Early outcome of children with complex atrial isomerism undergoing uni-ventricular cardiac palliation

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ABSTRACT

Objective: To review the postoperative intensive care unit (ICU) course and early outcome of children with complex atrial isomeric hearts undergoing cardiac surgery for uni-ventricular heart repair.

Methods: A retrospective review and analysis of ICU course of pediatric patients with atrial isomerism admitted from January 2000 to December 2004 in King Abdul-Aziz Medical City, Riyadh, Kingdom of Saudi Arabia, who underwent uni-ventricular repair.

Results: During the study period, 18 (n=18) patients were identified to have complex congenital heart disease (CHD) associated with atrial isomerism. They were in the form of right atrial isomerism (n=12), and left atrial isomerism (n=6). Eight patients did not meet the inclusion criteria of the study and were excluded. Ten of the 18 patients fulfilled the study criteria and underwent first stage uni-ventricular heart repair with 8 survivals (80%). Three of the 8 operated survival cases underwent second stage repair with 2 survivals (66%) and one patient completed Fontan surgery with a good outcome. An uneventful ICU course was noted in 3 of 10 operated patients (30%). Complications were noted in (40%) of cases including sepsis (n=4), tracheostomy (n=1), prolonged mechanical ventilation >7days (n=2). Over 50% of the operated patients required prolonged ICU stay (>2 weeks).

Conclusion: Atrial isomerism is frequently associated with complex cardiac defects that often present in the neonatal stage and requires multiple staged cardiac surgeries. The surgical repair and peri-operative management of this group of patients can be difficult, challenging, and with potential risk of significant morbidity or mortality. In our setting, we found the outcome of children with atrial isomerism undergoing uni-ventricular palliation comparable to the literature

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Atrial isomerism constitutes 0.4-2% of congenital heart diseases (CHD),[1] The nomenclature of atrial isomeric hearts were often linked to the presence or absence of the spleen as asplenia or polysplenia syndromes. Later evidence, however, showed no consistent correlation between splenic status, and particular cardiac anomalies.[2] Isomeric heart defects form a part of heterotaxy syndrome where lateralization of abdominal organs may also be defective.[3,4] The liver is often in the midline position with various other gastrointestinal anomalies such as gut malrotation, hepato-biliary tract malformation, and genitourinary tract anomalies.[3] The significance of atrial isomerism disorders is often associated with highly complex heart defects that may prove difficult to repair, often requiring multiple surgeries with poor surgical outcome, and considerable mortality as reported in the small number of currently published literature.[5,6] Patients with isomeric heart were once considered inoperable as their prognosis was often in doubt. Recently published data seem to suggest a better prognosis and outcome in some of the children undergoing a single ventricle repair, particularly in patients with left isomerism.[1] Due to the paucity of long-term follow-up studies at present, long-term prognosis for such patients is unclear, and often difficult to define. In order to have a better understanding of this group of patients with complex cardiac disease, we aim to evaluate the early outcome of children with atrial isomerism undergoing cardiac surgery

repair for single ventricle pathway and to identify the possible risk factors that may influence early surgical outcome.

Methods. A retrospective chart review and database analysis was performed on all patients admitted with atrial isomeric hearts between January 2000 and December 2004 at King Abdul-Aziz Cardiac Center, Riyadh, Kingdom of Saudi Arabia. Our hospital is a tertiary referral center for pediatric cardiac patients from inside the kingdom as well as nearby middle-east countries. Medical information of the patients was obtained from the departmental database and case notes of individual patients obtained from the medical records department. Diagnosis of atrial isomerism was established based on echocardiographic studies that were reviewed by at least 2 experienced pediatric cardiologists, the cardiac catheter findings, angiography, hemodynamics as well as the intra-operative findings documented by surgery. All patients had additional diagnostic workup for extra-cardiac anomalies including ultrasonography of the abdomen, splenic scans, and blood smear film for the presence of Howell-Jolly bodies that usually appear in the absence of functioning spleen.

