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

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

Methods: Analysis of 978 cardiopulmonary exercise tests of 227 patients who underwent either a TCPC, Fontan-Kreutzer or Fontan-Björk procedure

Fontan-Björk

1. A procedure in which the RA is connected to the RV (e.g. in treatment of tricuspid atresia)
2. Some patients develop RV growth and a pulsatile pulmonary blood flow

Patients with pulsatile PBF after the Fontan-Björk procedure show a better cardiopulmonary exercise performance compared to patients with laminar pulmonary perfusion

The results implicate the importance of pulsatile pulmonary blood flow to maintain the Fontan circulation.

TCPC: total cavopulmonary connection, RA: right atrium, RV: right ventricle, PBF: pulmonary blood flow
Impact of pulsatile pulmonary blood flow on cardiopulmonary exercise performance after the Fontan procedure

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Word Count: 3534 (<3500)
Glossary of Abbreviations

APC: atriopulmonary connection
AVC: atroventricular connection
BCPS: bidirectional cavopulmonary shunt
CI: confidence interval
HR: hazard ratio
IQR: interquartile ranges
OR: odds ratio
PB: plastic bronchitis
PBF: pulmonary blood flow
PLE: protein losing enteropathy
RA: right atrium
RV: right ventricle
TCPC: total cavopulmonary connection
VO2: oxygen uptake
Central Picture
Central Picture Legend

Dot-plot of predicted peak VO2 following various types of the Fontan procedure. (80/90)

total cavopulmonary connection (black), Fontan-Kreuzer (yellow), Fontan-Björk with (blue) and without (red) pulsatile pulmonary blood flow. VO2: oxygen uptake.

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. (199/200)

Perspective statement

In patients with Fontan circulation, non-pulsatile 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 non-pulsatile pulmonary blood flow. The creation of pulsatile pulmonary blood flow should be reconsidered to improve patients’ long-term outcomes.

(404/405)
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 two groups according to the pulmonary blood flow (PBF) pattern: patients with pulsatile PBF and those without. Peak oxygen uptake (VO2) was measured and percent-predicted VO2 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 (interquartile ranges (IQR): 2.1-8.2) years. A total of 978 cardiopulmonary exercise tests were performed at median follow-up of 17.7 (IQR: 11.3-23.4) years postoperatively. Analysis using linear mixed-effects models demonstrated that percent-predicted VO2 was higher in patients with pulsatile PBF after Fontan-Björk compared to patients after other types of Fontan procedure (p<0.001). The same results were obtained when the longitudinal percent predicted VO2 was performed using only patients with tricuspid atresia and double inlet left ventricle (p<0.001).

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.

(Key words: ) (Word count: 248/250)
atriopulmonary connection (Fontan-Kreutzer), atrioventricular connection (Fontan-Björk), total
cavopulmonary connection, exercise capacity, peak oxygen uptake, pulsatile pulmonary blood flow

**Graphical Abstract**

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

Methods: Analysis of 978 cardiopulmonary exercise tests of 227 patients who underwent either a TCPC, Fontan-Kreutzer or Fontan-Björk procedure

1. A procedure in which the RA is connected to the RV (e.g. in treatment of tricuspid atresia)
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TCPC: total cavopulmonary connection, RA: right atrium, RV: right ventricle, PBF: pulmonary blood flow
Introduction

Over the past 50 years, various types of Fontan procedures have evolved to treat patients with a functional single ventricle [1-4]. Currently, the 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 to 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 with the right ventricle to promote right ventricular growth as a pumping chamber which then creates a pulsatile PBF. Whereas TCPC or atrophic pulmonary anastomosis (APA) leads to a laminar pulmonary blood flow (PBF) in the pulmonary circulation [2, 9, 10]. Studies indicate that a non-pulsatile 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 occurs 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 atrioventricular connection (AFC or Fontan-Kreutzer) procedure, atrioventricular connection (AVC or Fontan-Björk) procedure, or TCPC to support the hypothesis that a pulsatile pulmonary blood flow contributes to a better exercise capacity.

