Impact of pulsatile pulmonary blood flow on cardiopulmonary exercise performance after the Fontan procedure

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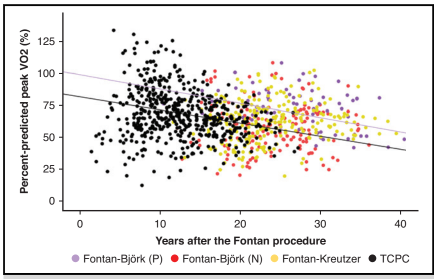
ABSTRACT

Objective: To evaluate the exercise capacity in patients following Fontan–Kreutzer, Fontan–Björk, and total cavopulmonary connection (TCPC).

Methods: Patients who performed exercise capacity tests at least once after the Fontan procedure between 1979 and 2007 were included. Patients after Fontan–Björk procedure were divided into 2 groups according to the pulmonary blood flow (PBF) pattern: patients with pulsatile PBF and those without. Peak oxygen uptake (VO_2) was measured and percent-predicted VO_2 was calculated.

Results: A total of 227 patients were nominated. The types of Fontan procedure included Fontan–Kreutzer in 48 (21.1%) patients, Fontan–Björk in 38 (16.7%); 11 (4.8%) with pulsatile PBF and 27 (11.9%) without pulsatile PBF; and TCPC in 141 (62.1%). Median age at the Fontan procedure was 4.5 years (interquartile range, 2.1-8.2 years). A total of 978 cardiopulmonary exercise tests were performed at median follow-up of 17.7 years (interquartile range, 11.3-23.4 years) postoperatively. Analysis using linear mixed-effects models demonstrated that percent-predicted VO_2 was greater in patients with pulsatile PBF after Fontan–Björk compared with patients after other types of Fontan procedure ($P < .001$). The same results were obtained when the longitudinal percent predicted VO_2 was performed using only patients with tricuspid atresia and double inlet left ventricle ($P < .001$).

Conclusions: Among long-term survivors after various types of Fontan procedures, patients with pulsatile PBF after the Fontan–Björk procedure demonstrated better exercise performance compared to those after TCPC, those after the Fontan–Kreutzer procedure, and those after the Fontan-Björk procedure with non-pulsatile PBF. The results implicate the importance of pulsatile PBF to maintain the Fontan circulation. (JTCVS Open 2023;16:811-22)



Dot-plot of predicted peak VO_2 following various types of the Fontan procedure.

CENTRAL MESSAGE

Percent-predicted peak oxygen uptake was significantly better in patients with Fontan–Björk procedure and pulsatile pulmonary blood flow compared to other types of Fontan procedure in the long term.

PERSPECTIVE

In patients with Fontan circulation, nonpulsatile laminar pulmonary blood flow demonstrates a decline in exercise capacity. Pulsatile pulmonary blood flow might prevent late mortality and morbidities and provides better exercise capacity compared with nonpulsatile pulmonary blood flow. The creation of pulsatile pulmonary blood flow should be reconsidered to improve patients' long-term outcomes.

See Discussion on page 823.

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Abbreviations and Acronyms

- AoP = aortic pressure
- AVV = atrioventricular valve
- CMRI = cardiac magnetic resonance imaging
- df = degrees of freedom
- IQR = interquartile ranges
- PAP = pulmonary artery pressure
- PB = plastic bronchitis
- PBF = pulmonary blood flow
- PLE = protein-losing enteropathy
- RA = right atrium
- RV = right ventricle
- SV = systemic ventricular
- TCPC = total cavopulmonary connection
- VO_2 = oxygen uptake

▶ Video clip is available online.

Over the past 50 years, various types of Fontan procedures have evolved to treat patients with a functional single ventricle.[1-4] Currently, total cavopulmonary connection (TCPC) is the preferred strategy because it provides better hemodynamics, an overall better survival, and fewer morbidities such as arrhythmia or thromboembolic complications, compared with the so-called "classic Fontan procedure."[5] However, the long-term outcome after the TCPC is still unclear regarding somatic development and exercise capacity.[6-8] Recently, we demonstrated that patients who showed a pulsatile pulmonary blood flow (PBF) long after the Fontan–Björk procedure had better exercise capacity than patients without pulsatile PBF.[9] The idea behind the Fontan–Björk procedure is to connect the right atrium (RA) with the right ventricle (RV) to promote right ventricular growth as a pumping chamber, which then creates a pulsatile PBF, whereas TCPC or atriopulmonary anastomosis leads to a laminar PBF in the pulmonary circulation.[2,9,10] Studies indicate that a nonpulsatile laminar flow may lead to structural vascular change, endothelial dysfunction, and increased vascular resistance.[11,12] On the contrary, a pulsatile PBF seems to decrease vascular resistance and show a better pulmonary perfusion.[13] Our previous studies demonstrated that pulsatile PBF was profitable in maintaining a Fontan circulation.[9]

Since the introduction of the TCPC, survival after a Fontan procedure has significantly improved, and patients often live beyond the age of 40 years.[14] However, complications such as arrhythmia, ventricular dysfunction, protein-losing enteropathy (PLE), plastic bronchitis (PB), or Fontan failure still occur in patients after TCPC, even in the long term.[15] Furthermore, cardiorespiratory exercise capacity is often decreased, which has a significant prognostic value in patients with congenital heart disease.[16] There are studies that evaluate the long-term data of patients and their exercise capacity,[17-21] but studies that compare patients' exercise capacity among different types of Fontan procedures are still rare.

Therefore, this study aimed to compare the exercise capacity of patients after different types of the Fontan procedures, including atriopulmonary connection (or Fontan–Kreutzer) procedure, atrioventricular connection (or Fontan–Björk) procedure, or TCPC to support the hypothesis that a pulsatile PBF contributes to a better exercise capacity.

METHODS

Data-Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical Statement

The institutional review board of the Technical University of Munich approved the study (approval number 2022-303-S-KH, on June 27, 2022) and waived the need for informed consent from the patients who were retrospectively analyzed in the study.

Patients

We reviewed all patients who underwent all types of the Fontan procedure, including Fontan–Kreutzer procedure, Fontan–Björk procedure, or TCPC at the German Heart Center in Munich between 1979 and 2007. Those who performed at least 1 cardiopulmonary exercise test at the German Heart Center were included in this study. As this study's aim was to analyze the exercise capacity of patients after the Fontan procedure and exercise capacity is measurable when patients are 10 years old, the year 2007 was chosen as the end of the study period. Medical records were collected, including data on clinical status, physical examination, echocardiography, cardiac magnetic resonance imaging, cardiac catheterization examinations, and cardiopulmonary exercise testing. The follow-up data from the time of the Fontan procedure until the last known record of the patients were collected using our institutional single-ventricle patient database system, which is regularly tracked.

