ORIGINAL ARTICLE

Left atrial isomerism: 10-year surgical outcomes at a single center

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Introduction. *Left atrial isomerism (LAI) is a complex entity with various treatments and outcomes. The aim of the study was to analyze the surgical outcomes of patients with LAI undergoing cardiac surgery.* ***Methods.*** *A retrospective study was carried out on patients with a diagnosis of LAI who underwent cardiac surgery were included, between January 1, 2010 and March 31, 2020. The demographic characteristics and perioperative conditions were described.* ***Results.*** *Twenty-seven patients were included; the median age was 6 years (IQR 3 -11), 40.7% males. The main diagnoses in patients undergoing the univentricular approach were atrioventricular canal (25.9%) and pulmonary atresia (11.1%), while cases undergoing the biventricular approach were atrial septal defect (44.4%) and ventricular septal defect (40.7%). The most common surgical procedures were modified Blalock–Taussig shunt (18.5%) in the univentricular approach and repair of septal defects (4.6%) in the biventricular approach. No early or late deaths were found.* ***Conclusions.*** *The survival of LAI in our center is similar to that of other referral centers. Patients with LAI must undergo a rigorous evaluation to determine an appropriate surgical strategy.*

Key words: *Congenital heart disease; Heterotaxy syndrome; Left atrial isomerism.*

Introducción. *El isomerismo auricular izquierdo (IAI) es una entidad compleja, con un tratamiento y resultados diversos. El objetivo del estudio fue analizar los resultados quirúrgicos de los pacientes con IAI sometidos a cirugía cardíaca.* ***Métodos.*** *Se realizó un estudio retrospectivo en el que se incluyeron pacientes con diagnóstico de IAI sometidos a cirugía cardiaca, del 1 de enero de 2010 al 31 de marzo de 2020. Se describieron las características demográficas y condiciones perioperatorias.* ***Resultados.*** *Se incluyeron 27 pacientes, la mediana de edad fue 6 años (RIQ 3 -11), el 40.7% fueron hombres. Los principales diagnósticos en pacientes llevados a estrategia univentricular fueron: el canal auriculoventricular (25.9%) y atresia pulmonar (11.1%), mientras que los casos llevados a estrategia biventricular fueron: comunicación interauricular (44.4%) y comunicación interventricular (40.7%). Los procedimientos quirúrgicos más comunes fueron la fístula sistémico pulmonar (18.5%) en la estrategia univentricular, y la reparación de los defectos septales (4.6%) en la estrategia biventricular. No se encontraron muertas tempranas, ni tardías.* ***Conclusiones.*** *La supervivencia de la IAI en nuestra institución es similar a la de otros centros de referencia. Los pacientes con IAI deben someterse a una evaluación rigurosa para determinar una estrategia quirúrgica adecuada.*

Palabras clave: *Cardiopatía congénita; Síndrome de heterotaxia; Isomerismo auricular izquierdo.*

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The prevalence of congenital heart disease (CHD) ranges from 2.1 to 12.3 per 1000 live births [1], with an incidence of 6 to 8 per 1,000 live births [2], with atrial isomerism (AI) being one of the most severe and rare forms with a prevalence of 1 per 10,000 to 20,000 live births [3,4].

AI is an alteration of the body's left-right axis, giving mirror images symmetrical to each other with the morphology of right or left-sided structures [4-6]. Left atrial isomerism (LAI) is associated with other cardiovascular malformations [3,4-7], where the diagnosis and medical and surgical management pose several methods and alternatives [7-10]; however, postoperative mortality is variable in this group of patients [4].

The aim of this study was to analyze the surgical outcomes of patients with LAI who underwent cardiac surgery at a single center.

