Cardiology in the Young

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Tachyarrhythmia after the total cavopulmonary connection: incidence, prognosis, and risk factors

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Original Article

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Abstract

Objective: The purpose of this study is to evaluate the incidence and outcomes regarding tachyarrhythmia in patients after total cavopulmonary connection. *Methods:* A retrospective analysis of 620 patients who underwent total cavopulmonary connection between 1994 and 2021 at our institution was performed. Incidence of tachyarrhythmia was depicted, and results after onset of tachyarrhythmia were evaluated. Factors associated with the onset of tachyarrhythmia were identified. *Results:* A total of 52 (8%) patients presented with tachyarrhythmia that required medical therapy. Onset during hospital stay was observed in 27 patients, and onset after hospital discharge was observed in 32 patients. Freedom from late tachyarrhythmia following total cavopulmonary connection at 5, 10, and 15 years was 97, 95, and 91%, respectively. The most prevalent late tachyarrhythmia was atrial flutter (50%), followed by supraventricular tachycardia (25%) and ventricular tachycardia (25%). Direct current cardioversion was required in 12 patients, and 7 patients underwent electrophysiological study. Freedom from Fontan circulatory failure after onset of tachyarrhythmia at 10 and 15 years was 78% and 49%, respectively. Freedom from occurrence of decreased ventricular systolic function after the onset of tachyarrhythmia at 5 years was 85%. Independent factors associated with late tachyarrhythmia were dominant right ventricle (hazard ratio, 2.52, $p = 0.02$) and weight at total cavopulmonary connection (hazard ratio, 1.03 per kilogram; $p = 0.04$). Type of total cavopulmonary connection at total cavopulmonary connection was not identified as risk. *Conclusions:* In our large cohort of 620 patients following total cavopulmonary connection, the incidence of late tachyarrhythmia was low. Patients with dominant right ventricle and late total cavopulmonary connection were at increased risk for late tachyarrhythmia following total cavopulmonary connection.

Tachyarrhythmia was one of the most common complications in patients after the classic Fontan procedure.[1–3] It predominantly occurred as a response to progressive atrial stretch and had a prognostic implication associated with increased morbidity and mortality. Since the introduction of the total cavopulmonary connection, the survival and complication rate have improved drastically.[4–6] Due to this improvement in life expectancy and functional status in patients with total cavopulmonary connection, the long-term follow-up complications have gained more and more importance.[7–9] Among these, tachyarrhythmia appears to be one of the main concerns, along with thromboembolism, protein-losing enteropathy, plastic bronchitis, and ventricular failure.[10–15] Commonly observed tachyarrhythmias are atrial fibrillation and atrial flutter with a previously described incidence of 9–60%, and ventricular tachyarrhythmia with a described incidence of 2–16%.[10–15] These rhythm disturbances could cause severe clinical problems not only affecting the long-term outcome but also requiring further therapy or interventions.[16,17] Time of follow-up, atriopulmonary anastomosis, older age at Fontan operation, pre-operative and early post-operative tachycardia, and moderate-to-severe atrioventricular valve regurgitation have been identified as risk factors for the appearance of atrial tachyarrhythmia.[10–15] There is vast literature investigating tachyarrhythmia in adult patients after the Fontan procedure.[18–20] However, there is limited data on the incidence, type, and treatment of tachyarrhythmia and their impact on late outcomes in a contemporary cohort of total cavopulmonary connection.[21–23]

In this study, we therefore aimed to determine the incidence and type of tachyarrhythmia in a large cohort of patients who underwent total cavopulmonary connection at our institution.

Additionally, we intended to investigate the effectiveness of the treatments and to determine their prognostic impact on late outcomes.

Methods

Ethical statement

This study was approved by the Institutional Review Board of the Technical University of Munich (approved number of 2022-303-S-KH on 27 June, 2022). Because of the retrospective nature of the study, the need for individual patient consent was waived.

Patients and data collection

A single-centre retrospective cohort study of 620 consecutive patients who underwent a total cavopulmonary connection from May 1994 to December 2021 was performed. Medical records included baseline morphology and demographics as well as perioperative data using electronic and paper chart reviews of each patient. The patients obtained outpatient follow-ups with paediatric cardiologists. The most current vital status and follow-up data including the onset of tachyarrhythmia and systemic ventricular systolic function were obtained from our institutional single-ventricle database, which is regularly tracked. The detail of the assessment of ventricular systolic function was described in our previous study.[24]

Operative techniques

Total cavopulmonary connection is defined as total cavopulmonary anastomosis (superior vena cava (SVC) is directly connected to the right pulmonary artery, and inferior vena cava (IVC) is connected to the right pulmonary artery using a lateral tunnel or extra-cardiac conduit technique), and the right atrium was excluded from the Fontan pathway. In patients with situs inversus, SVC and IVC are connected to the left pulmonary artery. On the contrary, "classic" Fontan procedure included atriopulmonary anastomosis (Fontan–Kreutzer procedure) and atrioventricular anastomosis (Fontan–Björk procedure). In the Fontan–Kreutzer procedure, SVC flow and IVC flow drained into the right atrium and both SVC flow and IVC flow together go through to the pulmonary artery via the atrial appendage–main pulmonary artery anastomosis. In the Fontan–Björk procedure, the right atrial appendage was anastomosed to the infundibular portion of the right ventricle. In "classic" Fontan procedure, the right atrium was used for the Fontan pathway. The operative techniques for total cavopulmonary connection are described in previous reports.[6,25] Fenestration was not routinely performed and was only used for high-risk patients.[6]

