RETROSPECTIVE REVIEW OF RIGHT-SIDED HEARTS AND ASSOCIATED CARDIAC MALFORMATIONS IN CHILDREN AT THE CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

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A research report submitted to the Faculty of Health Science, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for

the degree of Masters of Medicine in Paediatrics (MMed)

Johannesburg, 2014

DECLARATION

I, Nadia van Staden declare that this research report is my own work. It is being submitted for the degree of Masters of Medicine in Paediatrics in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

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ABSTRACT

Introduction

Right-sided hearts have three different causes. They are often associated with additional significant cardiac malformations (ASCM) and extracardiac abnormalities.

Objectives

- To determine the prevalence of right-sided hearts.
- To distinguish between dextrocardia, dextroversion and dextroposition.
- To examine patient demographics.
- To examine ASCM and extracardiac abnormalities.
- To document patient management.

Methods

A retrospective audit of patient records.

Results

Dextrocardia comprised 1.8% of all congenital heart defects and 58% of all right-sided hearts seen. Situs inversus was the dominant situs arrangement. Situs solitus and situs ambiguous had a high incidence of ASCM. Dextroposition made up 41% of all right-sided hearts and the majority had causes amenable to treatment. Two patients were diagnosed with dextroversion.

Conclusions

Dextrocardia as a cause of a right-sided heart shows no socio-economic or ethnic preference. ASCM are commonly seen in dextrocardia, and depends largely on the situs arrangement. Dextroposition is mostly secondary to extracardiac causes. Dextroversion is rare.

It is imperative to ascertain the cause of a right-sided heart, as this will influence patient management and outcome.

ACKNOWLEDGEMENTS

I gratefully acknowledge and thank:

- My supervisor, Professor Antoinette Cilliers.
- All patients whose data was used in this study.
- The Cardiology unit and staff for their assistance.
- The Medical Advisory Committee and the Chris Hani Baragwanath Hospital for allowing me to conduct our study.
- The Department of Paediatrics and the Faculty of Health Sciences of the University of the Witwatersrand.

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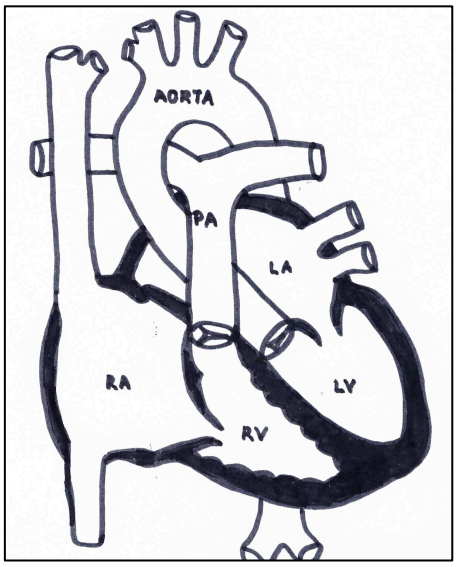
ABBREVIATIONS

CHBAH	Chris Hani Baragwanath Academic Hospital
ASCM	Additional significant cardiac malformations
RSH	Right-sided heart
RAA	Right atrial appendage
LAA	Left atrial appendage
RA	Right atrium
LA	Left atrium
RV	Right ventricle
LV	Left ventricle
AV	Atrioventricular
VA	Ventriculoarterial
PT	Pulmonary trunk
Ao	Aorta
FGF-8	Fibroblast growth factor 8
RAI	Right atrial isomerisation
LAI	Left atrial isomerisation
MPA	Main pulmonary artery
TGV/A	Transposition of the great vessels/arteries
IVC	Inferior vena cava
SVC	Superior vena cava
ASD	Atrial septal defect
AVSD	Atrioventricular septal defect
VSD	Ventricular septal defect
TR	Tricuspid regurgitation
PS	Pulmonary stenosis
PA	Pulmonary atresia
MV	Mitral valve
LVOT	Left ventricular outflow tract
RVOT	Right ventricular outflow tract
DORV	Double outlet right ventricle
BTS	Blalock-Taussig shunt
AV-VA	Atrioventricular-Ventriculoarterial
CCHD	Congenital cyanotic heart disease
MPA	Main pulmonary artery
CATCH-22	Acronym for: cardiac anomalies, abnormal facies, thymus hypoplasia, cleft palate, hypocalcaemia, hypoparathyroidism
VACTERL	Acronym for: vertebral abnormalities, ano-rectal malformations, cardiac abnormalities, trachea-oesophageal fistula/atresia, renal and limb abnormalities
RMB	Right main bronchus
HIV	Human Immunodeficiency Virus
USA	United States of America

1.0 INTRODUTION

Anatomically, the heart is located in the mediastinum, between the lungs and above the diaphragm. The bulk of the heart is situated to the left of the midline and the apex usually points inferiorly and to the left. This is the normal arrangement and is known as levocardia. There are several reasons why the heart can be deviated from this position, or for its apex to point in an unexpected direction.

Figure 1. Normal heart (illustration: author)



PA, Pulmonary artery; LA, Left Atrium; LV, Left Ventricle; RA, Right Atrium; RV, Right Ventricle;

1.1 Definitions of right-sided heart subgroups:

1.1.1 Dextrocardia

As a result of a variation in cardiac development the base-apex of the heart is directed rightwards, opposite to the normal leftwards orientation (1,2). This malposition is intrinsic to the heart and is not caused by extracardiac abnormalities (3). This mirror image arrangement occurs in approximately

0.01% of live births and is often accompanied by additional significant cardiac malformations (ASCM). ASCM have previously been described as those malformations that require medical or surgical treatment (1,4). For the purpose of this study, ASCM was used as a descriptive term for any additional cardiac defect diagnosed at time of echocardiographical assessment.

The diagnosis is often missed in the course of patient assessment and may be made unexpectedly in asymptomatic patients after a routine chest x-ray or astute physical examination (5). Dextrocardia with ASCM without the benefit of appropriate treatment may have important adverse consequences on the long-term survival of these children (1,3).

Diagnostic electrocardiographic features in dextrocardia include: inverted P, QRS, and T waves in lead I; right axis deviation and absent R-wave progression in the chest leads (dominant S waves throughout) (6,7).

Although it is rare, an awareness of the possibility of dextrocardia should be created amongst paediatricians, neonatologists and other health practitioners caring for children.

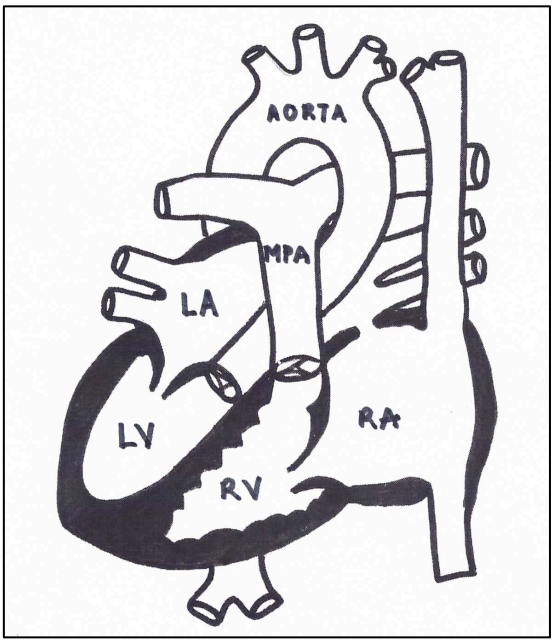


Figure 2: Dextrocardia (illustration: author)

MPA, Main pulmonary artery; LA, Left Atrium; LV, Left Ventricle; RA, Right Atrium; RV, Right Ventricle

1.1.2 Dextroposition

Dextroposition is the displacement of the heart to the right secondary to other extracardiac causes such as right lung hypoplasia, right pneumonectomy, atelectasis or diaphragmatic hernia (8). Although the heart is rightwardly positioned, the cardiac apex remains pointed normally to the left. In the majority of cases, this anatomic position is associated with an anatomically normal heart but may coincidently be coupled with congenital heart lesions (3,4,9). The risk for congenital heart lesions in patients with dextroposition is the same as for the general population (8).

An unusual example of a dextroposition is Scimitar syndrome, which is

often associated with cardiac lesions. The common association is hypoplasia of the right lung and anomalous pulmonary venous return from the abnormal lung (10,11). The chest x-ray characteristically demonstrates a curvilinear pattern created by the abnormal pulmonary veins on the right side draining into the inferior venous cava (12). Scimitar syndrome is often confused with right-sided lung pathology, such as tuberculosis with right lung collapse, which has a similar X-ray appearance (12,13).

1.1.3 Dextroversion

Dextroversion is the least familiar subgroup of dextrocardia and includes location of the heart in the right hemi thorax without inversion of the cardiac chambers (8,14). It results from a congenital malrotation of the ventricular part of the heart about its long axis with the atria remaining in the normal position (dextrocardia with normally related atria and viscera) (2). The embryogenesis of dextroversion is closely related to the embryogenesis of the cono-truncal region of the heart. This condition is associated with a high incidence of ASCM (4,6,9).

The electrocardiography features in dextroversion differ from those in dextrocardia. In dextroversion, the atria are in the normal position, therefore the direction of spread of atrial depolarization is the same as levocardia resulting in a normally upright P wave in lead I (6).

1.2 Classification

The classification and diagnosis of abnormal cardiac positions should be done using a segmental approach with the position of the viscera and atria (situs) defined first, then the ventricles, followed by the great vessels (1,15).

The atria maintain their laterality throughout development, and therefore underlie and define cardiac situs (6). Atrial positions are assigned once their various defining morphologies have been identified. Each atrium has features which differentiate the one from the other. The right atrial appendage (RAA) is triangular, while the left atrial appendage (LAA) is tubular. The RAA has a wide communication with the right atrium (RA) and has a rough surface due to the extensive pectinate muscles. The LAA has a narrow communication with the left atrium (LA) and has fewer pectinate muscles (16).

Once the anatomical-right and the anatomical-left atria are identified, their situs (positions) can be determined. The term situs is not only used to determine the atrial positions, but also to indicate the position of the abdominal and thoracic organs (16). Both the incidence and severity of complex cardiac anomalies are proportional to the failure of shift of the cardiac apex with respect to the abdominal viscera and situs (6,17,18).

There are three types of situs: situs solitus, situs inversus, and situs ambiguous (6,18).

Situs solitus is the normal anatomic state, with a trilobed right lung and a bilobed left lung. The morphological right atrium is to the right of the morphological left atrium and the cardiac apex is left-sided (1,6).
In situs solitus dextrocardia the cardiac apex points to the right, but the viscera are situated in their usual positions (15). The likelihood of diagnosing a severe cardiac lesion in situs solitus dextrocardia is high (6,17,18).

Situs inversus is the mirror image of situs solitus (6). The pulmonary anatomy is reversed with the left lung having three lobes and the right lung having two lobes. The liver and gallbladder are located opposite to the usual positions on the left, whereas the spleen and stomach are located on the right. The remaining internal structures are also a mirror image of the normal (3,18). In the example of dextrocardia and situs inversus, the anterior-posterior relationships of the heart are normal, but the right-left axis/orientation is reversed. This means that the morphologic right atrium is on the left, and the morphologic left atrium is on the right (11,19).

