Surgical outcomes in the treatment of children with atrioventricular septal defects

Inaugural Dissertation
Submitted to the
Faculty of Medicine
in partial fulfillment of the requirements
for the degree of Doctor of Medicine
in the Faculty of Medicine
of the Justus Liebig University of Giessen

Submitted by Mahmod, Abdalla Ahmed
From Libya, Born in El-Minia

Giessen (2008)

From Department of Paediatric Cardiology- Paediatric Heart Center Giessen

Director: Prof. Dr. D. Schranz
Faculty of Medicine, Justus Liebig University of Giessen

Committee Member: Prof. Dr. med. Dietmar Schranz

Committee Member: PD Dr. med. Martin Heidt

Date of Doctoral Defense: 27.08.2008

DEDICATION

To my wife, **Iwona Monika**, for her kindness, love, and support.

To my mother, **Ghania**, sisters and brothers, my loving family.

A. A. M.

CONTENTS

1. Introduction *3*

1.1. Definition **3**

1.2. Etiology **3**

1.3. History background **3**

1.4. Epidemiology **4**

1.5. Anatomy and Associated cardiac anomalies **4**
1.5.1. General morphologic anatomy 4
1.5.2. Partial atrioventricular septal defect 7
1.5.3. Complete atrioventricular septal defect 8
1.5.4. Rastelli classification 9
1.5.5. Associated cardiac anomalies 10

1.6. Pathophysiology, Natural history and Diagnostic methods **10**
1.6.1. Pathophysiology 10
1.6.2. Natural history 11
1.6.3. Diagnostic methods 11

2. Therapy options *12*

2.1. Medical therapy **12**

2.2. Surgical therapy **12**
2.2.1. Surgical indications 12
2.2.2. Aims of surgical repair 12
2.2.3. Surgical techniques 13
2.2.3.1. Two- patch technique for complete AVSD repair 13
2.2.3.2. Single- patch technique for complete AVSD repair 15
2.2.3.3. Repair of partial AV septal defect 17

2.3. Aims of the study **17**

3. Patients and methods *18*

3.1. Study design **18**

3.2. Diagnosis **19**

3.3. Anaesthesia and CPB **20**

3.4. Operative techniques **20**

3.5. Follow- up **21**

3.6. Statistical analysis **21**

4. Results *22*

4.1. Preoperative data **22**
4.1.1. General patients characteristics 22
4.1.2. Diagnosis 26
4.1.3. Preoperative anticongestive therapy 27
4.1.4. Preoperative palliative procedures 27

4.2. Intraoperative data **27**
4.2.1. Operative techniques 27
4.2.2. CPB duration and aortic- cross clamping 30
4.2.3. Intraoperative complications 31
4.2.4. Thorax closure 32

4.3. Postoperative data **33**
4.3.1. Catecholamine therapy 33

4.3.2. Additional therapy 33
4.3.3. Mechanical ventilation 33
4.3.4. Secondary thorax closure 34
4.3.5. Postoperative rhythm disturbances 34
4.3.6. Postoperative complications 35
4.3.7. Postoperative residual findings- echocardiography findings 37
4.3.8. Early mortality 39
4.3.9. Discharge 39

5. Late results and follow- up ***41***

5.1. Re- admissions **41**

5.2. Late operative interventions (Redo) **42**

5.3. Follow- up **48**
5.3.1. General findings 48
5.3.2. Electrocardigraphy findings 49
5.3.3. Echocardiography findings 49
5.3.4. Follow- up therapy 50

6. Discussion ***51***

6.1. Preoperative situation **51**
6.1.1. Preoperative findings 51
6.1.2. Medical therapy (Anticongestive therapy) 53
6.1.3. Palliative procedures 53
6.1.4. Preoperative diagnosis 54

6.2. Operative data **55**
6.2.1. Total bypass and aortic clamping time 55
6.2.2. Operative technique 55
6.2.3. Intraoperative echocardiography 56
6.2.4. Intraoperative complications 56
6.2.5. Thorax closure 57

6.3. Postoperative course **57**
6.3.1. Postoperative need for catecholamine and diuresis therapy 57
6.3.2. Postoperative pulmonary hypertensive crisis 58
6.3.3. Mechanical ventilation and Intensive care unit stay 59
6.3.4. Postoperative complications 59
6.3.5. AV valve function after AVSD repair 60
6.3.6. Left ventricular outflow obstruction 62
6.3.7. Complete AV- block and pacemaker implantation 62
6.3.8. Right ventricular outflow obstruction 63
6.3.9. Medical therapy at discharge 63
6.3.10. Survival and mortality 64
6.3.11. The need for reoperations 66

7. Summary / Zusammenfassung ***68***

7.1. Summary **68**

7.2. Zusammenfassung **71**

8. Abbreviations ***74***

9. References ***76***

10. Figures list ***83***

11. Tables list ***85***

12. Acknowledgments ***86***

13. Curriculum vitae ***87***

1. Introduction

1.1. Definition

Atrioventricular septal defects are congenital heart diseases in which the septal tissue immediately above and below the normal level of the AV valves is deficient or absent.
In all forms of atrioventricular septal defects there are abnormal AV valves to a varying degree. They have been also called endocardial cushion defects due to developmental disturbance in endocardial cushion, AV canal defects, ostium primum defects (when there is no VSD), and common AV valve (when there is only a single AV valve orifice) (1).

1.2. Etiology

During fetal life between 3-8 weeks, the embryologic abnormality in AV septal defects is disturbance of the proper development of the endocardial cushions, which are responsible for the septation of the atria and ventricles (membranous portion). But the exact causes are unknown (2).

1.3. History background

Abbot first recognized ostium primum ASD and common AV canal defect (3), but their morphologic similarity was recognized by Rogers and Edwards in 1948 (4). The terms partial and complete atrioventricular canal defects were introduced by Wakai and Edwards in 1956 and 1958 (5;6). The description of the position of the AV node and bundle of His, and the concept of ostium primum ASD (partial AV canal) and common AV orifice (complete AV canal) was done by Lev (7). The term intermediate and transitional was added by Wakai and Edwards and later by Bharati and Lev (8). Van Mierops studies added a great deal of knowledge to the overall anatomic features of AV septal defects during this periods (9). In 1966, Rastelli and colleagues described the morphology of AV valve leaflets in cases with common AV orifice (10). In 1976 the concept of leaflets bridging the ventricular septum introduced by Ugarte and colleagues, which was also used by Lev (11). In the late 1960s, based on anatomy and cineangiography and the description by Baron and colleagues and Van Mierop and colleagues, it was recognized that the basic defect was absence of AV septum, which can be imaged by echocardiography and in cineangiography in the right anterior oblique projection (12). These concepts were further expanded by Picoli and colleagues, and then R.H. Anderson who emphasized that all variations were part of a spectrum (13). Dennis

and Varco, in 1952 used a pump- oxygenator to close what they thought ASD. The patient died, and the autopsy showed that it was partial AV septal defect. The first successful repair of a complete AV septal defect was done by Lillehei and colleagues in 1954, by using cross circulation and direct suture of the atrial rim of the defect to ventricular septal crest (14). In 1955, Kirklin and colleagues closed partial AV septal defect by open cardiotomy and use of the pump- oxygenator (15). Early mortality rates for repair were 50%. The most common complications were complete heart block, mitral valve regurgitation and creation of subaortic stenosis (16). After delineation the bundle of His by Lev in 1958, the incidence of heart block reduced. The improved understanding of the structure and function of the common AV valve and the improved surgical techniques and cardiopulmonary bypass and a realization of the importance to close the mitral valve cleft without inducing stenosis lead to decreased short- and long-term incidence of mitral regurgitation with low morbidity and mortality rates. The single-patch technique was first described by Maloney and colleagues and later on by Gerbode in 1962 (17). The two- patch technique was described early by Dubost and Blondeau in 1959 (18).

1.4. Epidemiology

Seven to 8 babies per 1000 live births have congenital heart disease, and this accounts for 3% of all infant deaths and 46% of deaths due to congenital malformations. Around 18- 25% of affected infants die in the first year with 4% of those surviving infancy dying by 16 years (Dezateux et al. (19)). Atrioventricular septal defects represent approximately 4% of all congenital cardiac anomalies, and they are frequently associated with other cardiac malformations, especially patients with Down syndrome. Complete AVSD is frequently (60%-86%) associated with Down syndrome (20;21).

1.5. Anatomy and Associated cardiac anomalies

1.5.1. General morphologic anatomy

The deficiency or absence of AV septum above the AV valves results in an ostium primum defect and below the AV valves it results in a deficiency of the basal (inlet) portion of the ventricular septum. The patients with partial AV septal defects have ostium primum ASD and some deficiency in the basal (inlet) portion of the ventricular septum which is less than in patients with complete AV septal defects (22). The septal deficiency may or may not result in interatrial or interventricular communications, depending on attachments of the

AV valves. From the clinical point of view, there are partial, intermediate, and complete forms of AV septal defects. In the partial form, there exists an ostium primum ASD. Here the AV valves are attached to the crest of the interventricular septum, and there is usually no interventricular communication. The anterior leaflet of the mitral valve is considered to form part of a trileaflet mitral valve, because it has a cleft of varying degree. On occasion, this mitral valve may have some degree of incompetence, but most commonly, it is competent. In the intermediate form, the main distinguishing feature from partial AV septal defects is the incomplete attachement of the AV valves to the interventricular septum. So that some gaps may exist and some degrees of underdevelopment of the leaflet tissues may be present. In the complete AV septal defect, both the lower atrial and inlet (basal) ventricular septum are deficient or absent. The attachment and configuration of the AV valves to the ventricular septum are quite variable.

There is often variability in the number of leaflets, but usually five or more AV valves leaflets of variable size are present. There may be one (common) or two AV valve orifices. For left AV valve there is left superior leaflet (LSL), left inferior leaflet (LIL) and left lateral leaflet (LLL). For right AV valve there is right superior leaflet (RSL), right inferior leaflet (RIL) and right lateral leaflet (RLL) (Figure 1).

The ratio of anterior leaflet to posterior leaflet of the left AV valve in patients with AV septal defect is reversed to normal, this means that the posterior (left lateral) leaflet contributes to one- third (1/3) and the bileaflets anterior cusp (the left superior and inferior leaflets together) contributes to two- thirds (2/3) of the mitral valve annulus (Figure 2).

The hearts with AV septal defects are characterized by absence of the usual wedged position of the aortic valve in relation to both AV valves in normal hearts. This is due to down displacement toward the apex of AV valves because of deficiency of the inlet portion of the septum, so that aortic valve is elevated and displaced anteriorly (9). In addition, the left ventricular outflow tract is narrowed and elongated, although rarely sufficient to be of hemodynamic importance in the unrepaired heart, while the LV inflow tract is shortened (13). The AV node is displaced posteriorly and inferiorly toward the coronary sinus, so that it lies between it and the ventricular crest, in the nodal triangle (Koch triangle), which is bounded by the coronary sinus, the rim of the ASD, and the posterior attachment of the inferior bridging leaflet. The bundle of His courses antero- superiorly to run along the leftward aspect of the crest of the VSD, giving off the left bundle and continuing as the right bundle branch (7) (Figure 3).

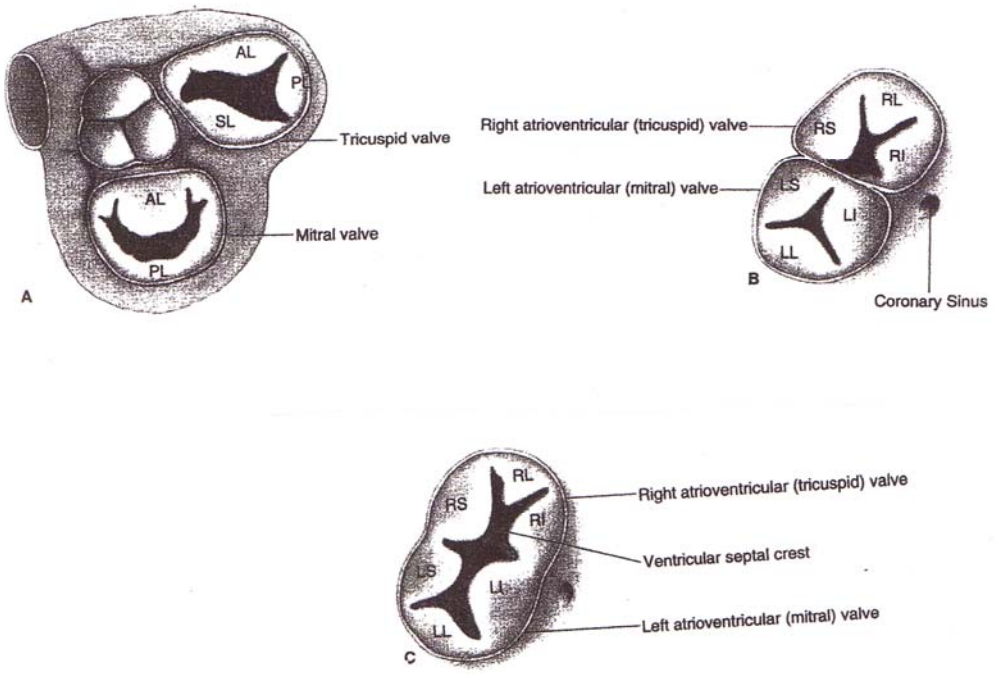

Figure 1: Mitral- tricuspid valve relationship. A: In the normal heart. B: Partial atrioventricular septal defect. C: Complete atrioventricular septal defect. (Modified from Khonsari (23)).

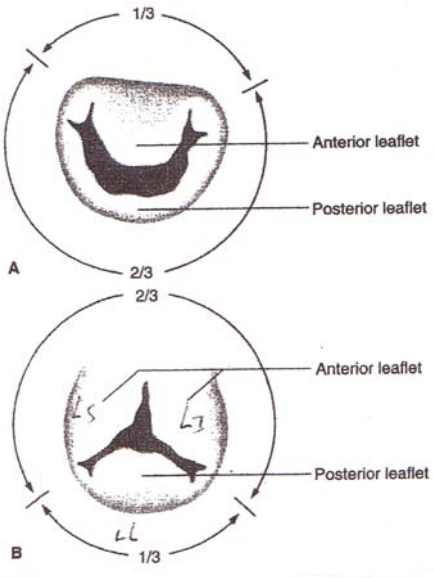

Figure 2: Mitral valve annular configuration. A. In the normal mitral valve. B. In an atrioventricular septal defect mitral valve. (Modified from Khonsari (23)).

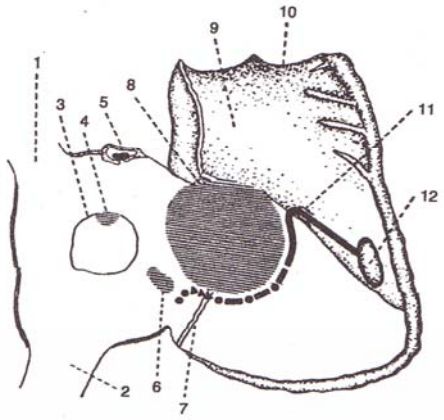

Figure 3: Sketch of the course AV node and His bundle. (Modified from Lev (7)).

Key: ●, AV node; ▲, penetrating portion of the AV bundle; ●—, branching of the AV bundle; —, right bundle branch; 1, SVC; 2, IVC; 3, limbus; 4, PFO; 5, cut edge of atrial appendage; 6, coronary sinus; 8, AV septal communication; 9, infundibulum; 10, base of pulmonary valve; 11, muscle of Lancisi; 12, cut edge of moderator band.

1.5.2. Partial atrioventricular septal defect

There is usually ostium primum ASD of moderate size which is bounded superiorly by a crescentic ridge of atrial septum that fuses with the AV valve annulus inferiorly only at its margins (Figure 4). This defect is characterized by presence of two AV valves, in which the mitral valve has a cleft between the left superior and left inferior leaflets and are joined to a variable extent anteriorly by leaflet tissue near the crest of the ventricular septum, so that it is a tricuspid valve in contrast to a normal valve. In most cases there is also a patent foramen ovale or ostium secundum ASD. The interatrial communication may be small in size and is restricted to the area normally occupied by the atrioventricular septum or because of the fusion of the base of the left superior or inferior leaflets to the edge of the adjacent atrial septum (24). Rarely, AV valve tissue is attached completely to the edge of the atrial septum, and no interatrial communication exists despite the deficiency in the septum (13;25). In unusual variants of partial AV septal defect some degree of deficiency of the inlet portion of the ventricular septum may be found, especially when the inlet portion is shortened and this leads to interventricular communication, but when the left superior and inferior leaflets are attached to the downward displaced septal crest, there is usually no interventricular communication. Occasionally there are one or more small interventricular communications beneath the AV valve.

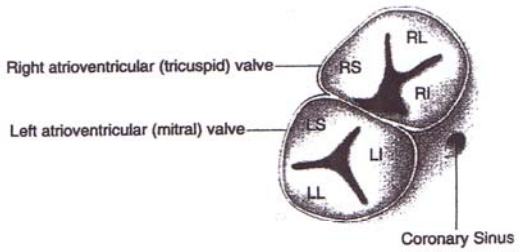

Figure 4: Partial atrioventricular septal defect. (Modified from Khonsari (23)).

Key: RS, RL, and RI, are right superior, right lateral, and right inferior leaflets respectively. LS, LL, and LI, are left superior, left lateral, and left inferior leaflets respectively.

1.5.3. Complete atrioventricular septal defect

Characterized by moderate to large interventricular communications, and common AV valve in which the left superior and left inferior leaflets are usually separated (Figure 5). The deficiency in inlet portion of the ventricular septum is usually more than in partial AV septal defect. The interventricular communication is large beneath left superior leaflet and smaller or none beneath left inferior leaflet. Very rare, there is no VSD beneath the left superior leaflet and a large one beneath left inferior leaflet (26;27).

Chordal attachments of the common AV valve in the LV are usually relatively normal, but displaced toward the apex of the heart due to deficiency of the inlet portion of the septum, this leads to no longer aortic valve between the AV valves (28-30). In LV a third papillary muscle may be present and the posterior papillary muscle is displaced laterally. There may be only one papillary muscle which is producing a parachute type valve that is difficult to repair. Rarely, the left AV valve is stenotic, but this is usually associated with hypoplasia of the LV (31). The right AV valve has also superior, inferior, and lateral leaflets. The right superior leaflet is small when the left superior leaflet bridging is extensive and large when the left superior leaflet bridging is mild or absent.

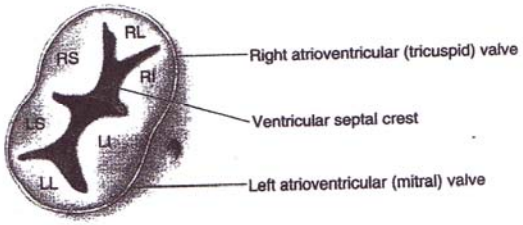

Figure 5: Complete atrioventricular septal defect. (Modified from Khonsari (23)).

Key: RS, RL, RI are right right superior, right lateral, and right inferior leaflets, respectively. LS, LL, LI are left superior, left lateral, and left inferior leaflets, respectively.

1.5.4. Rastelli classification

This classification based on whether the left superior leaflet bridges or not over the septal crest to the right ventricular side. It essentially focuses on the shape, size, location and details of the attachments of the left superior leaflet.

In type A, which is very often seen, the left superior leaflet is over the left ventricle and its chordal attachment is to the crest of the ventricular septal defect.

In type B, which is rarely seen, the chordal attachment of the left superior leaflet is to an abnormally located papillary muscle on the right ventricular aspect of the interventricular septum.

In type C, which is seen quite often, the left superior leaflet is large and bridges the ventricular septal defect and right ventricle and its chordal attachement are variable (10) (Figure 6).

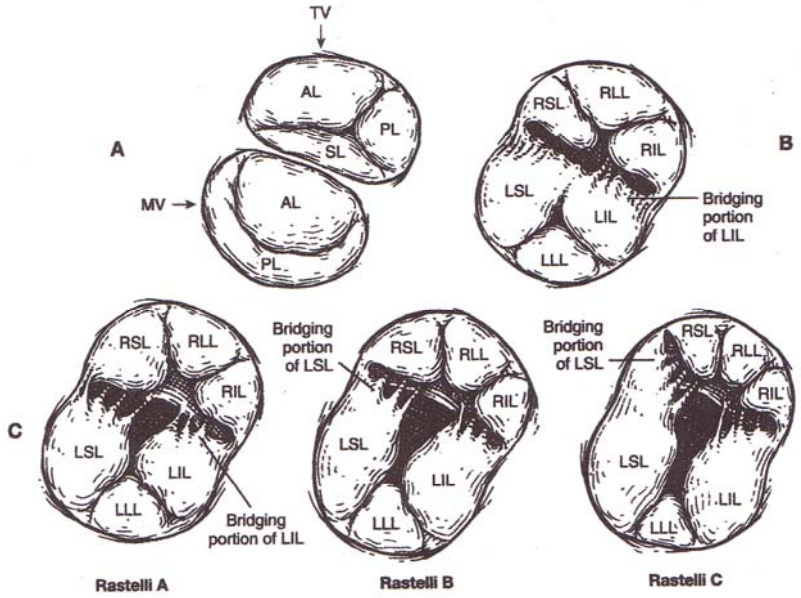

Figure 6: Atrioventricular valves viewed from atrial side. A. Normal mitral and tricuspid valves. B. Leaflets in partial atrioventricular septal defects. C. Rastelli´s classification of complete atrioventricular septal defects. (Modified from Kirklin/ Barratt-Boyes (32)).

1.5.5. Associated cardiac anomalies

Patent ductus arteriosus is present in about 10% of cases especially in complete AV septal defects. Tetralogy of Fallot is present in about 5% of patients with AV septal defects. Double outlet right ventricle without pulmonary stenosis is found in about 2% of patients. Completely unroofed coronary sinus with left superior vena cava is found in 3% of cases of the complete AV septal defects and 3% of cases of the partial AV septal defects (25). Pulmonary vascular disease is common in complete AV septal defect and usually appears early in life and progresses. Down syndrome is found in 75% of cases with complete AV septal defect, but is rare in cases with partial AV septal defects. Left ventricular outflow tract obstruction is rare in unoperated patients (about 1%) (25), but it becomes apparent as a postoperative complication (33).

1.6. Pathophysiology, Natural history and Diagnostic methods

1.6.1. Pathophysiology

Unless severe pulmonary hypertension or associated pulmonary stenosis, there is usually left to right shunt. In partial AV septal defect, it is at the atrial level and usually large, but sometimes it is small or moderate. If the shunt is large, and there is no AV valve

regurgitation, then it is hemodynamically similar to ASD of the secundum type, and only the RV stroke volume is increased. In case of important left AV valve regurgitation, the left to right shunt will be more, and the stroke volume of both LV and RV will be increased, and cardiomegaly and heart failure develop early. In case of complete AV septal defect, the left to right shunt is both at atrial and ventricular level and pulmonary artery pressure approaches the systemic pressure and if not corrected early the pulmonary resistance will be fixed and the risk of repair is increased (34).

1.6.2. Natural history

The natural history depends mostly on the extent of the three components of the septal defects; atrial shunt, ventricular shunt, and the AV valve regurgitation. In complete AV septal defects they usually are presented early in life with severe heart failure with or without pulmonary infections, which is complicated if it is associated with Down syndrome, because of the early tendency to develop fixed pulmonary vascular resistance. In the other end of the spectrum, the partial AV septal defect, the prognosis depends on the extend of shunt volume and AV valve regurgitation. The patients are usually asymptomatic and presented later in childhood or young adulthood. By complete AV septal defects the mean life expectancy by some patients is less than 6 months or even less in patients with a fixed pulmonary vascular resistance who developing symptoms of Eisenmenger- reaction (right to left shunt).