Diagnosis of tachyarrhythmia and corresponding therapies

Patients' rhythm were regularly checked in hospital and also in outpatient clinics during rest in supine position using a standard 12-lead electrocardiogram. Experienced analysts reviewed the record of patients undergoing 24-hour Holter recording during normal daily activity. Tachyarrhythmia was defined as a documented atrial fibrillation, atrial flutter including cavo-tricuspid and non-cavo-tricuspid-related intra-atrial reentry tachycardia, not further specified supraventricular tachycardia, or focal atrial tachycardia. Ventricular arrhythmias comprised sustained ventricular tachyarrhythmia and ventricular fibrillation. We identified the point of time at which an arrhythmia was first recognised. Frequency and type of treatment, as well as success rates, were analysed. Early arrhythmia was defined as tachyarrhythmia observed in hospital stay after total cavopulmonary connection, and late arrhythmia was defined as tachyarrhythmia observed after hospital discharge. Treatment was classified as pharmacologic treatment (class I – class IV), direct current cardioversion, or electrophysiology study with and without ablation. During electrophysiology study, acute success was defined as the termination of tachycardia. The primary end point was the onset of any tachyarrhythmia requiring treatment. To determine the prognostic impact of arrhythmia on long-term outcomes, we examined late end points of Fontan circulatory failure, defined as death, heart transplantation, Fontan takedown, protein-losing enteropathy, plastic bronchitis, or NYHA functional class III or IV at follow-up. Protein losing enteropathy was diagnosed as defined by Rychik and colleagues' statement[26] from the American Heart Association, by symptoms of oedema without another identified cause and also by an elevated a-1 antitrypsin clearance in a 24-hour stool collection or an elevated a-1 antitrypsin level in a single stool sample paired with the presence of serum hypoalbuminemia. The diagnosis of plastic bronchitis was made by expectoration of casts, bronchoscopy, and histologic examination.

Statistical analysis

Categorical variables are presented as absolute numbers and percentages. A chi-square test was used for categorical data. Continuous variables are expressed as medians with interquartile ranges. An independent sample t-test was used to compare normally distributed variables. The Mann–Whitney U-test was used for variables that were not normally distributed. Freedom from tachyarrhythmia and freedom from Fontan circulatory failure after the onset of tachyarrhythmia were estimated using the Kaplan–Meier method, and differences between groups were determined using log-rank test. Risk factor analysis for the early onset of tachyarrhythmia was performed using linear regression model, and analysis for late onset of tachyarrhythmia was performed using Cox regression model. Data analysis was performed using SPSS version 28.0 for Windows (IBM, Ehningen, Germany) and R-statistical software (state package).

Results

Patient characteristics and perioperative data

Tachyarrhythmia was observed in hospital following total cavopulmonary connection in 27 (4.3%) patients. The incidence of dominant right ventricle (77.8% versus 52.3%, $p = 0.009$), double-outlet right ventricle (29.6% versus 12.3%, $p = 0.009$), total anomalous pulmonary venous connection/partial anomalous pulmonary venous connection (18.5% versus 6.2%, $p = 0.013$), and isomerism (18.5% versus 7.3%, $p = 0.032$) were more frequently observed in patients with in-hospital tachyarrhythmia, compared to those without in-hospital tachyarrhythmia (Table 1, Fig. 1, and Fig. 2).

Median age and weight at total cavopulmonary connection were 2.3 years (interquartile ranges: 1.8–3.4) and 12.0 kg (10.7–14.0), respectively (Table 2). Lateral tunnel total cavopulmonary connection was performed in 50 patients and extra-cardiac total

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Table 1. Baseline characteristics of the 620 patients who underwent TCPC.

		Total	No in-hospital tachyarrhythmia	In-hospital tachyarrhythmia	
Variable	Level	N=620	N=593	N=27	p value
Gender	Female	235 (37.9)	226 (38.1)	9 (33.3)	0.617
	Male	385 (62.1)	367 (61.9)	18 (66.7)	
Dominant ventricle	Left	289 (46.6)	283 (47.7)	6 (22.2)	**0.009**
	Right	331 (53.4)	310 (52.3)	21 (77.8)	
Primary Diagnosis	HLHS	172 (27.7)	162 (27.3)	10 (37.0)	0.270
	UVH	131 (21.1)	123 (20.7)	8 (29.6)	0.269
	TA	95 (15.3)	93 (15.7)	2 (7.4)	0.243
	DILV	91 (14.7)	89 (15.0)	2 (7.4)	0.275
	PAIVS	32 (5.2)	30 (5.1)	2 (7.4)	0.590
	ccTGA	29 (4.7)	29 (4.9)	0 (0.0)	0.239
	UAVSD	25 (4.0)	24 (4.1)	1 (3.7)	0.914
	Others	46 (7.4)	45 (7.7)	1 (3.7)	0.439
Associated cardiac anomaly	TGA	208 (33.5)	202 (34.1)	6 (22.2)	0.202
	DORV	81 (13.1)	73 (12.3)	8 (29.6)	**0.009**
	CoA	79 (12.7)	75 (12.6)	4 (14.8)	0.741
	TAPVC/PAPVC	42 (6.8)	37 (6.2)	5 (18.5)	**0.013**
Isomerism	Yes	48 (7.7)	43 (7.3)	5 (18.5)	**0.032**
Dextrocardia/Situs Inversus	Yes	56 (9.0)	51 (8.6)	5 (18.5)	0.079
Initial palliation	Norwood	264 (42.6)	250 (42.2)	14 (51.9)	0.319
	AP Shunt	185 (29.8)	180 (30.4)	5 (18.5)	0.112
	PAB	90 (15.5)	87 (14.7)	3 (11.1)	0.608
Prior BCPS	Yes	571 (92.1)	546 (92.1)	25 (92.6)	0.922
Age at BCPS (months)	Median (IQR)	5.4 (3.6-10.5)	5.4 (3.6-10.7)	5.1 (3.2-8.6)	**<0.001**
Weight at BCPS (kg)	Median (IQR)	5.7 (4.8-7.1)	5.7 (4.8-7.2)	5.2 (4.3-6.7)	0.070

BCPS = bidirectional cavopulmonary shunt; ccTGA = congenitally corrected transposition of the great arteries; CoA= coarctation of the aorta; DILV = double-inlet left ventricle; DORV = double-outlet right ventricle; HLHS = hypoplastic left heart syndrome; PAB = pulmonary artery banding; PAIVS = pulmonary atresia with intact ventricular septum; TA = tricuspid atresia; TAPVC/PAPVC = total anomalous pulmonary vein connection/ partial anomalous pulmonary vein connection; TCPC, total cavopulmonary connection; TGA = transposition of the great arteries; UAVSD = unbalanced atrioventricular septal defect; UVH = univentricular heart.
Patient diagnosis of functional univentricular heart was classified according to the modified congenital Heart Surgery Nomenclature and Database Project classification.

cavopulmonary connection in 570. Fenestration was placed in only 46 (7%) patients. There were eight in-hospital deaths.