Demographic data includes age, gender, weight, diagnosis, type of surgical repair, total bypass time and cross clamp time, peri-operative intensive care unit (ICU) data including ventilation hours, duration of inotrope infusion, number of inotrope used, ICU length of stay, and peri-operative complications were collected. Any death that occurred during ICU stay or within 30 days of cardiac surgery was reported as mortality. All medical and surgical interventions were performed after obtaining consents. This study was approved by the research committee from our institute.

Results. During the study period, 2200 patients were admitted to our institute for pediatric cardiac evaluation and echocardiography assessment. Nine hundred cases required admission to the pediatric ICU. The majority of the cases admitted to our ICU were post-surgical cases (80%). Eighteen patients (6 male, 12 female) were identified to have atrial isomerism. They represented 2% of the total pediatric cardiac ICU admissions and 1% of pediatric cardiac diseases. Twelve patients were found to have right atrial isomerism (RAI) and 6 with left atrial isomerism (LAI). The average weight on presentation was 5.5±0.8 kg. Fourteen (77%) were newborn, 14 (77%) were cyanotic, and the other 4 (33%) presented with heart failure. Sixty percent (60%) had ductal dependent lesions requiring prostaglandin infusion in the newborn period.

The classification of cardiac anomalies associated with isomerism is represented in **Table 1**. Both forms of atrial isomerism were associated with complex intra-cardiac, systemic, or pulmonary venous anomalies. The most common intra-cardiac anomaly associated with RAI was right ventricular outflow tract obstruction (RVOTO) (67%) mainly in the form of pulmonary atresia (PA). Additionally, atrio-ventricular septal defects (AVSD), partial, or total anomalous pulmonary venous connection, and bilateral superior vena cava (SVC) were also seen. Most of the patients with LAI had left ventricular outflow tract obstruction (LVOTO) and interrupted inferior vena cava (IVC) with azygos vein continuity. Of the extra cardiac anomalies, 10 of 12 (83%) patients with RAI had asplenia, 3 of 6 (50%) with LAI had polysplenia, 2 had gastro-esophageal reflux disease (GERD), 2 had gut malrotation, one had inguinal hernia, and 2 had unilateral hydronephrosis.

Surgical decision. After initial evaluation of 18 isomerism cases, 5 of 18 patients were not offered any surgery, as they were considered to have lesions that are not suitable for surgical repair for various reasons. Three of 5 died in the hospital shortly after birth including one born prematurely. The remaining 2 were discharged and subsequently succumbed. One patient with isomeric heart had bi-ventricular repair attempt and was excluded from the study. Two out of 18 patients were found to have balanced lesions after birth. They have been followed up and are planned to have future corrective surgery. The remaining 10 who met the study criteria (3 LAI, 7 RAI) underwent various forms and stages of palliative surgical repairs of uni-ventricular heart as described in **Table 2**. Those 10 patients who had palliative surgeries represented 1.4% of all pediatric cardiac surgical cases performed at the same period (720 cases).

Surgical interventions. Ten patients underwent first stage operation, 6 were less than one month of age at the time of surgery. Only one patient (10%) died in the immediate postoperative period following Blalock-Taussing (BT) shunt surgery. The remaining 9 patients (90%) survived the first stage operations and were successfully discharged home following their initial repair. During the follow up of those 9 children, one case of BT shunt died suddenly at home, 3 patients underwent second stage cardiac repair, and 5 patients remained alive and currently are followed up for future corrective surgeries. Of the 3 cases that had second stage repair, 2 patients survived and were discharged home, and one died in the immediate postoperative ICU care.

Morbidity and mortality. Overall surgical survival of 70% was noted in this study. Three (one LAI+ 2 RAI) out of 10 patients died (30%). There were 2 deaths following first stage BT shunt operation (20%), and one additional death following second stage operation

Table 1 - Summary of 18 patients with isomeric heart with details of their cardiac lesions. Cases from 1 to 11 represent patients that had surgery (case one is excluded, cases 12 to 18 did not have surgery).