An important association in approximately 20% of patients with situs inversus and mirror image dextrocardia is Kartagener syndrome. This cilopathic autosomal recessive disease is typified by bronchiectasis, sinusitis, and situs inversus (6,18). The diagnosis should be considered in patients presenting with features of chronic lung disease and a right-sided heart.

When situs inversus totalis occurs with a structurally normal heart, longevity is normal, but when congenital heart disease coexists, longevity is determined by the

coexisting cardiac anomalies (1,15). Situs inversus with a normally positioned left-sided heart (levocardia) has a much greater incidence of severe cardiac abnormalities (6).

The third and most serious situs pattern associated with dextrocardia is **situs ambiguous** or heterotaxy syndrome ("hetero" different, "taxy" arrangement). A common synonym for heterotaxy is isomerism. In this situation sidedness is random, such that some organs are reversed and others are not. Thus situs cannot be determined. The liver may be in the midline, the spleen absent or multiple, the atrial morphology unclear, and the bowel may be malrotated. Often, normally unilateral structures are duplicated or absent. These cases are classified as laterality sequences. The 2 primary subtypes of situs ambiguous include (1) right isomerism, or asplenia syndrome, and (2) left isomerism, or polysplenia syndrome (1,3,17,18).

In classic right isomerism, or asplenia, bilateral right-sidedness occurs. These patients have bilateral right atria, a centrally located liver, an absent spleen, and bilaterally trilobed lungs, each with a short bronchus that branches early. The descending aorta and inferior vena cava are on the same side of the spine. Associated cardiac malformations include common atrioventricular canal, univentricular heart, transposition of the great arteries and total anomalous pulmonary venous return. These patients are usually immunocompromised (due to absence of the spleen) and this, together with the complex cyanotic cardiac anomalies results in a poor prognosis with a mortality rate of up to 80% in the first year of life (3,11,17).

In left isomerism, or polysplenia, bilateral left-sidedness occurs. These patients have bilateral left atria and multiple spleens, and both lungs have two lobes, each with a bronchus that branches distally. Cardiac anomalies are not as complex as in asplenic patients. Interruption of the inferior vena cava with azygous or hemizygous continuation may be present. Because of bilateral left-sidedness, a right superior vena cava joins a morphologic left atrium, and thus the sinus node is usually absent or hypoplastic. Many of these patients have heart block because of the abnormally formed sinus node. Up to 25% of patients have minor cardiac abnormalities, and the disorder may not be diagnosed until adulthood (3,17,18).

In patients with situs ambiguous where there may be bilateral right or left atria present, other extracardiac anatomical features may be used to decide situs. The tracheobronchial anatomy is one feature that is concordant with the atrial situs and can be recognized on chest x-rays to assist in the diagnosis of atrial positions. The morphological right main bronchus is eparterial with an early branching pattern and is consistently located above the morphologic right atrium, whereas the left main bronchus is hyparterial, divides more distally and is consistently located above the left atrium (6).

The next step after identifying the position of the viscera and atria, keeping to a segmental approach, is to differentiate between the right and left ventricle. The right ventricle (RV) has a moderator band and its apex has coarse trabeculations, while the left ventricle (LV) has fine trabeculations (16). In ventricular inversion, the ventricle in the left position may display morphological

features of a right ventricle, and the ventricle in the right position may demonstrate left ventricular morphology.
Despite opposite ventricular morphology, the pulmonary trunk will still arise from the right-sided ventricle and the aorta from the left-sided ventricle.

The final step is to determine the connections between the four heart chambers as well as between the heart chambers and the great vessels.

Atrioventricular concordance indicates a normal connection whereby the anatomical RA is connected to the anatomical RV, and the anatomical LA to the anatomical LV. Atrioventricular discordance implies that the anatomical RA is connected to the anatomical LV and the anatomical LA to the anatomical RV (16,19).

Ventriculoarterial concordance occurs in a normal heart when the aorta arises from the anatomical LV and the pulmonary trunk from the anatomical RV. Ventricular discordance is present if the aorta arises from the anatomical RV and the pulmonary trunk from the anatomical LV.

AV concordance and VA discordance implies complete transposition of the great arteries (TGA), while AV discordance and VA discordance indicates anatomically-corrected TGA (16).

Table 1 provides a summary of the various more common connections that can be found in the heart.

Table 1. Summary of some of the more common atrioventricular and ventriculoarterial connections that can be found in the heart

Anatomy/ Pathology	**AV connection**	**VA connection**	**Left heart**	**Right heart**
Normal heart	Concordance	Concordance	Left Atrium-Left Ventricle-Aorta	Right Atrium-Right Ventricle-Pulmonary Trunk
Complete TGA	Concordance	Discordance	Left Atrium-Left Ventricle-Pulmonary Trunk	Right Atrium-Right Ventricle-Aorta
Anatomically corrected TGA	Discordance	Discordance	Left Atrium-Right Ventricle-Aorta	Right Atrium-Left Ventricle-Pulmonary Trunk
Double-outlet RV	Any	>50% of Aorta and Pulmonary Trunk from RV	Hypoplastic or normal size	Normal size or hypoplastic
Single ventricle	Not defined	Both Aorta and Pulmonary Trunk from single ventricle	Single Ventricle with undefined left or right ventricular features	Single Ventricle with undefined left or right ventricular features

AV, atrioventricular; LV, left ventricle; RV, right ventricle; TGA, transposition of the great arteries; VA, ventriculoarterial

1.3. Genetics

The genetics involved in cardiac midline and lateral defects is very complex and not well understood. The aberrations are thought to occur along three geometric axes: anterior-posterior, dorsal-ventral and left-right. The expression of genes in the dorsal midline cells coordinate the development of the three anatomic axes which drives the cardiac tube to loop in the appropriate direction (15).

In the third week of gestation the right to left axis is established. When the primitive streak appears it secretes fibroblast growth factor 8 (FGF-8) which induces and maintains expression of *Nodal and Lefty-2 genes* and occurs only on the left side of the embryo. Both of these genes upregulate *PITX2,* the transcription factor responsible for establishing left sidedness. In order to prevent left-sided signals from crossing over, two genes *Lefty-1* and *Sonic hedgehog* are expressed on the left side of the neural tube floor plate and act as a barrier. They also repress left-sided gene expression on the right. Genes regulating right-sided development are not as well defined (20).

1.4. Embryology

Knowledge of the embryology of the heart formation facilitates comprehension of the disorders underlying cardiac malposition. As previously mentioned, it is the position of the atria as opposed to the bulbus cordis or the primitive ventricle, that determines the cardiac situs (as only the atria fully retain their laterality throughout cardiac development). Therefore, abnormalities of atrial position are usually associated with abnormalities in the situs of other organs (6).

The embryonic cardiac tube shows pulsatility on day 22 and undergoes constrictions that outline future cardiac chambers. Since the cardiac tube grows more rapidly than the pericardial cavity, it must undergo a series of complex foldings to be accommodated.

The primitive heart tube undergoes looping at day 23, and may loop to the right or to the left forming either a D-loop or an L-loop, respectively. With D-looping, the bulbus cordis is located to the right of the primitive ventricle. The proximal bulbus cordis gives rise to the right ventricle, and the primitive ventricle forms the morphologic left ventricle. Hence, in situs solitus with D-looping, atrioventricular concordance is established as the right atrium connects to the right ventricle and the left atrium to the left ventricle. The ventricles then undergoes horizontal shift (version) from right to left, resulting in the normal orientation of the apex toward the left. Therefore, normal is represented by cardiac situs solitus with D-looping and atrioventricular concordance. With L-looping, the bulbus cordis is to the left of the primitive ventricle resulting in dextrocardia (3,6).

1.5. Motivation for study

A heart in the right chest is uncommon and evaluation can be challenging.
It is important to recognize because it can be associated with important ASCM in patients with dextrocardia (1) and in cases of dextroposition may be coupled with important non-cardiac malformations which are usually the cause of the malposition of the heart (8).

The recognition of situs inversus and situs ambiguous has important implications for patients who present with abdominal symptoms. For example, appendicitis in patients with situs inversus will present with left-sided loin pain rather than right-sided loin pain because their abdominal visceral contents may be reversed. In addition, patients with situs ambiguous may have right atrial isomerism or heterotaxia. This is associated with asplenia placing them at risk for serious bacterial infections. Patients with both left and right-sided isomerism are at risk for malrotation of the bowel and consequently bowel ischaemia.

A right-sided heart may be secondary to mediastinal shift resulting from underlying chest pathology such as pneumothorax and congenital diaphragmatic hernias. These require prompt recognition and rapid treatment which may be life saving.

Failure to recognize reversed anatomy could therefore result in misdiagnosis and improper surgical and medical management. The prevalence of right-sided hearts and associated cardiac malformations has not previously been examined within a Southern African Tertiary Care Centre to the best of the authors' knowledge.

1.6. Aim

To review all children diagnosed with right-sided hearts at the Chris Hani Baragwanath Academic Hospital (CHBAH) Paediatric Cardiology Department (a Southern African tertiary care hospital) over a 21-year period, and to compare the findings to those reported from institutions in both first world and developing countries.

1.7. Objectives

Primary Objective

To determine the prevalence of various right-sided hearts in the patients seen by the CHBAH Paediatric Cardiology Department from 1 January 1991 to 2 November 2012.

Secondary Objectives:

- To distinguish dextrocardia from dextroposition and dextroversion.

- To establish age at diagnosis and gender predominance.

- To review the prevalence of associated significant cardiac malformation, the situs of the abdominal contents, and associated heterotaxia.

- To document management of the cardiac and other abnormalities.

2.0 STUDY DESIGN AND METHODS

2.1 Study Population

A retrospective, time series audit was performed, and included every paediatric patient seen at the CHBAH Paediatric Cardiology Department between 1 January 1991 and 2 November 2012. The total number of paediatric patients referred for cardiac assessment during this period was 18870.

Any patient on the database that was found to have a right-sided heart was included in the study.

2.2 Study Methods

Cardiology records in an electronic database were obtained from the CHBAH paediatric cardiology department. This electronic paediatric database was started on 1 January 1991 and includes every patient (both inpatient and outpatient) that is seen at the CHBAH paediatric cardiology department. The database is updated on a daily basis by Professor A.M. Cilliers (Head of CHBAH paediatric cardiology). All patients with right-sided hearts diagnosed between 1 January 1991 and 2 November 2012 were identified. Their electronic records were obtained and these were then crosschecked with the patients' clinical progress notes. All data was collected by one researcher, the author, in order to minimize observer bias.

Permission to conduct the study at CHBAH was obtained from the Medical Advisory Committee at the hospital. Permission was also obtained from the CHBAH Paediatric Cardiology Department for access to the electronic database

and patient files. Ethics approval to undertake the patient review was granted by the Human Research Ethics Committee (HREC), University of the Witwatersrand.

2.3 Statistical Analysis

Descriptive statistical analysis was performed.

Quantitative data was expressed as a mean (+/- one standard deviation).

Chi square test was used for analysis of nominal and for continuous variables. An unpaired Student's t-test or Mann-Whitney U test was used to compare data between the different diagnostic groups. A p-value <0.05 was used as the level of significance.

