Journal of Radiology and Imaging

NobleResearch
An Open Access Publisher
www.nobleresearch.org

Rokytska N et al., J Radiol Imaging. 2018, 3(3):10-18
http://dx.doi.org/10.14312/2399-8172.2018-3

Original research

Open Access

Computed tomography of congenital heart disease in patients with heterotaxy syndrome

Nadiia Rokytska[1,*], Raad Tammo[1], Tetyana Yalynska[1], Hanna Morkovkina[1], Halchenko Oleksandr[1] and Illia Yemets[1]

[1]Department of Radiology, Ukrainian children cardiac center (UCCC), 28/1 Chornovola St., Kiev, Ukraine

Abstract

Background: Heterotaxy syndrome (HS) or situs ambiguous, is determined as a type of congenital disorders which is caused by failure to establish normal left–right (L–R) asymmetry during embryonic development. One of the characteristics of the resulting defects is segmental discordances along the L–R axis. There are two types of "situs ambiguous" right and left isomerism, both variants are associated with complex cardiac and visceral malformations. *Material and method:* Forty three patients aged from one day to 12-years-old, with congenital heart disease (CHD) and suspected HS underwent multi-detector computed tomography (MDCT) between 2011 and 2016. The MDCT images were acquired on a 16 slices scanner in all patients after performing echocardiography. Statistical data was presented as mean ± standard deviation. *Results:* Heterotaxy syndrome with right isomerism was in 53% (n = 23) patients (3 girls, 20 boys), a mean age 9.32 ± 6.2 months, and 47% (n = 20) patients had heterotaxy syndrome with left isomerism (16 girls and 4 boys), a mean age 23.7 = 8.3 months. Dextrocardia was detected in 26% (n = 11) patients with right isomerism and in 7% (n = 5) patients with left isomerism. Complex CHD were detected in all patients, and were as follows: atrioventricular septal defects (AVSD) was detected in 37% (n = 16), double outlet right ventricle (DORV) – 30% (n = 13), single ventricle (SV) – 19% (n = 8), transposition of great arteries (TGA) – 30% (n = 13), pulmonary stenosis and pulmonary atresia (PS and PA) – 30% (n = 13), total anomaly pulmonary vein connection (TAPVC) and partial anomaly pulmonary vein connection (PAPVC) – 53% (n = 23), hypoplasia left heart syndrome (HLHS) – 2% (n = 1), isolated ventricular septum defect (VSD) – 2% (n = 1), aortic coarctation (CoA) – 2% (n = 1), interrupted IVC with hemiazygous continuation – 35% (n = 15) (only in patients with left isomerism). Single right-sided SVC was detected in 53% (n = 23), single left-sided SVC in 16% (n = 7) and bilateral SVC in 30 % (n = 13). *Conclusions:* Mostly patients with HS have complex CHD and require accurately assessment for future management. Multidetector computed tomography allows to obtain detailed data on the morphology of the heart, great vessels, the anatomy of the internal organs and their mutual arrangement, make an accurate diagnosis of HS.

Keywords: heterotaxy syndrome; congenital heart diseases; multidetector computed tomography

Introduction

Heterotaxy syndrome or situs ambiguous, is determined as a type of congenital disorders which is caused by failure to establish normal left – right (L – R) asymmetry during embryonic development. One of the characteristics of the resulting defects is segmental discordances along the L – R axis [1].

Originally, heterotaxy has been defined on the grounds of splenic anatomy with patients who were diagnosed with asplenia or polysplenia. Now, this approach is considered not to be perfect, heterotaxy is believed to be better defined on the grounds of isomerism of the atrial appendages rather than other features such as splenic anatomy because atrial appendage morphology is the most invariable feature and gives the most consistent "syndromic clustering" [2].

Atrial chambers sidedness within the body defines their arrangement. Lateralization is the term that describes the development of morphologically right-sided structures on one side of the body, and morphologically left-sided structures on the other side. "Situs solitus" is used for another term for normal lateralization. The mirror-imaged arrangement can be also called "situs inversus" [3].

"Situs ambiguous" is used to speak about any unusual symmetry of asymmetric thoracic and abdominal organs, and the atrial appendages within the heart. Patients who

***Corresponding author:** Dr. Nadiia Rokytska, MD, Radiologist of Radiology department of Ukrainian children cardiac center, 28/1 Chornovola St., 01135 Kyiv, Ukraine. Tel./Fax: (044) 284-03-21, 284-03-11; Mobile: +380-99-605-75-52; Email: rhope2107@gmail.com

Received 9 July 2018 *Revised* 4 October 2018 *Accepted* 15 October 2018 *Published* 24 October 2018

Citation: Rokytska N, Tammo R, Yalynska T, Morkovkina H, Oleksandr H, Yemets I. Computed tomography of congenital heart disease in patients with heterotaxy syndrome. J Radiol Imaging. 2018; 3(3):10-18. DOI: 10.14312/2399-8172.2018-3

have "situs ambiguous" can be subdivided into those who have heterotaxy with isomerism of the right atrial appendages and heterotaxy with isomerism of the left atrial appendages [4]. It should also be noted that one organism may have only one kind of arrangement of internal organs or situs solitus, or situs inversus, or situs ambiguous.

Left isomerism is related with paired left-sided viscera. However, right-sided viscera may be nonexistent. On the contrary, right isomerism has characteristics of a paired right-sided viscera, but left sided viscera may be absent. Both variants are connected with complex cardiac malformations, viscerocardiac heterotaxy (incoherent laterality of the heart axis, stomach, portal sinus, or gallbladder) and intestinal malrotation (Figure 1).

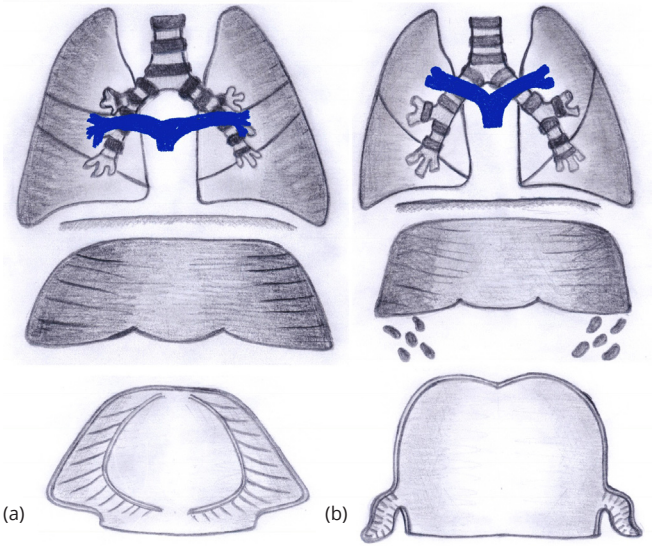

Figure 1 (a) Typical findings in right isomerism are bilateral morphologic right atrial appendages, bilateral morphologic right (three lobed) lungs with eparterial bronchi, spleen is absent (asplenia); (b) Typical findings in left isomerism are bilateral morphologic left atrial appendages, bilateral morphologic left (bilobed) lungs with hyparterial bronchi, multiple splenuli (polysplenia).