Case Number	Surgery	Isomerism type	Diagnosis
1	Excluded case	LI	AVSD, PA, ASD
2	Done x 1	LI	SV-HR V, TAPVD, Coa
3	Done x 1	LI	SV-HRV, PS, AVSD
4	Done x 2	RI	SV-HRV, TAPVD, ASD
5	Done x 2	LI	SV-HRV, VSD, PA
6	Done x 2	RI	DORV, PS, AVSD
7	Done x 3	RI	AVSD, PA-HRV, BSVC
8	Done x 1	RI	SV, PA-HRV, AVSD
9	Done x 1	RI	PA, VSD, TAPVD
10	Done x 1	RI	SV-HLV, TGA, AVSD, TAPVD
11	Done x 1	RI	DORV, PS, AVSD
12	Inoperable	RI	PA, AVSD
13	Inoperable	RI	SV, TAPVD
14	Planned in future	LI	TAPVD, TOF, DORV, PS
15	Inoperable	RI	Obstructed TAPVD, AVSD, multiple VSD
16	Planned in future	LI	Sub-valvular aortic stenosis, PDA, MV cleft, interrupted IVC
17	Inoperable	RI	PA, SV-HRV, AVSD, small pulmonary arteries branches, severe AVV regurgitation
18	Inoperable	RI	PA, IVS, DORV

LI - left isomerism, RI - right isomerism, AVSD - atrio-ventricular septal defect, PA - pulmonary atresia, ASD - atrial septal defect, SV - single ventricle, TAPVD - total anomalous pulmonary venous drainage, Coa - coarctation of the aorta, SV-HRV - single ventricle (hypoplastic right ventricle), PS - pulmonary stenosis, AVSD - atrio-ventricular septal defect, VSD - ventricular septal defect, PA - pulmonary atresia, DORV - double outlet right ventricle, PA-HRV - pulmonary atresia - hypoplastic right ventricle, SV-HLV - single ventricle-hypoplastic left ventricle, TGA - transposition of great arteries, TOF - tetralogy of fallot, PDA - patent ductal arteriosis, MV - mitral valve, IVC - inferior vena cava, AVV - atrio ventricular valve, IVS - intact ventricular septum, BSVC - bilateral superior vena cava

to make the overall mortality of 30% in our series of patients who went for uni-ventricular heart repair. The case that died during the second stage repair was bilateral cavo-pulmonary anastomosis with atrioventricular valve repair. Two of the mortality in our series were in-hospital deaths and one was a late home death. A difficult peri-operative ICU course characterized by low cardiac output, pulmonary hypertension crisis, unstable hemodynamics, renal failure, and so forth were noted in 4 of 7 survivors (57%) necessitating vigorous management while the remaining 3 of 7 survivors (43%) had uneventful ICU course after their surgery. Postoperative arrhythmia were observed in 3 cases mainly sinus type, however, it did not contribute to the mortality of the 2 cases who died in the hospital. The complexities of cardiac repair in this group of patients called for prolong mechanical ventilation and intensive hemodynamic support in many cases. The average ventilation time was 14±1.6 days, and the average duration of inotrope infusion was 5.6±0.6 days. The average lengths of stay in the ICU were 29±2 days, and in the hospital were 60±4.7 days. Sixty two percent of patients had significant postoperative morbidity due to various complications following surgery. Four of 10 patients had sepsis, and 2 died. *Staphylococcus epidermidis* was isolated in 3 patients and *Klebsiella* species in one. Two patients developed brain infarction, and one underwent tracheostomy due to persistent lung collapse secondary to diaphragm palsy.

