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ORIGINAL ARTICLE

Incidence, Associated Abnormalities, and Outcomes of Dextrocardia: A Registry-based Study in Saudi Arabia

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Abstract

Objective: **Dextrocardia refers to the right-sided positioning of the heart during embryonic development and may occur in isolation or in association with visceral malposition or other malformations. However, few studies have investigated this condition. This study aimed to determine the incidence of cardiac and non-cardiac malformations, as well as to analyze long-term follow-up and survival outcomes in patients with dextrocardia.**

Methods: **This was a retrospective chart review of dextrocardia cases at King Faisal Specialist Hospital & Research Centre in Riyadh, Saudi Arabia from April 22, 1975, to December 31, 2016. A total of 259,246 transthoracic echocardiograms from that period were reviewed, and 357 patients were included in the analysis.**

Results: **The incidence of dextrocardia was approximately 1 in 28,571 pregnancies (0.35 per 10,000 pregnancies). Most patients with dextrocardia were between 2 and 18 years old (n = 252, 70.6 %). The most common type was isolated dextrocardia (situs solitus), followed by situs inversus totalis, and situs ambiguous. The most common congenital cyanotic heart diseases were double outlet right ventricle (n = 55, 15.5 %) and pulmonary atresia (n = 35, 9.8 %). The most common acyanotic congenital abnormalities were ventricular (n = 152, 42.7 %) and atrial (n = 121, 34.2 %) septal defects. Overall survival in the study population was approximately 83 %. Survival rates varied by situs type, with the highest rates observed in patients with situs inversus (96 %), followed by those with situs solitus (91 %), and situs ambiguous (55 %). Moderate to severe pulmonary hypertension was significantly associated with a reduction in overall survival. The most common non-cardiac anomalies observed were gastrointestinal and urogenital abnormalities.**

Conclusion: **This study describes the largest regional cohort of patients with dextrocardia, providing important insights into dextrocardia and outcomes of different intracardiac defects in our community. Our findings confirm that complex**

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congenital cardiac disease is more common in patients with situs solitus and isomerism group. Patients in the isomerism group (12.6 %) had significantly higher mortality rates compared to those in the situs solitus (7.6 %) and situs inversus (3.7 %) groups.

Keywords: Dextrocardia, Situs inversus, Isolated dextrocardia, Situs ambiguous, Cardiac anomalies, Congenital cyanotic heart disease

1. Introduction

Dextrocardia is a condition in which the heart is positioned in the right hemithorax during embryonic development, with the axis directed caudally to the right, in the absence of mechanical shifting due to adjacent visceral abnormalities [1,2]. This complex embryological disease is frequently associated with congenital cardiac defects [3], which range from simple to complex cyanotic or acyanotic heart defects [4].

The incidence of dextrocardia is approximately 1 in 12,019 pregnancies (0.83 per 10,000 pregnancies) [1]. Nonetheless, reports on dextrocardia are rare and few, with only retrospective studies available in the literature.

There are three different types of dextrocardia based on the visceroatrial arrangement: situs solitus (isolated dextrocardia), situs inversus, and situs ambiguous (isomerism). Situs solitus is defined by the right inferior vena cava (IVC) and right superior vena cava draining into the morphological right atrium on the right side of the heart, with the viscera on the same side of the abdomen [3]. Situs inversus is identified when the left IVC and the left superior vena cava drain into the morphological right atrium located on the left side of the heart and the viscera are on the opposite side of the abdomen [4]. Situs ambiguous is defined as the abnormal distribution of the viscera in the abdomen and thorax; it is not a complete depiction of normal anatomical distribution [3–6]. Isomerism occurs when the viscera in the situs ambiguous situation are symmetrically distributed across the midline of the body. Right isomerism is characterized by two symmetric morphological right atria in the heart, two morphological right lungs with three lobes each, and the absence of a spleen (asplenia). Left isomerism is characterized by two symmetric morphological left atria in the heart, two morphological left lungs with two lobes each, and multiple spleens (polysplenia) [2,7].

Complex cardiac diseases and anomalies occur more frequently in situs solitus and situs ambiguus than in situs inversus [8–12]. To the best of our knowledge, this is the first and largest registry-based study that explores dextrocardia in our community.

Abbrevations

AR	Aortic regurgitation
AS	Aortic stenosis
ASD	Atrial septal defect
BAV	Bicuspid aortic valve
DORV	Double outlet right ventricle
D-TGA	D-loop transposition of the great arteries
ECG	Electrocardiogram
EF	Ejection fraction
ER	Emergency room
L-TGA	L-loop transposition of the great arteries
MR	Mitral regurgitation
MS	Mitral stenosis
PDA	Patent ductus arteriosus
PFO	Patent foramen ovale
PR	Pulmonary regurgitation
PS	Pulmonary stenosis
TAPVC	Total anomalous pulmonary venous connection
TGA	Transposition of the great arteries
TOF	Tetralogy of Fallot
TR	Tricuspid regurgitation

Using the registry of patients with dextrocardia at a quaternary care center in Saudi Arabia, we explored the clinical outcomes, associated cardiac defects, non-cardiac malformations, and the estimated incidence of dextrocardia in our population. We believe that this registry will improve the description of dextrocardia, as well as the understanding of the etiology, while outlining the typical presentation and advance care coordination amongst caretakers for better management of patients with dextrocardia.

