CONTEMPORARY RESULTS OF SURGICAL CORRECTION OF COMPLETE ATRIOVENTRICULAR SEPTAL DEFECT IN PATIENTS WITH OR WITHOUT DOWN SYNDROME – A RETROSPECTIVE REVIEW

Thesis Submitted By

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In Partial Fulfilment of The Requirement for The Degree Of

M.Ch in Cardiovascular and Thoracic Surgery

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Under the Guidance of

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DECLARATION

I, **Dr Nagananda L**, hereby declare that this thesis titled "Contemporary results of surgical correction of Complete Atrioventricular Septal Defect in patients with or without Down's Syndrome – A retrospective review" has been prepared by me under the capable supervision and guidance of **Dr. Sabarinath Menon**, Additional Professor, Department of Cardiothoracic and Vascular Surgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.

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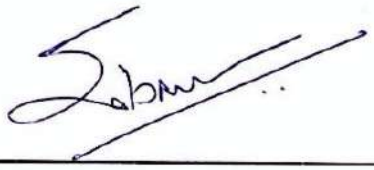
We hereby certify that this thesis titled

"Contemporary results of surgical correction of Complete Atrioventricular Septal Defect in patients with or without Down's Syndrome – A retrospective review" is the bonafide work of **Dr Nagananda L**, MCh CVTS resident, done under our guidance at Department of Cardiovascular and Thoracic surgery at Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.

He has shown keen interest in preparing this project.



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Institutional Ethics Committee
(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1503 /DECEMBER-2019 07.01.2020

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Dear Dr. Nagananda,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "CONTEMPORARY RESULTS OF SURGICAL CORRECTION OF COMPLETE ATRIOVENTRICULAR SEPTAL DEFECT IN PATIENTS WITH OR WITHOUT DOWN'S SYNDROME – A RETROSPECTIVE REVIEW (IEC/1503)" on 21st December, 2019.

The following documents were reviewed:

Original submission

1. *Covering letter addressed to the Chairman, IEC, SCTIMST dated 25.11.2019 with checklist*
2. *Full proposal*
3. *IEC Application Form*
4. *Observation chart*
5. *TAC Approval letter*
6. *Covering letter addressed to the Secretary, TAC (Clinical Studies) for waiver of Consent Form*
7. *CV of Principal Investigator and Co-Principal Investigators*

Revised submission

1. *Covering letter addressed to the Chairman, IEC, SCTIMST with checklist*
2. *Full proposal*
3. *IEC Application Form*
4. *Proforma*
5. *TAC Approval letter*
6. *Covering letter addressed to the Secretary, TAC (Clinical Studies) for waiver of Consent Form*
7. *CV of Principal Investigator and Co-Principal Investigators*

The following members of the Ethics Committee were present at the meeting held on 21st December, 2019 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
3.	Dr. K R S Krishnan	M.E., Ph.D.	Male	Medical Technology	Yes
4.	Dr. Anand Kumar A	MD, DM	Male	Clinician	No
5.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
6.	Dr. Harikrishna Varma PR	Ph.D(Materials Science)	Male	Medical Technology	Yes
7.	Dr. V. Raman Kutty	M D, M Phil, M P H	Male	Health Sciences Expert/Clinician	Yes
8.	Dr. P. Manickam	BSMS, MSc (Epid).,PhD	Male	Health Science Expert/ Social Scientist	No
9.	Dr. Aneesh V Pillai	BA. LLB (Hons.), LLM, Ph. D, SET (Law)	Male	Legal Expert	No
10.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
11.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC

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ACKNOWLEDGEMENTS

Writing this thesis has been fascinating and extremely rewarding. I would like to thank a number of people who have contributed to the final result in many different ways.

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LIST OF ABBREVIATIONS

AVSD – Atrioventricular Septal Defect

AVVR – Atrioventricular valve regurgitation

PAH – Pulmonary Arterial Hypertension

PVR – Pulmonary Vascular Resistance

EMT - Epithelial Mesenchymal Transformation

AV – Atrioventricular

CHD – Congenital Heart Disease

CPB – Cardiopulmonary Bypass

LSL - Left superior Leaflet

LLL - Left Lateral Leaflet

LIL – Left Inferior Leaflet

RSL – Right Superior Leaflet

RIL – Right Inferior Leaflet

LA – Left Atrium

LV – Left Ventricle

RVSP – Right Ventricular Systolic Pressure

RA – Right Atrium

RV – Right Ventricle

ACC – Aortic Clamp Time

MV – Mitral Valve

JET – Junctional Ectopic Tachycardia

SVT – Supra-ventricular Tachycardia

CHB – Complete Heart Block

VIS – Vasoactive Inotropic Score

MV – Mitral Valve

SYNOPSIS

Objectives: Down Syndrome is associated with complete AVSD and when compared to their normal counterparts have poorer outcomes. The aim of this study is to compare the midterm outcome of patients undergoing atrioventricular canal defect repair with respect to Down's and non-Down's Syndrome.

Methods: 77 infants underwent surgery for correction of Complete Atrioventricular septal defect in division of Paediatric cardiac surgery, department of CVTS at SCTIMST between 2008-2017, 42 (54.54%) had Down Syndrome and 35 (45.45%) were of normal chromosomal pattern.

Results: Mean age at surgery for Downs was 8.33 ± 2.08 and for non-Downs it was 7.6 ± 2.58. Two types of techniques were used, the double patch repair was done for 48 (62.33%) and modified single patch repair for 29 (37.66%). Except for the significant (P < 0.0001) less CPB and ACC time in modified single patch repair, there was no association on the technique used with the presence of Downs and non-Downs. Atrial ectopics being the most common arrythmia was seen more in non-Down infants and was statistically significant (P 0.008). Out of the 77 patients who underwent AVCD repair, there were 5 (6.49%) in-hospital mortality, in that 1 (2.38%) infant was Down's and the other 4 (11.42%) non-Down's (P value 0.11).

Out of the remaining 72 patients who were discharged, 3 (3.86%) had a late mortality at 2, 12 and 36 months from the date of surgery. The infants who died at 2 and 12 months were Down Syndrome whereas the child who died at 36 months belonged to the non-Down group.

Out of the remaining 69 in the study group 5 (6.49%) were lost to follow-up.

The remaining 64 (83.11%) children were followed up in OPD at regular intervals of 1 month, 3 months, 6 months, 1 year and 3 years and Echocardiography was done and assessed for any improvement or worsening of AVVR and PAH.

All patients had a significant fall in their PAH in the post-operative period. This fall in PAH when compared to the pre-operative PAH was statistically significant.

Patients with Downs syndrome had slightly increased incidence of moderate or moderate to severe AVVR (14.64%) in the immediate post-operative period when compared to the group with Non-Downs syndrome (12.9%).

The incidence of AVVR when followed up for 3 years showed a progression in the incidence of moderate to severe AVVR in both groups with 22.8% in patients with Downs Syndrome and 17.24% in Non-Downs.

Conclusion: Presence of Downs syndrome has no effect on the outcomes of surgical repair of complete AVSD. Both early and late results after surgical correction are comparable. There is a constant progression of residual left AVVR.

Recent advances in surgical practise and ICU management has resulted in reduced early and late mortality. Primary surgery of complete AVSD is safe and can be accomplished with minimal morbidity and mortality in Down and non-Down Syndrome infants.

Keywords: Atrioventricular septal defects, Down Syndrome, AVVR, PAH, Pulmonary Vascular Resistance.

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CONTEMPORARY RESULTS OF SURGICAL CORRECTION OF COMPLETE ATRIOVENTRICULAR SEPTAL DEFECT IN PATIENTS WITH OR WITHOUT DOWN'S SYNDROME – A RETROSPECTIVE REVIEW

INTRODUCTION

Infants having Complete Atrioventricular Septal Defect (AVSD) usually presents with congestive heart failure within the first 2–4 months of infancy if not repaired [1]. Clinical evaluation, 2D-Echocardiography with Doppler has become the standard methods to diagnose AVSD. These children ideally should be operated within the ages of 3 and 6 months of age because after 1 year it is frequently associated with the risk of elevated pulmonary vascular resistance and risk of becoming inoperable [1].

The prevalence of Congenital heart disease in infants with Down's Syndrome is 40% while it is only 0.3% in their chromosomally normal counterparts [2]. Complete AVSD is one of the most common congenital heart defects seen in patients with Down Syndrome [2]. Early onset of pulmonary vascular disease is a critical factor in patients with complete AVSD and Down Syndrome. Down Syndrome is also an independent risk factor in development of PAH. This along with any residual AVVR would further complicate the mid and long-term results in this subgroup of patients [2].

The various techniques described for repair of Complete Atrioventricular canal defect include the Single patch, Double patch, Modified Single patch and the No patch technique. Even though these different techniques hold the same principle of the operative management, studies suggests that the two-patch technique preserved the atrioventricular valve function better [3,4], whereas some suggest that the modified single patch technique is better as it minimizes the ischemic time and leads to an excellent outcome [5]. However, a review of each individual technique, has shown there is no significant difference in their long-term outcome [6]. The results of these various techniques can be evaluated by examining the operative mortality and the reoperation rates for mitral

insufficiency, pacemaker, and residual shunts. The operative mortality for AVSD repair was known to be low and most of previous studies achieved in-hospital death of less than 5 % [6]. Improvement in the techniques of cardiopulmonary bypass, anaesthesia and post-operative management have shown improved results with early primary surgical repair. In spite of these advances residual AVVR and severe PAH and the need for re-intervention remains a problem. This study is a retrospective study on midterm results with surgery and postoperative outcomes with respect to AVVR and PAH.

AIM OF THE STUDY

Aim of Study: To compare the midterm outcome of patients undergoing atrioventricular canal defect repair with respect to Down's and non-Down's Syndrome.

Hypothesis: Patients with Down's Syndrome who undergo Complete Atrioventricular Septal defect repair will have poor outcomes when compared to patients without Down's Syndrome.

Objectives:

1. Assess the midterm results of surgical repair of Complete Atrioventricular Septal defects.
2. Compare the early surgical outcomes in patients with and without Down's Syndrome.
3. Compare the late surgical outcomes with respect to degree of residual mitral regurgitation and Pulmonary arterial hypertension in both groups.
4. Analyze the re-intervention rates and cause for re-intervention.
5. Look into mortality rates and assess survival.
6. Review of the various surgical techniques used for repair.

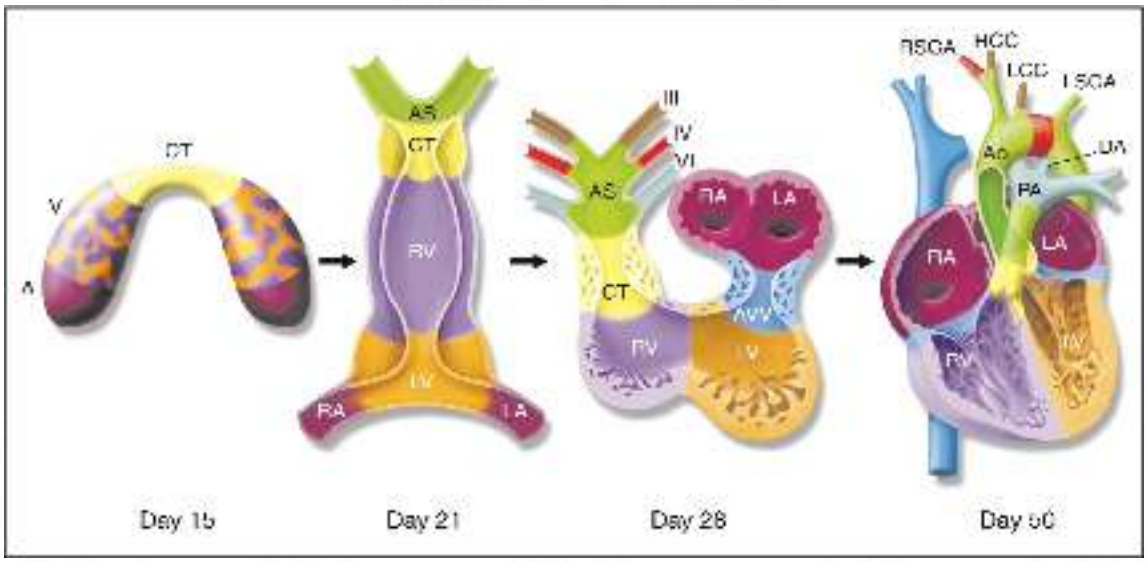
REVIEW OF LITERATURE

Morphogenesis of the Cardiovascular System

The heart is the first major organ to form in the developing embryo [7]. (Figure 1-1) depicts various stages in cardiac morphogenesis. A timeline of important stages occurring during the formation of the heart is depicted in (Figure 1-2).

The earliest identifiable cardiac structure is seen at day 15 of gestation when the cardiac progenitor cells have been committed to a cardiogenic fate in response to an inducing signal and are organized into a crescent shape [7] . At three weeks of gestation, the bilaterally symmetric heart primordial cells migrate to the midline and fuse to form a single linear heart tube which is comprised of an inner endothelial lining and an outer myocardial cell layer separated by cardiac jelly, an extracellular matrix secreted by the myocardial precursor cells.

