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Original Article

Clinical investigations over 13 years to establish the nature of the cardiac defects in patients having abnormalities of lateralization

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Abstract *Introduction:* The first step in diagnosing congenital cardiac malformations is to assess the arrangement of the atrial appendages. In patients with abnormal lateralization of the organs of the body, the arrangement of atrial appendages is neither normal, nor a mirror image of normal. There are 2 categories of abnormal arrangement based on the morphology of the atrial appendices, namely right isomerism and left isomerism, and in almost all instances these are found in the setting of so-called heterotaxy syndromes. *Objective:* To evaluate the various congenital cardiac malformations those are associated with abnormalities of lateralization, and to discuss the diagnostic tools, therapeutic options, and outcome for these patients. *Patients and methods:* We studied 134 patients, who had been admitted to our department of paediatric cardiology with known abnormalities of lateralization and congenital cardiac defects between 1990 and 2003. The data relating to each patient was evaluated retrospectively. The arrangement of the atrial appendages was established echocardiographically, and/or angiographically, and/or on the basis of morphologic investigations during the operation. These studies showed that 43 (32.1%) of the patients had right isomerism, and 88 (65.7%) had left isomerism. In 2 (1.5%), there was mirror-imaged arrangement, while in the final patient (0.07%), we were unable to determine sidedness with certainty. The median age at diagnosis was 0.66 years, and the females outnumbered the males in a ratio of 3 to 1. Patients in the 2 isomeric groups were compared with regard to age, cardiac defects, diagnostic tools and outcomes. *Results:* The difference in mean ages of the two groups of patients was statistically significant, those with right isomerism being 1.0 minus or plus 1.5 years, as opposed to those with left isomerism being 3.3 minus or plus 4.7 years (*P* is less than 0.005). Of the patients with right isomerism, 32 (74.4%) had left-sided, and 11 (25.6%) right-sided hearts, whereas in those with left isomerism, the hearts were left-sided in 65 (73.9%), and right-sided in 21 (23.9%), with 2 (2.2%) positioned in the midline. Extracardiac totally anomalous pulmonary venous connection was more common in those with right isomerism, being found in 13 patients (30.2%) as opposed to 5 patients (5.7%) with left isomerism. In only 8 of those with right isomerism did we find two perforate atrioventricular valves (18.6%), this arrangement being found in 34 (38.6%) of those with left isomerism. Pulmonary atresia and stenosis were present in 40 (93.0%) of those with right isomerism, but also in 41 (46.6%) of the patients with left isomerism. Angiographic and echocardiographic investigations were concordant in about three-quarters of patients with both right and left isomerism. All patients with extracardiac totally anomalous pulmonary venous connection died. Overall, 22 of the patients with right isomerism died (51.2%), as opposed to 20 (22.7%) of those with left isomerism. *Conclusion:* Our experience confirms that patients with right isomerism have more complex cardiac defects than those with left isomerism. Overall, the presence of isomerism carries a poor prognosis, the more so for right

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isomerism, with this related to the complex cardiac abnormalities. In our cohort, extracardiac totally anomalous pulmonary venous connection with pulmonary arterial obstruction was always a fatal combination. The mapping of cardiac and abdominal morphologies is still essential for proper diagnosis of these syndromes, especially in fetal life.

Keywords: Isomerism; morphology; prognosis

THE FIRST STEP IN DIAGNOSING CONGENITAL cardiac malformations is to assess the arrangement of the atrial appendages, this being the marker of cardiac lateralization. This is the initial step in the sequential segmental analysis of abnormal cardiac structure.[1–3] The most complex congenital malformations, typically involving abnormal systemic and pulmonary venous connections and isomeric atrial appendages, are known to be associated with malformations of the spleen.[4–6] The presence of isomeric atrial appendages obviously rules out the possibility of the cardiac structures being normally arranged, and in almost all instances the arrangement of the organs is the rest of the body is neither normal, nor a mirror image of normal. Isomerism itself can be divided into the categories of right and left isomerism.[2,3,5,7] It is now well established that, in all patients with isomerism, it is mandatory to identify with precision all the cardiac malformations, and the surgeon or cardiologist attempting palliation or correction must have a clear understanding of each anomaly.[8–10] Our aim in this study was to evaluate the varied cardiac malformations found in a cohort of patients known to have isomerism. Based on this experience, we then discuss the tools available for diagnosis, the therapeutic options, and the prognosis for these patients.

