Exercise capacity, quality of life, and daily activity in the long-term follow-up of patients with univentricular heart and total cavopulmonary connection

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Aims

Patients with congenital heart disease usually show diminished exercise capacity and quality of life. However, there is only little information about daily activity, a marker for lifestyle, exercise capacity, and the prevention of arteriosclerosis. This study investigated exercise capacity, quality of life, daily activity, and their interaction with univentricular heart physiology after total cavopulmonary connection (TCPC).

Methods and results

Fifty-seven patients (18 females, 39 males, age 8–52 years) after TCPC (lateral tunnel 28, extra-cardiac conduit 29) who underwent surgery during 1994–2001 were examined in our institution. They performed a symptom-limited cardiopulmonary exercise test. Those patients 14 years of age and older filled in the health-related quality-of-life questionnaire SF-36, and those who were 8–13 years of age, the CF-87. Daily activity parameters were obtained by using a triaxial accelerometer over the next three consecutive days. Exercise capacity was severely reduced after TCPC (25.0 mL/min/kg corresponding to 59.7% of age- and sex-related reference values). Daily activity was within the recommendations of the United Kingdom Expert Consensus Group (≥60 min, ≥3 metabolic equivalent, ≥5 days/week) in 72% of the investigated patients. It was reduced in older patients (Spearman \( r = -0.506, P < 0.001 \)) and patients with a lower peak oxygen uptake (Spearman \( r = 0.432, P = 0.001 \)). In children < 14 years, mental health was related to daily activity.

Conclusion

Despite their diminished exercise capacity, patients after TCPC show a fairly normal activity pattern. However, their activity depends not only on age, but also on exercise capacity, which, in contrast to healthy people, decreases already from early adolescence on.

Keywords

Congenital heart disease • Exercise capacity • Total cavopulmonary connection • Long-term follow-up • Quality of life • Daily activity

Introduction

Patients with congenital heart disease show decreased exercise capacity in diminished peak oxygen uptake (peak \( \dot{V}O_2 \)). Even those with heart defects considered to be ‘corrected’ after surgery show such kind of reduction in peak \( \dot{V}O_2 \), but the reasons are commonly unknown. Recently, Bjarnason-Wehrens et al. investigated motor developmental skills in schoolchildren with congenital heart disease. They reported on delays in coordination even in patients without haemodynamic burden and they assumed that the overprotection may be the cause for less activity and consecutively delayed motor development that also might result in impaired exercise capacity.

Daily activity is an important lifestyle factor for children and adolescents. Sport with children or adolescents of the same age helps them to gain friendship, to improve their exercise capacity and...
quality of life. This influences positive psychological development and prevents them from developing isolation later in life. Furthermore, it is essential for proper motor development.

However, studies measuring daily activity in patients with congenital heart disease are rare and are of conflicting results. Fredriksen et al. found, in their group of various congenital heart diseases, a reduced activity level only in boys. McCrindle et al. found limitations in both sexes of patients with several modifications of Fontan circulations. Therefore, we investigated patients with univentricular heart physiology after total cavopulmonary connection (TCPC), which is the current modification of the original Fontan procedure with expected improved results.

Hence, the aim of the study was to gain insight into the activity patterns of these patients and to determine the different factors on which daily activity might depend.

Methods

Study subjects
We investigated patients who had undergone a TCPC in our institution before 2002. Patients with an earlier Fontan modification converted to a TCPC were excluded from the study (Figure 1).

Of the 116 eligible patients, 17 died during the follow-up, 2 had heart transplantation, and 1 required a take-down operation. Twelve patients moved to remote or unknown areas and 18 patients refused to be studied.

From the total of 66 patients recruited to our study and examined from October 2006 to June 2007, 1 refused to wear the accelerometer, 3 were not able to perform a symptom-limited exercise test due to motoric handicaps, and another 5 could not fill out the quality-of-life questionnaire (two for language barriers and three for mental retardation). Hence, 57 patients between 8 and 52 years of age completed the whole protocol and were included in the study.

Cardiopulmonary exercise test
All patients underwent a symptom-limited cardiopulmonary exercise test on a bicycle in upright position according to international guidelines, with one of the authors present at all times. After a 3 min rest to define baseline values, patients had a 3 min warm-up without load, followed by a ramp-wise increase of load with 5, 10, or 15 W/min depending on the expected individual physical capacity estimated by the investigator. The aim was to reach a cycling time of about 8 to 12 min after warm-up. The end of the cardiopulmonary exercise test was marked by symptom limitation and was followed by a 5 min recovery period without cycling.

