

A retrospective analysis of cases with left atrial isomerism

Sol atriyal izomerik olguların retrospektif değerlendirilmesi

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ABSTRACT

Background: In this study, we aimed to evaluate accompanying cardiac pathologies in patients with left atrial isomerism and report the follow-up results.

Methods: A total of 72 patients (25 males, 47 females; mean age 44.6±65.8 months; range 0 day to 255 months) with left atrial isomerism in two congenital heart diseases centers were retrospectively analyzed between July 2002 and December 2016. Clinical, radiological, electrocardiographic, echocardiographic, and angiocardiographic findings of the patients, surgical and transcatheter procedures, and postoperative follow-up data were recorded.

Results: The mean follow-up was 108±49.5 (range 12 to 173) months. Of 72 patients, four did not require surgery, while a permanent pacemaker was implanted in two patients. Of 68 patients who needed surgery, 17 were the candidates of biventricular correction, while the remaining 51 patients were the candidates of univentricular correction. The Kawashima procedure was performed in 29 patients. The pulmonary antegrade flow was left open in seven of these patients. In four patients, hepatic veins were incorporated into the Fontan circulation at the same session. In six patients, hepatic veins were directed to the pulmonary artery due to progressive cyanosis during follow-up using extracardiac conduit. Three patients died after surgery. Mortality or progressive cyanosis was not observed in any patients in whom the hepatic veins were incorporated into the Fontan circulation at the same or in another session, or in the patients in whom the antegrade flow was left open.

Conclusion: The overall prognosis is excellent in patients with biventricular physiology. However, tissue oxygenation tends to fall in patients undergoing Kawashima procedure. Therefore, incorporation of the hepatic veins into the pulmonary circulation at the same session, or leaving the antegrade flow open in suitable cases seems to be a safe approach in patients undergoing Kawashima procedure.

Keywords: Interrupted vena cava inferior; isomerism; Kawashima.

ÖZ

Amaç: Bu çalışmada sol atriyal izomerik hastalarında eşlik eden kardiyak patolojiler değerlendirildi ve takip sonuçları sunuldu.

Çalışma planı: Temmuz 2002 - Aralık 2016 tarihleri arasında iki doğumsal kalp hastalıkları merkezinde sol atriyal izomerizmli toplam 72 hasta (25 erkek, 47 kız; ort. yaş 44.6±65.8 ay; dağılım 0 gün - 255 ay) retrospektif olarak incelendi. Olguların klinik, radyolojik, elektrokardiyografik, ekokardiyografik ve anjiyokardiyografik bulguları, cerrahi ve transkateter işlemler ve ameliyat sonrası takip verileri kaydedildi.

Bulgular: Ortalama takip süresi 108±49.5 (dağılım 12-173) ay idi. Yetmiş iki hastanın dördüne cerrahi gerekmez iken, iki hastaya kalıcı kalp pili takıldı. Cerrahi gereken 68 hastanın 17'si iki ventrikül tamiri adayı iken, geriye kalan 51 hasta tek ventrikül tamiri adayıydı. Yirmi dokuz hastaya Kawashima işlemi uygulandı. Bu hastaların yedisinde pulmoner antegrad akım açık bırakıldı. Dört hastada hepatik venler aynı seansta Fontan dolaşımına dahil edildi. Altı hastada takip sırasında ilerleyici siyanoz nedeniyle hepatik venler, ekstrakardiyak konduit yardımıyla, pulmoner artere yönlendirildi. Bu hastaların üçü hasta kaybedildi. Hepatik venlerin aynı seansta ya da ikinci bir seansta Fontan dolaşımına dahil edildiği hastalar veya antegrad pulmoner akımın açık bırakıldığı hastalarda mortalite veya ilerleyici siyanoz gözlenmedi.

Sonuç: İki ventrikül fizyolojisine sahip hastaların genel prognozu mükemmeldir. Ancak, Kawashima işlemi yapılan hastalarda doku oksijenasyonu düşme eğilimindedir. Bu nedenle, Kawashima işlemi yapılan hastalarda, aynı seansta hepatik venlerin dolaşıma dahil edilmesi veya uygun olgularda antegrad akımın açık bırakılması güvenli bir yaklaşım olarak görülmektedir.

Anahtar sözcükler: Kesintili inferior vena cava; isomerizm; Kawashima.