Follow-up and occurrence of tachyarrhythmia

Among 612 early survivors, 10 patients were lost to follow-up after their hospital discharge. The median follow-up period was 5.9 (interquartile ranges: 1.2–13.1) years in the remaining 602 patients. There were 15 late deaths, 4 heart transplantations, and no Fontan takedown. Transplant-free survival at 5, 10, and 15 years was 96.8, 94.6, and 94.2%, respectively. During the study period, 52 (8.4%) patients presented with tachyarrhythmia (Table 3). Tachyarrhythmia was observed in hospital following total cavopulmonary connection in 27 (4.3%) patients and was diagnosed during follow-up periods in 32 (5.2%) patients with median interval of 11.0 (4.6–16.9) years. Freedom from the onset of tachyarrhythmia after hospital discharge was 96.8% (95% confidence interval: 94.8–98.7) at 5 years, 95.0% (95% confidence interval: 92.5–97.6) at 10 years, and 90.7% (95% confidence interval: 86.5–95.0) at 15 years, respectively (Fig. 3).

Therapy for tachyarrhythmia

In 27 patients with early tachyarrhythmia, initial medication included class II in 19 patients, class I in 8 patients, and class III antiarrhythmics in 1 patient (Table 4). Three patients underwent direct current cardioversion. All patients were discharged with sinus rhythm, and late tachyarrhythmia was observed in seven patients with a median of 4.2 years after total cavopulmonary connection. At the last follow-up, 11 patients needed medication including class II in 8 patients, class I in 2, and class III in 2.

In 32 patients with late arrhythmia, medical therapy included class II in 21 patients, class I in 8, class IV in 2, and class III in 1. A single episode of tachyarrhythmia was observed in 16 patients

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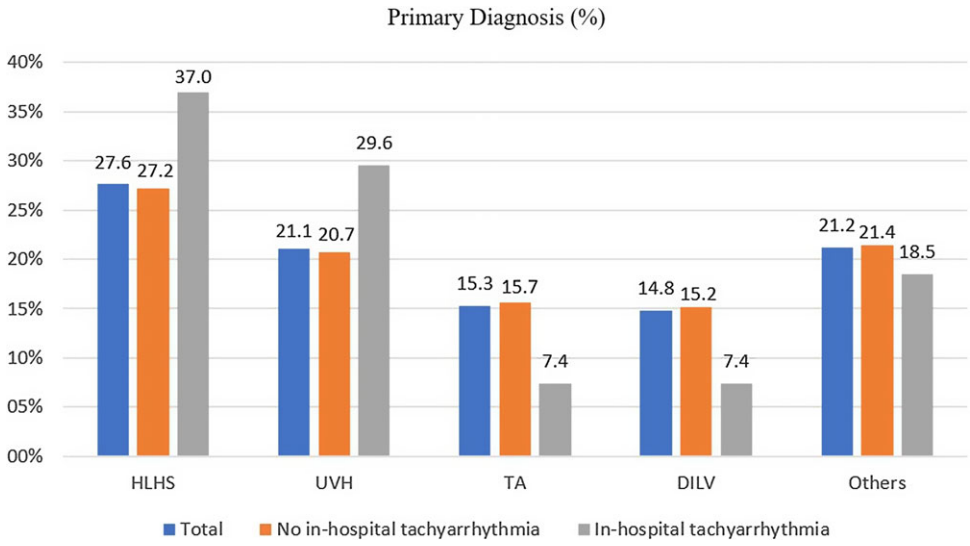

Figure 1. Bar chart comparing the primary diagnosis between patients with and without the onset of in-hospital tachyarrhythmia.

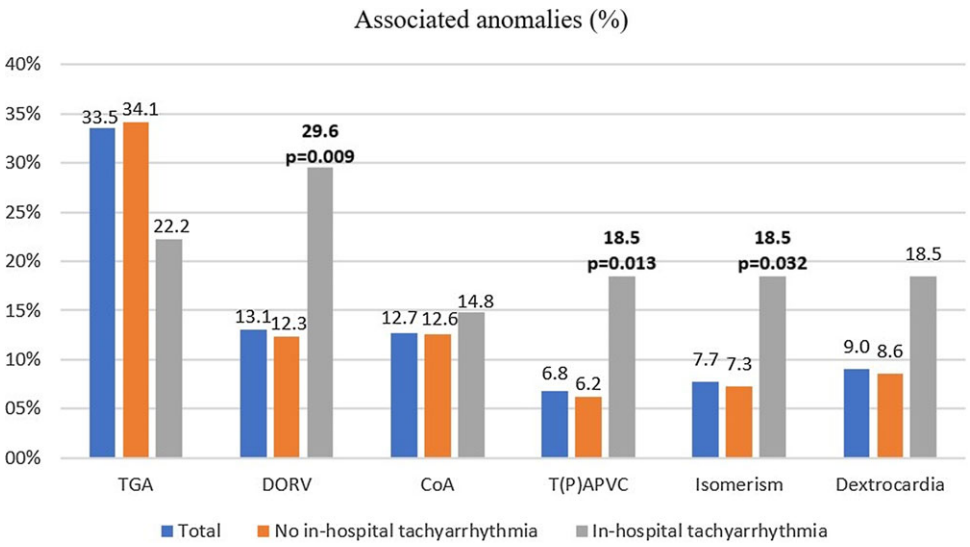

Figure 2. Bar chart showing the distribution of associated anomalies between patients with and without the onset of in-hospital tachyarrhythmia.