The exercise test featured a breath-by-breath gas exchange analysis using a metabolic chart (Vmax, SensorMedics, Viasys Healthcare, Yorba Linda, CA, USA). Peak VO2 was defined as the highest mean uptake of any 30 s time interval during the exercise.

Reference values (mL/kg/min) were calculated for 18 years and older according to Cooper and Storer.

For patients 12–17 years of age, reference values (mL/kg/min) were calculated according to Cooper and Weiler-Ravell.

Twenty-one patients had a double-inlet left ventricle, 15 tricuspid atresia, 11 hypoplastic left heart syndrome, 5 hypoplastic right heart syndrome, 3 double-outlet right ventricle with unbalanced ventricles, and 2 a complete atrioventricular septal defect with unbalanced ventricles. Heterotaxy was present in three patients.

Medication consists of oral anticoagulation (53 patients), ACE inhibitor (25), diuretics (9), beta-blocker (3), and digoxin (2).

A lateral tunnel was performed in 28 patients and an extra-cardiac conduit was performed in 29 patients during 1994–2001. Median age of the patients during follow-up was 14.0 (interquartile range 11.0–17.8) years. Total cavopulmonary connection was completed with a median age of 5.6 (3.7–8.4) years. In 56% (n = 32) of the patients, a partial cavopulmonary connection (PCPC) precedes the TCPC. A fenestration was created at surgery in 42% (n = 24) of the patients with only four fenestrations open during the follow-up.

Three patients suffered from intermittent or persistent protein-losing enteropathy with a total protein level in serum of less than 5.5 g/dL. NT-proBNP was within the normal range of less than 480 ng/L in all but four patients.

The study was in accordance with the Declaration of Helsinki (revision 2008). The study protocol was approved by the local ethical board (project number 1568/06). All patients gave written informed consent.

| Figure 1 | Patients’ inclusion. |
For patients younger than 12 years of age, we used the pooled data from both sexes:

\[
\text{peak } V_O^2 = \frac{37.1 \cdot \text{height (cm)} - 3770.6}{\text{weight (kg)}}
\]

Quality of life

Just before the exercise test, health-related quality of life was measured by two different questionnaires based on the age of the patients. For adolescents and adults of 14 years and older, the Medical Outcomes Study 36 item short form (SF-36) was used. It has an acceptable internal consistency and has proven useful in various specialties of medicine without any bias for symptoms of a specific disease. The SF-36 measures eight health constructs using subscales with 2 to 10 items per subscale (with a total of 36 questions). As described previously,\textsuperscript{10} we used the German version of the self-report form with a window of 4 weeks.\textsuperscript{11,12}

For children younger than 14 years of age, the Child Health Questionnaire CF-87 was used to estimate the quality of life. It is also a multi-dimensional generic instrument that has been designed and evaluated for children up to 5–18 years of age. It consists of 87 items within 11 dimensions.\textsuperscript{13}

The patients received the appropriate questionnaire at the beginning of the investigation and had to complete it without any help. In patients lacking reading ability, the investigator read the instructions and questions to the children.

Daily activity

Daily physical activity was measured by the triaxial accelerometer RT3 (Stayhealthy, Monrovia, CA, USA) over the next three consecutive days after the examination.

The RT3 is designed as a complete activity recording and measurement system for clinical and research applications. When wearing this RT3 on the waist over three consecutive days, it continuously tracks activity throughout the day with the use of piezoelectric accelerometer technology that measures motion in three dimensions and provides triaxial vector data in activity units. The accelerometer was removed only during showering or swimming and during bedtime.

In our scientific research, we used vector magnitudes calculated from the three dimensions with a sampling epoch of 1 min. Daily activity was defined as the mean value of activity units over these 3 days. The daily minutes in moderate (3–6 metabolic equivalents (METs)) and vigorous activity (>6 METs) were calculated, using the published cut-off points for moderate (>970 counts/min) and vigorous (>2333 counts/min) activity.\textsuperscript{14} For statistics, we used the pooled data from moderate-to-vigorous activities representing all activity >3 METs.