Materials and 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 (approved number of 2022-303-S-KH on 27th of June 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 one 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.
An experienced echo-cardiographer (CR) reviewed the pre- and post-Fontan echocardiogram images and assessed the systemic ventricular function and AVV regurgitation. Patients after Fontan-Björk procedure were divided into two groups by assessing their pulmonary blood flow (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 systemic ventricular function and atrioventricular valve regurgitation were 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, extra-cardiac 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 (VO2) was defined as the highest mean uptake
of any 30s 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 (RAP), main pulmonary artery (PAP), left atrium (LAP) and systemic ventricular systolic and end-diastolic pressure (SVSP, SVEDP). Pulmonary vascular resistance (PVR) and Cardiac Index (CI) were calculated.

Cardiac Magnetic Resonance Imaging

The Cardiac Magnetic Resonance Imaging (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, ECG-triggered cine CMRI. The systemic ventricular end-systolic volume (SV ESV) and systemic ventricular end-diastolic volume (SV EVD) were measured. Systemic ventricular ejection fraction (SV EF), systemic ventricular end-diastolic volume index (SV EDVI), systemic ventricular end-systolic volume index (SV ESVI), and systemic ventricular stroke volume index (SV SVI) were calculated.

Statistical analysis
Categorical variables are presented as absolute numbers and percentages. A chi-squared test was used for categorical data. Continuous variables are expressed as medians with interquartile ranges (IQR), or means with standard deviation (SD). The Student’s t-test was used to compare normally distributed variables, and the Mann-Whitney test was used for variables that were not normally distributed. For statistical analysis of longitudinal corrected peak VO2 values corrected for age and sex (percent normal peak VO2) 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 non-linear relation of the continuous predictors “postoperative period” and “type of Fontan” to the outcome “percent normal peak VO2”. 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 non-linear effect. Best subset selection guided by the Bayesian Information Criterion (BIC) 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, Ehningen, Germany) 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 Fontan-Björk procedure between 1979 and 1994, 48 patients who underwent 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. 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 exams at our institute and were included in this study. 9 patients who did not have a follow up exam at our clinic could not be included. Patient characteristics in each procedure are shown in Table 1. Briefly, 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 UVH (n=44, 31.2%). Patients who underwent the Fontan-Björk procedure were then divided into two 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 non-pulsatile PBF. Initial palliation in Fontan-Kreutzer patients included aorto-pulmonary shunt in 16 patients (33.3%), pulmonary artery banding in 17 (35.4%) and pulmonary artery reconstruction in 3 (6.3%). Regarding Fontan-Björk patients in group P, initial palliation included aorto-pulmonary 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, aorto-pulmonary 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. Prior to TCPC, initial palliation included Norwood type procedure in 34 (24.1%) cases, aorto-pulmonary shunt in 60 (42.6%), pulmonary artery 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 (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 AVV procedure in
In Fontan-Björk patients 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 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 veno-venous fistula was performed in 9 patients, and balloon dilatation of the PA in 1 patient. In Fontan-Björk patients in group P, stent implantation into the right atrium (RA) - right ventricle (RV) pathway was performed in two patients (18.2%) and two patients received trans-catheter valve implantation into the RA-RV pathway. In group N, stent implantation into the pulmonary artery was performed in 4 patients (14.8%) and trans-catheter 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 Fontan-Björk patients 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 VO2 in individual Fontan patients are shown in Figure 1. Percent predicted peak oxygen uptake (VO2) was higher in Fontan-Björk with pulsatile PBF (group P) compared to other types of the Fontan procedure (p<0.001). 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 VO2 after the Fontan procedure. Figure 2 demonstrates the longitudinal percent predicted VO2. There was a significant difference in postoperative percent predicted VO2 between Fontan-Björk with pulsatile PBF (group P) and other types of the Fontan procedure (p<0.001). 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 VO2 between Fontan-Björk with pulsatile PBF (group P) and Fontan-Björk with non-pulsatile PBF (group N) and Fontan-Kreuzer procedure (p=0.003).

When we compared the longitudinal percent predicted VO2 in patients with tricuspid atresia, there was still a significant difference in postoperative percent predicted VO2 between Fontan-Björk with pulsatile PBF (group P) and other types of the Fontan procedure (Supplementary Figure S1, p<0.001). The same results were obtained when we compared the longitudinal percent predicted VO2 in patients with tricuspid atresia and double inlet left ventricle (Supplementary Figure S2, p<0.001).

