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Intra-atrial reentrant tachycardia in adult patients after Fontan operation

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ABSTRACT

Background: : Atrial tachyarrhythmia is a major late complication in adult Fontan patients. This study examined the clinical features and risk factors of late intra-atrial reentrant tachyarrhythmia (IART) in adult patients after Fontan surgery and the mid-term outcome of Fontan conversion with or without antiarrhythmic surgery in these patients.
Methods: : We conducted a retrospective study on adult patients who were born before 1994 and survived at least 3 months after a Fontan operation at Seoul National University Children's Hospital.
Results: : We followed 160 patients over 20.9 ± 4.1 years. Sustained atrial tachycardia was identified in 51 patients, and IART was found in 41, appearing a mean 13.6 years after surgery. By the 25 year follow-up, 40% had developed IART. The incidence of IART significantly increased over time. Patients with an atriopulmonary connection (APC) (n = 65) had significantly longer follow-up duration and higher incidence of IART than patients with a lateral tunnel (n = 86) or extracardiac conduit Fontan (n = 9). On multivariate analysis, APC, sinus node dysfunction, and nonsustained atrial tachycardia were found to be significantly associated with IART. Twenty-four patients with IART underwent Fontan conversion. Over the follow-up period, IART severity scores in the 22 patients who survived after Fontan conversion decreased significantly, and New York Heart Association functional class significantly improved. On multivariate analysis, protein losing enteropathy and ventricular dysfunction were found to be significant risk factors for mortality.
Conclusions: : IART was common in adult Fontan patients, and Fontan conversion with or without antiarrhythmic surgery and pacemaker placement helped to control it.

1. Introduction

Atrial tachycardia is a troublesome problem, affecting morbidity and mortality in patients after Fontan operation. Fontan patients often have extensive atrial scarring and are prone to right atrial dilatation and fibrosis, which may act as arrhythmogenic substrates. Indeed, up to 50% of Fontan patients develop atrial tachyarrhythmia within 20 years of the operation [1,2]. Intra-atrial reentrant tachycardia (IART), a type of macroreentrant tachycardia, is the most common form of atrial tachyarrhythmia in Fontan patients [3,4]. In adult Fontan patients (a growing population), IART reduces quality of life and may even cause death in hemodynamically compromised patients [5]. Several studies have recommended that these patients be treated with Fontan conversion to the lateral tunnel (LT) or extracardiac conduit (ECC) Fontan with concomitant antiarrhythmic surgery [6–8]; however, outcomes of such a procedure have not been well identified. The aim of this study was to evaluate clinical features of and risk factors for late IART over an extended period and to assess mid-term outcomes of Fontan conversion with antiarrhythmic surgery.

2. Methods

2.1. Patients and definitions

We conducted a retrospective cohort study of 160 patients born before May 1994 who have been followed up at Seoul National University Children's Hospital after Fotan operation. Patients who were lost to follow-up, died within 3 months of their Fontan operation, or had incomplete medical records were excluded. We reviewed clinical notes, electrocardiograms, 24-hour Holter monitor records, echocardiograms, images and reports obtained through cardiac catheterization, electrophysiologic studies, and computed tomography scans.

Late IART was defined as sustained IART, documented by electrocardiography, Holter monitoring, or pacemaker monitoring, that occurred 3 months or more after Fontan surgery. Sinus node dysfunction (SND)

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was defined as sinus bradycardia with a resting heart rate more than 2 standard deviation lower than normal for the patient's age, predominant junctional rhythm, or sinus pause of ≥3 s, with or without escape beats [9–11]. Ventricular dysfunction was defined as ejection fraction < 50% of systemic ventricle on echocardiogram.

To evaluate clinical outcomes of Fontan conversion, we used a modified version of the multiscale IART severity score developed by Triedman et al. [12]. The instrument was composed of 4 categories; documented IART, IART severity, antiarrhythmic medications, and frequency of cardioversion for prior 3 months, which was modified to frequency of cardioversion for prior one year in this study. Scores on these 4 scales were summed to yield a total IART severity score ranging from 0 to 12 points, which was calculated for baseline (before Fontan conversion) and last follow-up. A favorable long-term outcome was defined as a score at last follow-up that was ≤3 or had decreased by ≥3 from the preoperative score. An unfavorable long-term outcome was defined as a follow-up score that was ≥4 or had decreased by ≤2 from the preoperative score.

