aim of avoiding potential late left-ventricular dysfunction secondary
to ongoing dilation. Although the most optimum approach for this group of patients would be transcathether closure, the other alternative might instead be conservative management. (Gabriel et al, 2002).

3) Asymptomatic patient with small ventricular septal defect and no left-ventricular dilation

Usually a conservative approach is warranted in this subgroup. (Gabriel et al, 2002)

4) Asymptomatic patient with small defect and prolapse or regurgitation of aortic valve

Children with peri-membranous ventricular septal defects and more than trivial aortic regurgitation should be referred for surgery. A reduced threshold for surgery might be justifiable in patients with juxta-arterial defects because of their high risk of aortic regurgitation and low rate of spontaneous closure. (Tweddell et al, 2006).

5) Patient with Eisenmenger’s syndrome

Treatment of these individuals is mainly supportive. Dehydration and exposure to high altitudes should be avoided. Venesection may be used to reduce the effects of polycythemia, although its benefits are questionable in asymptomatic patients, as it can worsen iron deficiency and exercise intolerance and can amplify risk of stroke. (Spence et al, 2007) Endothelial-based treatments, particularly those aimed either at blockade of the potent vasoconstrictor endothelin 1 or at prevention of catabolism of the nitric oxide-dependent vasodilator cGMP, are used increasingly in this population of patients. (Fine et al, 2009)

Electrocardiographic findings in VSD:

ECG can be normal in patients with small ventricular septal defects. Volume loading of the left ventricle might result in left-ventricular
hypertrophy, whereas raised right-ventricular pressure due to either pulmonary hypertension or obstruction to the pulmonary outflow tract could lead to right-ventricular hypertrophy.

**Chest X-ray:** shows left or biventricular enlargement with increased pulmonary vasculature

**Echocardiography** is the mainstay of modern diagnosis of VSD.

Transthoracic echocardiography is used to localize the defect, assess the hemodynamic effect and impact of the defect on the morphology and function of the cardiac chambers. This is done using 2D, color Doppler, continuous wave and pulsed wave. (*Badano et al, 2011*).

Trans esophageal echocardiography has assumed an important role in intraoperative assessment of ventricular septal defect because it greatly facilitates confirmation of repair and early identification and correction of any residual lesion. (*Ayres et al, 2005*).

Three-dimensional echocardiography is becoming widely available and could provide important diagnostic assistance for assessment of unusually positioned ventricular septal defects and those associated with complex congenital heart malformations. (*Chen et al, 2006*)

**Role of Cardiac catheterization**

It is rarely needed in patients with uncomplicated defects. This procedure is usually reserved either to measure pulmonary vascular resistance in individuals with suspected or actual pulmonary vascular disease or to close the malformation by a trans catheter approach. (*Penny and Vick, 2011*).