Study data was collected and managed using *REDCap* electronic data capture tools hosted at the University of the Witwatersrand (21). *REDCap* (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

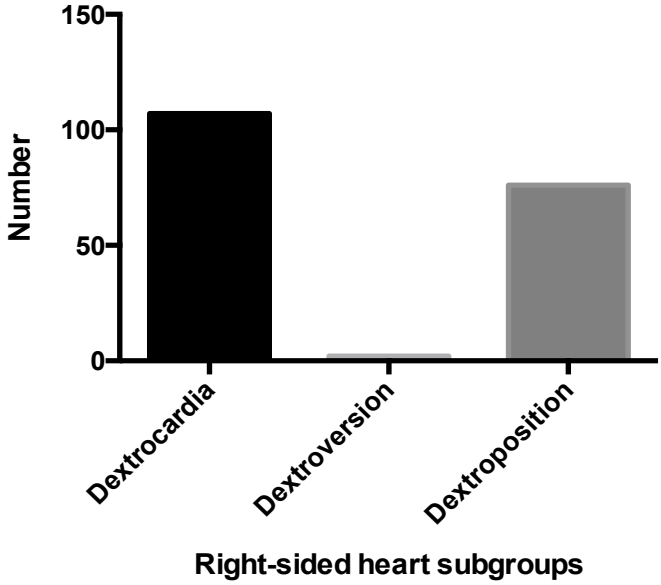
The data was then further analyzed using *Microsoft Excel* and *GraphPad Prism. Graphpad Prism* is a commercial scientific 2D graphing and statistics software published by *GraphPad Software, Inc*.

3.0 RESULTS

A total of 18870 paediatric patients were referred for cardiac assessment at the CHBAH Paediatric Cardiology Department between 1 January 1991 and 2 November 2012. Six thousand and fifteen congenital heart defects were diagnosed during this time. One hundred and eighty-seven children were found to have right-sided hearts.

Of the 187 patients with right-sided hearts, 111 had dextrocardia (109 patients with pure dextrocardia, plus two patients with confirmed dextroversion). A further 76 patients with right-sided hearts were found to have dextroposition as a cause. Right-sided hearts made up 1% of the total number of patients referred for cardiac assessment over the study period. Dextrocardia as a subgroup of right-sided hearts in the study cohort comprised 1.8% of all the congenital heart defects documented on the database.

Figure 3. Right-sided heart subgroups



Right-sided heart demographics

Age

The median age at diagnosis of a right-sided heart was 18 months (range, prenatal to 16 years).

Eighty-seven patients were diagnosed in the neonatal period (at, or before one month of age), 43 of these patients (49%) had ASCM. Fifty-eight patients were diagnosed in infancy (one month to one year), of which 25 (43%) had ASCM. Forty-two patients were diagnosed after one year of age. Thirty (71%) of them had ASCM.

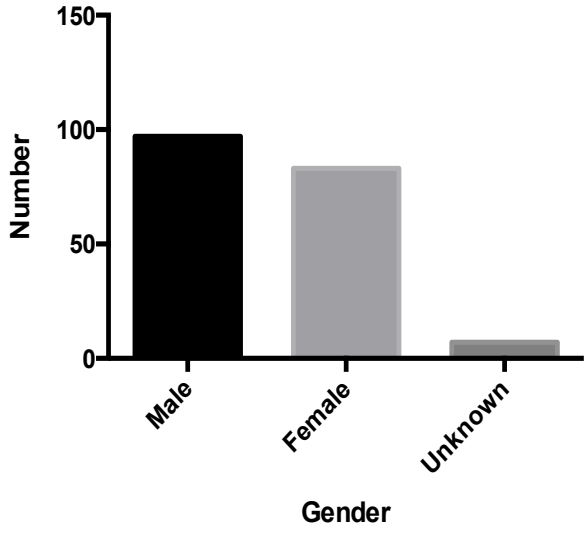
In the study, the majority of diagnoses of right-sided hearts (78%) were made before one year of age. However, if the diagnosis of a right-sided heart was made after one year of age, there was a greater risk of association with ASCM (p value = 0.0051).

Gender

There were 97 male patients and 83 female patients with right-sided hearts. The gender of seven patients had not been recorded. The male to female ratio of right-sided heart was 1: 0.85 (54% male, 46% female).

The male to female ratio for pure dextrocardia was similar at 1: 0.88.

Figure 4. Gender preponderance for right-sided hearts



Origins of right-sided heart patients

CHBAH services a large catchment area for Gauteng, as well as the surrounding provinces and neighbouring African countries. The table below (*table 2*) depicts patient origins provided by caregivers at the time of their first consultation.

Table 2. Origins of right-sided heart patients seen

LOCATION	**PATIENT NUMBER**
Gauteng	138
North West Province	22
Limpopo	3
Foreigners	3
Undefined	21
Total number	**187**

Figure 5. Origins of right-sided heart patients seen

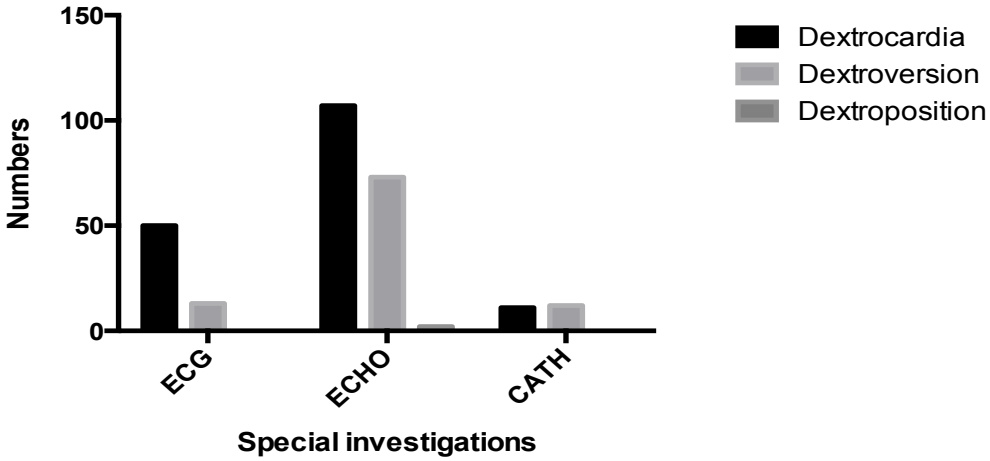
Special investigations

Chest X-rays, electrocardiograms, echocardiograms and cardiac catheterization reports were examined where available to confirm cardiac anatomy and situs information. The table below *(table 3)* depicts the number of special investigations (excluding chest X-rays) that were performed.

Table 3. Special investigations performed

SPECIAL INVESTIGATIONS	**NUMBER**
Electrocardiogram	63
Echocardiogram	182
Cardiac catheterization	23
Total number	**268**

Figure 6. Total number of special investigations performed per individual right-sided heart subgroup



3.1 Right-sided heart subgroups

3.1.1 Dextrocardia

One hundred and nine patients were diagnosed with pure dextrocardia (dextroversion excluded) during the study period. This comprised 58% of the total number of right-sided hearts that were seen, and made up 1.8% of the total congenital heart defects (6015 patients) that were diagnosed.
Of the 109 patients with dextrocardia, 78 (72%) had additional significant cardiac malformations.

Dextrocardia - Age at diagnosis

Ninety-one out of the 109 patients (83%) were diagnosed with dextrocardia before one year of age. Sixty-eight of these patients (75%) were found to have ASCM.
Of the 18 patients (17%) that were diagnosed with dextrocardia after one year of age, 11 had ASCM (61%).

Table 4: Dextrocardia and ASCM versus age at diagnosis – contingency table

	Diagnosis < 1 year of age	Diagnosis > 1 year of age
Dextrocardia and ASCM	68	11
Dextrocardia and no ASCM	23	7

ASCM, Additional significant cardiac malformation

When the association between the age at diagnosis of dextrocardia and the ASCM was compared, it was not found to be statistically significant (p value = 0.2566).

The mean age at diagnosis of dextrocardia was 11 months for those with ASCM and 13 months for those without ASCM.

Segmental Approach

The results follow a segmental approach previously mentioned in the text, whereby situs arrangements are determined first, followed by the ventricular configurations and lastly the great vessels connections are described.

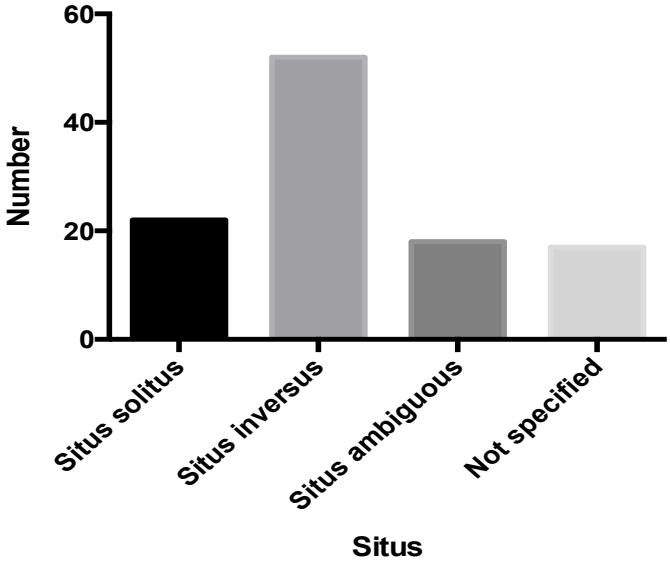
Dextrocardia - Situs arrangements

Situs solitus was confirmed in 22 (20%) out of the 109 patients with dextrocardia, while 52 patients (48%) had situs inversus. Eighteen patients (16%) were found to have situs ambiguous. The situs arrangements of 17 patients was not recorded and could not be further determined (*table 5* and *figure 7* below).

Table 5. Dextrocardia: Situs arrangements

SITUS	**NUMBER**
Situs solitus	22
Situs inversus	52
Situs ambiguous	18
Not specified	17
Total	**109**

Figure 7. Dextrocardia: Situs arrangements



Dextrocardia - Situs arrangements and ASCM

Of the 22 patients with dextrocardia and situs solitus, only seven (32%) were found to have a normal heart on echocardiogram, the remaining 15 patients (68%), had ASCM *(table 6).* Similarly, 35/52 (67%) patients with situs inversus dextrocardia were found to have ASCM with the other 17 patients (33%) having a normal echocardiogram.

Table 6 compares the situs arrangements and their association with ASCM. There was no statistical difference between those with situs solitus and situs inversus in terms of their association with ASCM (p value = 1.000).

Table 6. Dextrocardia: situs arrangements and ASCM – contingency table

SITUS	**ASCM**	**No ASCM**	**Total**
Situs solitus	15	7	22
Situs inversus	35	17	52
Total	**50**	**24**	**74**

ASCM, Additional significant cardiac malformation

Dextrocardia - Situs Ambiguous

There were 18 patients with situs ambiguous dextrocardia. Five were found to have right atrial isomerisation (RAI) and seven to have left atrial isomerisation (LAI). Situs ambiguous was diagnosed in a further six patients but the type of isomerisation was not clearly stated and could not be decided from the information in the patients' clinic notes.