1.6.3. Diagnostic methods

The exact diagnosis of AVSD can be made with two- dimensional echocardiography (35). Clinical presentation, chest radiograph, and electrocardiogram let suspect AVSD (36). The need for cardiac catheterization is not necessary before 6 months of age because the probability to develop fixed high pulmonary resistance is low, but it can be used when major cardiac anomalies coexist or evidence of pulmonary vascular disease or the echocardiographic examinations are not clear (29).

2. Therapy options

2.1. Medical therapy

Patients with partial AV septal defects present with signs and symptoms similar to those of secundum ASD´s and as such, they rarely need medical therapy. In patients with complete AV septal defects, medical therapy consists of anticongestive treatment for the signs and symptoms of congestive heart failure. The mainstays of medical therapy are Diuretics (for diuresis for the volume overloaded heart), digoxin (as a mild inotrope), and ACE-inhibitors (for afterload reduction), as reported by Montigny et al. (37). In our institution low dose B- blockers are successfully used due to blocking the sympathetic activity and by reducing systemic vascular resistance without decreasing blood pressure which is also described by Buchhorn et al. (38).

2.2. Surgical therapy

2.2.1. Surgical indications

The diagnosis of an AV septal defect is in principle an operation indication, because spontaneous closure does not occur and the hemodynamic derangement is nearly always present. By partial AV septal defect the optimal age for operation is 1 to 2 years, but this could be earlier if there is AV valve regurgitation, heart failure or severe growth failure.

In complete AV septal defect, operation is indicated early in the first year of life, usually before 6 months of age, but if refractory heart failure or severe growth failure is evident early, then repair at 2 to 4 months of age is indicated. Operation after the first year of age is associated with increased risk, because the pulmonary vascular disease may be already too severe to permit repair.

2.2.2. Aims of surgical repair

1- Closing the interatrial communication, which is always present.
2- Closing the interventricular communication, when one is present.
3- Creating, or maintaining two competent, nonstenotic AV valves.
4- Avoiding AV block induction by damage to the AV node and or His bundle.
   For these purposes there are many repair techniques, which, when used properly, provide good results (39;40), for example:

a. One or two patches may be used to repair the malformation when there is a large VSD (41).

b. A large bridging left superior leaflet, may be divided to facilitate the repair or left intact (25;42;43).
c. Damage to AV node and His bundle may be avoided by staying on the right side of the septum (25).
d. The cleft between the LSL and LIL, may be sutured or may be left as tricuspid valve to avoid valve stenosis (44;45).
e. The AV valves may be attached to the patch by simple or by pledgeted mattress sutures with some sort of sandwich method, to establish AV valve competence (25;44).

2.2.3. Surgical techniques

2.2.3.1. Two- patch technique for complete AVSD repair

After a median sternotomy, a piece of pericardium is taken and cleared from pleural fat, and set aside in 0.6% glutaraldehyde, after the remaining pericard is widely opened, stay sutures are placed and the anatomy is examined. The patient is heparinized and arterial cannula inserted. Two venous cannulae are used, one inserted through the right atrial appendage in the SVC, the other through the low right atrial wall in IVC. Direct caval cannulation can be done also. CPB is established with 34°C cold perfusate, and the patient cold to 31°C. The cardioplegic needle is now placed in the ascending aorta, the aorta is clamped, and the cold cardioplegic solution is infused. The caval tapes are snugged.

After that the right atrium is opened, the malformation is examined and each morphologic details are noted. Valve leaflets are often closed as they are in systole. If not, saline is injected into LV to close them, then the morphology of the leaflets is studied to plan the repair of any regurgitation or to accommodate any lack of left AV valve tissue. A fine polypropylene suture is placed between LSL and LIL and left loose. The leaflets are allowed to open and atrial and ventricular septal defects are studied. Position of coronary sinus is noted, and the course of AV node and His bundle is imaginated from knowledge of the anatomy. The leaflets are retracted and the depth of the ventricular septal defect estimated. Dacron patch is trimmed to a crescent shape of appropriate size. Suture line may begin anywhere, but it must be on the right ventricular side of all chordae from left side leaflets, including those from any bridging components of the LIL. Suture line should stay well back from ventricular crest and catch some of the base of the RIL to avoid His bundle injury. Suture line is completed anteriorly, here care must be taken to avoid LVOTO. The LSL and LIL are precisely fixed to the patch by using interrupted simple or mattress sutures. Here care must be taken to ensure that the mitral valve apparatus at the patch is

appropriately narrow so as not to create regurgitation and at the correct height so as not to produce LVOTO (too low) or mitral regurgitation (too high). Mitral valve cleft is closed by interrupted simple sutures, testing mitral valve for competence. The RSL and RIL are fixed to the Dacron patch, and any cleft closed also. The pericardial patch is trimmed to size the atrial defect, and a new suture line is begun with bites incorporating pericardial patch, the right AV valve, the Dacron patch and little fom left AV valve. The pericardial patch is sutured anteriorly, superiorly, and inferiorly by leaving coronary sinus draining into left atrium to avoid conduction system injury (Figure 7: A- D). After that rewarming is carried out, right atrium closed, the heart is filled, and the aortic cross clamp is removed after deairing procedures are performed. Then operation assessment is performed by transesophageal echocardiography.

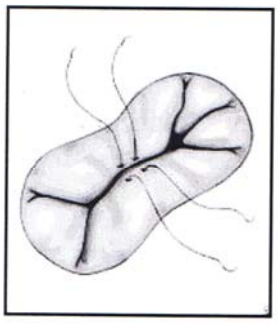

Figure 7- A: The common AV valve is floated to a closed position using saline solution. The central apposition points of the superior and inferior bridging leaflets are identified and marked with fine polypropylene. (Modified from Ohye (46)).

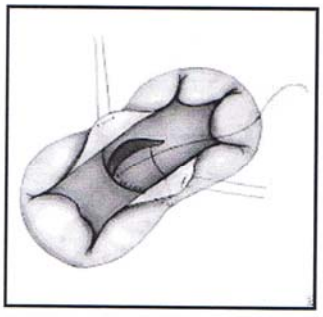

Figure 7- B: Two-patch technique. A patch of Goretex or Dacron is fashioned and secured along the crest of the ventricular septal defect. (Modified from Ohye (46)).

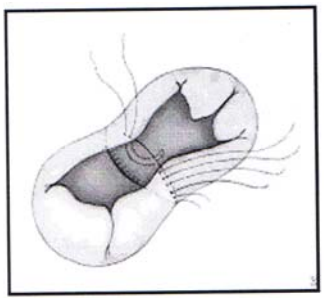

Figure 7- C: Two-patch technique. Interrupted horizontal mattress sutures are placed through the crest of the VSD patch and the inferior and superior bridging leaflet, dividing the common AV valve into right and left components. (Modified from Ohye (46)).

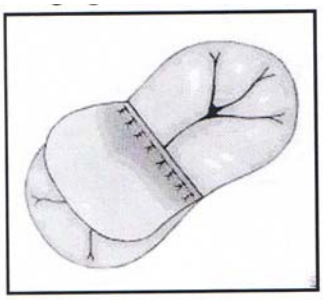

Figure 7- D: The pericardial patch is sutured to the crest of the prosthetic ventricular septum with the superior and inferior bridging leaflet sandwiched between the 2 patches. (Modified from Ohye (46)).

2.2.3.2. Single- patch technique for complete AVSD repair

Repairing differs from 2- patch technique in the following:

1. Single patch almost always pericardium.
2. The waist tailoring at the level of AV valve is critical.
3. Both left and right AV valves are sutured to the pericardial patch.

The preparation for bypass is the same as for two- patch technique. After aortic cross clamping and cardioplegic infusion, oblique right atriotomy is done, identifying the most anterior point of LSL and LIL, and 6-0 Prolene suture is placed and left loose, then the AV valve is tested by saline infusion. The bridging LSL and LIL is incised to allow access for suturing the pericardial patch (after trimming) to ventricular septal defect, to be later fixed again in the patch. The patch sutured on the right side of the septum, with care taken, to avoid injury to His bundle. The leaflets of both right and left AV valve are attached to the patch at its waist. The AV valve clefts are closed with interrupted simple suture and tested

with saline for competence. The same patch is also used to close the atrial septal defect, leaving the coronary sinus draining into the left atrium, in the same way as in two- patch technique (Figure 8: A- D).

After that rewarming, right atriotomy closure, deairing and aortic cross clamp removed. Then operation assessment by transesophageal echocardiography, if severe abnormalities are present, they should be corrected. Then the operation is completed in the usual manner after placing pulmonary artery catheter.

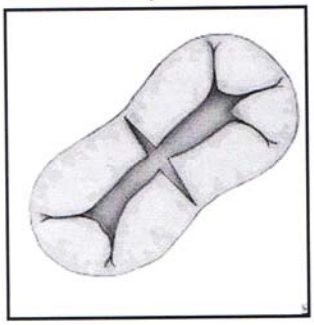

Figure 8- A: Single- patch technique. The superior and inferior bridging leaflets are divided into right and left component. (Modified from Ohye (46)).

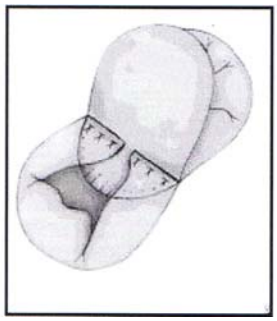

Figure 8- B: The leaflets are resuspended to the patch by passing sutures through the cut edge of the AV valve leaflet, the patch, and the cut edge of the right AV valve and tying the sutures. (Modified from Ohye (46)).

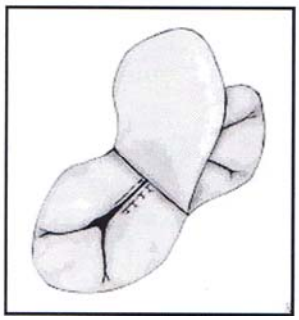

Figure 8- C: The cleft of the mitral valve between the superior and inferior bridging leaflets is closed. (Modified from Ohye (46)).

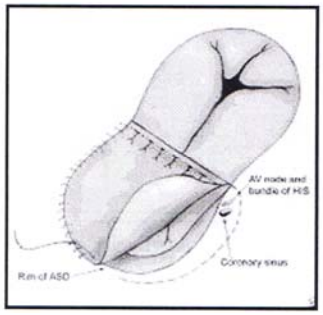

Figure 8- D: The atrial septal defect is closed with an autologous pericardial patch. The coronary sinus is placed in the left atrium to avoid injury to the conduction system. The rim of the ASD, the AV node, the bundle of His are indicated. The dashes represent the proposed suture line. (Modified from Ohye (46)).

2.2.3.3. Repair of partial AV septal defect

It is a single patch repair in which the atrial septal defect is closed by a pericardial patch and the mitral valve cleft is closed at the thickened and rolled edges. The same precaution to avoid injury to AV node and His bundle is taken, by suturing the pericardial patch, so that the coronary sinus is draining to the left atrium, as in complete AV septal defect repair. The coronary sinus can be left draining to right atrium also.

2.3. Aims of the study

In our study we analyzed the records (data) of 110 patients with atrioventricular septal defects (74 patients with Down syndrome and 36 patients with normal chromosomal pattern), who underwent repair between January, 1997 and December, 2007. To evaluate the impact of different preoperative, operative, and postoperative factors on the outcome after repair of AVSD, we compared the patients with Down syndrome and non- Down syndrome in the early postoperative period and long- term course.

3. Patients and methods

3.1. Study design

Between January 1997 and December 2007, 130 patients were diagnosed with atrioventricular septal defects (partial and complete) in the Pediatric Heart Center, Giessen. From these 110 patients underwent two- patch and single- patch repair (biventricular repair), 20 patients were excluded, because 18 of them underwent univentricular correction repair (total cavopulmonary connection), and 2 underwent pulmonary artery banding, and were waiting for the final repair. These cohort included all patients undergoing two- patch and single- patch repair with and without palliative procedures, and also patients that underwent Fallot tetralogy repair.

Institutional Review Board approval was obtained prior to study inclusion. Clinical preoperative patient characteristics, operative details and postoperative outcome data, including complications and mortality data were collected retrospectively.

The patients (110) were divided into 2 groups, 74 patients (67.3%) presented with Down syndrome (group D) and 36 patients (32.7%) without Down syndrome (group ND).

There were 58/110 females (52.7%) and 52/110 males (47.3%). A total of 100 patients (90.9%) had primary repair (one stage repair), 65 patients (87.8%) in group D and 35 patients (97.2%) in group ND. The mean age at primary repair was 1.9 ± 3.6 years, while the median age was 7.2 months (range, 92 days- 19.8 years). A total of 40 patients (36.4%) were younger than 6 months at the primary repair, 33 patients in group D and 7 patients in group ND. The median weight at repair was 5.82 kg (range, 3.35- 65 kg). A total of 3 patients (2.7%) underwent repair weighing less than 4 kg, 2 patients with Down syndrome and 1 patient without . The mean age at primary repair was 1.5 ± 3.5 years (median = 6.1 months) in group D and 2.6 ± 3.9 years (median = 14.5 months) in group ND. A total of 10 patients (9.1%) underwent palliative surgery 12 days to 6.9 years (mean = 0.9 ± 2.1 years, median = 3.7 months) before repair. There were 106 patients diagnosed as complete AV septal defects and 4 diagnosed as partial AV septal defects (Table 1). According to the intraoperatively assessed Rastelli classification: 84.5 % of the patients who underwent atrioventricular septal defect repair presented with type A, 10 % with type B, and 5.5 % presented with type C. Six of the patients who underwent primary repair had severe left side AV valve insufficiency, and 6 patients (5.5%) additionally associated with tetralogy of Fallot. Clinical follow- up was possible for 105 patients (96.3%) and the mean follow-up duration was 3.5 ± 3.2 years, range (13 days- 10.9 years) (Table 2).

Table 1: Patients clinical characteristics

	Total number	(%)
Complete AVSD	106/110	96.4
Partial AVSD	4/110	3.6
Female	58/110	52.7
Male	52/110	47.3
Down syndrome (group D)	74	67.3
Non- Down syndrome (group ND)	36	32.7

Table 2: Patients characteristics and follow- up (All patients)

	Number	(%)	Mean	SD	Median	Range
Operation Age			1.9 y	3.6 y	7.18 m	3.1 m- 19.8 y
Operation weight (kg)			9.3 kg	10.6 kg	5.82 kg	3.35- 65 kg
Follow-up	105/109	96.33	3.5 y	3.2 y	2.5 y	13 d- 10.9 y

3.2. Diagnosis

All patients with AV septal defects are diagnosed or the diagnosis confirmed by two-dimensional echocardiography (100%) particularly with Doppler color flow imaging and when possible, with transthoracic window, M- mode. Cardiac catheterization was done for 79 patients (71.8%) without anaesthesia in analgo- sedation and all were diagnostics. Direction and magnitude of shunting, pulmonary and systemic pressures, resistances and reversibility, if pulmonary vascular resistance was high, left and right ventricular pressures were measured. In addition to that, associated cardiac anomalies were confirmed or excluded. By all patients electrocardiography was done to check for cardiac rhythm, ventricular hypertrophy, PR- interval, QRS interval and vectorcardiogram. Chest radiography was done for all patients. Preoperatively all patients underwent screening for other congenital anomalies and metabolic diseases by newborn screening test. All patients underwent intraoperatively and postoperatively echocardiography examination (Table 3).

Table 3: Diagnostic methods

	Number	(%)
Echocardiography	110	100
Cardiac catheterization	79	71.8
Electrocardiography	110	100
Chest radiography	110	100

3.3. Anaesthesia and CPB

Induction of anaesthesia was performed with desflurane®, remifentanil® or fentanyl® together with muscle relaxant (atracurium®), and maintenance of anaesthesia was done with continuous infusions associating fentanyl®, propofol® (in patients more than 1 year of age) and or midazolam®. A radial or femoral arterial line and central venous line were placed. All patients underwent the procedure with a closed circuit including gas exchanger and a roller pump. The efficacy of perfusion was assessed by continuous monitoring of the oxygen venous saturation which was kept over 70%, continuous hemoglobin level measurement and discontinuous blood gas analysis. Temperature was measured with rectal, esophageal and arterial line probes. CPB was performed at a flow rate 2,6 L/min./m² in the hypothermic phase (31-32°C), using pH-stat blood gas management with a PaO2 maintained below 150 mmHg. The hematocrit is targeted to be at least 45% at the end of CPB.

3.4. Operative techniques

All procedures were performed by more than one surgeon, through median sternotomy. An autologous pericardial patch was harvested and kept moist in a cold saline after fixation in glutaraldehyde. CPB was established via standard aortic and bicaval venous cannulation. The left ventricle was decompressed by venting through the ASD or the patent foramen ovale after right atriotomy. Moderate hypohermia (31-32°C) and antegrade cold Bretschneider cardioplegia (30 ml/kg) were used for myocardial protection. Single- patch technique plus left AV valve cleft closure and or right AV valve repair was done in all patients with partial AV septal defects (n = 4). Two- patch technique or Single- patch technique plus AV valve repairs was done in all patients with complete AV septal defects (n = 106), this including the tetralogy of Fallot and persistent left superior vena cava patients. In some patients with complete AVSD, the VSD was closed by direct fixation of AV valve to the ventricular septal crest, or by a direct interrupted mattress suture

(modified single- patch technique), or simply left because it was already almost closed or covered by septal leaflet of the tricuspid valve (right side AV valve).

3.5. Follow- up

Follow- up data were obtained by review of clinical records, including echocardiography, cardiac catheterization and electrocardiography data. To assess the follow- up, all available clinical records at the Pediatric Heart Center, Giessen and clinical records from the local pediatric cardiologists are collected. Further telephone communications with the patients pediatricians and last polyclinic visit summary were gathered. The mean follow- up duration for all patients was 3.5 ± 3.2 years (range, 13 days- 10.9 years), and it was for 96.3% (105/109) of patients complete.

3.6. Statistical analysis

All the data were analyzed using a commercial statistical software program. Data (continuous variables) are presented as mean ± standard deviation, or median with range as appropriate. Binomial or ordinal data are expressed as percentages. Time- related changes in fredoom from re- operations and catheter- based intervention were estimated by using the Kaplan- Meier analysis (method). Time- related changes in survival estimation by using the Kaplan- Meier analysis was not used, because there was only 1 death. Statistical significance was reached when p- value was < 0.05 by using un-paired student´s t- test. All data were analyzed with statistical computer programs " WinSTAT and InSTAT".

4. Results

4.1. Preoperative data

4.1.1. General patients characteristics

From 110 patients who underwent AV septal repairs with two-patch and single- patch technique, 58 patients were females (52.73%), with 45.9% of the patients in group D (Down syndrome) and 66.7% in group ND (non- Down). The mean weight at repair was 9.3 ± 10.6 kg, the median weight at repair was 5.82 kg (range, 3.35- 65 kg) for all patients. In group D, the mean weight was 8.1 ± 9.8 kg (median = 5.6 kg), and in group ND the mean weight was 11.8 ± 11.9 kg (median = 8.15 kg). The two- tailed p- value was not quite significant between the 2 groups (p = 0.0865). For all patients the median age at the operation was 7.2 months (range: 3.1 months – 19.8 years), and the mean age was 1.9 ± 3.6 years. In group D the mean age was 1.5 ± 3.5 years (median = 6.1 months), while in group ND the mean age was 2.6 ± 3.9 years (median = 14.5 months). The two- tailed p- value was not significant between the 2 groups (p = 0.1393). From 110 patients, 106 were with complete AV septal defect (96.4%), and 4 patients (3.6%) were with partial AV septal defect, and by 55/110 patients (50%). In addition to ASD- I, there was also ASD- II or PFO in 50% of the patients in group D and also in 50% of the patients in group ND. According to Rastelli classification, type A was present in 93/110 of patients (84.5%), type B in 11/110 of patients (10%) and type C in 6/110 of patients (5.5%). There was no difference between group D and ND. By 5/110 patients the diagnosis of AV septal defect was done prenatal (4.55%) by using echocardiography. The preterm babies were 13/110 patients (11.82%), there was no difference between group D and ND. The presenting signs and symptoms were; heart murmur in 100%, pulmonary hypertension in 69/110 (62.7%), sweating by drinking 55/110 (50%), failure to thrive 40/110 (36.4%), tachypnea and dyspnea 37/110 (33.6%), cyanosis 29/110 (26.4%), pallor 25/110 (22.7%), respiratory infection 24/110 (21.8%), edema 21/110 (19.1%), hypothyrosis 17/110 (15.5%), and epilepsy in 1/110 (0.91%). Preoperative incomplete and complete RBBB were diagnosed in 38/110 patients (34.6%), and AV block grade I- II in 8/110 patients (7.3%). Only 1 patient had AV block grade II, Wenckebach type. The median preoperative oxygen saturation was 96% (range,78-100%) and the mean was 95% ± 4.3. Only 1 patient (0.91%) was admitted to the hospital intubated from regional hospital because of pulmonary hypertensive crisis (Table 4 and 5).

Table 4 : Preoperative data for all patients

	Number	(%)
cAVSD	106	96.4
pAVSD	4	3.6
ASD-II / PFO	55	50
Rastelli- A	93	84.5
Rastelli- B	11	10
Rastelli- C	6	5.5
Prenatal diagnosis	5	4.55
Preterm babies	13	11.8
Heart murmur	110	100
Pulmonary hypertension	69	62.7
Sweating	55	50
Failure to thrive	40	36.36
Tachypnea & dyspnea	37	33.64
Cyanosis	29	26.36
Pallor	25	22.73
Respiratory infection	24	21.82
Edema	21	19.09
Hypothyrosis	17	15.45
Epilepsy	1	0.91
Incomplete RBBB & Complete RBBB	38	34.55
AV block I- II	8	7.27
Preoperative intubation	1	0.91

Table 5: Oxygen saturation preoperatively

	Mean	SD	Median	Range
Oxygen saturation (%)	95	4.33	96	78- 100

The total number of patients who presented with signs and symptoms of heart failure (sweating, tachypnea, dyspnea and edema) were 74 patients (67.3%). In group D, 56 patients (75.7%) presented with pulmonary hypertension, 51 patients (68.9%) presented with symptoms and signs of congestive heart failure, and 20 patients (27%) presented with

respiratory infection. In group ND 13 patients (36.1%) presented with pulmonary hypertension, 23 patients (63.9%) with symptoms and signs of congestive heart failure, and 4 patients (11.1%) with respiratory infection (Figure 9). The preoperative analysis of both groups revealed that patients in group D exhibited a significantly higher pulmonary pressure compared with patients in group ND. From the patients with Down syndrome (D group), 62 patients (83.8%) were Rastelli type A, 8 patients (10.8%) were Rastelli type B, 4 patients (5.4%) were Rastelli type C, 5 patients with tetralogy of Fallot, and only 1 patient had preoperative severe mitral insufficiency grade (III) (Table 6). In group ND, 31 patients (86.1%) were Rastelli type A, 3 patients (8.3%) were Rastelli type B, 2 patients (5.6%) were Rastelli type C, 1 patient (2.8%) with tetralogy of Fallot, and 5 patients (13.9%) with severe mitral valve insufficiency (Table 7) and (Figure 10).

Table 6: Down syndrome patients characteristics (D)

	Number	(%)
Rastelli type A	62	83.8
Rastelli type B	8	10.8
Rastelli type C	4	5.4
Pulmonary hypertension	56	75.7
Tetralogy of Fallot	5	6.8
Severe MI	1	1.4

Table 7: Non- Down syndrome patients characteristics (ND)

	Number	(%)
Rastelli type A	31	86.1
Rastelli type B	3	8.3
Rastelli type C	2	5.6
Pulmonary hypertension	13	36.1
Tetralogy of Fallot	1	2.8
Severe MI	5	13.9

The incidence of severe mitral insufficiency was significantly lower among patients in group D compared with group ND, while the incidence of pulmonary hypertension, respiratory infection and associated tetralogy of Fallot was higher among patients in group D compared with group ND.