The study was approved by the Institutional Review Boards of Seoul National University Hospital.

2.2. Statistical methods

Continuous variables were recorded as mean ± standard deviation or as median and range, and values of the normally distributed ones were compared between groups by *t*-test and analysis of variance. Univariate analysis of categorical variables was performed using the log-rank test, Pearson's chi-square test, Fisher's exact test, and Cox regression to determine which ones might be risk factors for late IART and mortality. The Cox proportional-hazards model was used to estimate the hazard ratio for occurrence of late post-Fontan IART in relation to years of survival after the operation. Cumulative probability of freedom from IART was analyzed using the Kaplan–Meier estimator, both for the study sample as a whole and for each Fontan configuration. Multivariate logistic regression was conducted to determine which factors were associated with late post-Fontan IART and death. Statistical analyses were performed using SPSS version 21.0 (IBM, Armonk, NY, USA). A p-value of <0.05 was considered statistically significant.

3. Results

3.1. Fontan patients

Demographic and clinical characteristics of the patients included in this study are shown in Table 1. Age at Fontan operation ranged from 8 months to 36.3 years, and 3351.8 patient-years of follow-up were conducted over a median period of 20.9 years (range 6.3–31.6). Atriopulmonary connection (APC) Fontan was performed in 65 patients (40%) since 1982, lateral tunnel (LT) Fontan in 86 (53%) since 1990 and extracardiac conduit (ECC) Fontan in 9 (6%) since 1997.

The initial diagnosis of patients was categorized into 7 groups; tricuspid atresia in 29 patients (18%), common inlet ventricle with unbalanced atrioventricular septal defect in 39 (24%), mitral atresia in 29 (46%), double inlet ventricle in 33 (21%), complicated double outlet right ventricle in 9 (6%), complicated transposition of the great arteries in 7 (4%), and pulmonary atresia with intact ventricular septum in 2 (1%) (Table 1). Heterotaxy syndrome was diagnosed in 41 (25.6%) patients, of whom 21 had right isomerism and 20 had left isomerism. Most patients had a single ventricle of right ventricular type (88/160, 55%); 53 (33%) had a single ventricle of left ventricular type, and 19 (12%) had both ventricles type.

3.2. Supraventricular tachycardia

Sustained supraventricular tachycardia was identified in 51 patients (31.8%; Table 2), of whom 41 (25.6%) had late IART, including 6 patients with both IART and sustained atrial fibrillation. Paroxysmal atrial fibrillation without IART occurred in 1 patient, 23.1 years after Fontan

Table 1
Demographics and clinical characteristics.

Demographics and clinical variables		All patients (n = 160)	Patients with IART (n = 41)	Patients without IART (n = 119)	p
Age at Fontan (years)[a]		4.8 ± 4.7 3.2 (0.8–36.3)	5.0 ± 3.3 4.1 (0.8–15.4)	4.8 ± 5.1 3.0 (1.2–36.3)	NS
Follow-up time after Fontan (years)[a]		20.9 ± 4.1 20.9 (6.3–31.6)	23.3 ± 4.1 23.7 (12.8–30.6)	20.1 ± 3.8 20.2 (6.3–31.6)	<0.001
Gender, male		96 (60%)	25 (61%)	71 (60%)	NS
	APC	65 (41%)	31 (76%)	34 (29%)	
Fontan type	LT	86 (54%)	9 (22%)	77 (65%)	<0.001
	ECC	9 (6%)	1 (2%)	8 (7%)	
Type of single ventricle					NS
Right ventricle		88 (55%)	20 (49%)	68 (57%)	NS
Left ventricle		53 (33%)	14 (34%)	39 (33%)	NS
Both ventricles		19 (12%)	7 (17%)	12 (10%)	NS
Heterotaxia		41 (26%)	12 (29%)	19 (16%)	NS
Right isomerism		21 (13%)	5 (12%)	16 (13%)	NS
Left isomerism		20 (13%)	7 (17%)	13 (11%)	NS
Initial diagnosis					NS
Tricuspid atresia		29 (18%)	7 (17%)	22 (19%)	
Common inlet ventricle with Unbalanced AVSD		39 (24%)	9 (22%)	30 (25%)	
Mitral atresia		41 (26%)	11 (27%)	30 (25%)	
Double inlet ventricle		33 (21%)	6 (15%)	27 (23%)	
Complicated DORV		9 (6%)	3 (7%)	6 (5%)	
Complicated TGA		7 (4%)	4 (10%)	3 (3%)	
PA with IVS		2 (1%)	1 (2%)	1 (1%)	
Previous BT shunt		62 (39%)	20 (49%)	42 (35%)	NS
Sinus node dysfunction		38 (24%)	23 (14%)	15 (13%)	<0.001
Non-sustained atrial tachycardia		57 (39%)	28 (76%)	29 (27%)	<0.001
Protein losing enteropathy		9 (6%)	3 (2%)	6 (5%)	NS
Ventricle dysfunction		37 (24%)	13 (32%)	24 (20%)	NS
Moderate-to-severe AVVR		11 (7%)	5 (12%)	6 (5%)	NS
Death		13 (8.1%)	6 (14.6%)	7 (5.9%)	0.08