(50.0%), with no recurrence after a median follow-up of 5.2 (2.3–8.5) years. The remaining 16 patients (50.0%) had multiple episodes of tachyarrhythmia, and 3 patients (9.4%) experienced more than 3 symptomatic tachyarrhythmic episodes. Those who experienced a single versus multiple (>1) episodes of tachyarrhythmia showed no significant differences in the freedom from Fontan circulatory failure (single: 88% versus multiple: 84%, P = .17) at 5 years (Supplementary Figure S1). Direct current cardioversion was required in 12 (37.5%) patients, and a repeat direct current cardioversion was required in 4 patients (12.5%). Seven patients (21.9%) received an electrophysiology study at a median of 439 days after the first onset of tachyarrhythmia, and six of them (18.8%) underwent consequent catheter ablation. The results after electrophysiology study are shown in Supplementary Table S1. Acute success was obtained in five out of six patients, but three patients needed direct current cardioversion after ablation therapy. During follow-up after the onset of tachyarrhythmia, three patients died, two patients developed protein-losing enteropathy, one patient developed plastic bronchitis, and six patients developed NYHA class III or IV symptoms. No patient with tachyarrhythmia underwent heart transplantation. In total, seven patients reached the composite end point of Fontan circulatory failure. Freedom from Fontan circulatory failure after the onset of a tachyarrhythmia were 86.2, 77.5, and 48.5% at 5, 10, and 15 years, respectively (Fig. 4). At last follow-up, 19 patients (59.4%) needed anti-arrhythmic medication, including class II medications in 16 patients, followed by class I in 2, and class III in 1.

Among patients with tachyarrhythmia, reduced ventricular systolic function was observed in eight patients (8/32, 25%) before the onset of tachyarrhythmia in four patients and after the onset of tachyarrhythmia in four patients. After the onset of tachyarrhythmia, freedom from the onset of reduced ventricular systolic function at 5 years was 85%.

Risk factors for the onset of tachyarrhythmia

As for the early onset of tachyarrhythmia during hospital stay, double-outlet right ventricle (p = 0.01, odds ratio: 3.00), dominant

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Table 2. Perioperative variables.

Variables	Total cases N=620	No tachyarrhythmia N=568	Tachyarrhythmia N=52
Operative data			
Age at TCPC (years)	2.3 (1.8-3.4)	2.3 (1.8-3.2)	2.9 (1.9-6.4)
Weight at TCPC (kg)	12.0 (10.7-14.0)	12.0 (10.7-14.0)	12.6 (10.7-20.8)
Type of TCPC			
Intra-cardiac	50 (8.1)	36 (6.3)	14 (26.9)
Extra-cardiac	570 (91.9)	532 (93.7)	38 (73.1)
CPB time (min)	66 (47-102)	65 (46-97)	96 (61-130)
Aortic cross clamp (AXC)	161 (26.0)	138 (24.3)	23 (44.2)
AXC time (min)	46 (26-73)	44 (26-69)	65 (32-96)
Concomitant procedure	164 (26.5)		
DKS	17 (2.7)	15 (2.6)	2 (3.8)
AVV procedure	79 (12.7)	68 (12.0)	11 (21.2)
PA reconstruction	59 (9.5)	48 (8.5)	11 (21.2)
Atrioseptectomy	29 (4.7)	25 (4.4)	4 (7.7)
SAS/VSD enlargement	13 (2.1)	12 (2.1)	1 (1.9)
Pacemaker implantation	12 (1.9)	8 (1.4)	4 (7.7)
Fenestration at TCPC	46 (7.4)	33 (5.8)	13 (25.0)
Postoperative data			
ICU stay (days)	6 (4-9)	6 (4-9)	7 (5-11)
Hospital stay (days)	20 (14-28)	20 (14-27)	24 (20-36)
Complications			
Pleural effusion	301 (48.5)	277 (49.3)	24 (46.2)
Chylothorax	131 (21.2)	121 (21.6)	10 (19.2)
Secondary fenestration	11 (1.8)	8 (1.4)	3 (5.8)

AVV = atrioventricular valve; CPB = cardiopulmonary bypass; DKS = Norwood/Damus–Kay–Stansel; PA = pulmonary artery; SAS/VSD = subaortic stenosis/ventricular septal defect; TCPC = total cavopulmonary connection.

right ventricle ($p = 0.01$, odds ratio: 3.20), and isomerism ($p = 0.04$, odds ratio: 3.00) were risk factors using univariate analysis, and dominant right ventricle ($p = 0.01$, odds ratio: 3.20) was an independent risk factor using multivariate analysis (Table 5). As for the late onset of tachyarrhythmia, double-outlet right ventricle ($p = 0.01$, hazard ratio: 2.79), dominant right ventricle ($p = 0.04$, hazard ratio: 2.21), older age at total cavopulmonary connection ($p = 0.03$, hazard ratio per year: 1.05), and heavier weight at total cavopulmonary connection ($p = 0.01$, hazard ratio per kg: 1.03) were risk factors using univariate analysis, and dominant right ventricle ($p = 0.02$, hazard ratio: 2.52) and heavier weight at total cavopulmonary connection ($p = 0.04$, hazard ratio per kg: 1.03) were independent risk factors using multivariate analysis. The results of other variables are shown in Supplementary Table S2. As for the type of total cavopulmonary connection, patients with extra-cardiac total cavopulmonary connection had a tendency of better freedom from tachyarrhythmia than those with lateral tunnel total cavopulmonary connection, but p-value did not reach a significant difference ($p = 0.075$) in the late onset of tachyarrhythmia (Supplementary Figure S2). When we analysed the episode of an early tachyarrhythmia as a risk for late tachyarrhythmia, it was identified as a significant risk for late tachyarrhythmia ($p < 0.001$, hazard ratio: 15.641, 95% confidence interval = 6.355–38.492).