Of the five patients who had right atrial isomerisation, two were confirmed to have asplenia on abdominal ultrasound. Two of the RAI patients demised (both were male). The first patient had a single atrium and ventricle complex with normally related great vessels. He was diagnosed to have gastric outlet obstruction and

died unexpectedly at 20 months of age while awaiting corrective gastrointestinal surgery. The second patient was diagnosed with congenital cardiac heart disease immediately after birth. He had an Atrio-Ventricular Septal Defect associated with a single atrium and two ventricles and asplenia. He demised in the neonatal period, but the circumstances around his demise were not apparent from the clinical notes.

Left atrial isomerisation was diagnosed in seven patients. One had duodenal atresia. A complete heart block was found in one other. None of the LAI subgroup was reported to have demised at time of study.

Six patients had heterotaxy but further patient details were not outlined. One of them was found to have asplenia but no other indicators of RAI. Two patients in this subgroup had demised at time of study.

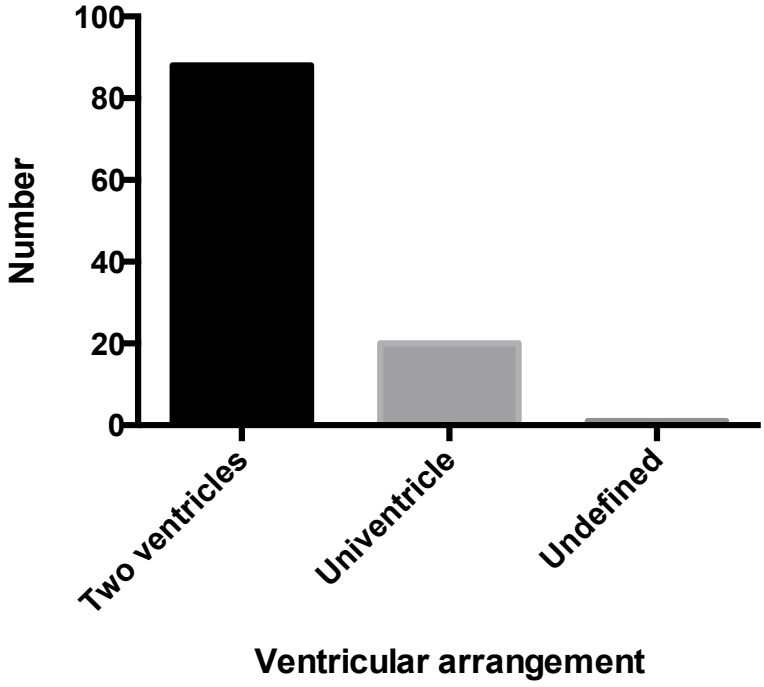
Dextrocardia - Ventricular configurations (Table 7, Figure 8)

Ventricular arrangements are represented in *table 7 and figure 8*.

Table 7. Dextrocardia: Ventricular arrangements

VENTRICLES	**NUMBER**
Univentricle	20
Two ventricles	88
Undefined	1
Total	**109**

Figure 8. Dextrocardia: Ventricular arrangements



An undefined ventricle was described in a case of Siamese twins, where twin II had dextrocardia. They were joined at the waist and had four arms, two legs and one genitalia (thoraco-omphalo-pagus conjoined twins). They shared a peritoneal sac. The echocardiographic examination of the twin hearts proved to be difficult and the AV and VA connections were classified as undefined. Both twins demised shortly after birth.

Dextrocardia - Atrioventricular (AV) relationships (Table 8, Figure 9)

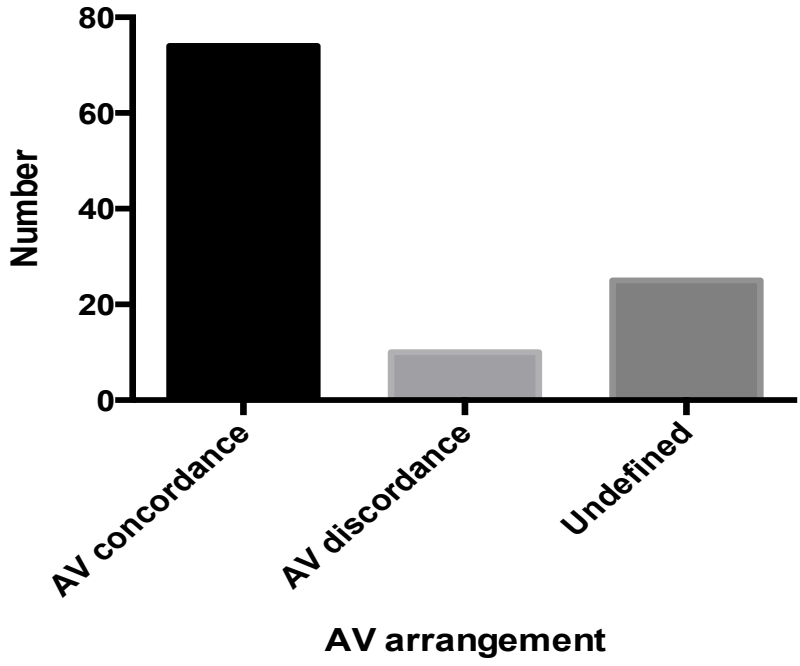
The majority of all the patients with dextrocardia (74 out of 109) had atrioventricular concordance (68%). Ten patients (9%) had atrioventricular discordance and 25 (23%) had AV relationships that were not clearly defined.

Table 8. Dextrocardia: Atrioventricular relationships

AV RELATIONSHIPS	**NUMBER**
AV concordance	74
AV discordance	10
Undefined	25
Total	**109**

AV, atrioventricular

Figure 9. Dextrocardia: Atrioventricular relationships



Dextrocardia - Ventriculoarterial (VA) relationships (Table 9, Figure 10)

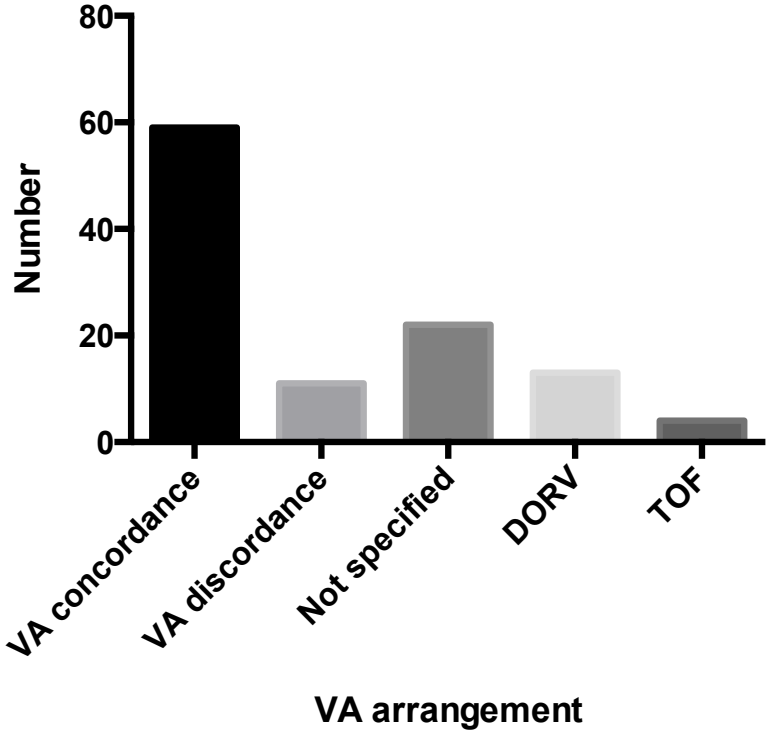
Sixty-three patients (58%) demonstrated ventriculoarterial (VA) concordance. (Four patients in this subgroup were diagnosed with Tetralogy of Fallot). Ventriculoarterial discordance was diagnosed in 11 patients (10%), while another 13 patients (12%) were found to have a double outlet right ventricle (DORV). The VA relationships in 22 patients (20%) were not clearly specified in the clinical notes.

Table 9. Dextrocardia: Ventriculoarterial relationships

VA RELATIONSHIPS	**NUMBER**
VA concordance	63
VA discordance	11
Double outlet right ventricle	13
Undefined	22
Total	**109**

VA, ventriculoarterial

Figure 10. Dextrocardia: Ventriculoarterial relationships



Dextrocardia - Two ventricles versus a single ventricle

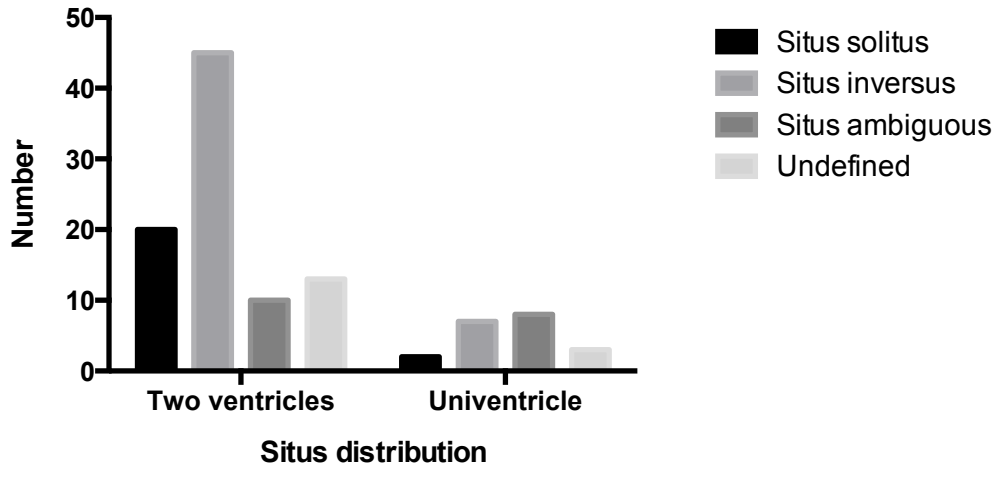
For further analysis of situs, atrioventricular-ventriculoarterial (AV-VA) relationships, ASCM and extracardiac defects, the patients were divided into two groups: those with two ventricles and those with a single ventricle.

If a comparison of the situs distribution in the patients with two ventricles is done to the situs distribution in those with a single ventricle, as in *table 10* below,
it can be seen that the majority of patients with two ventricles demonstrated situs inversus dextrocardia (45 patients), whereas there was a similar distribution between situs inversus dextrocardia (seven patients) and situs ambiguous dextrocardia (eight patients) in those with a single ventricle.
The situs difference per ventricular arrangement was not found to be statistically significant (p value = 0.061).