**Hemodynamic data and systemic ventricular volume data**

Cardiac catheterization data and CMRI data are shown in Table 4. When the systolic pulmonary artery pressure (PAP) of TCPC patients was compared with classic Fontan patients, PAP was significantly lower in TCPC patients than in classic Fontan patients (p=0.019). Systolic aortic pressure was lower in TCPC patients compared with classic Fontan patients (p=0.020). Cardiac index was higher in TCPC patients than in classic Fontan patients (p<0.001). When the data were compared between the pulsatile PBF patients (group P in Fontan-Björk) and non-pulsatile PBF patients (Fontan-Kreutzer, group N in Fontan-Björk, and TCPC), systolic SVP, systolic AoP, diastolic AoP, and mean AoP were higher in pulsatile PBF patients, compared with non-pulsatile PBF patients.

As for CMRI, the data of TCPC patients were compared to those of classic Fontan patients. SV EDV(I), the SV ESV(I), SV SVI and cardiac index were higher in TCPC patients compared to classic Fontan patients. When the data were compared between pulsatile PBF patients (group P in Fontan-Björk) and non-pulsatile PBF patients (Fontan-Kreutzer, group N in Fontan-Björk, and TCPC), SV EDVI was smaller in pulsatile PBF patients, compared with non-pulsatile PBF patients. Furthermore, the regurgitation fraction into the RA-RV connection was measured in 5 Fontan-Björk patients 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 higher percent predicted peak VO$_2$, compared with patients after other types of the Fontan procedure including TCPC, where patients showed laminar non-pulsatile PBF (Video 1).

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 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 circulation, such as protein losing enteropathy (PLE), plastic bronchitis (PB), tachyarrhythmia, and cardiac de-compensation, occur also following TCPC. Non-pulsatile 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 to patients with non-pulsatile 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 higher in TCPC patients compared to classic Fontan patients, whereas predicted peak VO2 measured by exercise tests was higher in patients after Fontan-Björk with pulsatile PBF compared to those after TCPC. Of course, patients after Fontan-Björk with pulsatile PBF had a considerably large right ventricle, which might support the pulmonary blood flow 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 Fontan subjects [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 non-pulsatile PBF patients. The functional status in patients with pulsatile systolic flow in the pulmonary circulation improved and we could, therefore, 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 pulmonary blood flow might prevent late mortality and morbidities and provide better exercise capacity compared to non-pulsatile pulmonary blood flow. On the other hand, 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 pulmonary blood flow 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. Björk patients 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
pace maker implantation.

**Conclusions**

Among the long-term survivors after different types of Fontan procedure, patients with pulsatile
pulmonary blood flow 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 non-pulsatile pulmonary blood flow (Figure 4). The results implicate the importance
of pulsatile pulmonary flow to maintain the Fontan circulation.
References