Figure 1: Schematic of Cardiac Morphogenesis

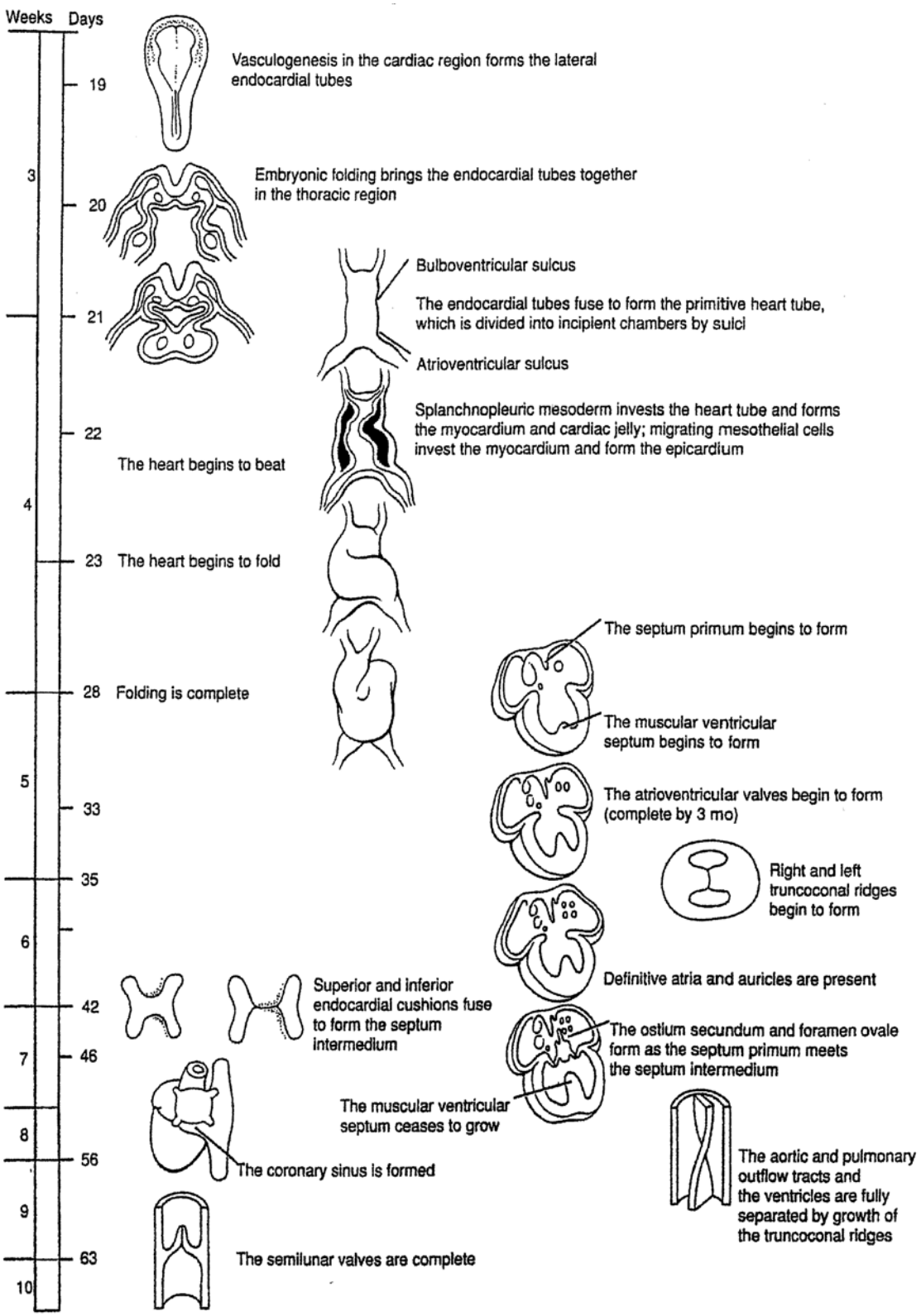


Note: A=atrium, Ao=aorta, AVV=atrioventricular valve segment, AS=aortic sac, CT=conotruncal segment, DA=ductus arteriosus, LA=left atrium, LCC=left common carotid, LSCA=left subclavian artery, LV=left ventricle, PA=pulmonary artery, RA=right atrium, RSCA=right subclavian artery, RCC=right common carotid, RV=right ventricle, V=ventricle.

The tube structure initiates rhythmic regular contractions at approximately day 23 [8]. The heart then undergoes rightward looping positioning the atria (inflow chambers) above the ventricles (outflow chambers) in response to the contractions. Rightward looping is essential for proper orientation of the ventricles and for alignment of the heart chambers [9].

Following cardiac looping, which is complete by day 28, the atrial and ventricular chambers of the heart become morphologically identifiable.

Figure 2: Timeline of Cardiac Morphogenesis



During this time, blood begins to circulate through the embryo and is unidirectional by day 24 [10]. Blood flow is said to be in series at this stage, indicating that the blood flows in sequence from the first pump (pulmonary circulation) into the second pump (systemic circulation) and back around to the first.

Atrial septation is the first step in the separation of the systemic and pulmonary circulations. The septum primum is a wedge of tissue that grows caudally from the roof of the atrium towards the AV canal. Prior to the closure of the interatrial opening (ostium primum), programmed cell death, or apoptosis, occurs near the superior edge of the septum primum creating a new opening (ostium secundum), maintaining an interatrial communication [10]. To the right of the septum primum, a second septal structure (septum secundum) forms. The septum secundum does not close completely, leaving an interatrial channel (foramen ovale), which is the interatrial communication that is present throughout fetal life. Concurrently, the muscular interventricular septum is formed from the bulboventricular sulcus.

At about 5 weeks, the endocardial cushions of the AV canal appear. The endocardial cushions are derived from the cardiac jelly. Two major processes occur during the development of the atrioventricular canal [8]. The first is growth and fusion of the superior and inferior endocardial cushions which results in septation of the atrioventricular canal. Secondly, there is closure of the ostium primum and the ventricular septum by the superior and inferior endocardial cushions. The AV canal subsequently shifts to the right to align the atria with their respective ventricle. In addition to septation of the atrioventricular canal, the endocardial cushions also contribute to the formation of the tricuspid and mitral valves.

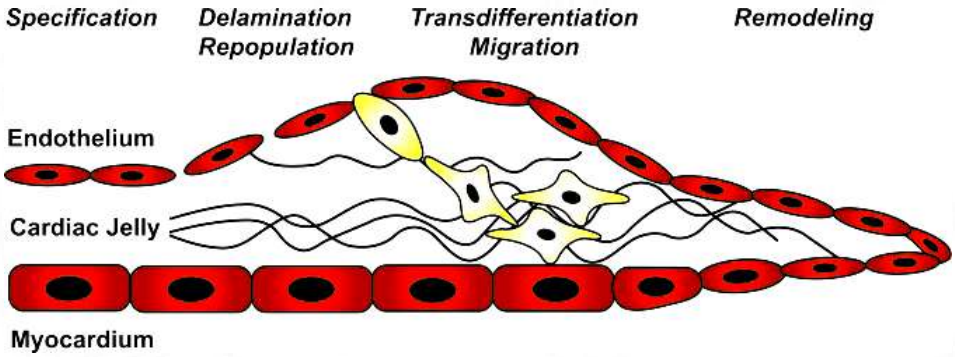
The outflow tract, also called as the conotruncus, undergoes septation separating the aorta from the pulmonary trunk. Swellings from the right and left walls of the bulbus cordis fuse to form the conal septum [10] . As these swellings grow in a spiral fashion, the aorta and pulmonary trunk twist around each other. Part of the conotruncal swellings fuse with the inferior endocardial cushion and the muscular interventricular septum to form the membranous interventricular septum, separating the right and left ventricles. Extensive valvar remodeling and ventricular growth then takes places to ultimately form the developed heart [7].

The major categories of developmental processes involved in cardiac morphogenesis along with associated heart defects are summarized below:

1. *Cellular migration*: Early in development, neural crest cell migration contributes cells that participate in conotruncal septation. Alterations in this process leads to conotruncal malformations, such as supracristal ventricular septal defects, tetralogy of Fallot, and transposition of the great arteries.
2. *Cardiac hemodynamics*: As blood passes through the developing heart, the differential pressure on the various areas of the chamber walls causes changes in the chamber shape and dimension. Abnormal cardiac hemodynamics can lead to abnormal distention of the cardiac chambers and valves, which can change their shape and function. Malformations linked to abnormal cardiac hemodynamics include hypoplastic left heart syndrome, coarctation of the aorta, and perimembranous ventricular septal defects.
3. *Cell death*: Apoptosis molds the developing heart by removing tissue, an important process in the formation of cardiac valves, the trabeculated ventricular wall, and the timely development of shunts between the developing right and left heart. Excessive cell death is associated with septal defects, while

insufficient cell death is associated with Ebstein's anomaly, a condition in which the tricuspid valve fails to separate from the ventricular wall.
4. *Extracellular matrix function*: Cardiac jelly is the one which forms the endocardial cushions at the AV orifice and in the outflow tract. The endocardial cushions act as anchors for the valves. Cardiac jelly fills the space between the inner wall and the outer surface. The cardiac jelly acts as the medium through which endothelial cells lining the atrioventricular lumen detaches and migrates into the jelly, where they undergo transformation, which gives rise to myocardial cells that proliferate and in turn give rise to the cardiac cells which contributes to cardiac valve formation. This process is known as epithelial-mesenchymal transformation (EMT). Figure 1- 3 illustrates the EMT process. Atrioventricular septal defects can occur if the extracellular matrix does not form fully functional cardiac cushions.

Figure 3: Anatomy of Heart Valve Formation via Epithelial-Mesenchymal Transformation



5. *Targeted growth*: This process is necessary for the formation of certain heart structures. The direction of pulmonary vein growth is determined by a specific growth signal from the left atrium. Abnormal targeted growth processes during heart development can lead to abnormalities, such as abnormal pulmonary

venous return and cor-triatriatum which stems from the faulty incorporation of the common pulmonary vein into the left atrium.

6. *Establishment of visceral situs and cardiac looping*: Establishment of right and left sides of the body and looping abnormalities result in ventricular inversion and reversed right or left position of organs.

Atrioventricular Septal Defects

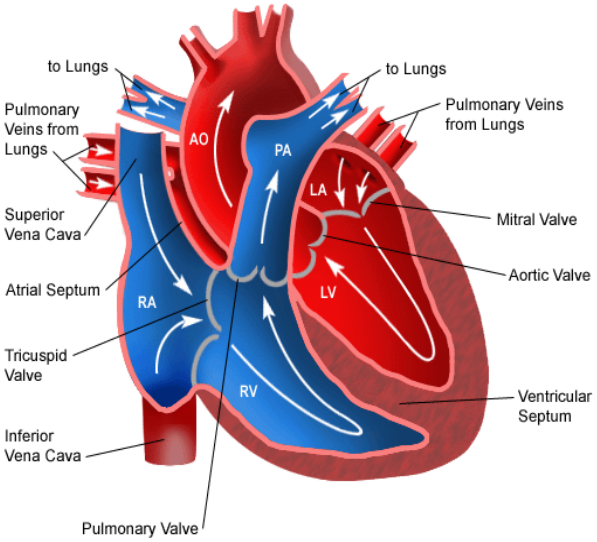
AVSDs, also known as atrio-ventricular canal defects or endocardial cushion defects, include anomalies categorized with involvement of the atrial septum, the ventricular septum, and one or both of the atrioventricular valves. (Figure 1-4) demonstrates defect components and mixing of blood.

AVSDs account for approximately 7% of all congenital heart defects [11] .

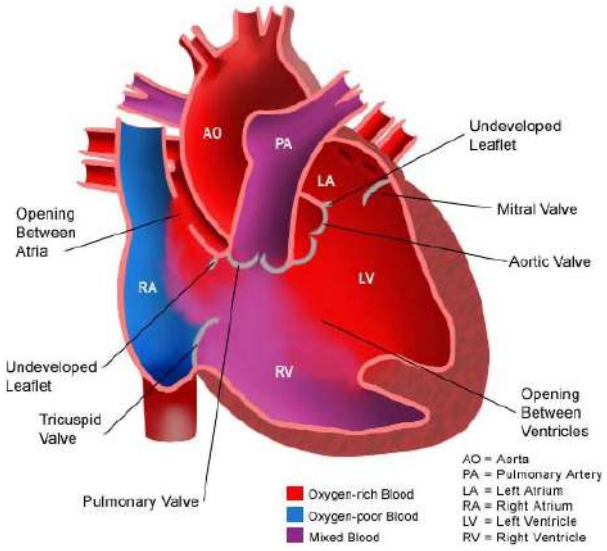
The AV septum and valves are formed from progenitor cardiac structures, endocardial cushions [12] . During morphogenesis, the endocardial cushions expand as they are infiltrated by extracellular matrix secreted from the surrounding myocardium. The cushions then fuse and undergo remodelling to form the AV valves and septa [13]. Formation of the AV valves occurs between estimated gestational ages of 52 and 56 days [14] .

AVSDs arise from the abnormal development of the endocardial cushions where the superior and inferior cushions do not fuse completely. The degree of severity of the defect is dependent on the stage at which the developmental failure occurs . As a consequence of non-fused cushions, the central part of the heart crux fails to form [12].

Figure 4: Normal Heart and Complete Atrioventricular Septal Defect Anatomy



a. Normal Heart



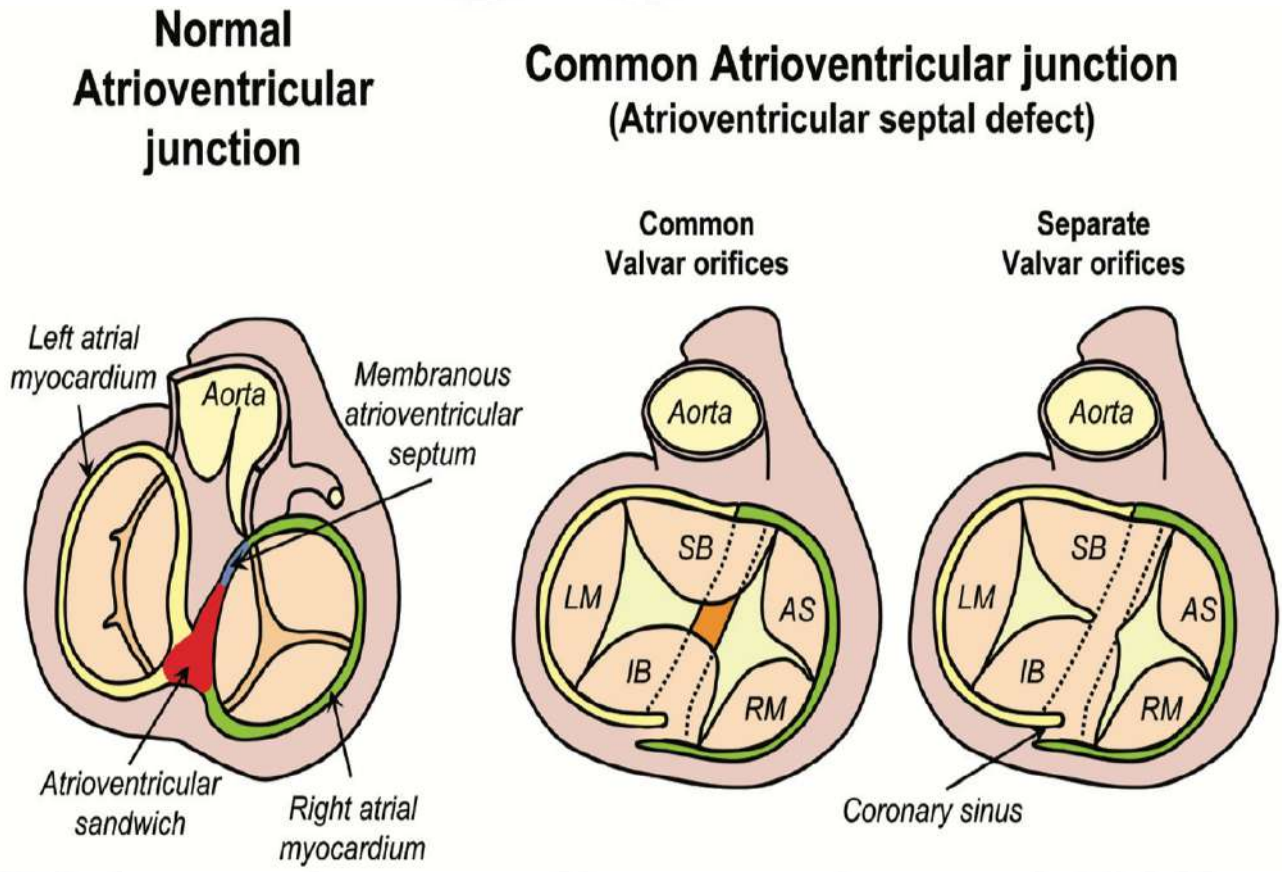
b. Complete Atrioventricular Septal Defect

ANATOMY

ATRIOVENTRICULAR JUNCTION AND VENTRICULAR MASS

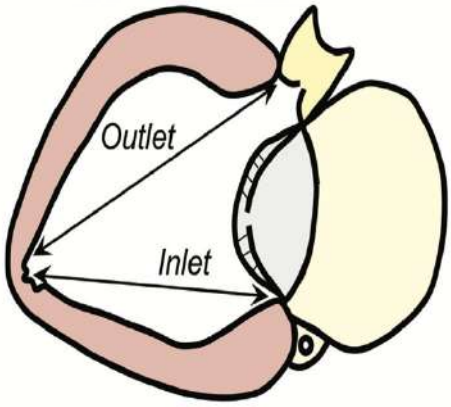
All hearts with AVSD have a common AV junction. This is in contrast to the figure-of-eight configuration of the AV junction in normal hearts [15](Figure 1-5). It is not same as the valvar junction with the valvar orifice(s). The valvar orifices can be double in the setting of a common atrioventricular junction, as in hearts with separate valvar orifices. Absence of the usual figure-of-eight configuration makes the aorta to lie more anteriorly than normal due to the lack of a recess to accommodate the aortic outflow tract. This anterior position of the aorta is part of the deformity of the ventricular mass; inner length is shorter than the outlet length (Figure 1-6). This inlet-outlet disproportion in AVSD contrasts normally structured hearts which has equal inlet-outlet length. The atrial septum fails to meet the ventricular septum, usually leaving a large defect which is the atrioventricular septal defect. The crest of the ventricular septum usually has a scooped appearance [15].