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MATERIAL

The local institutional Review Board approved the study, waving the need for patient consent. A descriptive, observational, retrospective study was performed; it included patients under 18 years, diagnosed with LAI who underwent cardiac surgery from January 1, 2010 to March 31, 2020. Patients with incomplete records were excluded. The variables were collected from the clinical and surgical notes. Demographic data, diagnoses, previous interventions, including surgical interventions such as cardiac catheterization, morbidity, and complications before discharge, were recorded. The diagnosis of LAI was made through the morphological method, considering a morphologic left atrium when it was located in a more cephalic position in the mediastinum concerning the right atrium, in addition to a thin and tubular appendage with a narrow neck and absence of the crista terminalis, and the vestibule of the mitral valve always confluent with the smooth side of the pulmonary venous component, that is, the pectineus muscles are only inside the appendage. It was complemented with bronchopulmonary morphology where the left bronchus was longer than the right bronchus (1.5 to 2 cm), and the left pulmonary artery crossed over the hypoarterial bronchus. The diagnosis was supported by echocardiogram, computed tomography, and cardiac catheterization (**Fig. 1**) (**Fig. 2**). Hypotension was considered when systolic blood pressure was below the 5% percentile according to age [11], and vascular injury was eventual damage to a vessel that may occur in anticipation of the surgical procedure. Major bleeding was defined as blood loss of 7 mL/kg/h or more for 2 or more consecutive hours during the first 12 postoperative hours or 84 mL/kg or more during the first 24 postoperative hours or the need for surgical re-exploration due to bleeding in the first 24 postoperative hours [12].

Patients were followed at the outpatient clinic one month, three months, six months, and 12 months after surgery, and then once per year, unless an earlier follow-up was required. Follow-up was documented as their last visit in March 2020. Early mortality was defined as death occurring in the first 30 days after surgery.

Statistical analysis

Descriptive statistics were used for the demographic variables. Frequencies and percentages were used to describe categorical variables, while mean ± standard deviation (±SD) or median (interquartile range [IQR]) were used for quantitative variables, according to the data distribution, through the Kolmogorov-Smirnov test. The software used was SPSS version 24.0, SPSS Inc., Chicago, IL.

RESULTS

Clinical-demographic characteristics

Twenty-seven patients were included. 40.7% (n=11) were male; the median age was 6 years (IQR 3 - 11), the median weight was 19.4 kg (IQR 12 - 30), and the median height was 119 (IQR 94 - 138).

Dextrocardia was present in 22.2% (n=6) and mesocardium in 7.4% (n=2). In addition, 11.1% (n=3) had stenosis in one of the pulmonary artery branches. They had at least one previous surgery in 29.6% (n=8) (**Table 1**).

The main diagnoses in patients undergoing the univentricular approach were atrioventricular canal (n=7; 25.9%) and pulmonary atresia (n=3; 11.1%), while cases undergoing biventricular approach were atrial septal defect (n=12; 44.4%) and ventricular septal defect (n=7; 40.7%) (**Table 2**).

During the preoperative, intubation and vasopressor support were required in 11.1% (n=3). Preoperative infection was present in 7.4% (n=2).

Surgical characteristics

Surgical procedures varied according to the palliation or repair approach (**Table 3**). In 48.1% (n=13) cases, the univentricular approach was used, being the most frequent procedure, the modified Blalock–Taussig shunt (MBTS) (n=5; 18.5%), and 51.9% (n=14) cases, the biventricular approach was used, where the most frequent procedure was the repair of septal defects (n=3; 4.6%): closure of ventricular septal de-