2. Methods

This retrospective study analyzed cases of dextrocardia at King Faisal Specialist Hospital & Research Centre in Riyadh, Saudi Arabia, spanning from April 22, 1975, to December 31, 2016. All data were obtained with full approval for publication following a thorough committee review. As one of the country's largest and earliest quaternary care centers, we reviewed 259,246 echocardiography cases from our institution, identifying 407 patients of both adult and pediatric age groups diagnosed with dextrocardia. Utilizing a stepwise approach, we systematically collected and analyzed data on

cardiac anatomy. The data reviewed included chest X-rays, ultrasonography, and computed tomography scan reports. The study's inclusion criterion required the actual long axis of the heart to be oriented towards the right side, with sufficient integrated data to ascertain the situs. In contrast, patients who had insufficient information, lung pathology, or dextroposition resulting from any other condition were excluded from the study.

Two experienced independent observers conducted a thorough review of all echocardiographic recordings, radiology data, and laboratory reports. Out of the 407 patients initially identified, 50 were excluded from the study due to technically inadequate information, reports that did not match the dextroposition of the heart, or inaccurate diagnosis of certain dextrocardia types. The medical records of the remaining 357 patients were then analyzed using the Integrated Clinical Information System, which provided detailed information on date registration, referrals, clinic visits, discharge notes, interventions, and management. Additionally, the results of imaging studies were also reviewed to ensure a comprehensive evaluation of the patients.

Patients were examined using left and right parasternal long- and short-axis, right apical, subcostal long axis, four-chamber, and suprasternal long- and short-axis views. Doppler color flow imaging, were performed according to international standards. When the standard views failed to provide adequate information with a poor transthoracic echocardiogram (TTE) windows, another TTE was reviewed. The classification of pulmonary hypertension was established primarily through the use of non-invasive methods, which involved a comprehensive evaluation of several factors including the assessment of right ventricular size and function, calculation of pulmonary artery systolic pressure (PASP) values based on the maximum tricuspid regurgitation velocity (TRV) in cases without coexisting cardiac defects especially in adult population, left heart assessment, cardiac anatomy, evaluation for associated cardiac lesions, and identification of other features of severe pulmonary hypertension. Dextrocardia was defined as the major axis of the heart (base to apex) pointing to the right, owing to congenital malposition, rather than pathology-associated pulling or pushing of the heart towards the right. The determination of atrial situs was primarily based on the location of the IVC, the descending aorta at the level of the diaphragm, and the site of hepatic venous drainage. To ensure the comprehensiveness of our findings, we also considered the location of the liver, stomach, and bronchial morphology, as seen on chest X-rays during the analysis phase. The identification of the cardiac chambers was based on their internal morphological characteristics. The morphology of the ventricles was assessed according to the presence of the tricuspid valve in the morphological right ventricle and the mitral valve in the morphological left ventricle. Additionally, the relation of the great arteries was defined by evaluating the relative position of the pulmonary artery and aorta at the semilunar valve level. In cases where we were unsure of the atrial situs, we reviewed subsequent echocardiographic exams to confirm our findings. All data collected were entered into an Excel sheet and afterwards transferred into a database designed for this study.

Descriptive statistical analyses were performed. Survival analysis was performed with overall survival (OS) in years as primary and secondary outcomes, respectively. Patients were followed up until they experienced the outcome of interest or until the date of the last follow-up. Univariate and multivariate analyses were conducted on all continuous variables, and Kaplan−Meier survival curves were generated as part of the statistical analysis. Clinically significant variables and variables that achieved nominal significance ($p < 0.05$) in univariate analysis were included in a stepwise forward multivariate Cox proportional hazards regression model. Variables that were removed from the model were tested for evidence of confounding and effect modification using the percentage hazard difference (>15 %) and likelihood ratio test ($p < 0.05$), respectively. Variables retained in the model were determined to be clinically or statistically significant if $p < 0.05$. Statistical analysis was performed using SPSS (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp).

3. Results

A total of 357 patients from April 22, 1975, to December 31, 2016, were included in this study. An average of eight cases of dextrocardia were diagnosed per year during the antenatal or postnatal periods. The incidence of dextrocardia was approximately 1 in 28,571 pregnancies, or 0.35 per 10,000 pregnancies.