Figure 5: Normal AV junction (left) and the common AV junction with a common valvar orifice (middle) and 2 separate orifices (right).



AS = anterosuperior, IB = inferior bridging, LM = left mural, SB = superior bridging, RM = right mural.

Figure 6: The inlet-outlet disproportion in hearts with atrioventricular septal defect.



LEAFLETS AND SUBVALVAR APPARATUS

The valve usually consists of 5 leaflets. 2 of these leaflets are across the interventricular septum, inserted into both the right and left ventricles through the supporting apparatus, called the bridging leaflets. One leaflet is completely in relation to the left ventricular chamber, over the lateral aspect of the valvar junction (left mural leaflet). The other 2 leaflets are related to the right ventricular cavity, one located antero-superiorly (anterosuperior leaflet) and the other inferiorly (right mural leaflet). If both bridging leaflets were connected through a strap of leaflet tissue, there would be separate valvar orifices seen as in the partial type.

The left-sided valve comprises 3 different leaflets: the mural and both bridging leaflets. This valve is wrongly called a mitral valve, because there is no similarity between the two. The mural leaflet in AVSD covers approximately 20% of the entire circumference of the left orifice, whereas the normal mitral valve supports approximately 67% of the circumference [15] (Figure 1-7). The

papillary muscles supporting the mitral leaflet in normal hearts are obliquely oriented, whereas those in AVSD are in a superior-inferior relationship to each other [15]. This is demonstrated in cross-sectional echocardiography. When the left valve in AVSD is different from the normal mitral valve it should be noted that the term cleft is inappropriate to describe the gap between the bridging leaflets. This is because, the cleft is used to describe a slit-like space within a single leaflet instead of a gap between 2 separate leaflets. If the gap in AVSD was an actual cleft, it would be possible to close the cleft without loss of effective valvar orifice area. Since the gap is a space between 2 separate leaflets, its closure will lead to loss of the effective valvar area.

The right-sided valve shares some features with the normal tricuspid valve, despite having 4 leaflets. The anterosuperior and mural leaflets in AVSD are comparable with those of the normal tricuspid valve. The circumferential proportion of the mural leaflet in the right valve is almost similar to that of the counterpart in the left valve, the ratio being almost consistent, irrespective of the degree of extension of the superior bridging leaflet into the right ventricle, ranging from minimal extension (Rastelli type A) to the most significant extension (Rastelli type C) [16]. As the superior bridging leaflet extends more into the right ventricle, there is associated reduction in the size of the anterosuperior leaflet [16] (Figure 1-8).

Figure 7: Normal mitral valve and "left-sided atrioventricular valve" in atrioventricular septal defect.

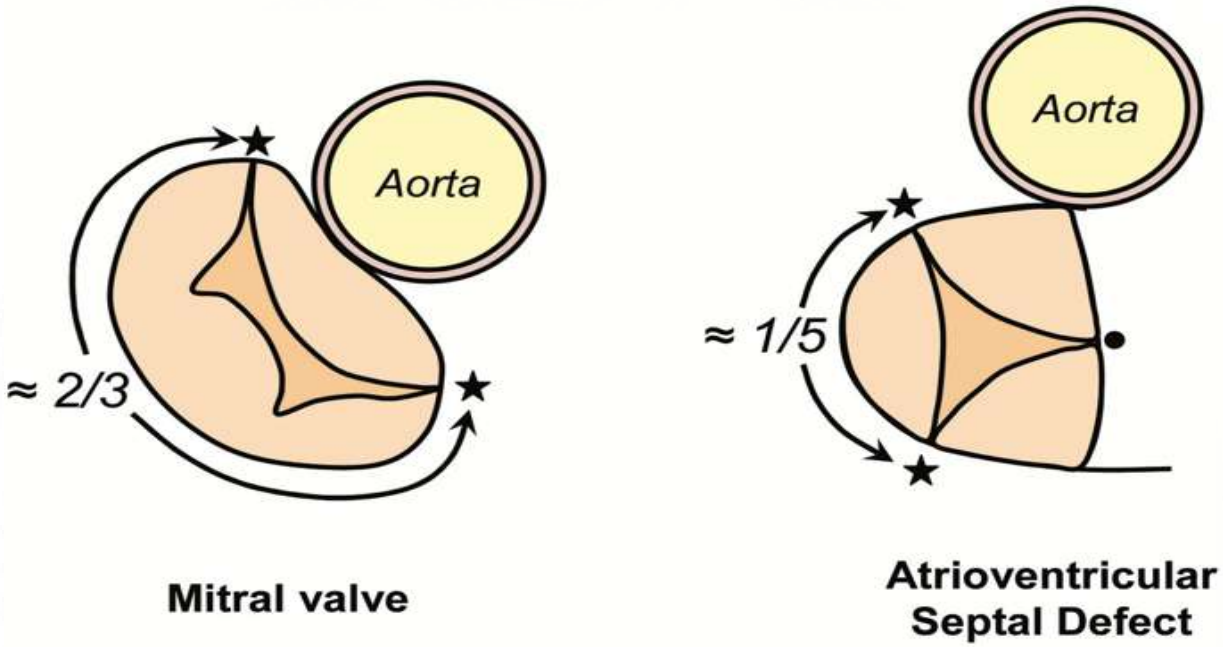
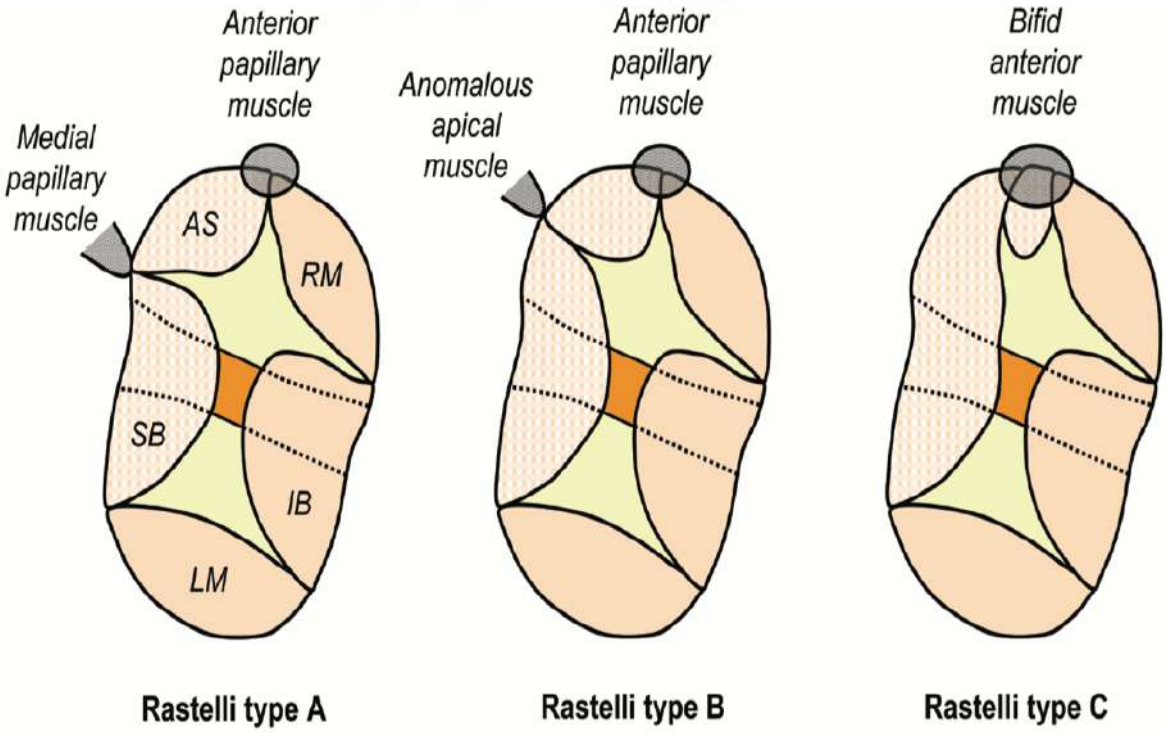


Figure 8: Anatomical variations of the atrioventricular valvar leaflets according to the Rastelli classification.



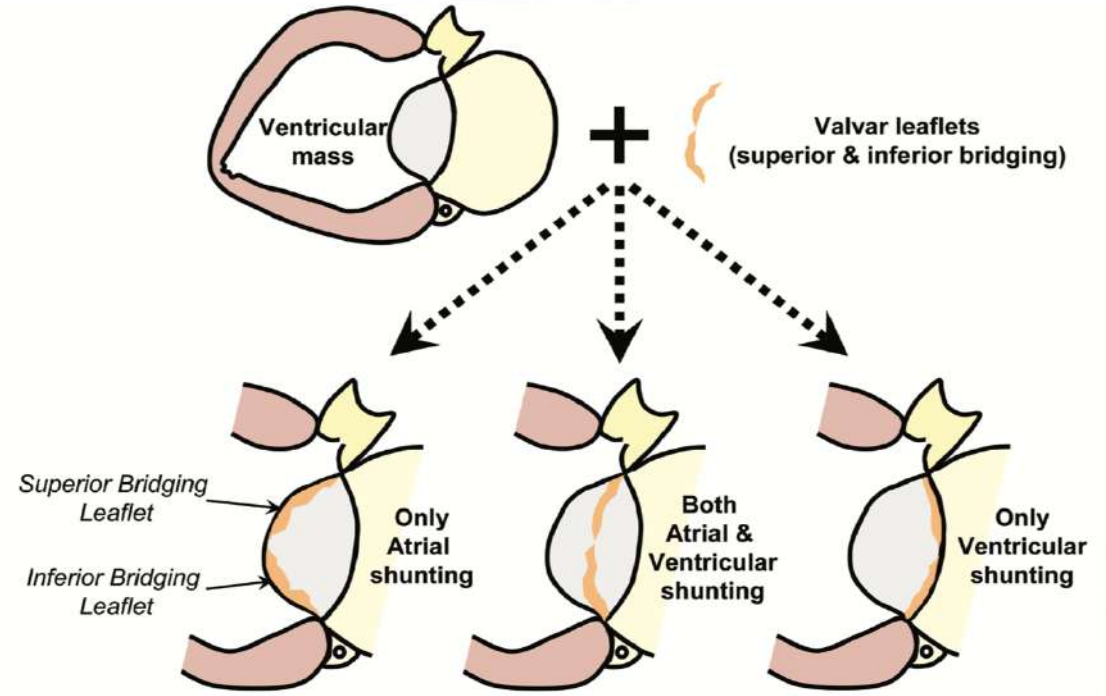
AS = anterosuperior, IB = inferior bridging, LM = left mural, SB = superior bridging, RM = right mural.

LEVEL OF INTRACARDIAC SHUNTING

AVSD are usually categorized according to the anatomic variation of the atrioventricular orifice, either being largely common to both ventricles or divided by the connecting leaflet tissue between the facing bridging leaflets [17]. From the surgical point of view, the decisive distinction is the level of intracardiac shunting that happens through the defect. Based on this 3 distinct patterns of shunting can exist: at the atrial level only, at both the atrial and ventricular levels, and at the ventricular level only. According to Becker and Anderson, “if the valve leaflets are removed, there is no way of distinguishing the variants of this group from one another” [17]. This is based on the observation that all hearts of AVSD have comparable features in the ventricular mass and a common atrioventricular junction, in other words, the major anatomical variations are determined by how the bridging leaflets are related to the septal structures. The level of intracardiac shunting is also because of this relationship (Figure 1-9). The bridging leaflets adhere to neither the crest of the ventricular septum nor the under surface of the atrial septum, making shunting to occur at both the atrial and ventricular levels. This is usually associated with a common atrioventricular valve, forming a complete type. The second common group has both bridging leaflets firmly attached to the crest of the ventricular septum, resulting in shunting being possible only at the atrial level. In this both bridging leaflets are usually connected, dividing the common orifice into separate right and left valvular orifices (partial form, or ostium primum defect). The other type is hearts with only interventricular shunting due to attachment of the leaflets to the underside of the atrial septum. Although these hearts have all the features of AVSD, mainly a common atrioventricular junction guarded by the characteristic 5-leaflet valve, there are some anatomical differences among these subtypes. First, the degree of cardiac deformity varies considerably. The

most severe abnormality characterized by a deeper ventricular scoop and larger inlet-outlet disproportion in the “complete” form, whereas hearts with only ventricular shunting were at the other end of the spectrum in a mild form, with the “partial” form having a moderate deformity. There is also a difference in the level of the bridging leaflets in relation to the level of the atrioventricular junction. The leaflets in hearts with only a ventricular component are always upwardly displaced (prolapsed), while those of an ostium primum defect are always downwardly displaced (tethered). Because the leaflet arrangement at the septal aspect cannot be corrected with surgery, such prolapsing and tethering would remain after repair of AVSD, the reason for development of the late valvular dysfunction.

Figure 9: The variations of the relationship between the bridging leaflets and the septal structures.



ATRIOVENTRICULAR CONDUCTION

Differences in the leaflets' relationship to the septum affect shunting level and the location of the atrioventricular node. In AVSD, the atrioventricular node is displaced more posteroinferiorly from the usual anatomical landmark, the apex of the triangle of Koch [18]. When closing the defect with a patch, the location of the displaced node and penetrating bundle of His should be carefully noted , to avoid conduction injury. The degree of displacement yet varies according to the shunting level. When only the ventricular component of the defect is present, due to the presence of shorter distance between the anterior and posterior margins of the defect, the node is located closer to the apex of the triangle of Koch compared to other forms (Figure 1-10). Because of this, the excision of the septum primum is limited to within the muscular rim of the fossa ovalis when entering the left atrium through a right atriotomy, as in typical AVSD repair. This anomalous/displaced node gives rise to the conduction bundle of His running on the crest of the ventricular septum and then branches to the left and right bundle after a relatively long non-branching portion (Figure 1-11). As with the other two subtypes, the distance between the orifice of the coronary sinus and the edges of the atrial and ventricular septum will determine whether it is safe to suture the patch here without causing any heart block. The other significant anatomical consideration to be noted is the course of the non-branching and branching bundle. It runs on the septal crest, slightly to the left side of the septal crest. In partial AVSD, fusion between the superior and inferior bridging leaflets and their adherence to the septal crest allow the entire atrioventricular conduction bundle to be protected by leaflet tissue when sutures are placed on the ventricular margins of the patch, whereas the branching atrioventricular bundle is exposed on the septal crest with a common valvular orifice. Consequently, if stitches need to be placed in the septum to

anchor the patch, the right ventricular aspect of the septum would be the safest to avoid branch injury.