Comment

Among 620 patients who underwent total cavopulmonary connection, freedom from late tachyarrhythmia after hospital discharge was 91% at 15 years. Dominant right ventricle and higher weight at total cavopulmonary connection were risks for the late onset of tachyarrhythmia. Freedom from Fontan circulatory failure after the first onset of arrhythmia was 86.2, 77.5, and 48.5% at 5, 10, and 15 years, respectively.

Incidence of tachyarrhythmia

Compared to patients after the classic Fontan procedure, the incidence of tachyarrhythmia after total cavopulmonary connection has been reported lower, ranging from 4 to 40%[4,5,12,15,22,23,27] at 10–15 years. Our results of 9% at 15 years were consistent with previous reports. In general, there is no progressive atrial stretch in patients after total cavopulmonary connection, and a lower incidence of

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Table 3. Type of tachyarrhythmia.

Variables	N	%
Total number of patients	620	
Early tachyarrhythmia (in hospital)	27	4.3
Supraventr. tachycardia (not specified)	13	2.1
Atrial flutter	6	1.0
Ventricular tachycardia	5	0.8
Atrioventricular reentrant tachycardia	4	0.6
Focal atrial tachycardia	4	0.6
Numerous SVES*	3	0.5
Junctional ectopic tachycardia	2	0.3
Late tachyarrhythmia (after discharge)	32	5.2
Atrial flutter	15	2.4
Supraventr. tachycardia (not specified)	8	1.3
Ventricular tachycardia	8	1.3
Focal atrial tachycardia	6	1.0
Atrioventricular reentrant tachycardia	3	0.5
Intraatrial reentry tachycardia	2	0.3
Atrioventricular nodal reentrant tachycardia	1	0.2

SVES = supraventricular extrasystole.

tachyarrhythmia is a great advantage of total cavopulmonary connection. In this study, we found the tendency that extra-cardiac total cavopulmonary connection was better in the freedom from tachyarrhythmia than lateral tunnel total cavopulmonary connection. However, there was no significant difference in the incidence of tachyarrhythmia in lateral tunnel total cavopulmonary connection and extra-cardiac total cavopulmonary connection. This issue is still controversial. Several studies demonstrated better freedom from tachyarrhythmia in extra-cardiac total cavopulmonary connection than lateral tunnel total cavopulmonary connection,[28–30] and other studies showed no significant difference in the incidence of arrhythmia between lateral tunnel total cavopulmonary connection and extra-cardiac total cavopulmonary connection[31–33] or better outcome after lateral tunnel total cavopulmonary connection in regard to tachyarrhythmia.[34] Therefore, we cannot conclude that extra-cardiac total cavopulmonary connection is definitively better than lateral tunnel total cavopulmonary connection in regard to late tachyarrhythmia.

In our study, we found atrial tachyarrhythmia in almost 75% and ventricular tachyarrhythmia in 25% of the patients, and atrial flutter was the most frequent atrial tachyarrhythmia. Other studies demonstrated that the most frequent tachyarrhythmia to be cavo-tricuspid and non-cavo-tricuspid-related intra-atrial reentry tachycardia.[10–15] These can be triggered by scar tissue in the atria, chronic atrial pressure, or volume overload.[13,14] Moreover, other factors associated with older age, such as higher body mass index, arterial hypertension, dyslipidemia, cigarette smoking, and coronary artery disease, might favour the presence of atrial flutter.[12,35]

Results after therapy

In this study, patients with early tachyarrhythmia showed a good response to medical therapy and direct current cardioversion, and all patients were discharged with sinus rhythm. Recurrent tachyarrhythmia was observed in only seven patients. Among 32 patients with late tachyarrhythmia, 21 patients needed direct current cardioversion and 7 patients, in whom pharmacologic