The majority of patients with dextrocardia in this study were between 2 and 18 years old (n = 252, 70.6 %), followed by those above 18 years old (n = 75, 21 %), infants aged 1 month to 2 years (n = 25, 7 %), and newborns (n = 5, 1.4 %). The majority of patients in the 2−18 years age group diagnosed with isolated dextrocardia (situs solitus), situs inversus totalis, and situs ambiguous (n = 117, 115, and 20, respectively),

accounting for 46.4 %, 45.6 %, and 8 % of cases, respectively. Situs solitus was the most commonly identified type of dextrocardia in this registry, followed by situs inversus totalis and situs ambiguous. No difference observed among the different types of dextrocardia and sex, although situs solitus (n = 94, 54.9 %) and situs ambiguous (n = 16, 66.7 %) were slightly more in male patients.

The most common acyanotic congenital heart defects identified in patients with dextrocardia were ventricular septal defect (VSD) (n = 152, 42.6 %), atrial septal defect (ASD) (n = 121, 33.9 %), patent ductus arteriosus (PDA) (n = 75, 21.0 %), and patent foramen ovale (PFO) (n = 38, 10.6 %) Table 1. A significant difference is noted in ASD and PDA among different types of dextrocardia.

The most common cyanotic abnormalities presented were double outlet right ventricle (DORV) (n = 55, 15.5 %), pulmonary atresia (n = 35, 9.8 %), single ventricle (n = 32, 9.0 %), hypoplastic right ventricle (n = 28, 7.9 %), D-loop transposition of great vessels (D-TGA) (n = 17, 4.7 %), total anomalous pulmonary vein connection (TAPVC) (n = 10, 2.8 %), tricuspid atresia (n = 7, 2.0 %), and tetralogy of Fallot (n = 6, 1.7 %). A significant difference is noted in TAPVC, pulmonary atresia, hypoplastic right sided ventricle, Single ventricle and DORV among different types of dextrocardia.

The most common type of dextrocardia observed in patients with transposition of the great arteries was situs solitus dextrocardia, which included both L-transposition of the great arteries (L-TGA) and D-transposition of the great arteries (D-TGA) (n = 51, 56%). This was followed by situs inversus totalis (n = 30, 33%) and situs ambiguous (n = 10, 11%).

The overall survival (OS) of different types of dextrocardia was estimated using a Kaplan−Meier survival curve (Fig. 1). Approximately 83% of patients survived, with the majority of mortality occurring during early childhood. Notably, most deaths occurred before the third decade of life.

The survival analysis in Fig. 2, displays the OS stratified by cardiac defects, revealed that cyanotic defects did worse than acyanotic heart defects. However, no significant difference was observed between these groups (Log rank 4.6, p = 0.098). The survival analysis depicted in Fig. 3 demonstrates that patients with situs ambiguous have significantly lower survival rates compared to those with isolated dextrocardia or situs inversus. This difference was statistically significant (Log rank 7.8, p = 0.020). Additionally, Fig. 4 demonstrates that patients with dextrocardia and moderate to severe pulmonary hypertension exhibited significantly reduced survival compared to those without pulmonary hypertension (Log rank 8.1, p =0.004). Anomalies associated with dextrocardia are summarized in Table 2, while death frequencies are presented in Table 3.

A significant difference (p = 0.011) was noted among the various types of dextrocardia. Univariate analysis identified age (hazard ratio [HR] 1.590, 95% confidence interval [CI] 1.114 -1.928, p < 0.0001) and the presence of moderate to severe pulmonary hypertension (PH) (HR 0.567, 95% CI 0.234 -0.891, p = 0.005) as significant predictors of increased mortality risk. In the multivariate model, after adjusting for all variables, both age (HR 1.114, 95% CI 1.031 -1.459, p < 0.0001) and pulmonary hypertension (HR 0.918, 95% CI 0.523 -0.987, p = 0.05) remained independent and significant predictors of mortality (see Table 4).

4. Discussion

Compared to previous studies that attempted to establish the incidence of dextrocardia, we used the number of all pregnancies as denominator [12], rather than that of live births. During the same time period, there were an estimated 247,085 pregnancies in Saudi Arabia [12]. Our study showed an incidence of dextrocardia of 0.35 per 10,000 pregnancies. A previous study suggested the incidence to be approximately 0.83 per 10,000 pregnancies [1]. Other studies showed similar results; Kidd et al. [14] reported 0.40 per 10,000 live births, Ferencz et al. [15] reported 0.53 per 10,000 live births, and Fyler et al. [16] reported 0.37 per 10,000 live births. We also found an incidence rate comparable to previous reports, while also identifying some limitations in the reported incidence, including the use of incidence per live birth rather than per pregnancy, the possibility of referral bias, and concerns about the adequacy of screening methods. These factors could potentially affect the accuracy and validity of the reported incidence.

