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Long-Term Effects of Percutaneous Fenestration Following the Fontan Procedure in Adult Patients with Congenital Univentricular Heart

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Background: The Fontan procedure, performed for univentricular heart, may also include the technique of percutaneous fenestration to create a small atrial septal defect (ASD) and a right-to-left shunt. The aim of this study was to evaluate the long-term effects of fenestration in adult patients who had a Fontan procedure for univentricular heart.

Material/Methods: Fontan surgery was performed in 39 patients, including 19 (49%) patients with fenestration (Group I), and 20 (51%) patients without the fenestration procedure (Group II). Laboratory tests in both groups included echocardiography, plethysmography, cardiopulmonary exercise testing, and 24-hour Holter monitoring.

Results: Compared with patients in Group I, patients in Group II had a significantly increased level of N-terminal pro-brain natriuretic peptide (NT-proBNP) (p=0.04), alkaline phosphatase (ALP) (p=0.01) and a significant increase in frequency of atrial fibrillation (p=0.04). Patients in Group I had a significantly increased systemic ventricular ejection fraction (SVEF) (p=0.05) and increased heart rate (HR) (p=0.006), heart rate reserve (HRR) (p=0.02), ventilatory equivalent (VE) (p=0.01), and VO_2 peak (p=0.05) on cardiopulmonary exercise testing (CPET). Renal, hematologic, and ventilatory parameters, and incidence of thromboembolism showed no significant differences between the groups.

Conclusions: Long-term follow-up of patients who underwent Fontan procedures with percutaneous fenestration had improved single ventricular function, lower NT-proBNP levels, improved exercise capacity, and reduced ALP levels. These findings indicate that percutaneous fenestration closure should be considered for adult patients who have undergone Fontan procedure for univentricular heart.

MeSH Keywords: **Exercise Tolerance • Fontan Procedure • Heart Defects, Congenital**

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Background

The Fontan procedure is used as a palliative surgical procedure for patients with congenital heart disease with univentricular heart [1]. Although about 85% of patients now reach adulthood following the Fontan procedure [1], in time, they develop a reduction of exercise capacity and multi-organ complications, including hepatic fibrosis, protein-losing enteropathy (PLE), and effects on respiratory function [2–5]. Since 1971, when the first Fontan operation was performed, this procedure has undergone many modifications [1].

Almost 30 years ago, in 1988, the technique of fenestration was developed, which is the creation of a small atrial septal defect (ASD) to allow a small right-to-left shunt [6]. A fenestration is a communication between the right and left atrium that allows a reduction in pressure in the right atrium and the cavopulmonary bypass and improves the preload on the single ventricle [6]. The cardiac surgical procedure of fenestration contributes to overcoming the period of low cardiac output in the early postoperative period, reduces the need for mechanical ventilation, and reduces the incidence of pleural effusion, but this is done at the expense of mild to moderate desaturation [7,8]. The benefits of fenestration, beyond the early postoperative period, include a reduction in fibrinous (plastic) bronchitis, PLE, and cardiac dysrhythmia [9,10]. However, the potential risks of fenestration include cyanosis and thromboembolism [10].

Currently, the long-term effects of fenestration are unclear, and closure of the fenestration remains an issue for debate [7,10–13]. Most of the current published studies on the outcome of fenestration refer to pediatric surgical cases, while there is less published information regarding the clinical outcome of fenestration in adult patients, including the influence of fenestration on exercise capacity.

The aim of this study was to evaluate the long-term effects of fenestration in adult patients who had a Fontan procedure for univentricular heart, including the effects, including the effects on cardiac rhythm, respiratory function, exercise capacity, and hematologic, hepatic, renal, and thromboembolic complications.

Material and Methods

Ethical approval

The study protocol was approved by the local Ethics Committee of Jagiellonian University Medical College. All the patients provided informed written consent to participate in the study. Patients were consecutively recruited who were adults, who were more than 18 years-of-age, and who had undergone Fontan procedure in childhood. The study was conducted between 2012–2015.