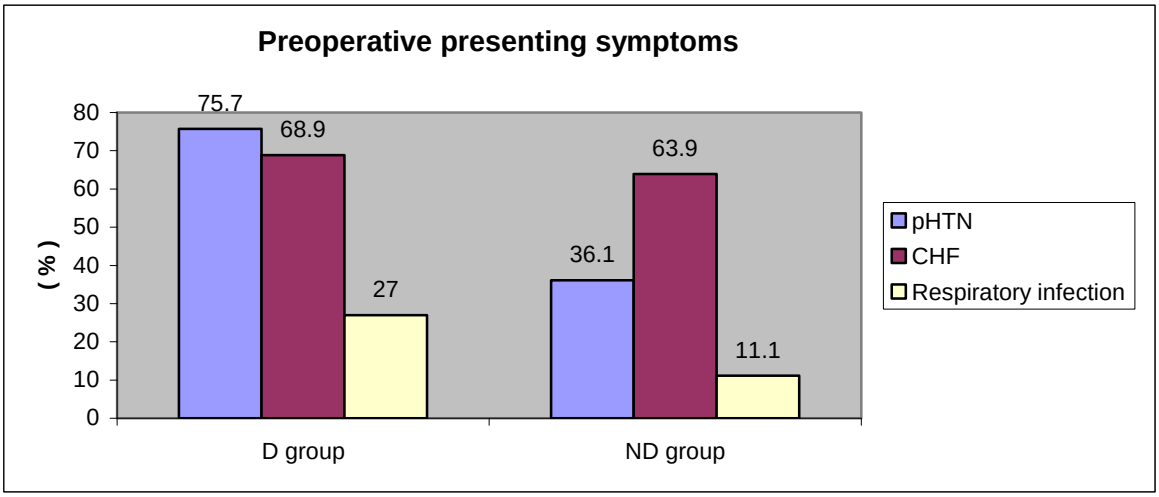

Figure 9: Preoperative presenting symptoms in Down and non- Down syndrome patients.

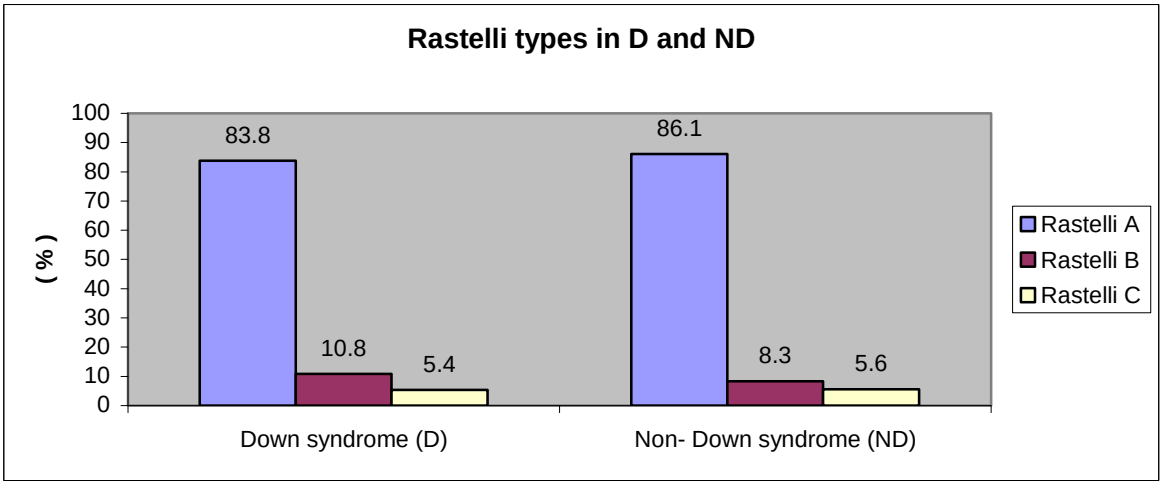

Figure 10: Rastelli types in Down syndrome and non- Down syndrome patients.

Other coexisting extracardiac congenital anomalies were observed in 11 patients (10%) all of them except one had Down syndrome, these anomalies including congenital cataract, Hirschsprung`s disease, congenital tracheal stenosis, anal atresia, und umbilical hernia.

4.1.2. Diagnosis

By all patients the diagnosis was made or confirmed by echocardiography and all patients were in sinus rhythm. In the preoperative echocardiography were 6 patients with mitral insufficiency grade III (5.5%), while 104 patients (94.5%) had no or mild mitral insufficiency. Cardiac catheterization was done for 79/110 (71.8%), only 2/79 (2.5%) had complications, 1 patient suffered of leg ischemia, the second had an arterio- venous fistula (femoral). Both were successfully treated without residual complications. In 74/110 patients (67.3%), AVSD was associated with Down syndrome, and the other most common coexisting cardiac anomalies were: patent ductus arteriosus 35/110 (31.8%), persistent left superior vena cava 7/110 (6.4%), RVOTO (Fallot tetralogy) 6/110 (5.5%), aortic coarctation 5/110 (4.6%), coronary origin anomalies 2/110 (1.8%), aberrant right subclavian artery 1/110 (0.91%). None of the patients presented with LVOTO (0%). In 25/110 patients (22.7%) the ventricles were unbalanced, out of these only 2/110 (1.82%) were with border line hypoplastic left ventricle, 24 patients with right ventricle dominance and 1 patient with left ventricle dominance (Table 8). Seventeen patients (22.9%) in group D and 8 patients (22.2%) in group ND were found to have unbalanced ventricles.

Table 8 : Coexisting cardiac anomalies and congenital anomalies

	Number	(%)
Down syndrome	74	67.3
Non- Down patients (ND)	36	32.7
Patent ductus arteriosus	35	31.8
Persistent left superior vena cava	7	6.4
RVOTO (Fallot tetralogy)	6	5.5
Aortic coarctation	5	4.6
Coronary artery anomalies	2	1.8
Aberrant right subclavian artery	1	0.9
Unbalanced ventricles	25	22.7
Hypolastic left ventricle (border line)	2	1.8
Mitral regurgitation grade III	6	5.5

4.1.3. Preoperative anticongestive therapy

The patients with AV septal defects, who required preoperatively medical therapy, were 70 (63.6%). This was consisting mainly of anticongestive drugs, the mainstays were lasix for diuresis, digoxin as a mild inotrope, and B- blockers plus ACE inhibitors for afterload reduction. In addition to that symptomatic treatment for example, thyroxine for hypothyrosis, and antibiotics for respiratory infection were administerd.

4.1.4. Preoperative palliative procedures

The choice to proceed to primary repair or to palliative procedure was based on the pre-operative clinical condition, echocardiography assessement and on the direct inspection of the heart at the time of operation. In 10/110 patients (9.1%) palliative procedures were done, including aorto- pulmonary shunts in 2/110 patients (1.8%), and pulmonary artery banding and rebanding in 8/110 (7.3%) (Table 9). In addition to that 3 patients underwent aortic coarctation repair (at the same time with banding). One of the aortic coarctation was left without correction because of its low grade and in the other patient, the correction was done at the same time with AV septal repair. All patients who underwent pulmonary artery banding procedures had pulmonary hypertension secondary to pulmonary overflow, 3 patients had right ventricle dominance, 4 patients had balanced ventricles, and 1 patient had left ventricle dominance. Those who underwent aorto- pulmonary shunt procedures (n = 2) had RVOTO, both of them had balanced ventricles. The palliative procedures were necessary in 9 patients (12.2%) in group D, and in 1 patient (2.8%) in group ND. This patient in the ND group underwent pulmonary artery banding.

Table 9: Palliative procedures

	Number	(%)
Aorto- pulmonary shunt	2	1.82
Pulmonary artery banding and coarctation repairs	8	7.27
Total	10	9.09

4.2. Intraoperative data

4.2.1. Operative techniques

After the routine aorto- bicaval cannulation, CPB with mild hypothermia had been established, antegrade cold Bretschneider cardioplegia was infused. Two- patch or single-

patch technique was done depending on the anatomical finding. Sixty- five patients (87.8%) in group D and 35 patients (97.2%) in group ND underwent primary AVSD repair. From those patients with Down syndrome 63/74 patients (85.1%) underwent two- patch technique repair and 11/74 patients (14.9%) underwent single- patch technique, while in group ND 18 patients (50%) underwent two- patch technique and 18 patients (50%) underwent single- patch technique. This revealed that more patients in group D underwent two- patch techniques compared with patients in group ND (Figure 11). The details of the operation of all patients were: one patient underwent a single-patch technique plus left side and right side AV valve repair and aorta coarctation repair (0.91%); 14 patients underwent a single- patch technique plus mitral valve repair (12.7%), 2 combined with PDA ligations; 14 patients underwent a single- patch technique plus left and right side AV valve repair (12.7%), 4 combined with PDA ligations; 3 patients underwent two- patch technique plus left and right side AV valve repair and pulmonary artery patch enlargement at the previous banding site (2.7%); 6 patients underwent 2- patch technique plus left and right side AV valve repair (1 patient had MV- replacement) and Fallot tatralogy correction (5.5%). From these, 1 patient received a Contegra graft, while the others had infundibular muscular resection and transannular patch enlargement or pulmonary valve commissurotomy; 19 patients underwent two- patch repair plus both AV valves repair and PDA ligation and resection (17.3%), 53 patients underwent two- patch technique plus left and right side AV valve repair (48.2%). In addition to AVSD repair there were 3 persistent left superior vena cava re-routing to the right. In total 29 patients (26.4%) underwent single- patch technique, including the patients with partial AVSD (n = 4). Eighty- one patients (73.6%) underwent two- patch technique (Table 10). In 99/110 patients (90%) the pericardial patch which used to close the ASD, was sutured so that the coronary sinus drained into the left atrium. By all patients the assessment of the morphologic and functional result was done by transesophageal two- dimentional color flow Doppler echocardiography. Seven patients required operative revision, from those, 5 patients with reinstitution of cardiopulmonary bypass; 4 patients showed severe residual mitral regurgitation, with 2 patients of them underwent MV repairs. The third patient was revised for residual mitral regurgitation and RVOTO. This patient underwent MV repair and pulmonary artery patch enlargement at the previous banding site. This patient later on underwent heart transplantation because of chronic heart failure. The fourth patient with residual mitral valve regurgitation underwent mitral valve replacement (mechanical, carbomedics- 16 mm). The fifth patient showed LVOTO. The reason of the obstruction was based on the VSD patch. This patient was

revised with the use of a new patch. Two patients suffering of cardiac tamponade underwent re-thoracotomy. In one of them an artificial 4 mm ASD was performed in the catheter lab because of high pulmonary pressure. We noticed, that only 1 patient (1.4%) in D group underwent revision with reinstitution of HLM, while 4 patients (11.4%) in group ND underwent revisions, which is quite significant.

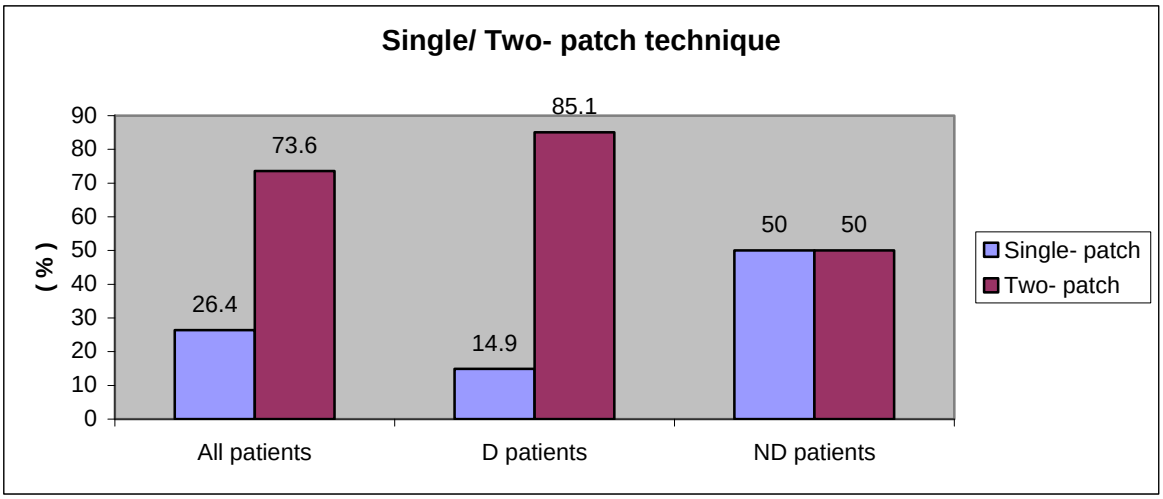

Figure 11: Single- patch and two- patch technique in all patients, Down syndrome patients and non- Down syndrome patients.

Table 10: Operative techniques

	Number	(%)
Single- patch + MV repair + TV repair + Coarctation repair	1	0.91
Single- patch + MV repair (2-PDA)	14	12.7
Single- patch + MV repair + TV repair (4-PDA)	14	12.7
Two- patch + MV repair + TV repair + PA-patching.	3	2.7
Two-patch + MV repair + TV repair + Fallot repair	6	5.5
Two-patch + MV repair + TV repair + PDA	19	17.3
Two-patch + MV repair + TV repair	53	48.2
Total single- patch technique	29	26.4
Total two- patch technique	81	73.6

Following surgery, the chest left open in 5 patients (closed only by pericardial membrane), in addition to that the chest was reopened in 1 patient because of hemodynamic instability. In all those patients, the chest was closed later on secondarly. In 4 patients the chest was closed directly after revision operations.

4.2.2. CPB duration and aortic- cross clamping

For all patients, the mean CPB time was 151 ± 60.5 min., while the median was 143 min. (range, 66- 326 min.), and the mean aortic cross clamping time was 88 ± 35 min., the median was 83.5 min. (range, 32- 207 min.) (Table 11). The mean CPB time in group D was 159.3 ± 56 min., and the mean CPB time in group ND was 133.9 ± 66.5 min.. The two- tailed p- value was considered significant (p = 0.0382) (Figure 12). The mean aortic cross clamping in group D was 95.3 ± 34.5 min., and in group ND was 73.1 ± 32.9 min.. The p- value was also considered significant (p = 0.0017). In 106/110 patients (96.4%), erythrocytes concentrates were used as a priming for ECC. The difference in CPB and aortic cross clamping times between the 2 groups may be attributed to the higher rate of using two- patch techniques in group D.

In the patient with the longest Bypass time (326 min.) the operative course was very complicated, because of the difficulty to repair the left sided AV valve, in the border line hypoplastic LV and difficulty to wean from HLM. This patient later on underwent successful heart transplantation.

Table 11 : Bypass time and aortic cross clamping

	Mean	SD	Median	Range
Bypass time (min.)	151	60.5	143	66- 326
Aortic cross clamping (min.)	88	35	83.5	32- 207

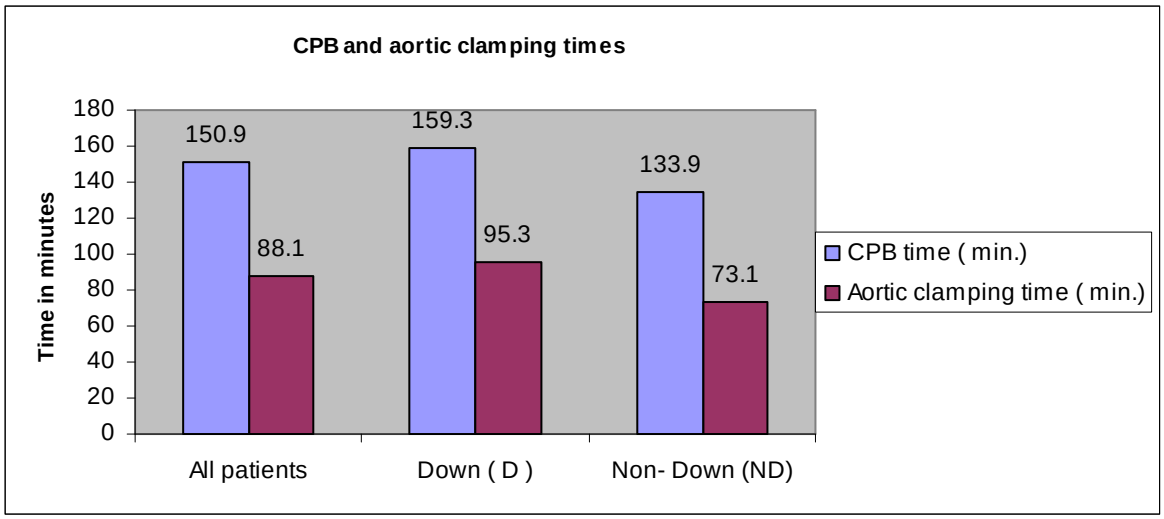

Figure 12: CPB and aortic cross clamping times.

4.2.3. Intraoperative complications

Pulmonary hypertensive crisis occurred in 13/110 of patients (11.8%), complete AV block occurred in 10 patients (9.1%), which necessitated external pacing (some of them were temporary). Weaning difficulty from HLM of different causes occurred in 6 patients (5.5%). Difficulty to repair mitral valve because of dysplastic AV valve and persistent mitral regurgitation grade III-IV, occurred in 4 patients (3.6%). Electrocardiography changes due to air embolism occured in 2/110 (1.8 %). Junctional ectopic rhythm occurred in 2 patients (1.8%), other rhythm disturbances (Sinus tachycardia, supraventricular extrasystole, sick sinus syndrome) occurred in 4 patients (3.6%). Right side AV valve regurgitation III-IV occurred in1 patient (0.9%). Intraoperative bleeding due to long CPB time occurred in 1 patient (0.9%). Protamine allergy occurred in 1 patient (0.9%). Operative mortality which is defined as death within the operative and postoperative hospitalization or within 30 days from surgery was 1 patient (0.91%) due to severe mitral regurgitation grade IV and pulmonary hypertensive crisis which lead to right ventricular failure (Table 12). In the group D, 10 patients (13.5%) had intropeative pulmonary hypertensive crisis, 7 patients (9.5%) had complete AV block, and 1 patient (1.4%) had severe MI. In group ND, 3 patients (8.3%) had pulmonary hypertensive crisis, 3 patients (8.3%) had complete AV block, 3 patients (8.3%) had severe MI, and 1 patient died (2.8%). The weaning difficulty from HLM was the same in both groups, with 3 patients for each group.

Table 12: Intraoperative complications and rhythm disturbances

		No.	(%)
1.	Pulmonary hypertensive crisis	13	11.8
2.	Complete AV block (some of them were temporary)	10	9.1
3.	Weanig difficulty from HLM	6	5.5
4.	Mitral valve insufficiency (III-IV) and difficult repair	4	3.6
5.	Electrocardigraphy changes	2	1.8
6	Junctional ectopic rhythm	2	1.8
7.	Other rhythm disturbance (SVES, Sinus tachycardia, SSS)	4	3.6
8.	Right side AV valve regurgitation (III-IV)	1	0.9
9.	Intraoperative bleeding	1	0.9
10.	Protamine allergy	1	0.9
11.	Operative death	1	0.9

4.2.4. Thorax closure

Primary thorax closure was possible in 105/110 of patients (95.5%), but later on in 1 patient from those who underwent primary closure, the chest was re-opened and closed only by pericardial membrane because of hemodynamic instability. In 6 patients (5.5%) thorax was left opened and closed only with a pericardial membrane, because of heart edema, hemodynamic instability and hemostasis problems (bleeding) (Table 13).

The primary thorax closure was done in 72 patients (97.3%) in group D and in 32 patients (88.9%) in group ND.

Table 13 : Thorax closure in all patients

	Number	(%)
Primary closure	105/110	95.5
Secondary closure	6/110	5.5
Operative revisions	7/110	6.4

4.3. Postoperative data

4.3.1. Catecholamine therapy

Inotropic agents like, epinephrine, norepinephrine, dobutamine,dopamine and milrinone® were used to support the circulation in the postoperative period in 82 patients (75.2 %).

The mean duration of catecholamines support was 3.3 ± 4.5 days, the median was 2 days (range, 0- 34 days). The mean duration of inotropic therapy in group D (n = 58) was 2.8 ± 2.2 days, and in group ND (n = 24) was 4.7 ± 7.5 days. The two- tailed p- value was 0.0467 which is considered significant. The patients in group ND showed a significantly longer period need for inotropic support compared to group D patients.

4.3.2. Additional therapy

For preload reduction nitroglycerine as a continuous infusion was used and for diuresis, lasix® was used as a single dose or continuous infusion. In addition to that 66/109 of patients (61%) discharged with aldactone, lasix , B- blockers and captopril therapy, which stopped during the follow- up period.

4.3.3. Mechanical ventilation

All patients were transferred from operating room to intensive care unit intubated and controlled ventilated. In the intensive care unit the patients were under pressure controlled mechanical ventilation, which was adjusted to optimize preload and decrease afterload. At first the oxygen concentration was 100%, which was later on in case of good oxygen saturation reduced gradually. The mean intubation time for all patients was 3.5 ± 4.8 SD days, the median was 2.5 days (range, 0- 39 days). The mean duration of mechanical ventilation in group D patients was 3.5 ± 3.2 days and in group ND patients was 3.6 ± 7.1 days, the p- value was 0.9189 which is considered not significant. The longest intubation time was in 1 patient (39 days) who had severe mitral regurgitation after AVSD repair. Then he underwent mitral valve repair which was failed, then he suffered chronic heart failure and lastly underwent heart transplantation. The mean intensive care unit stay was 6.5 ± 7.3 SD days, the median was 6 days (range, 0- 71 days) (Table 14).

The mean duration of intensive care unit stay, was in group D patients 6.5 ± 3.8 days, and in group ND patients was 6.4 ± 11.7 days, the p- value was 0.9469 which is considered not significant.

Table 14: Mechanical ventilation and ICU stay in days for all patients

	Mean	SD	Median	Range
Mechanical ventilation (d)	3.5	4.8	2.5	0- 39
ICU stay (d)	6.5	7.3	6	0-71

4.3.4. Secondary thorax closure

The secondary chest closure was done in 6 patients. Five patients already came from the operation room with open thorax. One patient was reopened after primary chest closure because of hemodynamic instability (pericard tamponade). Four of those patients who had opened thorax, had also postoperative revision, to be closed directly after the revision operation. The mean period for secondary chest closure was 3.8 days ± 1.8 SD and the median was 3 days (range, 2- 7 days) after surgical repair. Two patients (2.7%) from group D underwent secondary closure and 4 patients (11.4%) from group ND had secondary closure. None died from the patients who underwent secondary closure.

4.3.5. Postoperative rhythm disturbances

In the postoperative period, in 67 patients (61.5%) rhythm disturbances in the form of junctional ectopic tachycardia, supraventricular tachycardia, supraventricular extrasystole, ventricular extrasystole, ventricular tachycardia, sinus tachycardia, bradycardia (including temporary and permanent AV block from I-III grade), atrial fibrillation and flutter was found in electrocardiography. Almost in the majority they were temporary. Incomplete right bundle branch block was found in ECG of 35 patients (32.1%) and complete right bundle branch block was found in ECG of others 35 patients (32.1%) (Table 15). At discharge 100 patients had sinus rhythm (91.7%), 3 patients had AV junctional ectopic rhythm (2.8%), and 6 patients had permanent pacemaker because of complete AV block. In the patients in group D there were 71 patients (95.9%) with sinus rhythm, 2 patients (2.7%) with junctional ectopic rhythm and 1 patient (1.4%) required pacemaker implantation due to complete AV block. In group ND there were 29 patients (82.9%) with sinus rhythm, 1 patient (2.9%) with junctional ectopic rhythm and 5 patients (14.2%) required pacemaker implantation due to complete AV block. The patients in group ND had a significant higher rate of complete AV block compared with those in group D postoperatively.