Figure 10: Figures illustrating, the "Koch" area

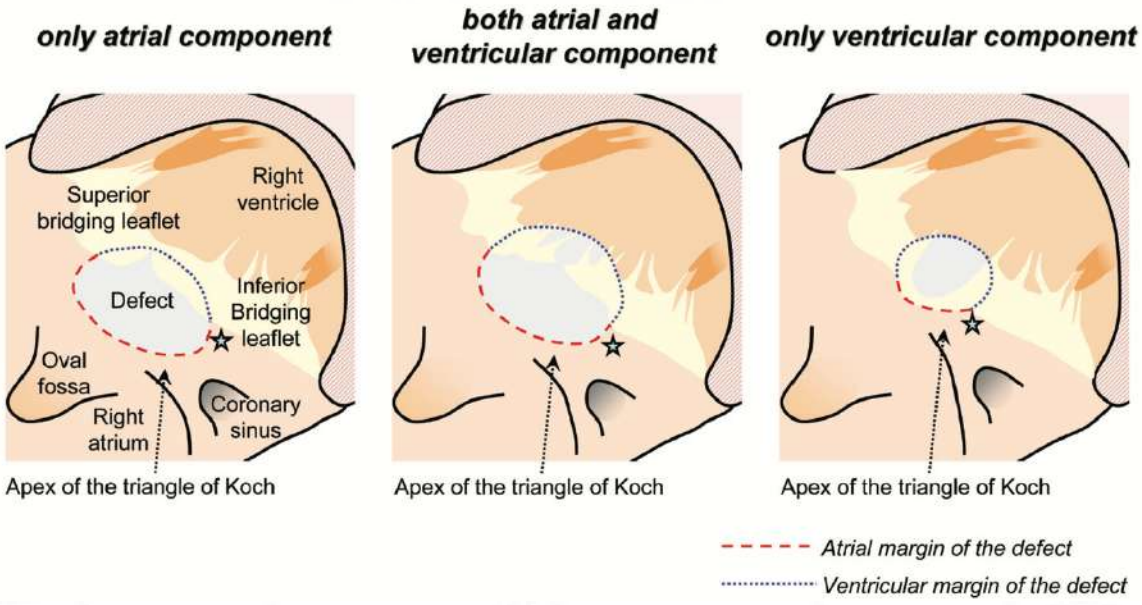
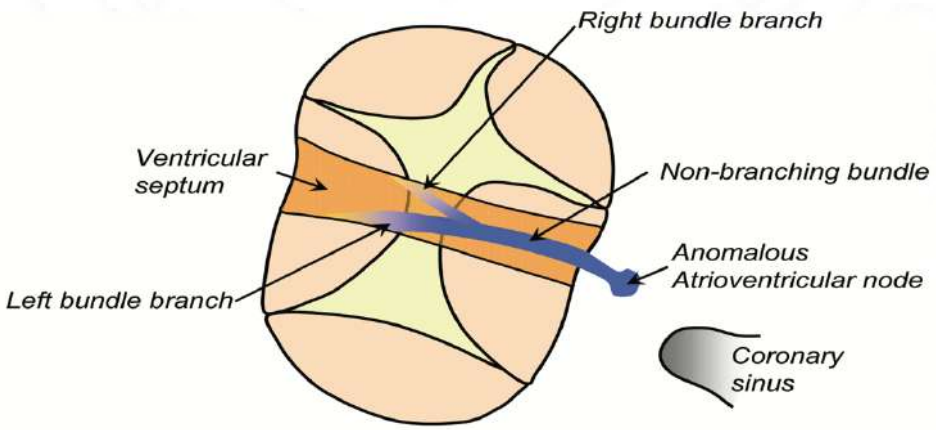


Figure 11: The displaced atrioventricular node and its continuation to the non-branching bundle.



Genetic Etiologies of Atrioventricular Septal Defects

The characteristic pattern of AVSD is associated with Down syndrome (trisomy 21). Down syndrome is the most common genetic syndrome with a prevalence of one in 700 live births [19]. Approximately 70% of cases of complete AVSDs occur in individuals with Down syndrome [20].

Down syndrome patients with certain types of CHDs, such as transposition of the great arteries, truncus arteriosus, and coarctation of the aorta, are rare, suggesting the possibility that the over-expression of the genes located on chromosome 21 may represent a protective factor for some types of CHDs [19]. As in most cases of significant chromosomal aberration, AVSDs are also associated with other noncardiac congenital defects. Not all children with trisomy 21 have AVSDs, so environmental factors, genetic factors on chromosome 21 or other chromosomes, partial trisomy, or all of these must contribute to the manifestation of the phenotype [21].

AVSDs seen in children with Down syndrome are more commonly of the complete form [19]. AVSDs in patients with or without Down Syndrome differ not only in terms of the prevalence of partial or complete forms, but also in terms of the distribution of associated cardiac malformations. Left-sided obstructive lesions are rare in children with Down syndrome, and they are more commonly seen in AVSD patients without Down syndrome [19].

Down Syndrome and Complete atrioventricular septal defects

Complete atrioventricular septal defect (CAVSD) is frequently (60%-86%) associated with Down Syndrome. Left-sided obstructions and right ventricular dominance, left atrioventricular valve abnormalities such as double orifice valve and single papillary muscle, are more prevalent in children with a normal chromosomal pattern, whereas Rastelli types B and C are more often found in patients with Down Syndrome [19].

Early progression of pulmonary vascular obstructive disease has been reported especially in patients with Complete AVSD associated with Down syndrome [22].

Children with Down syndrome may be at increased risk of perioperative and long term mortality [23] and have a predisposition to more operative complications requiring a longer duration of requiring mechanical ventilation post-operatively, ICU care and hospital stay [24].

Pulmonary predisposition in Down Syndrome

CAVSD in patients with Down Syndrome are reported to be associated with high incidence of pulmonary hypertension (PAH) and pulmonary vascular obstructive disease.

Studies on histological specimens have shown more severe form of pulmonary vascular disease in patients with Down syndrome, with significant differences in the amount of intimal lesions and medial thickness of the small pulmonary arteries compared to their normal chromosomal counterparts.

Surgical management of atrioventricular septal defects

History of surgical treatment [25]

In 1952 at the University of Minnesota Hospital in Minneapolis, Dennis and Varco attempted for the first time a cardiac operation in a human using a pump-oxygenator. The preoperative diagnosis was ASD, and at operation the defect was thought to be closed. The patient died, and autopsy showed the true diagnosis to be partial AV septal defect. The first successful repair of a complete AV septal defect was performed by Lillehei and colleagues in 1954, using cross-circulation and direct suture of the atrial rim of the septal defect to the crest of the ventricular septum.

In 1954, Kirkiln and colleagues successfully repaired a partial AV septal defect through the atrial well of Watkins and Gross, and in 1955 began repairing AV septal defects by open cardiotomy and use of pump-oxygenator.

Early surgeries of complete AV septal defects were all associated with a high hospital mortality, often related to complete heart block, post repair left AVVR or creation of subaortic stenosis.

In 1958, Lev's description of the location of the bundle of His provided the basis for repair techniques that avoid heart block.

In 1959, Dubost and Blondeau reported their early experience and emphasized that the "cleft" in the "mitral leaflet" need not be sutured in repairing partial AV septal defects.

In 1962, Maloney and colleagues described two cases in which a single patch was used to close both the defects and with the valve tissue suspended from the patch. This technique was again described by Gerbode in 1962 and was associated with decreased in-hospital mortality.

Mcgoon recognised the importance of "taking from the tricuspid valve" to leave sufficient tissue from which to create and adequate left AV valve.

TECHNIQUE OF OPERATION [26]

Surgical treatment of AV septal defects includes:

(1) closing the interatrial communication, which is always present.

(2) closing the interventricular communication if present

(3) avoiding damage to the AV node and bundle of His

(4) maintaining or creating two competent, non-stenotic AV valves.

Two-Patch Technique

After a median sternotomy is made, a large piece of pericardium is removed and set aside, and pericardial stay sutures are applied. External cardiac anatomy is evaluated and a left superior vena cava sought. If one is present, there is a 50% chance of associated unroofed coronary sinus syndrome. Purse-string sutures are placed.

In patients weighing less than 5 kg, repair may be performed with limited cardiopulmonary bypass (CPB) with a single venous cannula and hypothermic circulatory arrest; in larger patients, standard CPB is used. Alternatively, in both

infants and older children, hypothermic CPB at 20°C and cold cardioplegia may be used. In this method, the cavae are cannulated directly with thin-walled, right-angled metal cannulae. CPB flow is reduced to about 1.2 $L \cdot min^{-1} \cdot m^{-2}$ when the patient's temperature reaches 20°C. Short periods of circulatory arrest or low flow perfusion are occasionally used if visibility is not excellent. As cooling proceeds, the aorta is clamped, and cold cardioplegic solution is injected. The right atrium is opened widely, and a sump sucker is passed through the foramen ovale into the left atrium. Stay sutures are applied. Morphology examined (Figure 1-12).

Morphology of the LSL and LIL is noted carefully with the leaflets in both the closed and open positions. Cold saline solution is injected once or twice through the valve and the closure pattern and any regurgitant leaks studied.

The most anterior point of LSL-LIL opposing edges is found, and a double-armed 6-0 or 7-0 polypropylene suture is placed through it. Leaflet stay and marking sutures are placed, measurements are made, and the polyester interventricular patch is trimmed. The patch is sutured to the right side of the crest of the ventricular septum with continuous polypropylene suture. Chordae of the RSL and RIL stay on the right ventricular side of the patch; those of the LSL and LIL stay on the LV side, and some may be cut if they interfere with the suturing, because the anterior edges of these leaflets will be sutured to the polyester patch. When this phase is completed, the marking suture on the anterior edges of the coapting surfaces of the LSL-LIL complex is passed through the appropriate point of the edge of the polyester ventricular defect patch. The pericardial inter- atrial patch is then trimmed to appropriate shape and size, and the first part of its insertion is accomplished. For this, interrupted mattress sutures of 5-0 or 6-0 polyester are placed to enclose anterior edges of the LSL

and LIL between the polyester patch below and pericardial patch above. Alternatively, left-sided leaflet tissue is anchored as a separate manoeuvre to the polyester patch; the pericardial atrial septal patch is then sewn to the leaflet-patch line of attachment. Great care is taken to ensure alignment of left AV valve leaflets is perfect and without distortion during this process.

Saline solution is again injected through the left-sided portion of the AV valves (two orifices are present once the interventricular patch is in place) to study its closure pattern and competence. A few additional “tailoring sutures” are placed without tension along the coapting surfaces of the LSL and LIL near the patch, if needed, to prevent systolic eversion or prolapse; usually they are not required. If a central leak (at the point of junction of LSL, LIL, and LLL) persists, an annuloplasty stitch is placed in the region of the commissure between the LSL and LLL.

Assessment of both the left and right AV valves at this point includes consideration of their size. The diameter of each is estimated with Hegar dilators and considered acceptable if within 2 SD of normal for the size of the patient.

Repair is completed by suturing the rest of the pericardial interatrial patch in place, with the suture line passing around the AV node and bundle of His and not across them. The right-sided leaflets are usually not sutured to the patch because they close competently without this. If any commissural tissue between the LSL and RSL or LIL and RIL is cut, the right side of this (as well as the left side) is sutured to the patch. Rewarming of the patient is begun and patient is weaned of CPB (Figure 1-13 and 1-14).

Figure 12: Repair of complete atrioventricular (AV) septal defect; right atrial view [25]

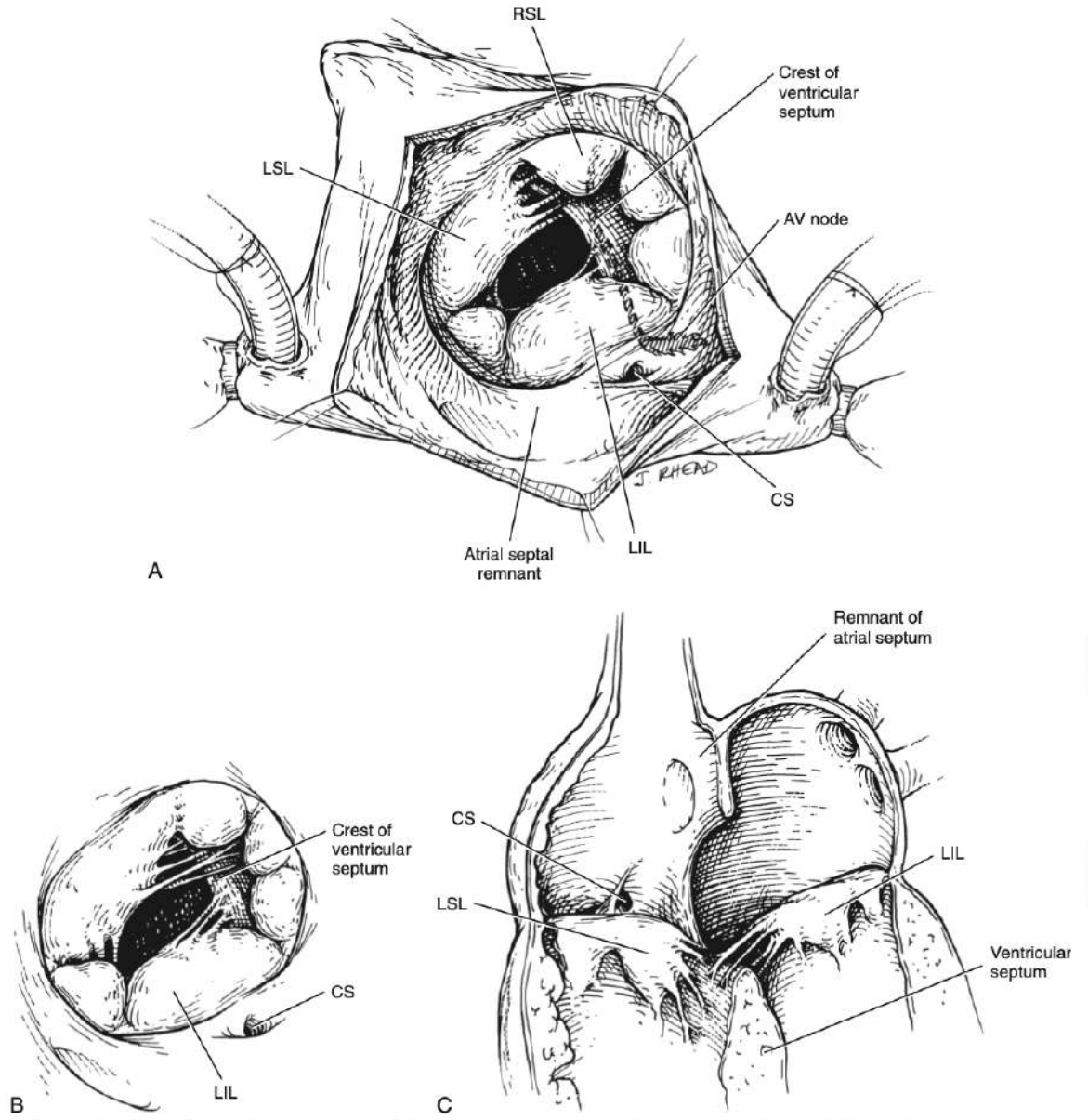


Figure 13: Repair of complete atrioventricular (AV) septal defect. [26]