Received: February 22, 2017 Accepted: April 11, 2017

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Cite this article as:

Erdem A, Zeybek C, Kamalı H, Yücel İK, Yıldırım A, Aydemir NA, et al. A retrospective analysis of cases with left atrial isomerism. Turk Gogus Kalp Dama 2017;25(4):550-7.

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Left atrial isomerism, one of heterotaxy syndromes, is a complex syndrome characterized by morphological left atrial manifestations of both atria accompanied by several cardiac and non-cardiac abnormalities.^[1-4] Due to bilateral left atrial morphology, the inferior caval vein (ICV)-right atrial connection is absent in nearly all cases.^[5-7] In cases with left atrial isomerism with single ventricular physiology, Kawashima procedure, cavopulmonary anastomosis, is applied in which all systemic venous return is directed to the pulmonary artery, except for hepatic veins.^[8] In the same session with Kawashima procedure or in another session, pulmonary circulation is separated from systemic circulation totally, when hepatic veins are directed to the pulmonary artery so.^[9] Hepatic inhibitor factor is directly reached the pulmonary artery through the inclusion of hepatic veins to the pulmonary artery and pulmonary arteriovenous fistula formation is inhibited or delayed.^[10,11]

In the present study, we aimed to evaluate cardiac pathologies, procedures and transcatheter interventions in patients who were diagnosed with left atrial isomerism followed in two congenital heart diseases centers and to discuss surgical approaches for single ventricular physiology and mid-term results of surgery. To the best of our knowledge, this is the first to evaluate left atrial isomerism cases in Turkey.

PATIENTS AND METHODS

Between July 2002 and December 2016, data of a total of 72 patients (25 males, 47 females; mean age: 44.6±65.8 years; range, 0 day to 255 months) who were admitted to two pediatric cardiology clinics and diagnosed with left atrial isomerism were retrospectively analyzed. During 14-year study period, 51 patients were admitted to Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Department of Pediatric Cardiology and were scheduled for treatment. In addition, between 2012 and 2016, 21 patients were admitted to Istanbul Medipol University, Department of Pediatric Cardiology were scheduled for treatment. The study protocol was approved by the Ethics Committees of Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital and Istanbul Medipol University. All patients were informed about the study and a written informed consent was obtained. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Consistent with the literature, left atrial isomerism was initially suspected in patients with an interrupted IVC as assessed by echocardiography and the diagnosis

was based on at least two suggestive signs.^[12] These signs included abdominal situs abnormalities with or without polysplenia, bilateral hyparterial bronchus or bilateral two-lobed lung appearance, electrocardiographic evidence of a p wave vector of 180° to 360°, congenital atrioventricular (AV) block, biliary atresia, intestinal malrotation abnormalities or definite surgical confirmation of left atrial pattern of both atria.^[12-14] At the initial admission, age, weight, pulse oxymetric oxygen saturation, and complaints on admission were recorded. Cardiac findings were classified based on electrocardiography, telecardiography, echocardiography, and angiocardiology. Pediatric cardiology and pediatric cardiac surgery committee reports and previous surgeries were noted. Previous echocardiography, cardiac catheterization, and operative data of patients who underwent surgery in an external center, but were followed in our study centers were recorded. The Kawashima procedure was defined as a bilateral or unilateral bidirectional cavopulmonary anastomosis which was performed to the patients with interrupted IVC-azygos continuation and in which hepatic veins were excluded from the pulmonary circulation.^[8] The Fontan procedure was defined as a procedure in which hepatic veins were included in the pulmonary circulation.

Statistical analysis

Statistical analysis was performed using the SPSS version 11.0 software (SPSS Inc., Chicago, IL, USA). Data were expressed in mean ± standard deviation (SD). In addition, median values were used, if SD was above the half of the mean values, depending on the minimum and maximum values.

RESULTS

The mean follow-up was 108±49.5 (range, 12 to 173) months. On admission, cyanosis was detected in 55 patients (76.4%), cardiac murmur in 32 patients (44.4%), heart failure in 13 patients (18.05%), and growth retardation in 14 patients (19.4%). Extracardiac abnormalities are presented in Table 1.