IART indicates intra-atrial reentrant tachycardia; APC, atriopulmonary connection Fontan; LT, lateral tunnel.
Fontan; ECC Extracardiac connection Fontan; AVSD, atrioventricular septal defect; DORV, double outlet of right ventricle; TGA, transposition of great artery; BT shunt, Blalock–Taussig shunt; AVVR, atrioventricular regurgitation.
[a] Data expressed as mean ± standard deviation and median value (range).

Table 2
Supraventricular tachycardia.

Supraventricular tachycardia	n	%
Sustained	51	32%
IART	41	26%
IART with atrial fibrillation	6	
IART with focal AT	1	
IART with JT	2	
IART with VT	1	
Atrial fibrillation only	1	1%
Focal AT	4	3%
AVRT	3	2%
Junctional tachycardia	7	4%
Nonsustained AT	57	36%

IART indicates intra-atrial reentrant tachycardia; AT, atrial tachycardia; JT, junctional tachycardia; VT, ventricular tachycardia; AVRT, atrioventricular reentrant tachycardia.

operation. Nonsustained atrial tachycardia (NSAT) was documented in 57 patients (35.6%) by 24 hour holter monitoring; 32 of these also showed a sustained supraventricular tachycardia, which was IART in 28.

3.3. IART

Median interval between initial Fontan operation and diagnosis of late IART was 12.9 years (range 3.3 months to 27.0 years, mean 13.6 ± 6.2 years). According to the Cox proportional-hazards model, the prevalence of IART significantly increased with each additional year of survival (hazard ratio 1.1, 95% confidence interval 1.008–1.200, $p = 0.032$). Patients with IART were followed up significantly longer than those without it (23.3 ± 4.1 years vs. 20.1 ± 3.8 years, $p < 0.001$) (Table 1), and patients with an APC Fontan were followed up significantly longer than those with an LT or ECC (mean 23.7 ± 3.6 years for APC, 19.4 ± 2.9 years for LT, and 15.2 ± 3.5 years for ECC; $p < 0.001$). IART had been diagnosed in 22.1% ± 3.5% of patients 20 years after the Fontan procedure and in 39.8% ± 7.3% 25 years later; 27 years after the operation, 50% of patients had developed IART (Fig. 1).

On univariate analysis, incidence of IART was significantly higher in patients with an APC Fontan (31/65, 47.7%) than in those with an LT (9/86, 10.5%) or ECC Fontan (1/9, 11.1%) ($p < 0.001$). However, there was no significant difference in IART incidence between LT and ECC Fontan, even after adjusting for follow-up time. Freedom from IART was significantly different between APC (61%) and LT (92%) at 20 years of follow-up ($p < 0.001$) (Fig. 2).

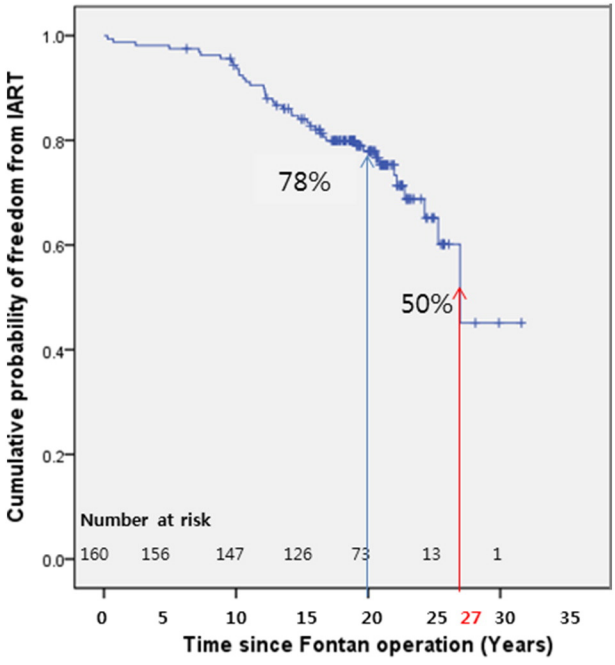

Fig. 1. Kaplan–Meier estimator of the probability of freedom from IART since Fontan operation. IART indicates intra-atrial reentrant tachycardia.

