Caval Blood Flow During Supine Exercise in Normal and Fontan Patients

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Background. Extracardiac total cavo-pulmonary connection (TCPC) bypasses the right atrium and has in theory better hemodynamics than intraatrial TCPC repair. Both are thought to have inferior hemodynamics compared with a normal circulation. Direct comparison of flow rates at rest and during exercise with magnetic resonance imaging technique have not been performed.

Methods. The study comprised 20 children. Six children (median age, 9.3 years; interquartile range, 2.2) had undergone extracardiac TCPC. Eight children (median age, 8.9 years; interquartile range, 5.0) had an intraatrial TCPC, and 6 children (median age, 10.3 years; interquartile range, 2.6) were healthy control subjects. Blood flows in the aorta, inferior vena cava, and superior vena cava were measured at rest and during two levels of submaximal supine bicycle exercise (0.5 W/kg and 1.0 W/kg) using a magnetic resonance imaging scanner mounted with a bicycle.

Results. Heart rate, respiratory rate, inspiratory fraction, and blood flow rates in the aorta and inferior vena cava increased equally in all three groups. If patients were grouped together, flow rates were significantly lower, and the inspiratory flow fraction in the inferior vena cava was significantly higher, than in control subjects. Retrograde flows were observed in all three groups at rest but tapered off with exercise.

Conclusions. At submaximal levels of lower limb exercise, patients with extracardiac as well as intraatrial TCPC showed a similar increase in respiration, heart rate, and aortic and caval flow rates as healthy control subjects. This is in accordance with the observation that many patients with TCPC perform well during daily life activities.


The total cavo-pulmonary connection (TCPC) is a palliative operation used in patients with complex cardiac malformations that preclude a biventricular repair. Different modifications have been used during the years. The intraatrial lateral tunnel TCPC experienced widespread use in the 1980s and 1990s. The unique resting flow dynamics driven by a combination of the cardiac pump and respiration have been described by several authors [1–4]. We recently described a peripheral pump that acts in addition to the cardiac pump and respiration during exercise [5]. In 1988 de Leval and coworkers [6] introduced the lateral tunnel TCPC, and 2 years later Marcelletti and associates [7] introduced the extracardiac TCPC. The operative technique seems to be easier and potentially cause less arrhythmia owing to fewer atrial suture lines [8, 9]. Speculations on which TCPC modification is the best remain.

In vitro models have documented better hemodynamics in the extracardiac TCPC compared with the intraatrial repair [10–12]. Explanted sheep heart preparations have further documented that energy dissipation is lower in the extracardiac TCPC, especially at high physiologic flow rates [13].

The aim of this study was to compare flows in the intraatrial TCPC with the extracardiac TCPC and with healthy control patients at rest and during exercise. We hypothesized that extracardiac TCPC has better hemodynamics than intraatrial but not as good as that of control subjects.

Patients and Methods

Study Group

Three groups of children were investigated. Group A comprised 6 children with an extracardiac TCPC, group B, 8 children with an intraatrial TCPC, and group C, 6 healthy control subjects. Seven of the patients in group B were studied as part of a previously reported study [5]. Compared with the previous study, this study adds a control group and a group of children with an extracardiac TCPC operation. Baseline data are shown in Table 1. The operations included a two-stage procedure with an end-to-side anastomosis between the superior vena cava (SVC) and the right pulmonary artery in both patient groups at the age of approximately 6 months. The extracardiac repair was performed with a 16- to 20-mm Gore-Tex (W.L Gore & Assoc, Flagstaff, AZ) tube connecting...
the inferior vena cava (IVC) to the inferior surface of the right pulmonary artery at the median age of 5.6 years. The intraatrial repair was performed with a prosthetic baffle connecting the IVC with the lower part of the SVC, which was anastomosed to the inferior surface of the right pulmonary artery or the pulmonary main trunk at a median age of 4 years. Surgical fenestration between the IVC channel and the right atrium was created in 3 patients in the extracardiac group and 4 patients in the intraatrial group.

Cardiac catheterization performed in all operated children approximately 6 months after surgery disclosed unobstructed pathways and absence of significant venovenous collaterals. The surgical fenestrations in 5 patients had closed spontaneously, and those of 2 patients had been closed percutaneously with an Amplatzer ASD occluder. At the time of the magnetic resonance (MR) flow measurement, 1 patient had an insignificant residual opening. Echocardiography performed within 3 months of the MR study showed good ventricular function and absence of aortic or more than mild atrioventricular valve incompetence in all patients.