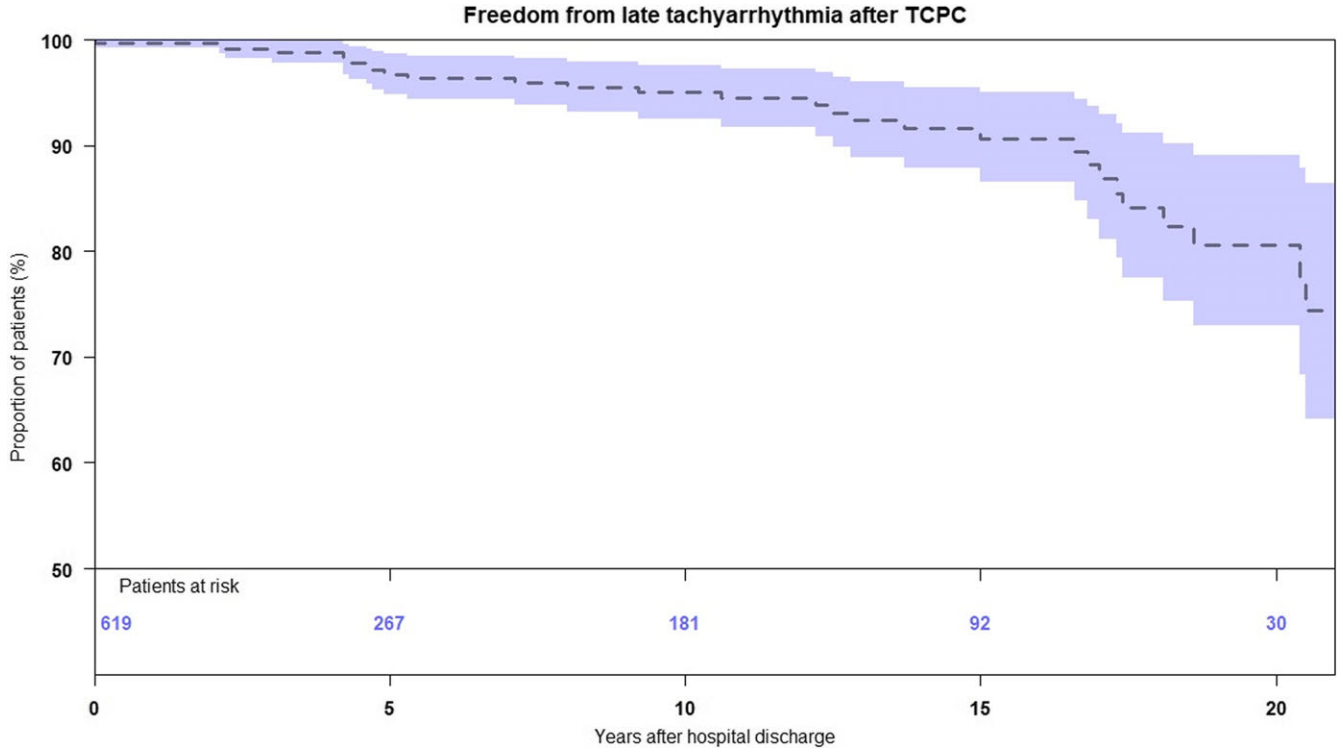

Figure 3. Kaplan–Maier estimate of freedom from the onset of tachyarrhythmia after hospital discharge following TCPC. TCPC, total cavopulmonary connection.

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Table 4. Therapy after the onset of tachyarrhythmia.

Variables	N	%
Total number of patients	620	
Early tachyarrhythmia (in hospital)	27	4.3
Medication	27	4.3
Class I	8	1.3
Class II	19	3.1
Class III	1	0.2
Cardioversion	3	0.5
Late arrhythmia (after discharge)	32	5.2
Medication	32	5.2
Class I	8	1.3
Class II	21	3.4
Class III	1	0.2
Class IV	2	0.3
Cardioversion	12	1.9
Electrophysiological study	7	1.1
Catheter ablation	6	1.0

treatment had been ineffective, received an electrophysiology study and 6 of them underwent subsequent ablation. Immediate success was achieved in all but one patient. The results were consistent with the results of other studies.[10–15] Acute procedural success in ablation therapy has been reported as a predictor of recurrence-free survival. In our study, recurrence of tachyarrhythmia after electrophysiology study was seen only in one patient, and all of the seven patients were alive.

There is concern that the onset of a late tachyarrhythmia is the first sign of deterioration or failure of the Fontan circulation. Patients who develop late atrial tachyarrhythmia are more prone to Fontan circulatory failure, ventricular systolic dysfunction, and hospitalisations. In this study, 7 of 32 patients who developed late tachyarrhythmia reached the composite end point of Fontan circulatory failure, and freedom from Fontan circulatory failure after the onset of arrhythmia was 78 % at 10 years and 49% at 15 years. These results were consistent with the report by Carins et al.[23] Survival after the onset of arrhythmia was surprisingly good: there were only 3 deaths among 32 patients, that is, more than 90% survival at 10 years after the onset of a tachyarrhythmia. Previous reports demonstrated that the onset of arrhythmia would be associated with a rapid decline in survival.[1–3]

Risks for late-onset tachyarrhythmia and future prospective

We found dominant right ventricle and heavier weight at total cavopulmonary connection to be predictors of developing late tachyarrhythmia. These findings are consistent with those previously reported by our group. In other studies, atriopulmonary Fontan, atrial isomerism, and dextrocardia were also reported as risk factors of developing tachyarrhythmia. In this study, isomerism was identified as a risk factor for early tachyarrhythmia, but not for late tachyarrhythmia. Of note, patients twith the extra-cardiac conduit total cavopulmonary connection were not less likely to experience a tachyarrhythmia compared with those with lateral tunnel total cavopulmonary connection. In this study, the median age and weight at total cavopulmonary connection were 2.3 years and 12 kg, respectively, and older age and heavier weight at total cavopulmonary connection were risks for late tachyarrhythmia. Our current strategy is to perform total cavopulmonary connection completion from 18 months of age and from 10 kg weight as soon as patients reach these criteria. These results support our rationale for this strategy. We are convinced that early farewell to cyanosis and preservation of the systemic ventricular systolic function is most important to prevent late Fontan complications including tachyarrhythmia.

It is of note that double-outlet right ventricle was identified as a risk for both early and late tachyarrhythmia. We think this is a new finding. There are case reports describing tachyarrythmia late after total cavopulmonary connection in patients with double-outlet right ventricle.[36,37] However, there was no study that demonstrated

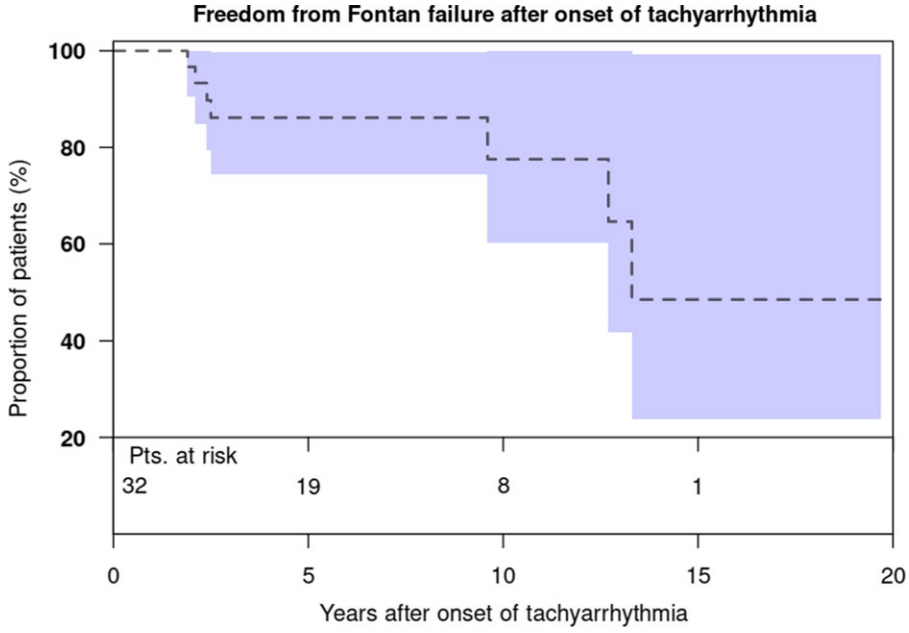

Figure 4. Kaplan–Maier estimate of freedom from Fontan circulatory failure after the onset of late tachyarrhythmia.