Table 1. Extracardiac abnormalities in patients with left atrial isomerism

	n	%
Polysplenia syndrome	37	51.4
Intestinal malrotation	2	2.8
Meningomyelocele	2	2.8
Esophageal atresia	1	1.4
Cleft palate	1	1.4
Omphalocele	1	1.4

Table 2. Cardiac signs in patients with left atrial isomerism

	n	%
Cardiac position		
Dextrocardia	24	33.3
Mesocardia	9	12.5
Levocardia	39	54.2
Superior vena cava		
Isolated right	26	36.1
Isolated left	12	16.7
Bilateral	34	47.2
Atrioventricular septal defect		
Balanced ventricles	15	20.8
Right ventricle dominant, unbalanced	17	23.6
Left ventricle dominant, unbalanced	5	6.9
Single atrium/large ASD	17	23.6
Double-outlet right ventricle	28	38.8
Double or common-inlet right ventricle	16	22.2
Double or common-inlet left ventricle	2	2.7
Pulmonary atresia	16	22.2
Confluent pulmonary arteries	11	15.3
Non-confluent pulmonary arteries	5	6.9
Pulmonary stenosis	28	38.8
Atrioventricular discordance	14	19.4
Extracardiac return of pulmonary veins	6	8.3
Total	2	2.8
Partial	4	5.6
Mitral stenosis or hypoplasia	4	5.6
Isolated ventricular septal defect	2	2.8
Isolated large atrial septal defect	2	2.8
Isolated patent ductus arteriosus	2	2.8
Complete atrioventricular block	2	2.8

ASD: Atrial septal defect.

Dextrocardia is observed in 24 patients, mesocardia in nine patients, and levocardia in 39 patients. In all 72 patients, interrupted IVC-azygos continuation was present. The azygos vein was opened to the right

superior caval vein (SCV) in 40 patients and the left SCV in 32 patients. Cardiac signs are presented in Table 2.

Of 72 patients, four did not require any surgical intervention. Of 68 patients requiring surgery, 17 were eligible for two-ventricle repair, while 51 were eligible for single-ventricle repair (Figure 1). In two patients with two-ventricle physiology, surgery was needed for only permanent pacemaker implantation.

In these two cases who were diagnosed with complete AV block with left atrial isomerism during the neonatal period, permanent pacemaker was surgically implanted. None of these cases had an intracardiac pathology. Five of the patients who were candidates for biventricular repair were accepted as inoperable due to pulmonary vascular disease at the time of admission to our centers. Three of these patients died, while two are still under follow-up with medical treatment. Of a total of 10 patients who were candidates for biventricular repair one had isolated ventricular septal defect (VSD) and the other one had double-outlet right ventricle associated with VSD. These patients underwent closure of VSD. Six patients underwent atrioventricular septal defect (AVSD) repair. In all patients who were candidates for biventricular repair, pulmonary veins drained to intracardiac chambers. The patients who did not require surgical repair had biventricular circulation. Two patients with isolated atrial septal defect (ASD) and two patients with isolated patent ductus arteriosus (PDA) underwent transcatheter closure (Figure 2a-e). One patient underwent permanent pacemaker implantation due to prolonged pauses associated with sinus node

