

Introduction

Ventricular septal defect (VSD) is the most common form of congenital heart disease in childhood, occurring in 50% of all children with congenital heart disease and in 20% as an isolated lesion. The incidence of VSDs, which has increased dramatically with advances in imaging and screening of infants, ranges from 1.56 to 53.2 per 1000 live births. The ease of detection of small muscular VSDs is reflected in the higher incidence rates. A large review of the literature estimated the median incidence of VSDs at 2829 per 1 million live births (*Ghosh et al., 2013*).

VSDs are defects in any portion in the interventricular septum and are classified to inlet, muscular, conoventricular, and conal septal defects. In the inlet (atrioventricular canal) type, this area of the septum is formed by endocardial cushion tissue. It is associated with abnormalities of the atrioventricular valves (*Moguillansky et al., 2010*).

The muscular type is the second most common defect accounting for 10 – 20 % of VSDs. It consists of several subtypes: apical, central, marginal and Swiss cheese when multiple defects are present (*Rudolph, 2009*).

In the conoventricular type, the defects are located between the conal septum and muscular-septal band septum. It includes the membranous, perimembranous and malalignment or hypoplasia of the conal septum (***Penny and Vick, 2011***).

The perimembranous type is the most common type of VSD and commonly associated with abnormalities of the aortic valve. It is surrounded by fibrous tissue which can be responsible for the spontaneous closure of the defect. The hypoplasia of the conal septum is typically anterior deviation of the conal septum and causes a right ventricular outflow tract obstruction. A posterior deviation causes a left ventricular outflow tract obstruction (VSD associated with coarctation of the aorta and/or hypoplastic or interrupted aortic arch) (***Anderson et al., 2013***).

The conal septal defect (VSD of the right ventricular outlet) accounts for 5% of the defects. It overlies the conal septum and is located below the pulmonary valve. It is also called supracristal, infundibular, or subpulmonary defect (***Mavroudis et al., 2013***).

Left ventricular (LV) torsion is due to oppositely directed apical and basal rotation and has been proposed as a sensitive marker of LV function. 2D Speckle Tracking

Echocardiography (STE) can measure LV torsional deformation noninvasively by automated tracking of speckles from apical and basal short-axis recordings. The magnitude and characteristics of this torsional deformation have been described in different clinical and experimental studies, and it is well established that LV rotation is sensitive to changes in both regional and global LV function. Therefore, assessment of LV rotation represents an interesting approach for quantifying LV function (***Geyer et al., 2010***).

Aim of the Study

The aim of the study was to assess left ventricular function by 2D STE parameters in surgically repaired VSD among patients attending Pediatric Cardiothoracic Surgery Department and Pediatric Cardiology Clinic, Children's Hospital, Faculty of Medicine, Ain Shams University.

Ventricular Septal Defect

Ventricular septal defect (VSD) is a developmental defect of the interventricular septum (IVS) wherein a communication exists between the cavities of the two ventricles. VSD is a common congenital cardiac anomaly, occurring in both children and adults. It can occur in isolation or as part of more complex defects. Isolated VSDs are the second most common congenital cardiac defect encountered after bicuspid aortic valves (*Mavroudis et al., 2013*).

The isolated VSDs can be repaired surgically with an acceptable mortality rate. Recently nonsurgical transcatheter device closure of VSD is in vogue (*Prapa et al., 2013*).

Understanding the nature of the anomaly, clinical picture, the physiologic data and the natural history of VSD is important for planning the management strategy (*Vijayalakshmi, 2013*).

About 20 percent of VSDs are associated with almost all forms of congenital heart disease (CHD). They occur frequently as an integral part of other anomalies like tetralogy of Fallot (TOF), truncus arteriosus,

atrioventricular septal defects, double-outlet right ventricle (DORV) and transposition of great arteries (TGA) or in association with coarctation of the aorta (COA), patent ductus arteriosus (PDA), atrial septal defect (ASD), pulmonary stenosis (PS), etc (*Ranucci et al., 2015*).