Due to the more complex type of cardiac malformations (Figure 2) neonates with right isomerism have significantly higher mortality and postoperative morbidity if they are compared to the ones with left isomerism. In the contrary, the greatest attrition in left isomerism occurs in the prenatal period and often connected with heart block and hydrops. Even though the cardinal cardiac defects mostly define morbidity and mortality in the neonatal period, the visceral anomalies may have a strong impact on these patients' long-term outcome. Long-term survival of the children with left isomerism is essentially affected by various degrees of malrotation and malfixation of the bowel (Figure 3), preduodenal portal vein, gastric volvulus, and biliary atresia [5].

One of the main reasons of infant mortality is congenital heart disease (CHD) as it influences one in every 130 newborns.

A rate of 1.44/10,000 for all cardiac defects connected with left–right asymmetry malformations (cardiac and/or non-cardiac) was assessed by the Baltimore–Washington Infant Study. It has been found out that having congenital

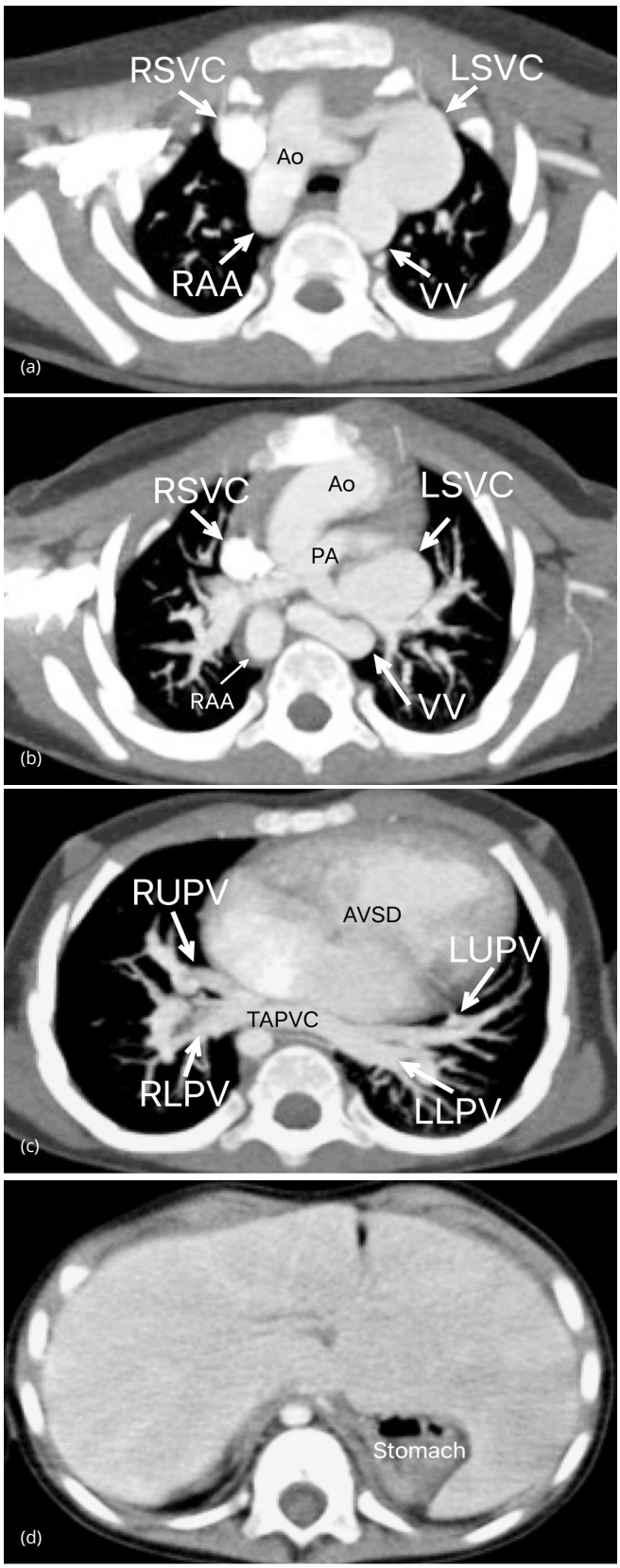

Figure 2 Maximum intensity projection (MIP) images of heterotaxy syndrome, right isomerism, levocardia, atrioventricular septal defect (AVSD), double outlet right ventricle (DORV) (c), supracardiac total anomalous pulmonary venous connection (TAPVC) into left superior vena cava (LSVC) (a, c), bilateral superior vena cava (SVC) (a, b), pulmonary stenosis (PS) (b), right aortic arch (RAA) (a, b); Liver is on the midline, stomach - on the left side (d); RUPV – right upper pulmonary veins, LUPV –left upper pulmonary veins, RLPV –right lower pulmonary veins, LLPV – left lower pulmonary veins, VV – vertical vein, RAA –right aortic arch, Ao – aorta, PA – pulmonary artery, LSVC – left superior vena cava, RSVC – right superior vena cava.