Table 15: Postoperative ECG rhythm disturbance findings

	Number	(%)
Junctional ectopic tachycardia.	20/109	18.4
Supraventricular tachycardia and or suprventricular extrasystole.	11	10
Ventricular tachycardia and or ventricular extrasystole.	4	3.7
Sinus bradycardia	25	22.9
Atrial fibrillation and or flutter	1	0.9
Sinus tachycardia	6	5.5
Temporary AV block	14	12.8
Permanent AV block	6	5.5
Incomplete right bundle branch block	35	32.1
Complete right bundle branch block	35	32.1

4.3.6. Postoperative complications

In the operative and postoperative period 48 patients (44%) suffered from pulmonary hypertensive crisis, characterized by rapid rise in pulmonary pressure, accompanied by bronchospasm and reduced blood pressure and oxygen saturation. All of them had remission under deep sedation, muscle relaxation, increased FiO2, hyperventilation, nitric oxide inhalation, illomedin and flolan therapy. The mean duration of therapy for all patients was 5.6 days ± 3.5, the median was 5 days (range, 1- 14 days). The mean duration of therapy in D group patients (n = 35) was 5.2 ± 2.9 days, and in ND group patients (n = 9) was 7.1 ± 5.3 days. The p- value was 0.0173 which is significant. At discharge there were only 10 patients with persistent pulmonary hypertension (14.5%) from the patients who have preoperatively pulmonary hypertension, which represents 9.2% from all patients (10/109). Seven patients of them were in group D (9.5%) and 3 in group ND (8.6%). All of them were discharged on sildenafil, illomedin and anticongestive therapy to be followed-up, one patient of them had normal pulmonary pressure after mitral valve replacement 2 months later. The other postoperative complications included: Thirty- two patients with respiratory infection, 28 patients with pleural effusion (only 3 patients required draining, while the others treated medically), 26 patients with atelectasis, 25 patients with respiratory obstruction and or stridor, 15 patients with pericardial effusion (only 2 required re-thoracotomy), 5 patients with lung edema, 4 patients with ascitis (all drained), 3 patients had chylothorax (treated medically), 3 patients suffered from a cardiogenic shock, 2

patients had severe bleeding (which was compensated after transfusion of fresh frozen plasma, platelets and erythrocytes concentrations), 2 patients had sepsis, 1 patient had postcardiotomy syndrome, 1 patient had renal dysfunction, and 1 patient had temporary neurological deficits (Table 16).

In group D patients, 24 patients (32.4%) had respiratory infection, 22 patients (29.7%) had pulmonary atelectasis, 21 patients (28.4%) had stridor, and 3 patients (4.1%) had pulmonary edema, while in group ND, 8 patients (22.9%) had respiratory infection, 4 patients (11.4%) had atelectasis, 4 patients (11.4%) had stridor and 2 patients (5.7%) had pulmonary edema (Figure 13). The patients with Down syndrome had a higher rate of respiratory infection, more tendency to develop stridor and atelectasis compared to group ND but this was not associated with long mechanical ventilation or ICU stay in group D.

Table 16: Postoperative complications

	Number	(%)
Pulmonary hypertensive crisis	48	44.04
Respiratory infection	32	29.4
Pleural effusion	28	25.7
Atelectasis	26	23.9
Respiratory obstruction and or stridor	25	22.9
Pericardial effusion	15	13.8
Lung edema	5	4.6
Ascitis	4	3.7
Chylothorax	3	2.8
Cardiogenic shock	3	2.8
Bleeding	2	1.8
Sepsis	2	1.8
Postcardiotomy syndrome	1	0.9
Renal dysfunction	1	0.9
Temporary neurological deficits	1	0.9

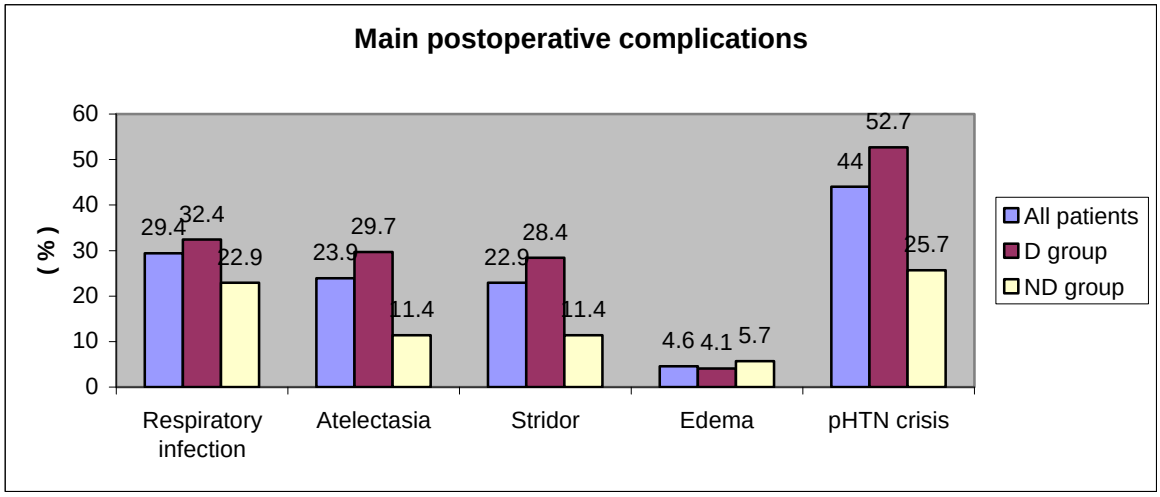

Figure 13: Main postoperative complications.

4.3.7. Postoperative residual findings- echocardiography findings

In all living patients (109) postoperative control echocardiography was done which was used not only to judge the hemodynamic situation but also in the decision making for revisions in 7 patients in the postoperative period. Four patients of them had already open chest in the postoperative period, due to hemodynamic instability. The echocardiography findings by discharge in all patients (109): mitral valve regurgitation was grade (0-I) in 75 patients, MI grade (II) in 27 patients, MI grade (III) in 7 patients, and MI grade (IV) no patient. From those patients who had preoperative MI grade III (n = 6), 2 patients postoperatively still had MI grade (III), 3 patients had MI grade (II), and 1 patient had MI grade (I). Mild grade mitral stenosis was seen in 2 patients which was hemodynamically not significant. Tricuspid valve regurgitation was grade (0-I) in 101 patients, TI grade (II) in 7 patients, and TI grade (III) in 1 patient. Aortic valve regurgitation was grade (I–II) in 2 patients, and pulmonary valve regurgitation was grade (I –II) in 2 patients. Residual small VSD without gradient was seen in 31 patients (Table 17).

Table 17: Echocardiographic residual findings at discharge

	Number	(%)
Mitral regurgitation grade (0–I)	75	68.8
Mitral regurgitation grade (II)	27	24.8
Mitral regurgitation grade (III)	7	6.4
Mitral regurgitation grade(IV)	0	0
Mitral stenosis (mild)	2	1.8
Tricuspid regurgitation grade (0-I)	101	92.7
Tricuspid regurgitation grade (II)	7	6.4
Tricuspid regurgitation grade (III)	1	0.9
Aortic regurgitation grade (I-II)	2	1.8
Pulmonary regurgitation grade (I-II)	2	1.8
Small residual VSD without shunt	31	28.4

From those patients who underwent two- patch technique (81 patients), 1 patient died, 43/80 patients had mitral valve regurgitation (I), 21 patients had mitral valve regurgitation (II), 7 patients had mitral valve regurgitation (III), and 9 patients had no mitral valve regurgitation. In 29 patients with single- patch technique, 22 patients had mitral valve regurgitation (I), 6 patients had mitral valve regurgitation (II), and 1 patient had no mitral valve regurgitation. In the group of Down syndrome patients, 70 patients (94.6%) had no or mild mitral valve regurgitation, and 4 patients (5.4%) had moderate to severe mitral regurgitation. In the ND group, 32 patients (91.4%) had no or mild mitral valve regurgitation and 3 patients (8.6%) had moderate to severe mitral valve regurgitation (Table 18 and 19) (Figure 14).

Table 18: Two/ Single- patch technique and MV regurgitation postoperatively

	MI (I)	MI (II)	MI (III)	MI (IV)
Two- patch technique (80/81)	43	21	7	0
Single- patch technique (29)	22	6	0	0

Table 19: Down /non- Down patients and MV regurgitation postoperatively

	D group	(%)	ND group	(%)
No or mild MI	70	94.6	32	91.4
Moderate to severe MI	4	5.4	3	8.6

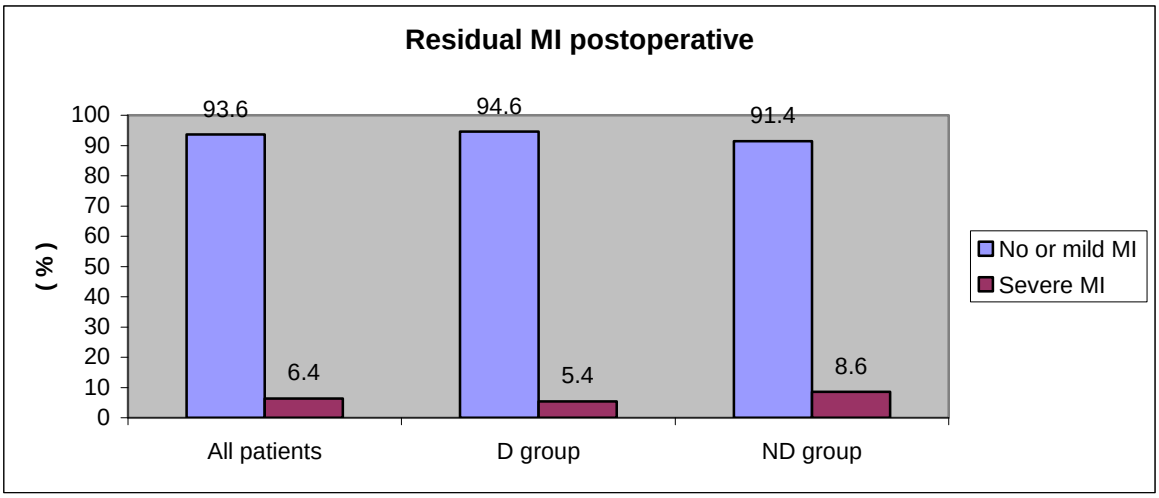

Figure 14: Residual MI postoperatively.

4.3.8. Early mortality

The early mortality after atrioventricular septal defect repair was 1/110 patient (0.91%). This occurred in the operation room, due to severe mitral valve regurgitation, which was difficult to repair. Pulmonary hypertensive crisis developed which lead to right ventricular dilatation and right ventricular failure. This patient belonged to group ND (2.8%) and had right ventricular dominance. Several variables were analyzed to assess if they were risk factors for operative mortality. These variables included age, sex, body weight of patients, preoperative palliative procedures and respiratory compromise requiring ventilation. Only age (< 4 months), body weight (< 4 kg), and in addition to that, non- Down patients were identified as an independent risk factor for early mortality.

The life expectancy for all patients expected to be a straight line (99.1%), because only one patient (0.91%) died intraoperatively and that is the reason not to use Kaplan- Meier method for estimating survival.

4.3.9. Discharge

The mean hospital stay was 16.7 ± 12.4 days, the median was 13 days (range, 3- 80 days). The mean hospital stay for group D patients was 16.7 ± 10.5 days (median = 14.5 days), while for group ND patients was 16.8 ± 15.8 days (median = 14.5 days). The p- value was 0.9688 and is considered not significant. The longest stay was in a patient with complicated postoperative course with severe dysplastic mitral valve, long CPB and aortic cross clamp

durations 323/205 min., respectively. At discharge only 10 patients still had pulmonary hypertension with good response to therapy (9.2%), 100 patients had sinus rhythm (91.7%), 6 patients needed a permanent pacemaker (5.5%) and 3 patients were with atrioventricular junctional rhythm (2.8%). Also at discharge only 66 patients were on temporary anticongestive therapy including, Diuretics, ACE inhibitors and B- blocker (61%). The mean oxygen saturation at discharge was 98 % ± 1.6, the median was 99 % (with range, 94- 100 %). The mean pulmonary artery pressure was 21.8 mmHg ± 6.6, the median was 21 mmHg (range,10- 55 mmHg). From 109 living patients were 94 patients (86.2%) discharged to home and 15 patients (13.8%) to the referring hospital (Table 20 and Table 21).

Table 20: Clinical profile at discharge

	Mean	SD	Median	Range
Hospital stay (d)	16.7	12.4	13	3- 80
Oxygen saturation (%)	98	1.6	99	94- 100
Mean pulmonary pressure (mmHg)	22.1	7.4	21	10- 56
Discharge weight (kg)	9.2	10.4	5.96	3.39-64.7

Table 21: Clinical findings at discharge

	Number	(%)
Persistent pulmonary hypertension	10	9.2
Sinus rhythm	100	91.7
Permanent pacemaker	6	5.5
Junctional ectopic rhythm	3	2.8
Anticongestive therapy (temporary)	66	61
Discharge to home	94	86.2
Discharge to referring hospital	15	13.8

5. Late results and follow- up

5.1. Re- admissions

During the follow- up period 32 patients were readmitted (30.5%) to the different departments, with a total number of admissions equal to 75 times. The readmissions for surgical purposes were in different surgical departments and also for interventional cardiac catheterization. The readmissions for medical treatment were also in different departments, including paediatric cardiology and paediatric neurology. Cardiac catheterization was done in 16 patients, including 14 times for diagnostic purposes and 2 times for therapeutic purposes. For therapeutic purposes, 1 case was for implantation of VSD occluder system, which was complicated with injury to one of the aortic valve cusps, repaired surgically in the same day with the use of cardiopulmonary bypass. In the second case the patient underwent implantation of coils in patent ductus arteriosus (PDA). The other operative causes of readmission, included adenoidectomy, tonsillectomy, congenital cataract operation and teeth extraction. For therapy adjustment, it was 1 time for immunosuppresive therapy and 2 times for marcumar adjustment. The readmissions included also 5 times pacemaker implantation and or change and 2 times pacemaker explantations (Table 22).

Table 22: The causes of readmission

	Number of patients	(%)
Redo and or transplantation	21	20
Cardiac catheterization (diagnostic and therapeutic)	16	15.2
Other operative causes (non- cardiac)	8	7.6
Respiratory infection	6	5.7
LVOTO / Subaortic stenosis	6	5.7
Cardiac failure	5	4.8
Pacemaker implantation or change	5	4.8
Fever	4	3.8
Marcumar or Immunosuppresive adjustment	3	2.9
Pacemaker explantation	2	2.9
Bronchoscopy	2	2.9
Endocarditis	1	0.95
Pericardial effusion	1	0.95

5.2. Late operative interventions (Redo)

Twenty- one patients (21/105 = 20%) underwent 24 reoperations during the follow- up period plus 2 patients in the direct postoperative period who did not need further interventions during follow- up, one of them had MV repair and the other one had permanent pacemaker implantation, so that the total patients who needed reoperations were 23 patients (21.9%). Those included subaortic fibromuscular ridge resections (n = 5), left ventricular outflow tract obstruction due to VSD Dacron patch (n = 1), Mitral valve repair (n = 9), mitral valve replacements (n = 5), VSD occluder implantation in the catheter lab (n = 1), and PDA coil closure (n = 1). These 24 reoperations, included 2 heart transplantations after atrioventricular septal defects repair. The cause of transplantation in the first case was severe residual mitral regurgitation and chronic cardiac failure 20 months after the first operation. In the second case, the cause was severe residual mitral valve regurgitation after revision and end stage cardiac failure. This patient had a hypoplastic left ventricle and preoperative pulmonary artery banding, and received heart transplantation 34 days after AVSD repair. In addition to that; 5 patients underwent revisions in the direct postoperative period, 4 of them came later on for mitral valve replacement or repair or sub-aortic obstruction revision and for transplantation, and the fifth patient had no further intervention. Three of the patients (3/6) who had preoperatively severe left side AV valve insufficiency, underwent mitral valve repair or replacement in the follow- up period. This shows a higher rate of MV reoperations in patients who had preoperatively severe MI (Table 23). The mean time from the AVSD repair to the first reoperation or transplantation for all patients was 22.3 months ± 22.6, the median was 16 months (range, 34 days- 7.6 years). The mean time from the AVSD repair to the second reoperation or transplantation was 5.6 years ± 4.3, the median was 5 years (range, 1.7- 10.2 years) (Table 24).

Within the follow- up period 9/71 patients (12.7%) in group D and 14/34 patients (41.2%) in group ND required reoperation after AVSD primary repair. In total there were 9 reoperations in group D plus 2 catheter interventions and 3 pacemaker implantations. The reoperations included; 5 MV reoperations (MV repair,n = 3 and MV replacement,n = 2), 4 LVOTO repairs. In group ND there were 16 reoperations, plus 2 heart transplantations and 6 pacemaker implantations. The reoperations included; 13 MV reoperations (9 MV repair and 4 MV replacement), 3 LVOTO repairs and 2 heart transplantations. This shows that the main indication for reoperation in both groups was severe mitral valve insufficiency, followed by pacemaker implantations, and LVOTO repairs, with higher rate of reoperations in group ND compared to group D. The freedom from any type of reoperations at 10 years

for all patients was 80% (Figure 15). The freedom from MV repair reoperation at 10 years was 87% (Figure 16), the freedom from MV replacement reoperation at 10 years was 95% (Figure 17), the freedom from LVOTO repair reoperation at 10 years was 88% (Figure 18), and the freedom from pacemaker implantation at 10 years was 92% (Figure 19). In Down syndrome patients the freedom from any redo at 10 years was 90% (Figure 20) and in ND patients group the freedom from any redo at 10 years was 50% (Figure 21).

Table 23: Type of reoperations

	Number	(%)
Mitral valve replacement (mechanical valves)	5	4.8
Mitral valve repair	9	8.6
Subaortic fibromuscular resection	5	4.8
LVOTO patch reconstruction or reposition	1	0.95
Heart transplantation	2	1.9
VSD occluder implantation	1	0.95
PDA coil closure	1	0.95
Total number of reoperations	24	22.9

Table 24: The duration to first & second redo after AVSD repair

	Mean	SD	Median	Range
First reoperation	22.3 (m)	22.6 (m)	16 (m)	34 (d)- 7.6 (y)
Second reoperation	5.6 (y)	4.3 (y)	5 (y)	1.7 (y)- 10.2 (y)

It should be noted that 22 patients underwent revisions or reoperations with a total of 29 reoperations or interventions, with 7 patients underwent re-re-operations, all of them except one underwent two-patch technique. Sixteen patients underwent two- patch technique (19.8%) with 22 reoperations (75.9%), and 6 patients underwent single- patch technique (20.7%) with 7 reoperations (24.1%) (Table 25 and 26).

Table 25: Two- patch technique and reoperations

	Patients	(%)	Reoperations	(%)
Two- patch technique (Total)	16/81	19.8	22/29	75.9
Mitral valve repair and or replacement	11/81	13.6	12/29	41.4
Subaortic obstruction repair	4/81	4.9	6/29	20.7
Transplantation	2/81	2.5	2/29	6.9
VSD occluder implantation	1/81	1.2	1/29	3.4
PDA coil closure	1/81	1.2	1/29	3.4

Table 26: Single- patch technique and reoperations

	Patients	(%)	Reoperations	(%)
Single- patch technique (Total)	6/29	20.7	7/29	24.1
Mitral valve repair and or replacement	6/29	20.7	6	20.7
Sub-aortic obstruction repair	1/29	3.4	1	3.4

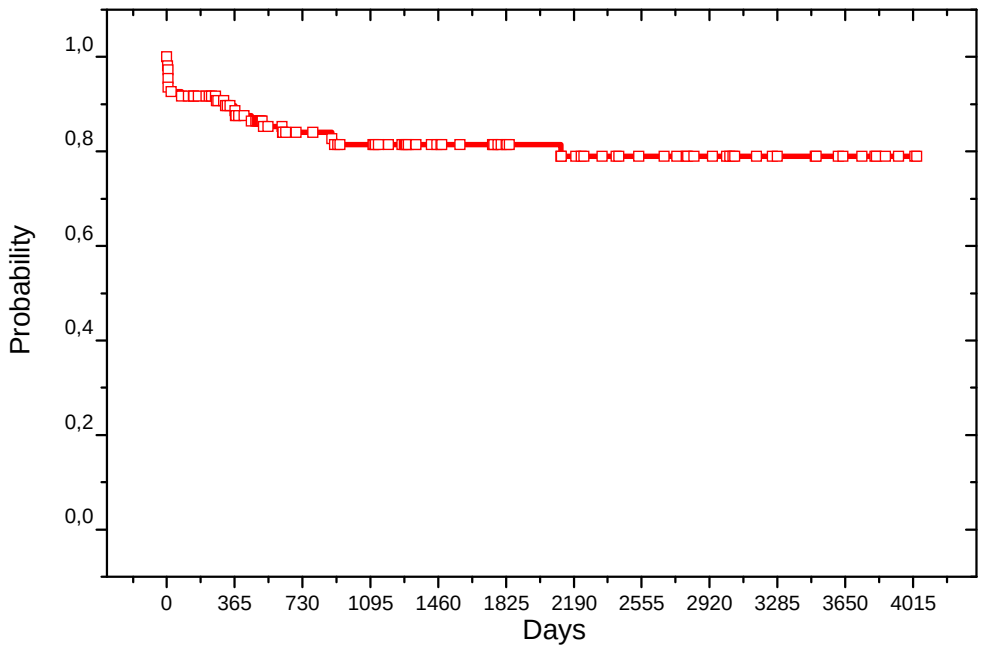

Figure 15: Kaplan-Meier estimate of freedom from any reoperation for all patients.

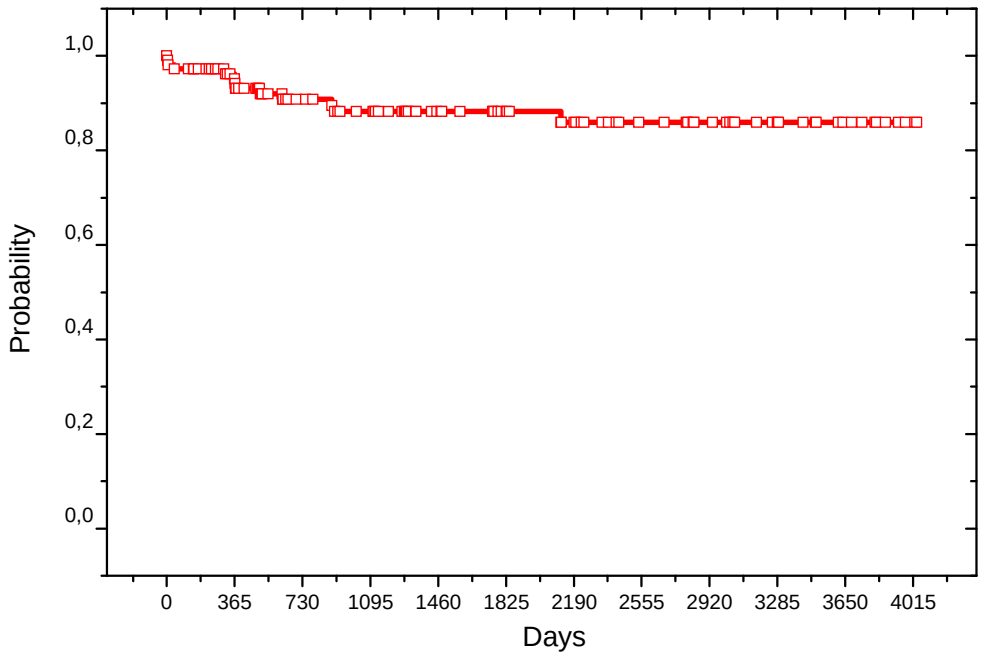

Figure 16: Kaplan-Meier estimate of freedom from MV repairs reoperation.