Patients and methods

We identified 134 patients admitted to our department of paediatric cardiology with abnormalities of lateralization and congenital cardiac defects between 1990 and 2003. For each patient, we evaluated the data retrospectively.

The cardiac sidedness was established by direct morphologic investigation of atrial appendages and arrangement of the abdominal great vessels during any surgical operations, the angiographic findings regarding the arrangement of the abdominal great vessels, and/or angiograms of the atrial appendages, and angiography and bronchial sidedness, or echocardiography and bronchial sidedness. Diagnosis of the isomerism according to the arrangement of the abdominal great vessels was based on the definitions published by Huhta et al.[11] A patient was diagnosed as having right isomerism when the aorta and inferior caval vein were positioned adjacent to each other, and either to the right or the left side of the spine, with the inferior caval vein anterolateral to the abdominal aorta. A patient was diagnosed with left isomerism when the inferior caval vein was itself interrupted, and continued through the azygos or hemiazygos venous system posterior and on the same side of the spine as the abdominal aorta.

Based on these diagnostic criterions, we found that 43 (32.1%) of our patients had right isomerism, 88 (65.7%) had left isomerism, 2 (1.5%) had mirror-imaged arrangement, while we were unable to determine sidedness with certainty in the final patient (0.07%).

The median age at diagnosis was 0.66 years, and the females outnumbered the males in a ratio of 3 to 1. For each patient, we recorded age, gender, electrocardiography results (if available), abdominal ultrasound findings (if available), cardiac morphology, sidedness of the bronchial tree, methods of treatment, and outcome.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (version 11.0; SPSS, Chicago, III, USA). Results for the patients with right as opposed to left isomerism were compared using a two-tailed *t* test.

Results

The major complaint and/or cause of referral of the patients was cyanosis in 77 (57.5%), with other presenting complaints being respiratory distress in 18 (13.4%), suspicions of cardiac disease in 14 (10.4%), cyanosis coupled with fatigue in 8 (6%), and recognition of a systolic murmur in 6 (4.5%), with the symptoms being non-specific in the remaining 11 patients (8.2%). There was parental consanguineous in 9 (20.9%) of those with right isomerism, and in 27 (30.7%) of the patients with left isomerism. Those with right isomerism presented at an age of 1.0 year plus or minus 1.5 years, as opposed to 3.3 years plus

of minus 4.7 years for those with left isomerism, this difference being statistically significant *P* is less than 0.005).

Of the 43 patients with right isomerism, 32 (74.4%) had left-sided hearts and 11 (25.6%) had right-sided hearts. Of those with left isomerism, 65 (73.9%) had left-sided hearts, 21 (23.9%) had right-sided hearts, with the heart positioned in the midline in the remaining 2 patients (2.2%).

None of the patients with right isomerism exhibited interruption of the inferior caval vein. In these patients, the inferior caval vein was on the right of the vertebral column in the abdomen in 29 (67.4%), and on the left in the other 14 (32.6%). The inferior caval vein was interrupted in 83 (94.3%) of the patients with left isomerism. The hepatic veins drained directly into the right-sided atrium in 60 (68.2%) of these patients, into the left-sided atrium in 20 cases (22.7%), and into both atriums in 3 cases (3.4%). Of the 5 (5.7%) patients without interruption of the inferior caval vein, the vein was on the right of the vertebral column in the abdomen in 4, and on the left in the other. In these patients, the diagnosis of left isomerism was established by the direct identification of the atrial appendages during surgical operations.

In 2 of the patients in whom a mirror-imaged arrangement had been suggested by echocardiography, angiocardiography and bronchial morphology, the atrial appendages were both found to have right morphology during surgical operations. Another patient had been diagnosed as having right isomerism on the basis of angiocardiography and bronchial appearance, but a definitive diagnose of mirror-imagery of the appendages was established by direct investigation during the surgical operation.

We found bilateral superior caval veins in 13 (30.2%) of those with right isomerism, and 41 (46.6%) of the patients with left isomerism.