All patients were in New York Heart Association functional class I to II, in sinus rhythm, and without clinical signs of congestive heart failure. All patients had resting transthoracic oxygen saturations greater than 94%. One patient in each group was on angiotensin-converting enzyme inhibitor and diuretics. Two patients in the extracardiac group and 3 patients in the intraatrial group received therapy with sodium warfarin.

Informed consent under a protocol approved by the Danish Research Ethical Committee was obtained from all subjects or their parents.

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Extracardiac TCPC (n = 6)</th>
<th>Intraatrial TCPC (n = 8)</th>
<th>Controls (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>9.3 (2.2)</td>
<td>8.9 (5.0)</td>
<td>10.3 (2.6)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>4/2</td>
<td>4/4</td>
<td>5/1</td>
</tr>
<tr>
<td>Age at surgery (y)</td>
<td>5.6 (2.2)</td>
<td>4.0 (3.1)</td>
<td>…</td>
</tr>
<tr>
<td>Time since surgery (y)</td>
<td>3.7 (0.3)</td>
<td>4.8 (3.1)</td>
<td>…</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>28 (2)</td>
<td>31 (15)</td>
<td>41 (17)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>137 (11)</td>
<td>131 (19)</td>
<td>144 (14)</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.05 (0.09)</td>
<td>1.08 (0.33)</td>
<td>1.25 (0.31)</td>
</tr>
<tr>
<td>Diagnosis (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricuspid atresia</td>
<td>0</td>
<td>3</td>
<td>…</td>
</tr>
<tr>
<td>Double-inlet left ventricle</td>
<td>2</td>
<td>4</td>
<td>…</td>
</tr>
<tr>
<td>Mitral atresia</td>
<td>0</td>
<td>1</td>
<td>…</td>
</tr>
<tr>
<td>Hypoplastic right heart</td>
<td>3</td>
<td>0</td>
<td>…</td>
</tr>
<tr>
<td>Complex DORV</td>
<td>1</td>
<td>0</td>
<td>…</td>
</tr>
</tbody>
</table>

Numbers and those in parentheses represent median (interquartile range).

BSA = body surface area; DORV = double-outlet right ventricle; TCPC = total cavo-pulmonary connection.

Study Design

The children were investigated according to an exercise protocol and MR setup previously described in detail [5]. In brief, they were placed supine in the MR imaging scanner with their feet strapped in the pedals of an ergometer bicycle mounted on the scanner table. The electrocardiogram was recorded continuously. Inspiration and expiration were monitored with an air-filled belt mounted on the abdomen.

Heart rate and MR imaging flows during inspiration and expiration were measured during rest and at workloads of 0.5 W/kg and 1.0 W/kg when the heart rate had been stable for 2 minutes. Real-time flow measurements were performed by phase-contrast flow acquisition during two full respiratory cycles with a time resolution of approximately 20 frames per second. Superior vena caval flow was measured immediately above the pulmonary anastomosis in TCPC patients and above the right atrium but below the azygos vein in control subjects. Inferior vena caval flow was measured in the middle of the conduit in group A, in the intraatrial tunnel above the coronary sinus in group B, and at the top of the IVC just beneath the right atrium in control subjects. Aortic flow was measured in the middle of the ascending aorta. The following variables were recorded in each individual: mean heart and respiratory rates, duration of inspiration and expiration, and mean flow rates in IVC, SVC, and aorta during inspiration and expiration and overall at each workload. From these measurements we calculated the inspiratory fraction as the duration of inspiration relative to a full respiratory cycle, the inspiratory flow fraction as inspiratory flow relative to mean flow, and percentage of retrograde flow relative to mean forward flow. All flow rates were corrected for body surface area and expressed as liters per minute per meter squared.

Statistical Analysis

The Mann-Whitney U test was used to compare groups (extracardiac (TCPC), intraatrial (TCPC) and control subjects), and the Wilcoxon W test was used to compare paired data. We considered a probability value less than 0.05 (two-tailed) to be statistically significant. The statistical analyses were performed using a spreadsheet (Microsoft Excel; Microsoft Corp, Redmond, WA) and Analyse-it software version 1.71.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agreed to the manuscript as written.