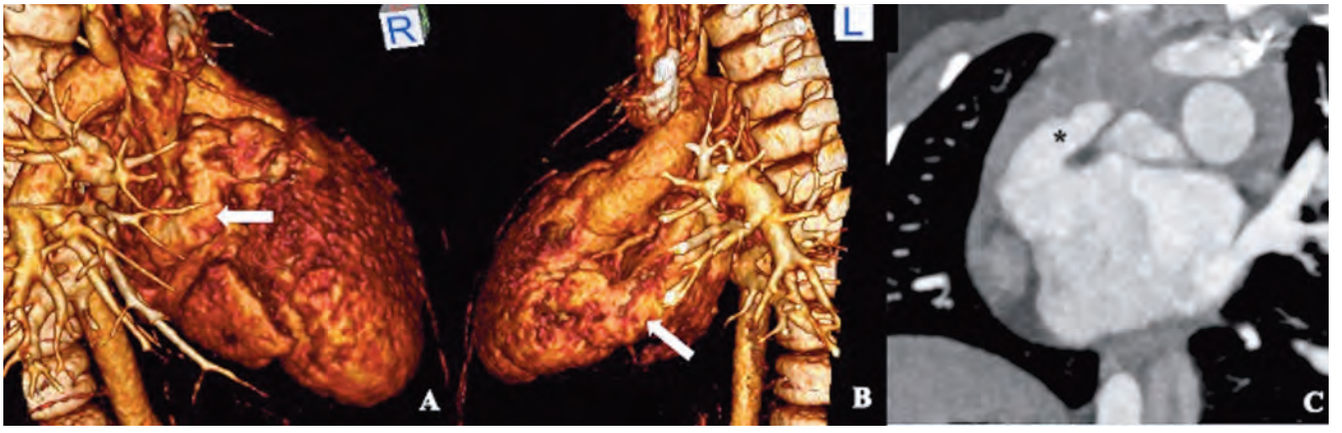

Figure 1. 3D reconstruction: A) shows morphologically left atrial appendage (arrow) in the right topographic position, B) "digitiform" shaped appendage typical of the morphologically left atrial appendage. C) Axial reconstruction shows the morphologic left atrium (*) in the right topographic position.

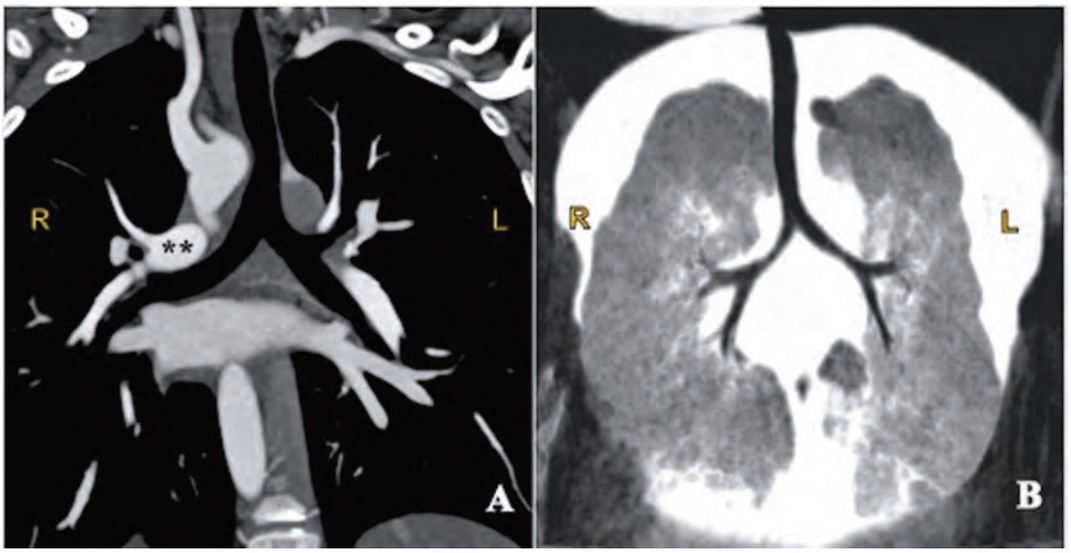

Figure 2. A) CT reconstruction shows right hypoarterial bronchus (**), B) long bronchi, and bilobed lungs.

fect and atrial septal defect. We identified 2 (7.4%) patients who required emergency surgery, in whom MBTS was performed.

Postoperative and follow-up

Seventeen (62.9%) procedures were performed with cardiopulmonary bypass with a median of 129 minutes (IQR 82 -148) and aortic clamping with a median of 89 minutes (IQR 67 - 107) (**Table 4**). The main transoperative complications were: arrhythmias (n=9; 33.3%), hypotension (n=8; 29.6%) and vascular injury (n=1; 3.7%).

The median length of stay in the pediatric intensive care unit was 3 days (IQR 2 - 8), and the median number of hours of mechanical ventilation was 21.5 hours (IQR 9.7 - 134.5) (Table 4). Postoperative complications such as heart failure (n=21; 77.8%), pulmonary hypertension (mild n=5, 18.5%; moderate n=3,11.1%), arrhythmias (n=6; 22.2%), pleural effusion (n=5; 18.5%), infections (n=3; 11.1%), and major bleeding (n=2; 7.4%). One (3.7%) case required management with nitric oxide.