In Table 1, we list the types of atrioventricular connections found in the two groups of patients stratified on the basis of the morphology of the atrial appendages. Totally anomalous pulmonary venous connection, of course, is universally present in patients with isomerism of the right atrial appendages. In 30 of our patients, however, the pulmonary veins, although anomalously connected in that they joined an atrium with a right atrial appendage, did join to the atrial chambers, with 5 of these draining to the right-sided atrium via a common channel, and one to a divided atrial chamber. In the other 7 patients with right isomerism, the pulmonary venous return was to the brachiocephalic vein via a vertical vein in 6, and infradiaphragmatically to the portal venous sytem in the other. In 2 patients with left isomerism, the pulmonary venous return was also anatomically anomalous, draining to the atrial chambers via a coronary sinus in 1, and infradiaphragmatically to the portal venous system in the other. In 3 other patients, all pulmonary veins drained to the right-sided atrium via a common channel. These differences in pulmonary venous connection between patients having right and left isomerism were statistically significant (*P* is less than 0.05).

A common atrioventricular junction was frequent in both groups, being found in 72.1 % of those with right isomerism, and 48.9% of those with left isomerism. The common junction was guarded by a common valve in 49.6%, but by two valvar orifices with an "ostium primum" defect in the remaining 10 patients. Separate atrioventricular junctions guarded by tricuspid and mitral valves were found in 8 (18.6%) of the patients with right isomerism, and 34 (38.6%) of those with left isomerism.

Table 2 details the ventriculoarterial connections present in the 2 groups. Concerning the nature of the ventricular mass, of the 43 patients with right isomerism, 6 (14.0%) had a hypoplastic right ventricle, with either double inlet to a dominant left ventricle or absence of one atrioventricular connection, 16 (37.2%) had a hypoplastic left ventricle, again with either double inlet to the right ventricle, or a dominant right ventricle with absence of one atrioventricular connections, 1 (2.3%) had a solitary ventricle of indeterminate morphology, and 20 (46.5%) had balanced ventricles. Within the overall group of those with two ventricles, the topology was right-handed in 74.2%, and left handed in the remaining 25.8%. Of the 88 patients with left isomerism, 5 (5.7%) had a hypoplastic right ventricle with either double inlet to the dominant left ventricle, or absence of one atrioventricular connection, 24 (27.3%) had a hypoplastic left ventricle with double inlet or absence of one atrioventricular connection, the right ventricle being dominant, 2 (2.3%) had solitary and indeterminate ventricles, and 57 (64.8%) had balanced ventricles. Within this group of patients with left isomerism, the ventricular mass showed right hand topology in 72.2% of those with two ventricles, and left hand topology in the remaining 27.8%. Pulmonary atresia or stenosis was found in 40 (93.0%) of those with right isomerism, and 41 (46.6%) of the group with left isomerism. In contrast, aortic stenosis, atresia, or coarctation was found in none of those with right isomerism, and 6.8% of those with left isomerism.

When we analyzed the level of agreement between the diagnostic tools used to assess the identified abnormalities of lateralization, we found 76.3% concordance between echocardiography and angiography in the group with right isomerism, and 73.8% concordance in those with left isomerism.

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Table 1. The type and mode of atrioventricular connection in the groups with right isomerism and left isomerism. With regard to ventricular topology, this is described only for those with functionally biventricular arrangements.

	Right isomerism (n = 43)	Left isomerism (n = 88)
Type of atrioventricular connection		
Biventricular	31 (72.1%)	72 (81.8%)
Double inlet ventricle	10 (23.3%)	6 (6.8%)
Absent AV connection	2 (4.6%)	10 (11.4%)
Mode of atrioventricular connection		
Two separate and perforated valves	8 (18.6%)	34 (38.6%)
Common AV valve	30 (69.8%)	35 (39.8%)
Two valves with ostium primum defect	1 (2.3%)	9 (10.2%)
Absent RAV connection	1 (2.3%)	0
Absent LAV connection	2 (4.6%)	8 (9.1%)
Common AV junction with imperforate right AV valve	0	1 (1.1%)
Common AV junction with imperforate left AV valve	1 (2.3%)	1 (1.1%)
Ventricular topology		
Functionally univentricular	12 (29.9%)	16 (19.8%)
Functionally biventricular with right-hand topology	23 (53.5%)	52 (59.1%)
Functionally biventricular with left-hand topology	8 (18.6%)	20 (22.7%)

Abbreviation: AV: atrioventricular

Table 2. Ventriculoarterial connections in the groups with right atrial isomerism and left atrial isomerism.