Table 1. Patient characteristics and data of initial Fontan procedure

<table>
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<tr>
<th>Characteristics</th>
<th>APA N (%) or median (IQR)</th>
<th>AVA (Björk) N (%) or median (IQR)</th>
<th>Non-pulsatile N (%) or median (IQR)</th>
<th>TCPC N (%) or median (IQR)</th>
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<td>N (%) or median (IQR)</td>
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<td>0 (0)</td>
<td>0 (0)</td>
<td>20 (14,2)</td>
</tr>
<tr>
<td>CoA</td>
<td>4 (8,3)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>18 (12,8)</td>
</tr>
<tr>
<td>Dextrocardia</td>
<td>4 (8,3)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>14 (9,9)</td>
</tr>
<tr>
<td>Dominant RV</td>
<td>1 (2,1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>56 (39,7)</td>
</tr>
<tr>
<td>Initial palliation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norwood/DKS</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>34 (24,1)</td>
</tr>
<tr>
<td>Aorto-pulmonary shunt banding</td>
<td>16 (33,3)</td>
<td>2 (18,2)</td>
<td>9 (33,3)</td>
<td>60 (42,6)</td>
</tr>
<tr>
<td>Pulmonary artery banding</td>
<td>17 (35,4)</td>
<td>5 (45,5)</td>
<td>4 (14,8)</td>
<td>31 (22)</td>
</tr>
<tr>
<td>PA Reconstruction</td>
<td>3 (6,3)</td>
<td>3 (27,3)</td>
<td>7 (25,9)</td>
<td>30 (21,3)</td>
</tr>
<tr>
<td>Prior Pacemaker</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implantation</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (3,7)</td>
<td>6 (4,3)</td>
</tr>
<tr>
<td>Prior BCPS</td>
<td></td>
<td></td>
<td></td>
<td>105 (74,5)</td>
</tr>
<tr>
<td>Age at BCPS (months)</td>
<td></td>
<td></td>
<td></td>
<td>10,3 (5,8-24,6)</td>
</tr>
<tr>
<td>Weight at BCPS (kg)</td>
<td></td>
<td></td>
<td></td>
<td>7,4 (6,0-10,3)</td>
</tr>
<tr>
<td>Height at BCPS (cm)</td>
<td></td>
<td></td>
<td></td>
<td>70 (65-84)</td>
</tr>
<tr>
<td>Age at Fontan operation (year)</td>
<td>8,1 (5,2-13,2)</td>
<td>6,1 (2,2-9,5)</td>
<td>5,7 (2,1-7,3)</td>
<td>2,9 (1,9-6,5)</td>
</tr>
<tr>
<td>Weight at Fontan (kg)</td>
<td>14,7 (13,3-30,6)</td>
<td>20,5 (14,7-28,4)</td>
<td>14,7 (13,3-19,1)</td>
<td>19,5 (13,0-30,0)</td>
</tr>
<tr>
<td>Height at Fontan (cm)</td>
<td>107 (100-145)</td>
<td>125 (97-141)</td>
<td>103 (95-121)</td>
<td>93 (85-117)</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>101 (79-123)</td>
<td>81 (15-28)</td>
<td>93 (75-107)</td>
<td>88 (52-131)</td>
</tr>
<tr>
<td>AXC time (min)</td>
<td>52 (36-67)</td>
<td>45 (28-66)</td>
<td>54 (43-63)</td>
<td>60 (32-92)</td>
</tr>
</tbody>
</table>

CPB=cardiopulmonary bypass; ACX= aortic cross-clamp
Table 2