Data analyses

Since data were skewed, all descriptive data were expressed in median values and interquartile ranges (Q1–Q3). The percentage of subjects, meeting the current physical activity guidelines of the United Kingdom Expert Consensus Group performing >60 min at a minimum of 3 METs on 5 days per week or more, was calculated.\textsuperscript{15} Furthermore, the individual values for combined moderate and vigorous activities were plotted relative to the 50th percentile for normal, healthy children reported by Pate et al.\textsuperscript{15}

Non-parametric Mann–Whitney U tests were calculated to find differences between the described surgical variables. The non-parametric Spearman correlation was used to find associations between daily activity, exercise capacity, and quality-of-life data.

All analyses were performed using SPSS 15.0 software (SPSS, Inc., Chicago, IL, USA). P-values <0.05 were considered significant.

Results

Exercise capacity

Median peak \( V_O^2 \) was 25.0 (20.6–28.7) mL/min/kg corresponding to 59.7% (51–69%) of the age- and sex-related reference values.

In children <14 years of age, exercise capacity was estimated to be 62.1% (56.6–73.9%) of age- and sex-related reference values and in the teenager and adult group, mean percentage of relative peak \( V_O^2 \) was slightly lower with 56.0% (47.7–65.5%) of the reference value, outlining that even age- and sex-corrected peak \( V_O^2 \) decreased with increasing age (Spearman \( r = -0.339, P = 0.010 \)). A closer look at the data revealed that especially in males, there was not the usual increase of exercise capacity during puberty but rather a progressive decline from early adolescence on (Figure 2).

Exercise capacity was related to NT-proBNP (Spearman \( r = -0.322, P = 0.017 \)). However, we failed to find relationships to systemic ventricular morphology, type of TCPC, fenestration, and protein-losing enteropathy. Exercise cyanosis, defined as oxygen saturation below 85% during exercise, was observed in 12 patients.

Quality of life

Self-estimated quality of life was fairly good. In many scales, the best imaginable result was achieved in many patients (Table 1).

Daily activity

From 57 data samples, a median of 87 min/day (48–112 min) was spent in moderate activity and a median of 12 min/day (6–24.5 min) was spent in vigorous activity. The pooled data of these two activity intensities were 98 min/day (53–135 min). Daily activity was within the recommendations of the United Kingdom Expert Consensus Group (≥60 min, ≥3 metabolic equivalent, ≥5 days/week) in 41 patients (72% of the investigated patients) (Figure 3).

Time spent in moderate and vigorous activity correlated significantly with age (Spearman \( r = -0.506, P < 0.001 \)) and exercise capacity expressed as percentage of expected (Spearman \( r = 0.432, P = 0.001 \)), representing decreased activity with increasing age and decreasing exercise capacity. No significant differences between males and females were found.

In the subgroup of children aged younger than 14 years, the mean activity was 119 min/day (77–178 min, \( n = 28 \)) showing an inverse correlation only to age (Spearman \( r = -0.451, P = 0.016 \)). Patients who were 14 years or older achieved 73 min/day mean activity (43–118 min, \( n = 29 \)) with a moderate relationship only to exercise capacity (Spearman \( r = 0.477, P = 0.009 \)).

Neither surgical parameter (extra-cardiac or lateral tunnel TCPC, fenestration, prior PCPC) nor other signs of a failing Fontan circulation (protein-losing enteropathy, NT-proBNP) showed any relationship to daily activity.

Only in the children’s group, a significant but weak correlation to the Mental Health subscale (Spearman \( r = 0.380, P = 0.046 \)) representing anxiety and depression in the CHQ-87 instrument could be detected. No other relationship of any scale of
the quality-of-life questionnaires could be found with daily activity in our TCPC cohort, not even to vitality or physical functioning.

Furthermore, seasonal effects in the study period for a higher activity in the months of spring were only small and failed significance (Kruskal–Wallis $X^2 = 13.9, P = 0.085$).