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Table 5. Risk factors for the onset of tachyarrhythmia.

	Univariate			Multivariate		
Variables	P-value	OR	95% CI	P-value	OR	95% CI
Early tachyarrhythmia						
DORV	0.01	3.00	1.27-7.01			
Dominant RV	0.01	3.20	1.27-8.03	0.01	3.20	1.27-8.03
Isomerism	0.04	2.91	1.05-8.06			
	Univariate			Multivariate		
Variables	P-value	HR	95% CI	P-value	HR	95% CI
Late tachyarrhythmia						
DORV	0.01	2.79	1.29-6.04			
Dominant RV	0.04	2.21	1.06-4.62	0.02	2.52	1.19-5.34
Age at TCPC (per year)	0.03	1.05	1.01-1.09			
Weight at TCPC (per kg)	0.01	1.03	1.01-1.05	0.04	1.03	1.01-1.05

CI = confidence interval; DORV = double-outlet right ventricle; HR = hazard ratio; RV = right ventricle; OR = odds ratio; TCPC = total cavopulmonary connection.

that double-outlet right ventricle is a risk for tachyarrhythmia after the Fontan procedure. Wilkinson et al. demonstrated in their 22 specimens study that the conduction system originated from a normally placed atrioventricular node in 4 out of 6 cases and was related to the trabecular septum in 5. The penetrating bundle usually descended onto the crest of the septum at the "crux" of the heart and bifurcated astride it. In two cases with an absent atrioventricular connection, the penetrating bundle originated from an abnormally placed node and in one of these specimens a sling of conducting tissue was identified with dual pathways.[38] These varieties of the conduction system might cause the higher incidence of tachyarrhythmia after total cavopulmonary connection. Further studies are mandatory to clarify the exact abnormalities of conductive tissue and the incidence of tachyarrhythmia in patients with double-outlet right ventricle.

Limitation

This study was limited by its retrospective and single-centre design. Changes in surgical and medical management have occurred with time that may not be covered by our analyses, and that may affect the long-term results. Changes in surgical management include the introduction of extra-cardiac total cavopulmonary connection since 1999 and the no fenestration policy since 2001. A tangible change regarding post-operative management was the adoption of an early extubation strategy even for unstable patients. The limited number of outcome events might limit the reliability of the Cox regression results in some cases (end points). In addition, the small number of outcomes limits the statistical power of analysis. Data were not available at consistent follow-up periods for every patient. Patients referred from other institutions might have a different history and quality of their remote medical and surgical management, and these factors could affect long-term outcomes.

Conclusions

Freedom from late tachyarrhythmia at 15 years was 91% following total cavopulmonary connection. Electrophysiology study and subsequent ablation demonstrated high rate of success in patients. Patients with dominant right ventricle and heavier weight at total cavopulmonary connection were at increased risk for late tachyarrhythmia. Freedom from Fontan circulatory failure after the first onset of an arrhythmia was 77.5% at 10 years, and close surveillance of clinical condition is required for this cohort.

Supplementary material. For supplementary material accompanying this paper visit https://doi.org/10.1017/S1047951123003141

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References

1. Poh CL, Zannino D, Weintraub RG, et al. Three decades later: the fate of the population of patients who underwent the atriopulmonary Fontan procedure. Int J Cardiol 2017; 231: 99–104.
2. Ghai A, Harris L, Harrison DA, et al. Outcomes of late atrial tachyarrhythmias in adults after the Fontan operation. J Am Coll Cardiol 2001; 37: 585–592.
3. Weipert J, Noebauer C, Schreiber C, et al. Occurrence and management of atrial arrhythmia after long-term Fontan circulation. J Thorac Cardiovasc Surg 2004; 127: 457–464.
4. d'Udekem Y, Iyengar AJ, Cochrane AD, et al. The Fontan procedure: contemporary techniques have improved long-term outcomes. Circulation 2007; 116: I157–64.
5. Nakano T, Kado H, Tatewaki H, et al. Results of extracardiac conduit total cavopulmonary connection in 500 patients. Eur J Cardiothorac Surg 2015; 48: 825–832.
6. Ono M, Kasnar-Samprec J, Hager A, et al. Clinical outcome following total cavopulmonary connection: a 20-year single-centre experience. Eur J Cardiothorac Surg 2016; 50: 632–641.
7. Pundi KN, Johnson JN, Dearani JA, et al. 40-year follow-up after the fontan operation: long-term outcomes of 1,052 patients. J Am Coll Cardiol 2015; 66: 1700–1710.
8. Khairy P, Fernandes SM, Mayer JE. Jr, etal, long-term survival, modes of death, and predictors of mortality in patients with fontan surgery. Circulation 2008; 117: 85–92.