The prevalence of VSD worldwide is relatively constant. However, the type of VSD that predominates in a region widely varies. In the United States, perimembranous VSDs are the most common types while in Asia, subaortic VSDs (outlet type) are the most common encountered types (*Kapoor and Gupta, 2008*).

Table (1): The relative frequencies of the major congenital heart defects

Lesion	Percentage of all lesions (%)
Ventricular septal defect	25-30
Atrial septal defect	6-8
Patent ductus arteriosus	6-8
Coarctation of aorta	5-7
Tetralogy of fallot	5-7
Pulmonary valve stenosis	5-7
Aortic valve stenosis	4-7
D–Transposition of great arteries	3-5
Hypoplastic left ventricle	1-3
Hypoplastic right ventricle	1-3
Truncusarteriosus	1-2
Total anomalous pulmonary venous return	1-2
Tricuspid atresia	1-2
Single ventricle	1-2
Double–outlet right ventricle	1-2
Others	5-10

(*Bernstien, 2012*)

Embryologic Background

The normal development of the IVS is a complex process and depends upon the endocardial cushions, conotruncal ridges, growth of tissues at the crest of the IVS and the muscular septum (*Van Lodewynk and Lynn, 2013*).

The VSDs result from a deficiency of growth or a failure of alignment or fusion of the component parts of the IVS beyond the first 7 weeks of intrauterine life. The reason for this delayed or incomplete closure is still unknown. The membranous VSD occurs as a result of failure of fusion of the endocardial cushions, the conotruncal ridges and the muscular septum (*Wenink, 2013*).

The outlet VSD may occur because of failure of fusion of the conal septum. The inlet VSD may occur due to the incomplete fusion of the right endocardial cushion with the muscular septum. Muscular defects may occur because of lack of merging of the walls of the trabecular septum or excessive resorption of muscular tissue during ventricular growth and remodeling. The fetal circulation is not altered significantly in uncomplicated VSDs (*Ciro and Borruto, 2014*).

Genetic Background

A high rate of chromosomal anomalies, syndromes and extra cardiac malformations are observed in patients with CHD. Chromosomal abnormalities are observed mostly in CHD associated with other malformations while the mutations in moreover, transcription factor genes are only observed in isolated defects. Genetic disorders responsible for these alterations can be classified into chromosomal disorders, Single gene disorders and Polygenic disorders (*Altin et al., 2015*).

Chromosomal disorders

Table (2) shows some of the chromosomal syndromes commonly associated with VSD.

This group of disorders are caused by absence or Duplicated chromosomes include trisomy 21 (Down syndrome), 22q11 deletion (DiGeorge syndrome), and 45X deletion (Turner syndrome). Five to eight percent of patients with CHD have an underlying chromosomal disorders. The recurrence risk of an offspring is that of the chromosomal disorder (*Hussein et al., 2009*).

Single-gene disorders

These disorders are caused by deletions, missense mutations and duplications within a gene. These disorders follow autosomal-dominant, autosomal-recessive, or X-linked inheritance patterns. Some examples are Holt-Oram syndrome, atrial septal defect with conduction defect, and supraventricular aortic stenosis. Three percent of patients with congenital heart disease have a single-gene disorder.

Recurrence risk is high in the first-degree relatives of patients with these disorders (*Brunea, 2008*).

Septation defects have recently been the subject of molecular studies, with the identification of the NKX2.5 gene implicated in nonsyndromic reticular atrial septal defect. Furthermore, studies of families with Holt-Oram syndrome in the elucidation of the TBX5 mutation causing atrial septal defects and VSDs. Further studies have shown an interaction between TBX5, GATA4, and NKX2.5 suggesting that transcriptional activation may be responsible for septal defects (*Chang et al., 2013*).

Polygenic disorders

This group encompasses many congenital heart defects.