Echocardiography

An experienced echo-cardiographer (C.R.) reviewed the pre- and post-Fontan echocardiogram images and assessed the systemic ventricular (SV) function and atrioventricular valve (AVV) regurgitation. After undergoing the Fontan–Björk procedure, patients were divided into 2 groups by assessing their PBF pattern 15 years' postoperatively using pulsed-wave Doppler assessment: patients with pulsatile PBF who demonstrated pulsatile systolic flow in the main pulmonary artery (group P), and patients without pulsatile PBF who showed pulseless continuous systolic-diastolic flow, respiratory-dependent pulmonary flow, or minimally accelerated flow in the end-diastolic phase (group N). The details on how the pulmonary flow pattern was measured are described in our previous study.[9] The evaluation of SV function and atrioventricular valve regurgitation was determined according to our previous study.[22]

Operative Techniques

The Fontan–Björk procedure was indicated for patients with tricuspid atresia/stenosis or double-inlet left ventricle who had a normal relation of the great arteries. The intracardiac procedure was performed according to the original method, with some modifications.[2] The Fontan–Kreutzer procedure was initially performed using its original technique[3] and more recently according to the techniques after Fontan–Lins modified techniques. The operative techniques for TCPC are described in previous reports.[15,23] Lateral tunnel TCPC was performed in 50 patients in the early era. In January 1999, extracardiac TCPC was introduced and has been our standard procedure since May 2002.[23]

Cardiopulmonary Exercise Capacity Testing

A symptom-limited cardiopulmonary exercise test on a bicycle in upright position was performed according to our institutional protocol.[24] The exercise test featured a breath-by breath gas exchange analysis using a metabolic chart. Peak oxygen uptake (VO_2) was defined as the greatest mean uptake of any 30-second time interval during exercise. Age- and sex-related reference values (% of Normal) were calculated according to the report of Cooper and Storer.[25]

Cardiac Catheterization

Cardiac catheterizations were performed when clinically indicated under local anesthesia, conscious sedation as needed, and spontaneous room air ventilation. Pressure measurement was performed in the right atrium pressure, main pulmonary artery pressure (PAP), left atrium pressure, and SV systolic and end-diastolic pressure. Pulmonary vascular resistance and cardiac index were calculated.

Cardiac Magnetic Resonance Imaging (CMRI)

CMRI was performed on a 1.5-T whole-body scanner using a phase array cardiac coil. The standardized CMRI protocol was used according to the guidelines.[26] The ventricular image stack was typically analyzed by demarcating endocardial and epicardial borders of the right ventricle with the assistance of software tools. By cross-referencing the short-axis ventricular images with the long-axis images and observing the wall motion in a cine fashion, accurate determination of the atrioventricular and semilunar valves planes was facilitated. In patients with ventricular conduction delay, the end-systolic and end-diastolic frames may not be the same for the right and left ventricles and should thus be selected independently to yield the minimum and maximum volumes respectively. After locating the long axis of the heart, contiguous true short-axis slices were acquired using breath-hold, electrocardiogram-triggered cine CMRI. The SV end-systolic volume and SV end-diastolic volume were measured. SV ejection fraction, SV end-diastolic volume index, SV end-systolic volume index, and SV stroke volume index were calculated.

Statistical Analysis

Categorical variables are presented as absolute numbers and percentages. A χ^2 test was used for categorical data. Continuous variables are expressed as medians with interquartile ranges, or means with standard deviation. The Student *t* test was used to compare normally distributed variables, and the Mann–Whitney *U* test was used for variables that were not normally distributed. For statistical analysis of longitudinal corrected peak VO_2 values corrected for age and sex (percent normal peak VO_2) by cardiopulmonary exercise test, linear mixed-effects models with a random intercept were used to account for repeated measures within patients. Natural cubic splines were used to model the potentially nonlinear relation of the continuous predictors "postoperative period" and "type of Fontan" to the outcome "percent normal peak VO_2." Therefore, the degrees of freedom (df) of the splines were varied from 1, which corresponds to a linear effect, to 5, which corresponds to a very flexible nonlinear effect. Best subset selection guided by the Bayesian information criterion was used to select a model from all combinations of df for the splines, as well as from models involving main effects only or additional interaction effects of the predictors. This selection resulted in a model of main effects only with 3 df for the spline of "postoperative period" and 1 df for the spline of "type of Fontan TCPC." Data analysis was performed with SPSS 28.0 for Windows (IBM Corp) and R statistical software 4.2.1 (R Foundation for Statistical Computing).

RESULTS

Patients

Of all patients who underwent either Fontan–Björk procedure, Fontan–Kreutzer procedure, or TCPC between 1979 and 2007, a total of 227 patients performed cardiopulmonary exercise testing during the postoperative follow-up period, including 38 patients who underwent the Fontan–Björk procedure between 1979 and 1994, 48 patients who underwent the Fontan–Kreutzer procedure between 1984 and 1992, and 141 patients who underwent TCPC between 1994 and 2007. The Fontan–Björk procedure was performed on 66 patients between 1978 and 1995. In total, 14 patients died within the first 15 years of postoperative follow-up. Among the 52 patients who survived longer than 15 years' postoperatively, 43 had follow-up examinations at our institute and were included in this study. Nine patients who did not have a follow-up examination at our clinic could not be included. Patient characteristics in each procedure are shown in Table 1. To summarize, the Fontan–Kreutzer procedure was performed at a median age of 8.1 years, and the most frequent diagnosis was tricuspid atresia (n = 26, 54.2%). The Fontan–Björk procedure was performed at a median age of 5.9 years, and the most frequent diagnosis was also tricuspid atresia (n = 36, 94.7%). The TCPC was performed at a median age of 2.9 years, and the most frequent diagnosis was univentricular heart (n = 44, 31.2%). Patients who underwent the Fontan–Björk procedure were then divided into 2 groups (group P and group N) according to the PBF that was assessed using echocardiography 15 years' postoperatively. Group P consisted of 11 patients who showed a pulsatile PBF and group N consisted of 27 patients who showed nonpulsatile PBF.

Initial palliation in patients who underwent Fontan–Kreutzer included aortopulmonary shunt in 16 patients (33.3%), pulmonary artery banding in 17 (35.4%), and pulmonary artery reconstruction in 3 (6.3%). Regarding patients who underwent Fontan–Björk in group P, initial palliation included aortopulmonary shunt in 2 (18.2%) patients, pulmonary artery banding in 5 (45.5%), and pulmonary artery reconstruction in 3 (27.3%) patients. In group N, aortopulmonary shunt was performed in 9 (33.3%) patients, pulmonary artery banding in 4 (14.8%) patients, and pulmonary artery reconstruction in 7 (25.9%) patients. Before TCPC, initial palliation included Norwood type procedure in 34 (24.1%) cases, aortopulmonary shunt in 60 (42.6%), pulmonary artery