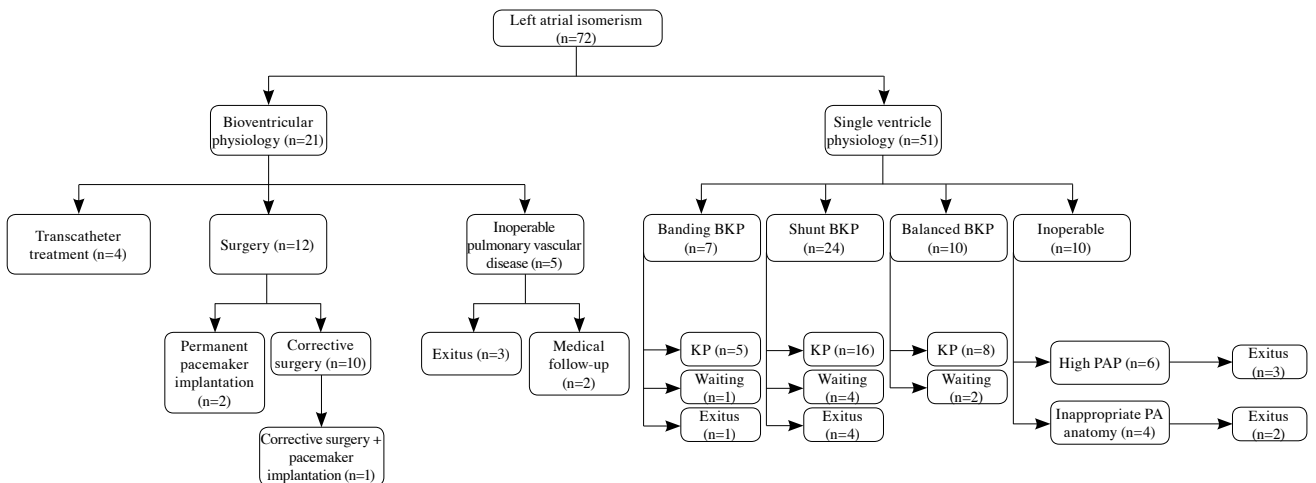


Figure 1. Diagram of 72 patients with left atrial isomerism.

BKP: before Kawashima procedure; KP: Kawashima procedure; PA: pulmonary artery; PAP: Pulmonary artery pressure.

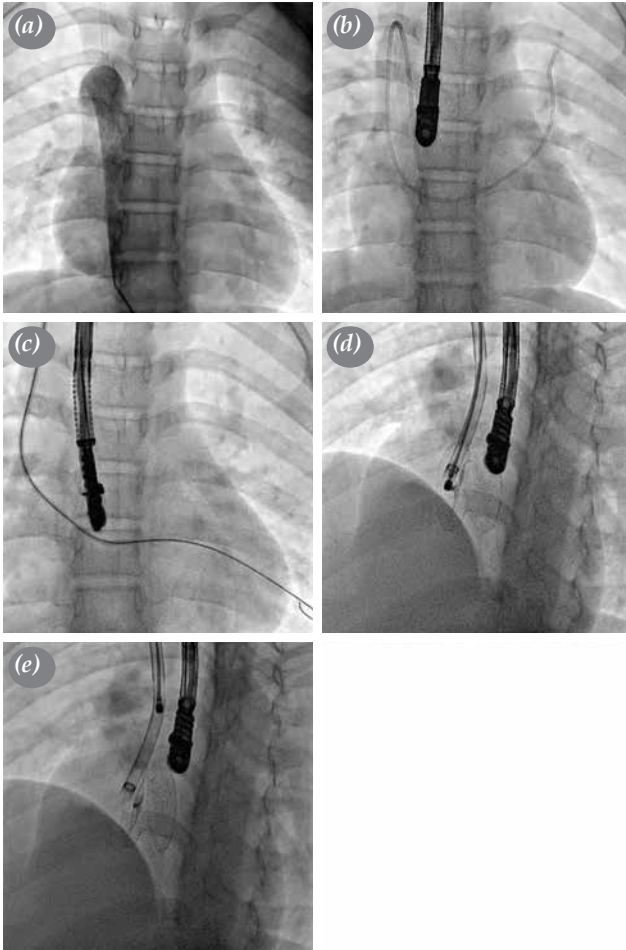


Figure 2. Transcatheter closure of ASD through superior vena cava in a case with left atrial isomerism. (a) Angiography showing azygos continuation; (b) guidewire advancing through femoral vein; (c) guidewire advancing superior vena cava; (d) view before the device release; and (e) view after the device release.

dysfunction. In this patient with dextrocardia, ASD, and perimembranous VSD (No. 10 in the biventricular repair group) was previously implanted a permanent pacemaker during closure of the surgical defects at two years of age. In other patients, postoperative AV block was not observed. Two other adult patients who previously underwent Kawashima procedure were applied ablation due to intraatrial reentrant tachycardia.

A total of 24 patients who were candidates for univentricular repair underwent aortopulmonary shunt surgery, while seven patients underwent pulmonary artery banding before Kawashima procedure. Four of these patients were accepted as inoperable due to aortopulmonary collateral-dependent pulmonary circulation or inappropriate pulmonary artery anatomy, while six patients were inoperable due to high pulmonary artery pressure at the time of admission and the final goal of Kawashima procedure were unable to be achieved. Of these patients, five died, while the others are still under follow-up with medical treatment. Eight of 10 patients who had balanced physiology and did not required any palliation underwent Kawashima procedure, while two are still under waiting for the procedure at a later time.