Five patients (18.5%) had a reoperation: 2 (7.4%) because of major bleeding and 3 (11.1%) because of surgical site infection. In addition, 14.8% (n=4) required cardiac catheterization after the surgical procedure, required the placement of a stent in the fenestration 2 (7.4%) cases, and in the other 2 (7.4%) patients, no additional therapeutic measure was performed. Postoperative follow-up was 28.1 ± 26.6 months, with no early or late mortality cases.

DISCUSSION

AI is a complex entity associated with various malformations, both cardiovascular and in other devices and systems [3,13], which, according to The Society of Thoracic Surgeons database [14], represents 1.95% of surgical procedures in patients with congenital heart disease.

We agree that the least frequent form and with the best outcome is LAI [13,15-20,21], reporting a prevalence in our center of 41.5% among patients with AI, agreeing with Baban et al. and Alongi et al. in that determining the diagnosis is a challenge [15,16]; nevertheless, in our experience, all cases could be diagnosed in the preoperative stage with the support of the diagnostic assistants of our center.

There were no cases of obstruction of the pulmonary venous system. This situation differs from that reported by Alsoufi et al. [20], where the obstruction was found in 9%, a condition considered morbidity and mortality factor [16,18,22] by Chen et al. (OR: 44.33, p = 0.005) [13] and Alongi et al. (HR: 4.40, p = 0.01) [16], which according to Banka et al. is important in decision making and fetal counseling, as well as for early postnatal care [22]. On the other hand, 11.1% (n=3) had some degree of stenosis in one of the branches of the pulmonary artery (Table 1) without this situation affecting the outcome of survival, coinciding with McGovern et al. who reported in their cohort that 50% had stenosis in one of the branches of the pulmonary artery, but this was not related to mortality in this group (p = 0.37) [23].

Of the cohort, 66.7% had some degree of valvular regurgitation (Table 1), of which 22.2% (n=6) were moderate, and 18.5% (n=5) were severe, a situation that in some reports is associated with mortality [16,23]; whereas in our cohort no patient had a fatal outcome.

Given the variety of associated cardiac malformations, it marks a challenge for the analysis of repair strategies, where it stands out that our group used a univentricular approach in 48.1% (n=13) and 51.9% (n=14) of the patients the biven-

Table 1. Overall patient characteristics.

Characteristics, n (%)	Total n = 27 (100)
Gender, n (%)	
Male	11 (40.7)
Female	16 (59.3)
Age (years), median (IQR)	6 (3 - 11)
Weight (kg), median (IQR)	19.4 (12 - 30)
Height (cm), median (IQR)	119 (94 - 138)
Previous surgeries, n (%)	
0	18 (66.7)
1	8 (29.6)
2	1 (3.7)
RACHS-1, n (%)	
2	7 (25.9)
3	20 (74.1)
Cardiac intrathoracic position, n (%)	
Levocardium	19 (70.4)
Dextrocardium	6 (22.2)
Mesocardium	2 (7.4)
Atrioventricular valve regurgitation, n (%)	
None	9 (33.3)
Mild	7 (25.9)
Moderate	6 (22.2)
Severe	5 (18.6)
Anomalous pulmonary venous connection, n (%)	
Partial	3 (11.1)
Total	0
Pulmonary venous connection, n (%)	
Right Atrium	2 (7.5)
Left atrium	21 (77.7)
Both atria	4 (14.8)
Pulmonary artery branches, n (%)	
Normal	24 (88.9)
Stenosis	3 (11.1)

RACHS-1: Risk Adjustment for Congenital Heart Surgery 1, IQR: interquartile range.

tricular approach was used, with the most frequent procedure being MBTS in 18.5% (n=5), similar to that reported by Alongi et al.[16].

Finally, although the absence of the spleen or the presence of multiple accessory spleens has been considered a complementary part of the diagnosis of this pathology, in recent reports, several varieties of presentation have been observed in each group [15,16,18,23], where polysplenia can be found in 84% to 88% of patients with LAI [15,16], so that in some way in this group the infectious process is not an important mortality factor concerning right atrial isomerism, as reported by Bhaskar et al. (HR: 2, p = 0.008) [18] and Banka et al. (HR: 1.67, p = 0.044) [22].

Table 2. Associated defects in patients with left atrial isomerism.