Table 10. Situs distribution per ventricular arrangement – contingency table

	Situs solitus	Situs inversus	Situs ambiguous
Two ventricles	20	45	10
Single ventricle	2	7	8

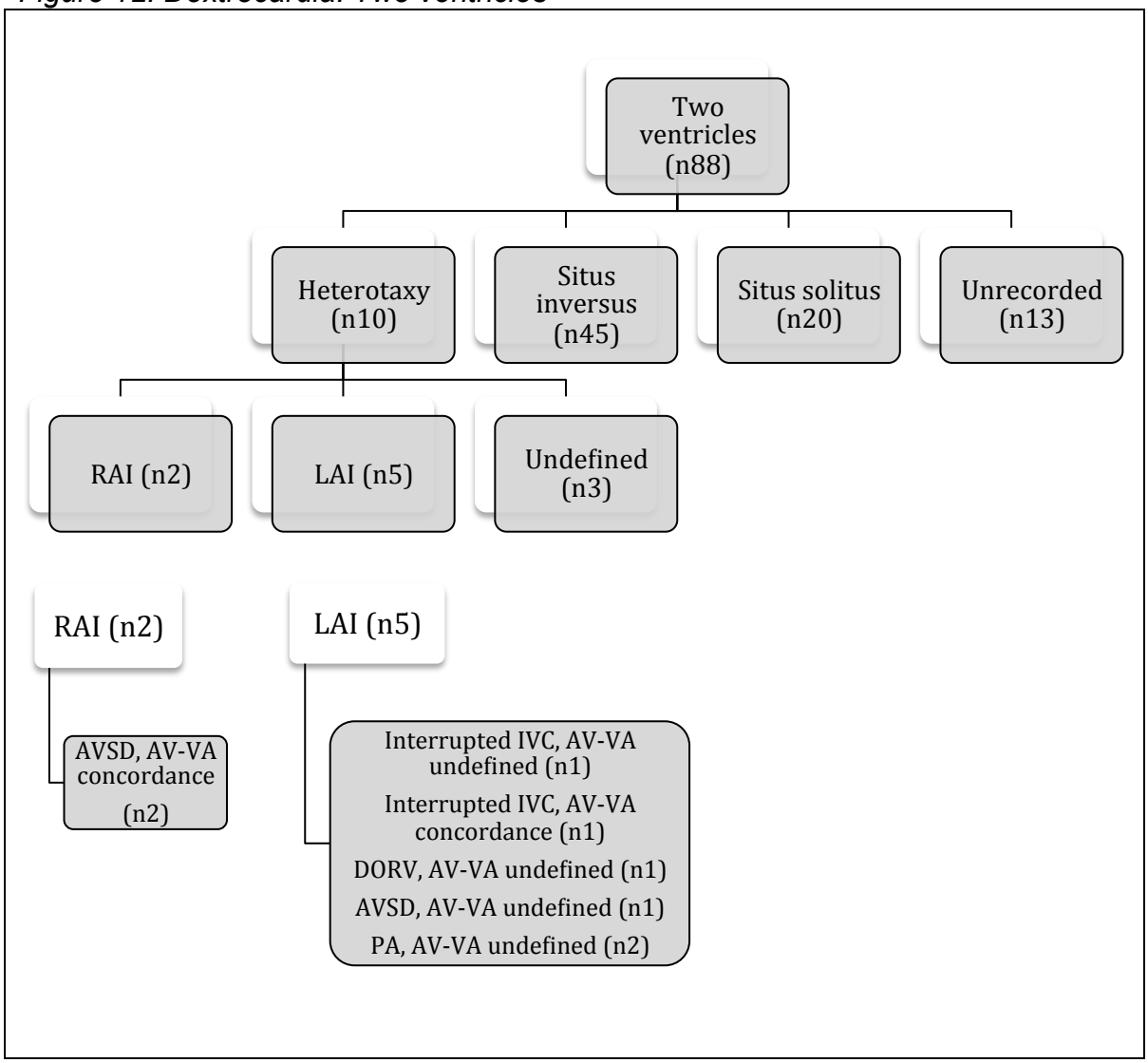
Figure 11. Situs distribution per ventricular arrangement



Fifty-seven out of the 88 patients with two ventricles (65%) were found to have ASCM. All 20 (100%) of the patients with a single ventricle had ASCM.

Figure 12 summarizes the data on the patients with dextrocardia and two ventricles, including the specific additional significant cardiac malformations in those with situs ambiguous dextrocardia.

Figure 12. Dextrocardia: Two ventricles



RAI, right atrial isomerisation; LAI, left atrial isomerisation; AVSD, atrioventricular septal defect; AV-VA, atrioventricular-ventriculoarterial; IVC, inferior vena cava; DORV, double outlet right ventricle

The table below summarises the patients with two ventricles and RAI.

Table 11. Two ventricles and RAI

Echocardiography	AV connection	VA connection	Extracardiac Abnormalities	Cardiac Surgery	Outcome
Incomplete AVSD. Interrupted IVC (right). ASD	Con-cordant	Con-cordant	Immotile Ciliary Dyskinesia	Nil	Lost to follow up
AVSD. Right aortic arch. Large VSD. Aortic valve atresia	Con-cordant	Con-cordant	Asplenia	Nil	Died

AV, atrioventricular; VA, ventriculoarterial; AVSD, atrioventricular septal defect; IVC, inferior vena cava; ASD, atrial septal defect; VSD, ventricular septal defect

The table below summarises the patients with two ventricles and LAI.

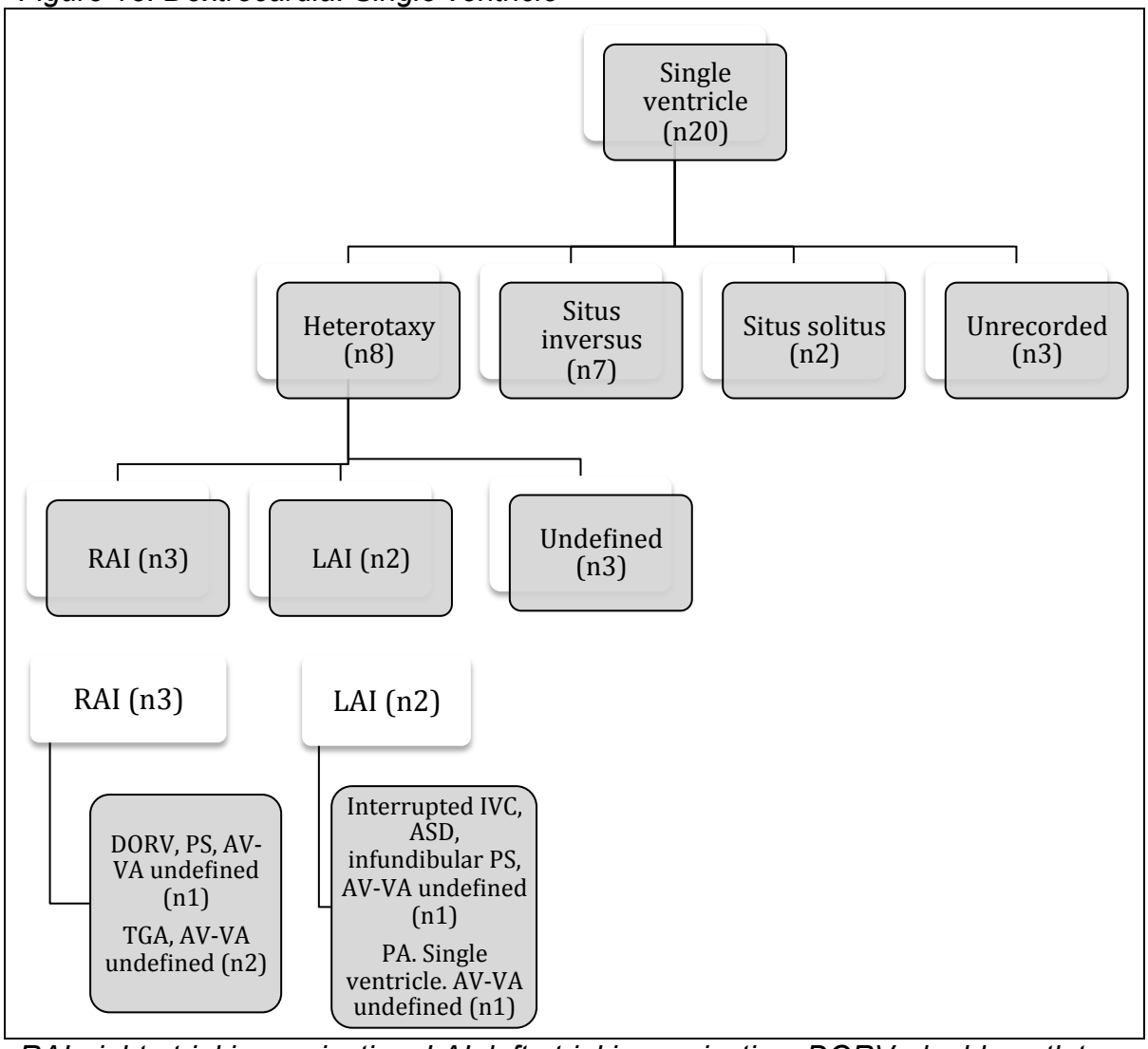
Table 12. Two ventricles and LAI

Echocardiography	AV connection	VA connection	Extracardiac Abnormalities	Cardiac Surgery	Outcome
Interrupted IVC. Bilateral SVCs. Single atrium. Large inlet VSD.	Undefined	Undefined	Duodenal atresia	Nil	Lost to follow up
AVSD. Severe TR. Non compaction RV. Heart block	Undefined	Undefined	Dysmorphic features	Nil	Lost to follow up
DORV. Single atrium. Single aortic valve. Large inlet VSD. Interrupted IVC. Hypoplastic segment of aortic arch	Undefined	Undefined	Nil	Coarctation repair; PDA ligation; PA banding	Lost to follow up
Interrupted IVC. Left-sided SVC. LVOT gradient 47mmHg. No VSD	Con-cordant	Con-cordant	Nil	Nil	Lost to follow up

AV, atrioventricular; VA, ventriculoarterial; IVC, inferior vena cava; SVC, superior vena cava; VSD, ventricular septal defect; AVSD, atrioventricular septal defect; TR, tricuspid regurgitation; RV, right ventricle; DORV, double outlet right ventricle; LVOT, left ventricle outflow tract; PA, pulmonary artery

Figure 13 summarizes the data on the patients with dextrocardia and a single ventricle including specific additional significant cardiac malformations in those with situs ambiguous dextrocardia.

Figure 13. Dextrocardia: Single ventricle



RAI, right atrial isomerisation; LAI, left atrial isomerisation; DORV, double outlet right ventricle; IVC, inferior vena cava; ASD, atrial septal defect; TGA, transposition of the great arteries; AV-VA, atrioventricular-ventriculoarterial; PS, pulmonary stenosis

The table below summarises the patients who presented with a single ventricle and RAI.

Table 13. Single ventricle and RAI

Echocardiography	AV connection	VA connection	Extracardiac Abnormalities	Cardiac Surgery	Outcome
Hypoplastic left heart. Complex CCHD. DORV. Valvular PS. Atretic mitral valve. ASD secundum. Large VSD. Mild TR	Undefined	Undefined	Failure to thrive	Glenn procedure	Lost to follow up
TGA. Single aortic valve. Pulmonary venous return to inferior chambers	Undefined	Undefined	Asplenia; Severe recurrent bronchopneumonia	Nil	Lost to follow up
Single aortic valve. TGA with hypoplastic MPA. Infundibular stenosis.	Undefined	Undefined	Gastric outlet obstruction	Nil	Died

AV, atrioventricular; VA, ventriculoarterial; CCHD, congenital cyanotic heart disease; DORV, double outlet right ventricle; PS, pulmonary stenosis; ASD, atrial septal defect; VSD, ventricular septal defect; TR, tricuspid regurgitation, TGA, transposition of the great arteries; MPA, main pulmonary artery

The table below summarises the patients who presented with a single ventricle and LAI.