They result from an interplay between environmental and genetic factors. Although there is no direct genetic

testing at this time for VSDs which are neither associated with chromosomal disorders nor they are associated with single gene disorders, recurrence risk can still be used for counseling reproductive adults as with paternal VSD, the recurrence risk in an offspring is 2% while with maternal VSDs, the recurrence risk rises up to (6-10%) (**Garcia, 2009**).

Table (2): Syndromes commonly associated with VSD

Syndrome	Percentage of CHD	Type Of CHD
Edwards syndrome (Trisomy 18)	100%	VSD TOF DORV
Patau syndrome (Trisomy 13)	80%	VSD ASD TOF
Partial Trisomy 4q (Del 4q, 21, 32)	60%	VSD ASD
Cri du chat syndrome (Del 5p)	30-60%	VSD
DiGeorge syndrome (Del 22q11)	50%	TA TOF VSD
Down syndrome (Trisomy 21)	40-50%	AVSD VSD

ASD: Atrial septal defect; AVSD: Atrio-ventricular septal defect; DORV: Double-outlet right ventricle; TA: Truncus arteriosus; TOF: Tetralogy of fallot; VSD: Ventricular septal defect.

(Ramaswamy, 2009)

Classification

Many classifications of VSDs have been proposed. Soto et al classified VSDs depending on their location in the IVS as seen from the right ventricular side. They are divided into four types of defects: 1. Perimembranous, 2. Muscular, 3. Outlet and 4 Inlet (*Gan et al., 2015*).

Anderson et al classified the VSDs according to i.e.:

- i. The relation of the defect to the atrioventricular conduction axis; The membranous septum.
- ii. The relation of the defect to the atrioventricular valves.
- iii. The relation of the defect to the arterial valves.
- iv. The position of the defect within the ventricular septum,
i.e. the inlet, trabecular or outlet part of the septum.

They have classified VSDs into four types: perimembranous, muscular defects, doubly committed juxta-arterial and juxtatricuspid (non-perimembranous) defects (*Gómez et al., 2014*).

Anatomical Classification

I. Perimembranous defects (infracristal, subaortic, membranous, conoventricular): They are the most common and account for 80 percent of all VSDs. These defects involve the membranous septum with extension into the-adjacent inlet, outlet or muscular septum. They lie in the outflow tract of the left ventricle (LV), immediately beneath the aortic valve. There is fibrous continuity between the aortic and tricuspid valves. The conduction bundle is always found in the posteroinferior margin of the defect. In perimembranous VSD, rarely LV to right atrium (RA) shunt (Gerbode defect) may be seen. Van Praagh's classification considers that 'perimembranous' is a misnomer for this VSD as 'peri' is the Greek prefix meaning 'around'. They suggest that the appropriate terminology should be 'paramembranous' VSD as the defect lies beside the membranous septum (**Hussain et al., 2014**).

In paramembranous defect, there can be a variable degree of anterior malalignment between the infundibular septum and the anterior ventricular septum such that the aortic valve appears to override the defect. Posterior or

leftward malalignment also occurs, producing subaortic stenosis. Anterior malalignment of the conal septum is seen in TOF and posterior malalignment is seen in interrupted aortic arch (IAA) (*Gan et al., 2015*).