The mean time from first surgery to Kawashima procedure was 13.4 ± 5.3 months in 16 patients who underwent aortopulmonary shunt. Four patients are still waiting for the procedure at a later time. Three of 24 patients who underwent aortopulmonary shunting died postoperatively, while another patient died after the second shunt surgery. The mean time from surgery to Kawashima procedure was 17.5 ± 7.8 months in five patients who underwent pulmonary artery banding. One of these patients died in the early postoperative period, while another is still waiting for the procedure at a later time.

A total of 29 patients underwent Kawashima procedure (Figure 3). The median age at the time of surgery was 3.5 years (range, 11 months to 14 years). The mean preoperative angiographic pulmonary artery pressure was 12.7 ± 6.4 mmHg and the mean McGoon pulmonary artery index was 1.68 ± 0.6 . The mean preoperative oxygen saturation was $74 \pm 7\%$ (range, 65 to 84%), while the mean postoperative oxygen saturation increased to $89.4 \pm 17.6\%$. A total of seven patients underwent Kawashima procedure with open pulmonary antegrade flow. Five of these patients received the procedure without any palliative intervention, while one patient underwent the procedure after aortopulmonary shunt surgery and another after pulmonary artery banding. In four of the patients who

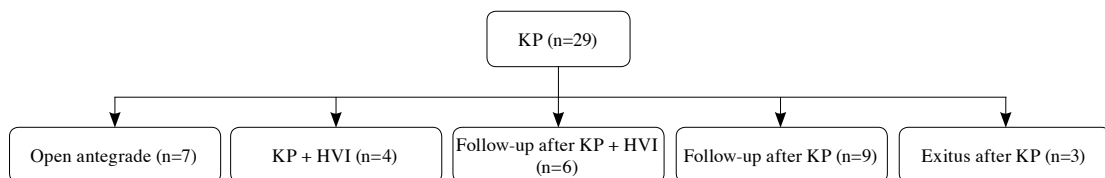


Figure 3. Diagram of 29 patients undergoing Kawashima procedure.

KP: Kawashima procedure; HVI: Hepatic vein inclusion.

underwent Kawashima procedure, hepatic veins were included in the Fontan circulation in same session. In six patients in whom hepatic veins were unable to be included in the Fontan circulation in the initial session, hepatic veins were directed to the pulmonary artery using an extracardiac conduit after a median time of 74 months in a second session due to progressive cyanosis and asthenia. None of these patients had open antegrade flow in the initial session.

After Kawashima procedure, one patient died in the early postoperative period, while two died in the late postoperative period (after 7 months and 3 years, respectively). In none of these patients, hepatic veins were unable to be included in the pulmonary circulation. No mortality was seen in the patients in whom hepatic veins were included in the pulmonary circulation in a same or second session and in whom the antegrade pulmonary flow was open.

At a median postoperative period of 63 months, the mean oxygen saturation was $92.7 \pm 10.6\%$ in four patients in whom hepatic veins were included into the Fontan circulation at a single session. At a median postoperative period of 34 months, the mean oxygen saturation was $86.7 \pm 11.3\%$ in the remaining patients in whom hepatic veins were included into the Fontan circulation at a separate session and these patients are still stable. In another 16 patients, the mean oxygen saturation was $84.9 \pm 13.7\%$ and these patients are still under follow-up, and in three of them, the inclusion of hepatic veins to the pulmonary circulation were planned.

In one patient who underwent Kawashima procedure and in whom hepatic veins were directed to the pulmonary artery nine years later underwent stent implantation due to localized stenosis in the pulmonary artery leading to pleural effusion and ascites four months after the procedure. After treatment with stent implantation, this patient was hemodynamically and clinically stable.

DISCUSSION

The mortality rate of right atrial isomerism, in which atrial appendages are in bilateral right appendage morphology, is $\geq 85\%$ under one year of age in patients with severe cyanotic cardiac pathologies, if left untreated. In case of left atrial isomerism, atrial appendages are bilateral and in left appendage morphology and cardiac pathologies present clinically milder than in right atrial isomerism. However, there are reports showing a mortality rate higher than 50% in left atrial isomerism.^[15] In the literature, there is a limited number of large-scale studies involving left atrial isomerism and,

to the best of our knowledge, this is the first study conducted in Turkey.