Study participants

This study included 39 adult patients who were more than 18 years-of-age, who underwent Fontan operation for a diagnosis of a functionally single-ventricle heart. Of these 39 patients, 13 patients (33.3%) had tricuspid atresia; ten patients (26.0%) had pulmonary stenosis with transposition of the great arteries; nine patients (23.1%) had right ventricular hypoplasia; two patients (5.1%) had double-inlet right ventricle; and one patient (2.5%) had a complete atrioventricular canal (CAVC) defect.

The classic Fontan operation, in which the right atrium (RA) is directly connected to the main pulmonary artery (MPA) via the right atrial (RA) appendage, was the surgical procedure in three patients (8%); intracardiac total cavopulmonary connection (lateral tunnel) was the surgical procedure in the remaining patients. A left single ventricle was present in 30 patients (77%), and a right single ventricle was present in nine patients (23%). Patients were clinically stable for three months before inclusion in the study. Exclusion criteria included a history of asthma, neoplasia, infection, major trauma, pregnancy, diabetes, or alcohol abuse.

The Fontan surgery had been performed in 39 patients, including 19 (49%) patients (Group I) with fenestration, and 20 patients (51%) (Group II) who did not undergo the fenestration procedure.

Study protocol

Clinical information was recorded for each participant in the study and included the New York Heart Association (NYHA) functional class. Clinical data was recorded on vital signs, body weight, height, oxygen saturation, type of cardiac malformation, history of cardiac surgery, history of thromboembolic complications (pulmonary embolism, venous thrombosis, ischemic stroke), electrocardiography (ECG), cardiopulmonary exercise test (CPET), body plethysmography, and 24-hour Holter monitoring studies.

Laboratory investigations

Hematological tests included the red blood cell counts (RBC), hematocrit (HCT), hemoglobin (Hb), and red blood cell distribution width (RDW). N-terminal pro-brain natriuretic peptide (NT-proBNP) was measured. Tests of liver function included alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), total bilirubin level, and alpha-fetoprotein (AFP).

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Tests of renal function included creatinine levels, cystatin C, and the urine albumin to creatinine ratio (ACR).

Electrocardiography (ECG)

The single ventricle ejection fraction (SVEF) on ECG was semi-quantified by two experienced cardiologists using the Vivid 7 high-end cardiac ultrasound machine (GE Medical Systems, USA). Atrioventricular valve regurgitation was evaluated semi-quantitatively, and the fenestrations were evaluated by Doppler color flow imaging.

Cardiopulmonary exercise testing (CPET)

Each study participant underwent cardiopulmonary exercise testing (CPET) with a modified 30 minute Bruce protocol to evaluate exercise tolerance. The following parameters were recorded: time of exercise (T); heart rate (HR); blood pressure (BP); ventilatory equivalent (VE); maximum oxygen uptake (VO_{2max}); respiratory exchange ratio (RER); maximum ventilatory equivalent of oxygen (VE/VO_2); maximum ventilatory equivalent of carbon dioxide (VE/VCO_2); breathing reserve (BR); and oxygen saturation. Maximum oxygen uptake (VO_{2max}) was defined as the highest value at peak workload in ml/kg/min, and percentage of predicted value was obtained.

Ventilatory anaerobic threshold (VAT) as a measure of exercise tolerance used the V-slope method. Oxygen pulse (pulse-O_2) was defined as the amount of oxygen consumed per systole. The ventilatory equivalent of oxygen (VE/VO_2) was defined as the amount of ventilation needed for the uptake of a given amount of oxygen. The ventilatory equivalent for carbon dioxide (VE/VCO_2) was defined as the amount of ventilation needed for the elimination of a given amount of carbon dioxide. The respiratory exchange ratio (RER) was calculated by dividing the VO_2 by the VCO_2. The heart rate reserve (HRR) was calculated as the difference between peak and resting heart rate. Oxygen saturation at rest ($SatO_{2rest}$), peak saturation ($SatO_{2peak}$) and the difference between rest and peak saturation ($\Delta SatO_2$) were measured [3,14].