TABLE 1. Patient characteristics and data of initial Fontan procedure

Characteristics	APA	AVA (Björk) Pulsatile	AVA (Björk) Nonpulsatile	TCPC
N (%) or median (IQR)	48 (21.1)	11 (4.8)	27 (11.9)	141 (62.1)
Male sex	26 (54.2)	5 (45.5)	13 (48.1)	94 (66.7)
Primary diagnosis				
Tricuspid atresia	26 (54.2)	10 (90.9)	26 (96.3)	28 (19.9)
DILV	16 (3.3)	1 (9.1)	1 (3.7)	26 (18.4)
ccTGA	0 (0)	0 (0)	0 (0)	7 (5)
UVH	4 (8.3)	0 (0)	0 (0)	44 (31.2)
HLH	0 (0)	0 (0)	0 (0)	14 (9.9)
PAIVS	2 (4.2)	0 (0)	0 (0)	8 (5.7)
UAVSD	0 (0)	0 (0)	0 (0)	2 (1.4)
Others	0 (0)	0 (0)	0 (0)	12 (8.5)
Cardiac anomaliy				
TGA	23 (47.9)	0 (0)	0 (0)	76 (53.9)
DORV	4 (8.3)	0 (0)	0 (0)	20 (14.2)
CoA	4 (8.3)	0 (0)	0 (0)	18 (12.8)
Dextrocardia	4 (8.3)	0 (0)	0 (0)	14 (9.9)
Dominant RV	1 (2.1)	0 (0)	0 (0)	56 (39.7)
Initial palliation				
Norwood/DKS	0 (0)	0 (0)	0 (0)	34 (24.1)
Aortopulmonary shunt	16 (33.3)	2 (18.2)	9 (33.3)	60 (42.6)
Pulmonary artery banding	17 (35.4)	5 (45.5)	4 (14.8)	31 (22)
PA reconstruction	3 (6.3)	3 (27.3)	7 (25.9)	30 (21.3)
Previous pacemaker implantation	0 (0)	0 (0)	1 (3.7)	6 (4.3)
Previous BCPS				105 (74.5)
Age at BCPS, mo				10.3 (5.8-24.6)
Weight at BCPS, kg				7.4 (6.0-10.3)
Height at BCPS, cm				70 (65-84)
Age at Fontan operation, y	8.1 (5.2-13.2)	6.1 (2.2-9.5)	5.7 (2.1-7.3)	2.9 (1.9-6.5)
Weight at Fontan, kg	14.7 (13.3-30.6)	20.5 (14.7-28.4)	14.7 (13.3-19.1)	13.0 (11.0-19.5)
Height at Fontan, cm	107 (100-145)	125 (97-141)	103 (95-121)	93 (85-117)
CPB time, min	101 (79-123)	81 (15-28)	93 (75-107)	88 (52-131)
AXC time, min	52 (36-67)	45 (28-66)	54 (43-63)	60 (32-92)

APA, Atriopulmonary anastomosis; *AVA*, atrioventricular anastomosis; *TCPC*, total cavopulmonary connection; *DILV*, double-inlet right ventricle; *ccTGA*, congenitally corrected transposition of the great arteries; *UVH*, univentricular heart; *HLH*, hemophagocytic lymphohistiocytosis; *PAIVS*, pulmonary atresia with intact ventricular septum; *UAVSD*, unbalanced atrioventricular septal defect; *TGA*, transposition of the great arteries; *DORV*, double-outlet right ventricle; *CoA*, coarctation of the aorta; *RV*, right ventricle; *DKS*, Damus–Kaye–Stansel; *PA*, pulmonary artery; *BCPS*, bidirectional cavopulmonary shunt; *CPB*, cardiopulmonary bypass; *ACX*, aortic crossclamp.

banding in 31 (22%), and pulmonary artery reconstruction in 30 (21.3%). Furthermore, BCPC was performed in 105 (74.5%) patients at a median age of 10.3 months.

Post-Fontan Morbidities

The median follow-up period was 20.0 years (15.9-29.9 years) in all patients. Postoperative morbidities are shown in Table 2. Regarding reoperations after the Fontan–Kreutzer, 12 (25.0%) patients received TCPC conversion, Fontan pathway revision was performed in 1 (2.1%) patient, and an AVV procedure in 3 (6.3%). In patients who underwent Fontan–Björk in group P, TCPC conversion was performed once (9.1%), Fontan pathway revision twice (18.2%), and surgical tricuspid valve implantation was performed in 4 (36.4%) patients. In group N, 6 (22.2%) patients received TCPC conversion, 3 (11.1%) Fontan pathway revision, and 3 (11.1%) patients an AVV procedure. After the TCPC, Fontan pathway revision was performed in 6 (4.3%) patients and AVV procedure in 5 (3.5%).

As for interventions after the Fontan–Kreutzer, occlusion of venovenous fistula was performed in 9 patients, and balloon dilatation of the pulmonary artery in 1 patient. In patients who underwent Fontan–Björk in group P, stent

TABLE 2. Patient postoperative data

Characteristics	All	APA	AVA (Björk) Pulsatile	AVA (Björk) Nonpulsatile	TCPC
N (%) or median (IQR)	227	48 (21.1)	11 (4.8)	27 (11.9)	141 (62.1)
Follow up period, y	20.0 (15.9-29.9)	31.3 (26.3-33.6)	35.2 (31.5-38.0)	31.7 (28.0-35.0)	17.1 (14.6-20.0)
Reoperation	54 (23.8)	18 (37.5)	6 (54.5)	11 (40.7)	19 (13.5)
Conversion to TCPC	19 (8.3)	12 (25.0)	1 (9.1)	6 (22.2)	0 (0)
Fontan pathway revision	12 (5.3)	1 (2.1)	2 (18.2)	3 (11.1)	6 (4.3)
TV implantation	4 (1.8)	0	4 (36.4)	0 (0)	0
AVV procedure	11 (4.8)	3 (6.3)	0 (0)	3 (11.1)	5 (3.5)
Intervention					
Balloon dilatation PA	4 (1.8)	1 (2.1)	0 (0)	1 (3.7)	2 (1.4)
Stent implantation PA	14 (6.2)	0 (0)	0 (0)	4 (14.8)	10 (7.1)
Stent implantation RARV	2 (0.9)	0 (0)	2 (18.2)	0 (0)	0 (0)
TV implantation RARV	4 (1.8)	0 (0)	2 (18.2)	2 (7.4)	0 (0)
Occlusion of fistula	15 (6.6)	9 (18.8)	1 (9.1)	0 (0)	5 (3.5)
Fenestration closure	4 (1.8)	0 (0)	0 (0)	0 (0)	4 (2.8)
Atrial tachyarrythmia	88 (38.8)	41 (85.4)	9 (81.2)	25 (92.6)	13 (9.2)
Ablation	46 (20.3)	18 (37.5)	5 (45.5)	17 (63.0)	6 (4.3)
Cardioversion	41 (18.1)	18 (375)	5 (45.5)	14 (51.9)	4 (2.8)
Systemic ventricular dysfunction	83 (36.6)	12 (25)	1 (9.1)	8 (29.6)	62 (44)
Pacemaker implantation	45 (19.8)	18 (37.5)	3 (27.3)	10 (37)	14 (9.9)
Other postoperative morbidities					
PB	2	0 (0)	0 (0)	0 (0)	2 (1.4)
PLE	13	4 (8.3)	0 (0)	2 (7.4)	7 (5.0)

APA, Atriopulmonary anastomosis; *AVA*, atrioventricular anastomosis; *TCPC*, total cavopulmonary connection; *IQR*, interquartile range; *TV*, tricuspid valve; *AVV*, atrioventricular valve; *PA*, pulmonary artery; *RARV*, right atrium and right ventricle; *PB*, plastic bronchitis; *PLE*, protein-losing enteropathy.

implantation into the RA–RV pathway was performed in 2 patients (18.2%), and 2 patients received transcatheter valve implantation into the RA-RV pathway. In group N, stent implantation into the pulmonary artery was performed in 4 patients (14.8%) and transcatheter valve implantation in 2 (7.4%). After the TCPC, stent implantation into the pulmonary artery was done in 10 (7.1%) patients and fenestration closure was performed in 4 (2.8%). As for the RA-RV regurgitation in patients who underwent Fontan–Björk in group P, grade of regurgitation was none or trivial in 7 patients, mild in 3 patients, and moderate in 1 patient at their first exercise capacity tests.