SND and NSAT both appeared to be significant risk factors for IART on univariate analysis (Table 1). SND was more prevalent in patients with an APC (33%) than those with an LT or ECC (18%) ($p = 0.026$), with no significant difference between the latter two. Multivariate logistic regression confirmed that in the sample as a whole, the APC Fontan, SND, and NSAT were significantly associated with IART (Table 3); in patients with an APC, the risk factors were SND and NSAT, whereas in patients with an LT or ECC, the risk factors were SND and moderate- to-severe atrioventricular regurgitation.

Age at Fontan operation, heterotaxy syndrome, classification of original heart anomaly, ventricular dysfunction, single ventricle type, and history of pre-Fontan palliative surgery or Blalock–Taussig shunt did not significantly affect the risk of IART.

3.4. Management of IART and outcomes of Fontan conversion in patients with IART

Fontan conversion was performed in 36 patients in this study, with the first conversion being performed in 1996. Of the patients with IART ($n = 41$), 24 (58.5%) underwent Fontan conversion (APC to LT in 3, APC to ECC in 19, LT to ECC in 2), of whom 21 patients underwent concomitant antiarrhythmic surgery and 22 received a pacemaker concomitantly with or after Fontan conversion.

In the 24 patients with IART who underwent Fontan conversion, the median interval from initial Fontan operation to conversion was 15.2 years (range 3.7–26.7, mean 15.8 ± 5.2), and median follow-up duration after Fontan conversion was 8.1 years (range 0.1–15.5, mean 6.9 ± 4.5). Reasons for conversion included recurrent IART ($n = 9$), IART with right atrial thrombosis ($n = 8$), IART with heart failure or moderate to severe atrioventricular regurgitation ($n = 3$), and protein-losing enteropathy ($n = 1$). Three patients underwent Fontan conversion concomitantly with surgery for subaortic stenosis or pulmonary artery stenosis. Right Maze was performed in 10 patients and biatrial Maze in 4 with IART and atrial fibrillation. Seven patients underwent right atrial isthmus cryoablation. Other procedures performed concomitantly with Fontan conversion included atrioventricular valve repair or replacement, subaortic muscle bundle resection, mitral valve obliteration, and pulmonary artery angioplasty.

IART patients who required Fontan conversion had poorer long-term function status than those who did not, with lower New York Heart Association (NYHA) functional class ($p = 0.034$), higher incidence of atrial thrombus ($p = 0.014$), and higher incidence of ventricular dysfunction ($p = 0.013$).

IART recurred in 9 of 24 patients who underwent Fontan conversion with antiarrhythmic surgery (37.5%) at a median 2.0 years (range 0.3–7.6) after the operation. However, among the 22 Fontan conversion patients who survived after the operation, IART severity scores decreased significantly over a median follow-up period of 7.8 years, from 6.9 ± 2.1 before conversion to 2.4 ± 2.7 at last follow-up ($p < 0.001$) (Fig. 3). Two of the patients in whom IART recurred received pacemakers for atrial pacing that prevented IART for 12 and 20 months. Another 2 patients with recurred IART were placed on a class III antiarrhythmic drug and remained IART-free for the last 5 years before the end of follow-up.

Seventeen of the 22 patients who survived after the operation were classified as having favorable outcomes, whereas 3 of the 22 patients had unfavorable outcomes despite medication and atrial pacing by a permanent pacemaker. Early postoperative IART developed more frequently in patients with an unfavorable outcome (3/3) than in those with a favorable outcome (2/17), whereas there was no difference between the groups in the frequency of perioperative complications, such as acute kidney injury, bleeding, and prolonged pleural effusion.