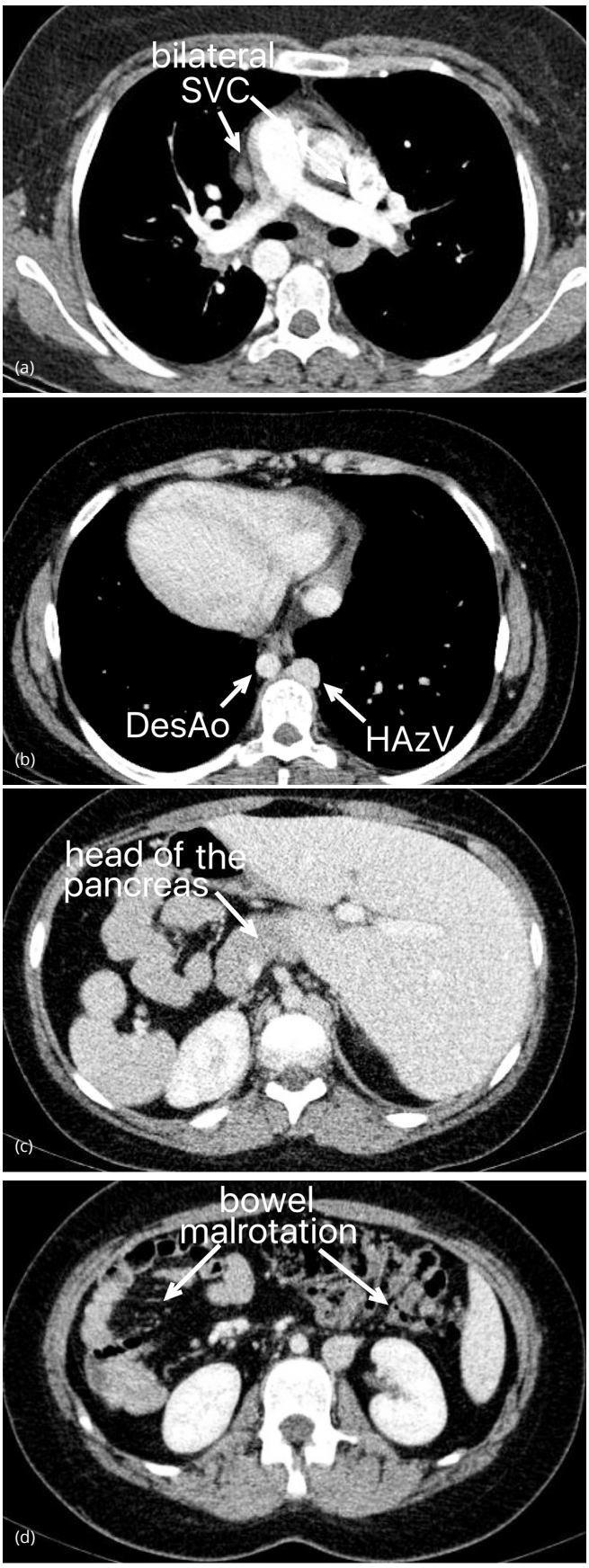

Figure 3 Transversal images of heterotaxy syndrome, left isomerism, dextrocardia, left aortic arch (LAA) (b), bilateral SVC (a), liver is on the left side, stomach on the right side (c), interruption of the inferior vena cava with hemiazygous continuation (b), multiple spleen, hypoplasia the body and tail of the pancreas (c), bowel rotation abnormality (d); (DesAo – descending aorta, HAzV – hemiazygos vein).

heart disease in 50-100% of cases and only 5% may survive beyond the age of five years old [6].

Patients with heterotaxy syndrome (HS), right isomerism in 90-99% suffer from severe congenital heart anomalies. Complex cardiac anomalies can be the cause for the high mortality rate among these patients. Mortality rate in right isomerism (79% in the first year of life) is a higher than in left isomerism (61% in the first year) [7].

With the development of multidetector computed tomography and magnetic resonance imaging (MRI), with their extensive use in the diagnosis of CHD, knowledge of the bodily arrangement has become necessary for the radiologist in the complex diagnostics heterotaxy syndrome.

The aim of this article is to demonstrate possibility multidetector computed tomography in diagnosis of CHD and extracardiac vascular anomalies in patients with heterotaxy syndrome, based on own data. Besides the purpose of our work was to study the issue of how often different types of CHD occur among the patients with heterotaxy syndrome depending on the type of isomerism.

Material and methods

Forty-three patients aged from 1 day to 12-years-old, with CHD and suspected heterotaxy syndrome underwent non-gated multidetector computed tomography between 2011 and 2016.

The multidetector computed tomography (MDCT) images were acquired on a 16 slices scanner in all patients after performing echocardiography. MDCT dose parameters used in our little patients were so low as it possible, average CTDI vol was within 11 mGy, DLP - 20 mGy x cm,, the average effective dose equivalent - 0.7 mSv. MDCT parameters of 80 kV and 40 mAs with tube current modulation were set for all patients. CT data were obtained using the following parameters: detector collimation, 1.5 mm; slice thickness, 2 mm; Increment, 1 or 2 mm; Feed /Rotation, 18 mm/sec; gantry rotation time, 0.5 sec. The scan range was from the thoracic inlet to the top of the iliac wings. In all scans, dose modulation (CARE Dose 4D) was used to minimize the radiation dose. Nonionic iodinated contrast material (320 mg/ml) was injected at a rate varying from 1.2 ml/sec to 2.5 ml/sec. The scan delay was determined using bolus tracking in the descending aorta with a 4 seconds delay after trigger, repetitive monitoring scans were performed within the lumen of the descending aorta as the region of interest with the threshold of starting the diagnostic scans as 80 HU.

We followed such diagnostic criteria to assessment organs arrangement in patients with CHD: position and morphology of the atria; aorta and inferior vena cava position with respect to the midline; stomach position and its malrotation presence; position of the liver and gall bladder; heart apex position; presence or absence of spleen/ spleens; position of the bronchus (eparterial, hyparterial), morphology of the lungs (three or two lobes on both sides); position of the intestine and presence of

its malrotation. Statistical data was presented as mean ± standard deviation. The statistical evaluation of the validity of the difference between the comparative indices was carried out by using Pearson's chi-squared test (χ^2), the correlation between them was done by using correlation coefficient (r), and on the basis of correlation coefficient the coefficient of determination (R^2x100) was identified, which defines the contribution of the factor to the change of the dependent variable.

Results

Heterotaxy syndrome with right isomerism was in 53% (n = 23) patients (3 girls, 20 boys), a mean age 9.32 ± 6.2 months, and 47% (n = 20) patients had heterotaxy syndrome with left isomerism (16 girls and 4 boys), a mean age 23.7 ± 8.3 months.