Pulmonary function tests (PFT)

Patients participating in the study underwent whole-body plethysmography. The American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines were followed for all lung function measurements [15]. Pulmonary functions measurements were expressed as absolute values and percentage of predicted values (%N) based on the age, sex, height, and ethnicity of the study participants.

The following pulmonary function parameters were noted: total lung capacity (TLC); vital capacity (VC); forced expiratory volume in one second (FEV_1); forced vital capacity (FVC); tidal volume (TV); expiratory reserve volume (ERV); reserve volume (RV); peak expiratory flow (PEF); maximal expiratory flow (MEF); and total resistance (R_{tot}).

Statistical analysis

Continuous variables were expressed as the mean and standard deviation (SD). The conformity of continuous variables to the normal distribution was analyzed with the Shapiro-Wilk test for normality. The χ^2 test (Chi-square test), Mann-Whitney U test, student's t-test, and Kruskal-Wallis test were performed, where appropriate. To exclude the influence of age on fenestration interactions, and the time from the fenestration procedure on analyzed parameters, a two-way analysis of variances (ANOVA) was performed. Statistical significance was set at a p-value <0.05. The data were analyzed using Statistica version 10.0.1011.7 (StatSoft Inc., USA).

Results

Patient characteristics

Thirty-nine patients were included in the study, who had undergone a Fontan procedure, and who had a median age of 25 years (range, 19–44 years). The median age of the patients at the time of the Fontan procedure was 5 years (range, 1–16 years). The mean postoperative duration from Fontan procedure to inclusion in the study was 19 years (range, 12–34 years).

Of the 39 patients who underwent Fontan surgery, there were 19 (49%) patients with fenestration (Group I), and 20 (51%) patients without the fenestration procedure (Group II). The baseline characteristics of the two groups of patients who underwent Fontan procedures, with and without fenestration, are shown in Table 1.

Atrial fibrillation

Atrial fibrillation was recorded in 23% of the total number of patients who underwent Fontan procedures, with and without fenestration. The groups of patients who underwent a Fontan procedure without fenestration (Group II) showed that the frequency of atrial fibrillation was significantly greater (p=0.04). Two-way of analysis of variance (ANOVA) showed that neither the age nor the time from surgery influenced the statistical significance of this finding. Furthermore, there was no age effect on fenestration and no effect of the time from the fenestration operation on the evaluated parameters.

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Table 1. Comparison of baseline characteristic and laboratory parameters between Fontan patients with or without fenestration.

	Fenestration		No fenestration		p Value
Number of patients, (n)	19		20		–
Number of males, n(%)	11	(58)	13	(65)	–
Age, (years)	24	(20–33)	30.5	(19–44)	**0.0004**
Age at operation, (years)	4	(2–15)	5	(1–16)	0.2
Time from operation, (years)	19	(18–22)	23.5	(12–34)	**0.002**
Type of Fontan procedure					
APC, n(%)	2	(11)	4	(20)	0.7
TCPC, n(%)	17	(89)	16	(80)	0.7
Type of systemic ventricle					
LV, n(%)	16	(84)	15	(75)	0.6
RV, n(%)	3	(16)	5	(25)	0.6
HR, (betas/min)	83	(50–97)	76.5	(58–109)	0.3
BP, (mmHg)					
Systolic	130	(110–160)	130	(85–170)	0.5
Diastolic	70	(40–80)	80	(45–90)	0.2
SVEF, (%)	55	(30–75)	50	(30–60)	**0.05**
NT-proBNP, (pg/ml)	102	(10–697)	271.9	(40.1–3185)	**0.04**
RBC, (10^9/µl)	5.6	(4.3–7)	5.4	(4.5–6.7)	0.2
Hb, (g/dl)	16.9	(13.1–19.5)	16.4	(13–20)	0.5
HCT, (%)	48.5	(38.7–55.1)	47.4	(38.8–61.7)	0.7
Platelet count, (10^3/µl)	145±39		150±60		0.8
ALT, (IU/l)	24	(18–46)	26.5	(11–69.7)	0.13
AST, (IU/l)	24±6		28±7		1
GGTP, (IU/l)	64	(26–155)	81	(22.6–240)	0.1
Bilirubin, (µmol/l)	16.5	(7.4–101.8)	23	(3.5–135.4)	0.5
ALP, (IU/l)	67±21		86±21		**0.01**
AFP, (ng/ml)	2.5	(1.5–10.3)	2.8	(0.8–18.6)	1
Total protein, (g/dl)	76.5	(69.2–81.9)	73.4	(39.2–87.6)	0.4
Albumin, (g/dl)	44.4	(38.9–48.5)	42.1	(20.5–50.2)	0.3
Creatinine, (µmol/l)	77.5	(62–113)	77.5	(31–173)	1
Cystatin C, (mg/l)	1	(0.7–1.2)	0.9	(0.6–4.1)	1
ACR, (g/mg)	10.1	(2.9–39)	10	(3.3–86.4)	0.9