In case of left atrial isomerism, clinical signs are non-specific and vary depending on cardiac pathologies. Some of the patients with left-to-right shunt cardiac septal defects are asymptomatic and present only with cardiac murmur, while the others may present heart failure and growth retardation. In case of reduced pulmonary blood flow, cyanosis, murmur and growth retardation may present. In case of mixed physiology, the majority of patients may present with cyanosis. In certain patients with left atrial isomerism, intracardiac anatomy is normal and the definite diagnosis can be made while investigating extracardiac diseases such as biliary atresia and malrotation.^[16] In addition, some patients may present with rhythm problems such as AV block. As our centers are tertiary setting cardiac surgery services, the majority of patients are those who were previously diagnosed with congenital heart disease in external centers and referred to our centers. The initial complaints of our patients are also consistent with the literature data.^[12,13]

Some left atrial isomerism cases presenting with mild pathologies may be overlooked during clinical examination. In addition, IVC interruption can be detected in some cases during catheter-angiography and these patients are incidentally diagnosed with left atrial isomerism, which complicates the scheduled procedure. In such cases, as the distance of the catheter advancing through venous route to the right atrium is longer and manipulation is more difficult, cardiac defects should be closed through different techniques. In our clinical practice, we encountered two such cases. In one case, we attempted to close PDA through antegrade route; however, complete AV block occurred. Therefore, we used transarterial closure. In another case, we closed PDA transarterially. In two cases, we used jugular veins for ASD closure and achieved successful outcomes. To reach the left atrium through jugular vein and atrial defect and to insert a guidewire into the pulmonary vein, we used a Lima catheter and a steerable sheath to carry the device (Figure 2a-e).

In patients with left atrial isomerism, bradycardia associated with sinus node dysfunction is an expected condition. In our study, one of the patients developed bradycardia associated with sinus node dysfunction. This patient underwent biventricular repair. However, we inserted a permanent pacemaker due to prolonged pauses as assessed by Holter monitoring before surgery. In addition, surgery-related AV conduction abnormalities and atrial arrhythmias in patients with

single ventricle are common. During neonatal period, two of our patients were diagnosed with complete AV block and left atrial isomerism. These patients underwent pacemaker implantation. None of these patients developed postoperative AV block. Also, two elderly patients who underwent Kawashima procedure were applied ablation due to intraatrial reentrant tachycardia.

Previous studies have shown a remarkable female predominance in patients with left atrial isomerism.^[17,18] Our study is also consistent with the literature data. Gilljam *et al.*^[12] reported that the age of the diagnosis varied from 1 day to 16 years. In our study, this rate was also ranging from 1 day to 29 years. Although the majority of the patients were diagnosed during the neonatal period, some were diagnosed late. In our study, the latest age of diagnosis was 21 years. In this patient the absence of right ventricular outflow tract obstruction and significant left to right shunt presenting with heart failure signs precluded early diagnosis. This patient was admitted to our clinic due to pulmonary hypertension related to the left-to-right shunt with a significant decrease in the exercise capacity.

The rate of interrupted infrahepatic IVC-azygos continuation ranges from 85 to 100% in patients with left atrial isomerism.^[18] In our study, all patients had an interrupted IVC. This finding indicates that isomerism of the atrial appendages may be overlooked in case of cardiac pathologies without an interrupted IVC. In the literature, the most common concomitant cardiac pathology is AVSD in patients with left atrial isomerism.^[14] Our study is also consistent with the literature. Although pulmonary atresia and single-ventricle pulmonary stenosis are specific to the right atrial isomerism, we observed a higher rate in patients with left atrial isomerism, compared to the literature findings, which might have contributed to the increased morbidity and mortality rates.

Treatment of left atrial isomerism depends on the presence of intracardiac pathology. Two-thirds of patients are eligible for biventricular repair, while few are eligible for single-ventricle repair.^[16] In our study, contrast to the literature findings, the number of patients with biventricular physiology was lower. This suggests that segmental analysis was less commonly performed in acyanotic patients who might be eligible for biventricular repair and patients with mild cardiac pathologies are infrequently admitted to the healthcare centers or delayed. If early total correction or pulmonary artery banding is unable to be performed in AVSD patients, emerging pulmonary

vascular disease may complicate surgery and increases mortality. In our study, two such patients were diagnosed with pulmonary vascular disease and were not operated. These patients were scheduled for follow-up with medical treatment. In some cases, intracardiac pathologies can be treated through transcatheterization without surgery. Similarly, in our study, two patients with isolated PDA and two patients with isolated large ASD were treated with transcatheterization.