Dextrocardia was detected in 26% (n = 11) patients with right isomerism and in 12% (n = 5) patients with left isomerism. Complex CHD were detected in all patients (Table 1), and were as follows: atrioventricular septal defects (AVSD) was detected in 37% (n = 16), double outlet right ventricle (DORV) – 30% (n = 13), single ventricle (SV) - 19% (n = 8), transposition of great arteries (TGA) – 30% (n = 13) (Figure 4), pulmonary stenosis and pulmonary atresia (PS and PA) – 30% (n = 13) (Figure 5), total anomaly pulmonary vein connection (TAPVC) (Figure 6) and partial anomaly pulmonary vein connection (PAPVC) – 53% (n = 23) (Figure 7), hypoplasia left heart syndrome (HLHS) – 2% (n = 1), interrupted aortic arch (IAA) – 2% (n = 1) (Figure 8), isolated ventricular septum defect (VSD) – 2% (n = 1), aortic coarctation (CoA) – 2% (n = 1) (Figure 9), interrupted inferior vena cava with hemiazygous continuation – 35% (n = 15) (only in patients with left isomerism). Single right-sided superior vena cava was detected in 53% (n = 23), single left-sided superior vena cava in 16% (n = 7) and bilateral superior vena cava in 30% (n = 13).

Table 1 Congenital heart disease in patient with heterotaxy syndrome (left and right isomerism).

CHD	*Heterotaxy syndrome (n = 43 patients)*							*Pearson's chi-squared test* (χ^2)	*Correlation coefficient* (r)	*Coefficient of determination* (R^2x100)	p
	Left isomerism			*Right isomerism*							
	n	*%*	*The number of cases per 100 patients*	*n*	*%*	*The number of cases per 100 patients*	*Multiplicity of* of excess over left isomerism				
AVSD	1	2%	5	15	35%	65.2	13 times				
DORV	2	5%	10	11	26%	47.4	4.7 times				
SV	-	-	-	8	19%	34.8					
TGA	1	2%	5	12	28%	52.2	10.4 times				
PA	3	7%	15	8	19%	34.8	2.3 times				
PS	-	-	-	2	5%	8.7					
TAPVC	3	7%	15	18	42%	78.3	5.2 times				
PAPVC	2	5%	10	-	-	-		36.84	0.679	46.1%	< 0.01
Interrupted of IVC with hemiazygous continuation	15	35%	75	-	-	-					
Bilateral SVC	3	7%	15	10	23%	43.5	2.9 times				
VSD	1	2%	5	-	-	-					
HLHS	-	-	-	1	2%	4.3					
IAA	-	-	-	1	2%	4.3					
CoA	1	2%	5	-	-	-					
Total	32		160.0 ± 16.7	86		373.5 ± 16.7	2.3 times	t-distribution ± 9.57	-	-	< 0.01
Number of cases	20			23			-	-	-	-	-

It can be seen from the table 1, that the Correlation coefficient (r) at the level of 0.679 with a 99 % confidence ($p < 0.01$) indicates that there is from moderate to strong uphill (positive) relationship between the isomerism factor and the incidence of various types of congenital heart disease among the patients with heterotaxy syndrome.

Coefficient of determination ($R^2 \times 100$) shows that the isomerism factor in 46% causes changes in the incidence of congenital heart defects among the patients with HS.

In general, in all types of congenital heart defects, the total index of their frequency with right isomerism was 373.5 ± 16.7 cases per 100 patients, and with left

isomerism – 160.0 ± 16.7 per 100 patients, which in 2.3 times more (t-distribution = 9.57, p < 0.01). More clearly, the distribution of congenital heart disease in patients with left and right isomerism is shown in Figure 10.