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ALL</th>
<th>APA</th>
<th>AVA (Björk)</th>
<th>TCPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%) or median (IQR)</td>
<td>227</td>
<td>48 (21.1)</td>
<td>11 (4.8)</td>
<td>27 (11.9)</td>
</tr>
<tr>
<td>Follow up period (year)</td>
<td>20.0</td>
<td>31.3</td>
<td>35.2</td>
<td>31.7</td>
</tr>
<tr>
<td></td>
<td>(15.9-29.9)</td>
<td>(26.3-33.6)</td>
<td>(31.5-38.0)</td>
<td>(28.0-35.0)</td>
</tr>
<tr>
<td>Re operation</td>
<td>54 (23.8)</td>
<td>18 (37.5)</td>
<td>6 (54.5)</td>
<td>11 (40.7)</td>
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<tr>
<td>Conversion to TCPC</td>
<td>19 (8.3)</td>
<td>12 (25.0)</td>
<td>1 (9.1)</td>
<td>6 (22.2)</td>
</tr>
<tr>
<td>Fontan pathway revision</td>
<td>12 (5.3)</td>
<td>1 (2.1)</td>
<td>2 (18.2)</td>
<td>3 (11.1)</td>
</tr>
<tr>
<td>TV implantation</td>
<td>4 (1.8)</td>
<td>0</td>
<td>4 (36.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>AVV procedure</td>
<td>11 (4.8)</td>
<td>3 (6.3)</td>
<td>0 (0)</td>
<td>3 (11.1)</td>
</tr>
<tr>
<td>Intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Balloon dilatation PA</td>
<td>4 (1.8)</td>
<td>1 (2.1)</td>
<td>0 (0)</td>
<td>1 (3.7)</td>
</tr>
<tr>
<td>Stent implantation PA</td>
<td>14 (6.2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (14.8)</td>
</tr>
<tr>
<td>Stent implantation RARV</td>
<td>2 (0.9)</td>
<td>0 (0)</td>
<td>2 (18.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>TV implantation RARV</td>
<td>4 (1.8)</td>
<td>0 (0)</td>
<td>2 (18.2)</td>
<td>2 (7.4)</td>
</tr>
<tr>
<td>Occlusion vv fistula</td>
<td>15 (6.6)</td>
<td>9 (18.8)</td>
<td>1 (9.1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Fenestration closure</td>
<td>4 (1.8)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>Atrial Tachyarrhythmia</td>
<td>88 (38.8)</td>
<td>41 (85.4)</td>
<td>9 (81.2)</td>
<td>25 (92.6)</td>
</tr>
<tr>
<td>Ablation</td>
<td>46 (20.3)</td>
<td>18 (37.5)</td>
<td>5 (45.5)</td>
<td>17 (63.0)</td>
</tr>
<tr>
<td>Cardioversion</td>
<td>41 (18.1)</td>
<td>18 (37.5)</td>
<td>5 (45.5)</td>
<td>14 (51.9)</td>
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<tr>
<td>Systemic ventricular dysfunction</td>
<td>83 (36.6)</td>
<td>12 (25)</td>
<td>1 (9.1)</td>
<td>8 (29.6)</td>
</tr>
<tr>
<td>Pacemaker Implantation</td>
<td>45 (19.8)</td>
<td>18 (37.5)</td>
<td>3 (27.3)</td>
<td>10 (37)</td>
</tr>
<tr>
<td>Other postoperative morbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PB</td>
<td>2</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>PLE</td>
<td>13</td>
<td>4 (8.3)</td>
<td>0 (0)</td>
<td>2 (7.4)</td>
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</table>
Table 3