In patients undergoing Kawashima procedure, all systemic veins are included into the pulmonary artery, except for hepatic veins. Several studies have shown that inclusion of hepatic inhibitor factor secreted by the liver into the systemic circulation bypassing the lungs may lead to pulmonary arteriovenous fistulas.^[19,20] Following total cavopulmonary anastomosis, the rate of pulmonary arteriovenous fistula ranges from 17 to 58%.^[19] Following Kawashima procedure, developing collaterals between hepatic veins and systemic veins and pulmonary arteriovenous fistulas worsen the prognosis, contributing to the progression of cyanosis.^[20]

Several studies have shown that early inclusion of hepatic veins to the pulmonary artery may prevent pulmonary arteriovenous fistula formation, decrease progressive cyanosis, and reduce morbidity and mortality.^[11,21] In our study, following Kawashima procedure, we included hepatic veins using an extracardiac conduit approach in six patients who developed progressive cyanosis during follow-up and we included hepatic veins into the pulmonary circulation in a single session in four patients starting from 2012, based on our experience and literature data. No mortality was seen in these patients and all are stable and still under follow-up without desaturation.

In the present study, of 72 patients with left atrial isomerism, 16 (22%) died. Many of these patients were unable to be intervened and died from pulmonary vascular disease and non-confluent pulmonary arteries and these patients were often admitted at late stage. In our study, the mortality rate of shunt surgery was 20.8%, which is consistent with the literature findings.^[22,23] In the literature, the mortality rate of Kawashima procedure varies from 0 to 33%,^[24,25] while in our study, only one patient died in the early postoperative period and the mortality rate was 3.4%. Another patient who developed protein-losing enteropathy died from recurrent ascites and effusions.

The main limitation of our study is that all patients were unable to be followed in our clinic as of birth and some patients were admitted at older age. Therefore,

we are unable to make a conclusion about the prognosis of left atrial isomerism. We have also insufficient knowledge about why inoperable patients due to high pulmonary artery pressure at the time of this study were left untreated or why these patients did not receive pulmonary artery rehabilitation and missed the chance of Kawashima procedure. We consider that these patients without rhythm disorder or any anatomical cardiac pathology were not meticulously examined. Another limitation is our small sample size: we were unable to conduct a statistical comparison between the patients in whom the antegrade flow was left open and the patients in whom the hepatic veins were included in the circulation early or late.