Ventriculoarterial connections	Right isomerism (n = 43)	Left isomerism (n = 88)
Concordant	7 (16.3%)	46 (52.3%)
Discordant	4 (9.3%)	8 (9.1%)
Double-outlet right ventricle	22 (51.2%)	28 (31.8)
Double-outlet left ventricle	0	1 (1.1%)
Single-outlet ventricle	10 (23.3%) (all via an aorta)	5 (5.7%) 1 via a pulmonary trunk, and remaining 4 via the aorta)

In our patients, data was available concerning bronchial sidedness in 22 (51.2%) of those with right isomerism, and 60 (59.2%) of those with left isomerism. The findings were concordant in 16 of the 22 with right isomerism in whom it was available, and in 52 of the 60 patients with left isomerism. The p-wave axis showed normal polarity in 27 (62.8%) of those with right isomerism, but was abnormal in 41 (46.6%) of those with left isomerism. Details of the electrocardiographic findings and bronchial arrangement in the 2 groups are shown in Table 3.

Extracardiac anomalies

In those with right isomerism, 1 patient had anal atresia, 1 had an omphalocele, 1 had isolated cleft palate, and 1 had right-sided renal agenesis. In the patients with left isomerism, 1 patient had Down's syndrome, 1 patient had been the product of "in vitro" fertilization, and 1 had gastroschisis.

Table 3. Electrocardiographic findings and bronchial morphology in the groups of patients with right and left isomerism.

	Right isomerism (n = 43)	Left isomerism (n = 88)
Electrocardiography findings		
No record	15 (34.9%)	32 (36.4%)
Normal sinus rhythm	27 (62.8%)	11 (12.5%)
p-wave abnormalities	1 (2.3%)	41 (46.6%)
Complete AV block	0	4 (4.6%)
Bronchial arrangement		
Right isomerism	16 (37.2%)	0
Left isomerism	0	52 (59.1%)
Usual	0	2 (2.3%)
Mirror-imaged	2 (4.7%)	2 (2.3%)
Uncertain	4 (9.3%)	4 (4.6%)
No record	21 (48.8%)	28 (31.8%)

Abdominal ultrasonographic findings

In all, details of abdominal ultrasonographic examination were available in 16 patients. This showed that, in those with right isomerism, 5 had asplenia, 2 had normal visceral arrangement, 2 had mirror-imaged arrangement, and 1 had a normal spleen with a midline liver. In the group with left isomerism, 2 had polysplenia, 3 had normal visceral arrangement, and 1 had mirror-imaged arrangement.

Therapeutic procedures

Of the 42 patients with right isomerism, 20 (46.5%) individuals underwent a total of 26 surgical interventions. All of them were palliative procedures, with 18 (69.2%) being creation of systemic-to-pulmonary shunts, 3 (11.5%) being conversions to the Fontan

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circulation, one being a fenestrated procedure, 3 (11.5%) being constructions of bidirectional cava-pulmonary connections, 1 (3.9%) procedure being exploratory, and the final procedure being closure of the fenestration. Total correction was not attempted in any patient.

In the patients with left isomerism, surgical procedures were performed in 61 (69.3%). In all, these patients required 72 surgical procedures, with 22 being systemic-to-pulmonary shunts (30.6%), 22 (30.6%) total corrections, 8 (11.1%) banding of the pulmonary trunk, 5 (6.9%) closure of a persistently patent arterial duct, 4 (5.5%) Fontan conversions, with 1 fenestration, 4 (5.5%) bidirectional cavapulmonary connections, 2 (2.8%) pulmonary valvotomies, 2 (2.8%) exp1orations, 2 atrial septectomies (2.8%), and the final one again being the closure of the fenestration. In 6 patients, a permanent pacemaker was inserted because of complete atrioventricular dissociation. Details the surgical procedures are summarized in Table 4.

Outcomes

In total, 22 (51.2%) of those with right isomerism, and 20 (22.7%) of those with left isomerism died, this difference being statistically significant (*P* is less than 0.005). In those with right isomerism, 7 died with severe haemodynamic instability in the early period after surgery, 7 patients died 5 or more days after surgery for various reasons, including respiratory failure, severe neurologic problems, disseminated intravascular coagulopathy, sepsis, and heart failure with cardiac tamponade, while 3 patients died early after an angiographic procedure. The remaining 5 patients died at home or another health centre, mostly from cardiac causes.

In the group with left isomerism, 13 patients died with severe haemodynamic instability in early period after surgery, 3 died 5 or more days after surgery due to sepsis, pulmonary embolus, or respiratory failure, and 3 died early after an angiographic procedure. The remaining patient died at home owing to cardiac causes. All 18 patients within the 2 groups with a totally anomalous extracardiac pulmonary venous connection died. In Table 5, we summarise the outcomes of the surgical procedures.