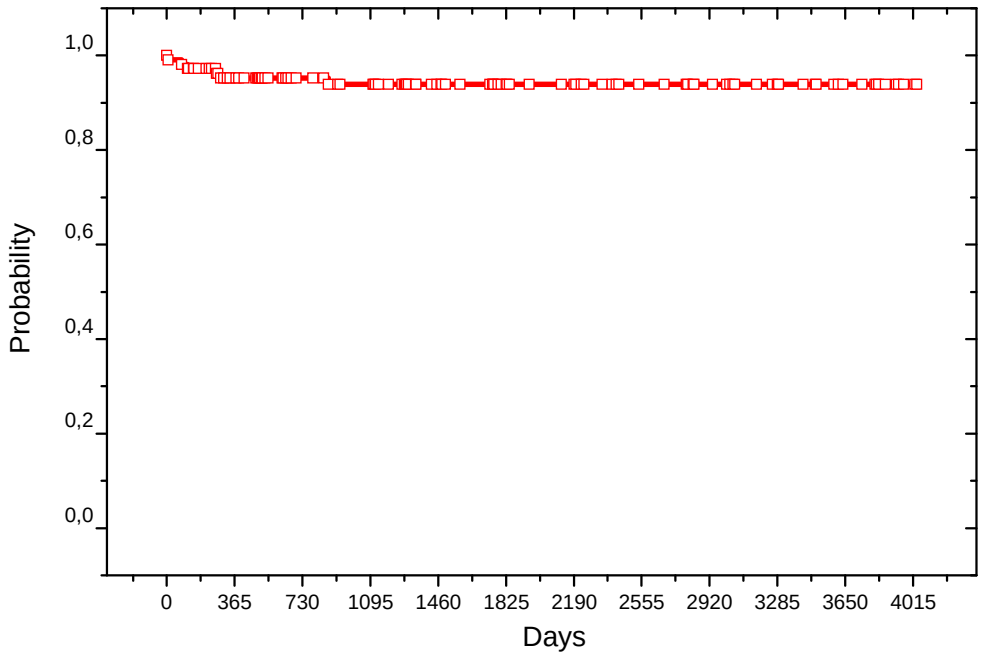

Figure 17: Kaplan-Meier estimate of freedom from MV replacements reoperation.

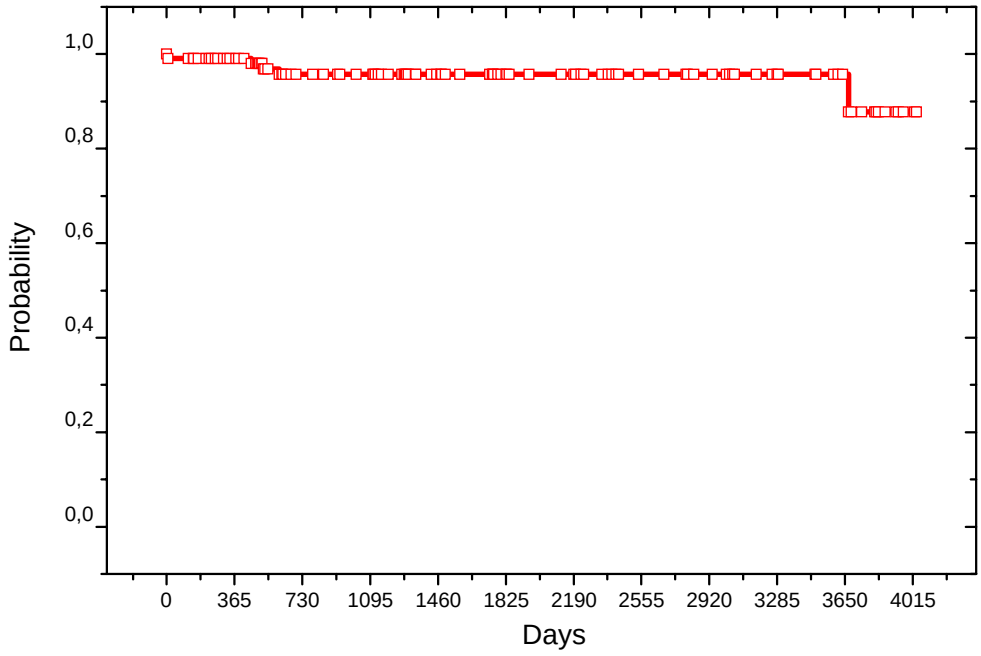

Figure 18: Kaplan-Meier estimate of freedom from LVOTO repairs reoperation.

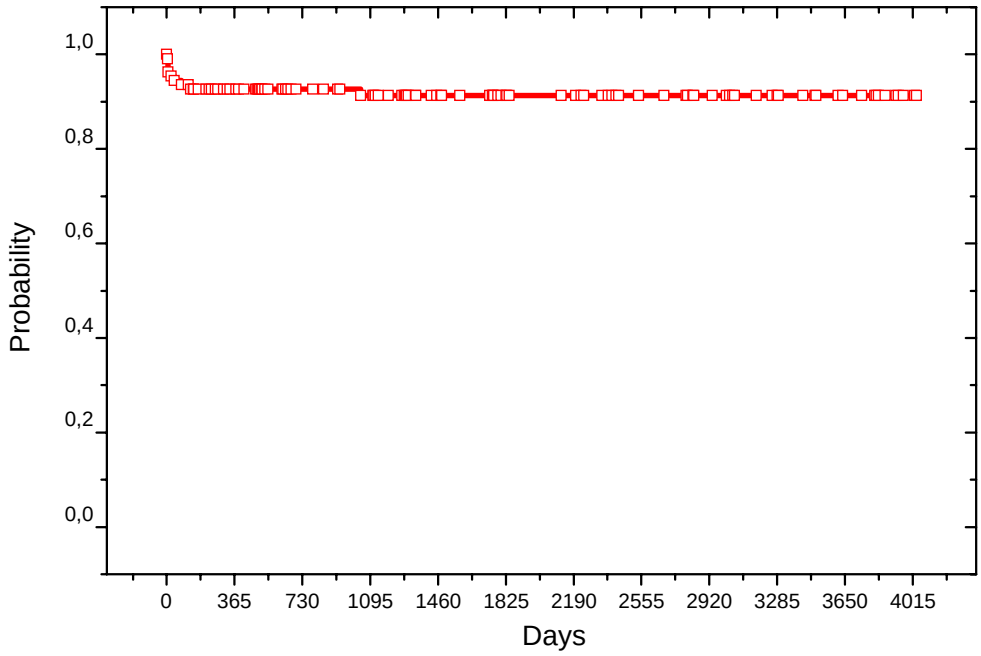

Figure 19: Kaplan-Meier estimate of freedom from pacemaker implantations.

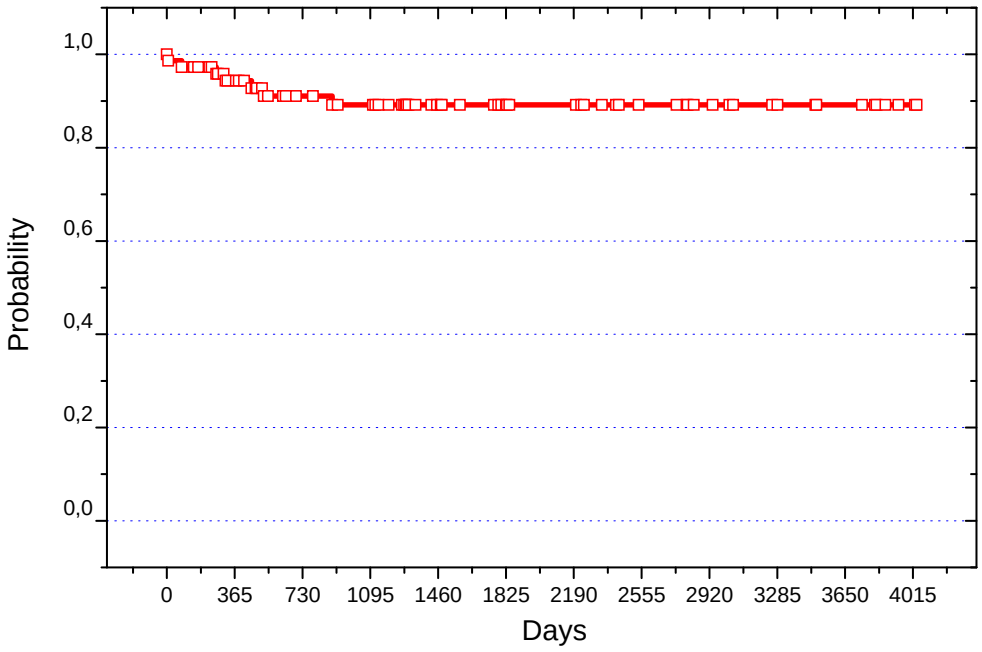

Figure 20: Kaplan-Meier estimate of freedom from any reoperation by Down´s patients.

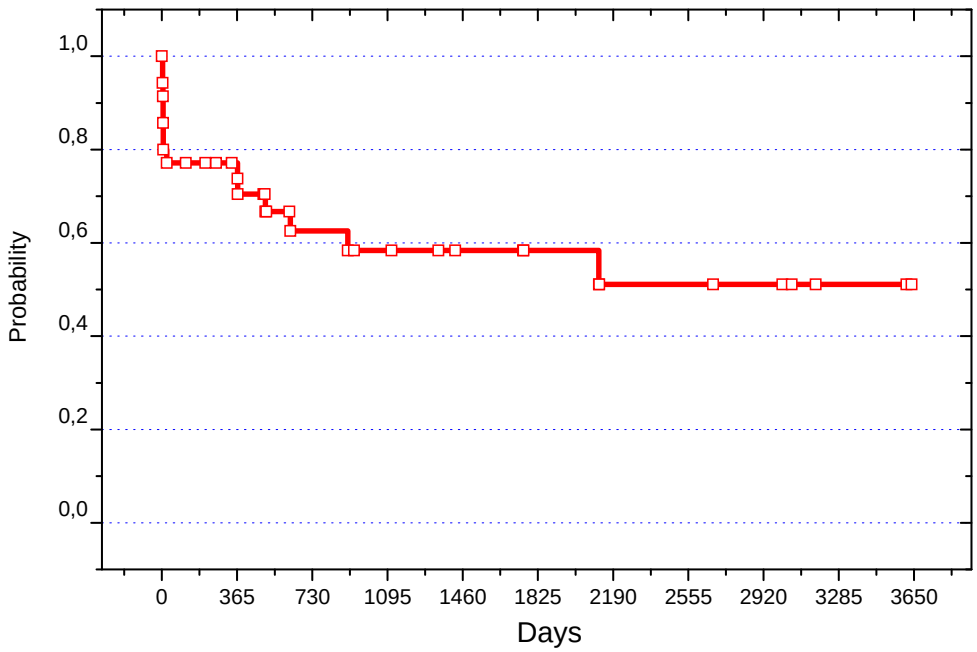

Figure 21: Kaplan-Meier estimate of freedom from any redo by non- Down´s patients.

5.3. Follow- up

5.3.1. General findings

After discharge from hospital, the follow- up was conducted in the polyclinic of the department of pediatric cardiology, in the Pediatric Heart Center, Giessen as well as by pediatric cardiologists of the regional hospitals. The follow- up was possible for 105 patients from 109 patients who were discharged living from the hospital (96.3%). The other 4 patients were lost. During follow- up visit, the general condition of the patients was assessed, in addition to that the patient´s body weight, height, blood pressure were measured. The patient´s present complaints as well as medication was inquired. Then general physical and cardiopulmonary examinations were performed, additionally to that also electrocardiography and echocardiography. Only 16 patients needed cardiac catheterization (including, 2 times therapeutic interventional and 14 times diagnostic for those patients who were dischraged with signs of pulmonary hypertension and also before reoperation to assess the pulmonary vascular resistance). The mean follow- up period was 3.5 ± 3.2 years, the median period was 2.5 years (range, 13 days- 10.9 years). No deaths were recorded, 97 patients were found with functional status NYHA I (92.4%), 7 patients with NYHA II (6.7%), and 1 patient with NYHA IV (0.95%). The mean follow- up for D group 71/74 patients was 3.5 ± 3.2 years, and for ND group 34/35 patients was 3.4 ± 3.3 years. The functional status, electrocardiographic, and echocardiographic findings in Down and non- Down patients are summarised in Table 27.

Table 27: Follow- up findings in D and ND patients

	D	(%)	ND	(%)
Good biventricular function	70/71	98.6	34/34	100
NYHA I-II	70	98.6	34	100
NYHA IV	1	1.4	0	0
Severe mitral valve regurgitation	2	2.8	2	5.9
Sinus rhythm	67	94.4	31	91.2
Permanent pacemaker due to complete AV block	3	4.2	3	8.8

From the table we can see that the group ND patients are more prone to severe mitral insufficiency and complete AV block compared to group D patients.

5.3.2. Electrocardigraphy findings

Ninety- eight patients were found to have sinus rhythm (93.3%), 6 patients having permanent pacemaker because of complete AV block (5.7%), including 3 patients who already were discharged with permanent pacemaker after the primary repair of AVSD and 3 other patients who got complete AV block during the follow- up period and consequently underwent permanent pacemaker implantation, and 1 patient with atrioventricular ectopic rhythm (0.95%). Forty- four patients were found with complete right bundle branch block (41.9%), 34 patients were found with incomplete right bundle branch block (32.4%).

5.3.3. Echocardiography findings

The echocardiography findings for 105 patients during follow- up can be summarized as 104 patients (99.1%) had good biventricular function and 1 patient (0.95%) had reduced ventricular function. Eight patients (7.6%) had no mitral regurgitation, mitral valve regurgitation grade I was found in 68 patients (64.8%), mitral regurgitation grade II in 25 patients (23.8%), mitral regurgitation grade III in 3 patients (2.9%), and mitral regurgitation grade IV in 1 patient (0.95%). Tricuspid regurgitation grade I was found in 63 patients (60%), tricuspid regurgitation grade II in 7 patients (6.7%) and tricuspid regurgitation grade IV in 1 patient (0.95%). At the same time pulmonary valve regurgitation grade I was found in 10 patients (9.5%), and aortic valve regurgitation grade I-II in 9 patients (8.6%). In none of the patients any signs of mitral stenosis or tricuspid stenosis were diagnosed. Residual small VSD without shunt was found in 16 patients (15.2%), signs of pulmonary hypertension were found in 2 patients (1.9%), and LVOTO was found in 2 patients (1.9%), one of those patients with a LVOTO had a gradient equal to 22 mmHg, the other had a gradient equal to 25 mmHg (Table 28).

Table 28: Follow- up findings in all patients

	Number	(%)
Total follow- up	105	96.3
Sinus rhythm	98	93.3
Complete RBBB	44	41.9
Good biventricular function	104	99.1
NYHA- I	97	92.4
NYHA- II	7	6.7
NYHA- IV	1	0.95
Mitral regurgitation- I	68	64.8
Mitral regurgitation- II	25	23.8
Mitral regurgitation- III	3	2.9
Mitral regurgitation- IV	1	0.95
Tricuspid regurgitation- I	63	60
Tricuspid regurgitation- II	7	6.7
Tricuspid regurgitation- IV	1	0.95
Residual small VSD (without shunt)	16	15.2
Pulmonary regurgitation (I)	10	9.5
Aortic regurgitation (I-II)	9	8.6
Signs of pulmonary hypertension	2	1.9
LVOTO (light obstruction)	2	1.9
Incomplete RBBB	34	32.4
Anticongestive therapy	21	20

5.3.4. Follow- up therapy

Anticongestive therapy was applicated in 21 patients (20%) during the follow- up. This included diuretics, ACE- inhibitors and B- blockers. This therapy was given to the patients with NYHA III-IV, or the patients with mitral and tricuspid regurgitation grade III-IV, or in the direct postoperative period.

6. Discussion

6.1. Preoperative situation

6.1.1. Preoperative findings

In our retrospective study, we reviewed the biventricular repair of atrioventricular septal defects in both Down syndrome patients and non- Down syndrome patients. The key factor to proceed for biventricular repair is whether the ventricles are balanced or not. Both left and right AV valves may equally share the common AV valve orifice, this arrangement termed a balanced defect. But when the AV valve sits more over one ventricle than the other, the contralateral ventricle is typically hypoplastic. When the AV orifice favors the right AV valve (right dominance is existent), and when favors the left AV valve (left dominance is existent). The ventricular balance is based on the size of the ventricular inlet, not on the size of the ventricular chamber, and is assessed with echocardiography, on the 4-chamber view (46). This improvement in the understanding of morphologic anatomy, a considerable advance in surgical technique, more efficient myocardial protection and better postoperative care leads to a reduced mortality rate of less than 4% (3.6%) even in young children, as reported by Tweddell et al. (47) and by Dragulescu et al. (48). In addition to that the improved management of postoperative pulmonary artery hypertensive crisis using nitric oxide and pharmacologic resources decreased significantly the operative mortality. The main surgical techniques used to repair AVSD are two- patch technique as described by George Trusler in the article by Mills et al. (49) or single- patch technique as described by Rastelli et al. (41) depend on the morphologic anatomical findings intraoperatively.

We report on the experience of the Pediatric Heart Center, Giessen in the period from 1997 to 2007, in which both two- patch and single- patch techniques were used for biventricular repair of AV septal defects. Only in 5 patients (4.5%) the diagnosis was performed prenatally. The others were diagnosed postnatally (95.5%) either during a routine echocardiography examination for patients with Down syndrome (67.3%) or they were presented with symptoms and signs of heart failure or accidentally during medical examination for respiratory infection. The clinical presentation of the patients with partial AVSD was late compared to the patients with complete AVSD because they were asymptomatic or had only mild symptoms. The operation date of the partial AVSD patients was also later. The patients with complete AVSD were presented in the clinic during the first months of life as a result of progressive heart failure (sweating, tachypnea, dyspnea and edema). Heart murmur was found in 100% of these patients, pulmonary hypertension in 62.7%, failure to thrive in 36.4%, cyanosis in 26.4%, and respiratory infection in 21.8%.

Down syndrome was associated with atrioventricular septal defect in 67.3% of our patients, Lange et al. reported 71.6% (50). Pulmonary hypertension was diagnosed in 62.7% of all our patients and in 75.6% of the patients with Down syndrome, similar to the reports by Chi et al. (51). Only 1 patient (1.4%) from Down syndrome group had severe left side AV valve insufficiency preoperatively, which was very low compared with the non- Down patients, in which 5 patients (13.9%) had severe MI. Lange et al. reported that Rastelli type B and C were more frequent in patients with Down syndrome (50), which we could not find. The combination with tetralogy of Fallot in our series was seen in 6 patients (5.5%), Studer et al. reported 6.5% (25), which was comparable. Regarding the population we studied, we must stress on the concept of an early surgical correction of AV septal defect before development of fixed pulmonary vascular resistance, which is suggested by Böning et al. (52) and by Lange et al. (50). The median age at operation for all patients was 7.2 months in our patients and the mean age at operation was 1.9 ± 3.6 years. The patients in our study had a wide range of ages between 92 days and 19.8 years and this explains why the mean age at operation was more than 6 months. The median weight at operation was 5.8 kg (range 3.4- 65 kg). Böning et al. (52) reported a median age of 1.2 years and a median weight of 7.6 kg. Backer et al. (53) reported a median age at operation of 8 months (range, 1 month- 108 months), while Moran et al. (54) reported a median age of 6 months. Yamaki et al. indicated that pulmonary vascular obstructive disease in patients with complete AVSD and Down syndrome may progress more rapidly than it does in non-Down syndrome patients (55). Therefore, in order to avoid progression to irreversible pulmonary vascular obstructive disease, surgical intervention before 4 months of life may be appropriate in Down syndrome patients, as suggested by Ando et al. (56). By comparing our results with the other studies and with taking into consideration, that the pulmonary vascular disease usually appears early in life and progresses rapidly especially in complete AV septal defects with large VSDs, it is our protocol to operate before the development of pulmonary vascular resistance, cardiomegaly and severe AV valve insufficiency (between 4- 6 months). This wide range of operation ages in our patients was due to the patients with partial and or intermediate AV septal defects, who were operated later in their life (more than 6 months of age).

6.1.2. Medical therapy (Anticongestive therapy)

Patients with partial AV septal defect who are presented with signs and symptoms similar to those with secundum ASD, as such rarely need medical therapy. They are operated later in their life. Some of them may be presented with signs and symptoms of congestive heart failure, as reported by Manning et al. (57). The patients with complete AV septal defect tend to develop symptoms and signs of congestive heart failure and pulmonary vascular obstructive disease as a result to large left to right shunt and associated AV valve regurgitation. They should undertake initial aggressive medical management to relieve the symptoms, as suggested by Driscoll et al. (58). An earlier intervention is indicated if medical management fails to stablize the patient. In 1985, Bull et al. (59) questioned the advisability of repairing complete AVSD in patients with Down syndrome, on the assumption that early repair carries a high risk for an uncertain prospect. They reported a survival of 80% at 15 years with medical management and recommended medical treatment, unless a unit can offer exceptional surgical results. In our series 70 patients needed anticogestive therapy before the surgical correction (63.6%) consisting mainly of diuretics, B- blockers, ACE inhibitors and digoxin. All those patients who required medical therapy before operation were patients with complete AV septal defect, with 52 patients (72.3%) from group D and 18 patients (50%) from group ND. The higher rate of medical therapy in group D compared to group ND is due to pulmonary hypertension, pulmonary congestion and respiratory infections. Our policy is early surgical repair of patients with complete AVSD and associated Down syndrome which is safe and accomplished with very low mortality rate and excellent short and long- term results.

6.1.3. Palliative procedures

The treatment of choice for an atrioventricular septal defect is primary surgical repair. The palliative procedures, like pulmonary artery banding for palliation of congestive heart failure have a very limited role in the treatment of AV septal defect. The indication for pulmonary artery banding are patients with AV septal defect with associated anomalies, preterm patients, severely unbalanced defects, or preparation for Fontan circulation and poor clinical condition due to comorbidity conditions precluding major surgical intervention. In our series, 10 patients underwent palliative procedures (9.1%), including 8 pulmonary artery banding (7.3%) and 2 aorto- pulmonary shunt (1.8%), which is less than that found in the literature. Lange et al. reported 20% of patients with complete AV septal defect underwent palliative procedures (50) and Ando et al. reported 12% (56). All those

patients who underwent pulmonary artery banding had secondary pulmonary hypertension due to pulmonary overflow and 4 patients of them had unbalanced ventricles. In those who underwent aorto-pulmonary shunt, both of them had right ventricular outflow tract obstruction (Fallot tetralogy). This means that 90.9 % of our patients underwent primary repair (one stage repair) and palliative procedures were only done in preterm infants or in those who had coexisting cardiac anomalies or those who had comorbidities which were not feasible for primary repair. The median age at palliation procedures in our institute was 3.7 months (range, 12 days- 6.9 years). The primary repair reduces residual lesions following correction, and may avoid problems related to delaying surgery such as development of fixed pulmonary vascular resistance, complications related to pulmonary artery banding or aorto- pulmonary shunt, a less complicated postoperative course and fewer repeat surgeries as suggested by Najm et al. (60) and McElhinney et al. (61). On the other hand staged treatment of AV septal defect remains a valid option and continues to be utilized as described by Silvermann et al. (62) and William et al. (63).

6.1.4. Preoperative diagnosis

The diagnosis of AV septal defect is usually based on clinical history, physical examination, ECG, chest radiogram, and echocardiography, which make the diagnosis in almost all cases certain. Shashi et al. reported that the diagnosis of complete AVSD in patients with Down syndrome can be done by physical examination and ECG in 78% of patients (64). Cardiac catheterization and cineangiogram are only required when major cardiac anomalies coexist and when the operability is questioned because of pulmonary vascular disease especially in Down syndrome patients as suggested by Soudon et al. (65). Kwiatkowska et al. (66) reported that echocardiography is usually sufficient for the full assessment of AVSD and the choice of further treatment. In our study, beside clinical history, physical examination, ECG, chest radiogram, in all patients echocardiography and color Doppler were used (100%) and cardiac catheterization was used in 79 patients (71.8%) which is relative more than other reports of many centers. This means that cardiac catheterization also was used for AV septal defect patients without coexisting cardiac anomalies and in whom the anatomy or physiology was unclear after an adequate echocardiogram.