In the registry, situs solitus dextrocardia was the most common, accounting for 47.9 % of cases, followed by situs inversus at 45.3 %, and situs ambiguous at 6.7 %. Our findings were similar to those by Tripathi et al., with rates of 43.3 %, 38 %, and 18.7 % for situs solitus, inversus, and ambiguous, respectively [12]. However, our rates were slightly higher than those reported by Garg et al. and Bohun et al. [1,4]. This difference may be attributed to the relevance of our quaternary care and the early detection of dextrocardia due to the complexity of our patients.

4.1. Situs solitus dextrocardia

Situs solitus is commonly linked to congenital heart disease, although the literature has noted

Table 1. Demographic, general, and morphological characteristics of the patients with different types of dextrocardia.

Variables	Valid (n = 357)	Total cases (%)	Situs solitus (n = 171) (%)	Situs inversus totalis (n = 162) (%)	Situs ambiguous (n = 24) (%)	χ^2	p-value
Demographics							
Age							
<1 month	5	1.4	3 (1.7)	2 (1.2)	0		
1 month−2 years	25	7	16 (9.3)	5 (3.1)	4 (16.7)		
2−18 years	252	70.6	117 (68.0)	115 (71.0)	20 (83.3)		
>18 years	75	21	35 (20.9)	40 (24.7)	0		
Sex							
Male	192	53.6	94 (54.9)	82 (50.6)	16 (66.7)		
Female	165	46.4	78 (45.6)	80 (49.4)	8 (33.3)		
ECG							
1st degree	34	9.5	13 (92.9)	20 (80.0)	1 (50.0)		
2nd degree	3	0.84	0 (0.0)	3 (12.0)	0 (0.0)		
3rd degree	4	1.1	1 (7.1)	2 (8.0)	1 (50.0)		
EF							
≥55 %	341	95.6	160 (93.0)	159 (98.1)	23 (95.8)		
54−30 %	13	3.6	10 (5.8)	2 (1.2)	1 (4.2)		
<30 %	3	0.8	2 (1.2)	1 (0.6)	0 (0.0)		
Cyanotic abnormality							
TOF	6	1.7	1 (0.6)	5 (3.1)	0 (0.0)	3.627	0.163
TAPVC	10	2.8	4 (2.4)	2 (1.2)	4 (16.7)	**18.408**	**0.0001**
D-TGA	17	4.7	7 [4]	9 (5.5)	1 (4.2)	0.4122	0.813
Tricuspid atresia	7	2	5 (2.9)	1 (0.6)	1 (4.2)	2.944	0.229
Pulmonary atresia	35	9.8	21 (12.3)	7 (4.3)	7 (29.2)	**16.759**	**0.0001**
Hypoplastic right sided ventricle	28	7.8	13 (7.6)	9 (5.5)	6 (25.0)	**10.857**	**0.004**
Single ventricle[a]	32	9.0	17 (10.0)	9 (5.5)	6 (25.0)	**10.104**	**0.018**
DORV	55	15.4	18 (10.5)	27 (16.6)	10 (41.7)	**16.021**	**0.0003**
Acyanotic abnormalities							
VSD	152	42.5	77 (45.0)	64 (39.5)	11 (45.8)	1.133	0.567
ASD	121	34.0	68 (40.0)	44 (27.1)	9 (37.5)	**6.043**	**0.049**
PFO	38	10.6	23 (13.4)	15 (9.2)	0 (0.0)	4.621	0.099
PDA	75	21.0	38 (22.2)	27 (16.6)	10 (41.7)	**8.08**	**0.018**
Total TGA							
TGA	91	25.5	51 (30.0)	30 (18.5)	10 (41.7)	**9.075**	**0.011**
Valvular heart disease							
MR	37	10.4	18 (10.5)	17 (10.5)	2 (8.3)	0.12	0.942
AR	21	5.9	12 (7.0)	8 (5.0)	1 (4.2)	0.79	0.674
TR	81	22.7	38 (22.2)	40 (24.7)	3 (12.5)	1.847	0.397
PR	14	3.9	7 (4.1)	7 (4.3)	0 (0.0)	1.068	0.586
MS	5	1.4	4 (2.3)	1 (0.6)	0 (0.0)	2.154	0.341
PS	91	25.8	48 (28.1)	32 (19.7)	11 (45.8)	**8.541**	**0.014**
AS	1	0.3	0 (0.0)	1 (0.6)	0 (0.0)	1.208	0.547
Bicuspid AV	2	0.6	2 (1.1)	0 (0.0)	0 (0.0)	2.189	0.335
Pacemaker							
Yes	20	5.6	10 (5.8)	9 (5.6)	1 (4.2)	0.123	0.940
No	336	93.3	161 (93.0)	153 (94.0)	23 (94.4)		
Average ER triage visits, n			1.25	2.18	2.17	42.750	0.274
Hospital admission, n			2.40	2.32	3.21	33.734	0.09
Mortality, %			3.6	1.68	0.84		

ECG, electrocardiogram; TOF, tetralogy of Fallot; TAPVC, total anomalous pulmonary vein connection; D-TGA, D-loop transposition of the great arteries; L-TGA, L-loop transposition of the great arteries; DORV, double outlet right ventricle; VSD, ventricular septal defect; ASD, atrial septal defect; PFO, patent foramen ovale; PDA, patent ductus arteriosus; TGA, transposition of the great arteries; MR, mitral regurgitation; AR, aortic regurgitation; TR, tricuspid regurgitation; PR, pulmonary regurgitation; MS, mitral stenosis; PS, pulmonary stenosis; AS, aortic stenosis; BAV, bicuspid aortic valve; EF, ejection fraction; ER, emergency room.