9. Oster ME, Knight JH, Suthar D, et al. Long-term outcomes in single-ventricle congenital heart disease. Circulation 2018; 138: 2718–2720.
10. Okólska M, Karkowski G, Kuniewicz M, et al. Prevalence of arrhythmia in adults after fontan operation. J Clin Med 2022; 11: 1968.
11. Collins KK. The spectrum of long-term electrophysiologic abnormalities in patients with univentricular hearts. Congenit Heart Dis 2009; 4: 310–317.
12. Egbe AC, Connolly HM, Niaz T, McLeod CJ. Outcome of direct current cardioversion for atrial arrhythmia in adult Fontan patients. Int J Cardiol 2016; 208: 115–119.
13. Stephenson EA, Lu M, Berul CI, et al. Arrhythmias in a contemporary Fontan cohort: prevalence and clinical associations in a multicenter cross-sectional study. J Am Coll Cardiol 2010; 56: 890–896.
14. Fishberger SB, Wernovsky G, Gentles TL, et al. Factors that influence the development of atrial flutter after the Fontan operation. J Thorac Cardiovasc Surg 1997; 113: 80–86.
15. Lasa JJ, Glatz AC, Daga A, Shah M. Prevalence of arrhythmias late after the fontan operation. Am J Cardiol 2014; 113: 1184–1188.
16. Moore BM, Anderson R, Nisbet AM, et al. Ablation of atrial arrhythmias after the atriopulmonary Fontan procedure: mechanisms of arrhythmia and outcomes. JACC Clin Electrophysiol 2018; 4: 1338–1346.
17. Pujol C, Hessling G, Telishevska M, et al. Prevalence and treatment outcomes of arrhythmias in patients with single ventricle physiology over the age of 40 Years. J Clin Med 2022; 11: 6568.
18. Egbe AC, Connolly HM, Khan AR, et al. Outcomes in adult Fontan patients with atrial tachyarrhythmias. Am Heart J 2017; 186: 12–20.
19. Kürer CC, Tanner CS, Vetter VL. Electrophysiologic findings after Fontan repair of functional single ventricle. J Am Coll Cardiol 1991; 17: 174–181.
20. Gandhi SK, Bromberg BI, Schuessler RB, et al. Characterization and surgical ablation of atrial flutter after the classic Fontan repair. Ann Thorac Surg 1996; 61: 1666–1678.
21. Egbe AC, Miranda WR, Devara J, et al. Recurrent sustained atrial arrhythmias and thromboembolism in Fontan patients with total cavopulmonary connection. Int J Cardiol Heart Vasc 2021; 33: 100754.
22. Quinton E, Nightingale P, Hudsmith L, et al. Prevalence of atrial tachyarrhythmia in adults after Fontan operation. Heart 2015; 101: 1672–1677.
23. Carins TA, Shi WY, Iyengar AJ, et al. Long-term outcomes after first-onset arrhythmia in Fontan physiology. J Thorac Cardiovasc Surg 2016; 152: 1355–1363.
24. Dahmen V, Heinisch PP, Staehler H, et al. Longitudinal analysis of systemic ventricular function and atrioventricular valve function after the Fontan procedure. Eur J Cardiothorac Surg 2023; 63: ezad078.
25. Schreiber C, Hörer J, Vogt M, et al. Nonfenestrated extracardiac total cavopulmonary connection in 132 consecutive patients. Ann Thorac Surg 2007; 84: 894–899.
26. Rychik J, Atz AM, Celermajer DS, et al. Evaluation and management of the child and adult with Fontan circulation: a scientific statement from the American heart association. Circulation 2019; 140: e234–e284.
27. Schmiegelow MD, Idorn L, Gislason G, et al. Cardiovascular complications in patients with total cavopulmonary connection: a nationwide cohort study. Int J Cardiol 2020; 305: 120–126.
28. Azakie A, McCrindle BW, Van Arsdell G, et al. Extracardiac conduit versus lateral tunnel cavopulmonary connections at a single institution: impact on outcomes. J Thorac Cardiovasc Surg 2001; 122: 1219–1228.
29. van den Bosch E, Bossers SSM, Bogers AJJC, et al. Staged total cavopulmonary connection: serial comparison of intra-atrial lateral tunnel and extracardiac conduit taking account of current surgical adaptations. Interact Cardiovasc Thorac Surg 2019; 29: 453–460.
30. Robbers-Visser D, Miedema M, Nijveld A, et al. Results of staged total cavopulmonary connection for functionally univentricular hearts; comparison of intra-atrial lateral tunnel and extracardiac conduit. Eur J Cardiothorac Surg 2010; 37: 934–941.
31. Lasa JJ, Glatz AC, Daga A, et al. Prevalence of arrhythmias late after the Fontan operation. Am J Cardiol 2014; 113: 1184–1188.
32. Zheng J, Li Z, Li Q, Li X. Meta-analysis of Fontan procedure : extracardiac conduit vs. intracardiac lateral tunnel. Herz 2018; 43: 238–245.
33. Balaji S, Daga A, Bradley DJ, et al. An international multicenter study comparing arrhythmia prevalence between the intracardiac lateral tunnel and the extracardiac conduit type of Fontan operations. J Thorac Cardiovasc Surg 2014; 148: 576–581.
34. Brown JW, Ruzmetov M, Deschner BW, et al. Lateral tunnel Fontan in the current era: is it still a good option? Ann Thorac Surg 2010; 89:556–562.
35. Lewis M, Whang W, Biviano A, et al. Predictors and rates of recurrence of atrial arrhythmias following catheter ablation in adults with congenital heart disease. Congenit Heart Dis 2019; 14: 207–212.
36. Ferrari I, Shehu N, Stern H, et al. Junctional rhythm produces retrograde flow in the whole Fontan system: cardiac magnetic resonance-derived flow documentation-a case report. Eur Heart J Case Rep 2023; 7: ytad126.
37. Mizuno T, Nishii N, Morita H, et al. Pacemaker implantation via femoral vein and successful arrhythmia management in an elderly patient with Fontan circulation: a case report. Eur Heart J Case Rep 2022; 6: ytac003.
38. Wilkinson JL, Keeton B, Dickinson DF, et al. Morphology and conducting tissue in univentricular hearts of right ventricular type. Herz 1979; 4: 151–160.

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