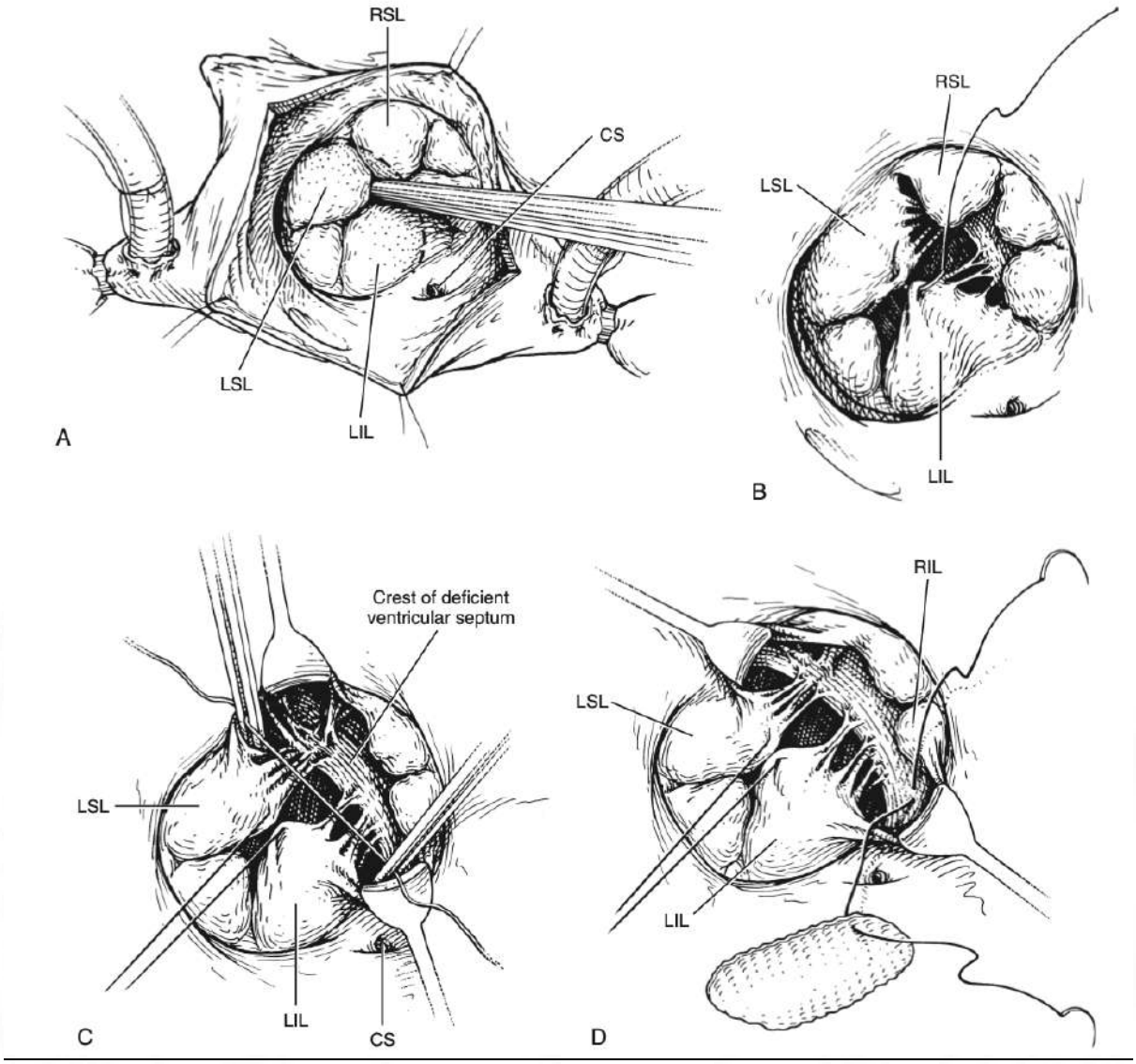


Figure 14: Repair of complete atrioventricular (AV) septal defect (cont….) [25]

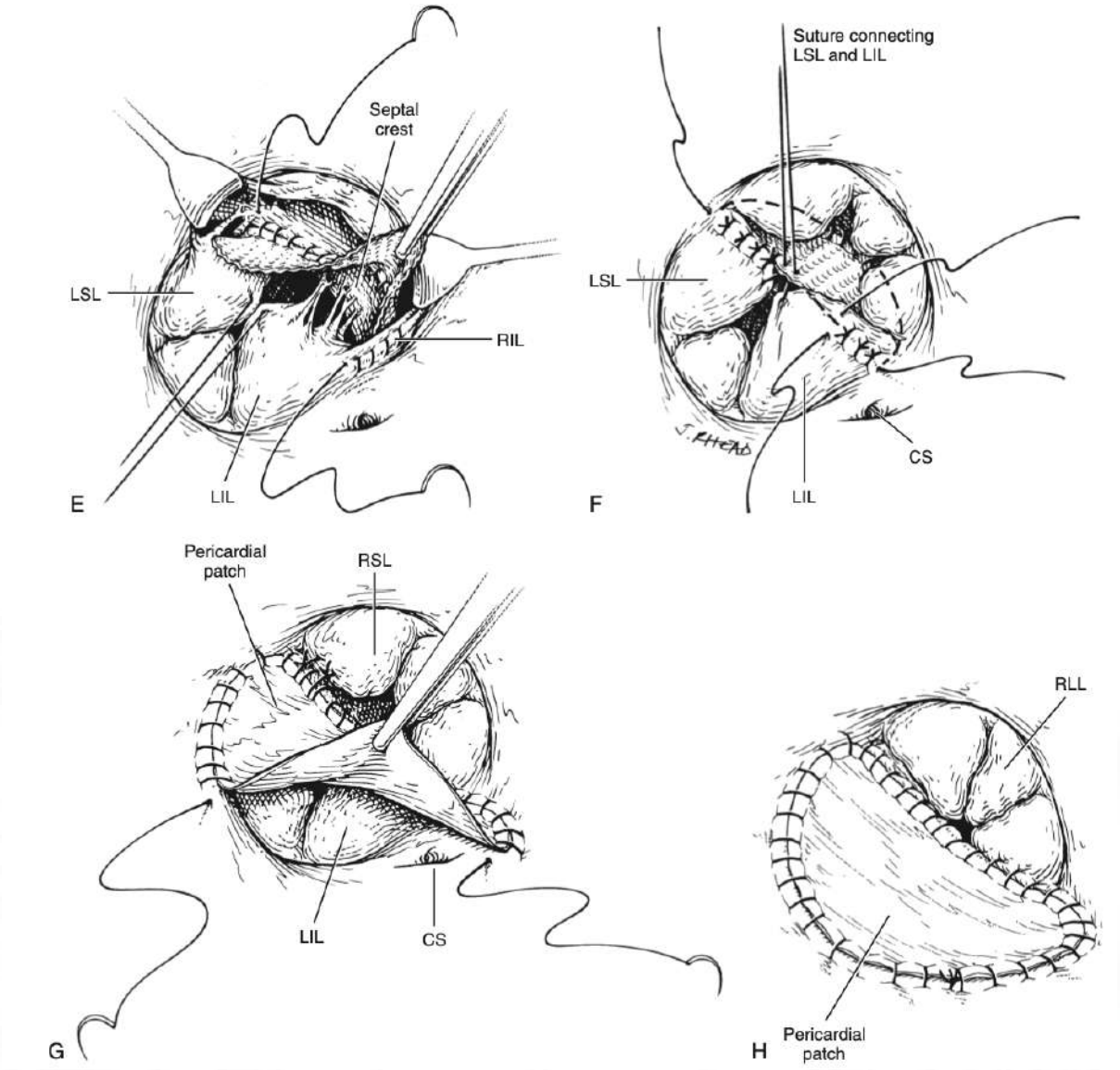
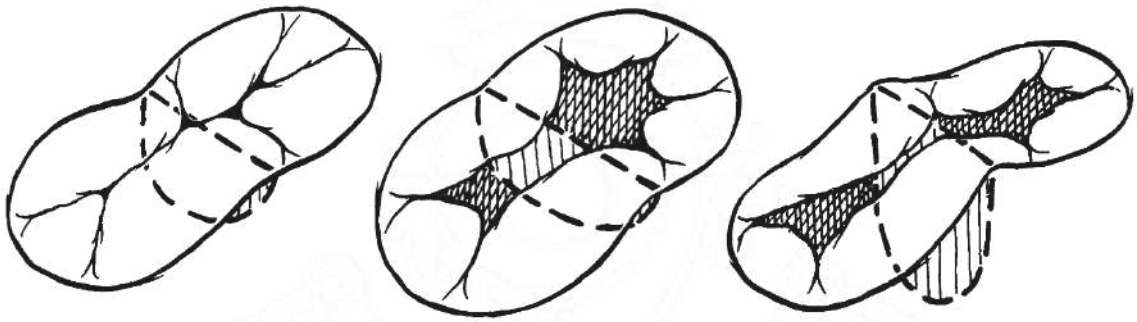


Figure 15: Figure depicting VSD portion of two-patch technique. [26]



Modified Single-Patch Technique (Figure 1-16)

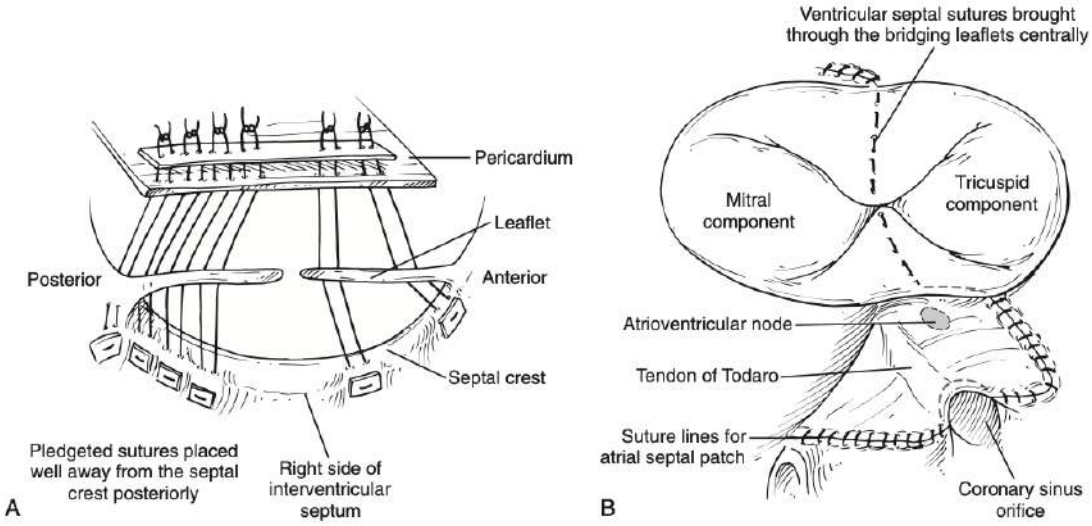
In 1997, Wilcox and colleagues reported direct suturing of the AV valves to the ventricular septum in complete AV septal defects with a small ventricular component.

The advantages of this procedure are (1) simplicity by avoiding a separate patch for VSD closure, (2) no division of valve leaflets or chordae, and (3) reduced operative time.

Interrupted pledgeted 5-0 braided sutures are placed on the right side of the interventricular septal crest and passed through the bridging LSL and LIL. These sutures are then passed through the edge of the autologous pericardial patch used to close the atrial defect and through a thin strip of polyester whose length is slightly shorter than the corresponding ventricular septum, with the intent of producing a central annuloplasty of the LSL and LIL. These sutures are tied, and the remainder of the operation proceeds as in the single- or two-patch techniques.

Nunn and colleagues reported uniform application for all patients with complete AV septal defects, 30 day mortality of less than 2%, no reoperations for residual VSDs, and no reoperations for LV outflow tract obstruction. This procedure has been widely applied in the setting of shallow ventricular defects.

Figure 16: Repair of complete atrioventricular septal defect with modified single-patch technique [26]



MATERIALS AND METHODS

Study type – Retrospective Observational study with Prospective follow up of patients

Study design – Single centre retrospective Observational model.

Patient data from medical records was collected, which includes pre-operative, Intra operative and post-operative follow up records of patient from OPD. Patient was followed up in OPD during their regularly yearly follow up and data was collected from OPD records.

Aim of Study: To compare the midterm outcome of patients undergoing atrioventricular canal defect repair with respect to Down's and non-Down's Syndrome.

Objectives:

1. Assess the midterm results of surgical repair of Complete Atrioventricular Septal defects.
2. Compare the early surgical outcomes in patients with and without Down's Syndrome.
3. Compare the late surgical outcomes with respect to degree of residual mitral regurgitation and Pulmonary arterial hypertension in both groups.
4. Analyse the re-intervention rates and cause for re-intervention.
5. Look into mortality rates and assess survival.

6. Review of the various surgical techniques used for repair.

Sampling method – Non Random

POPULATION

All patients who underwent cardiac surgery for correction of Complete Atrioventricular septal defect in division of Paediatric cardiac surgery, department of CVTS at SCTIMST between 2008-2017.

Data collection procedure – Hospital Medical records

Inclusion Criteria

All infants who underwent complete AVSD repair in division of paediatric cardiac surgery, SCTIMST between 2008-2017.

Exclusion criteria

1. All patients with age greater than 1 year are excluded from the study.
2. Patients with Partial Atrioventricular septal defects or Transitional Atrioventricular septal defects are excluded from the study.
3. All patients with Complete Atrioventricular Septal defects with unbalanced ventricles not suitable for a bi-ventricular repair are excluded from the study.

APPROVAL FROM TECHNICAL ADVISORY COMMITTEE (TAC):

TAC approval was obtained before commencing the study.

APPROVAL FROM INSTITUTIONAL ETHICS COMMITTEE (IEC):

IEC approval was taken before commencing the study.

METHODOLOGY

Patients who satisfied the inclusion criteria were included in the study. Data was collected with a semi structured questionnaire from hospital records and analysed. Pre-operative details, immediate post-surgery echocardiography parameters, follow up echocardiography details were collected from hospital records. Data was analysed after consultation with the statistician.