[a] (Undetermined ventricle; Significant p value less than <0.05).

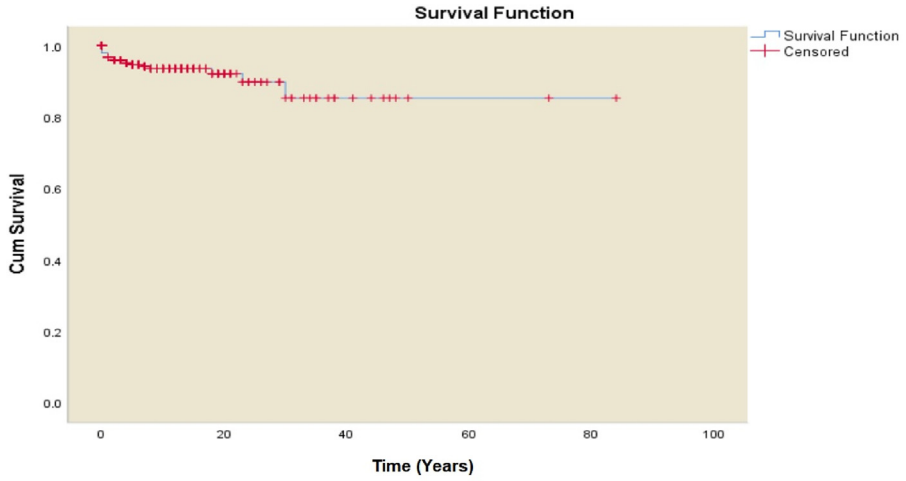
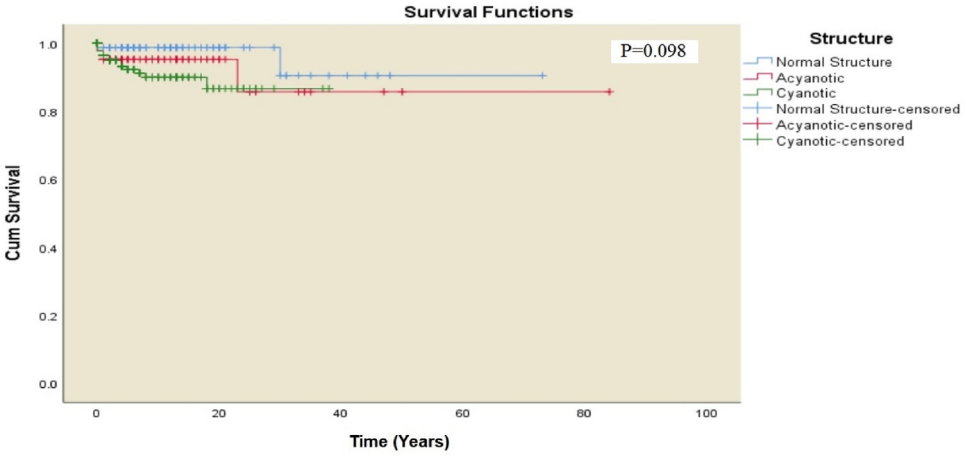


Fig. 1. Kaplan -Meier survival curve for patients with dextrocardia. The curve depicts overall survival in the studied cohort.