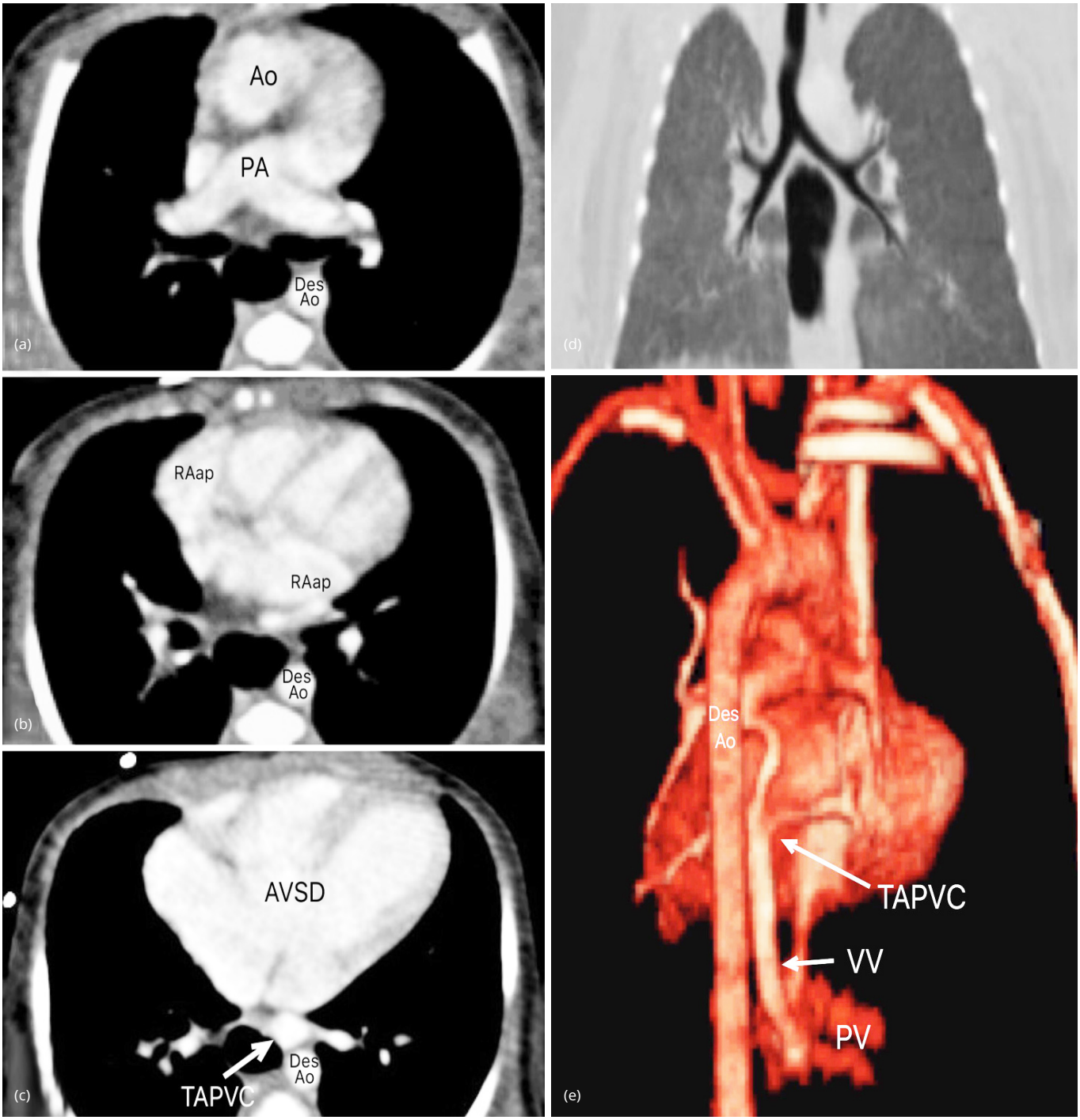

Figure 4 Transversal images (a, b, c), Minimum intensity projection (MiniP Thin) (d) and volume rendering technique (VRT) (e) images of heterotaxy syndrome, right isomerism, levocardia, transposition of great arteries (TGA), pulmonary atresia (PA) (a), infracardiac total anomalous pulmonary venous connection (TAPVC) draining into portal vein (c, e), atrioventricular septal defect (AVSD) (c), left aortic arch (LAA); eparterial bronchi (d); (RAap - right atrium appendage).

Discussion

In our study right isomerism was detected in 53%, whereas in studies of other institution left isomerism much more common than right isomerism [8, 9]. Left isomerism is usually associated with less severe cardiac defects and can occur without any cardiac defects.

Of the patients with right isomerism, 12 (52%) had levocardia, and 11 (48%) dextrocardia, in those with left isomerism, levocardia was in 15 (75%) patients, and dextrocardia was in 5 (25%), nearly similar findings being reported by Yildirim et al. [8].

It is very important for surgeon to know if patients have bilateral superior vena cava. We detected bilateral superior vena cava in 43% (n = 10) patients with right isomerism, and 15% (n = 3) of those with left isomerism, whereas Yildirim et al. [8] showed that patients with left isomerism

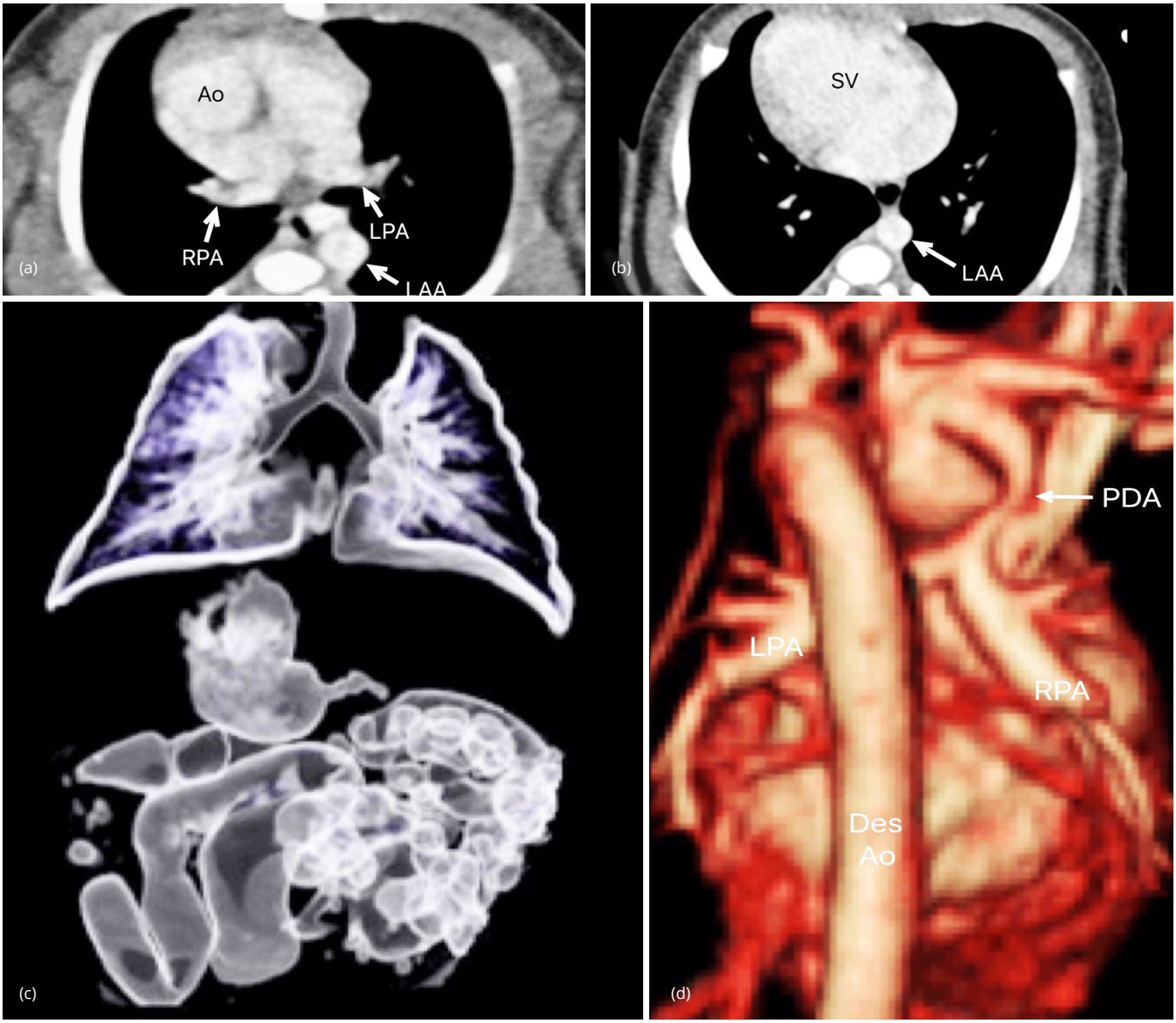

Figure 5 Transversal images (a, b) and VRT (c, d) of heterotaxy syndrome, right isomerism, dextrocardia, pulmonary atresia (PA), patent ductus arteriosus (PDA), left aortic arch (LAA), single ventricle (SV) (b); Intestinal malrotation (c); (RPA – right pulmonary artery, LPA – left pulmonary artery).