Statistical Analysis:

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Non normally distributed quantitative variables were summarized by median and interquartile range (IQR). Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots.

All Quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro- wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of >0.05 was considered as normal distribution.

For normally distributed Quantitative parameters the mean values were compared between study groups using Independent sample t-test (2 groups) / ANOVA (>2 groups) . For non-normally distributed Quantitative parameters, Medians and Interquartile range (IQR) were compared between study groups using Mann Whitney u test (2 groups) / Kruskal Wallis test (> 2 groups). The change in the quantitative parameters, before and after the intervention was assessed by paired t-test (In case of two time periods) or one way repeated measures ANOVA (In case of comparison across more than 2 time periods).

If statistically significant difference was found in ANOVA, appropriate post -hoc test (LSD/ Bonferroni) was used to assess statistical significance of pair wise comparisons.

Categorical outcomes were compared between study groups using Chi square test /Fisher's Exact test (If the overall sample size was < 20 or if the expected number in any one of the cells is < 5, Fisher's exact test was used.)

P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

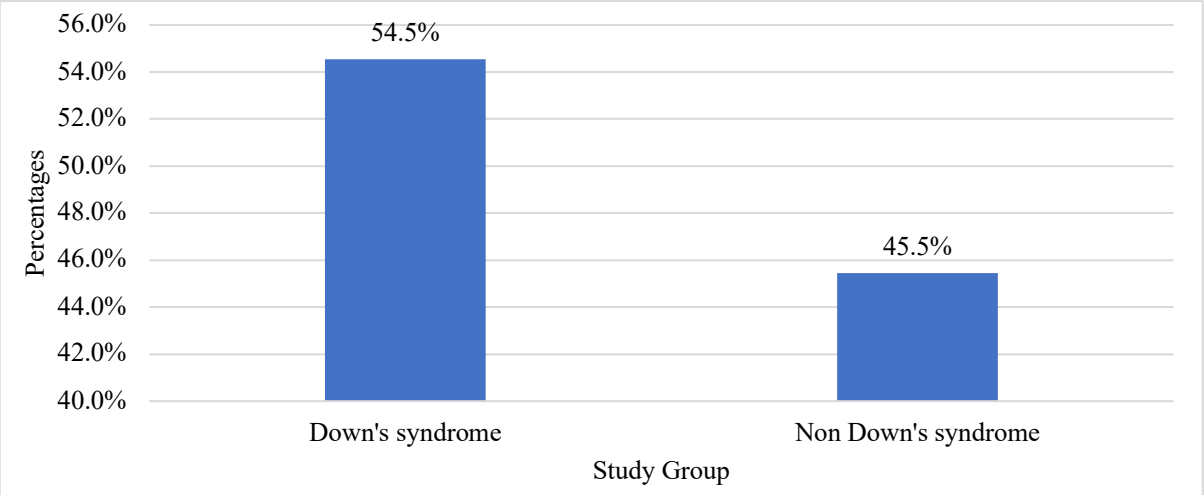
RESULTS

The study group included 77 patients all aged less than 1 year at surgery. Out of this 42 patients were of Down Syndrome (54.55%) and 35 with normal chromosomal pattern (45.45%).

Table 1: Descriptive analysis of study group in the study population (N=77)

Study Group	Frequency	Percentages
Down's syndrome	42	54.55%
Non Down's syndrome	35	45.45%

Chart 1: Bar chart of study population (N=77)



The mean age at surgery (months) for Down Syndrome 8.33 ± 2.08 and non-Down Syndrome 7.6 ± 2.58, with mean weight (kilograms) of 5.55 ± 1.02 and 5.17 ± 1.24 in Down and non-Down respectively.

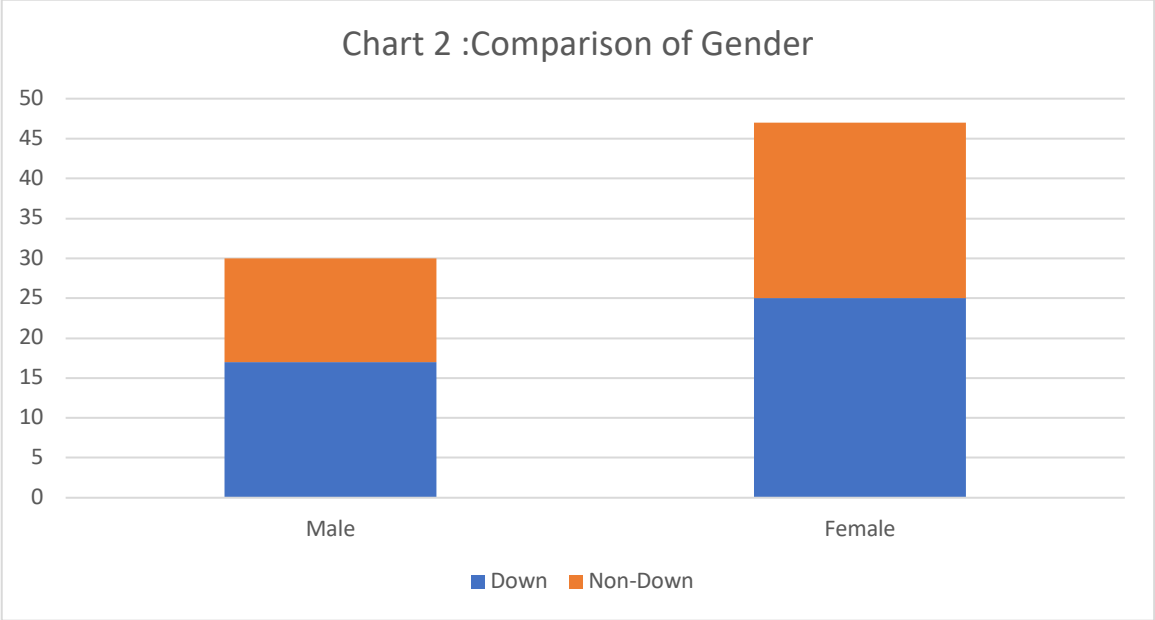
Table 2: Comparison of mean of age at surgery in months between study group(N=77)

Parameter	Study group (Mean± SD)		P value
	Down's syndrome (N=42)	Non-Down's syndrome (N=35)	
Age at surgery in months	8.33 ± 2.08	7.6 ± 2.58	0.171

Total number of male children were 30, of which 17 were Down's and 13 non-Down's. Whereas 47 were of the female sex, of which 25 were Down's and 22 non-Down's.

Table 3: Comparison of gender between study group (N=77)

Gender	Study Group		Chi square	P value
	Down's Syndrome (N=42)	Non-Down's Syndrome (N=35)		
Male	17 (40.48%)	13 (37.14%)	0.089	0.765
Female	25 (59.52%)	22 (62.86%)		



The mean of weight in each groups were 5.55 ± 1.02 and 5.17 ± 1.24 in Down's and non-Down's respectively.

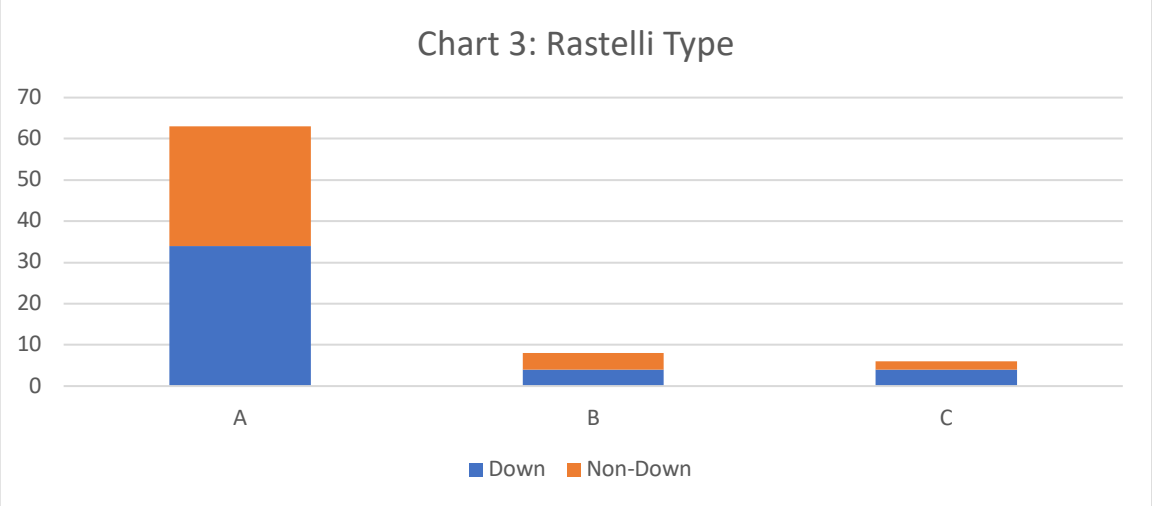
Table 4: Comparison of mean of weight (in kg) between study group(N=77)

Parameter	Study group (Mean± SD)		P value
	Down's syndrome (N=42)	Non-Down's syndrome (N=35)	
Weight (in kg)	5.55 ± 1.02	5.17 ± 1.24	0.141

Of the 77 patients, 63 were of Rastelli type A, 8 of Rastelli type B and 6 of Rastelli type C. Group wise break up is shown in Table 5.

Table 5: Comparison of Rastelli type between study group (N=77)

Rastelli Type	Study Group		Chi square	P value
	Down's syndrome (N=42)	Non-Down's syndrome (N=35)		
A	34 (80.95%)	29 (82.86%)	0.431	0.806
B	4 (9.52%)	4 (11.43%)		
C	4 (9.52%)	2 (5.71%)		

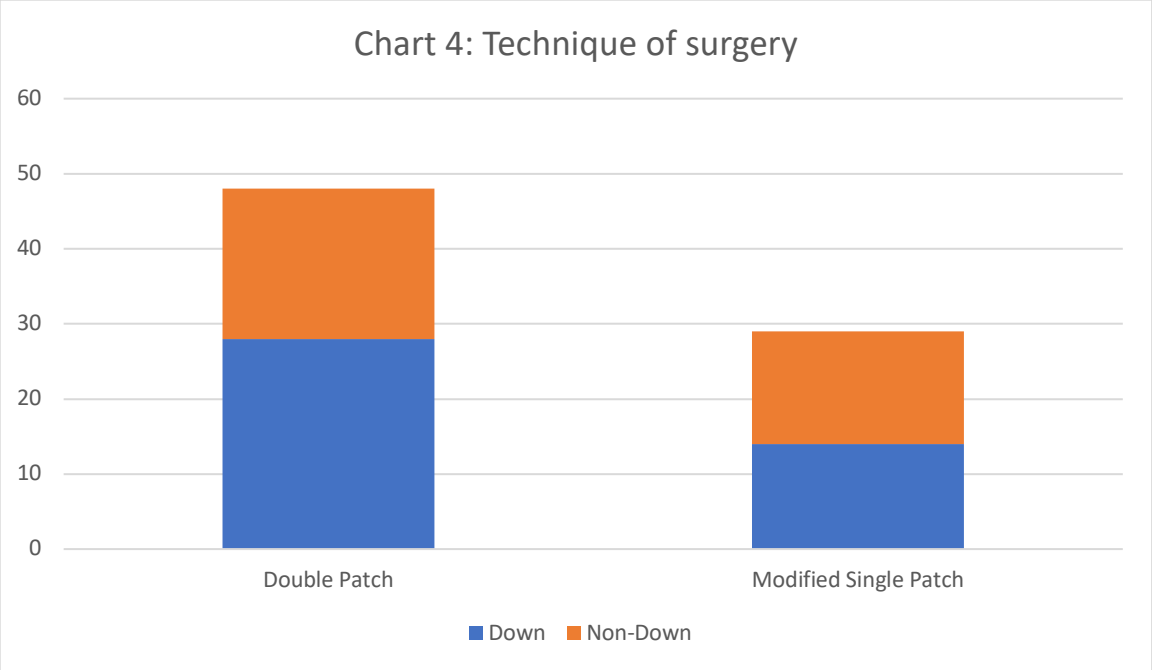


Out of 42 Down Syndrome infants 6 were hypothyroid, while their normal chromosomal counterparts did not show any associated anomaly.

Only Double patch and modified Single patch techniques were done at the institute during the study period.
48 patients (62.33%) underwent a double patch technique whereas 29 patients (37.66%) underwent a modified single patch repair.

Table 6: Comparison of technique of surgery between study group (N=77)

Technique of surgery	Study Group		Chi square	P value
	Down's syndrome (N=42)	Non-Down's syndrome (N=35)		
Double Patch Repair	28 (66.67%)	20 (57.14%)	0.738	0.390
Mod Single Patch	14 (33.33%)	15 (42.86%)		



Out of 77 patients, 41 (53.24%) infants underwent concurrent additional repair of the MV of which 21 (50%) were Down's and 20 (57.14%) non-Down Syndrome.

1 patient in the non-Down's group had to undergo right femoral thrombectomy for a complication following arterial line insertion.
1 patient underwent RUPV plasty in the Down's group and 1 in non-Down's underwent rerouting of PAPVC to LAA.
1 patient in the non-Down's group underwent tracheostomy for prolonged ventilation requiring frequent tracheal toileting.

The total CPB time average for the whole study population was 161.87 min and for ACC time the average being 111.43 min.

Table 7: Comparison of mean of total CPB and ACC time (in min) between study group(N=77)

Parameter	Study group (Mean± SD)		P value
	Down's syndrome (N=42)	Non-Down's syndrome (N=35)	
Total CPB time (in min)	160.38 ± 43.36	163.66 ± 41.39	0.737
ACC time (in min)	112.43 ± 32.89	112.29 ± 29.19	0.984

A total of 11 (14.28%) patients were shifted to ICU with their sternum open of which 4 (9.52%) were Down's and remaining 7 (20%) were non-Down's.

Table 8: Comparison of open or closed sternum between study group (N=77)

Sternum	Study Group		Chi square	P value
	Down's syndrome (N=42)	Non-Down's syndrome (N=35)		
Open	4 (9.52%)	7 (20%)	1.711	0.191
Closed	38 (90.48%)	28 (80%)		

Table 9: Comparison of mean of VIS between study group(N=77)

Parameter	Study group (Mean± SD)		P value
	Down's syndrome (N=42)	Non-Down's syndrome (N=35)	
VIS	10.64 ± 5.95	10.13 ± 4.25	0.670

Table 10: Comparison of median No. of days in ICU between study group(N=77)

Parameter	Study group		P value
	Down's syndrome (N=42) Median (IQR)	Non-Down's syndrome (N=35) Median (IQR)	
No. of days in ICU	6 (5, 8)	7 (5, 9)	0.062

Out of the 77 patients, 63 patients did not any re-intubations of which 35 patients (83.33%) of patients were having Down Syndrome and 28 (80%) belonged to the Non-Down group.