6.2. Operative data

6.2.1. Total bypass and aortic clamping time

Many studies identified the CPB time as a predictive risk factor for postoperative mortality as suggested by Ando et al. (56). The CPB generally promotes an inflammatory reaction, therefore, an effort to minimize CPB time is another key to the reduction of postoperative morbidity and mortality. By contrast in the report of Alexi-Meshkivili et al. the procedural times were no risk factor for perioperative mortality (67). In our study the mean CPB and aortic cross clamping times for all patients were 150.9 ± 60.5 and 88.1 ± 35.4 min., respectively. The mean CPB and aortic clamping times were significant more in group D compared to group ND. The cause of that was that more patients in group D underwent two- patch technique (85.1%). Backer et al. reported that the mean CPB and ischemia times were 157 ± 37 min. and 123 ± 28 min., respectively (53). Ando et al. reported that the mean CPB and aortic clamping times were 123.6 ± 31.7 min. and 87.7 ± 23.6 min., respectively. In all patients of our study repair was performed using continuous extracorporeal circulation with mild to moderate hypothermia (pharyngeal temperature 31-32°C) and myocardial protection was provided with cold crystalloid cardioplegia (Bretschneider).

6.2.2. Operative technique

Skillful surgical technique is an important factor in the biventricular repair of AVSD. Left ventricular size plays an important role in the postoperative course, as reported by Van Vida et al. (68). The volume of LV can be increased by precise sizing of the patch and the attachment of the ventricular septal patch a little more to the right of the ventricular crest. At the same time avoiding of the oversizing which results in patch redundancy with the potential for left AV valve insufficiency. The undersizing of the patch results in LVOTO. It is our policy to close the cleft of the left AV valve which is a controversial issue in several studies, because this may lead to left AV valve stenosis, which is suspected in 2 cases of our patients. This was corrected intraoperatively by the removal of cleft sutures. But at the same time, if this cleft is left open it leads to increased incidence of left AV valve insufficiency as suggested by Alexi et al. (67). The most important factor to improve leaflet coaptation is avoiding placement of sutures on the leaflet of left AV valve side during closure of ASD, by trying to place the suture more on the right side, thus increasing valve surface area and preventing leaflet puckering. Our biventricular repair of AVSD either by two- patch or by single- patch technique depends on the morphologic anatomical situation. If it is with two- patch technique (73.6%), it provides good access to the marging of the

VSD, thus allowing sufficient orientation to the LVOT, the aortic valve, and the conduction system. The same technique is suggested also by Alexi et al. (67). If single- patch is used (26.4%) it involves direct closure of the ventricular element of the defect, thus avoiding the use of a patch for the ventricular component, or direct suturing of the common AV valve leaflet to the crest of the ventricular septum, as proposed and reported by Wilcox et al. (69) and Nicholson- Nun (70) respectively. In most cases in our study (90%) we left the coronary sinus draining into the left atrium, in order to reduce the incidence of complete AV block.

6.2.3. Intraoperative echocardiography

The transesophageal or transthoracic echocardiography (if the infant is small) are of great help in the operating room to verify complete closure of the interatrial, interventricular communications and absence of important AV valve regurgitation or LVOTO. In our study all patients had intraoperative echocardiography, which was the key factor to remove the cleft suture from a left AV valve in 2 patients (1.8%) because of difficulty in weaning from HLM due to a left AV valve stenosis. Kim et al. suggested that in a complete AVSD repair, intraoperative echocardiography did not show the same finding, as that of follow- up echocardiography in some cases (71). However, this discrepancy is not so great as to require reoperation in early to mid-term follow- up. Therefore, intraoperative echocardiography may be used as tool to predict durability of surgical results and to decrease the incidence of reoperation in complete atrioventricular septal defects.

6.2.4. Intraoperative complications

The AVSD repairs are associated with intraoperative complications, including rhythm disturbances, pulmonary hypertensive crisis, low cardiac output syndrome, difficult AV valve repair mainly of the left side, difficult weaning from HLM, and bleeding. In our study 13 patients had intraoperative pulmonary hypertensive crisis (11.8%), 10 patients (9.1%) had complete AV block grade III , 6 patients (5.5%) had weaning problems from HLM, due to different reasons for example, severe MI, or low cardiac output syndrome, 2 patients (1.8%) had air embolism in coronary artery with ECG changes. Rhythm disturbances occurred in 6 patients (5.5%), that were mostly junctional ectopic rhyhm, supraventricular ectopic extrasystole, and sinus tachycardia. In 4 patients mitral valve repair was difficult (3.6%), due to severe dysplastic left AV valve, while tricuspid valve repair difficulty, protamine allergy, hemostasis difficulty, and LVOTO occurred in 1

patient each. There was 1 intraoperative death due to severe mitral insufficiency and pulmonary hypertensive crisis which lead to right heart dilatation with right heart failure (0.9%), which is very low compared to reports from Böning et al. in which the early mortality was (10.7%) (52).

6.2.5. Thorax closure

Primary chest closure is usually performed if the patient is hemodynamically stable after weaning from HLM. But sometimes open heart operations in children may lead to myocardial swelling and increasing lung water. Decreasing intrathoracic space may then make chest closure difficult. Delayed closure may be beneficial in this setting. Potential risks of delayed sternal closure are sepsis and sternal instability. In the reports from Iyer et al. the sternum was left open for 3.8 ± 0.29 days, and no patient required reexploration for mediastinitis and no patient had an unstable sternum (72). Six of our patients underwent secondary thorax closure (5.5%), the mean duration for secondary thorax closure was 3.8 ± 1.8 days and the median was 3 days (range, 2- 7 days). The main reasons to leave the thorax open were hemodynamic instability, myocardial swelling or hemostasis difficulty. Four patients underwent operative revisions to be closed directly after revision; none of these patients died. The delayed chest closure using a pericardial membrane is a safe procedure in children with compromised cardiac output and myocardial swelling after AVSD repair avoiding cardiac tamponade.

6.3. Postoperative course

6.3.1. Postoperative need for catecholamine and diuresis therapy

In the postoperative course, the catecholamine support therapy plays an important role in supporting the circulation, especially in patients who develop preoperatively or intraoperatively severe cardiopulmonary instability. The indications to use catecholamine are to stablize systemic blood pressure, to increase cardiac output or to increase peripheral vascular resistance after weaning from HLM intraoperatively or postoperatively in the intensive care unit especially following long CPB and aortic clamping times. Catecholamines can be used with nitroglycerine to reduce preload. Norepinephrine was used to reduce postoperative volume needs and consequentlly edema development while nitroglycerine was used in low doses to reduce coronary spasm. The use of phosphodiesterase-3- inhibitors like milrinone® as an inodilatator leads to a reduction in the use of catecholamine as inotropes. Alexi- Meskishvilli et al. (67) reported the need for

use catecholamine in the postoperative period especially in patients with preoperative severe cardiopulmonary instability or difficult intraoperative repair of dysplastic AV valve. In our patients, catecholamines were used intraoperatively and postoperatively in 75.2%. The mean duration for catecholamine therapy was 3.3 ± 4.5 days and the median duration was 2 days (range, 0- 34 days). The use of catecholamine was significantly higher in group ND patients compared to group D patients because of the complicated postoperative course of the ND patients. Generally almost all patients required diuretics therapy after AVSD repair, due to the effects of CPB on renal function and interstitial fluid distribution. A long period of CPB increases the risk of acute renal failure and volume overload. All patients in our study received in the postoperative period loop diuretics like, lasix® and dopamine agonists to reduce the volume overload especially in the lungs.

6.3.2. Postoperative pulmonary hypertensive crisis

This serious syndrome of hyperacute rise in pulmonary artery pressure is usually accompanied by brochospasm, often followed within seconds, or accompanied by profound reduction in cardiac output and fall in arterial oxygen saturation. This usually occurs in infants who are intubated after AVSD repair. The crisis may appear spontaneously, but usually occurs during or shortly after suctioning of the endotracheal tube. The prevalence is more after 18 hours after operation, but it can occur before or after that time. During an acute hypertensive crisis, atypical cardiac tamponade can result from acute right ventricular dilatation as reported by Atsumi et al. (73). Lindberg et al. (74) reported that the incidence of pulmonary hypertensive crisis in the postoperative period was 14%. In our study, 48 patients (44%) had pulmonary hypertensive crisis in the postoperative period. All of them had satisfactory response to therapy, which included deep sedation, increased inspired oxygen concentration, vasodilators use like nitroprusside, flolan®, ilomedin® and nitric oxide. The mean duration of therapy was 5.6 ± 3.5 days, and the median duration was 5 days (range, 1- 14 days). Preoperatively there were 69 patients with pulmonary hypertension. It should be noted that more patients in group D (52.7%) had pulmonary hypertensive crisis compared to group ND (25.7%), but the mean duration of crisis therapy was significantly less in D group compared to ND group (5.2 ± 2.9 days and 7.1 ± 5.3 days, respectively). Only 10 patients were discharged with persistent pulmonary hypertension (9.2%). This indicates the effectiveness of preventive measures used in our ICU by maintenance of paralysis and sedation for at least 24 hours and for at least another 24 hours if the patient remains intubated. Unnecessary suction of the endotracheal tube

especially in patients who are known to have pulmonary hypertension should be avoided. The dosage of catecholeamine should be reduced if the patient´s hemodynamic situation allows it. Postoperative pulmonary hypertensive crisis is common after a complete AVSD repair and in most cases can be managed successfully with conventional treatment and has a favourable postoperative outcome.

6.3.3. Mechanical ventilation and Intensive care unit stay

In general, extubation is best performed, when the patient is hemodynamically stable, with enough oxygenation, and there is no contraindication for extubation. The mean intubation time reported by Böning et al. (52) was 5.0 ± 5 .1 days, and the median was 2.5 days, while the mean ICU stay was 5.0 ± 3.8 days.

The mean intubation time in our study was 3.5 ± 4.8 days, and the median was 2.5 days (range, 0- 39 days). The mean ICU time was 6.4 ± 7.3 days, and the median was 6 days (range, 0- 71 days). There was no significant difference in the mechanical ventilation time and ICU stay between group D and group ND. The longest intubation time and longest ICU stay was in one patient from group ND, who had a complicated operative and postoperative course, and underwent heart transplantation later. We could not find a correlation between long CPB and aortic clamping time on the one hand and the intubation and ICU time on the other hand, because some patients who had long CPB and ischemia times, had short intubation and ICU times. Neirotti et al. suggested early extubation within 6 hours postoperatively (75), because some of the problems following surgery are related to the endotracheal tube and mechanical ventilation and the interventions necessary to maintain them. Even they also reported, that early extubation is not feasible in all patients. Ito et al. suggested the use of continuous positive airway pressure in the postextubation period especially for Down´s patients because of higher tendency to develop stridor (76). In our study, the incidence of stridor was higher in group D patients (28.4%) compared to group ND (11.4%), with the use of continuous positive airway pressure in all these patients.

6.3.4. Postoperative complications

A clinical condition of fluid retention and generalized edema is common in infants after major cardiosurgical interventions. CPB contributes to the development of many adverse effects like acute renal injury, which leads to fluid retention and global heart insufficiency with edema. Surgery can be the primary cause of chylothorax due to injury of the thoracic duct, hemorrhagic pleural effusion, and pneumothorax. The other complications are

associated with bacterial infections for example, respiratory infections, sepsis, or wound infection. In our study, early after surgery, 32 patients (29.4%) had respiratory infections, 28 patients (25.7%) had pleural effusion, 26 patients (23.9%) had atelectasis, 25 patients (22.9%) had stridor, 15 patients (13.8%) had pericardial effusion, 6 patients (5.5%) had complete AV-block, 5 patients (4.6%) had lung edema, 3 patients (2.8%) had circulatory collapse with need for resuscitation, 2 patients (1.8%) had bleeding, 2 patients (1.8%) had sepsis, 1 patient (0.9%) had renal dysfunction, 1 patient (0.9%) had temporary neurological deficit. Most of these complications were treated medically and some of them required surgical intervention, for example, 3 times pleural effusion draining, 2 times rethoracotomy for pericardial effusion and tamponade, and 6 times permanent pacemaker implantations. Böning et al. (52) reported postoperative complications like: infections (27.7%), complete AV-block III (29.8%), pleural effusion (14.1%), pericardial effusion (18.2%), renal dysfunction (7.6%), cardiac insufficiency (17.7%). The high incidence of respiratory infection and stridor in the postoperative period in our study, are attributed to that, that many of these patients are Down´s patients with pulmonary hypertensive crisis. Interestingly our patients tended to had a very low incidence of renal dysfunction and neurologic deficits (less than 1%) probably due to the fact that in our center inotropes and vasopressors doses are targeted to maintain enough cardiac output and arterial pressure direct in the operation room and in the postoperative period in the ICU as well as intraoperative myocardial and brain protection. None of our patients had wound healing problems, which are the same findings in the literature, as reported by Iyer et al. (72). Ando et al. (56) reported 2% wound infections and dehiscence. Apart from minor rhythm disturbances, like SVES, JET, VES, which were temporary in the postoperative period, only 3 patients were discharged with JET, major rhythm disturbances like complete AV-block were found in 6 patients who underwent permanent pacemaker implantation (5.5%). When comparing Down patients with non- Down patients, we recognized that Down patients had more respiratory complications and less complete AV block than non- Down patients.

6.3.5. AV valve function after AVSD repair

AV valve insufficiency is common in patients with AVSD as well as after the surgical repair. Only 6 of our patients had preoperatively severe mitral valve insufficiency, 1 of them was a Down syndrome patient and the remaining patients had trivial or mild mitral insufficiency. The same findings were also reported by Lange et al. (50). Studer et al. (25)

reported that preoperative AV valve insufficiency was a risk factor for reoperation. Alexi-Meskishvilli et al. (67) found an incidence of more complicated left AV valve anomalies of patients with Down syndrome compared with those without. In our study, the patients with non- Down syndrome presented a significantly higher incidence of left AV valve anomalies (dysplastic valve), and this result is compatible the findings of other authors (77). In all of our patients mitral valve cleft was closed, but in 2 patients intraoperatively, the cleft sutures were removed because the mitral side of AV valve was small. This is comparable with reports from Alexi-Meskishvili et al. (67) and Günther et al. (78).

Marino (79), stated that Rastelli type C is more prevalent in patients with Down syndrome, Lange et al. (50) reported that Rastelli type B and C are more prevalent in Down patients. Both findings we could not confirm in our study because more than 80% of our patients showed Rastelli type A. In the direct postoperative period, 4 patients with severe mitral valve insufficiency underwent surgical revisions, this included 3 cases of mitral valve repair and 1 case of mitral valve replacement, because of impossible repair. In the control echocardiography, postoperatively and before discharge, there were 7 patients with moderate to severe mitral valve insufficiency grade III (6.4%), 2 patients of them had preoperatively severe mitral insufficiency, all of them underwent two- patch technique repair and 4 of them were Down patients. At the same time 75 patients had no or trivial mitral valve insufficiency (68.8%), and 27 patients had mitral insufficiency grade II (24.8%). This means that 102 patients had no or trivial to mild mitral insufficiency (93.6%). We could not identify the Down syndrome as a risk factor for mitral valve insufficiency postoperatively. In the last echocardiography control during the follow- up period, 101 patients (96.2%) had no or trivial to mild mitral valve insufficiency, while 4 patients had moderate to severe mitral valve insufficiency (3.8%). Two patients of each group had severe MI. This is comparable with the reports from Böning et al. (52) and Bando et al. (80) (93.9% and 94%, respectively, absent and mild MV insufficiency), but better than that reported by Weintraub et al. (81) and Wetter et al. (82) (84% and 78%, respectively, absent and mild MV insufficiency after surgery). In our patients, in the time between the first control before discharge and the last control during follow- up, 17 patients underwent reoperations on mitral valve, including 12 times mitral valve repair and 6 times mitral valve replacements. Only 2 patients in the following- up period showed deterioration of the mitral valve insufficiency from garde II to grade III-IV, taking into consideration that all patients except 2 patients in our study underwent mitral valve cleft closure. One patient from those patients in whom the mitral cleft left unsutured, underwent later on mitral valve

replacement. Wetter et al. (82) reported an increase in the degree of valve insuffuciency postoperatively in 15%, predominantly in patients without cleft closure. There was no correlationship between the existance of a preoperative AV valve insufficiency and the amount of mitral insufficiency in the postoperative period or at the last follow- up, as reported also by Böning et al. (52) and Weinraub et al. (81).

6.3.6. Left ventricular outflow obstruction

Differences exist regarding the association between left AV valve insufficiency and the presence of left ventricular outflow obstruction, as reported by Marino and de Biase (79;83). In the unoperated patients the incidence of important LV outflow tract obstruction in all types of AVSD is very small, about 1% of cases is reported by Studer et al. (25). On the other hand, the LV outflow tract obstruction becomes often apparent as a postoperative complication as suggested by Piccoli et al. (84).

In our series, none of the patients had preoperatively LVOTO, but in the direct postoperative period, 1 patient underwent surgical revision in the fourth postoperative day due to narrowing of the left ventricular outflow tract by the VSD patch. The same patient required reintervention for the same reason after 63 days. After that the patient was free from any obstruction. During the follow- up, only 5 patients (4.8%) underwent reoperations for LVOTO, 4 of them had discrete subaortic stenosis due to acquired fibromusclar ridge, which was resected. In the last control during the follow- up, 2 patients (1.9%) had light LVOTO (pressure gradient less than 25 mmHg). We did not classify this subaortic LVOTO as a complication related to the surgical procedure since the appearance of this subaortic membrane is an independent factor related to the treatment of the long, narrow LV outflow tract, which is common in patients with complete AVSD.

6.3.7. Complete AV- block and pacemaker implantation

This surgical technique related variable can be considered to occur more frequently in complex malformations, but since Lev described the conduction system in AVSD defects in 1958, the prevalence of surgically induced complete AV block has been reduced to about 1% as reported by Lev et al. (7). In our series 6 patients (5.5%) required implantation of permanent pacemaker postoperatively. During the follow- up control, 3 patients underwent pacemaker explantation (2 patients recovered and had sinus rhythm, and 1 patient had heart transplantation), and another 3 patients required permanent pacemaker implantation, so that at the last follow- up control, there were 6 patients (5.7%) with permanent pacemaker due

to complete AV- block. Böning et al reported 7.4% (52). The tendency for pacemaker implantation was significantly higher in group ND (14.3%) compared with group D (1.4%). Lange et al. (50) reported that 5.1% of Down patients and 6.3% of non- Down patients required permanent pacemaker. There was no death of the patients who had a permanent pacemaker in our study. In the last follow- up control, 98 patients (93.3%) were in sinus rhythm without any other rhythm disturbances and 1 patient (0.95%) with JET with 92% freedom from pacemaker implantation after 10 years. Backer et al. (85) reported 3.5% of his patients required permanent pacemaker due to heart block.

6.3.8. Right ventricular outflow obstruction

In our study 6 patients (5.5%) were associated with right ventricular outflow tract obstruction (Fallot tetralogy). All of them underwent two- patch technique repair, and in addition to that, 1 patient required a Contegra graft, 1 patient required pulmonary valvotomy, 2 patients required only infundibular muscular resection, and 2 patients required a ventriculotomy plus infundibular muscular resection and a transannular patch enlargement. When compared to the other 104 patients, these 6 patients did not present worse results with respect to reoperation. There is a trend for these patients to be operated on later than those with AVSD alone. RVOTO in these patients prevents the development of pulmonary hypertension and enables surgery to be delayed. In the last follow- up only 2 patients had pulmonary insufficiency grade I-II, which is common in transannular patch repair. Only 2 patients (33.3%) underwent a pulmonary systemic shunt before the primary repair. In our center primary repair in these patients, whenever possible was given the preference, because the early palliative not only adds an inherent mortality, but also tends to make definitive repair more difficult without offering any mortality benefits as suggested by Najm et al. (86).

6.3.9. Medical therapy at discharge

The need for medical therapy in the postoperative period for patients with AVSD included antiarrhythmic and anticongestive therapy, for example, Diuretics, B- blockers, ACE inhibitors, digitalis, and amiodarone® in order to bring cardiac performance to an adequate level by reducing afterload, preload and controlling rhythm disturbances. These drugs are used mainly in ICU and continuous in normal station, till the patients clinical condition stablized. Many of these drugs were reduced or stopped before the patients were discharged from hospital but some patients were discharged from the hospital under this treatment to

be stopped after the first follow- up control, 2 weeks after discharge. In our series 66 patients (60.6%) were discharged under diuretics, digitalis, ACE-I, and B-blockers therapy, this included the patients with moderate to severe mitral insufficiency and the patients with persistent pulmonary hypertension. In group D 70.3% of patients were discharged on medical therapy and in group ND 40% of patients were discharged on medical therapy. In all patients, 55 patients (50.5%) with diuretics, 32 patients (29.4%) with ACE-I, 15 patients (13.8%) with digitalis, 10 patients (9.2%) with B-blockers, and 10 patients (9.2%) with sildenafil, ilomedin. The therapy protocol of our patients with AVSD after repair and at discharge was the same as reported by other literature (Monteiro et al. (87)).

In our study, 94 patients (86.2%) were discharged to their home because of stable clinical condition and 15 patients (13.8%) to the referring hospital under medical therapy and to be under medical observation.

6.3.10. Survival and mortality

The natural history of complete AVSD was very poor because of early progression of obstructive pulmonary vascular disease (88). The hospital mortality after repair of AVSD is generally reduced in recent years to less than 4% as reported by Tweddell et al. (47). This is achieved by improved understanding of the morphology of this complex malformation, better surgical techniques, general improvements in cardiac surgery in infants, and also improved physiological control during extracorporeal circulation, more efficient myocardial protection and better postoperative care in the treatment of pulmonary hypertensive crisis. Due to these improvements, many factors which were recognized as a risk factor for mortality are now neutralized, like young age, Down syndrome, and major associated cardiac anomalies, but some factors, like severe preoperative NYHA functional class, accessory valve orifice (double-orifice left AV valve), and severe preoperative AV valve regurgitation still represent elevated risk for mortality after AVSD repair. In our series we could not identify the risk factors for mortality, this is because only 1 patient (0.9%) in our series, died intraoperatively. The cause of death was severe mitral valve regurgitation which was difficult to repair and pulmonary hypertensive crisis which lead to right ventricular dilatation and right heart failure. This patient could not be weaned from the cardiopulmonary bypass. She was less than 4 months of age at operation, less than 4 kg weight, had preoperatively pulmonary hypertension, and was on anticongestive therapy. The patient had no associated cardiac anomalies, preoperatively AV valve insufficiency grade I-II, and she was a non- Down syndrome patient. The only risk factor in this patient

was preoperative pulmonary hypertension. Böning et al. (52) reported that preoperative pulmonary hypertension was a risk factor for early mortality and recommended early surgical repair of AVSD, as delayed timing of surgery rather results in further elevation of pulmonary vascular resistance and fixed pulmonary hypertension. He reported also that the diagnosis of a complete AVSD, ECC more than 110 minutes, two- patch technique and ommittance of cleft closure as a specific risk factors for mortality. In our study 73.6 % of patients underwent two- patch technique, 67.3% were associated with Down syndrome, 62.7% had preoperatively pulmonary hypertension, 5.5% had severe mitral valve insufficiency preoperatively, and the early mortality was less than 1%, and no late death (the probability of survival after 10 years was almost 100%). These results compare favourably with other studies, for example, Tlaskal et al. (89) and Litwin et al. (90). There are some arguments about the impact of Down syndrome on the the early and late outcomes of surgical repair of complete AVSD. Yamaki et al. (55) and Clapp et al. (91) reported that Down syndrome was a risk factor for rapid progression of obstructive pulmonary vascular disease. Morris et al. (21) reported that Down syndrome might be associated with high perioperative mortality compared to non- Down patients because of associated pulmonary vascular disease. The same less favourable results were also reported by Studer et al. and Pozzi et al. (25;92). But on the other side Rizzoli et al. (93) reported that Down syndrome was not an independent risk factor for operative mortality and the patients with Down syndrome underwent fewer reoperations. Many of the recent reports from Tweddell et al., Al-Hay et al., Günther et al., Bando et al., Najm et al. and Prifti et al. using multivariate analysis failed to indicate a presence of Down syndrome as a predictor for operative mortality (47;77;78;80;86;94). Bull et al. (59) assumed that surgical repair of complete AVSD in children with Down syndrome carries a high risk and recommended medical treatment, unless a unit can offer exceptional surgical results. In our study the long- term survival in those with and without Down syndrome was similar. Down syndrome does not have an impact on the long-term survival of surgically operated patients, at least when the defect is repaired during the first year of life, as reported also by Masuda et al. (95). We conclude, that biventricular repair whether by two- patch or single-patch techniques for treating AVSD is effective, safe, associated with low mortality rate and the associated Fallot tetralogy and Down syndrome did not increase mortality or reoperation rate.