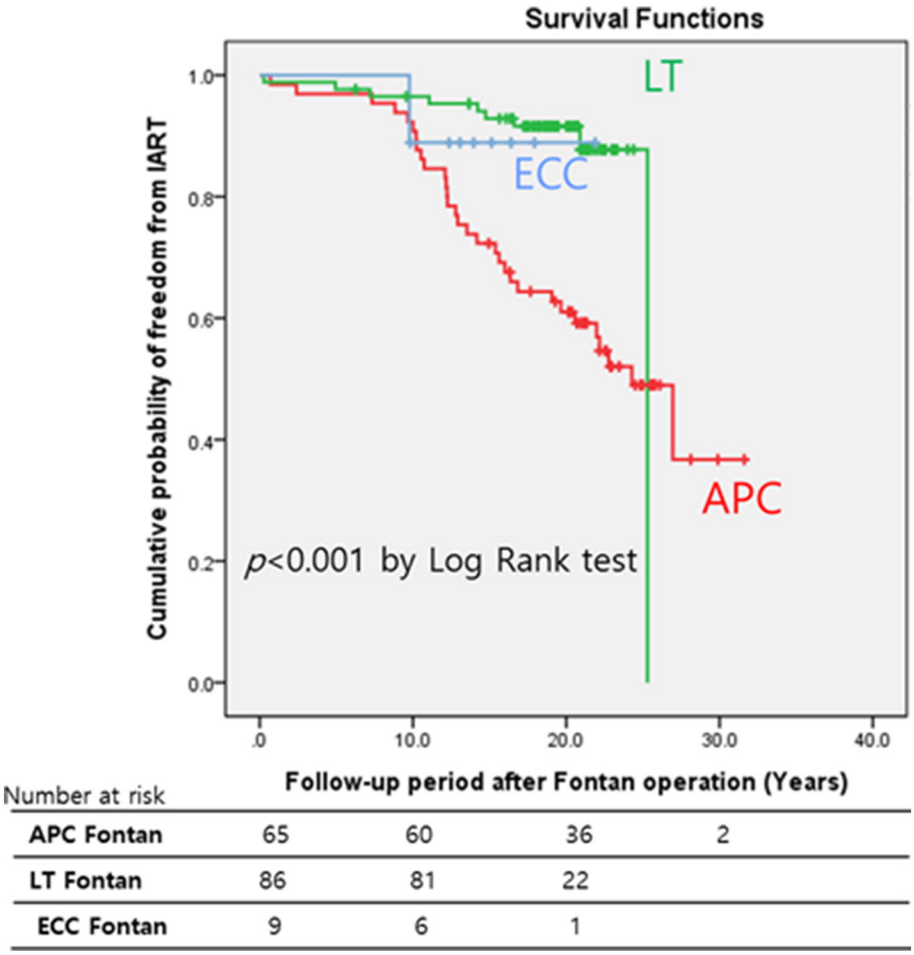

Fig. 2. Kaplan–Meier estimator of the probability of freedom from IART according to Fontan type. IART indicates intra-atrial reentrant tachycardia; LT, lateral tunnel Fontan; ECC, Extracardiac connection Fontan; APC, atriopulmonary connection Fontan.

Before Fontan conversion, NYHA functional class was I in 6 patients, II in 10 patients, III in 5 patients, and IV in 3 patients. NYHA class improved in 13 of the 22 Fontan conversion patients who survived for at least 3 months after the operation; in the other 9, in whom NYHA class was I or II, there was no change. Thus, Fontan conversion produced a significant improvement in NYHA.

One Fontan conversion patient with intractable protein losing enteropathy died during the early postoperative period (2.8% of the Fontan conversion group). Three Fontan conversion patients died during the late postoperative period (8.3%); 1 death occurred 4 months after Fontan conversion owing to severe ventricular dysfunction with junctional tachycardia, 1 was due to intractable protein-losing enteropathy and sepsis, and 1 died suddenly at home 12 years after Fontan conversion.

Radiofrequency ablation using the CARTO system (Biosense Webster, Diamond Bar, California, USA) was performed in 2 patients with

Table 3
Multivariate analysis of risk factors for late IART and late mortality.