Table 3. Cardiopulmonary exercise tests

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Classic Fontan</th>
<th>APA</th>
<th>AVA (Björk)</th>
<th>TCPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spiroergometry</td>
<td>mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postop period (year)</td>
<td>23.9 ± 5.3</td>
<td>27.1 ± 6.0#</td>
<td>23.8 ± 5.1</td>
<td>12.4 ± 4.9*</td>
</tr>
<tr>
<td>peak VO2 (ml/kg/min)</td>
<td>21.1 ± 7.2</td>
<td>23.7 ± 6.4</td>
<td>20.1 ± 6.2</td>
<td>27.7 ± 8.7*</td>
</tr>
<tr>
<td>% predicted peak VO2</td>
<td>61.8 ± 16.0</td>
<td>73.5 ± 15.8#</td>
<td>58.4 ± 18.4</td>
<td>68.5 ± 20.5*</td>
</tr>
</tbody>
</table>

TCPC vs. classic Fontan: *: p<0.01
Björk Pulsatile vs.others: #: p<0.01

Table 4

Table 4. Cardiac catheterization and CMRI data

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Classic Fontan</th>
<th>APA</th>
<th>AVA (Björk)</th>
<th>TCPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac catheterization</td>
<td>mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postop period (years)</td>
<td>14.8 ± 5.1</td>
<td>18.1 ± 8.2#</td>
<td>15.3 ± 4.6</td>
<td>10.5 ± 7.8**</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>14.5 ± 2.4</td>
<td>14.7 ± 1.6</td>
<td>14.0 ± 1.9</td>
<td>14.2 ± 2.3</td>
</tr>
<tr>
<td>Systolic PAP (mmHg)</td>
<td>13.6 ± 4.1</td>
<td>20.1 ± 9.4</td>
<td>16.0 ± 6.8</td>
<td>12.6 ± 4.3*</td>
</tr>
<tr>
<td>Diastolic PAP (mmHg)</td>
<td>11.2 ± 4.0</td>
<td>10.2 ± 4.7</td>
<td>10.4 ± 4.5</td>
<td>10.7 ± 3.5</td>
</tr>
<tr>
<td>Mean PAP (mmHg)</td>
<td>13.0 ± 3.2</td>
<td>14.3 ± 4.0</td>
<td>12.0 ± 3.8</td>
<td>11.8 ± 2.8</td>
</tr>
<tr>
<td>LAP (mmHg)</td>
<td>8.0 ± 3.6</td>
<td>8.0 ± 5.1</td>
<td>7.9 ± 5.3</td>
<td>7.9 ± 3.7</td>
</tr>
<tr>
<td>Systolic SVP (mmHg)</td>
<td>98.4 ± 15.3</td>
<td>106.1 ± 18.6#</td>
<td>96.7 ± 16.3</td>
<td>93.7 ± 15.3</td>
</tr>
<tr>
<td>Endodiastolic SVP (mmHg)</td>
<td>8.8 ± 4.1</td>
<td>9.2 ± 4.9</td>
<td>8.6 ± 4.3</td>
<td>9.0 ± 3.6</td>
</tr>
<tr>
<td>Systolic AoP (mmHg)</td>
<td>98.2 ± 15.1</td>
<td>106.8 ± 16.2#</td>
<td>95.0 ± 15.1</td>
<td>92.9 ± 12.5*</td>
</tr>
<tr>
<td>Diastolic AoP (mmHg)</td>
<td>60.0 ± 13.2</td>
<td>68.3 ± 13.0##</td>
<td>53.8 ± 19.4</td>
<td>56.3 ± 8.6</td>
</tr>
<tr>
<td>Mean AoP (mmHg)</td>
<td>71.7 ± 14.4</td>
<td>80.9 ± 13.7##</td>
<td>67.5 ± 19.5</td>
<td>68.4 ± 9.1</td>
</tr>
<tr>
<td>Rs</td>
<td>25.7 ± 14.9</td>
<td>27.3 ± 10.2</td>
<td>27.4 ± 10.7</td>
<td>16.8 ± 5.7**</td>
</tr>
<tr>
<td>Rp</td>
<td>2.1 ± 1.6</td>
<td>1.9 ± 1.2</td>
<td>2.2 ± 1.3</td>
<td>1.5 ± 1.0**</td>
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<tr>
<td>MRI</td>
<td>N=22</td>
<td>N=5</td>
<td>N=17</td>
<td>N=70</td>
</tr>
</tbody>
</table>

TCPC vs. classic Fontan: *: p<0.05, **: p<0.01
Björk Pulsatile vs.others: #: p<0.05,##: p<0.01

Qp= total pulmonary blood flow; Qs= cardiac index;
Rp= pulmonary vascular resistance; Rs= systemic vascular resistance
Figure legends

Figure 1.
Dot-plots of predicted peak VO2 following TCPC (black), Fontan-Kreuzer procedure (orange) and Fontan-Björk procedure with pulsatile PBF (blue) and non-pulsatile PBF (red).

Figure 2.
Longitudinal predicted peak VO2 following TCPC (black), Fontan-Kreuzer procedure (orange) and Fontan-Björk procedure with pulsatile PBF (blue) and non-pulsatile PBF (red). Fontan-Björk procedure with pulsatile PBF had a significant better predicted peak VO2, compared with other types of Fontan procedure (p<0.001).

Figure 3.
Longitudinal predicted peak VO2 following Fontan-Kreuzer procedure (orange) and Fontan-Björk procedure with pulsatile PBF (blue) and non-pulsatile PBF (red). Fontan-Björk procedure with pulsatile PBF had a significant better predicted peak VO2, compared with other types of Fontan procedure (p<0.001).

Video legend
The author briefly explains the importance and relevance of the study.
Impact of pulsatile pulmonary blood flow on cardiopulmonary exercise performance long after the Fontan procedure

Methods: Analysis of 978 cardiopulmonary exercise tests of 227 patients who underwent either a TCPC, Fontan-Kreutzer or Fontan-Björk procedure

1. A procedure in which the RA is connected to the RV (e.g. in treatment of tricuspid atresia)
2. Some patients develop RV growth and a pulsatile pulmonary blood flow

Patients with pulsatile PBF after the Fontan-Björk procedure show a better cardiopulmonary exercise performance compared to patients with laminar pulmonary perfusion

The results implicate the importance of pulsatile pulmonary blood flow to maintain the Fontan circulation.

TCPC: total cavopulmonary connection, RA: right atrium, RV: right ventricle, PBF: pulmonary blood flow