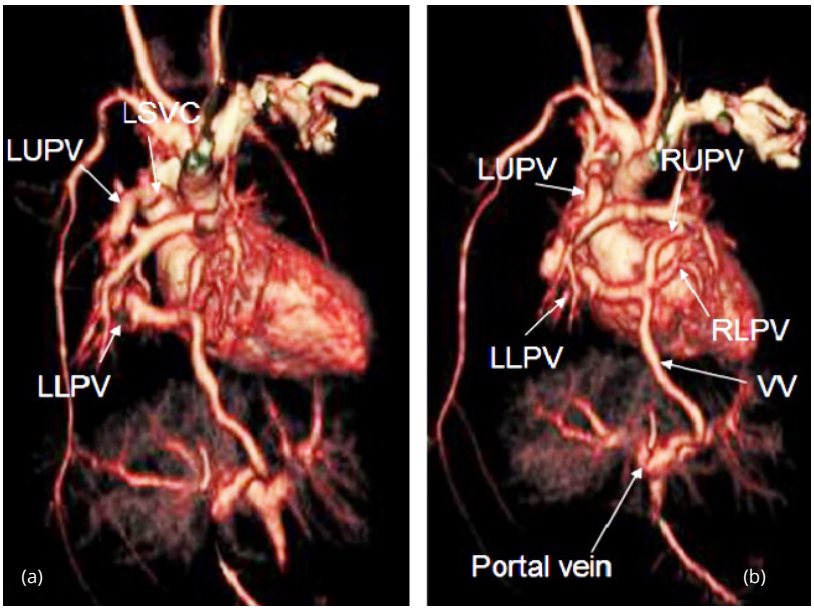

Figure 6 Volume rendering technique (VRT) images: (a) front side, and (b) back side, of heterotaxy syndrome, right isomerism, dextrocardia, atrioventricular septal defect (AVSD), double outlet right ventricle (DORV), transposition of great arteries (TGA), right aortic arch (RAA), total anomalous pulmonary venous connection (TAPVC) mixed (left upper pulmonary veins (LUPV) drain into left superior vena cava (LSVC), left and right lower and right upper pulmonary veins (LLPV+RUPV+RLPV via vertical vein (VV) drains into portal vein).

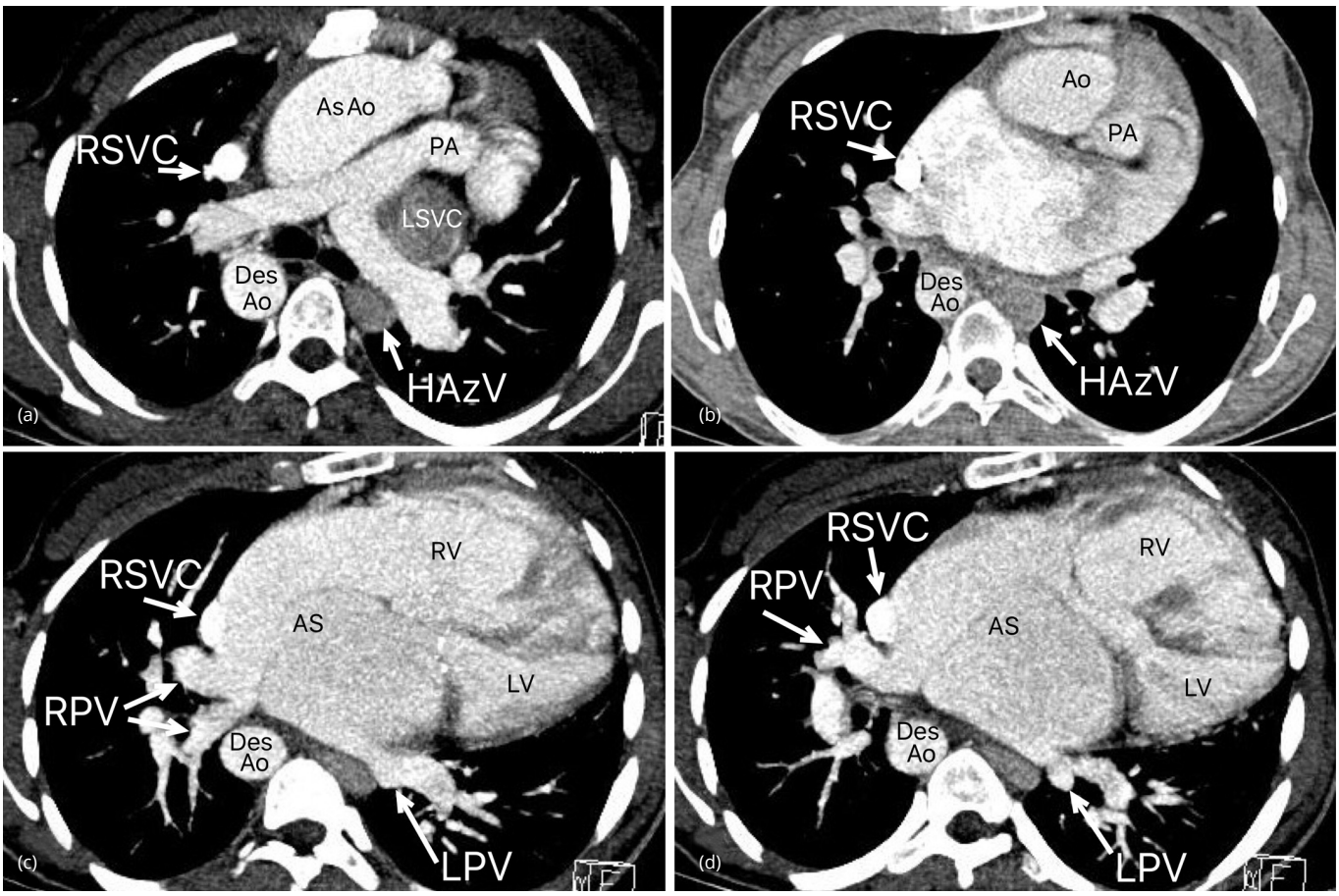

Figure 7 Multiplanar (MPR) images of heterotaxy syndrome, left isomerism, levocardia, double outlet right ventricle (DORV), transposition of great arteries (TGA) (a, b.), partial anomalous pulmonary venous connection (PAPVC) (c, d) – right pulmonary veins (RPV) drained into right sided atrium, left pulmonary veins (LPV) drained into left sided atrium, double superior vena cava (SVC), hemiazigos continuation into left superior vena cava (LSVC). (AS – atrial septum).