HR – heart rate; BP – blood pressure; SVEF – single ventricle ejection fraction; NT-proBNP – N-terminal B-type natriuretic peptide; RBC – red blood cells; HCT – hematocrit; Hb – hemoglobin; ALT – alanine aminotransferase; AST – aspartate aminotransferase; GGTP – gamma-glutamyl transpeptidase; ALP – alkaline phosphatase; AFP – alpha fetoprotein; ACR – albumin/creatynin ratio. Values are reported as mean ±SD or median (range) depending on the variable distribution.

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Table 2. Comparison of CPET parameters between Fontan patients with or without fenestration.

	Fenestration		No fenestration		p Value
T, (min: sec)	15: 19	(7: 59–20: 01)	14: 09	(9: 50–23: 00)	0.8
HR_{peak}, (beats/minute)	169	(121–191)	150	(71–180)	**0.006**
HRR, (beats/minute)	34	(7–78)	51	(9–112)	**0.02**
Puls $O2_{peak}$, (ml/beat/kg)	17.7±5.0		16.5±6.0		0.4
SBP_{peak}, (mmHg)	130	(110–160)	130	(85–170)	0.7
DBP_{peak}, (mmHg)	70	(40–80)	80	(45–90)	0.2
RER_{peak}	1.1	(1.0–1.3)	1.0	(0.9–1.2)	0.6
$VO2_{peak}$, (ml/kg/min)	27±10		21.5±6		**0.04**
$VO2_{peak}$, (%pred)	72±23		58±18		**0.05**
$VE/VO2_{peak}$	33.2	(25.3–46.1)	32.3	(23.9–49.7)	0.9
$VE/VCO2_{peak}$	31.1	(24.6–41.9)	30.6	(24.5–40.6)	0.8
VE, (l/min)	61	(36–102)	43	(30–109)	**0.01**
BR, (l/min)	70±22		81±20		0.1
$SatO2_{rest}$, (%)	90.5	(85–96)	89	(70–97)	0.3
$SatO2_{peak}$, (%)	82	(64–88)	80	(65–90)	0.97
ΔSatO2, (%)	8.5	(6–27)	6.5	(2–16)	0.2

CPET – cardiopulmonary exercise test; T – exercise time; HR – heart rate; HRR – heart rate reserve; Puls $O2_{peak}$ – peak oxygen pulse; SBP_{peak} – peak systolic blood pressure; DBP_{peak} – peak diastolic blood pressure; RER_{peak} – peak respiratory exchange ratio; VO_{2peak} – peak oxygen uptake; VE/VO_{2peak} – peak ventilator equivalent for oxygen; VE/VCO_{2peak} – peak ventilator equivalent for carbon dioxide; $SatO_{2rest}$ – rest oxygen saturation; $\Delta SatO_2$ – drop in $SatO_2$ during exercise; BR – breath reserve. Values are reported as mean ±SD or median (range) depending on the variable distribution.