Exercise Capacity

A total of 978 cardiopulmonary exercise tests were performed in 227 patients (mean 4.3 examinations per patient) at a mean follow-up of 17.9 ± 7.9 years postoperatively. Results of cardiopulmonary exercise tests are shown in Table 3, and yearly distributions in percent peak VO_2 in individual Fontan patients are shown in Figure 1. Percent predicted peak oxygen uptake (VO_2) was greater in patients who underwent Fontan–Björk with pulsatile PBF (group P) compared with other types of the Fontan procedure ($P < .001$). Although the interval between the Fontan procedure and the cardiopulmonary exercise tests was longer. Linear mixed-effects models were used to analyze the longitudinal percent predicted VO_2 after the Fontan procedure. Figure 2 demonstrates the longitudinal percent predicted VO_2. There was a significant difference in postoperative percent predicted VO_2 between Fontan–Björk with pulsatile PBF (group P) and other types of the Fontan procedure ($P < .001$). When patients after TCPC were excluded in the analysis, the same results were obtained (Figure 3). There was a significant difference in postoperative percent predicted VO_2 between Fontan–Björk with pulsatile PBF (group P) and Fontan–Björk with nonpulsatile PBF (group N) and Fontan–Kreuzer procedure ($P = .003$).

When we compared the longitudinal percent predicted VO_2 in patients with tricuspid atresia, there was still a significant difference in postoperative percent predicted VO_2 between Fontan–Björk with pulsatile PBF (group P) and other types of the Fontan procedure (Figure E1, $P < .001$). The same results were obtained when we compared the longitudinal percent predicted VO_2 in patients with tricuspid atresia and double-inlet left ventricle (Figure E2, $P < .001$).

Hemodynamic Data and SV Volume Data

Cardiac catheterization data and CMRI data are shown in Table 4. When the systolic PAP of patients who underwent

TABLE 3. Cardiopulmonary exercise tests

Characteristic	Classic Fontan			
		AVA (Björk)		
Mean ± SD	APA	Pulsatile	Nonpulsatile	TCPC
Spiroergometry	N = 225	N = 68	N = 157	N = 526
Postoperative period, y	23.9 ± 5.3	27.1 ± 6.0*	23.8 ± 5.1	12.4 ± 4.9†
Peak VO_2, mL/kg/min	21.1 ± 7.2	23.7 ± 6.4	20.1 ± 6.2	27.7 ± 8.7†
% predicted peak VO_2	61.8 ± 16.0	73.5 ± 15.8*	58.4 ± 18.4	68.5 ± 20.5†

APA, Atriopulmonary anastomosis; *AVA*, atrioventricular anastomosis; *TCPC*, total cavopulmonary connection; *SD*, standard deviation; *VO_2*, oxygen uptake. *Björk pulsatile versus others: $P < .01$. †TCPC versus classic Fontan: $P < .01$.

TCPC was compared with patients who underwent a classic Fontan, PAP was significantly lower in patients who underwent TCPC than in patients who underwent a classic Fontan ($P = .019$). Systolic aortic pressure was lower in patients who underwent TCPC compared with patients who underwent a classic Fontan ($P = .020$). Cardiac index was greater in patients who underwent TCPC than in patients who underwent a classic Fontan ($P < .001$). When the data were compared between the patients with pulsatile PBF (group P in Fontan–Björk) and patients with nonpulsatile PBF (Fontan–Kreutzer, group N in Fontan–Björk, and TCPC), systolic ventricular pressure, systolic aortic pressure (AoP), diastolic AoP, and mean AoP were greater in patients with pulsatile PBF compared with patients with nonpulsatile PBF.

As for CMRI, the data of patients who underwent TCPC were compared with those of patients who underwent a classic Fontan. SV EDV (I), the SV end-systolic volume (I), SV stroke volume index, and cardiac index were greater in patients who underwent TCPC compared with patients who underwent a classic Fontan. When the data were compared between patients with pulsatile PBF (group P in Fontan–Björk) and patients with nonpulsatile PBF (Fontan–Kreutzer, group N in Fontan–Björk, and TCPC), SV end-diastolic volume index was smaller in patients with pulsatile PBF, compared with patients with nonpulsatile PBF. Furthermore, the regurgitation fraction into the RA-RV connection was measured in 5 patients who underwent Fontan–Björk in group P, which showed a regurgitation fraction of 8%, 12%, 20%, 20%, and 33%, respectively.

DISCUSSION

The present study evaluated the long-term serial change in exercise capacity of percent predicted peak VO_2 in patients after different types of the Fontan procedures at our center over 35 years of follow-up. Although percent predicted peak VO_2 declined over the follow-up, patients after Fontan–Björk procedure with pulsatile PBF demonstrated greater percent predicted peak VO_2 compared with patients after other types of the Fontan procedure including TCPC, where patients showed laminar nonpulsatile PBF (Video Abstract).

Historical Changes of the Fontan Procedure

In 1979, Björk presented the Fontan–Björk modification for patients with tricuspid atresia.[2] The rationale of this modification was to incorporate the rudimental right

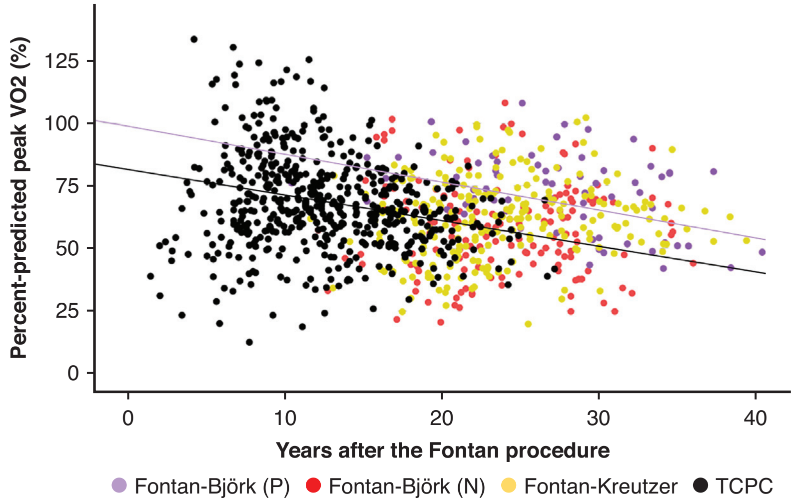

FIGURE 1. Dot-plots of predicted peak VO_2 following TCPC (*black*), Fontan-Kreuzer procedure (*orange*), and Fontan–Björk procedure with pulsatile PBF (*blue*) and nonpulsatile PBF (*red*). *VO_2*, Oxygen uptake; *TCPC*, total cavopulmonary connection.