In conclusion, left atrial isomerism may present with a broad range of spectrum ranging from normal intracardiac anatomy to severe cyanotic single-ventricle pathologies. The Kawashima procedure can be performed directly or after palliative operations in patients who are candidates for single-ventricle repair. Of note, tissue oxygenation tends to decrease due to pulmonary arteriovenous fistulas following the Kawashima procedure. Therefore, inclusion of hepatic veins to the circulation in a single session or in the early postoperative period or leaving the antegrade flow open in selected cases appear to be safe.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Alharthi M, Mookadam F, Collins J, Chandrasekaran K, Scott L, Tajik AJ. Images in cardiovascular medicine. Extracardiac venous heterotaxy syndrome: complete noninvasive diagnosis by multimodality imaging. *Circulation* 2008;117:498-503.
2. Tonkin IL, Tonkin AK. Visceroatrial situs abnormalities: sonographic and computed tomographic appearance. *AJR Am J Roentgenol* 1982;138:509-15.
3. Van Praagh R, Van Praagh S. Atrial isomerism in the heterotaxy syndromes with asplenia, or polysplenia, or normally formed spleen: an erroneous concept. *Am J Cardiol* 1990;66:1504-6.
4. Ferdman B, States L, Gaynor JW, Hedrick HL, Rychik J. Abnormalities of intestinal rotation in patients with congenital heart disease and the heterotaxy syndrome. *Congenit Heart Dis* 2007;2:12-8.
5. Moller JH, Nakib A, Anderson RC, Edwards JE. Congenital cardiac disease associated with polysplenia. A developmental complex of bilateral "left-sidedness". *Circulation*. 1967;36:789-99.
6. Stanger P, Rudolph AM, Edwards JE. Cardiac malpositions. An overview based on study of sixty-five necropsy specimens. *Circulation* 1977;56:159-72.
7. Sharma S, Devine W, Anderson RH, Zuberbuhler JR. Identification and analysis of left atrial isomerism. *Am J Cardiol* 1987;60:1157-60.
8. Kawashima Y, Kitamura S, Matsuda H, Shimazaki Y, Nakano S, Hirose H. Total cavopulmonary shunt operation in complex cardiac anomalies. A new operation. *J Thorac Cardiovasc Surg* 1984;87:74-81.
9. Uemura H, Yagihara T, Hattori R, Kawahira Y, Tsukano S, Watanabe K. Redirection of hepatic venous drainage after total cavopulmonary shunt in left isomerism. *Ann Thorac Surg* 1999;68:1731-5.
10. McElhinney DB, Kreutzer J, Lang P, Mayer JE Jr, del Nido PJ, Lock JE. Incorporation of the hepatic veins into the cavopulmonary circulation in patients with heterotaxy and pulmonary arteriovenous malformations after a Kawashima procedure. *Ann Thorac Surg* 2005;80:1597-603.
11. Brown JW, Ruzmetov M, Vijay P, Rodefeld MD, Turrentine MW. Pulmonary arteriovenous malformations in children after the Kawashima operation. *Ann Thorac Surg* 2005;80:1592-6.
12. 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;36:908-16.
13. Van Mierop LH, Patterson DF, Schnarr WR. Pathogenesis of persistent truncus arteriosus in light of observations made in a dog embryo with the anomaly. *Am J Cardiol* 1978;41:755-62.
14. Jacobs JP, Anderson RH, Weinberg PM, Walters HL, Tchervenkov CI, Del Duca D, et al. The nomenclature, definition and classification of cardiac structures in the setting of heterotaxy. *Cardiol Young* 2007;17:1-28.
15. Bartz PJ, Driscoll DJ, Dearani JA, Puga FJ, Danielson GK, O'Leary PW, et al. Early and late results of the modified fontan operation for heterotaxy syndrome 30 years of experience in 142 patients. *J Am Coll Cardiol* 2006;48:2301-5.
16. Kim SJ. Heterotaxy syndrome. *Korean Circ J* 2011;41:227-32.
17. Sapire DW, Ho SY, Anderson RH, Rigby ML. Diagnosis and significance of atrial isomerism. *Am J Cardiol* 1986;58:342-6.
18. Berg C, Geipel A, Kamil D, Knüppel M, Breuer J, Krapp M, et al. The syndrome of left isomerism: sonographic findings and outcome in prenatally diagnosed cases. *J Ultrasound Med* 2005;24:921-31.
19. Kim SJ, Bae EJ, Cho DJ, Park IS, Kim YM, Kim WH, et al. Development of pulmonary arteriovenous fistulas after bidirectional cavopulmonary shunt. *Ann Thorac Surg* 2000;70:1918-22.
20. Gatzoulis MA, Shinebourne EA, Redington AN, Rigby ML, Ho SY, Shore DF. Increasing cyanosis early after cavopulmonary connection caused by abnormal systemic venous channels. *Br Heart J* 1995;73:182-6.
21. Setyapranata S, Brizard CP, Konstantinov IE, Iyengar A, Cheung M, d'Udekem Y. Should we always plan a Fontan

- completion after a Kawashima procedure? *Eur J Cardiothorac Surg* 2011;40:1011-5.
22. Jacobs JP, Pasquali SK, Morales DL, Jacobs ML, Mavroudis C, Chai PJ, et al. Heterotaxy: lessons learned about patterns of practice and outcomes from the congenital heart surgery database of the society of thoracic surgeons. *World J Pediatr Congenit Heart Surg* 2011;2:278-86.
 23. Marcelletti C, Di Donato R, Nijveld A, Squitieri C, Bulterijs AH, Naeff M, et al. Right and left isomerism: the cardiac surgeon's view. *Ann Thorac Surg* 1983;35:400-5.
 24. Alejos JC, Williams RG, Jarmakani JM, Galindo AJ, Isabel-Jones JB, Drinkwater D, et al. Factors influencing survival in patients undergoing the bidirectional Glenn anastomosis. *Am J Cardiol* 1995;75:1048-50.
 25. McElhinney DB, Reddy VM, Moore P, Hanley FL. Bidirectional cavopulmonary shunt in patients with anomalies of systemic and pulmonary venous drainage. *Ann Thorac Surg* 1997;63:1676-84.