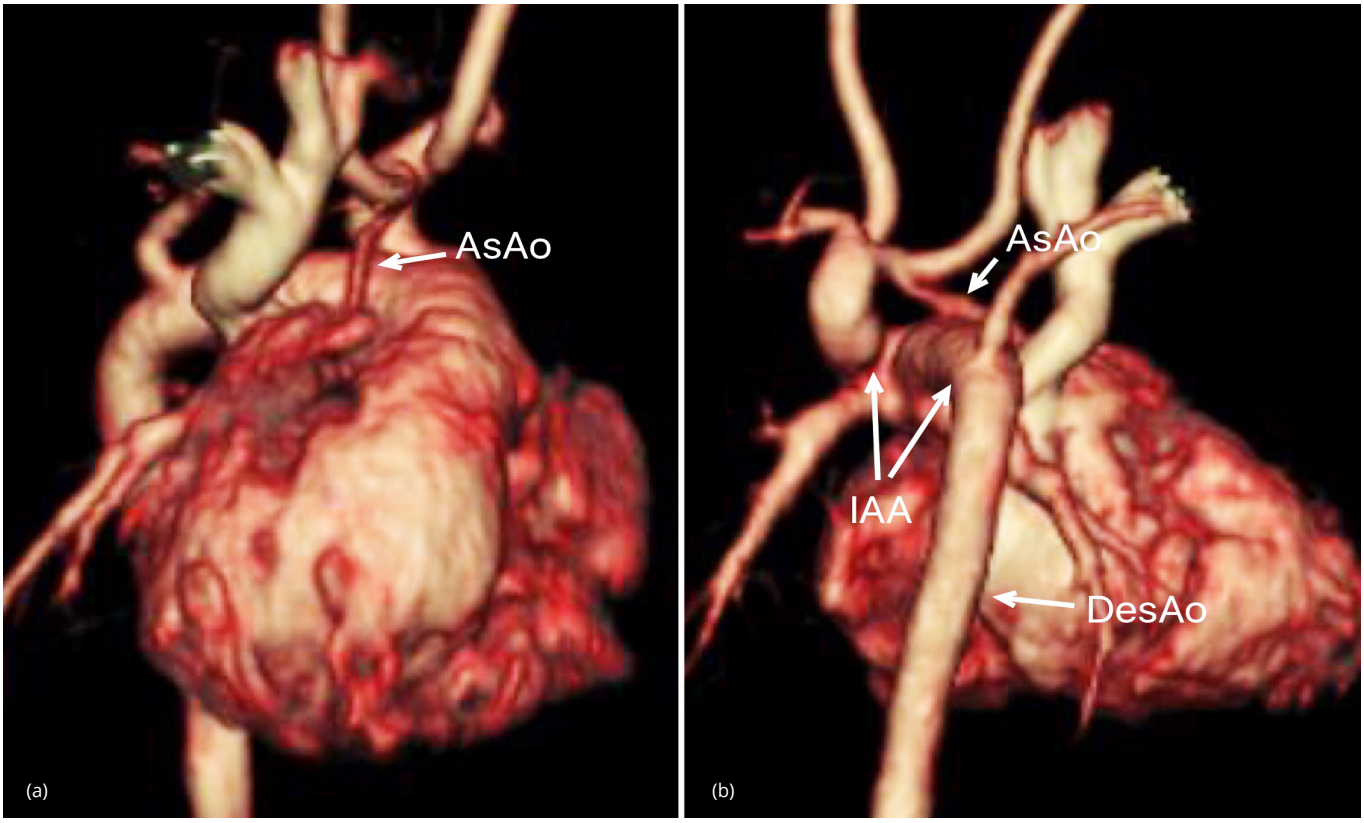

Figure 8 Volume rendering technique (VRT) images: (a) - front side, (b) - back side of heterotaxy syndrome, right isomerism, hypoplasia left heart syndrome (HLHS), interrupted aortic arch (IAA).

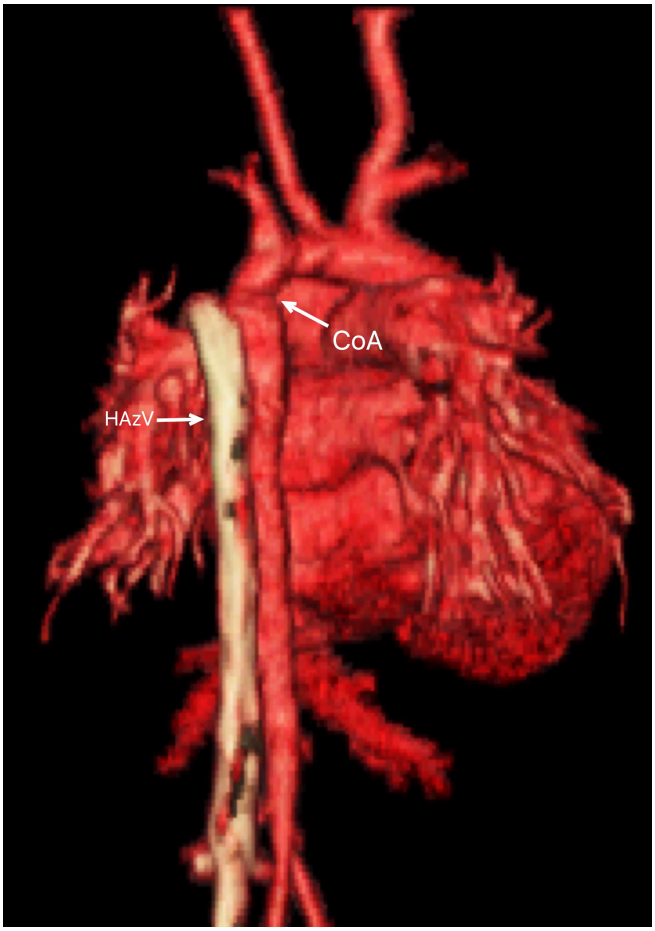

Figure 9 Volume rendering technique (VRT) image of heterotaxy syndrome, left isomerism, aortic coarctation (CoA), interrupted inferior vena cava with hemiazygos continuation.

had bilateral superior vena cava more often than patients with right isomerism (46.6% and 30.2% prospectively).

The most frequent cardiac defects detected in both group are atrioventricular septal defect, transposition of great arteries and double outlet right ventricle, whereas single ventricle, pulmonary stenosis, hypoplasia left heart syndrome and mostly atrioventricular septal defect (except one patient) was founded in patients with right isomerism. Interrupted inferior vena cava with hemiazygous continuation, partial anomalous pulmonary venous connection and aortic coarctation were detected only in patients with left isomerism. Gilljam et al. [10] noted that atrioventricular septal defect was frequent in both types of isomerism. It is worth mentioning that our data and Gilljam et al. [10] data regarding TAPV isomerism were almost the same (7% and 8% accordingly). This fact was surprising because both atrial chambers tend to be morphologically left in this setting.