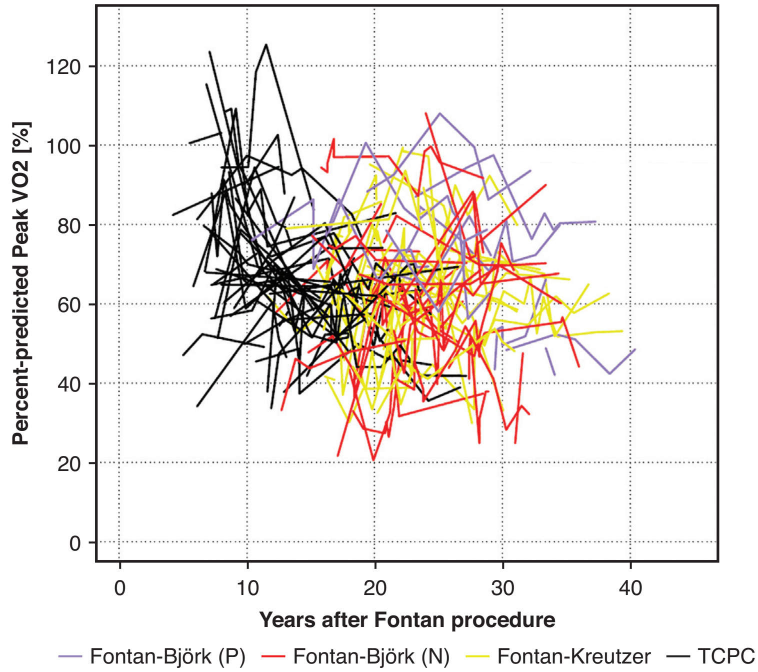

FIGURE 2. Longitudinal predicted peak VO_2 following TCPC (*black*), Fontan-Kreuzer procedure (*orange*), and Fontan–Björk procedure with pulsatile PBF (*blue*) and nonpulsatile PBF (*red*). Fontan–Björk procedure with pulsatile PBF had a significant better predicted peak VO_2, compared with other types of Fontan procedure ($P < .001$). *TCPC*, Total cavopulmonary connection; *VO_2*, oxygen uptake.

ventricle as a pumping chamber to improve the pulmonary circulation. However, due to stenosis and regurgitation over the atrioventricular connection, and due to arrhythmias and unfavorable hemodynamics, this modification was abandoned in favor of the TCPC.[5] Following the introduction of the TCPC, the short- to mid-term results after univentricular Fontan procedure improved significantly.[6,15] However, the late sequelae of a Fontan

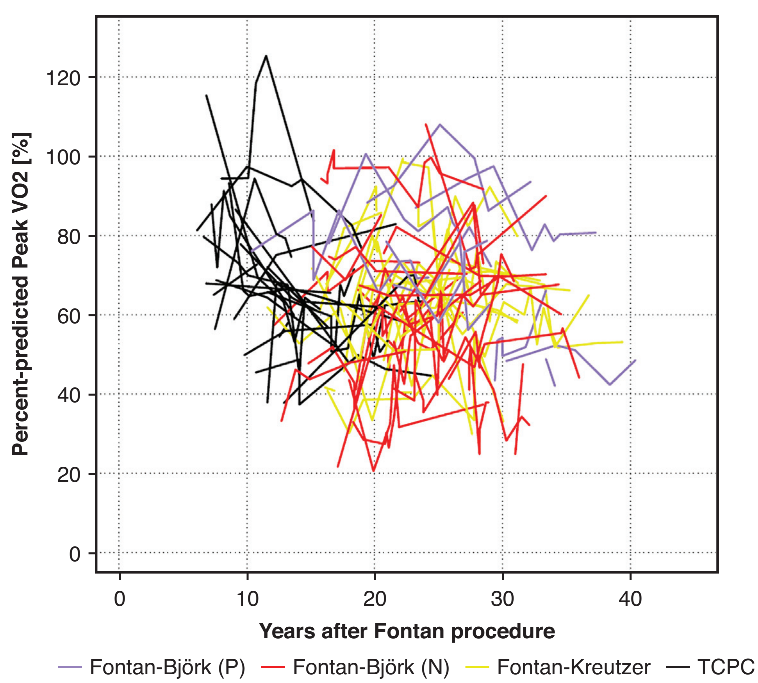

FIGURE 3. Longitudinal predicted peak VO_2 following Fontan–Kreuzer procedure (*orange*) and Fontan–Björk procedure with pulsatile PBF (*blue*) and nonpulsatile PBF (*red*). Fontan–Björk procedure with pulsatile PBF had a significant better predicted peak VO_2, compared with other types of Fontan procedure ($P < .001$). *TCPC*, Total cavopulmonary connection; *VO_2*, oxygen uptake.

TABLE 4. Cardiac catheterization and CMRI data

Characteristic Mean ± SD	Classic Fontan			TCPC
		AVA (Björk)		
	APA	Pulsatile	Nonpulsatile	TCPC
Cardiac catheterization	N = 42	N = 10	N = 25	N = 74
Postoperative period, y	14.8 ± 5.1	18.1 ± 8.2*	15.3 ± 4.6	10.5 ± 7.8†
Hemoglobin, g/dL	14.5 ± 2.4	14.7 ± 1.6	14.0 ± 1.9	14.2 ± 2.3
Systolic PAP, mm Hg	13.6 ± 4.1	20.1 ± 9.4	16.0 ± 6.8	12.6 ± 4.3‡
Diastolic PAP, mm Hg	11.2 ± 4.0	10.2 ± 4.7	10.4 ± 4.5	10.7 ± 3.5
Mean PAP, mm Hg	13.0 ± 3.2	14.3 ± 4.0	12.0 ± 3.8	11.8 ± 2.8
LAP, mm Hg	8.0 ± 3.6	8.0 ± 5.1	7.9 ± 5.3	7.9 ± 3.7
Systolic SVP, mm Hg	98.4 ± 15.3	106.1 ± 18.6*	96.7 ± 16.3	93.7 ± 15.3
End-diastolic SVP, mm Hg	8.8 ± 4.1	9.2 ± 4.9	8.6 ± 4.3	9.0 ± 3.6
Systolic AoP, mm Hg	98.2 ± 15.1	106.8 ± 16.2*	95.0 ± 15.1	92.9 ± 12.5‡
Diastolic AoP, mm Hg	60.0 ± 13.2	68.3 ± 13.0§	53.8 ± 19.4	56.3 ± 8.6
Mean AoP, mm Hg	71.7 ± 14.4	80.9 ± 13.7§	67.5 ± 19.5	68.4 ± 9.1
Qs cardiac index, L/min/m^2	2.9 ± 1.2	2.7 ± 0.7	2.4 ± 0.8	3.6 ± 1.1†
Qp	2.7 ± 1.1	2.6 ± 0.9	2.5 ± 0.8	3.0 ± 0.9‡
Rs	25.7 ± 14.9	27.3 ± 10.2	27.4 ± 10.7	16.8 ± 5.7†
Rp	2.1 ± 1.6	1.9 ± 1.2	2.2 ± 1.3	1.5 ± 1.0†
MRI	N = 22	N = 5	N = 17	N = 70
Postoperative period, y	24.7 ± 4.0	27.3 ± 5.9*	23.5 ± 5.2	16.6 ± 5.0†
SV EF, %	55.2 ± 10.7	52.8 ± 7.3	51.6 ± 11.7	51.8 ± 9.2
SV EDV, mL	128.0 ± 39.4	114.4 ± 24.8	135.4 ± 31.2	147.1 ± 52.3‡
SV ESV, mL	58.8 ± 25.8	54.2 ± 14.0	67.1 ± 26.8	73.5 ± 37.6‡
SV stroke volume, mL	69.2 ± 22.1	60.2 ± 15.6	69.2 ± 21.7	73.7 ± 21.0
SV EDVI, mL/m^2	74.0 ± 21.8	66.6 ± 7.7§	75.0 ± 15.6	87.1 ± 26.0†
SV ESVI, mL/m^2	34.1 ± 15.1	31.6 ± 5.3	37.2 ± 17.0	43.3 ± 20.0‡
SV SVI, mL/m^2	38.4 ± 11.1	37.8 ± 2.9	36.5 ± 7.4	44.3 ± 10.2†
Cardiac index, L/m^2	3.0 ± 0.9	2.3 ± 0.6	2.5 ± 0.5	3.4 ± 0.9†