Thromboembolism

Thromboembolic complications were found in 12 (31%) of the total number of patients who underwent Fontan procedures, with and without fenestration. Four patients presented with a pulmonary thrombosis, two patients developed thrombus in a lateral tunnel, three patients had a history of ischemic cerebral stroke, and three patients were diagnosed with chronic venous thrombosis. All the patients with thromboembolic complications were treated with oral anticoagulants. There was no significant association observed (χ^2 test, p=0.7) between the absence of fenestration (Group II) and thromboembolic complications.

Laboratory test results

Laboratory parameters in patients in Group II, without fenestration, had significantly greater N-terminal pro-brain natriuretic peptide (NT-proBNP) levels compared with patients in Group 1, with fenestration. Hematological parameters, including red blood cell counts (RBC), hematocrit (HCT), and hemoglobin (Hb) showed no significant differences between patients in Group I and Group II. For liver function laboratory test results, patients in Group II, who did not undergo fenestration (Group II), had significantly greater alkaline phosphatase (ALP) levels compared with patients in Group I who underwent fenestration. Other laboratory parameters, including aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), total bilirubin level and alpha-fetoprotein (AFP), did not differ significantly between patients in Group I and Group II (Table 1). Laboratory tests for renal function, including creatinine level, cystatin C and the urine albumin to creatinine ratio (ACR) showed no statistically significant differences between fenestrated (Group I) and non-fenestrated (Group II) patients (Table 1).

Echocardiography

The median ejection fraction, determined by echocardiography, was 50% (range, 30-55%) in the total number of patients who underwent Fontan procedures with and without fenestration. The Group I (fenestrated) patients had a greater single ventricle ejection fraction when compared with the Group II (non-fenestrated) patients.

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Table 3. Bodypletysmography results in fenestrated and unfenestrated Fontan patients.

	Fenestration	No fenestration	p Value
TLC, (l)	4.9±1.4	5.0±1.6	1
FEV1, (l)	3.1±0.9	3.0±1.2	0.8
VC, (l)	3.5±1.1	3.5±1.4	1
FVC, (l)	3.5±1.1	3.5±1.5	0.9
FEV1%VC, (%)	88.6 (74.9–93.2)	85.1 (74–100)	0.2
FEV1%FVC, (%)	88.7 (75.8–93.2)	85.7 (78.4–100.0)	0.8
TV, (l)	0.8 (0.5–1.9)	0.8 (0.4–2.1)	1
ERV, (l)	1.4 (0.4–2.1)	1.0 (0.2–2.7)	0.12
RV, (l)	1.4±0.4	1.4±0.3	0.7
RV/TLC, (%)	114.1 (84.1–143.6)	100.2 (78.8–202.1)	0.7
R_{tot}	107.4 (56.0–272.2)	142.8 (54.0–357.8)	0.6

TLC – total life capacity; FEV_1 – forced expiratory volume in 1 s; VC – vital capacity; FVC – forced vital capacity; TV – tidal volume; ERV – expiratory reserve volume; RV – reserve volume; R_{tot} – total resistance. Values are reported as mean ±SD or median (range) depending on the variable distribution.

Atrioventricular regurgitation was mild in 16 patients (41%), moderate in 13 patients (33%) and severe in three patients (8%) in the total number of patients who underwent Fontan procedures with and without fenestration. However, the degree of atrioventricular valve regurgitation did not differ significantly between patients in Group I and Group II, with and without fenestration (p>0.1).

Cardiopulmonary exercise test (CPET) and pulmonary function tests

As shown in Table 2, CPET results showed significant differences between patients who underwent Fontan procedures with fenestration (Group I) and without fenestration (Group II) in heart rate (HR), heart rate reserve (HRR), maximal VO_2, maximal VO_2 (% of predicted value), and ventilatory equivalent (VE).

The results of pulmonary function tests in patients with and without fenestration are shown in Table 3. There were no significant differences between the groups of patients who underwent Fontan procedures with fenestration (Group I) and without fenestration (Group II), in dynamic pulmonary function parameters, including total lung capacity (TLC), vital capacity (VC), forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), tidal volume (TV), expiratory reserve volume (ERV), reserve volume (RV), peak expiratory flow (PEF), maximal expiratory flow (MEF), and total resistance (R_{tot}).