Variables	Odds ratio	p value	95% C.I.
Risk factors for IART in all patients			
APC Fontan	4.8	0.002	1.731–13.059
Sinus node dysfunction	6.8	<0.001	2.42–18.973
NSAT	4.7	0.003	1.723–12.886
Risk factors for IART in patients with APC Fontan			
NSAT	12.7	0.001	2.838–56.798
Sinus node dysfunction	4.7	0.038	1.093–20.333
Risk factors for IART in patients with LT or ECC Fontan			
Sinus node dysfunction	47.6	0.004	3.300–616.398
Moderate-to-severe AVVR	45.1	0.001	4.942–458.964
Risk factors for late mortality			
Protein losing enteropathy	7.3	0.015	1.467–35.976
Ventricular dysfunction	3.5	0.050	1.002–11.988

IART indicates intra-atrial reentrant tachycardia; APC, atriopulmonary connection; NSAT, nonsustained atrial tachycardia; LT, lateral tunnel; ECC, extracardiac conduit; AVVR, atrioventricular regurgitation.

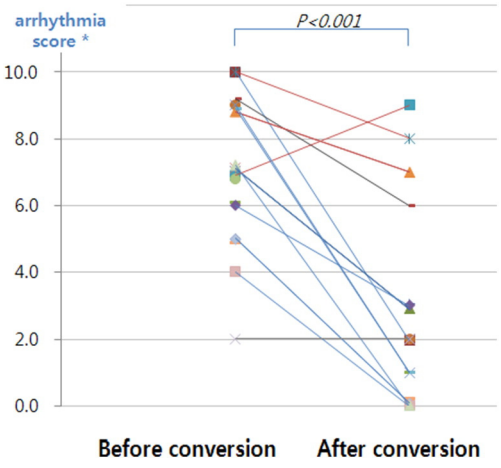

Fig. 3. IART clinical arrhythmia score before Fontan conversion and at last follow-up. *see definitions in Method section.

APC Fontan and severely dilated right atrium, but IART recurred in both patients at 3 and 7 months, respectively. Fontan conversion to ECC Fontan with right side maze operation and pacemaker implantation was performed in both patients, of whom IART did not recur for 1.1 and 2.4 years.

Medications taken by the IART patients are shown in Table 4. Class III anti-arrhythmic drugs were more frequently used in the medication-only group than the Fontan conversion group (65% vs. 33%, $p = 0.047$). Among the 17 IART patients who received only medical management, 4 died.

3.5. Late mortality in Fontan patients

There were 13 late deaths (>3 months after the Fontan operation) in this study, with a mean interval of 17.8 ± 5.1 years (range 9.6–30.1) after the operation. The mean age at death was 23.1 ± 8.4 years (range 11.2–47.6). Factors appearing to be significantly associated with death on univariate analysis included protein losing enteropathy ($p = 0.027$), moderate-to-severe atrioventricular valve regurgitation ($p = 0.043$), and ventricular dysfunction with ejection fraction <50% ($p = 0.039$). IART ($p = 0.087$) also increased the risk of death, although not statistically significantly so. Multivariate logistic regression confirmed protein losing enteropathy and ventricular dysfunction as significant risk factors for death (Table 3). Three of the 13 patients who died had intractable protein losing enteropathy. Three patients with a history of IART died owing to decompensated heart failure from severe ventricular dysfunction with atrial tachyarrhythmia or severe atrioventricular valve regurgitation. One patient with right isomerism and ventricular dysfunction died from pneumococcal septic shock, and 1 patient with left isomerism died from malignant pheochromocytoma with multiple metastasis and subsequent ventricular dysfunction. Sudden death of unknown origin was noted in 4 patients, of whom 1 had a history of IART and 1 had a history of sustained ventricular tachycardia.

Fontan type, heterotaxy syndrome, age at Fontan operation, single ventricle of right ventricle type, SND, and history of Blalock–Taussig shunt were not correlated with death.

4. Discussion

This study examined long-term outcomes for Fontan procedure and mid-term outcomes for Fontan conversion in an adult cohort and was comparable to previous studies in terms of follow-up duration.