APA, Atriopulmonary anastomosis; *AVA*, atrioventricular anastomosis; *TCPC*, total cavopulmonary connection; *SD*, standard deviation; *PAP*, pulmonary artery pressure; *LAP*, left atrium pressure; *SVP*, systolic ventricular pressure; *AoP*, systolic AoP; *Qs*, cardiac index; *Qp*, total pulmonary blood flow; *Rs*, systemic vascular resistance; *Rp*, pulmonary vascular resistance; *MRI*, magnetic resonance imaging; *SV*, systemic ventricular; *EF*, ejection fraction; *EDV*, end-diastolic volume; *ESV*, end-systolic volume; *EDVI*, end-diastolic volume index; *ESVI*, end-systolic volume index. *Björk pulsatile versus others: $P < .05$. †TCPC versus classic Fontan: $P < .01$. ‡TCPC versus classic Fontan: $P < .05$. §Björk pulsatile versus others: $P < .01$.

circulation, such as PLE, PB, tachyarrhythmia, and cardiac decompensation, occur also following TCPC. Nonpulsatile flow in the pulmonary circulation and relatively high central venous pressure might be the main cause of these complications. It is of note that patients after Fontan–Björk procedure with pulsatile PBF had no incidence of PLE or PB in this study.

Exercise Capacity After the Fontan Procedure

Our results demonstrated that exercise capacity was better in patients after the Fontan–Björk procedure with pulsatile PBF, compared with patients with nonpulsatile PBF, although the patients after the Fontan–Björk procedure were highly selected and the statistical methods were complex due to the difference of the follow-up period of each group. The pulsatile PBF might maintain a good pulmonary circulation and therefore provides better cardiac output in the long term. Interestingly, cardiac index at rest, measured by cardiac catheterization or CMRI, was greater in patients who underwent TCPC compared with patients who underwent classic Fontan, whereas predicted peak VO_2 measured by exercise tests was greater in patients after Fontan–Björk with pulsatile PBF compared with those after TCPC. Of course, patients after Fontan–Björk with pulsatile PBF had a considerably large right ventricle, which might support the PBF during exercise. Both factors, pulsatile PBF and increased ejection of the right ventricle might contribute to better exercise capacity in patients after Fontan–Björk procedure. It is well known that exercise capacity progressively declines in subjects who undergo Fontan.[27] However, decline in exercise capacity was slight in patients after Fontan–Björk procedure with pulsatile PBF.

Future Prospective

We found that late exercise capacity, which is a useful objective measure of ventricular function, was significantly reduced in patients with nonpulsatile PBF. The functional status in patients with pulsatile systolic flow in the pulmonary circulation improved and we could, therefore,

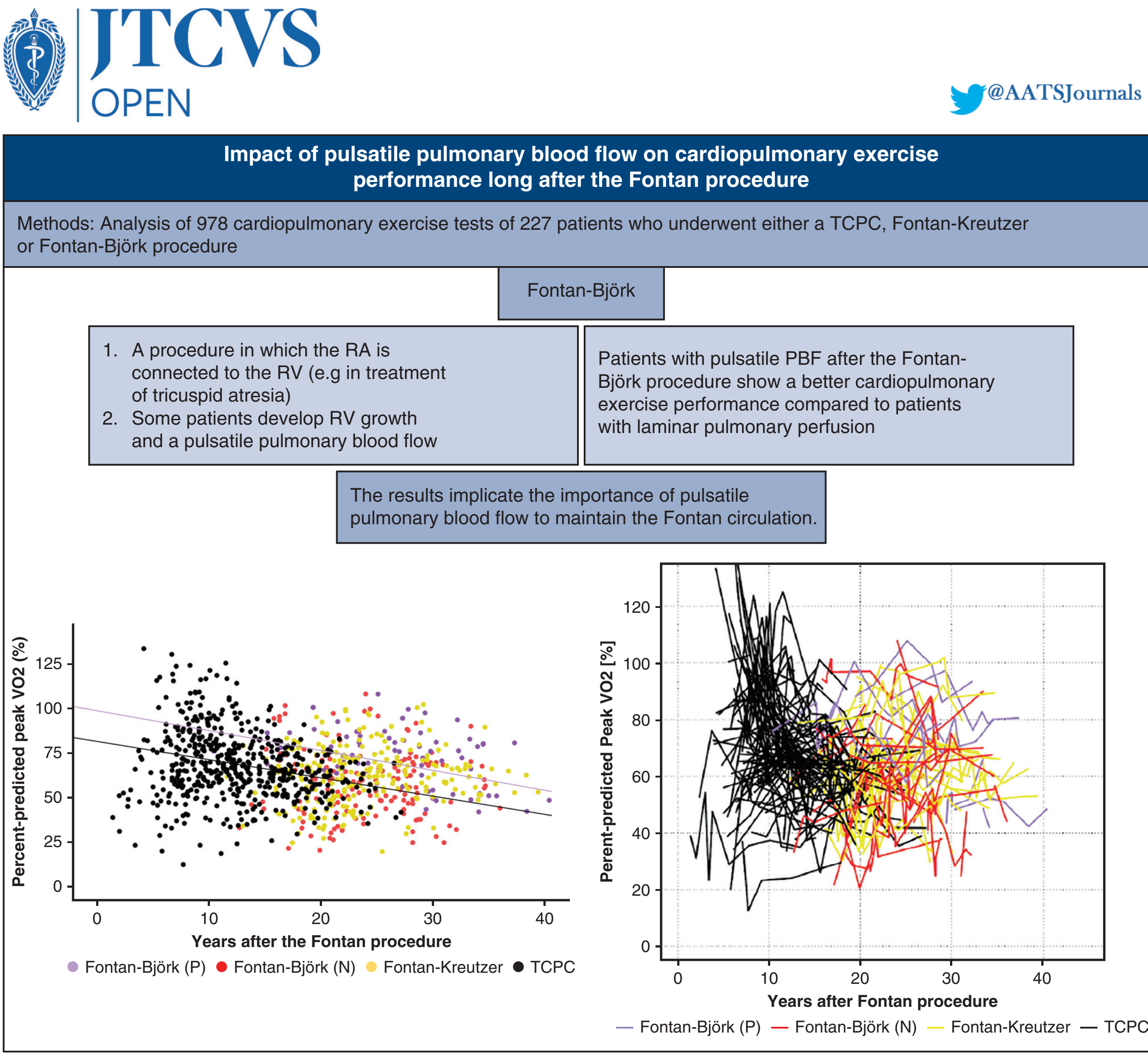

FIGURE 4. A summary of the article. *TCPC*, Total cavopulmonary connection; *RA*, right atrium; *RV*, right ventricle; *PBF*, pulmonary blood flow.