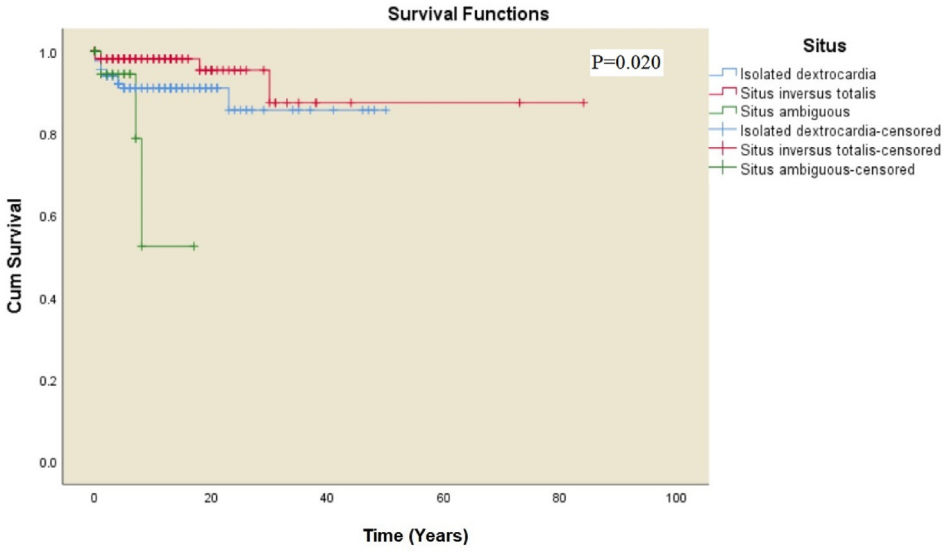


Log Rank Test	P-value	Status
4.656	0.098	Not Significant

Fig. 2. Kaplan -Meier survival curves stratified by structural heart defect. Comparison of survival curves using the log-rank test showed no statistically significant difference in mortality among the different structural heart defects (log-rank = 4.6, p = 0.098).

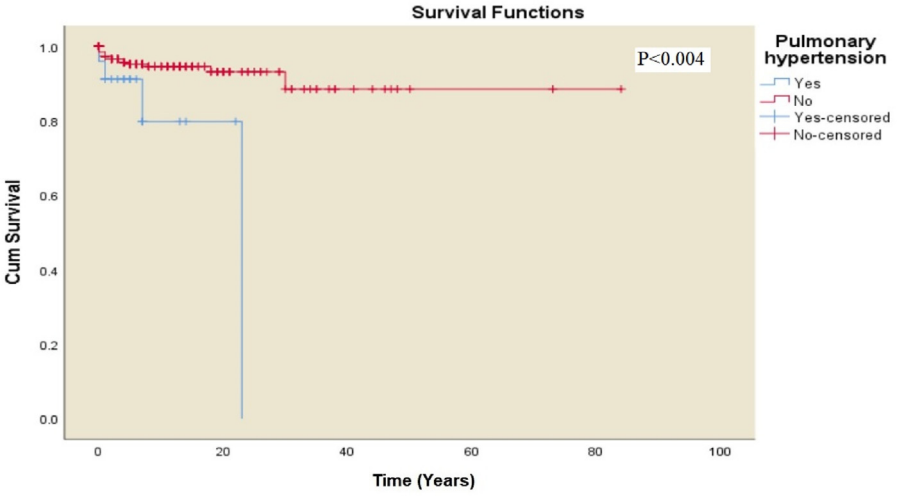
some overestimation [4,8,10,12,17]. In our study, we found a high prevalence of cyanotic congenital heart disease (CCHD), with the majority of cases displaying pulmonary valve atresia and DORV (n = 21, 12.3 %; n = 18, 10.5 %), followed by single ventricle and PS, as shown in Table 1. Furthermore, our cohort analysis showed that acyanotic heart defects were most frequently observed in situs solitus dextrocardia, particularly VSDs and ASDs (n = 77, 45 %; n = 68, 40 %, respectively), either independently or in combination with other defects.

The results from Table 1 indicate a higher incidence of transposition of the great arteries (n = 51; 30 %) in patients with situs solitus dextrocardia, with a significant proportion of cases being attributed to congenitally corrected transposition of the great arteries or L-TGA (n = 17, 9.9 %). Although the percentage of L-TGA was higher than what was reported [1], our findings were in line with previous studies conducted by Garg et al. and Bohun et al. [1,4]. Another study by Tripathi et al. reported similar findings, with DORV (n = 36; 22.1 %), single ventricle (n = 26; 16 %), congenitally corrected transposition of the great arteries (n = 51; 31.3 %), and pulmonary atresia [12].



Log Rank Test	P-value	Status
7.805	0.020	Significant

Fig. 3. Kaplan–Meier survival curves for the different types of dextrocardia. The overall survival for isolated dextrocardia and situs inversus totalis are similar, but the isomerism group has lower overall survival rates. The log-rank test for comparisons of survival curves indicated significant difference in the mortality for the difference in dextrocardia types, especially in the first decade of life (Log rank 7.805, p = 0.020).



Log Rank Test	P-value	Status
8.178	0.004	Significant

Fig. 4. Kaplan–Meier survival curves in moderate to severe pulmonary hypertension among dextrocardia patients. The log-rank test for comparisons of survival curves indicated a significant difference in the mortality (Log rank 8.178, p = 0.004).

4.2. Situs inversus dextrocardia

Garg et al. and Bohun et al. [1,4] have reported situs inversus to be more commonly associated with a structurally normal heart configuration, as demonstrated by the number of defects in Table 1. In our cohort, DORV was the most prevalent CCHD (n = 27, 16.6 %), followed by single ventricle,

Table 2. Anomalies associated with different types of dextrocardia.