Pulmonary atresia and stenosis were revealed in 10 (23%) of the patients with right isomerism, and 3 (7%) of the group with left isomerism. To the contrary, hypoplasia left heart syndrome was discovered in 2% of the patients with right isomerism, and coarctation of aorta in 2 % of the patients with left isomerism.

Conclusion

Mostly patients with heterotaxy syndrome have complex congenital heart disease (CHD) and require accurately assessment for future management. Multidetector computed tomography allows to obtain detailed data on the morphology of the heart, great vessels, the anatomy of

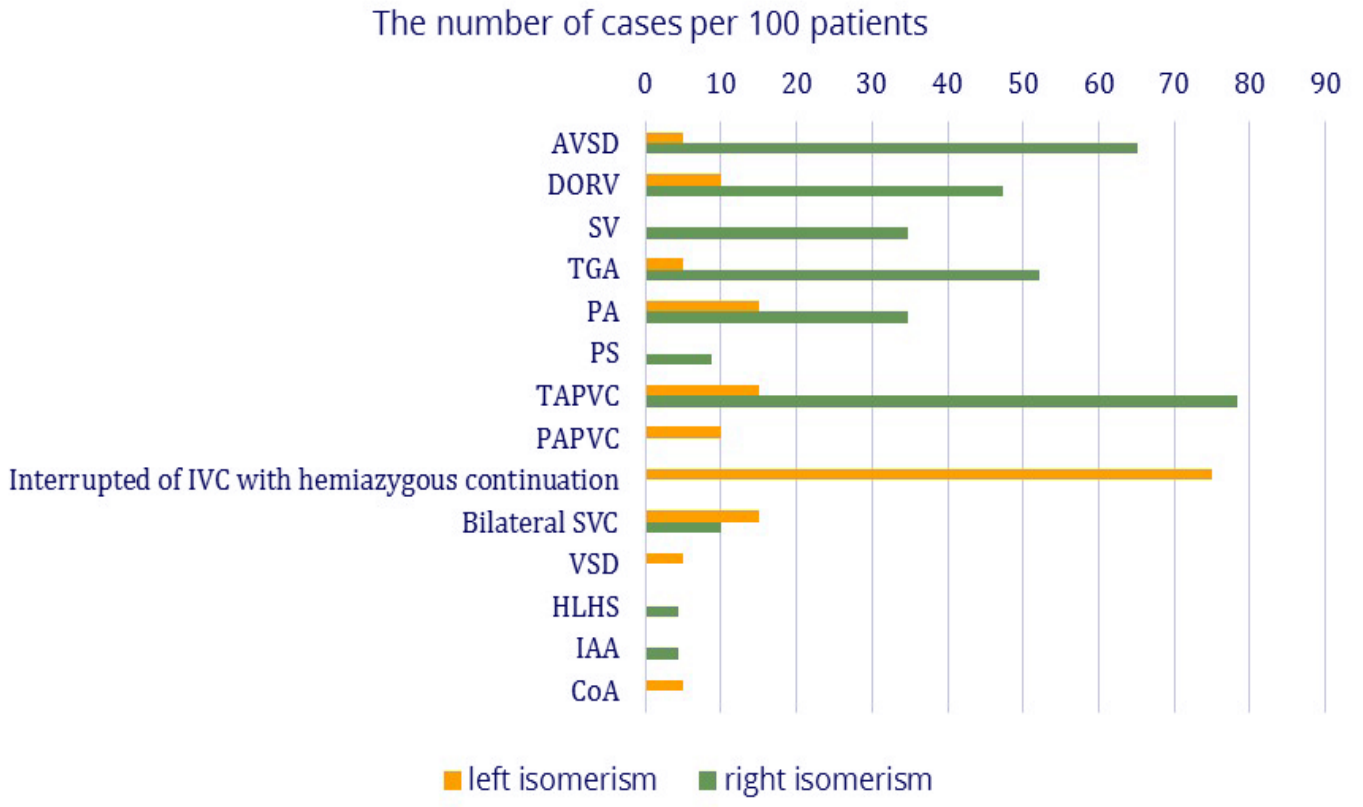

Figure 10 The number of cases of congenital heart diseases per 100 patients with right and left isomerism.

the internal organs and their mutual arrangement, make an accurate diagnosis of heterotaxy syndrome. Frequency and distribution of CHD in patients with heterotaxy syndrome and right isomerism higher than in patients with heterotaxy syndrome and left isomerism.

Conflicts of interest

Authors declare no conflicts of interest.

References

[1] Zhu L, Belmont JW, Ware SM. Genetics of human heterotaxias. Eur J Hum Genet. 2006; 14(1):17–25.

[2] Loomba R, Shah PH, Anderson RH, Arora Y. Radiologic Considerations in Heterotaxy: The need for detailed anatomic evaluation. Cureus. 2016; 8(1):e470.

[3] Van Praagh R. Terminology of congenital heart disease. Glossary and commentary. Circulation. 1977; 56 (2):139–143.

[4] Kim SJ. Heterotaxy syndrome. Korean Circ J. 2011; 41(5):227–232.

[5] Berg C, Geipel A, Kamil D, Knüppel M, Breuer J, et al. The syndrome of left isomerism: Sonographic findings and outcome in prenatally diagnosed cases. J Ultrasound Med. 2005; 24(7):921–931.

[6] Casey B. Two rights make a wrong: Human left-right malformations. Hum Mol Genet. 1998; 7(10):1565–15671.

[7] Abut E, Arman A, Guveli H, Bolukbas C, Kendir T, et al. Malposition of internal organs: A case of situs ambiguous anomaly in an adult. Turk J Gastroenterol. 2003; 14(2):151–155.

[8] Yildirim SV, Tokel K, Varan B, Aslamaci S, Ekici E. Clinical investigations over 13 years to establish the nature of the cardiac defects in patients having abnormalities of lateralization. Cardiol Young. 2007; 17(3):275–282.

[9] Qureshi AU, Kazmi U, Kazmi T, Sadiq M. Congenital heart defects associated with atrial heterotaxy. J Coll Physicians Surg Pak. 2012; 22(9):549–552.

[10] Gilljam T, McCrindle BW, Smallhorn JF, Williams WG, Freedom RM. Outcomes of left atrial isomerism over a 28-year period at a single institution. J Am Coll Cardiol. 2000; 36(3):908–916.