Defects, n (%)	Total n = 27 (100)
ASD	**12 (44.4)**
VSD	11 (40.7)
PDA	8 (29.6)
AV canal	7 (25.9)
DORV	6 (22.2)
Pulmonary stenosis	4 (14.8)
Pulmonary atresia	3 (11.1)
PAPVC	3 (11.1)
Hypoplastic left ventricle	2 (7.4)
Coarctation of the aorta	2 (7.4)
TOF	1 (3.7)
Absence left AV valve	1 (3.7)
Subaortic stenosis	1 (3.7)
Hypoplastic aortic arch	**1 (3.7)**
LSVC	1 (3.7)

ASD: atrial septal defect, AV: atrioventricular, DORV: double outlet right ventricle, LSVC: left superior vena cava, PAPVC: partial anomalous pulmonary venous connection, PDA: patent ductus arteriosus, TOF: tetralogy of Fallot, VSD: ventricular septal defect.

Table 3. Cardiac operations performed.

Surgery, n (%)	Total n = 27 (100)
Univentricular Palliation	
MBTS	5 (18.5)
PAB	2 (7.4)
PAB + PDA ligation	1 (3.7)
TCPC with an extracardiac conduit fenestrated	1 (3.7)
TCPC with an intracardiac conduit fenestrated	1 (3.7)
TCPC with an intracardiac conduit fenestrated + LPA angioplasty	1 (3.7)
Extended coartectomy + PDA ligation + PAB	1 (3.7)
Mechanical AV valve replacement	1 (3.7)
Biventricular repair	
VSD closure with BPP + ASD closure with BPP	3 (11.1)
AV canal correction with atrial septation with BPP	2 (7.4)
AV canal correction with atrial septation with BPP + mitral commissurotomy	1 (3.7)
AV canal correction with atrial septation with BPP + AV valve repair + right atrial appendage exclusion + PAPVC repair	1 (3.7)
AV canal correction with atrial septation with BPP + MPA angioplasty	1 (3.7)
AV canal correction with atrial septation with BPP + pulmonary valve commissurotomy + infundibular resection	1 (3.7)
AV canal correction with atrial septation with BPP + pulmonary valve replacement	1 (3.7)
PAPVC repair	1 (3.7)
PAPVC repair + ASD closure + PDA ligation.	1 (3.7)
Mitral mechanical valve replacement + tricuspid valve repair	**1 (3.7)**
Subaortic membrane resection	1 (3.7)

AV: atrioventricular, BCPC: bidirectional cavopulmonary connection, BPP: bovine pericardial patch, LPA: left pulmonary artery, MAP: main pulmonary artery, MBTS: modified Blalock-Taussig shunt, PAB: pulmonary artery banding, PAPVC: partial anomalous pulmonary venous connection, PDA: patent ductus arteriosus, RPA: right pulmonary artery, TCPC: total cavopulmonary connection, VSD: ventricular septal defect.

Table 4. Transoperative and postoperative characteristics.

Characteristics	Total n = 27 (100)
Surgery with CPB, n (%)	**17 (62.9)**
CPB time (min), median (IQR)	129, 82-148
Aortic cross-clamp time (min), median (IQR)	67, 59-101
Mechanical ventilation in PICU, n (%)	25 (92.6)
Mechanical ventilation time (min); median (IQR)	36, 17-116
Reintubation, n (%)	2 (7.4)
PICU LOS, n (%)	
< 1 day	0
1 - 7 days	20 (74.1)
8 - 15 days	6 (22.2)
> 15 days	1 (3.7)

CPB: cardiopulmonary bypass, LOS: length of stay, IQR: interquartile range, PICU: pediatric intensive care unit.

Limitations

The study is subject to the usual limitations of a retrospective, unicentric, non-randomized study. In addition, the study included a small cohort of patients with few adverse outcomes. However, this first report of our experience brings important information about the management of these patients in our country. This information is important to identify prognostic factors that can be modified, implemented, and/or complemented with new therapeutic options.

As a conclusion, the analysis of this cohort shows excellent survival in patients with LAI comparable to the experience of other centers. Rigorous evaluation is important to determine an appropriate palliation or repair strategy to obtain satisfactory results with low morbidity and mortality rates in this complex patient population.

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