**Table 1** Health-related quality of life of children <14 years (CHQ-87) and adolescents/adults 14–52 years (SF-36) with univentricular heart disease after total cavopulmonary connection

<table>
<thead>
<tr>
<th>CHQ-87 (&lt;14 years)</th>
<th>SF-36 (≥14 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimension</td>
<td>Median (Q1–Q3)</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>92 (85–96)</td>
</tr>
<tr>
<td>Role—emotional</td>
<td>100 (100–100)</td>
</tr>
<tr>
<td>Role—behavioural</td>
<td>100 (100–100)</td>
</tr>
<tr>
<td>Role—physical</td>
<td>100 (92–100)</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>100 (73–100)</td>
</tr>
<tr>
<td>General behaviour</td>
<td>87 (78–92)</td>
</tr>
<tr>
<td>Mental health</td>
<td>78 (71–89)</td>
</tr>
<tr>
<td>Self esteem</td>
<td>84 (77–93)</td>
</tr>
<tr>
<td>General health</td>
<td>62 (53–73)</td>
</tr>
<tr>
<td>Family activities</td>
<td>90 (83–99)</td>
</tr>
<tr>
<td>Family cohesion</td>
<td>85 (85–100)</td>
</tr>
</tbody>
</table>

**Figure 2** Exercise capacity according to age. Median measured values (full lines) are compared with the median of the individual reference values (dashed lines), depicting that in males there is no pubertal increase in exercise capacity and in females there is an enhanced decline of exercise capacity starting already in childhood.

**Discussion**

**Exercise capacity**

This study shows a substantial reduction of exercise capacity, measured as peak $\dot{V}O_2$ in a cardiopulmonary exercise test, in the TCPC patients. These findings are in concordance with previous work.
patterns in Fontan patients and patients after arterial switch in the extra-cardiac conduit subgroup. Up to now, only electrophy-
hood and declined from early adolescence on.
our patient group, exercise capacity stayed unchanged during child-
ents who increase muscle mass substantially during puberty. In
during puberty in males. This is in contrast to healthy male adoles-
study revealed that there was no increase of peak oxygen uptake
of peak 


Figure 3 Daily time spent in moderate or vigorous physical activity for each total cavopulmonary connection patient by patient’s age for males and females. Reference lines are the age group 50th percentiles for normal, healthy children according to Pate and >17 years of age the recommendations for physical activity according to the United Kingdom Expert Consensus Group.

studies that have reported exercise limitations in patients with
diverse congenital heart disease\textsuperscript{5,16} as well as in Fontan patients.\textsuperscript{5,17} Like the longitudinal study of Giardini et al.,\textsuperscript{17} we found a decrease of peak VO\textsubscript{2} in adults over the years when compared with the normal decline in healthy subjects. Additionally to this dispropor-
tionate decline with proceeding age, the gender analysis in our
study revealed that there was no increase of peak oxygen uptake
during puberty in males. This is in contrast to healthy male adoles-
cents who increase muscle mass substantially during puberty. In
our patient group, exercise capacity stayed unchanged during child-
hood and declined from early adolescence on.

Furthermore, we speculated on a better exercise performance
in the extra-cardiac conduit subgroup. Up to now, only electrophys-
siologic variables could show a clinical advantage of an extra-
cardiac conduit over a lateral tunnel TCPC.\textsuperscript{18–20} We also failed to find any differences in exercise capacity. However, our extra-
cardiac TCPC patients were slightly older at TCPC and at follow-up than our lateral tunnel TCPC patients making a realistic comparison impossible.

Daily activity
Nevertheless, our study showed a fairly normal daily activity
pattern in our TCPC patients. According to the recommendations
of the United Kingdom Expert Consensus Group, our patient
group after TCPC mostly complied with the standards for daily
activity in moderate (87 min/day) and vigorous (12 min/day) exer-
cises. In only 16 of our 57 patients (28%), a functional reduction of
daily activity, missing the recommended 60 min/day, was noted.
Therefore, our group of TCPC patients was substantially more
active than the congenital heart disease groups of McCrindle
et al.\textsuperscript{5} and Massin et al.\textsuperscript{21} who reported reduced physical activity
patterns in Fontan patients and patients after arterial switch
operation. Compared with McCrindle et al.’s all-kind-of-Fontan
group, we speculate that the main factor for increased physical
activity in our cohort was the better haemodynamic situation of
the TCPC, representing the contemporary standard of surgical
treatment in univentricular hearts and outperforming the long-
term results of other Fontan procedures such as atroplunmonary
connection or atrioventricular connection.\textsuperscript{17}

Another factor for increased daily activity might be the changing
aftercare philosophy of our department within the last 5 years.
Exercise and sport were not categorically discouraged. On the
contrary, we encourage our patients after a solid check-up to par-
ticipate in school sports and moderate exercises.