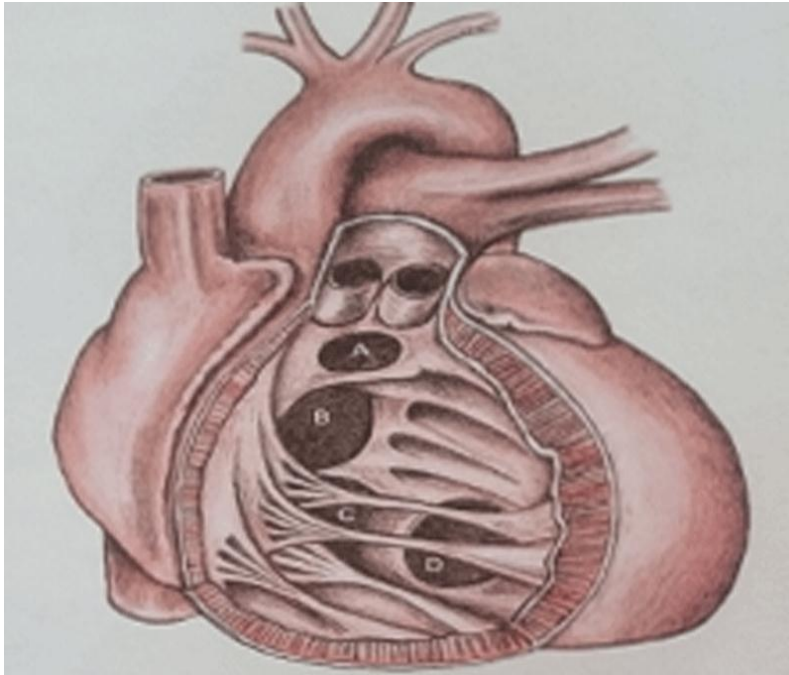
II. Muscular defects (trabecular): They account for 5 to 20 percent of all the VSDs. They are entirely bounded by the muscular septum and are often multiple, when viewed from the right side. Kirklin et al. further subclassified them depending on their location in the muscular septum as: (a) anterior, (b) midmuscular, (c) apical, (d) posterior. An anterior or marginal muscular defect is anterior to the septal band. A central midmuscular defect is posterior to the septal band. Apical defects are inferior to the moderator band and the posterior defects are beneath the septal leaflet of the TV (*Yoshimura et al., 2015*).

When multiple muscular defects are seen, it is often referred to as 'Swiss cheese' type of VSDs. Some believe that a Swiss cheese septum is actually an entity distinct from multiple VSDs. The morphology of the Swiss cheese septum is believed to originate from septal non-compaction during embryologic development. Thus unlike a group of muscular VSDs, Swiss cheese defects cannot close spontaneously (*Ganame, 2015*).

III. Subarterial or Outlet defects (supracristal, conal, infundibular, subpulmonary, doubly committed subarterial, doubly committed juxta-arterial): They occur in 5 to 7 percent of VSDs. They are situated just beneath the pulmonary valve and communicate with the right ventricular outflow tract above the supraventricular crest. The incidence is as high as 30 percent in Asian populations. This defect frequently leads to prolapse of the right coronary cusp or less likely the noncoronary cusp of the aortic valve causing aortic regurgitation (AR). In the perimembranous outlet defects there may be considerable degree of malalignment of the ventricular with the infundibular septum. The conduction system is remote to the outlet defects (**Penny and Vick, 2011**).

IV. Inlet defects (conal type, endocardial cushion type, atrioventricular septum type, juxtatricuspid): These VSDs account for about 8 percent of all the VSDs. They are located posteriorly and inferior to the membranous septum. A muscular inlet defect can be remote or have the conduction system bordering the defect superiorly. In the perimembranous inlet defects there may be some degree of malalignment of the ventricular and the atrial septum. There can then be

overriding or straddling of the tricuspid or mitral valve
(Vijayalakshmi, 2013).



A= Doubly committed subarterial ventricular septal defect; B= Perimembranous ventricular septal defect; C=Inlet or atrioventricular canal type ventricular septal defect; D=Muscular ventricular septal defect.

Figure (1): Schematic representation of the location of various types of VSDs (Ramaswamy, 2009).

Kirklin's Classification

Type I: VSDs are termed as supracristal, infundibular, juxtaarterial or conal. This defect lies caudal to the pulmonary valve in the infundibular portion of the right ventricular outflow tract.

Type II: VSDs are termed as perimembranous or paramembranous and are located adjacent to the