Discussion. Atrial isomerism form complex heart defects and constitute 0.4-2% of CHD.[1] It is usually associated with intra-cardiac, vascular, or extra cardiac anomalies that are to be carefully probed in pre-operative evaluation. In our series, we found that atrial isomerism represents 2% of our ICU admissions similar to other previously reported literatures.[6,7] Concurrent with other studies,[8,9] we found a frequent association between RAI with PA, complete AVSD, anomalous pulmonary venous connections, and bilateral SVC. Similarly, LAI was commonly associated with LVOTO, common atrium, and interrupted IVC. When atrial isomerism is suspected in a patient, identifying the presence or absence of spleen is an important step during the evaluation of such a patient.[4] The importance of determining the spleen status is diagnostic as well as

Table 2 - Type, stages, and outcome of different surgical repairs in each patient with isometric heart.

Diagnosis of 11 patients with isomeric heart who underwent surgery	First surgery	Second stage surgery	Third stage surgery	Outcome
AVSD, PA, HRV, ASD	MBT shunt			Died post –operatively
Coa, TAPVD, SV,	Coa repair, PAB	Waiting for future surgery		Alive
SV, HRV, AVSD, PS,	Glenn + Kawashima	Waiting for future surgery		Alive
TAPVD, SV, HRV	PAB, TAPVD repair	BCPA, AVSD repair		Died post-operatively
PA, HRV, VSD, SV, IIVC	Excluded case	Biventricular repair		Excluded from study
AVSD, DORV, PS	LMBT shunt	BBCPA		Alive
AVSD, PA, HRV, BIL SVC	MBT shunt	BCPA, AVSD repair	Fontan	Alive
PA, AVSD, SV, HRV	LMBT shunt	Waiting for future surgery		Alive
TAPVD, PA, VSD	BCPA, TAPVD repair	Waiting for future surgery		Alive
AVSD, SV, HLV, TGA, TAPVD	LMBT shunt	Waiting for future surgery		Alive
DORV, AVSD, PS	RMBT shunt			Died at home, 8 weeks post-operatively

AVSD - atrio-ventricular septal defect, PA - pulmonary atresia, ASD - atrial septal defect, Coa - coarctation of the aorta, TAPVD - total anomalous pulmonary venous drainage, SV - single ventricle, HRV - hypoplastic right ventricle, PS - pulmonary stenosis, VSD - ventricular septal defect, DORV - double outlet right ventricle, HLV - hypoplastic left ventricle, IIVC - interrupted inferior vena cava, TGA - transposition of great arteries, MBT - modified Blalock-Taussing, PAB - pulmonary artery bonding, LMBT - left modified Blalock-Taussing, RMBT - right modified Blalock-Taussing, BCPA - bi-directional cavo-pulmonary anastomosis, BBCPA - bilateral bi-directional cavo-pulmonary anastomosis, BIL SVC - bilateral superior vena cava

therapeutic. A patient with absent spleen should receive life-long prophylactic antibiotic and vaccination against encapsulated organism. In our study, asplenia was noted in 83% of RAI cases and polysplenia in 50% of LAI. This association has been observed by others and found different results. Uemura et al[10] reported in an autopsy series, the presence of asplenia in 56.5% of RAI and polysplenia in 63.8% of LAI. Gut anomalies such as malrotation, GERD, and inguinal hernia were observed in 27% of our patients associated mainly with LAI conforming earlier studies that report an incidence of 36% in such cases.[6]

In our series of 18 cases, 5 (28%) were not offered any form of surgical intervention and declared not suitable for surgical repair. All non operated cases died either soon after birth or in early newborn life. Cardiac surgery is not always attainable in all cases of atrial isomerism, and in many instances only compassionate care can be provided for the highly complex cases particularly in association with non-cardiac anomalies or prematurity.[1] The majority of non operated cases succumbed early in life. The high mortality in non operated infants is well recognized and it may even reach up to 95% mortality as it was presented in a report describing RAI patients.[1,5] Three patients with LAI underwent cardiac palliative surgery. Among the 3 patients with LAI, one had BT shunt, one with pulmonary artery banding with coarctation repair, and one had Glenn with Kawashima surgery. Of the 3 patient with LAI who had surgery, one died at home following BT shunt surgery, and the other 2 survived waiting for second-stage repair. Two out of 3 patients with left isomerism survived the first-stage operation, which resulted in 66% survival percentage in this sub-group of patients.