Discussion

The first step in sequential segmental analysis in any patient suspected of having congenital cardiac disease is to evaluate the arrangement of the atrial chambers. In the past, it was often thought that there were three types of arrangement, namely the usual arrangement, or "situs solitus", its mirror-imaged variant, often called "situs inversus", and so-called "situs ambiguus", in which the atrial chambers were considered to show a complex and indeterminate pattern[2]. As was shown by Uemura et al.,[4–6] however, when following the tenets of Van Praagh as expressed in the "morphological method", namely to identify the atrial chambers according to their most constant component, the appendage, then all patients with presumed ambiguous arrangement can be stratified into the groups with isomerism of either the right or left atrial appendages. Determination of the cardiac arrangement in this fashion is important for the physician who performs surgery or any angiographic intervention, albeit that, in the clinical setting, it is not always possible to identify the appendages with certainty. In these patients, nonetheless, who have some of the most complex forms of congenital cardiac diseases associated with abnormalities of lateralization in the heterotaxy syndromes,[4,7,8,12–14] it is possible, as shown by our experience, still to stratify into those with right or left isomerism depending on the constellations of malformations in the different groups.

It is also possible to stratify the patients on the basis of the echocardiographic findings relating to the arrangements of the abdominal great vessels, as first demonstrated by Huhta et al.[11] As these authors, and as was confirmed by Van Praagh et al.[15] and Rubino et al.[13] in the syndrome they described as "asplenia", the inferior caval vein continues without interruption in almost in all cases. The situation is more complicated in left isomerism. In the autopsy series analysed by Uemura et al.,[4] the inferior caval vein was interrupted in 86% of cases, while in the series reported by Van Praagh et al.,[15] albeit described in terms of "polysplenia", 80% of the cases were from patients with interrupted inferior caval veins. In our series, we found interruption of the inferior caval vein in 94%, of those shown to have left isomerism, which is very close to the 92% incidence reported by Gilljam et al.[16] in their patients with left isomerism. In the series of Gilljam et al.,[16] however, some of their patients were found to have usual atrial arrangement despite interruption of inferior caval vein. Indeed, it is well recognized that interruption of the inferior caval vein is not necessarily a marker of isomerism of the atrial appendages, even when associated with multiple spleens.[17]

The findings of arrangement of the organs as determined by different methods, specifically echocardiography, angiography and magnetic resonance imaging, were compared by Wang et al.,[18] and by Geva et al.[19] They suggested that angiography was a more useful tool for establishing the systemic venoatrial connections, but that magnetic resonance imaging was better for showing the pulmonary venous connections than the other methods. In our experience,

Table 4. Surgical procedures performed.

Procedure	Right isomerism (n = 20, total intervention = 26)	Left isomerism (n = 61, total intervention = 72)
Aortopulmonary shunt	18 (69.2%)	22 (30.6%)
Biventricular repair with open-heart surgery	–	22 (30.6%)
Banding of the pulm. trunk	–	8 (11.1%)
Closure of arterial duct	–	5 (6.9%)
BCPC	3 (11.5%)	4 (5.5%)
Fontan procedure	3 (11.5%)	4 (5.5%)
Pulmonary valvotomy	–	2 (2.8%)
Atrial septectomy	–	2 (2.8%)
Closure of the fenestration	1 (3.9%)	1 (1.4%)
Explorative surgery	1 (3.9%)	2 (2.8%)

Abbreviation: BCPC: bidirectional cavapulmonary connection

Table 5. Outcomes related with the surgical procedure.

Procedure	Those dying with right isomerism	Those dying with left isomerism
Aortopulmonary shunt	9/18 (50%)	2/22 (9.1%)
Biventricular repair with open-heart surgery	–	6/22 (27.3%)
Banding	–	3/8 (37.5%)
Closure of duct	–	2/5 (40%)
BCPC	3/3 (100%)	1/4 (25%)
Fontan procedure	2/3 (66.6%)	0/4
Pulmonary valvotomy	–	0/2
Atrial septectomy	–	2/2 (100%)
Closure of the fenestration	–	0/1
Explorative surgery	0/1	0/2
Total	15/25 (60%)	16/72 (22.2%)

Abbreviation: BCPC: bidirectional cava pulmonary connection

we found the concordance between echocardiography and angiography to be about three-quarters for both groups of patients.