Table 14. Single ventricle and LAI

Echocardiography	AV connection	VA connection	Extracardiac Abnormalities	Cardiac Surgery	Outcome
PA. Single ventricle	Undefined	Undefined	Nil	Left BTS	Lost to follow up
Interrupted IVC. Sinus venosus ASD. Infundibular PS. Bilateral SVCs	Undefined	Undefined	Nil	Glenn procedure	Lost to follow up

AV, atrioventricular; VA, ventriculoarterial; PA, pulmonary atresia; ASD, atrial septal defect; PS, pulmonary stenosis; SVC, superior vena cava; IVC, inferior vena cava; BTS, Blalock Taussig shunt

Dextrocardia - Additional significant cardiac malformations

Table 15 systematically categorises the ASCM that were diagnosed at time of patient echocardiography. This approach follows the diagnostic hierarchy as described by Fyler D.C. in the *Report of the New England Regional Infant Cardiac Program. Pediatrics 1980;65(suppl)(2):377-461.*

Table 15. Diagnostic categories of ASCM (22)

Categorical Hierarchy	**Categorical Diagnosis**	**ASCM (Patient number)**
01	Heterotaxias	18
02	Single ventricle	12
03	Hypoplastic left ventricle	2
04	Tricuspid atresia	6
05	Truncus arteriosus	0
06	Double outlet right ventricle	12
07	D-transposition of great arteries	4
08	L-transposition of great arteries	3
09	Endocardial cushion defects	2
10	Total anomalous pulmonary venous return	2
11	Pulmonary atresia with intact ventricular septum	0
12	Tetralogy of Fallot	4
13	Coarctation of the aorta	2
14	Ventricular septal defect	8
15	Aortic stenosis	0
16	Pulmonary stenosis	0
17	Myocardial disease	0
18	Atrial septal defect secundum	1
19	Patent ductus arteriosus	3
20	No significant heart disease	28
21	Lung disease	0
22	Other	2
	TOTAL	**109**

Dextrocardia - Extracardiac abnormalities

Listed below are all the additional significant extracardiac abnormalities that were diagnosed in the patients with dextrocardia.

Table 16. Dextrocardia – Extracardiac abnormalities

Genetics and Chromosomal abnormalities		8
Trisomy 21	1	
Marfan syndrome	1	
Holt-Oram syndrome	1	
CATCH-22	1	
Pentalogy of Cantrell	1	
Siamese twins	1	
VACTERL syndrome	2	
Oncological tumours		1
Ovarian Mass	1	
Cardiovascular abnormalities		9
Heart block	7	
SVC syndrome	2	
Neurological conditions		1
Sturge Weber Syndrome	1	
Surgical conditions		9
Tracheo-oesophageal fistula	1	
Biliary Atresia	1	
Omphalocele	3	
Duodenal atresia	1	
Jejunal atresia	2	
Gastric outlet obstruction	1	
Other		1
Kartagener syndrome	8	
Foetal alcohol syndrome	1	

CATCH-22 (acronym for cardiac anomalies, abnormal facies, thymic hypoplasia, cleft palate, hypocalcaemia, hypoparathyroidism); VACTERL (acronym for vertebral abnormalities, ano-rectal malformations, cardiac abnormalities, trachea-oesophageal fistula/atresia, renal abnormalities and limb abnormalities)

Dextrocardia – Surgical intervention

Cardiac surgery was performed in 25 of the patients with dextrocardia (23%). Details on the cardiac abnormalities that required surgery are listed below, again using the diagnostic hierarchy as described by Fyler D.C. (22).

Table 17. Diagnostic categories of the patients with dextrocardia who underwent surgery

Categorical Hierarchy	**Categorical Diagnosis**	**Patient number**
01	Heterotaxias	1
02	Single ventricle	5
04	Tricuspid atresia	4
06	Double outlet right ventricle	2
07	D-transposition of great arteries	3
08	L-transposition of great arteries	1
10	Total anomalous pulmonary venous return	1
12	Tetralogy of Fallot	3
14	Ventricular septal defect	3
19	Patent ductus arteriosus	2
	TOTAL	**25**

A further 11 patients underwent general surgical procedures as listed below.

Table 18. General surgical procedures performed in patients with dextrocardia

PROCEDURE	**NUMBER**
Pneumonectomy	1
Kasai for biliary atresia	1
Tracheo-oesophageal fistula repair	1
Jejunal atresia	2
Duodenal atresia	1
Gastric outlet obstruction	1
Omphalocele	4
Total	**11**

Dextrocardia – Patient outcome

Twenty-two out of the 109 patients diagnosed with dextrocardia (20%) had demised at time of study. Of the 25 patients who underwent cardiac surgery, six (24%) subsequently demised. Another 22 patients (20%) were reported to be alive, and 65 (60%) had been lost to follow up.

3.1.2 Dextroversion

There were only two patients with confirmed dextroversion.

Dextroversion – Age at diagnosis

Both patients were diagnosed in the neonatal period.

Dextroversion – Situs arrangements and ASCM

One patient had situs solitus and one had situs inversus. Both patients had two ventricles. There was atrioventricular concordance in both, but ventriculoarterial discordance in one (transposition of the great arteries).

One patient had ASCM (TGV) while one had normal cardiac anatomy at echocardiography.

Dextroversion – Surgical intervention and outcome

Neither of these patients underwent surgery and both were alive at time of study.

3.1.3 Dextroposition

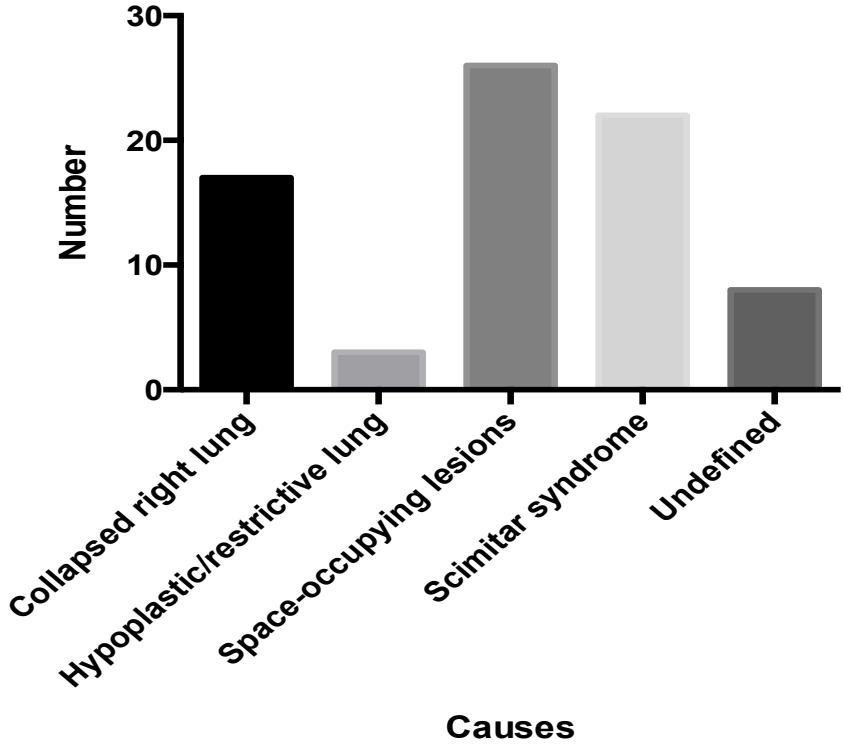
A total number of 76 patients were diagnosed with dextroposition.

Dextroposition - Causes

Table 19. Causes of dextroposition

CAUSES	NUMBER
Collapsed Right Lung	17
Hypoplastic lungs/restrictive lung disease	3
Space occupying lesions	26
Scimitar syndrome	22
Unrecorded	8
Total	**76**

Figure 14. Causes of dextroposition



A space-occupying lesion was defined as a mass or tumour that caused local pressure or compression on the right hemi thorax leading to displacement of the normal anatomy and subsequently the heart. Examples included congenital diaphragmatic hernias, omphaloceles, chest tumours etc.

Dextroposition - Age at Diagnosis

Seventy percent of patients (53/76) were diagnosed with dextroposition as the cause of their right-sided heart before one year of age. The remaining 23 patients (30%) were diagnosed after one year of age (range, newborn to 15 years).

Dextroposition - Scimitar syndrome

Twenty-two patients were confirmed to have Scimitar syndrome, five of whom were diagnosed before one month of age, and 13 (59%) before one year. The median age at diagnosis was 21 months.

Scimitar syndrome - Diagnosis before one year of age

Of the 13 patients with Scimitar syndrome that were diagnosed before one year of age, three patients (23%) had associated acyanotic congenital heart lesions. Seven (54%) had documented evidence of pulmonary hypertension, and one presented in congestive cardiac failure. Two patients had trachea-oesophageal fistulae, both of which were surgically repaired. One patient was found to have an accessory spleen, another duodenal atresia, while a single kidney was discovered in a third patient. Six patients had recorded episodes of bronchopneumonia requiring hospitalization. (Many were recurrent episodes). One patient was proven to have pulmonary tuberculosis.

Five out of the 13 patients (38%) underwent cardiac surgery (the majority required percutaneous occlusion of the feeder artery to the sequestrated lung tissue). Two of the patients who underwent cardiac surgery (40%) subsequently demised. Three out of the 13 patients (23%) diagnosed before one year of age had demised at time of study.

Scimitar syndrome - Diagnosis after one year of age

There were nine patients that were diagnosed after one year of age. One patient was found to have an atrial septal defect, one patient had Turner syndrome, two had documented episodes of bronchopneumonia requiring hospitalization, and one was reported to have pulmonary hypertension. Two patients (22%) underwent percutaneous occlusion of the feeder artery. All were reported to be alive at time of study.

Dextroposition – Situs, ventricular, and great vessels arrangements

Seventy-five of the 76 patients with dextroposition were documented to have situs solitus. The situs arrangement in one other patient was not recorded. All 76 patients were diagnosed to have normal atrioventricular and ventriculoarterial relationships.

Dextroposition – Extracardiac abnormalities (including Scimitar syndrome)

Listed below (*table 20*) are the additional significant extracardiac abnormalities that were diagnosed in the patients with dextroposition (including the patients with Scimitar syndrome).