In agreement with other studies in healthy children\textsuperscript{15,22} as well
as in Fontan patients,\textsuperscript{5} we observed a strong age-related decline
in physical activity. Only a closer look at the individual activity
data revealed that the lack of physical activity compared with
healthy peers is most prominent in the youngest age group
below 9, when physical activity in healthy children seems to be
most liberal throughout the life. Overprotection has been
reported as an important issue for exercise limitation in the
younger patients with congenital heart disease.\textsuperscript{23} It is not aston-
ishing that, in accordance with McCrindle et al.,\textsuperscript{5} the youngest chil-
dren are farthest away with regard to daily activity from their
healthy counterparts. They are usually under close control of
their parents and kept away from different type of sports and
thus controlling their activity even with their exercise capacity
being closest to normal in this lifespan.\textsuperscript{17} Teenagers aged 12–16
years were less active, but nearer to norm values. With this age,
we assume, they start to ignore the care from their parents and
develop their own activity patterns.

In the adolescent and adult group of 14 years of age or older
effects of aging diminished. In that age group, there was clear
coherence between daily activity and exercise capacity. This can
be interpreted as only patients with a higher exercise capacity
show a more active daily life. This might be a sign that indeed
the reduced exercise capacity curtails the patient’s daily life
despite they do not report that in health-related quality-of-life
questionnaires (present study).\textsuperscript{10,16} In this older age group, we
speculate on this direction of the cause and effect relationship,
as exercise diminished capacity is moderately to severely,
whereas daily activity is close to normal. However, the reduced
activity, especially the reduced vigorous activity in early childhood,
might be an important contributor for deconditioning and proper
muscle build-up in childhood and puberty. This cause-and-effect
relationship, we propose in children, is supported by the fact,
that none of the investigated variables of heart failure in Fontan
patients, for example, the incidence of sinus node dysfunction or
protein-losing enteropathy, showed any relation to exercise
capacity or daily activity.

Daily activity and self-reported quality
of life
In contrast to the patient group 14 years of age or older, we only
noted in the children subgroup a correlation between daily activity
and mental health. This correlation outlines that depression, prob-
ably more important anxiety, transferred from overprotecting
parents and health care provider to the young patients is an important reason for the diminished activity seen in that age group.

Furthermore, the lack of correlation between self-estimated vitality and objectively measured physical activity seems to be astonishing. However, these results are in concordance with McCrindle et al.,5 who reported only poor coherence in perceived general health and decreased physical activity patterns after Fontan operation. Other aspects of functional status as well as the answers in a physical activity questionnaire did not show any correlation to measured daily activity in their study. Maybe this is the same phenomenon as previously reported by Hager and Hess10 and in a larger cohort by Gratz et al.16 comparing objectively measured exercise capacity and self-reported physical functioning of adults with congenital heart disease. They reported on a reasonable misinterpretation of the patients concerning their own physical capacity. Others also speculated about this misconception when comparing the results of direct psychological tests to the results of these subscales in self-reported quality-of-life instruments.

**Conclusion**

Patients with TCPC show a reduced exercise capacity reaching only about 60% of their reference values. Nevertheless, they seem to be fairly active. Many of them show normal activity patterns, achieving the claimed 60 min of at least 3 METs per day by objective accelerometric measurement. As in healthy children, daily activity decreases with age. However, children younger than 9 years are most prominently curtailed in physical activity compared with their healthy peers, maybe due to overprotection. Later in adolescence, daily activity of TCPC patients is mainly related to exercise capacity that declines from the early adolescence on.

**Study limitation**

The measurement of daily activity over the next three consecutive days after examination was affected by weekday and weekend alteration. For future assessments of daily activity, recording over 1 week should be aspired. Furthermore, the study period should be as small as possible to exclude seasonal effects.

The patients studied here represent a ‘positive’ selection of the total patient group of TCPC patients. The excluded patients could either not perform an exercise test or could not fill out a quality-of-life questionnaire, had heart transplantation or TCPC take-down, or even died during follow-up. So, we can only state that patients with a good result of their TCPC can achieve a normal activity pattern in daily life despite severely diminished exercise capacity.

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**References**