reconsider the incorporation of the subpulmonary ventricle in patients with tricuspid atresia and normal position of the great arteries, to establish a biventricular circulation or to perform a one- and one-half repair. We agree, however, that it might be challenging to predict whether the right ventricle will "grow" after this Fontan modification and reach a sufficient size. In our observation, and also in other reports, it seems that the patients with pulsatile pulmonary flow had relatively rapid growth of the right ventricle within a few years postoperatively, suggesting the importance of favorable preoperative conditions.[9,28] In these patients, successful late tricuspid valve implantation in RA-RV connection has been reported.[29-33] Pulsatile PBF might prevent late mortality and morbidities and provide better exercise capacity compared to nonpulsatile PBF. In contrast, adding a pulsatile pump without a valve results in transmission of pressure in both directions, which ultimately results in complications such as cirrhosis, protein losing enteropathy and plastic bronchitis. To realize this concept, we need a small atrioventricular prosthesis that has long durability, growth potential, and no risk for thromboembolic complications. With such a prosthesis, we could revive a Björk procedure. In summary, the creation of pulsatile PBF by recruiting the sub-pulmonary ventricle should be reconsidered to improve patients' long-term outcomes. One and one-half repair might be an alternative option.[34]

Study Limitations

This study is limited by its retrospective and single-center design. There are limitations due to the small group of patients. Patients who underwent Fontan–Björk procedure were highly selected in terms of long-term survival and available examinations at our center, which might lead to a bias in this study's results. In addition, there were differences in the study periods between the various types of the Fontan procedure regarding spiroergometry, cardiac catheterization, and CMRI. There was also a difference in the average number of spiroergometry examinations between the patients after the "classic" Fontan procedure and those after TCPC, which possibly lead to a bias. Therefore, we needed complex statistical methods, which might be a limitation. CMRI could not be performed in patients following pacemaker implantation.

CONCLUSIONS

Among the long-term survivors after different types of Fontan procedure, patients with pulsatile PBF after the Fontan–Björk procedure demonstrated a better exercise performance than patients after TCPC, those after the Fontan–Kreutzer procedure, and those after the Fontan–Björk procedure with nonpulsatile PBF (Figure 4). The results implicate the importance of pulsatile pulmonary flow to maintain the Fontan circulation.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

References

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. *Thorax*. 1971;26:240-8.
2. Björk VO, Olin CL, Bjarke BB, Thorén CA. Right atrial-right ventricular anastomosis for correction of tricuspid atresia. *J Thorac Cardiovasc Surg*. 1979;77:452-8.
3. Lee CN, Schaff HV, Danielson GK, Puga FJ, Driscoll DJ. Comparison of atriopulmonary versus atrioventricular connections for modified Fontan/Kreutzer repair of tricuspid valve atresia. *J Thorac Cardiovasc Surg*. 1986;92:1038-43.
4. Bull C, de Leval MR, Stark J, Taylor JF, Macartney FJ. Use of a subpulmonary ventricular chamber in the Fontan circulation. *J Thorac Cardiovasc Surg*. 1983; 85:21-31.
5. de Leval MR, Kilner P, Gewillig M, Bull C. Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations. Experimental studies and early clinical experience. *J Thorac Cardiovasc Surg*. 1988;96:682-95.
6. Sittiwangkul R1, Azakie A, Van Arsdell GS, Williams WG, McCrindle BW. Outcomes of tricuspid atresia in the Fontan era. *Ann Thorac Surg*. 2004;77: 889-94.
7. Diller GP, Dimopoulos K, Okonko D, Li W, Babu-Narayan SV, Broberg CS, et al. Exercise intolerance in adult congenital heart disease: comparative severity, correlates, and prognostic implication. *Circulation*. 2005;112:828-35.
8. Paridon SM, Mitchell PD, Colan SD, Williams RV, Blaufox A, Li JS, et al. A cross-sectional study of exercise performance during the first 2 decades of life after the Fontan operation. *J Am Coll Cardiol*. 2008;52:99-107.
9. Ono M, Vogt M, Cleuziou J, Kasnar-Samprec J, Burri M, Strbad M, et al. Improved exercise performance in patients with tricuspid atresia after the Fontan–Björk modification with pulsatile systolic pulmonary flow. *Ann Thorac Surg*. 2016;101:1012-9.
10. Ansari ST, Agarwala B. Bjork surgery for tricuspid atresia—revisited. *Pediatr Cardiol*. 2009;30:1166-8.
11. Henaine R, Vergnat M, Bacha EA, Baudet B, Lambert V, Belli E, et al. Effects of lack of pulsatility on pulmonary endothelial function in the Fontan circulation. *J Thorac Cardiovasc Surg*. 2013;146:522-9.
12. Khambadkone S, Li J, de Leval MR, Cullen S, Deanfield JE, Redington AN. Basal pulmonary vascular resistance and nitric oxide responsiveness late after Fontan-type operation. *Circulation*. 2003;107:3204-8.
13. Kaapa P, Usha Raj J, Hillyard R, Anderson J. Segmental vascular resistance during pulsatile and steady perfusion in 3- to 5-wk-old rabbit lungs. *Am J Physiol*. 1991;261:H506-13.
14. Pujol C, Schiele S, Maurer SJ, Hock J, Fritz C, Hager A, et al. Patients with single-ventricle physiology over the age of 40 years. *J Clin Med*. 2020;9:4085.
15. Ono M, Kasnar-Samprec J, Hager A, Cleuziou J, Burri M, Lagenbach C, et al. Clinical outcome following total cavopulmonary connection: a 20-year single-centre experience. *Eur J Cardiothorac Surg*. 2016;50:632-41.
16. Talwar S, Kumar MV, Sreenivas V, Gupta VP, Choudhary SK, Airan B. Exercise performance after univentricular palliation. *Ann Pediatr Cardiol*. 2018;11:40-7.
17. Bossers SS, Helbing WA, Duppen N, Kuipers IM, Schokking M, Hazekamp MG, et al. Exercise capacity in children after total cavopulmonary connection: lateral tunnel versus extracardiac conduit technique. *J Thorac Cardiovasc Surg*. 2014; 148:1490-7.
18. Talwar S, Desai M, Talwar A, Choudhary SK, Sreenivas V, Saxena A, et al. Cardiopulmonary exercise performance after total cavopulmonary connection with or without prior superior cavopulmonary connection. *J Card Surg*. 2014;29:244-50.
19. Weinreb SJ, Dodds KM, Burstein DS, Huang J, Rand EB, Mancilla E, et al. End-organ function and exercise performance in patients with Fontan circulation: what characterizes the high performers? *J Am Heart Assoc*. 2020;9:e016850.
20. van Genuchten WJ, Helbing WA, Ten Harkel ADJ, Fejzic Z, Kuipers Md IM, Slieker MG, et al. Exercise capacity in a cohort of children with congenital heart disease. *Eur J Pediatr*. 2023;182:295-306.
21. Illinger V, Materna O, Slabý K, Jičínská D, Kovanda J, Koubský K, et al. Exercise capacity after total cavopulmonary anastomosis: a longitudinal paediatric and adult study. *ESC Heart Fail*. 2022;9:337-44.
22. Dahmen V, Heinisch PP, Staehler H, Schaeffer T, Burri M, Röhlig C, et al. Longitudinal analysis of systemic ventricular function and atrioventricular valve function after the Fontan procedure. *Eur J Cardiothorac Surg*. 2023;63:ezad078.
23. Schreiber C, Hörer J, Vogt M, Cleuziou J, Prodan Z, Lange R. Nonfenestrated extracardiac total cavopulmonary connection in 132 consecutive patients. *Ann Thorac Surg*. 2007;84:894-9.
24. Müller J, Christov F, Schreiber C, Hess J, Hager A. Exercise capacity, quality of life, and daily activity in the long-term follow-up of patients with univentricular heart and total cavopulmonary connection. *Eur Heart J*. 2009;30:2915-20.
25. Cooper CB, Storer TW. *Exercise Testing and Interpretation: A Practical Approach*. Cambridge University Press; 2001:278.
26. Fratz S, Chung T, Greil GF, Samyn MM, Taylor AM, Valsangiacomo Buechel ER, et al. Guidelines and protocols for cardiovascular magnetic resonance in children and adults with congenital heart disease: SCMR expert consensus group on congenital heart disease. *J Cardiovasc Magn Reson*. 2013; 13:15-51.
27. Giardini A, Hager A, Pace Napoleone C, Picchio FM. Natural history of exercise capacity after the Fontan operation: a longitudinal study. *Ann Thorac Surg*. 2008; 85:818-21.
28. Coles JG, Leung M, Kielmanowicz S, Freedom RM, Benson LN, Rabinovitch M, et al. Repair of tricuspid atresia: utility of right ventricular incorporation. *Ann Thorac Surg*. 1988;45:384-9.
29. Shah AH, Horlick EM, Eicken A, Asnes JD, Bocks ML, Boudjemline Y, et al. Transcatheter valve implantation for right atrium-to-right ventricle conduit