The association between the APC Fontan and IART has been well established by other reports [13,14]. Patients with an APC Fontan may develop chronic atrial stretch, increased pressure, dilatation, fibrosis, extensive scar tissue, and increased wall thickness, which can result in diffuse atrial mechano-electrical remodeling [15,16]. Duration of Fontan circulation is also well known as a risk factor for IART [1,2,17], which is consistent with the findings of this study. In this series, late IART incidence was about 22% at the 20-year follow-up and 40% at the 25-year follow-up, as estimated using the Kaplan–Meier estimator. Patients with an APC had significantly longer follow-up duration (mean 23.7 years vs. 19.4 years for LT and 15.2 years for ECC), which could account for the apparent higher incidence of IART in these patients than in the LT and ECC groups. However, multivariate analysis adjusting for follow-up duration confirmed APC configuration as a significant risk factor. Likewise, incidence of IART at the 20-year follow-up was higher in APC patients (39%) than LT patients (9%) ($p < 0.001$), whereas it did not differ between LT and ECC patients. A previous multicenter study ($n = 1271$) reported that the time-adjusted incidence of late tachyarrhythmias was not different between ECC and LT configurations [18]. However, that study was a medium-term study with a median follow-up duration of 9.2 years for the LT group and 4.7 years for the ECC group. As we included adult patients (>18 years) after Fontan surgery with long-term follow-up duration, the ECC group was composed of relatively few members, making it difficult to compare the incidence of late tachyarrhythmia between the ECC group and other groups.

To control IART, we primarily utilized Fontan conversion with elimination of dilated and diseased atrial tissue and correction of atrial fibrillation. After Fontan conversion, IART severity score and NYHA functional class improved significantly, with relatively low operative mortality. As the IART severity score we used was developed to assess the outcome of radiofrequency ablation of IART in patients with congenital heart disease [12], it had some limitations with regard to patients who underwent Fontan conversion. Frequency of cardioversion, one of the 4 IART severity scales, might have been underestimated in some cases. For example, in some patients who had developed a large thrombus and IART, Fontan conversion was performed at the first IART episode, and frequency of cardioversion was rated only 1 point. However, we believe that IART severity scores reflected overall severity of IART before and after Fontan conversion well, as they also accounted for symptom severity, documented IART, and antiarrhythmic medications. In the 3 patients with an unfavorable outcome, the recurrence of IART could be due to failure of the maze procedure as a result of poor surgical access, as 1 of these patients had very complex anatomy with a dual Fontan pathway (Fig. 4), and the other 2 had an anteriorly located aorta and a posterior Fontan pathway.

Fontan conversion from APC to LT or ECC Fontan, with or without concomitant antiarrhythmic surgery, has been performed in patients with refractory supraventricular arrhythmias since the late 1990s [6–8,19–23]. In patients with supraventricular tachyarrhythmia, cryoablation of the arrhythmia circuit during Fontan conversions was

Table 4
Antiarrhythmic drugs in patient with IART.

Antiarrhythmic drugs	Conversion group	Medication group
	n = 24	n = 17
Sotalol or amiodarone + atenolol or carvedilol ± digoxin	3 (13%)	3 (18%)
Sotalol or amiodarone ± digoxin	5 (21%)	7 (41%)
Flecainide + amiodarone + digoxin	0	1 (6%)
Atenolol or carvedilol ± digoxin	8 (33%)	2 (12%)
None or digoxin only	8 (33%)	4 (24%)

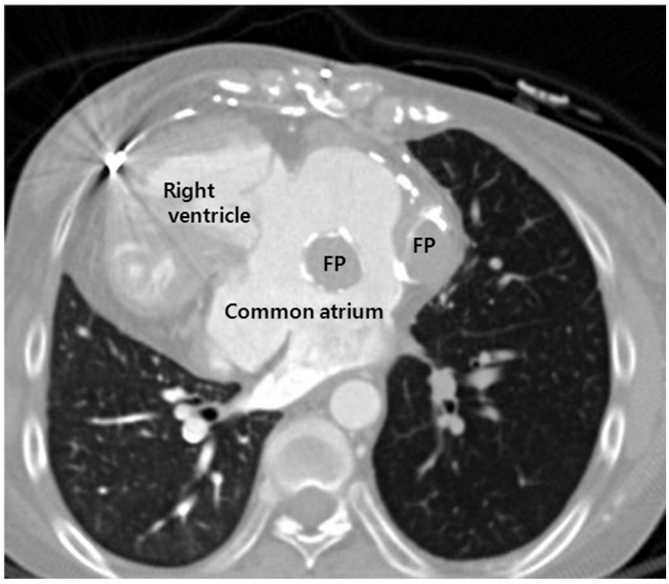

Fig. 4. Chest CT scan of a patients with highly recurrent IART. This patient had right ventricle type single ventricle with mitral atresia, left isomerism, dextrocardia and dual Fontan pathway after LT Fontan conversion. In this patient, IART was highly recurrent despite Fontan conversion, right side maze operation and atrial pacing. FP indicates Fontan pathway.

more effective than Fontan conversion alone, and a modified right atrial maze procedure was superior to isthmus ablation [6,8,24,25]. Previous studies in various health centers have reported early postoperative mortality after Fontan conversion to be 0–13.3% and late mortality to be <9.8% [8,19–22,26]. In patients who underwent Fontan conversion, early mortality (within 1 month of conversion) was 2.8% in our series, and there were 3 further deaths (8.3%) during the late postoperative period.