Table 11: Comparison of no of failed extubation between study group (N=77)

No of failed extubation	Study Group	
	Down's syndrome (N=42)	Non-Down's syndrome (N=35)
0	35 (83.33%)	28 (80%)
1	6 (14.29%)	5 (14.29%)
3	0 (0%)	2 (5.71%)
4	1 (2.38%)	0 (0%)

Table 12: Postop arrythmia

Arrythmia	Total (77)	Down Syndrome (42)	Non-Down Syndrome (35)
Atrial Ectopics	24 (31.68%)	10 (23.8%)	14 (40%)
CHB	1 (1.29%)	0	1 (2.85%)
SVT	2 (2.59%)	0	2 (5.71%)
JET	3 (3.89%)	0	3 (8.57%)

The overall incidence of arrythmia was found to be more in Non-Down (n=20 out of 35) when compared to Down (n=10 out of 42).

Table 13: Post-op Infection

Infection Source	Total (77)	Down Syndrome (42)	Non-Down Syndrome (35)
Blood	6 (7.79%)	2 (4.76%)	4 (11.42%)
Respiratory	15 (19.48%)	9 (21.42%)	6 (17.14%)

Urine	1 (1.29%)	0	1 (2.85%)
Wound	1 (1.29%)	0	1 (2.85%)

Re-Intervention in same admission:

One patient in the non-Down Syndrome group who had developed CHB in post-op period underwent permanent pacemaker implantation.

One patient in the non-Down group underwent redo-MV repair for severe AVVR on post-op day 2 and also underwent tracheostomy for need of prolonged ventilation.

One patient in the non-Down group underwent residual VSD closure on post-op day 2 and one patient of the Down group who had undergone a Double Patch technique underwent Redo to a single patch repair due to infective endocarditis.

Mortality and Survival:

Out of the 77 patients who underwent AVCD repair, there were 5 (6.49%) in-hospital mortality, in that 1 (2.38%) infant was Down's and the other 4 (11.42%) non-Down's (P value 0.11). The cause of death of 2 non-Down's infant being PAH crisis the remaining 3 died of sepsis.
Out of the remaining 72 patients who were discharged, 3 (3.86%) had a late mortality at 2, 12 and 36 months from the date of surgery. The infants who

died at 2 and 12 months were Down Syndrome whereas the child who died at 36 months belonged to the non-Down group.

Out of the remaining 69 in the study group 5 (6.49%) were lost to follow-up.

The remaining 64 (83.11%) children were followed up in OPD at regular intervals of 1 month, 3 months, 6 months, 1 year and 3 years and Echocardiography was done and assessed for any improvement or worsening of AVVR and PAH.

Among the patients who had in-hospital mortality 4 (80%) patients had underwent modified-single patch repair (N 29) and 1 (20%) patient had underwent double patch repair (N 48).
Similarly, late mortality was also observed more in patients of modified single patch repair 2 out of 3, and 1 patient had undergone double patch repair.

Table 14: Comparison of in-hospital mortality between study group (N=77)

Mortality	Study Group		Chi square	Fisher exact P value
	Down's syndrome (N=42)	Non-Down's syndrome (N=35)		
Yes	1 (2.38%)	4 (11.43%)	2.574	0.171
No	41 (97.62%)	31 (88.57%)		

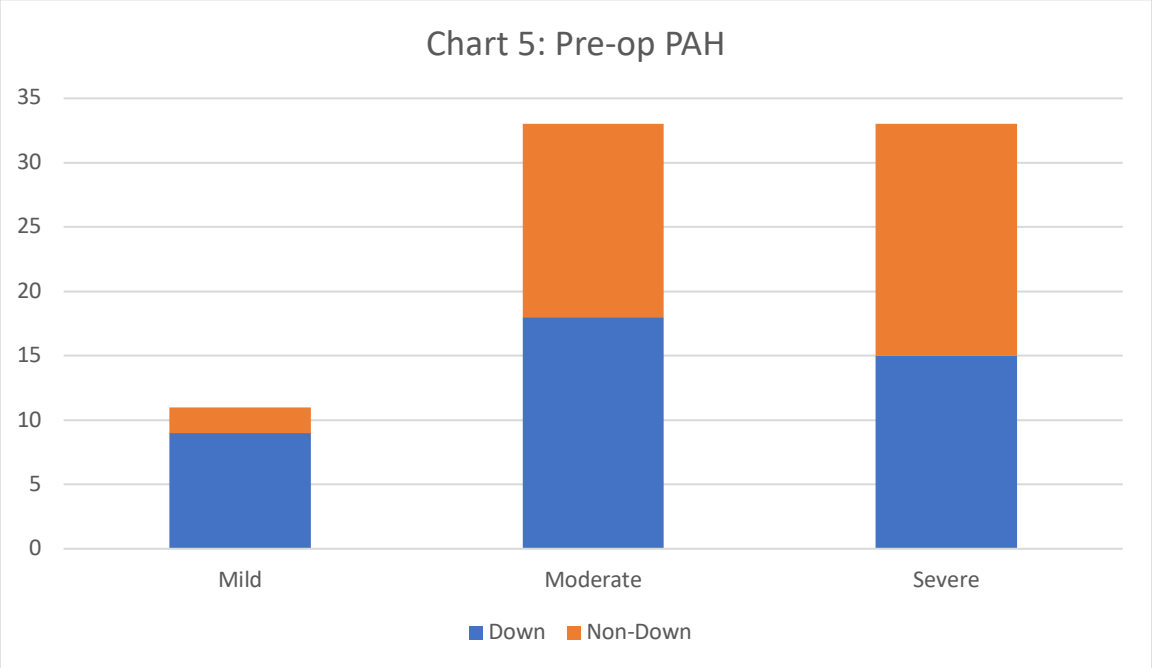
The pulmonary arterial hypertension was classified on basis of echo derived parameter (RV systolic pressure + RA pressure) into mild (20-40mm hg), moderate (41-59mm hg) and severe (> 60mm hg).

Pre-op PAH:

Out of 77 patients 11 (14.28%) had mild PAH, 33 (42.85%) each in moderate and severe PAH group.

In Down Syndrome group 9 (21.4%) had mild PAH, 18 (42.8%) had moderate and 15 (35.7%) had severe PAH.

In Non-Down group 2 (5.7%) had mild, 15 (42.8%) had moderate and 18 (51.4%) had severe PAH.

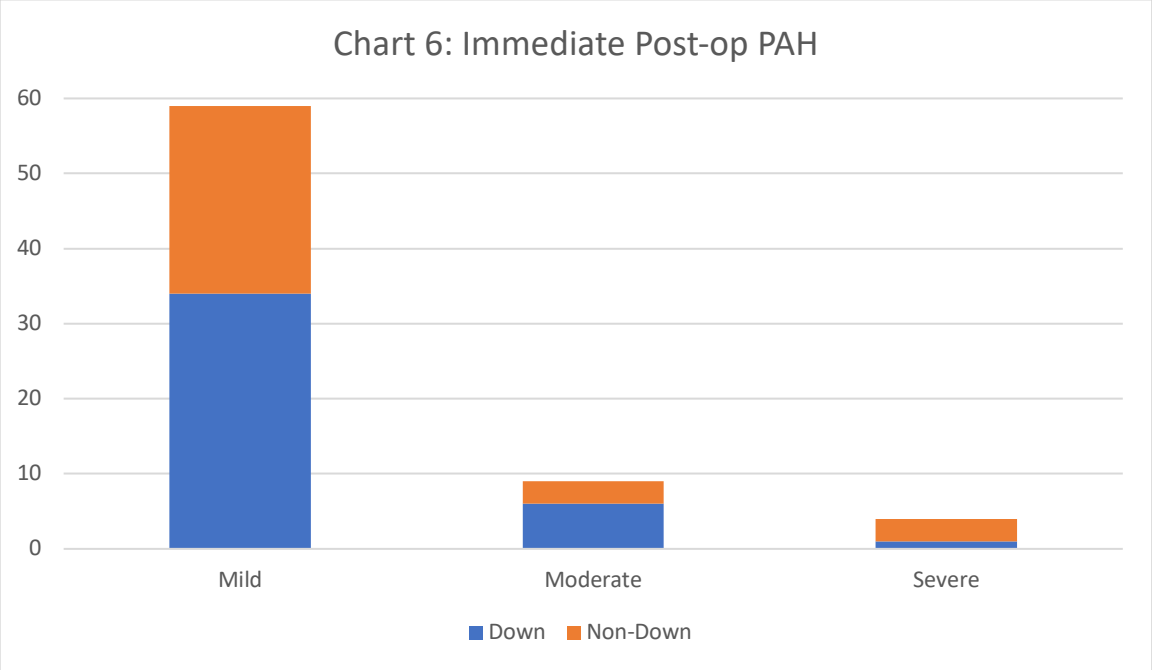


Immediate post-op:

Out of 72 patients 59 (81.94%) had mild PAH , 9 (12.5%) had moderate and 4 (5.55%) had severe PAH.

In Down Syndrome (N 41) 34 (82.9%) had mild, 6 (14.6%) had moderate and 1 (2.4%) had severe PAH.

In Non-Down Syndrome (N 31), 25 (80.6%) had mild, 3 (9.6%) had moderate and 3 (9.6%) had severe PAH.



Last follow up :

64 patients who were on regular follow up, the last follow up (3 years) was taken to compare the PAH.

59 (92.18%) patients had mild PAH and 5 (7.8%) had moderate PAH whereas there were no patients having severe PAH at 3rd year follow up.

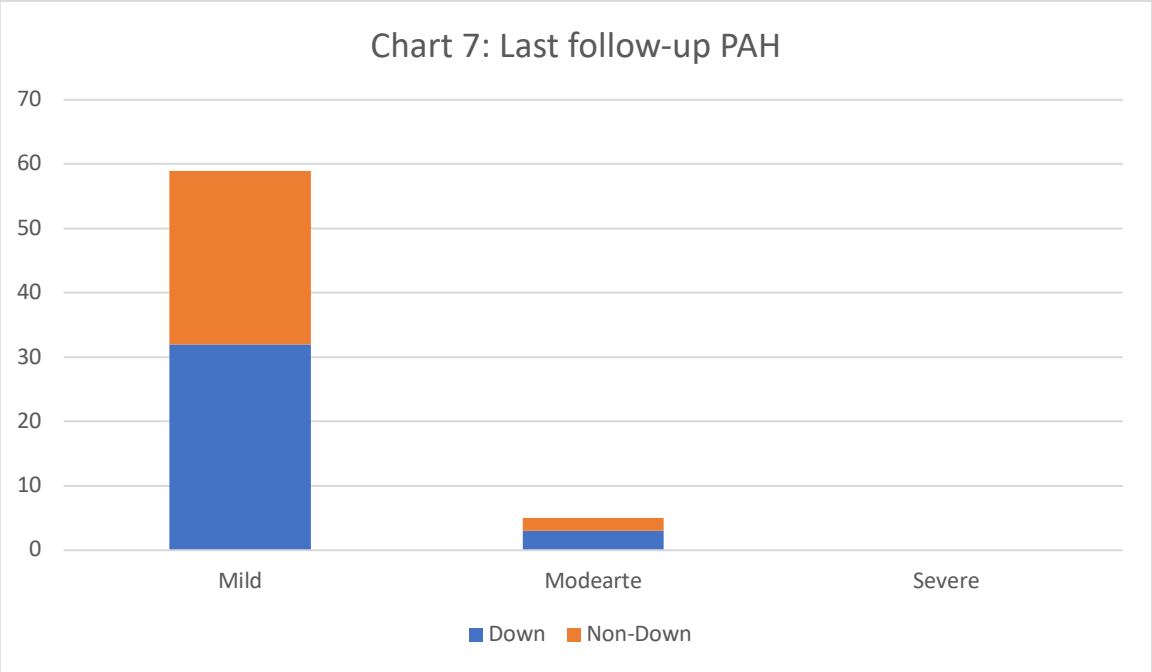
In Down Syndrome (N 35) group 32 (91.42%) had mild PAH and 3 (8.5%) had moderate PAH.

In Non-Down group (N 29), 27 (93.10%) had mild and 2 (6.8%) had moderate PAH.

Statistically both the Down and non-Down group had significant reduction in PAH in immediate post-op echo.

Compared to immediate post-op PAH there was no statistically significant change of PAH at last follow-up in either groups.

The mean PAH in terms RVSP+RA is 56.07+/- 14.98 mm hg, with Down Syndrome patients having a mean PAH of 54.43 ± 15.93 mm hg and non-Down Syndrome patients having a mean of 58.06 ± 13.72 mm hg



PAH at regular follow up is shown in table 15.

Table 15: Comparison of mean of PAH (RVSP) different time periods between study group(N=77)

PAH (RVSP)	Study group (Mean± SD)		P value
	Down's syndrome	Non-Down's syndrome	
Preop (N=77)	54.43 ± 15.93	58.06 ± 13.72	0.293
Immediate postop (N=72)	31.02 ± 11.21	31.68 ± 12.75	0.818
1st month Follow up (N=70)	32.23 ± 11.77	27 ± 7	0.032
3rd month follow up (N=68)	31.81 ± 9.36	27.84 ± 7.02	0.056

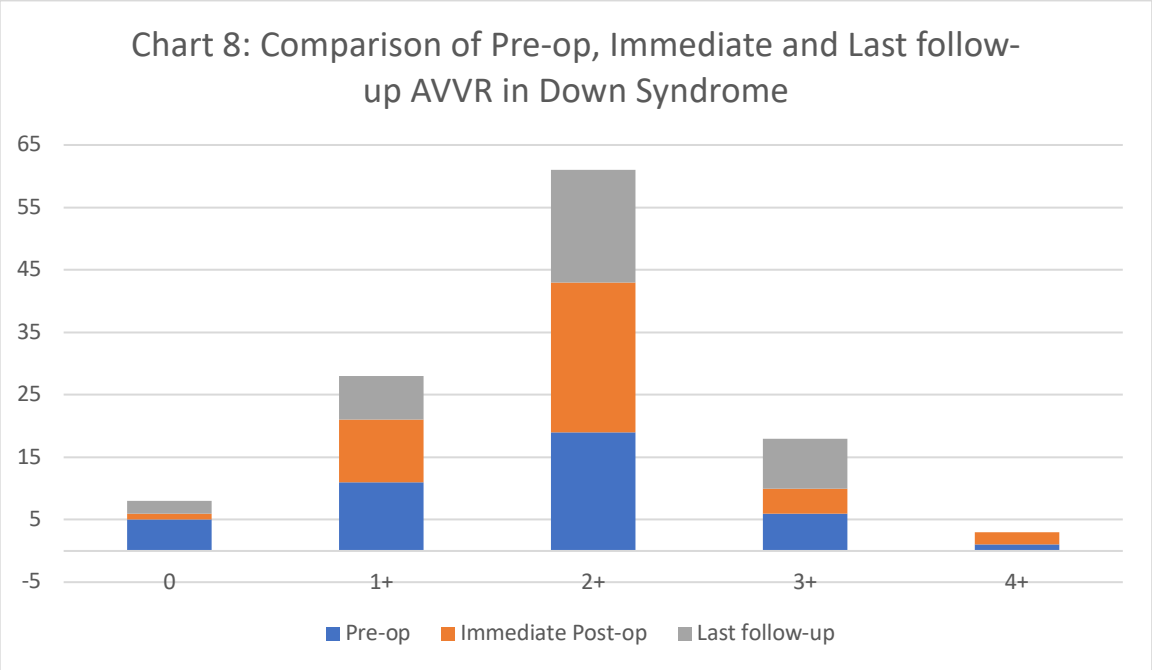
6th month follow up (N=67)	29.08 ± 9.37	25.35 ± 7.57	0.081
1st year Follow up (N=64)	27.66 ± 11.69	24.38 ± 10.01	0.238
3rd year follow up (N=64)	29.57 ± 7.89	23.1 ± 6.62	0.001