Table 20. Dextroposition – Extracardiac abnormalities/complications

Respiratory		18
Bronchopneumonia	12	
Pulmonary tuberculosis	3	
Bronchiectasis	3	
Chromosomal abnormalities		3
Trisomy 21	1	
Trisomy 18	1	
Turners syndrome	1	
Oncological abnormalities		6
Neutropaenic sepsis	1	
Acute lymphoblastic leukaemia	1	
Lymphoma	1	
Mucoepidermoid carcinoma RMB	1	
Metastatic Wilms tumour	1	
Disseminated germ cell tumour	1	
Benign chest masses	3	3
Neurological conditions		4
Cerebral palsy	1	
Myelomeningiocele	2	
Spinal Muscular Atrophy	1	
Surgical conditions		21
Left ventricular aneurysm	1	
Congenital diaphragmatic hernia	11	
Tracheo-oesophageal fistula	3	
Omphaloceles	3	
Duodenal atresia	1	
Prune belly syndrome	1	
Bowel rotation	1	

RMB, right main bronchus

Dextroposition – Surgical intervention

Nine patients with dextroposition were documented to undergo cardiac or vascular interventions, the majority of whom had Scimitar syndrome. Seven underwent percutaneous coiling of the feeder artery in patients with Scimitar syndrome. Another patient had a surgical repair of a left ventricular aneurysm. This patient was Human Immunodeficiency Virus (HIV) positive and had previously been diagnosed with pulmonary tuberculosis. The aetiology of the aneurysm was unclear but was thought to be due to his underlying tuberculosis and HIV. At angiography, the aneurysm appeared thin walled and the concern was that it would rupture. Elective repair was performed, which confirmed a false aneurysm with two necks (submitral/aortic). The ninth patient had non-Hodgkin's lymphoma with a left mediastinal mass complicated by superior vena cava syndrome. He underwent surgical resection of the left mediastinal tumour, but subsequently demised post operatively in the intensive care unit from vascular complications.

A wide variety of other non-cardiac surgeries were undertaken in the remaining patients to treat underlying gastrointestinal malformations or surgery in relation to the various space-occupying lesions.

Dextroposition – Patient outcome

Three of the patients who underwent surgery subsequently demised (33%). Two of the three patients had Scimitar syndrome. The third patient had non-Hodgkin's lymphoma and demised from post-operative complications.

In total, eight patients out of the 76 patients were reported to have demised at time of study (11%), while 11 patients (14%) were confirmed to be alive. Fifty-seven patients (75%) had been lost to follow up.

4.0 DISCUSSION

4.1 Demographics

4.1.1 Incidence

A right-sided heart is uncommon and made up 1% of the total number of patients referred for cardiac assessment at CHBAH Paediatric Cardiology Department over the study period. Dextrocardia as a sub-group of a right-sided heart comprised 1.8% of all the congenital heart defects that were seen. Results from similar studies reveal a lower incidence of dextrocardia, namely 0.01% of all live births in two first world countries (1,5) and a slightly higher incidence of 0.35% in third world settings (2,23). The denominators used to determine the incidence of dextrocardia differed between the various studies e.g. one reported the incidence as a percentage of all live births whereas another calculated the incidence as a percentage of all congenital hearts seen. Consequently a real comparison of the incidence of dextrocardia could not be made between the various studies. It was possible however, to determine the number of new cases diagnosed per year which was further compared to other studies. An average of eight to nine study patients were diagnosed to have right-sided hearts per year, whereas approximately five new cases of dextrocardia were diagnosed per year. These results are similar to those documented by Evans et al. in 2010 (1), at the Children's Heart Center in Nevada, where 61 patients with dextrocardia were diagnosed over a 10-year period giving an average of six new cases of dextrocardia per year. Another study undertaken in Saudi Arabia within a tertiary care center showed 30 patients to have dextrocardia over a four and a half year period which translated into six to seven new cases of dextrocardia per year (23).

4.1.2 Age at diagnosis

4.1.2.1 Right-sided hearts - Age at diagnosis

The median age at diagnosis of a right-sided heart in the study was 18 months. The majority of right-sided heart diagnoses (78%) were made before one year of age, with 63% having dextrocardia, 36% having dextroposition and 1% of the patients with dextroversion.

4.1.2.2 Dextrocardia – Age at diagnosis

The median age at diagnosis of dextrocardia as a subgroup of right-sided hearts was 12 months. In the study conducted by Evans et al. (1) dextrocardia was diagnosed later at a median age of 20 months.

The current study showed that the majority of patients (91/109 (83%)) with dextrocardia presented before one year of age. Seventy-five percent of these patients had ASCM. Only 18/109 patients (17%) in the study case series presented with dextrocardia after one year of age, of which 61% had ASCM. Those with ASCM had an earlier mean age of presentation as compared to those who did not. When the age at diagnosis of dextrocardia and ASCM was compared, it was however, not found to be statistically significant (p value = 0.2566). The early diagnosis of dextrocardia as a subgroup of right-sided hearts may be due to the association with ASCM causing the patients to become symptomatic at an early age.

4.1.3 Gender

There was a male preponderance in all right-sided hearts in our study (54%, 97 males and 83 females). This was also demonstrated in the dextrocardia subgroup

which showed a 53% male preponderance). The study results correlate well in terms of the gender distribution in other studies which report a 60% male and 40% female distribution. (1,2,23).

4.1.4 Places of origin of right-sided heart

The majority of patients were reported to originate from Gauteng Province (74% of all right-sided hearts) and is a reflection of the total number of patients referred to the CHBAH Paediatric Cardiology Department. For example, in 2012, 78% of all paediatric cardiology patients provided a home address from the Gauteng Province. There is speculation that some patients who originate from other regions and provinces may provide a local Gauteng address in order not to be turned away from CHBAH. The classification of origin of patients with right-sided hearts may therefore not be accurately represented.

4.2 Dextrocardia

4.2.1 Dextrocardia: Situs arrangements (study comparisons)

The situs arrangements in the study patients is similar to studies conducted elsewhere in the world (*Table 21*).

Table 21. Study comparisons: Dextrocardia and situs arrangements

	Situs solitus	Situs inversus	Situs ambiguous	Situs unrecorded	Total study numbers
The study	22 (20%)	52 (48%)	18 (17%)	17 (15%)	109
First world setting (1)	20 (33%)	30 (49%)	11 (18%)	-	61
Third world setting (2)	43 (34%)	49 (39%)	33 (27%)	-	125
Third world setting (23)	14 (47%)	14 (47%)	2 (6%)	-	30
Third world setting (24)	4 (29%)	8 (57%)	2 (14%)	-	14

Situs inversus was the dominant situs arrangement in patients with dextrocardia in all of the studies described (*table 21),* followed by situs solitus. Situs ambiguous was the least common in all the studies listed.

The study performed in Saudi Arabia (23), showed a larger percentage of patients with situs solitus and a smaller percentage of situs ambiguous compared to all the other studies. Both this study and a study from India (2) showed an equal distribution of patients with dextrocardia having situs solitus and situs inversus. This is in contrast to the study patients and to the remaining two publications (1,24) where situs inversus dextrocardia was the more common subgroup.

A possible explanation for the higher prevalence of situs solitus dextrocardia in some studies, is that situs inversus dextrocardia is theoretically more likely to be accompanied by a structurally normal heart, which may evade detection, thus providing a skewed representation of fewer patients in this group.

4.2.2 Dextrocardia: Situs arrangements and ASCM

Situs solitus dextrocardia is more likely to be associated with abnormal cardiac anatomy, as demonstrated in the study patients, where only seven out of 22 patients (32%) with situs solitus dextrocardia had a normal heart diagnosed echocardiographically. The remaining 15 out of 22 patients with situs solitus dextrocardia (68%) (*table 6*) had ASCM.

In the study case series, the prevalence of ASCM in situs solitus dextrocardia (68%) was similar to the prevalence of ASCM in the situs inversus dextrocardia (67%) (See *table 6*). Therefore there was no statistical difference in the prevalence of ASCM between these two situs arrangements (p value = 1.000).

4.2.2.1 Study comparisons: Situs arrangements and ASCM

A comparison of the current study was made with a case series recorded in the Middle East (24). (See also *table 21* above). This specific study was conducted over a five-year period in Tehran, Iran. The frequency of the various situs arrangements in patients with dextrocardia was found to be similar *(table 21)*. The incidence of congenital heart disease among the Iranian study participants as compared to the current study are documented in *table 22* below.

Table 22. Dextrocardia: Incidence of ASCM per situs arrangement

Situs arrangement	ASCM: Iranian study (24)	ASCM: Current study
Situs solitus	75%	68%
Situs inversus	50%	67%
Situs ambiguous	100%	94%

ASCM, additional significant cardiac malformations

Situs inversus dextrocardia. The literature reports the incidence of congenital heart disease or ASCM in situs inversus dextrocardia to be relatively low (estimated at 3%) (24). However, both the current study and the Iranian study showed a much higher incidence of congenital heart disease in patients with situs inversus and situs ambiguous compared to other published literature. A possible explanation for the apparent increased incidence of ASCM in situs inversus dextrocardia in the current study may be as a result of the study definition of ASCM that was used. ASCM was defined as any additional cardiac defect diagnosed at time of echocardiographical assessment. Other studies define ASCM as only those cardiac defects that require medical or surgical intervention. The current study's more lenient definition of ASCM most likely allowed for larger numbers of ASCM being diagnosed, thus over representing ASCM in situs inversus dextrocardia. It may also be possible that some patients in the situs

inversus subgroup had situs inversus levocardia instead of dextrocardia, making ASCM more likely.

In the current study, 15% of the patients with situs inversus dextrocardia were confirmed to have Kartagener syndrome. It therefore becomes important to consider a ciliopathy in patients with recurrent respiratory infections and a right-sided heart and to refer these patients for further close follow up.

Situs solitus dextrocardia. The incidence of congenital heart disease was higher in situs solitus dextrocardia in both the Iranian and the current study (*table 22*). These results were unsurprising and are in keeping with previously published literature which show that situs solitus dextrocardia is less likely to be associated with normal cardiac anatomy (1,3,11,17,18).

Situs ambiguous dextrocardia. In the current study, 17 out of the 18 patients with situs ambiguous dextrocardia had ASCM. One patient was excluded because of poor documentation. A similar finding was reported in the Iranian study, where 100% of the patients with situs ambiguous dextrocardia had ASCM. (24).

Additional significant cardiac malformations. Another study of patients with dextrocardia conducted in the Middle East in Saudi Arabia (23) revealed 83.4% of all the patients with dextrocardia to have associated congenital heart disease compared to 60% in the Iranian study (24) and 72% (78 out of 109 patients) in the current study group. In contrast, the percentage of dextrocardia and ASCM was significantly lower in the study conducted by Evans et al in the USA which found a

49% association (1). The smaller proportion in Evans et al. case series may again be explained by the definition of ASCM used for their study, which included only those cardiac malformations that required medical or surgical treatment. They did not include as part of their definition as in our study, all cardiac defects diagnosed at time of echocardiography

4.2.3 Further comparisons to similar studies

In order to provide perspective the study patient findings were compared to studies undertaken by institutions from other parts of the world such as North America and the Middle East.

4.2.3.1 Two ventricles versus a single ventricle

A comparison was undertaken with a study from the USA (Evans et al. 2010) where patients with dextrocardia were divided into those with two ventricles and those with a single ventricle.

Figures 15,16 and Tables 23,24.