Acute procedural success rate of radiofrequency catheter ablation for IART in Fontan patients is reported as 40–75%, however recurrence rate is as high as 60%, which is higher than other congenital heart diseases [12,27,28]. In our center, radiofrequency ablation was not actively considered for recurrent IART of Fontan patients due to its highly recurrent property after ablation and less cost-effectiveness.

SND is a frequently reported complication after Fontan operation [9,29–31]. In this series, SND was a significant risk factor regardless of Fontan configuration. The Mustard/Senning procedures and the Fontan procedure expose the sinoatrial node to injury and create extensive atrial suture lines, which may result in SND. The bradycardia may result in ectopic beats and a prolonged refractory period, which can then induce atrial reentrant tachycardia. Previous studies in Fontan patients have reported SND to be a significant risk factor for late postoperative atrial flutter, which was corroborated by our findings [1,32]. Pacing can decrease the atrial refractory period, dispel conduction delay, and suppress ectopic beats. Antibradycardia pacing may prevent recurrence of atrial tachycardia and improve hemodynamics in patients with SND [33].

NSAT documented by 24 hour Holter monitoring is a risk factor for IART, and this is the first study to report its significance in Fontan patients. Not only is NSAT a sign of a diseased atrium, it may act as a trigger to induce sustained IART. Antiarrhythmic drugs are not usually used to control NSAT but may need to be considered for this purpose as an aggressive option in Fontan patients.

Multivariate analysis found late postoperative mortality to be associated with protein losing enteropathy and ventricular dysfunction. Protein losing enteropathy is a known risk factor for mortality and morbidity in Fontan patients [34,35]. In our study, 2 patients with intractable protein-losing enteropathy underwent Fontan conversion but nevertheless died from uncontrollable massive diarrhea and sepsis. Chronic protein losing enteropathy, peripheral edema, thromboembolism, immunodeficiency, poor nutritional status, and failure to thrive are all problematic complications that make patients prone to infection and intolerant of major surgery.

IART also increased the risk for death, although not statistically significantly so. IART can reduce the cardiac output of a single-ventricle heart, especially in patients with ventricular dysfunction and valve regurgitation, leading to eventual death. In our study, sudden death occurred in 4 patients, of whom 2 had a history of atrial and ventricular tachycardia; otherwise, the 4 had good ventricular function and no significant valve regurgitation. The main cause of sudden death in Fontan patients may be arrhythmia. Giannakoulas et al. reported that supraventricular tachyarrhythmia was a significant risk factor for death in adult Fontan patients [5]. Diller et al. reported a similar result in a multicenter study of 321 patients, finding clinically relevant (usually supraventricular) arrhythmia to be a significant risk factor for death or transplantation (hazard ratio 6.0, 95% confidence interval 2.382–13.158) [36]. Therefore, IART should be controlled aggressively in Fontan patients.

4.1. Study limitations

This study was limited by its retrospective nature. Future evaluations of the efficacy and safety of Fontan conversion should have longer follow-up periods and a larger sample size. In our study, the relatively small sample size and relatively short-term follow-up of ECC patients made it difficult to compare the incidence rates of IART and mortality between the ECC configuration and the others. We performed electrophysiological mapping in only 2 patients with APCs, so we could not compare the outcome of radiofrequency catheter ablation with that of other surgical approaches in this series. As we performed arrhythmia correction surgery without preoperative or intraoperative electrophysiological mapping, we had limited ability to identify the IART circuit and target surgical cryoablation. We did not include hemodynamic parameters in this study due to some loss of catheterization data, which can be a limitation of analysis for risk factors.

5. Conclusions

IART was common in adult Fontan patients. The atriopulmonary connection Fontan, coexisting sinus node dysfunction, and nonsustained atrial tachycardia were associated with increased risk of IART. Protein losing enteropathy and ventricular dysfunction were significant risk factors for late postoperative death in adult Fontan patients. Fontan conversion with or without arrhythmia surgery, along with pacemaker placement, can help control IART; however, long-term monitoring is required.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

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