6.3.11. The need for reoperations

The follow- up was possible for 105 patients (96.3%) in our series, Böning et al. reported 94.8% follow- up completeness (52). The first follow- up usually 2 weeks after correction, then after 1, 3, 6 months examinations in the first year after operation, and then every year, Paulsen et al. suggested the follow- up every year or every second year (96). Although reoperation within 30 days postoperatively may contribute to a better long- term outcome, in general the most common causes for reoperation are severe mitral insufficiency, subaortic obstruction, pacemker implantation, and residual VSD closure, and these are associated with added risk of death. In our study reoperations were necessary in 23/105 patients (21.9%). In the patient group analyzed by Böning, the reoperations were necessary in 14% of patients (52). In our study 5 patients (4.5%) underwent revisions in the direct postoperative period, this included 3 mitral valve repairs (1 patient later on had MV replacement and another one patient had heart transplantation), 1 mitral valve replacement (this later on underwent heart transplantation), and 1 LVOTO reconstruction (this patient underwent re-revision later on). During follow- up there were 9 mitral valve repairs, 5 mitral valve replacements (1 had early MV repair), 6 LVOTO repairs (in 5 patients), 2 heart transplantations (1 had early MV replacement and 1 had MV repair previously), 1 VSD occluder implantation, and 1 PDA coil closure. Total MV replacements were 6 times, MV repairs were 12 times, LVOTO repairs were 7 times, with the tendency for reoperation more in group ND. None of the patients with partial AVSD underwent reoperation, and only 9 patients (12.2%) with Down syndrome had reoperation (3 cases MV repairs, 2 cases MV replacements, and 4 cases LVOTO repairs). In group ND 14 patients (41.2%) underwent reoperation. Lange et al. (50) reported that 11.1% of Down´s patients required reoperation and 22.7% of non- Down´s patients required reoperations, which is comparable with group D in our results, but in group ND their results were very low than our results. The overall freedom from reoperation at 10 years in our series was 80% of patients, freedom from MV repair was 87%, freedom from MV replacement 95%, and pacemaker implantation 92%, while the freedom from LVOTO repair at 10 years was 88%. The overall freedom from reoperations is comparable to that reported by Böning et al. (52) with 78.6% at 10 years and to that reported by Pozzi et al. (92) with 84.2%. We notice from our results, that patients with Down syndrome have lower incidence of reoperation for mitral valve insufficiency compared to patients without Down syndrome, presumably because severe mitral valve anomalies were less prevalent in patients with Down syndrome (only 1 patient in our study in D group had preoperatively severe mitral regurgitation). Formigari et

al. (97) also reported a higher incidence of subaortic stenosis in children with non- Down syndrome. In our study only 5 patients required reoperation (total reoperations = 7) for subaortic obstruction, 3 patients were associated with Down syndrome (4.2%) and 2 patients were not associated with Down syndrome (5.9%). The overall freedom from any redo in Down syndrome patients at 10 years was 90%, while the overall freedom from any redo by non- Down syndrome patients at 10 years was 50%. This data show that the non-Down syndrome patients had a significant higher rate of reoperations compared to Down syndrome patients, which means that the children with normal chromosomal pattern are at increased risk for reoperations more than Down syndrome patients, which has been already reported by Al-Hay et al., Weintraub et al. and Formigari et al. (77;81;97).

7. Summary / Zusammenfassung

7.1. Summary

The atrioventricular septal defect is a rare congenital malformation of the heart. The prevalence is 3-4% of all congenital cardiac malformation. Congenital heart disease has an incidence between 33 and 48% in Down syndrome, and AVSD is the most common heart defect (15-20%). The natural history of surgically untreated AVSD patients depends on morphologic and functional details of their malformation. The natural history for patients with a partial AV septal defect with mild left AV valve insufficiency is better than that with moderate to severe left AV valve insufficiency, but both of them have a very better natural history than those with a complete AV septal defect, in which the natural history is unfavourable. There is more than one strategy suggested for repair of AVSD (matter of controversy), depending on the ventricular balance (dominance). Univentricular palliation is mostly performed to correct severely unbalanced complete AVSD with hypoplastic left ventricle or other functional single ventricle, while biventricular repair, if feasible, remains a satisfactory option and the treatment of choice. Two techniques are widely used in the repair of complete AVSD, namely a single- patch technique and two- patch technique. We reviewed the records of 110 patients with AVSD (74 with Down syndrome and 36 without), who underwent a biventricular repair between January 1997 and December 2007.
In all patients preoperative, intraoperative and postoperative data including the long-term follow-up were recorded. Preoperative data included clinical course, diagnostic and palliative therapy. Intraoperative data recorded total cardiopulmonary bypass and aortic cross clamping times, delayed sternal closure and intaoperative complications. Postoperative data included duration of catecholamines and postoperative hypertensive crisis therapy, length of mechanical ventilation support and intensive care unit stay. These data were taken as the major factors influencing the postoperaive course. In the long-term follow- up all records including, physical examination, echocardiography, electrocardiogaphy, and cardiac catheterization results were evaluated.
<u>The following results could be identified:</u>

- The patients with complete AVSD were presented at an earlier age than patients with partial AVSD and 63.6% of them were under anticongestive therapy.
- All patients presented with heart murmur, while 67.3% of patients presented with signs and symptoms of congestive heart failure, 36.4% of patients presented with failure to thrive, 26.4% of patients with cyanosis and 21.8% of patients with respiratory infections.

- The patients who presented with pulmonary hypertension were 62.7% in our series, all of them were patients with complete AVSD.
- Down syndrome patients represented 67.3% of all patients, and 75.6% of the Down syndrome patients had pulmonary hypertension.
- The patients with severe mitral valve insufficiency preoperatively represented only 5.5% of all patients and 1.4% of all Down syndrome patients.
- The patients with associated Fallot tetralogy represented 5.5% of all patients and 2 patients of them had aorto- pulmonary palliative shunt.
- Only 9.1% of all patients (n = 10) underwent palliative procedures (pulmonary artery banding and aorto- pulmonary shunt), and none of them died.
- Two- patch technique was done in 73.6% of all patients (n = 81), while single-patch technique was done in 26.4% of all patients (n = 29).
- The overall early mortality was less than 1% (0.91%), with no late mortality, the cause of death was right heart failure due to pulmonary hypertensive crisis and severe mitral valve insufficiency.
- The total CPB and aortic clamping times were comparable to other studies.
- The postoperative course was uncomplicated in 73.4% of 109 living patients, and complicated in 26.6% of patients, mostly due to pulmonary hypertensive crisis (44%) and respiratory problems (29.4%).
- Most of the postoperative complications were well controlled under conventional medical therapy.
- Reoperation rate was 21.9% of the patients, within the follow- up period (total reoperations number = 29), most of these reoperations, were due to mitral valve insufficiency (12 MV repairs, 6 MV replacements), while the others included, 7 LVOTO repairs, 2 heart transplantations, 1 VSD occluder implantation, and 1 PDA coil closure.
- The freedom from any reoperation at 10 years was 80% of all patients, the freedom from MV repairs was 87%, the freedom from MV replacements was 95%, and the freedom from pacemaker implantations was 92%, while the freedom from LVOTO repair at 10 years was 88%. By Down´s patients the freedom from any redo at 10 years was 90%, while by non- Down´s patients at 10 years it was 50%.
- The patients who required permanent pacemaker implantations were 9 patients (8.2%), 3 patients of them underwent pacemaker explantation due to sinus

rhythm recovery (n = 2) and heart transplantation (n = 1). The freedom from pacemaker implantation at 10 years was 92%.

- During the follow- up period 93.3% of the patients showed a normal sinus rhythm. Six patients had permanent pacemaker (5.7%), 1 patient had junctional ectopic rhythm (0.95%), and 44 patients had complete RBBB (41.9%).
- In follow- up most of the patients were in functional status NYHA-I (92.4%), and in echocardiography examination, 101of the patients (96.2%) had no or mild mitral regurgitation, 4 patients (3.8%) had severe mitral insufficiency (2 of them are Down patients), and only 2 patients still had pulmonary hypertension (1 is Down syndrome patient).
- Only a small number of patients was postoperatively investigated by cardiac catheterization, most of them for pulmonary hypertension follow- up.

<u>According to these results the following conclusions could be drawn:</u>

- The biventricular repair of atrioventricular septal defects can be performed with good outcomes, a low mortality rate and primary repair is the treatment of choice and can be accomplished with good results.
- The age at surgical correction should be as early as possible and before 6 months of life particularly in Down syndrome patients to avoid the development of irreversible pulmonary vascular obstructive diseases and to avoid progressive ventricular dilatation from volume overload with progressive AV valve annular dilatation.
- Down syndrome is not a contraindication to surgical repair because Down syndrome is not a risk factor for operative death in recent era.
- Almost all AVSD can be adequately and sufficiently diagnosed by echocardiography, and it should be preferred to preoperative cardiac catheterization. An exception is in cases, in which AVSD associated with major cardiac anomalies or the morphologic anatomy not clear by echocardiography.
- The duration of the total CPB and aortic cross clamping is not associated with an increased morbidity or mortality.
- In long-term follow- up, the biventricular repair of AVSD even with small LV in our series are deemed satisfactory as evidenced by very low early mortality, absence of late mortality, and relative low incidence of reoperation.

- The reconstructed atrioventricular valve shows a good and long-lasting performance without an increase in late mortality or morbidity and the patients with Down syndrome had a lower incidence of any redo or mitral valve insufficiency reoperations compared with non- Down patients.

7.2. Zusammenfassung

Der Atrioventrikuläre Septum Defekt ist eine seltene, angeborene Fehlbildung des Herzens. In 3-4% aller angeborener Herzfehler findet sich eine AVSD. In 33-48% aller Down Syndrom- Patienten findet sich eine angeborene Herzfehlbildung und am häufigsten ein AVSD. Die Prognose und das Ausmaß der pathophysiologischen Beeinträchtigung hängen überwiegend vom Ausmaß der drei Komponenten des Defekts ab: atrialem Defekt, ventriculärem Defekt und AV-Klappeninsuffizienz. Bei Vorliegen eines partiellen AV-Kanal ist die Prognose vor allem durch das Ausmaß des Shuntflusses und eventuell zusätzlich vorhandene Vitien beeinträchtigt. Beim kompletten AV-Kanal kann bereits im frühen Säuglingsalter eine schwere Herzinsuffizienz das Überleben infrage stellen. Die Wahl des Zeitpunktes für Korrektur hängt von der Schwere der hämodynamischen Beeinträchtigung ab. Üblicherweise wird primäre Korrektur angestrebt (Ein-/ Zwei- Flicken Technik), in seltenen Ausnahmefällen ist ein Banding des Truncus pulmonalis sinnvoll, wenn Zweifel bezüglich einer möglichen Imbalance der Ventrikel bestehen. In unserer retrospektiven Studie wurden insgesamt 110 Patienten mit AVSD untersucht, bei denen zwischen Januar 1997 und Dezember 2007 eine AVSD Korrektur durchgeführt wurde.

Bei allen Kindern wurden die präoperativen, intraoperativen und postoperativen Daten einschließlich des Langzeitverlaufs erfasst. Im Rahmen der präoperativen Datenerhebung wurde der klinische Verlauf und die diagnostischen Methoden berücksichtigt. Als intraperative Daten wurde die Bypassdauer und Ischämiezeit, der Zeitpunkt des Thoraxverschluß und intraoperative Komplikationen erfasst. Im postoperativen Verlauf wurden Dauer der Katecholamintherapie, Dauer der postoperativen Behandlung pulmonalhypertensiver Krisen, die Beatmungsdauer und die Verweildauer auf der Intensivstation als wesentliche Merkmale für den unmittelbar postoperativen Verlauf herangezogen. Im Rahmen der Langzeituntersuchung wurden elektrokardiographische, echokardiographische Befunde sowie Herzkatheter- Befunde untersucht.

Wir kamen zu folgenden Ergebnissen:

- Bei Patienten mit komplettem AVSD konnte die Diagnose deutlich früher als bei den Patienten mit partiellem AVSD gestellt werden und 63.6% der Patienten wurden antikongestiv behandelt.
- Bei allen Patienten wurde ein Herzgeräusch angegeben, bei 67.3% der Fälle wurde der Herzfehler diagnostiziert, bei 62.7% der Patienten wurde pulmonale Hypertonie diagnostiziert, bei 36.4% wurde schlechtes Gedeihen angegeben, bei 26.4% Zyanose und bei 21.8% wurde Atemwegsinfektionen angegeben.
- In 67.3% der Patienten fand sich assoziiert ein Down Syndrom und in 5.5% eine assoziierte Fallot-Tetralogie.
- In 5.5% der Fälle fand sich eine höhergradige Insuffizienz der Mitralklappe.
- Insgesamt erfolgten 10 palliative Operationen (8 x Banding des Truncus pulmonalis und 2 x ein aortopulmonaler Shunt) (9.1%).
- In 73.6% der Fälle wurde eine Zwei- Patch- Technik durchgeführt und in 26.4% der Fälle wurde eine Ein- Patch- Technik durchgeführt.
- Die Frühmortalität im gesamten Kollektiv betrug 0.91%, die Spätmortalität 0%.
- In unserem Patientenkollektiv die Bypassdauer und Ischämiezeiten sind mit der Literatur vergleichbar.
- Schwerwiegende Komplikationen traten im postoperativen Verlauf selten auf (26.6%) und in die meisten Fälle waren pulmonal-hypertensive Krisen (44%) und pulmonalen Infektionen (29.4%), die mit mit einer medikamentösen Therapie gut kontrolliert werden konnten.
- Die Reoperationsrate betrug 21.9%.
- Die Wahrscheinlichkeit für ein reoperationsfreies Überleben lag bei 80% nach 10 Jahren. Die Wahrscheinlichkeit für ein MK- Rekonstruktionsfreies Überleben lag bei 87%, MV Ersatz bei 95% und LVOTO Rekonstruktion bei 88% nach 10 Jahren.
- Die Wahrscheinlichkeit für ein schrittmacherfreies Überleben lag bei 92% nach 10 Jahren. Bei 93.3% der nachuntersuchten Patienten lag ein normaler Sinusrhythmus vor (Schrittmacherversorgter AV-Block 3.Grades: 6/105 Patienten).
- Die Wahrscheinlichkeit für ein reoperationsfreies Überleben lag bei 90% bei Patienten mit Down Syndrom und bei 50% in nicht- Down Syndrom Patienten nach 10 Jahren.

- Die 10- Jahres-Überlebenswahrscheinlichkeit war bei allen Patienten sehr gut (bei fast 100%).
- Das funktionelle Ergebnis war nach AVSD Korrektur sehr gut (92.4% der Patienten befanden sich in NYHA-Stadium I), in der Echokardiographie wurde nur bei 3.8% der Patienten eine schwere Mitralklappeninsuffizienz und bei 1.9% der Patienten pulmonale Hypertonie festgestellt.
- Postoperative Herzkatheteruntersuchungen wurden nur bei wenigen Kindern durchgeführt (meist wegen einer pulmonalen Hypertonie).

Es können aufgrund dieser Ergebnisse folgende Schlussfolgerungen gezogen werden:

- Die biventriculäre AVSD- Korrektur kann mit guten Langzeitergebnissen und einem niedriegem Mortalitätrisiko durchgeführt werden, und wird üblicherweise als primäre Korrektur angestrebt.
- Das Alter zum Zeitpunkt der operativen Behandlung sollte möglichst früh gewählt werden, besonders bei Patienten mit Down Syndrom.
- Das Down Syndrom ist keine Kontraindikation für eine chirurgische Korrektur.
- Auf eine präoperative Herzkatheteruntersuchung kann bei ausreichender echokardiographischer Darstellung des Herzfehlers verzichtet werden.
- Die länge Bypassdauer and Ischämiezeiten sind nicht mit einer erhöhten Morbidität oder Mortalität assoziiert.
- Unserer Meinung nach bestätigen die sehr guten Langzeitergebnisse, dass die AVSD Korrektur sowohl bei Patienten mit Down Syndrom als auch bei nicht-syndromalen Patienten mit einem geringen Morbiditäts- und Mortalitätsrisiko durchführbar ist.

8. Abbreviations

ACE-I	Angiotensin converting enzyme inhibitors
ASD	Atrial septal defect
AV	Atrioventricular
AVSD	Atrioventricular septal defect
cAVSD	Complete atrioventricular septal defect
CPB	Cardiopulmonary bypass
D	Down syndrome
ECC	Extracorporeal circulation
ECG	Electrocardiography
ECHO	Echocardiography
HLM	Heart lung machine
ICU	Intensive care unit
i.e.,	That is to say
IVC	Inferior vena cava
JET	Junctional ectopic tachycardia
Kg	Kilogramm
LIL	Left inferior leaflet
LLL	Left lateral leaflet
LSL	Left superior leaflet
LVOTO	Left ventricular outflow tract obstruction
LV	Left ventricle
m.	Month
MI	Mitral insufficiency
min.	Minute
MV	Mitral valve
NYHA	New York Heart Association
ND	Non- Down syndrome
p	Probability
PA	Pulmonary artery
PAP	Pulmonary artery pressure
pAVSD	Partial atrioventricular septal defect
PDA	Patent ductus arteriosus
PFO	Patent foramen ovale

PLSVC	Persistent left superior vena cava
RBBB	Right bundle branch block
RIL	Right inferior leaflet
RLL	Right lateral leaflet
RSL	Right superior leaflet
RVOTO	Right ventricular outflow tract obstruction
RV	Right ventricle
SD	Standard deviation
SVC	Superior vena cava
SVES	Supraventricular extrasystole
SVT	Supraventricular tachycardia
TI	Tricuspid insufficiency
TV	Tricuspid valve
VES	Ventricular extrasystole
VSD	Ventricular septal defect
VT	Ventricular tachycardia
y	year

9. References

Reference List

(1) Becker AE, Anderson RH. Atrioventricular septal defects: What's in a name? J Thorac Cardiovasc Surg 1982 Mar;83(3):461-9.

(2) Van Mierop LH, Alley RD, KAUSEL HW, STRANAHAN A. The anatomy and embryology of endocardial cushion defects. J Thorac Cardiovasc Surg 1962 Jan;43:71-83.

(3) Abbot ME. Atlas of congenital cardiac disease. The American Heart association 1936;34-50.

(4) Rogers H, Edwards JE. Incomplete division of the atriovetricular canal with patent interatrial fpramen primum (persistent common atrioventricular ostium): reports of five cases and review of the literature. Am Heart J 1948;36:28.

(5) Wakai C, Edwards JE. Development and pathologic considerations in persistent common atrioventricular canal. Proc Myao Clin 1956;31:487.

(6) Wakai C, Edwards JE. Pathologic study of persistent common atrioventricular canal. Am Heart J 1958;56:779.

(7) Lev M. The architecture of the conduction system in congenital heart disease. I. Common atrioventricular orifice. AMA Arch Pathol 1958;65:174.

(8) Bharati M, Lev M. The spectrum of common atrioventricular orifice (canal). Am Heart J 1973;86:553.

(9) Van Mierop LH. Pathology and pathogenesis of endicardial cushion defect. Surgical implications. In Davilla JC, ed Second Henry Ford Hospital International Symposium on Cardiac surgery 1977;201.

(10) Rastelli GC, Kirklin JW. Anatomic observations on complete form of persistent common atrioventricular canal with special reference to atrioventricular valves. Mayo Clin Proc 1966;41:296.

(11) Ugarte M, Enriquez de SF, Quero M. Endocardial cushion defects: an anatomical study of 54 specimens. Br Heart J 1976 Jul;38(7):674-82.

(12) Baron MG, WOLF BS, STEINFELD L, VANMIEROP LH. ENDOCARDIAL CUSHION DEFECTS. SPECIFIC DIAGNOSIS BY ANGIOCARDIOGRAPHY. Am J Cardiol 1964 Feb;13:162-75.

(13) Picoli G, WOLF BS, Wilkinson JL, Lozsadi K, Macartney FJ, Anderson R. Morphology and classification of atrioventricular defects. Br Heart J 1979;42:621-33.

(14) Lillehei CW, Cohen M, Warden HE, Varco RL. The direct-vision intracardiac correction of congenital anomalies by controlled cross circulation: results in thirty-

two patients with ventricular septal defects, tetralogy of Fallot, and atrioventricular communis defects. Surgery 1955;38:11.

(15) Kirklin J, Daugherty G, Burchell H, Wood E. Repair of the partial form of persistent common atrioventricular canal: so called ostium primum type of atrial septal defect with interventricular communication. Ann Surg 1955;142:858.

(16) Chin AJ, Keane JF, Norwood WI, Castaneda A. Repair of complete common Atrioventricular canal in infancy. J Thorac Cardiovasc Surg 1982;84:437.

(17) Gerbode F. Surgical repair of endocardial cushion defect. Ann Chir Thorac Cardiovasc 1962;1:753.

(18) Dubost C, Blondeau P. Canal atrio-ventricular et ostium primum. J Chir 1959;78:241.

(19) Dezateux C KRGIBJBCWC. Newborn screening for congenital heart defects: a systemmatic review and cost-effectiveness analysis. Health Technology Assessment 2005 Feb;9(44).

(20) Amark K, Sunnegardh J. The effect of changing attitudes to Down's syndrome in the management of complete atrioventricular septal defects. Arch Dis Child 1999 Aug;81(2):151-4.

(21) Morris CD, Magilke D, Reller M. Down's syndrome affects results of surgical correction of complete atrioventricular canal. Pediatr Cardiol 1992 Apr;13(2):80-4.

(22) Gutgesell HP, Huhta J. Cardiac septation in atrioventricular canal defect. J Am Coll Cardiol 1986;8:1421.

(23) Khonsari S, Sintek C. Atrioventricular septal defects. Cardiac Surgery: Safeguard and Pitfalls in Operative Techniques 2003;3rd ed.:244.

(24) Virdi I, Keeton B, Shore D. Atrioventricular septal defect with a well developed primary component of the atrial esptum (septum primum). Int J Cardiol 1985;9:243.

(25) Studer M, Blackstone EH, Kirklin JW, Pacifico AD, Soto B, Chung GK, et al. Determinants of early and late results of repair of atrioventricular septal (canal) defects. J Thorac Cardiovasc Surg 1982 Oct;84(4):523-42.

(26) Anderson RH, Neches WH, Zuberbuhler JR, Penkoske PA. Scooping of the ventricular septum in atrioventricular septal defect. J Thorac Cardiovasc Surg 1988 Jan;95(1):146.

(27) Ebels T. Surgery of the left atrioventricular valve and of the left ventricular outflow tract in atrioventricular septal defect. Cardiol Young 1991;1:344.

(28) Baron MG. Abnormalities of the mitral valve in endocardial cushion defects. Circulation 1972 Mar;45(3):672-80.