Discussion

This study was designed to analyze the long-term complications of the use of fenestration in in adult patients who had previously undergone Fontan procedure for the congenital cardiac abnormality of univentricular heart. The main findings of this study showed that in long-term follow-up, patients who underwent Fontan procedures with fenestration (Group I) had improved single ventricular function, lower N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, improved exercise capacity, and reduced serum alkaline phosphatase (ALP) levels, when compared with patients who underwent Fontan procedure without the use of fenestration (Group II).

Recently published studies have reported that adult patients who underwent Fontan procedures have decreased ventricular systolic function, and significant deterioration of atrioventricular valve regurgitation in long-term follow-up [5,10]. However, the clinical impact of the use of fenestration on systolic ventricular fraction and atrioventricular valve competence has been controversial [5,10]. In 2011, a study published by Atz and colleagues showed, that a patient who had the Fontan procedure with fenestration did not significantly differ in echocardiographic variables and NT-proBNP levels in 8±3 years of follow-up observation [7]. However, the present study analyzed older patients with postoperative follow-up of 21.7±4.2 years. Also, it was recently shown that patients who had undergone a fenestrated Fontan procedure with total cavopulmonary connection (TCPC) showed an increased cardiac index compared with other types of Fontan procedure, including the lateral tunnel procedure [10]. The presence of fenestration in the Fontan circuit resulted in improved cardiac output, indicating a beneficial effect of fenestration for late clinical outcome [10].

The use of fenestration may play a role in the improved control of cardiac output that was previously impaired due to the lack

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of an effective pulmonary circulatory pump, as in the Fontan circulation, the preload reserve of the systemic ventricle is reduced or absent, as the cardiac output in the Fontan circulation at rest is 70% that of the cardiac output of the normal biventricular heart [16]. An interesting finding of this study was that adult patients who underwent Fontan procedures with fenestration (Group I) had a greater maximal heart rate (HR), maximal VO_2 (absolute and percentage of predicted value) and ventricular ejection fraction (VEF) at the peak of exercise in cardiopulmonary exercise testing, when compared with the non-fenestrated group (Group II), 20 years after the procedure. Of particular interest from the findings of the present study was that the maximal heart rate at the peak of exercise was significantly increased in the fenestrated group (Group I). In patients who undergo Fontan procedures, the heart rate (HR) plays an important role in controlling cardiac output during exercise [16]. It is also believed that abnormal autonomic control and dysfunction of the sinus node can contribute to the lower heart rate reserve (HRR) to exercise in patients who undergo Fontan procedures [17].

The data concerning the impact of fenestration closure on exercise capacity in Fontan patients remain unclear, especially in adult patients observed during long-term follow-up. In a study published by Meadows et al., the fenestration closure procedure did not influence the exercise capacity [11]. However, in the same study, ventilatory abnormalities, following fenestration closure, and during exercise improved dramatically, but did not normalize [11]. Mays et al. demonstrated that in the pediatric population with a single ventricle, after the Fontan procedure, the fenestration closure improved exercise arterial oxygen saturation and aerobic capacity, despite a restricted cardiac output at rest, when documented by cardiac catheterization immediately after the closure procedure [18]. However, in another study that described a pediatric population with a shorter follow-up than in the present study, it was shown that exercise variables did not differ according to the fenestration status [7].

Data regarding the incidence of cardiac dysrhythmia and arrhythmia in adults after the Fontan procedure are limited. In our study atrial fibrillation was recorded in 23% of all patients following the Fontan procedure. However, in the patients without the fenestration procedure (Group II), the frequency of atrial fibrillation was significantly greater when compared with patients who underwent the fenestration procedure (Group 1). According to previously published studies, the frequency of cardiac dysrhythmia and arrhythmia is estimated to be between 3–32% of patients in patients who undergo Fontan procedures [19]. What is important is that supraventricular arrhythmia may aggravate hemodynamics in the Fontan circulation and lead to heart failure over a short period. The observations from the present study are in line with other studies, which have demonstrated that in patients with fenestration closure, cardiac dysrhythmia and arrhythmia may be aggravated and necessitate an increase in the dose of antiarrhythmic agents given during patient follow-up [10,12].