obstruction or regurgitation after modified Björk-Fontan procedure. *Catheter Cardiovasc Interv*. 2017;89:298-305.
30. Eicken A, Fratz S, Hager A, Vogt M, Balling G, Hess J. Transcutaneous Melody valve implantation in "tricuspid position" after a Fontan Björk (RA-RV homograft) operation results in biventricular circulation. *Int J Cardiol*. 2010;142:e45-7.
31. Schamroth Pravda N, Kornowski R, Vaknin Assa H, Bruckheimer E, Birk E, Shapira Y, et al. Complex catheter-based structural heart reconstruction in a patient with tricuspid atresia and Björk palliative conduit. *JACC Case Rep*. 2021;3:212-6.
32. Rybicka J, Kowalski M, Różański J, Hoffman P. Successful reoperation of the valveless calcified right atrium to right ventricle conduit in an adult patient with tricuspid atresia after Fontan procedure. *Eur J Cardiothorac Surg*. 2012;41:e18-20.
33. Shiina Y, Kilner PJ, Uebing A, Uemura H. Tricuspid valve implantation after Bjork procedure to establish biventricular physiology. *Ann Thorac Surg*. 2013;96:309-11.
34. Hopkins KA, Brown JW, Darragh RK, Kay WA. Converting Fontan–Björk to 1.5- or 2-ventricle circulation. *Ann Thorac Surg*. 2019;107:e259-61.

Key Words: atriopulmonary connection (Fontan–Kreutzer), atrioventricular connection (Fontan–Björk), total cavopulmonary connection, exercise capacity, peak oxygen uptake, pulsatile pulmonary blood flow

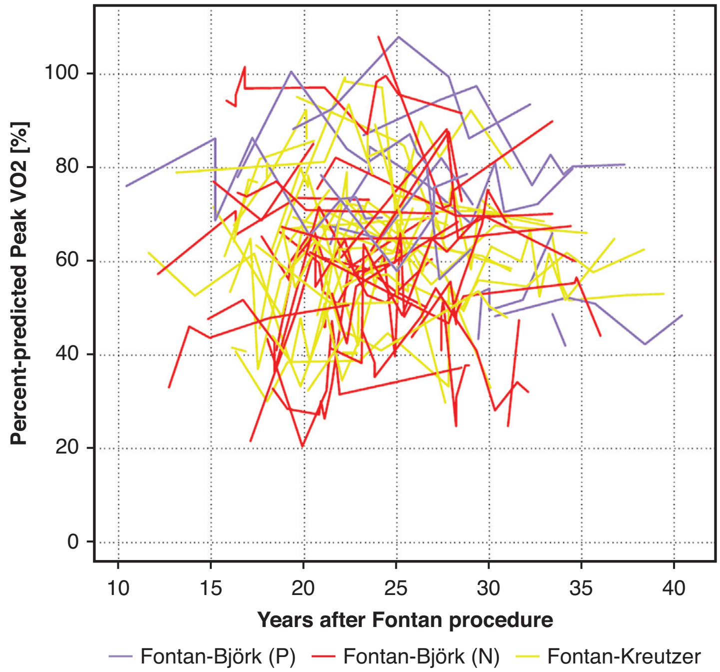

FIGURE E1. Longitudinal predicted peak VO_2 in patients with tricuspid atresia following TCPC (*black*), Fontan-Kreuzer procedure (*orange*) and Fontan-Björk procedure with pulsatile PBF (*blue*) and non-pulsatile PBF (*red*). *VO_2*, Oxygen uptake.

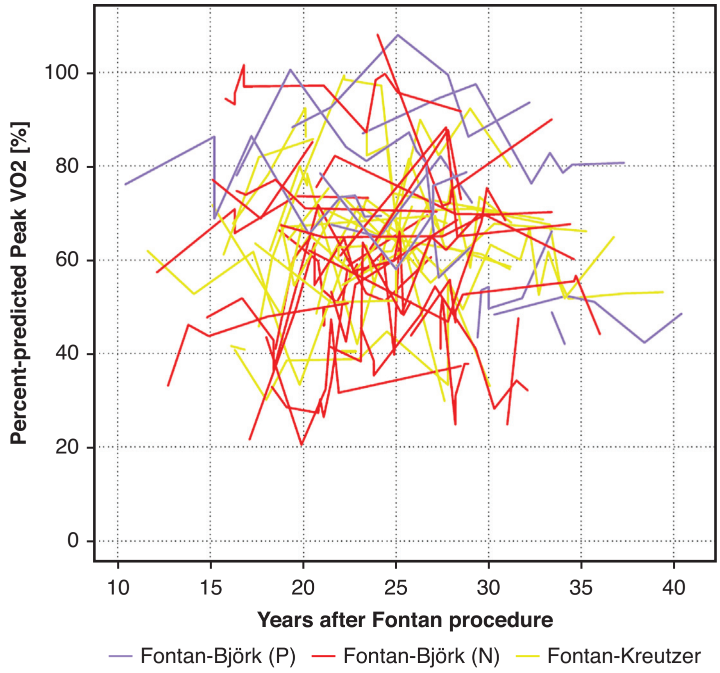

FIGURE E2. Longitudinal predicted peak VO_2 in patients with tricupid atresia and double inlet left ventricle following TCPC (*black*), Fontan-Kreuzer procedure (*orange*) and Fontan-Björk procedure with pulsatile (*blue*) and non-pulsatile (*red*). *VO_2*, Oxygen uptake.