Anomalies	No. of patients
Scimitar syndrome	29
Polysplenia	24
Asplenia	16
Diaphragmatic hernia	13
Kartagener syndrome (primary ciliary dyskinesia)	12
Poland syndrome	1
Prune belly syndrome with Vesicoureteral reflux and undescended testis.	1
Rt multicystic kidney disease/solitary kidney (with biliary hypoplasia)	4
Horseshoe kidney/bilateral hydronephrosis	
Lung agenesis/hypoplasia/pneumothorax	2
Liver cirrhosis/biliary atresia	2
Wandering spleen.	1
Short pancreas syndrome	1
Tracheoesophageal fistula	1
Kniest syndrome	1
Escobar syndrome	1

hypoplastic right heart syndrome, pulmonary atresia, and stenosis, as outlined in Table 1. These results are consistent with global trends documented by Garg et al. and Bohun et al. [1,4]. Acyanotic defects, such as VSDs and ASDs, were commonly observed alone or with other anomalies.

In another report by Tripathi et al., DORV (22.9 %), structurally normal heart (16.7 %), and left-to-right shunt lesions (16.0 %) were the most frequently diagnosed conditions.

The implications of these findings for congenital heart defect diagnosis are significant, and underestimation may occur due to the absence of associated cardiac and non-cardiac anomalies. Moreover, the reported disease burden estimates may be misleading, depending on the methods of early detection described in the literature [4,8,10,16]. Therefore, it is essential to consider the broader clinical context and employ rigorous diagnostic criteria.

4.3. Situs ambiguous dextrocardia

Our study reaffirms the high prevalence of CCHD in patients with isomerism, consistent with prior reports [1,4]. Specifically, DORV, single ventricle, hypoplastic right heart syndrome, and PS were among the most frequently occurring CCHDs.

The data presented in Tables 1 and 3 indicate that both patients with situs solitus and those with isomerism had a high prevalence of CCHD, but the mortality rate was higher in the isomerism group (12.6 %). These results suggest that the cardiac and non-cardiac malformations in patients with isomerism were more severe than those in patients with situs solitus. These findings underscore the importance of vigilant screening and prompt diagnosis of

Table 3. Death frequencies categorized by different types of dextrocardia and structural heart disease.

Type of dextrocardia	Number (%)	Total deaths (%)	Death per type (%)
Situs solitus	171/357 (48 %)	13/22 (59 %)	13/171 (7.6 %)
Situs inversus	162/357 (45.4 %)	6/22 (27 %)	6/162 (3.7 %)
Situs ambiguous	24/357 (6.6 %)	3/22 (13.6 %)	3/24 (12.6 %)
Structural heart disease			
Normal	78/357 (22 %)	2/22 (9 %)	
Acyanotic	98/357 (27 %)	5/22 (23 %)	
Cyanotic	181/357 (51 %	15/22 (68 %)	

Table 4. Univariate and multivariate Cox proportional regression analyses of the combined primary endpoint of all-cause death.

	Univariate Model			Multivariate Model		
	HR	χ^2	p-value	HR	χ^2	p-value
Age	1.590	17.165	**<0.0001*** **	71.228	1.114	**<0.0001*** **
Sex	0.437	0.269	0.134			
Acyanotic defects	0.326	5.086	**<0.005****	0.131	0.224	0.864
Cyanotic defects	0.952	7.021	**<0.005****	0.417	0.111	0.328
Normal structure	0.851	4.396	**<0.005****	0.156	0.231	0.604
Isolated dextrocardia	0.209	0.956	0.784			
Situs inversus totalis	0.363	0.820	0.495			
Situs ambiguous	0.425	0.714	0.652			
Pulmonary hypertension	0.567	5.042	**<0.005****	0.918	6.284	**<0.05***
Pulmonary stenosis	0.453	2.309	0.173			

HR, hazard ratio; χ^2, chi-square. $p < 0.05$ is considered statistically significant. *, $p < 0.05$; **, $p < 0.005$; ***, $p < 0.0001$.

CCHDs in patients with isomerism to facilitate timely and appropriate interventions.

In our registry, right isomerism was typically associated with CCHD, male sex, and immunocompromised patients, due to the absence of the spleen. Notably, all deaths observed in cases of situs ambiguous were related to right isomerism (n = 3, 14 %). According to Applegate and Tonkin et al. [18,20], patients with right isomerism typically have a poor prognosis and may not survive beyond the first year of life due to cardiovascular compromise. However, some patients may survive into adulthood, potentially due to less severe PS, absence of arrhythmias or overwhelming infections [13,18–20]. Nevertheless, the exact cause of survival remains unclear, and further research is needed.

Left isomerism is typically associated with acyanotic congenital heart defects, female sex, interrupted IVC, multiple spleens, gut malrotation, and biliary atresia, as demonstrated in Tables 1 and 2. Most patients with left isomerism survive until mid-adolescence, consistent with previous research [8–10].