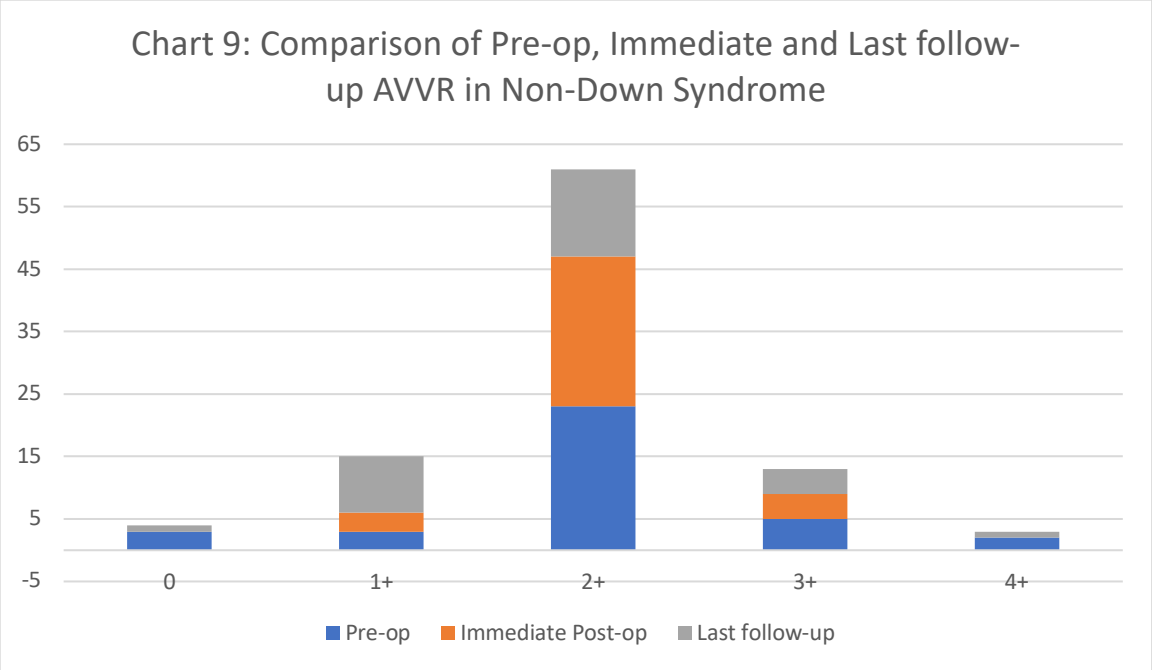
Degree of AVVR was assessed by colour Doppler imaging and scored as 0 (no regurgitation), 1+ (hemodynamically insignificant regurgitation), 2+ (mild regurgitation), 3+ (moderate regurgitation) and 4+ (severe regurgitation)

Table 16: Comparison of AVVR between study group (N=77)

AVVR	Study Group		Chi square	P value
	Down's syndrome	Non-Down's syndrome		
Preop AVVR	**(N=42)**	**(N=35)**		
0	5 (11.9%)	2 (5.71%)	6.076	0.194
1+	11 (26.19%)	3 (8.57%)		
2+	19 (45.24%)	23 (65.71%)		
3+	6 (14.29%)	5 (14.29%)		
4+	1 (2.38%)	2 (5.71%)		
Immediate Postop	**(N=41)**	**(N=31)**		
0	1 (2.44%)	0 (0%)	*	*
1+	10 (24.39%)	3 (9.68%)		
2+	24 (58.54%)	24 (77.42%)		
3+	4 (9.76%)	4 (12.9%)		
4+	2 (4.88%)	0 (0%)		
1st month Follow Up	**(N=39)**	**(N=31)**		
0	2 (5.13%)	1 (3.23%)	0.951	0.917
1+	12 (30.77%)	8 (25.81%)		
2+	20 (51.28%)	17 (54.84%)		
3+	4 (10.26%)	3 (9.68%)		
4+	1 (2.56%)	2 (6.45%)		
3rd month follow up	**(N=37)**	**(N=31)**		
0	0 (0%)	1 (3.23%)	*	*

1+	9 (24.32%)	5 (16.13%)		
2+	22 (59.46%)	17 (54.84%)		
3+	6 (16.22%)	7 (22.58%)		
4+	0 (0%)	1 (3.23%)		
6th month follow up	**(N=36)**	**(N=31)**		
0	4 (11.11%)	1 (3.23%)		
1+	3 (8.33%)	6 (19.35%)		
2+	19 (52.78%)	18 (58.06%)	*	*
3+	10 (27.78%)	4 (12.9%)		
4+	0 (0%)	2 (6.45%)		
1st year follow up	**(N=35)**	**(N=29)**		
0	2 (5.71%)	2 (6.9%)		
1+	11 (31.43%)	9 (31.03%)		
2+	20 (57.14%)	12 (41.38%)	*	*
3+	2 (5.71%)	5 (17.24%)		
4+	0 (0%)	1 (3.45%)		
3rd year follow up	**(N=35)**	**(N=29)**		
0	2 (5.71%)	1 (3.45%)		
1+	7 (20%)	9 (31.03%)		
2+	18 (51.43%)	14 (48.28%)	*	*
3+	8 (22.86%)	4 (13.79%)		
4+	0 (0%)	1 (3.45%)		





In pre-op AVVR patients having 1+ AVVR were 11 and 3 in Down and Non-Down respectively with P value of 0.04, with 2+ AVVR 19 and 23 in Down and non-Down Syndrome respectively with P value of 0.074.

In immediate post-op AVVR of 1+, 10 were Down and 3 were non-Down Syndrome, with P value of 0.11.

At 3rd year follow up, there was no statistically significant difference between the Down and non-Down group.

Comparing the immediate and last follow up AVVR, in Down Group there was no statistically significant change or improvement.

Table 17: Comparison of CPB time between the two techniques used

Double Patch Technique (N 48)	Modified Single Patch (N29)	P Value
178.98+/-38.04	140.10+/-40.32	<0.0003

Table 18: Comparison of ACC time between the two techniques used

Double Patch Technique (N 48)	Modified Single Patch (N29)	P Value
126.27+/-26.55	89.34+/-23.55	<0.0001

DISCUSSION

Complete AV septal defect continues to remain a common congenital heart disease requiring early corrective surgery during infancy to prevent the development of pulmonary vascular disease. The association of complete AVSD with Downs syndrome is well documented. There is documented early development of pulmonary vascular disease in these patients if associated with Downs syndrome.

The mean age of patients at the time of surgical correction is 8.33 ± 2.08 for Downs and 7.6 ± 2.58 for non-Downs which is comparable with a study done by Sivakumar Sivalingam *et al*. The male to female ratio is 1 : 1.56 but is not statistically significant. The mean weight of the patients in our study is 5.37 kilogram which is similar to the study done by James D. St. Louis *et al*. The age, weight and sex were similar between the two groups.

In our study the incidence of hypothyroidism was more in the Downs syndrome group, while no patient in the Non-Downs group had hypothyroidism. This difference is according to what has already been well described in literature [27]. The incidence of PAH and the presence of moderate or severe AVVR in the pre-operative period was also similar.

Double patch technique and Modified single patch technique were used in this study. There was no statistical difference between the type of procedure used for repair between the two groups. The mean clamp time and the cardio-pulmonary by-pass time between the two groups were similar compared to the study done by Ruediger Lange *et al.*

The mean CPB and ACC time between the two techniques were compared showed statistically significant less time in both CPB and ACC in the Modified Single Patch technique, which was comparable to the study done by Laura S. Fong *et al*.

All patients had a significant fall in their PAH in the post-operative period. This fall in PAH when compared to the pre-operative PAH was statistically significant. This is along expected lines as the large shunt is removed and with use of ultrafiltration during the procedure and pulmonary vasodilators like sildenafil , the PAH in the post-operative period was significantly less.

Patients with Downs syndrome had slightly increased incidence of moderate or moderate to severe AVVR (14.64%) in the immediate post-operative period when compared to the group with Non-Downs syndrome (12.9%). This difference was however not statistically significant (p-value 0.8), this result compares to the study done by Ruediger Lange *et al.*

The incidence of AVVR when followed up for 3 years showed a progression in the incidence of moderate to severe AVVR in both groups with 22.8% in patients with Downs Syndrome and 17.24% in Non-Downs. The difference between the two group however was not statistically significant. This result when compared to a study done by Andrew M. Atz *et al* showed similar results. The incidence of additional procedure for mitral valve apart for closure of the cleft (posterior annuloplasty, kay's annuloplasty, neo chordae placement) were similar in both groups.

The overall mortality in this study is 8 (10.38%) with early mortality of 5 (6.49%) and late mortality of 3 (3.89%). This was comparable to an Asian study done by Sivakumar Sivalingam *et al,* but slightly higher than the western population at 5.1% in a study done by Ruediger Lange *et al*.

The common cause of early mortality were PAH crisis and cardiac arrest and sepsis. Change in practice like the use of both classical and modified ultrafiltration intra-operatively and the use of pulmonary vasodilators has resulted in no early mortality since 2012. The post-operative Vasoactive inotropic score and the ICU days were similar in both groups. The most common arrythmia in both groups was atrial ectopics, however the incidence of all arrythmias was significantly higher in the Non-Downs group, this result when compared to a 47 year follow up study done by Rohit k. Kharbanda *et al* showed similar results. which was statistically significant. The total number of failed extubation in both groups were similar.

Limitations of the study:

This study was mainly retrospective involving only one centre. The patient volume was low because of which the strength of the statistical analysis is low.

CONCLUSION

Presence of Downs syndrome has no effect on the outcomes of surgical repair of complete AVSD. Both early and late results after surgical correction are comparable. There is a constant progression of residual left AVVR.

Recent advances in surgical practise and ICU management has resulted in reduced early and late mortality. Primary surgery of complete AVSD is safe and can be accomplished with minimal morbidity and mortality in Down and non-Down Syndrome infants.

Contemporary results of surgical correction of Complete Atrioventricular Septal Defect in patients with or without Down's Syndrome – A retrospective review

PROFORMA

DEMOGRAPHIC DATA:

Age at surgery
Sex
Weight
Down's/ Non-Down's
Rastelli Type
Any other associated anomaly

PRE-OPERATIVE ECHOCARDIOGRAPHIC DATA:

AVVR
PAH (RVSP+RA)

OPERATIVE DATA:

Technique of Surgery
Additional Procedure
Total CPB time
Aortic Cross clamp time

IMMEDIATE POSTOPERATIVE DATA:

Sternum open/close
Vasoactive Inotropic score
Number of days in ICU
Number of days on ventilator
Number of failed extubations
Any post-op infection
Any post-op arrythmia
Re-intervention in the same admission

Mortality

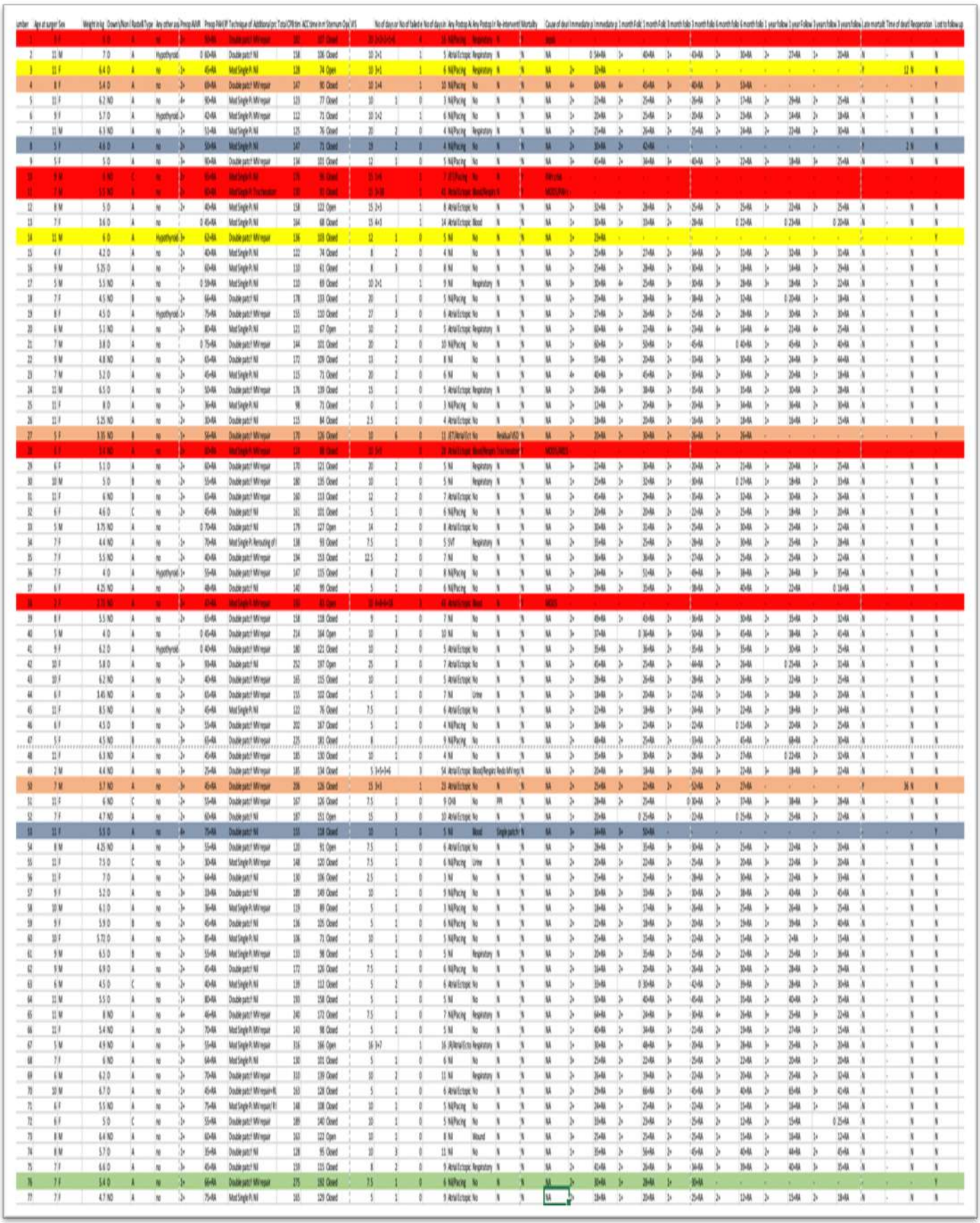
IMMEDIATE POST-OPERATIVE ECHOCARDIOGRAPHIC DATA:

AVVR
PAH

FOLLOW UP at 1month, 3 months, 6 months, 1 year and 3 years

AVVR
PAH
Mortality
Re-operation

MASTER CHART



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PLAGIARISM CHECK REPORT

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