Results

All children completed the protocol. One of the control subjects was moving excessively during exercise and it was not possible to achieve valid IVC flow measurements in that specific child. Age, height, weight, and body surface area did not differ between the three groups (Table 1).
Heart and Respiratory Rates

Heart rate tended to be lower in patients with intraatrial TCPC than in the extracardiac TCPC and in the control subjects, although the difference was not statistically significant. The heart rate increased with increasing levels of exercise ($p < 0.05$; Table 2). There was the same absolute increase with exercise in the three groups, with the intraatrial group reaching the lowest level.

No statistically significant difference in respiratory rate at rest and during exercise was found among the groups. The respiratory rate increased with exercise in all three groups ($p < 0.05$). The inspiratory fraction tended to increase during exercise, although no statistical difference was reached within or among groups (Table 2).

Flow Rates

Flow rates in the aorta, IVC, and SVC at rest and during exercise in the three groups are shown in Figure 1. At rest, flow rates were slightly higher in healthy control subjects than in each of the patient groups but not significantly so. Within all three groups flow rates in the aorta and IVC increased significantly with increasing levels of lower body exercise, whereas SVC flows were unchanged. The absolute increase in aorta and IVC flow with exercise did not differ significantly among groups and neither did the resultant flow rates during exercise. However, if data from the two patient groups were pooled together, control subjects had significantly higher flow rates in the aorta and IVC at rest and during exercise, but the increase in flow rates with exercise was similar in patients and control subjects (Table 3).

Periods of retrograde flow were present in all groups at rest, but minute in the aorta and SVC. In the IVC, the median regurgitant fraction relative to mean forward flow at rest was similar in both patient groups and control subjects (intraatrial, 7%; range, 1% to 32; extracardiac, 5%; range, 0% to 17%; control subjects, 6%; range, 0% to 20%). With increasing levels of exercise retrograde flow diminished in patients (intraatrial, 1%; range, 0% to 11%; extracardiac, 1%; range, 0% to 7%), and vanished completely in control subjects (0%; range, 0% to 0% at 1 W/kg).

Respiratory Influence on Flows

The effects of respiration expressed as inspiratory flow fraction of IVC flow at rest and during exercise in the two patient groups and in control subjects are shown in Figure 2. The inspiratory flow fraction in the IVC was significantly higher and more variable in both patient
groups than in control subjects. With exercise this effect of respiration vanished in control subjects and diminished but remained significantly higher in both patient groups.

Comment

This study compares real-time blood flow during exercise in children undergoing intraatrial and extracardiac TCPC operations with that of healthy children. The overall result was that both patient groups were able to respond to a submaximal lower limb exercise with a similar increase in heart rate and respiration and in IVC and aortic flows, which did not differ from the response in healthy children. The IVC flow in the two patient groups varied more with respiration than in the age-matched control subjects, but the influence tapered off with exercise. Only when data from the two patient groups were pooled together did healthy control subjects have significantly higher resting flow rates in the aorta and IVC and reach higher levels during exercise, but the increase in flow rates with submaximal exercise did not differ between the two groups.

This finding of reduced blood flow rates at rest and during exercise in the combined groups of patients having TCPC operations is similar to results from other studies that used gas exchange [14–16] or dye dilution [17] techniques to calculate cardiac output. In these studies resting heart rate and minute ventilation was higher in TCPC patients than in control subjects [14, 15], whereas we found similar heart and respiratory rates in the two groups both at rest and during exercise. Thus, our study does not suggest chronotropic incompetence [18] in Fontan patients at submaximal levels of supine bicycle exercise. Previous studies have likewise demonstrated a similar increase in heart rate in TCPC patients and control subjects during supine as well as upright bicycle exercise of comparable workloads [14, 19]. Most previous studies [14–17, 19] have included patients with the classic atriovenous connection. In one study [15] but not in another [14] there was an impaired increase in cardiac output with exercise in the classic atriovenous connection compared with intraatrial TCPC.

Hsia and colleagues [20] found that resting Doppler flows in the infrahepatic IVC, the hepatic veins, and the two combined were similar in patients with extracardiac and intraatrial TCPC, with marked respiratory dependency and small quantities of periodic retrograde flow. This respiratory variability in flows diminished significantly when patients changed position from upright to supine. Healthy control subjects exhibited lesser respiratory and positional variability in IVC return. We confirmed these observations with respect to supine flows in patients and control subjects and further showed that the cardiorespiratory response to exercise was similar in extracardiac and intraatrial TCPC. Thus this study did not support the concept of superior hemodynamics in extracardiac compared with intraatrial TCPC. This is in accordance with a recent clinical study, which showed similar early and late mortality and morbidity in the two groups [21].