Figure 15. Study comparisons: Dextrocardia and two ventricles

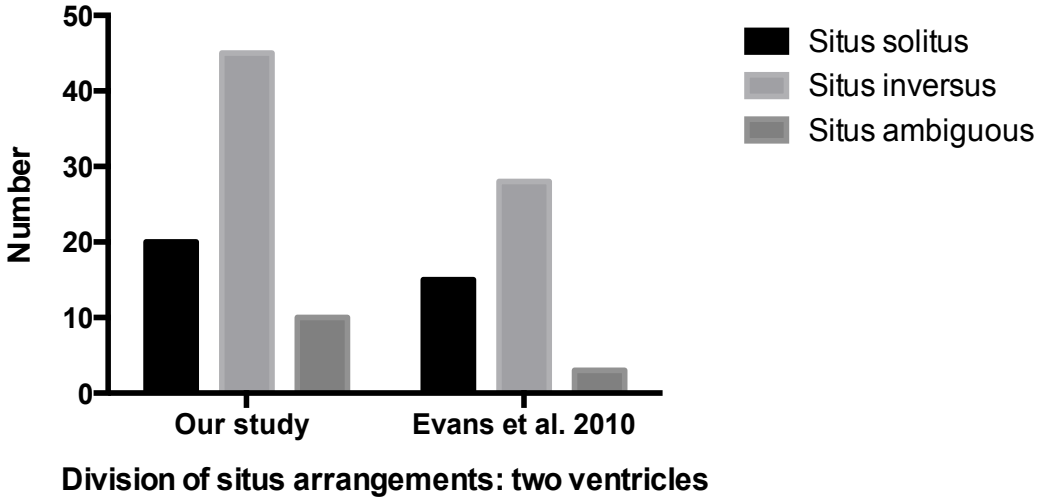


Table 23. Dextrocardia and two ventricles – contingency table

	Total number	Situs Solitus	Situs inversus	Heterotaxy
Evans et al.(1)	46 (75%)	15 (33%)	28 (61%)	3 (7%)
Current study	88 (81%)	20 (23%)	45 (51%)	10 (11%)

Both studies showed a similar distribution of the different types of situs arrangements in patients with dextrocardia and two ventricles.

In the current study, situs inversus was two times more likely than situs solitus and four and a half times more likely than heterotaxy. This compared well with Evans et al. (1), who showed that if there were two ventricles, situs inversus was also two times more likely than situs solitus. However, they found situs inversus to be nine times more likely than heterotaxy. This was two times more than what our study results revealed.

Twenty out of the 109 patients with dextrocardia (18%) in the study cohort were found to have a single ventricle.

Figure 16 compares the study results with those of Evans et al. (1).

Figure 16.Study comparisons: Dextrocardia and a single ventricle

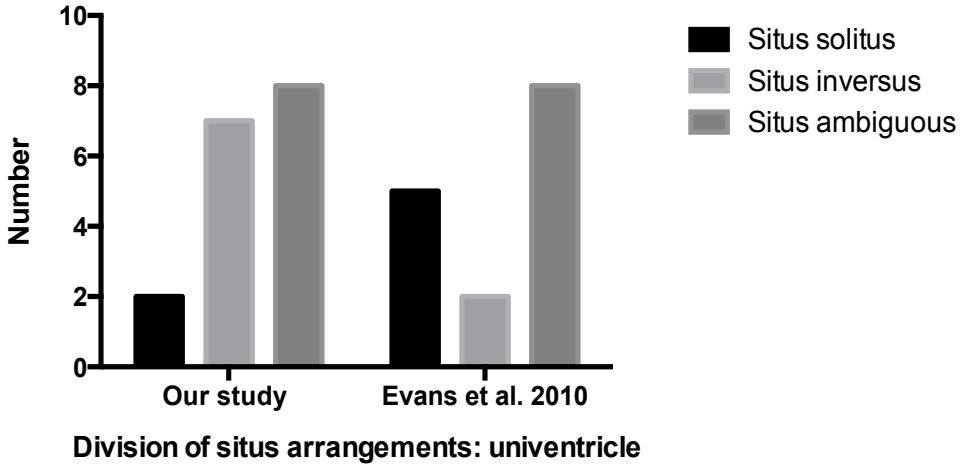


Table 24. Dextrocardia and a single ventricle – contingency table

	Total number	Situs Solitus	Situs inversus	Heterotaxy
Evans et al.	15 (25%)	5 (33%)	2 (13%)	8 (53)
Current study	20 (18%)	2 (10%)	7 (35%)	8 (40%)

The total number of patients that presented with dextrocardia and a single ventricle were similar in both studies, however marked differences in situs arrangements were noted between them. Situs solitus was three times more likely and situs inversus was almost three times less likely in the study conducted by Evans et al. as compared to the current study.

4.2.3.2 Situs ambiguous subgroup

A closer examination of the heterotaxy subgroup showed that the study findings were in keeping with those of the Evans et al. series for both the group with two ventricles, as well as the group with a single ventricle (1). Evans et al. reported a sum incidence of situs ambiguous at 18% (1). The study incidence of heterotaxia in patients with dextrocardia was found to be similar at 17%. This also compares well to other studies e.g. Garg et al. reported an incidence of heterotaxia of 26% (2); and Roodpeyma et al. reported an incidence of 14% (24).

Both the RAI and the LAI groups in the study demonstrated some of the more common documented serious cardiac and non-cardiac complications.

Right Atrial Isomerisation. Two out of the five patients with RAI had associated asplenia, one had immotile ciliary dyskinesia and one patient had gastric outlet obstruction. Two patients with RAI had demised at time of study (40%).

Left Atrial Isomerisation. Of the seven patients with LAI, three had an interrupted inferior vena cava, one patient reportedly had a complete heart block and duodenal atresia was diagnosed in one patient. No patients in the LAI group had demised at time of study.

Due to the small numbers in the heterotaxia group, it was not possible to analyse the subgroups further. However, in keeping with previously published literature (3,11,17), and as our study has shown, the mortality rate is usually higher in the RAI group as compared to the LAI group**.**

4.2.4 Dextrocardia – Patient outcome

One fifth of the patients with dextrocardia had demised at time of study. Nearly two thirds of the patients (60%) were reportedly lost to follow up. A possible explanation for the high percentage of patients lost to follow up may be that many patients who do not have severe ASCM and who remain asymptomatic are not given chronic medication or other medical treatment. Clinical examination and echocardiographical assessment are performed annually or biannually. Thus appointment compliance wanes over the years.

4.3 Dextroversion

There were only two patients with confirmed dextroversion. One patient had transposition of the great arteries and therefore ventriculoarterial discordance. The other patient had normal cardiac anatomy. Because of the small number in this group we were unable to draw any significant conclusions.

In a case series by Garg et al., in India in 2003 (2), 43 cases of dextroversion were found in 125 cases of confirmed dextrocardia (34%). Less than half of the cases (17 out of 43 patients) had concordant atrioventricular and ventriculoarterial connections. The majority had cardiac anomalies with only two patients having normal hearts (2). All data collected for the study was retrospective with no opportunity to clarify the accuracy of the data so that it is likely that some patients with dextroversion were incorrectly classified in the study cohort.

4.4 Dextroposition

A substantial number of patients were diagnosed with dextroposition as the cause of their right-sided heart (41% of the total right-sided hearts seen). The right heart positions were mostly secondary to extracardiac causes included right lung hypoplasia, space occupying lesions and also Scimitar syndrome.

4.4.1 Dextroposition: Age at diagnosis

The majority of patients with dextroposition presented before one year of age (70%). This is likely due to the fact that patients with secondary causes of a right-sided heart are usually symptomatic and present earlier.

4.4.2 Dextroposition – Scimitar syndrome

Review of the patients with Scimitar syndrome revealed that 59% of them were diagnosed before one year of age. These patients had a more severe clinical picture when compared to those diagnosed at an older age. These results were consistent with the results of a large case series reported on by Dusenbery et al, at the Boston Children's Hospital in 2013 (13). In their study, Scimitar syndrome was diagnosed under the age of one year in more than half of their study patients (58%). They found that those patients who presented before one year of age, had a higher incidence of symptoms, aortopulmonary collaterals, coexisting congenital heart disease, extracardiac anomalies and pulmonary hypertension (13).

A third of the patients with Scimitar syndrome underwent percutaneous coiling of the feeder artery. Three patients (14%) with Scimitar syndrome had demised at

time of study. (Two of the patients had previously undergone percutaneous coiling of the feeder artery). Dusenbery et al. demonstrated a slightly higher mortality rate (24%) in their case series (13).

4.4.3 Dextroposition – Surgical intervention

The majority of patients with dextroposition in our study had causes that were amenable to surgical rectification or medical treatment. For example, 21 patients had potentially rectifiable surgical conditions, six patients with oncological tumours and a further 18 patients with respiratory illnesses that required medical intervention *(see table 20)*. This reiterates the importance of the correct and timeously diagnosis of dextroposition as a cause of right-sided hearts.

4.4.4 Dextroposition – Patient outcome

The large majority of patients (57 out of 76) were lost to follow up. This is because most of these patients had documented normal cardiac anatomy at time of echocardiography.

5.0 STUDY LIMITATIONS

The retrospective design of the study provided a multitude of study limitations. Some of the study patients had incomplete database information and also incomplete or missing clinic files which resulted in a critical selective reporting bias. As a result, certain unexpected study findings could not be further investigated or properly validated due to a paucity of the additional required information.

Some of the recorded findings in the clinic notes were unclear, or difficult to categorise. This may have allowed for incorrect interpretation, which would have altered the results obtained.

6.0 CONCLUSION

Right-sided hearts in children in Southern Africa have not been previously described, except in isolated case study publications. This study scrutinized all three causes of a right-sided heart, as well as the associated significant cardiac malformations.

The study results were comparable to institutions in first world countries (Canada, North America) as well as institutions in third world settings (Iran, India, Saudi Arabia) (1,2,5,23,24).

Findings compared most favourably with results obtained by Evan et al. (1) (first world case series) and Roodpeyma et al. (24) (third world study).

This suggests that dextrocardia as a cause of a right-sided heart shows no socio-economic or ethnic preference.

The study confirmed a high association of ASCM amongst patients with dextrocardia. A careful systematic analysis in every case of a right-sided heart is therefore required.

In keeping with previously published literature, the most common situs arrangement in the study was situs inversus dextrocardia, found in nearly half of the patients with dextrocardia (48%). The incidence of ASCM in situs inversus dextrocardia was higher than expected at 67%.

Those with a single ventricle had an equal likelihood of having situs inversus or

situs ambiguous dextrocardia.

A significant number of patients with situs inversus dextrocardia were diagnosed with Kartagener syndrome in the study. This highlights the importance of considering this diagnosis in any patient who presents with recurrent respiratory infections and situs inversus dextrocardia.

As expected, situs solitus was less common, demonstrated in only one-fifth of the study patients. A high percentage of these patients (68%) had abnormal cardiac anatomy at time of echocardiography.

Situs ambiguous dextrocardia was rare (17%). Many of these patients demonstrated known cardiac and extracardiac abnormalities associated with left and right atrial isomerisation. These are a complex group of patients. Extensive extracardiac abnormalities may influence patient management and outcomes. Those with right atrial isomerisation are known to have a higher mortality and morbidity rate (as demonstrated by the study), making it essential that the appropriate precautionary measures get taken (i.e. immunization against encapsulated organisms in RAI and asplenia).

It is imperative to timeously diagnose the cause of a right-sided heart as dextroposition which usually has a secondary cause, is often amenable to surgical rectification or medical treatment as was shown in the study.

In the study, patients with Scimitar syndrome who presented early appeared to

have a more severe clinical picture and a poorer prognosis when compared to those diagnosed at an older age. Cognizance needs to be taken of the fact that radiographically it may be confused with pulmonary tuberculosis or other lung pathology.

In conclusion, a better understanding and high index of suspicion is required to timeously diagnose a child with a right-sided heart in order to provide the best management for each category of lesion.

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