(29) Soto B, Bargeron LM, Jr., Pacifico AD, Vanini V, Kirklin JW. Angiography of atrioventricular canal defects. Am J Cardiol 1981 Sep;48(3):492-9.

(30) Brandt PW. Axially angled angiocardiography. Cardiovasc Intervent Radiol 1984;7(3-4):166-9.

(31) Bloom KR, Freedom RM, Williams CM, Trusler GA, Rowe RD. Echocardiographic recognition of atrioventricular valve stenosis associated with endocardial cushion defect: pathologic and surgical correlates. Am J Cardiol 1979 Dec;44(7):1326-31.

(32) Kouchoukos N, Blackstone EH, Doty D, Hanley FL, Karp R. Atrioventricular septal defect. Kirklin/Barratt-Boyes: Cardiac surgery, Morphology, Diagnostic criteria, Natural history, Techniques, Results, and Indications 2003;Vol.1, 3rd ed.:802.

(33) McGrath LB, Kirklin JW, Soto B, Bargeron LM, Jr. Secondary left atrioventricular valve replacement in atrioventricular septal (AV canal) defect: a method to avoid left ventricular outflow tract obstruction. J Thorac Cardiovasc Surg 1985 Apr;89(4):632-5.

(34) Newfeld E, Sher M, Paul M, Nikaidoh H. Pulmonary vascular disease in complete atrioventricular canal defect. Am J Cardiol 1977;39:721.

(35) Barrea C, Levasseur S, Roman K, Nii M, Coles JG, Williams WG, et al. Three-dimensional echocardiography improves the understanding of left atrioventricular valve morphology and function in atrioventricular septal defects undergoing patch augmentation. J Thorac Cardiovasc Surg 2005 Apr;129(4):746-53.

(36) Narchi H. Neonatal ECG screening for congenital heart disease in Down syndrome. Ann Trop Paediatr 1999 Mar;19(1):51-4.

(37) Montigny M, Davignon A, Fouron JC, Biron P, Fournier A, Elie R. Captopril in infants for congestive heart failure secondary to a large ventricular left-to-right shunt. Am J Cardiol 1989 Mar 1;63(9):631-3.

(38) Buchhorn R, Hulpke-Wette M, Nothroff J, Paul T. Heart rate variability in infants with heart failure due to congenital heart disease: reversal of depressed heart rate variability by propranolol. Med Sci Monit 2002;8(10):661-6.

(39) Lacour-Gayet F, Planche C, Langlois J, Bruniaux J, Gentile M, Chambran P, et al. [Surgical treatment of complete atrioventricular canals, regular and irregular forms, in 75 patients]. Arch Mal Coeur Vaiss 1986 May;79(5):708-16.

(40) Lee CN, Danielson GK, Schaff HV, Puga FJ, Mair DD. Surgical treatment of double-orifice mitral valve in atrioventricular canal defects. Experience in 25 patients. J Thorac Cardiovasc Surg 1985 Nov;90(5):700-5.

(41) Rastelli GC, Ongley PA, Kirklin JW, McGoon DC. Surgical repair of complete form of persistent common atrioventricular canal. J Thorac Cardiovasc Surg 1968;55:299.

(42) Bender HW, Jr., Hammon JW, Jr., Hubbard SG, Muirhead J, Graham TP. Repair of atrioventricular canal malformation in the first year of life. J Thorac Cardiovasc Surg 1982 Oct;84(4):515-22.

(43) Rastelli GC, Ongley PA, McGoon DC. Surgical repair of complete atrioventricular canal with anterior common leaflet undivided and unattached to ventricular septum. Myao Clin Proc 1969;44:355.

(44) Carpentier A. Surgical anatomy and management of the mitral component of atrioventricular canal defects. In Anderson RH, Shinebourne EA, eds Pediatric cardiology London:Churchill Livingstone 1978;477.

(45) Rastelli GC, Weidman WH, Kirklin JW. Surgical repair of the partial form of persistent common atrioventricular canal, with special reference to the problem of mitral valve incompetence. Circulation 1965;31:31.

(46) Ohye R, Bove EL. Atrioventricular septal defect: surgical perspective. emedicine 2006.

(47) Tweddell JS, Litwin SB, Berger S, Friedberg DZ, Thomas JP, Frommelt PC, et al. Twenty-year experience with repair of complete atrioventricular septal defects. Ann Thorac Surg 1996 Aug;62(2):419-24.

(48) Dragulescu A, Ghez O, Fraisse A, Gaudart J, Amedro P, Kreitmann B, et al. [Long-term results of complete atrio-ventricular canal correction]. Arch Mal Coeur Vaiss 2007 May;100(5):416-21.

(49) Trusler GA, Mills NL, Ochsner IL, King TD. Correction of type C complete atrioventricular canal Surgical considerations. J Thorac Cardiovasc Surg 1976;71:20-8.

(50) Lange R, Guenther T, Busch R, Hess J, Schreiber C. The presence of Down syndrome is not a risk factor in complete atrioventricular septal defect repair. J Thorac Cardiovasc Surg 2007;134(2):304-10.

(51) Chi TPL. The pulmonary vascular bed in children with Down syndrome. J Pediatr 1975 Apr;86(4):533-8.

(52) Boening A, Scheewe J, Heine K, Hedderich J, Regensburger D, Kramer HH, et al. Long-term results after surgical correction of atrioventricular septal defects. Eur J Cardiothorac Surg 2002 Aug;22(2):167-73.

(53) Backer CL, Stewart RD, Bailliard F, Kelle AM, Webb CL, Mavroudis C. Complete atrioventricular canal: comparison of modified single-patch technique with two-patch technique. Ann Thorac Surg 2007 Dec;84(6):2038-46.

(54) Moran AM, Daebritz S, Keane JF, Mayer JE. Surgical management of mitral regurgitation after repair of endocardial cushion defects: early and midterm results. Circulation 2000 Nov 7;102(19 Suppl 3):III160-III165.

(55) Yamaki S, Yasui H, Kado H, Yonenaga K, Nakamura Y, Kikuchi T, et al. Pulmonary vascular disease and operative indications in complete atrioventricular canal defect in early infancy. J Thorac Cardiovasc Surg 1993 Sep;106(3):398-405.

(56) Ando M, Kobayashi M, Takahashi Y. Ideal timing of surgical repair of isolated complete atrioventricular septal defect. Interact Cardiovasc Thorac Surg 2007;6:24-6.

(57) Manning PB, Mayer JE, Jr., Sanders SP, Coleman EA, Jonas RA, Keane JF, et al. Unique features and prognosis of primum ASD presenting in the first year of life. Circulation 1994 Nov;90(5 Pt 2):II30-II35.

(58) Driscoll DJ. Left-to-right shunt lesions. Pediatr Clin North Am 1999 Apr;46(2):355-68, x.

(59) Bull C, Rigby ML, Shinebourne EA. Should management of complete atrioventricular canal defect be influenced by coexistent Down syndrome? Lancet 1985 May 18;1(8438):1147-9.

(60) Najm HK, Van Arsdell GS, Watzka S, et al. Primary repair is superior to initial palliation in children with atrioventricular septal defect and tetralogy of Fallot. J Thorac Cardiovasc Surg 1998;116(6):905-13.

(61) McElhinney DB, Reddy V, Silverman N, et al. Atrioventricular septal defect with common valvar orifice and tetralogy of Fallot revisited: making a case for primary repair in infancy. Young 1998;8(4):455-61.

(62) Silverman N, Levitsky S, Fisher E, DuBrow I, Hastreiter A, Scagliotti D. Efficacy of pulmonary artery banding in infants with complete atrioventricular canal. Circulation 1983 Sep;68(3 Pt 2):II148-II153.

(63) Williams WH, Guyton RA, Michalik RE, Plauth WH, Jr., Zorn-Chelton S, Jones EL, et al. Individualized surgical management of complete atrioventricular canal. J Thorac Cardiovasc Surg 1983 Dec;86(6):838-44.

(64) Shashi V, Berry MN, Covitz W. A combination of physical examination and ECG detects the majority of hemodynamically significant heart defects in neonates with Down syndrome. Am J Med Genet 2002 Mar 15;108(3):205-8.

(65) Soudon P, Stijns M, Tremouroux-Wattiez M, Vliers A. Precocity of pulmonary vascular obstruction of Down's syndrome. Eur J Cardiol 1975 Apr;2(4):473-6.

(66) Kwiatkowska J, Tomaszewski M, Bielinska B, Potaz P, Erecinski J. Atrioventricular septal defect: clinical and diagnostic problems in children hospitalised in 1993-1998. Med Sci Monit 2000 Nov;6(6):1148-54.

(67) exi-Meskishvili V, Ishino K, Dahnert I, Uhlemann F, Weng Y, Lange PE, et al. Correction of complete atrioventricular septal defects with the double-patch technique and cleft closure. Ann Thorac Surg 1996 Aug;62(2):519-24.

(68) Vida VL, Sanders SP, Milanesi O, Stellin G. Biventricular repair of right-dominant complete atrioventricular canal defect. Pediatr Cardiol 2006 Nov;27(6):737-40.

(69) Wilcox BR, Jones DR, Frantz EG. Anatomically sound, simplified approach to repair of " complete" atrioventricular septal defect. Ann Thorac Surg 1997;64:487-94.

(70) Nicholson IA, Nunn GR, Sholler GF, Hawker RE, Cooper SG, Lau KC, et al. Simplified single patch technique for the repair of atrioventricular septal defect. J Thorac Cardiovasc Surg 1999 Oct;118(4):642-6.

(71) Kim HK, Kim WH, Hwang SW, Lee JY, Song JY, Kim SJ, et al. Predictive value of intraoperative transesophageal echocardiography in complete atrioventricular septal defect. Ann Thorac Surg 2005 Jul;80(1):56-9.

(72) Iyer RS, Jacobs JP, de Leval MR, Stark J, Elliott MJ. Outcomes after delayed sternal closure in pediatric heart operations: a 10-year experience. Ann Thorac Surg 1997 Feb;63(2):489-91.

(73) Atsumi N, Kanemoto S, Terada Y, Jikuya T, Sakakibara Y, Mitsui T, et al. [Inhaled nitric oxide for postoperative pulmonary hypertensive crisis in a patient with complete atrioventricular canal associated with Down's syndrome: a case report]. Kyobu Geka 1996 Aug;49(9):729-32.

(74) Lindberg L, Olsson AK, Jogi P, Jonmarker C. How common is severe pulmonary hypertension after pediatric cardiac surgery? J Thorac Cardiovasc Surg 2002 Jun;123(6):1155-63.

(75) Neirotti RA, Jones D, Hackbarth R, Paxson FG. Early extubation in congenital heart surgery. Heart Lung Circ 2002;11(3):157-61.

(76) Ito H, Sobue K, So MH, Sugiura T, Sasano H, Takeuchi A, et al. Postextubation airway management with nasal continuous positive airway pressure in a child with Down syndrome. J Anesth 2006;20(2):106-8.

(77) Al-Hay AA, MacNeill SJ, Yacoub M, Shore D, Shinebourne E. Complete atrioventricular septal defect, Down syndrome, and surgical outcome. Risk factors. Ann Thorac Surg 2003;75:412-21.

(78) Guenther T, Mazzitelli D, Haehnel CJ, Holper K, Sebening F, Meisner H. Long-term results after repair of complete atrioventricular septal defects: analysis of risk factors. Ann Thorac Surg 1998;65:754-60.

(79) Marino B. Complete atrioventricular septal defect in patients with and without Down's syndrome. Ann Thorac Surg 1994 Jun;57(6):1687-8.

(80) Bando K, Turrentine MW, Sun K, Sharp TG, Ensing GJ, Miller AP, et al. Surgical management of complete atrioventricular septal defects. A twenty-year experience. J Thorac Cardiovasc Surg 1995 Nov;110(5):1543-52.

(81) Weintraub R, Brawn WJ, Venables A, Mee RB. Two-patch repair of complete atrioventricular septal defect in the first year of life. Results and sequential assessment of atrioventricular valve function. J Thorac Cardiovasc Surg 1990;99(2):320-6.

(82) Wetter J, Sinzobahamvya N, Blaschzok C, Brecher A-M, Graevinghoff LM, Schmaltz A.A.and Urban AE. Closure of the zone of apposition at correction of complete atrioventricular septal defect improves outcome. Eur J Cardiothorac Surg 2000;17:146-53.

(83) De BL, Di C, V, Ballerini L, Bevilacqua M, Marcelletti C, Marino B. Prevalence of left-sided obstructive lesions in patients with atrioventricular canal without Down's syndrome. J Thorac Cardiovasc Surg 1986 Mar;91(3):467-9.

(84) Piccoli GP, Ho SY, Wilkinson JL, Macartney FJ, Gerlis LM, Anderson RH. Left-sided obstructive lesions in atrioventricular septal defects: an anatomic study. J Thorac Cardiovasc Surg 1982 Mar;83(3):453-60.

(85) Backer CL, Mavroudis C, Alboliras ET, Zales VR. Repair of complete atrioventricular canal defects: results with the two-patch technique. Ann Thorac Surg 1995 Sep;60(3):530-7.

(86) Najm HK, Coles JG, Endo M, Stephens D, Rebeyka IM, Williams WG, et al. Complete atrioventricular septal defects: results of repair, risk factors, and freedom from reoperation. Circulation 1997 Nov 4;96(9 Suppl):II-5.

(87) Monteiro AJ, Canale LS, Rangel I, Wetzel E, Pinto DF, Barbosa RC, et al. Surgical treatment of complete atrioventricular septal defect with the two-patch technique: early-to-mid follow-up. Interact Cardiovasc Thorac Surg 2007 Dec;6(6):737-40.

(88) Frontera-Izquierdo P, Cabezuelo-Huerta G. Natural and modified history of complete atrioventricular septal defect--a 17 year study. Arch Dis Child 1990 Sep;65(9):964-6.

(89) Tlaskal T. [Surgical technique and results of correction of partial, transitional and total forms of atrioventricular septal defects]. Rozhl Chir 2001 Nov;80(11):562-71.

(90) Litwin SB, Tweddell JS, Mitchell ME, Mussatto KA. The double patch repair for complete atrioventricularis communis. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2007;21-7.

(91) Clapp S, Perry BL, Farooki ZQ, Jackson WL, Karpawich PP, Hakimi M, et al. Down's syndrome, complete atrioventricular canal, and pulmonary vascular obstructive disease. J Thorac Cardiovasc Surg 1990 Jul;100(1):115-21.

(92) Pozzi M, Remig J, Fimmers R, Urban AE. Atrioventricular septal defects. Analysis of short- and medium-term results. J Thorac Cardiovasc Surg 1991 Jan;101(1):138-42.

(93) Rizzoli G, Mazzucco A, Maizza F, Daliento L, Rubino M, Tursi V, et al. Does Down syndrome affect prognosis of surgically managed atrioventricular canal defects? J Thorac Cardiovasc Surg 1992 Oct;104(4):945-53.

(94) Prifti E, Bonacchi M, Bernabei M, Crucean A, Murzi B, Bartolozzi F, et al. Repair of complete atrioventricular septal defects in patients weighing less than 5 kg. Ann Thorac Surg 2004 May;77(5):1717-26.

(95) Masuda M, Kado H, Tanoue Y, Fukae K, Onzuka T, Shiokawa Y, et al. Does Down syndrome affect the long-term results of complete atrioventricular septal defect when the defect is repaired during the first year of life? Eur J Cardiothorac Surg 2005;37(3):405-9.

(96) Paulsen A, Edvardsen E, Brunvand L. [Follow-up of children with atrioventricular septal defect]. Tidsskr Nor Laegeforen 2003 Aug 14;123(15):2024-6.

(97) Formigari R, Di Donato RM, Gargiulo G, Di CD, Feltri C, Picchio FM, et al. Better surgical prognosis for patients with complete atrioventricular septal defect and Down's syndrome. Ann Thorac Surg 2004 Aug;78(2):666-72.

10. Figures list

Figure 1: Mitral- tricuspid valve relationship. A: In the normal heart. B: Partial atrioventricular septal defect. C: Complete atrioventricular septal defect. (Modified from Khonsari (23)). 6

Figure 2: Mitral valve annular configuration. A. In the normal mitral valve. B. In an atrioventricular septal defect mitral valve. (Modified from Khonsari (23)). 6

Figure 3: Sketch of the course AV node and His bundle. (Modified from Lev (7)). 7

Figure 4: Partial atrioventricular septal defect. (Modified from Khonsari (23)). 8

Figure 5: Complete atrioventricular septal defect. (Modified from Khonsari (23)). 9

Figure 6: Atrioventricular valves viewed from atrial side. A. Normal mitral and tricuspid valves. B. Leaflets in partial atrioventricular septal defects. C. Rastelli´s classification of complete atrioventricular septal defects. (Modified from Kirklin/ Barratt-Boyes (32)). 10

Figure 7- A: The common AV valve is floated to a closed position using saline solution. The central apposition points of the superior and inferior bridging leaflets are identified and marked with fine polypropylene. (Modified from Ohye (45)). 14

Figure 7- B: Two-patch technique. A patch of Goretex or Dacron is fashioned and secured along the crest of the ventricular septal defect. (Modified from Ohye (45)). 14

Figure 7- C: Two-patch technique. Interrupted horizontal mattress sutures are placed through the crest of the VSD patch and the inferior and superior bridging leaflet, dividing the common AV valve into right and left components. (Modified from Ohye (45)). 15

Figure 7- D: The pericardial patch is sutured to the crest of the prosthetic ventricular septum with the superior and inferior bridging leaflet sandwiched between the 2 patches. (Modified from Ohye (45)). 15

Figure 8- A: Single- patch technique. The superior and inferior bridging leaflets are divided into right right and left component. (Modified from Ohye (45)). 16

Figure 8- B: The leaflets are resuspended to the patch by passing sutures through the cut edge of the AV valve leaflet, the patch, and the cut edge of the right AV valve and tying the sutures. (Modified from Ohye (45)). 16

Figure 8- C: The cleft of the mitral valve between the superior and inferior bridging leaflets is closed. (Modified from Ohye (45)). 17

Figure 8- D: The atrial septal defect is closed with an autologous pericardial patch. The coronary sinus is placed in the left atrium to avoid injury to the conduction system. The rim of the ASD, the AV node, the bundle of His are indicated. The dashes represent the proposed suture line. (Modified from Ohye (45)). 17
Figure 9: Preoperative presenting symptoms in Down and non- Down syndrome patients. 25
Figure 10: Rastelli types in Down syndrome and non- Down syndrome patients. 25
Figure 11: Single- patch and two- patch technique in all patients, Down syndrome patients and non- Down syndrome patients. 29
Figure 12: CPB and aortic cross clamping times. 31
Figure 13: Main postoperative complications. 37
Figure 14: Residual MI postoperative. 39
Figure 15: Kaplan-Meier estimate of freedom from any reoperation for all patients. 44
Figure 16: Kaplan-Meier estimate of freedom from MV repairs reoperation. 45
Figure 17: Kaplan-Meier estimate of freedom from MV replacements reoperation. 45
Figure 18: Kaplan-Meier estimate of freedom from LVOTO repairs reoperation. 46
Figure 19: Kaplan-Meier estimate of freedom from pacemaker implantations. 46
Figure 20: Kaplan-Meier estimate of freedom from any reoperation by Down´s patients. 47
Figure 21: Kaplan-Meier estimate of freedom from any redo by non- Down´s patients. 47

11. Tables list

Table 1: Patients clinical characteristics 19

Table 2: Patients characteristics and follow- up (All patients) 19

Table 3: Diagnostic methods 20

Table 4 : Preoperative data for all patients 23

Table 5: Oxygen saturation preoperatively 23

Table 6: Down syndrome patients characteristics (D) 24

Table 7: Non- Down syndrome patients characteristics (ND) 24

Table 8 : Coexisting cardiac anomalies and congenital anomalies 26

Table 9: Palliative procedures 27

Table 10: Operative techniques 29

Table 11 : Bypass time and aortic cross clamping 30

Table 12: Intraoperative complications and rhythm disturbances 32

Table 13 : Thorax closure in all patients 32

Table 14: Mechanical ventilation and ICU stay in days for all patients 34

Table 15: Postoperative ECG rhythm disturbance findings 35

Table 16: Postoperative complications 36

Table 17: Echocardiographic residual findings at discharge 38

Table 18: Two/ Single- patch technique and MV regurgitation postoperatively 38

Table 19: Down /non- Down patients and MV regurgitation postoperatively 38

Table 20: Clinical profile at discharge 40

Table 21: Clinical findings at discharge 40

Table 22: The causes of readmission 41

Table 23: Type of reoperations 43

Table 24: The duration to first & second redo after AVSD repair 43

Table 25: Two- patch technique and reoperations 44

Table 26: Single- patch technique and reoperations 44

Table 27: Follow- up findings in D and ND patients 48

Table 28: Follow- up findings in all patients 50

12. Acknowledgments

I would like to thank gratefully Prof. Dr. D. Schranz for his supervision, friendly assistance and supporting this work.

I would like also gratefully acknowledge PD Dr. J. Bauer for his care, his patience and his supporting this work from the beginning, in the methods, contents and statistical analysis to the end of this work.

I would like to express my sincere thanks to PD Dr. I. Michel- Behnke who has given freely of her time and expertise to revise this work.

And my special gratefull thanks to Dr. H. Akintürk for his assistance and great support, that made this work possible.

Last but not least, I would like also to thank and appreciate the assistance of the following persons:

Wilfried Fischer, Johanes Gehron, Sussane Nisztuk, Britta Haunert, Maschonow Jurij, Dr.Lehmann, N. Mazhari, J. Monaci, Irmgard Lindemann, Sophie Volk, S. Possehn.

13. Curriculum vitae

Name	Abdalla Ahmed Mahmod
Date of birth	28.11.1968
Place of birth	El-Minia
Family state	Married
Nationality	Libyan
Address	Unterhof 67, App. 9012
	35392 Giessen
	Germany

Education:

Primary school	1973- 1979 / El-Minia
Preparatory school	1980- 1983 / Benghazi
Secondary school	1983- 1986 / Benghazi
Medical school	1986- 1994 / Faculty of Medicine, Al-Arab Medical University Benghazi (M.B.Ch.B. degree), including practical year.

Posts held as a Senior house officer (Assistenzarzt):

General surgery department, Benghazi teaching hospitals, Libya	01.06.1994- 31.05.1996
Diagnostic radiology department, Benghazi teaching hospitals	01.06.1996- 31.07.1998
Anaesthesia department, Benghazi teaching hospitals, Libya	01.08.1998- 28.02.2001
German course, Goethe-Institut, Freiburg	03.04.2001- 23.11.2001
Cardiac surgery department, Kerckhoff- Clinic, Bad Nauheim	01.12.2001- 06.02.2006
Cardiac and Thorax surgery department,University-Clinic,Gießen	07.02.2006- 28.04.2006
Cardiac surgery department, Kerckhoff- Clinic, Bad Nauheim	29.04.2006- 18.02.2007
Vascular surgery department, Harvey Clinic, Bad Nauheim	19.02.2007- 02.03.2007
Cardiac surgery department, Kerckhoff- Clinic, Bad Nauheim	03.03.2007- 30.04.2007
Pediatric cardiac surgery, University- Clinic, Giessen	01.05.2007- 31.08.2007

Academic work:

Scientific research for the PhD degree, Pediatric Heart Center, University Clinic, Giessen	01.09.2007- till now
Recognition as a cardiac surgeon specialist (Facharzt)	09.01.2008.

´´I declare that I have completed this dissertation single- handedly without the unauthorized help of a second party and only with the assistance acknowledged therein. I have appropriately acknowledged and referenced all text passages that are derived literally from or are based on the content of published or unpublished work of others, and all information that relates to verbal communications. I have abided by the principles of good scientific conduct laid down in the charter of the Justus Liebig University of Giessen in carrying out the investigations described in the dissertation.``

Abdalla A. Mahmod