Previous studies have reported that gastrointestinal and urogenital abnormalities are the most common anomalies observed in patients with congenital heart defects, which is consistent with our findings [1,4]. Scimitar syndrome was the most prevalent anomaly observed in our study, particularly in association with CCHD, as shown in Table 2. Additionally, our study identified other conditions associated with dextrocardia, including Kniest syndrome, Escobar syndrome, and wandering spleen.

As shown in Figs. 1 and 2, a normal structural heart had a 97 % survival rate, acyanotic 96 %, and cyanotic 88 %, with a similar median. Using the log-rank test, there was no significant difference between the three subgroups. Survival over two decades based on the type of dextrocardia, as shown in Fig. 3, was highest for situs inversus (96%), followed by situs solitus (91%) and situs ambiguous (55%). These results are similar to those reported by Bohun et al. (87%, 67%, and 46%, respectively) [1]. The survival rates declined steadily for patients with pulmonary hypertension, as shown in Fig. 4, indicating a worse prognosis for those with advanced disease. The pathophysiology of pulmonary hypertension may present with cardiac ischemia, either from residual defects or anomalies (e.g., Poland syndrome) associated with coagulopathy that may lead to microvascular dysfunction, as described in Italian case series or isolated pulmonary hypertension secondary to lung disease or rheumatologic disease [21,22]. It is crucial to acknowledge that the diagnosis and treatment of pulmonary hypertension have evolved over time, leading to a lack of standardized guidelines to follow in our study cohort, particularly in the pediatric congenital age groups. Although the types of cardiac defects associated with dextrocardia were significant in the univariate analysis, only age and pulmonary hypertension remained significant in the stepwise multivariate analysis (Table 4).

A major strength of the present study is the use of a robust analytical method to examine survival rates in patients with congenital heart defects. Specifically, a multivariable Cox regression was employed, allowing for the analysis of survival rates in patients with varying follow-up periods and appropriately accounting for censored data.

This study has some limitations. Obtaining a complete dataset was not feasible, which may affect the relevance of certain demographic variables within dextrocardia. We must also acknowledge that limitations in the searching process may have resulted in an underestimation of the actual number of dextrocardic cases. Moreover, assumptions were made regarding the referral system to our quaternary center and screening process, which may have introduced bias to the study results. Additionally, it is worth noting that most cases included in the study were not community referrals, which may limit the generalizability of the findings. Furthermore, limitations in imaging modalities may have prevented the identification of all cases of non-cardiac anomalies, and some deaths may not have been documented due to the use of intention-to-treat follow-up in the survival analysis. However, it is noteworthy that no dextrocardia diagnosis was made using only one imaging modality, and we followed the protocol as described in the methodology. This registry represents the largest group of dextrocardiac patients in the region, and we hope that our findings will contribute to the current understanding of this condition.

It is important to note that this study included a cumulative number of patients spanning over four decades, during which our hospital was the first quaternary hospital in the kingdom. As a result, we presume that the study sample was highly heterogeneous and representative of the population in the kingdom. Moreover, the participants exhibited favorable outcomes despite their complex congenital cardiac defects, type of surgical intervention, and long-term follow-up. Therefore, when interpreting the results of this study, it is essential to consider the significant advancements in the surgical and medical management of dextrocardia over the years. Our findings highlight the importance of ongoing research and quality improvement initiatives to further enhance the clinical outcomes and quality of life for dextrocardiac patients.

In conclusion, the most common cardiac defects associated with dextrocardia were acyanotic defects, followed by CCHDs. Despite the high prevalence of complex cardiac malformations in dextrocardiac patients, those with isomerism exhibited a significantly higher mortality rate compared to other patients, which may be attributed to the higher frequency of both complex cardiac and noncardiac malformations in this group. In contrast to patients with situs inversus, the situs solitus group is more susceptible to developing complex cardiac lesions, while the former is generally associated with a low incidence of both cardiac and noncardiac defects. The early identification of cardiac abnormalities allows healthcare providers to plan and implement appropriate interventions, including timely referrals to specialized centers for advanced care.

Author contributions

Conception and design of Study: NSA, BA. Literature review: NSA, BA, SAA, FA, KSA, FF. Acquisition of data: NSA, BA, SA, HH, RA, FA, AA, MA, GTA, SAA. Analysis and interpretation of data: NSA, GTA, SAA, FA, KSA. Research investigation and analysis: NSA, BA, SA, HH, RA, FA, AA, MA, GTA. Data collection: NSA, BA, SA, HH, RA, FA, AA, MA, GTA. Drafting of manuscript: NSA, BA, SAA, FA, KSA, FF. Revising and editing the manuscript critically for important intellectual contents: NSA, FA, KSA, FF. Data preparation and presentation: NSA, BA. Supervision of the research: NSA, FF. Research coordination and management: NSA, BA.

Ethics information

Institutional Review Board Statement: This article has obtained approval from the Institutional Review Board (IRB) at King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia with the reference RAC number: 2161005.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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