Furthermore, the published data concerning respiratory function in adult patients who have undergone Fontan procedures with and without fenestration are scarce. Several studies have shown that patients who underwent Fontan procedures may develop a restrictive pattern of lung disease due to weak respiratory muscles, a restrictive thoracic cage, or paralysis of the diaphragm after surgery [2]. However, in the present study, significant differences in dynamic ventilatory parameters in patients with fenestration were not observed when evaluated using whole body plethysmography.

Previously published studies have indicated that fenestration increases the risk of thromboembolic complications, including stroke, by providing a pathway of systemic venous emboli to the systemic circulation [20]. In the present study, thromboembolic complications occurred in 33% of patients, but there was no significant relationship between the fenestration status of the patient, and the incidence of thromboembolic complications. This finding is consistent with some previous reports, which did not demonstrate a difference in the number of ischemic strokes and the occurrence of thrombosis in Fontan patients with patent fenestrations [12,21].

Multi-organ complications including liver disease have been reported in survivors following the Fontan operation [1]. However, the clinical impact of structural hepatic abnormalities in these patients remains largely unknown [1]. It has been hypothesized that the increase in central venous pressure in the Fontan circulation can result in hepatic congestion, portal hypertension, and chronic hepatic injury [1]. The role of fenestration in hepatic impairment in patients with Fontan circulation is unknown. The present study demonstrated that non-fenestrated patients (Group II) had an increased level of alkaline phosphatase (ALP) when compared with the fenestrated group (Group I), whereas other hepatic parameters were comparable between Groups I and Group II. A Fontan-associated liver disease (FALD) has been defined as abnormalities in liver function and structure and is a serious problem for patients who undergo Fontan procedures [21]. However, the prevalence of FALD and the predictors for FALD remain unknown. ALP, as well as bilirubin, is considered to be a cholestatic marker, and recent studies have shown that elevated levels of ALP or bilirubin are associated with all-cause mortality, cardiovascular death, or hospitalization in patients with advanced heart failure [20]. A previously published study by Yamazoe et al. showed that ALP is an independent predictor of impaired renal function in patients with acutely decompensated heart failure [21]. In this study, the analysis of renal complications showed that

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there were no significant differences in renal parameters between the fenestrated patients (Group I) and non-fenestrated patients (Group II).

Currently, closure of a fenestration remains a controversial issue, as some studies demonstrate that fenestration closure improves oxygenation and may reduce the effects of medication for heart failure; other studies have suggested that fenestration closure may result in increased use of anti-arrhythmia medications [12]. Also, as reported by Kotani et al., persistent fenestration has been shown to be a marker for physiologic intolerance, as noted by increased rates of mortality and a higher incidence of Fontan failure and complications in a previously reported study conducted on pediatric Fontan patients [13]. However, some authors suggest that indications for routine fenestration closure should be carefully reconsidered because of the potential long-term benefits resulting from increased cardiac output and reduction in tachyarrhythmias in patients undergoing Fontan procedures with fenestration [10].

There were several limitations of this study. The patient cohort was of small size, and the study population was heterogeneous regarding their initial diagnoses and the type of Fontan surgery. This study was performed at a single center, while the data was analyzed and interpreted by the study authors, all of which may have introduced study bias. Furthermore, liver and renal function were assessed indirectly by commonly used clinical markers, not by quantitative measurements.

Conclusions

This study included long-term follow-up of adult patients who underwent Fontan procedure for univentricular heart, and compared patients with and without percutaneous fenestration. On long-term follow-up, the findings were that patients with fenestration had improved single ventricular function, lower N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, reduced alkaline phosphatase (ALP) levels, reduced liver impairment, and improved exercise capacity. The presence of fenestration did not influence hematologic, renal, pulmonary, or thromboembolic complications. These findings indicate that percutaneous fenestration should be carefully considered for these patients.

Conflict of interest

None.

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