Overall, nonetheless, it is now well established that the arrangement of the atrial appendages correlates relatively poorly with splenic status, somewhat better with pulmonary lobation, but best with bronchial morphology. Thus, the findings reported by Uemura et al.[6] for right isomerism, and by Van Praagh et al.[15] for "asplenia", show that the correlation with bronchial arrangement was 89%, and 69%. For those with left isomerism, and "polysplenia", the figures were 98% and 48%, respectively. This in itself demonstrates the advantage to be gained in describing cardiac arrangement on the basis of the morphology of the appendages rather than the state of the spleen. In this respect, Gilljam et al.[16] in their clinical study, found the correlation with bronchial morphology to be 96%. In our series, information concerning bronchial arrangement was available in only a proportion of patients. In those in whom we were able to extract this information by direct radiography, we found correlations of 72.7% for those with right isomerism, and 86.7% for those with left isomerism.

For the surgeon, it is important to know whether the patients have bilateral superior caval veins prior to any attempted surgical procedure. We found bilateral superior caval veins in 31% of our patients with right isomerism, and 46% of those with left isomerism, similar findings being reported by Hashmi et al.,[20] and by Gilljam et al.[16]

The worst outcome for patients with isomeric atrial appendages occurs when there is totally anomalous pulmonary venous connection to an extracardiac site together with restricted flow of blood to the lungs. The pulmonary veins, of course, are always totally anomalously connected whenever the patient has isomeric atrial appendages, and Uemura et al.[4] showed that the pulmonary venous connection was potentially obstructed even when the veins come back to the heart. It is important, therefore, to check for obstructed venous return in all patients identified as having right isomerism. The prognosis for these patients remains poor, inspirit of developments in modern congenital heart surgery.[9,10,21] It should

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also be noted that Gilljam et al.[16] found totally anomalous pulmonary venous connection in 8% of their patients with left isomerism, this being an unexpected finding, since both atrial chambers are trying to be morphologically left in this setting. We found, nonetheless, that 6% of our patients had totally anomalous pulmonary venous connection in the setting of left isomerism.

It is well established that the cardiac malformations are much more complex in right isomerism than in left, and hence it is hardly surprising that these patients have a poorer outcome.[21] Other than totally anomalous pulmonary venous connection, pulmonary arterial stenosis or atresia are common in patients with isomerism, especially in right isomerism, and this feature has a major negative affect on outcome.[17,20] In our series, pulmonary arterial obstruction was common, being found in over nine-tenths of the patients with right isomerism, and in almost half of those with left isomerism.

A common atrioventricular junction is also frequent in both types of isomerism, usually guarded by a common valve, but sometimes seen in the setting of the so-called "ostium primum" defect. We found separate atrioventricular junctions guarded by mitral and tricuspid valves in only one-sixth of our patients with right isomerism, but in over one-third of those with left isomerism. These findings are in keeping with results of autopsy examination of patients with "heterotaxy syndromes".[15,16,20]

It is also well established that the outcome for patients having isomerism of the right atrial appendages is far worse than for those with left isomerism, despite the introduction of modern surgical techniques.[21] The possibility of correction remains low for those with right isomerism, with no such patients in our series undergoing total correction. This is a more realistic option for those with left isomerism, and the outcome is known to be better. Amongst our cohort, the overall mortality rate was greater than 50% for those with right isomerism, but only 23% for those with left isomerism. The neonatal period was particularly critical for those having right isomerism.

An added problem for those with right isomerism is its known association with absence of the spleen, and the potential complications produced by the lack of splenic tissue. We have limited records concerning the state of the spleen in our patients, so we cannot with any confidence discuss the outcomes with regard to absence of the spleen, or multiple spleens. Knowing, nonetheless, that patients with right isomerism do typically have absence of the spleen, and that this predisposes to severe infections,[22,23] we recommend vaccination for all these patients , especially against pneumococcal infections.

In conclusion, our experience confirms that patients with isomeric atrial appendages continue to have poor outcomes, with mortality rates being particularly high for those with right isomerism.[21] Surgery is palliative in the majority of such patients, albeit that even in our cohort, total correction was possible for one-third of the patients with left isomerism. In our experience, nonetheless, the associations of extracardiac total anomalous pulmonary venous connection with pulmonary arterial obstruction always proved fatal. The detailed mapping of both cardiac and abdominal morphology in the setting of abnormalities of lateralization, therefore, remains essential, especially during fetal life.

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