The limitation of the study is that with only 6 and 8 patients in each group, this study does not allow for detection of minor differences, but major differences would likely have been disclosed. The low number of patients also precludes speculations about the importance of the underlying pathophysiology in the individual patients. At rest, 2 patients in the intraatrial group had very high IVC forward flow at inspiration and significant retrograde flow at expiration. The combination explains the very high inspiratory flow fractions. Conclusions are unaltered without the two outliers.

The patients who underwent intraatrial tunnel TCPC were younger at the time of operation than those having extracardiac tunnel TCPC. At the time of investigation,

Table 3. Aortic, Inferior Vena Cava, and Superior Vena Cava Flow

<table>
<thead>
<tr>
<th>Variable</th>
<th>Extracardiac and Intraatrial TCPC (n = 14)</th>
<th>Controls (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta</td>
<td>Rest 3.1 (1.2)*</td>
<td>4.0 (0.7)*</td>
</tr>
<tr>
<td></td>
<td>0.5 W/kg 4.2 (1.0)*</td>
<td>4.9 (0.6)*</td>
</tr>
<tr>
<td></td>
<td>1.0 W/kg 4.3 (0.5)*</td>
<td>5.4 (0.3)*</td>
</tr>
<tr>
<td>IVC</td>
<td>Rest 1.6 (0.4)*</td>
<td>2.1 (0.3)*</td>
</tr>
<tr>
<td></td>
<td>0.5 W/kg 2.7 (1.0)*</td>
<td>3.4 (0.1)*</td>
</tr>
<tr>
<td></td>
<td>1.0 W/kg 2.9 (1.2)*</td>
<td>4.5 (0.3)*</td>
</tr>
<tr>
<td>SVC</td>
<td>Rest 1.3 (0.7)</td>
<td>1.5 (0.2)</td>
</tr>
<tr>
<td></td>
<td>0.5 W/kg 1.5 (1.0)</td>
<td>1.8 (0.6)</td>
</tr>
<tr>
<td></td>
<td>1.0 W/kg 1.1 (0.3)*</td>
<td>1.6 (0.2)*</td>
</tr>
</tbody>
</table>

*Values are significantly different from surgical groups (p < 0.05).

Numbers and those in parentheses represent median (interquartile range).

IVC = inferior vena cava; SVC = superior vena cava; TCPC = total cavo-pulmonary connection.
age, weight, height, and body surface area did not differ between groups, and all values are indexed to body surface area. The male to female distribution differed between groups. In this age group, however, there are no sex-related differences in the oxygen uptake and kinetic response to moderate intensity exercise [22].

Lower limb activity in the supine position is uncommon. Perhaps the cardiorespiratory response to daily life submaximal exercise in the upright position would be significantly reduced in patients owing to the more pronounced effect of gravity on IVC flow in the TCPC circulation. The choice of supine bicycle exercise was, however, dictated by the use of an MR scanner equipped with an MR-compatible bicycle and with magnetic field strength and gradient systems sufficient for performing the real-time flow measurements during exercise. We did not study cardiorespiratory response to maximal workloads. Differences between the two types of Fontan circulation may be present at higher exercise levels.

The real-time MR technique used is limited by a relatively low spatial resolution that might potentially lead to partial volume-related overestimation of flow values in the smallest vessels. No systematic errors were detected related to this phenomenon, and the average difference between the total arterial and total venous flow was less than 5% for all exercise levels. Because of the small field of view it was not possible to perform phase correction based on stationary tissue as discussed before [5]. The real-time echo planar imaging technique based MR technique used has an inherently lower signal to noise ratio than standard MR techniques, but has nevertheless been demonstrated to be of sufficient accuracy for quantitative flow measurements in the large vessels of children [23]. The real-time aspect secured insensitivity to motion, and identical image quality was obtained at all exercise levels.

In conclusion, at submaximal levels of lower limb exercise, patients with extracardiac as well as intraatrial TCPC showed a similar increase in respiration, heart rate, and aortic and caval flow rates as healthy control subjects. This is in accordance with the observation that many patients with TCPC perform well during daily life activities.

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References