Seven patients with right isomerism had initial surgery as systemic to pulmonary shunt (5 cases), bilateral cavo-pulmonary anastomosis (one case), and PA band (one case). All 7 patients survived the initial operation except one that died unexpectedly at home 8 weeks following BT shunt surgery. Subsequently, 3 of the 6 survivals underwent second stage surgery with single mortality in the postoperative period, and 2 survivals. One of the 2 patients who survived the second-stage surgery completed the third-stage, consisted of extra-cardiac fenestrated Fontan operation and repair of incompetent atrio-ventricular (AV) valve with good outcome. Recent literature series showed better, early and midterm outcomes following Fontan surgery in children born with isomerism.[11,12] In the presence of insufficient AV valve, however, many authors recommend to perform AV valvuloplasty before Fontan surgery to enhance the outcome.[11,12] Three out of 7 patients with RAI in our series had total anomalous pulmonary venous drainage. Those were the most difficult and challenging cases to manage. Among them, one died during the second-stage repair, and the rest had prolonged postoperative ICU course. In total, out of 7 patients with RAI who had first and second surgeries, 2 patients died (28%) and the rest survived.

Overall survival for all isomeric cases in our series was 80% after the first stage surgery and 70% after the second stage repair. The overall mortality of 30% in our study is comparable to previously published data.[6,9,13,14] We observed a possible trend toward better prognosis in patients with right isomerism (77%) as compared to left isomerism (66%). Further studies are needed to confirm such trend.

Regardless of the type of surgery, the postoperative course can be difficult and challenging, necessitating rigorous hemodynamic support and prolonged mechanical ventilation in some instances. Uneventful ICU course was noticed in 3 patients (30%) only. The rest of the patients had more difficult and challenging ICU course. With the application of modern surgical techniques and advancement in intensive care treatment, patients survive the initial stage operation in early life or later during infancy. In our cases, 6 patients underwent first stage surgical palliation at less than one month of age with 80% survival rate. Our results as well as others indicate that surgical palliation in the neonatal period is achievable with acceptable outcome despite the high complexity and potential co-morbidity.[14] The difficulties in the management of these cases are related to multiple factors including the high complexities of the cardiac lesions, the associated extra-cardiac anomalies, and susceptibility to infection. In fact, sepsis was a major cause of morbidity and mortality in our series. It occurred in 4 patients (40%) and contributed directly to mortality in 2 of them, who succumbed to fulminant sepsis. The increase susceptibility to infection in this group of children is likely to be related to impaired splenic function. Obviously, the high incidence of complications leads to prolonged ICU stay, prolonged hospitalization, and substantial utilization of resources in comparison to other type of cardiac patients.

In conclusion, atrial isomerism represents almost 2% of patients undergoing cardiac surgery in our center. Atrial isomerism is frequently associated with cardiac and extra cardiac anomalies especially related to spleen status. Due to the high complexity of heart disease or the co-existence of other malformations, surgical repair was attainable in only 2 out of 3 of the cases. When surgery is undertaken, the complexity of cardiac repair, and susceptibility to infection contribute to high incidence of co-morbidity and prolong ICU care. However, with single ventricle repair route, 80% of our patients tolerated the first stage repair and 66% tolerated second stage repair. Our study has many limitations due to the small number of these rare cases, the retrospective nature of the study, and the unavailability of all management options such as heart transplant. We hope that the progress in surgical technique, peri-operative care and technology support may improve the ICU outcome and survival in this group of children with complex cardiac lesions.

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