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# Functional outcome in contemporary children with total cavopulmonary connection – Health-related physical fitness, exercise capacity and health-related quality of life

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ABSTRACT

*Objective:* Children and adolescents with an univentricular heart after total cavopulmonary connection (TCPC) have functional impairments. This study assesses health-related physical fitness (HRPF) and exercise capacity, as well as their relation to health-related quality of life (HRQoL) in patients with an univentricular heart after total-pulmonary connection (TCPC).

*Patients and methods:* Between July 2014 and October 2016 a total of 78 children and adolescents with TCPC (12.0 ± 3.2 years, 21 female) performed a motor test including five tasks for strength and flexibility during their routine follow-up appointment. They also underwent a symptom limited cardio-pulmonary exercise test and filled in a HRQoL questionnaire (KINDL-R). Patients' data were compared to a recent sample of healthy children (n = 1650, 12.6 ± 2.4 years, 49% female).

*Results:* Multivariable regressions corrected for sex, age and BMI showed that TCPC patients achieved 12.4 repetitions of curl-ups ($p < 0.001$) and 2.6 push-ups ($p = 0.010$) less than healthy counterparts. They had impairments in trunk (−8.5 cm; $p < 0.001$), shoulder (−7.5 cm; $p < 0.001$) and lower limb flexibility (−4.7 cm; $p < 0.001$). Peak oxygen uptake was reduced to 34.8 ± 7.5 ml/min/kg and 77.7% respectively, compared to peers ($p < 0.001$). Ventilatory efficiency was also impaired (healthy: 27.5 ± 2.9 vs. TCPC: 31.6 ± 3.3; $p < 0.001$). HRQoL did not differ significantly ($p = 0.233$).

*Conclusions:* Children and adolescents with TCPC still present impaired HRPF and exercise capacity whereas HRQoL is similar to healthy peers. Since low HRPF may yield to worse motor competence and exercise capacity, early screening for HRPF and early treatment, if indicated, is recommended.



## 1. Introduction

About 1% of all alive new-born children have a congenital heart disease (CHD) and about 3% of them are born with an univentricular heart [1]. Unfortunately, those patients are not amenable to biventricular repair but nonetheless have to undergo a three staged palliative surgical procedure to ensure survival [2,3]. The final step is the total cavopulmonary connection (TCPC). After completion the venous blood is passively conducted to the lungs through an extracardial conduit or lateral tunnel, bypassing the right heart structures. After oxygenation, the blood pours into the remaining single ventricle that drives the systemic circulation.

Albeit functional mid and long-term outcomes improved over the past decades due to surgical progress and medical aftercare, children with TCPC still depict impaired motor development in motor skill [4], limited exercise capacity [5] and reduced health-related quality of life (HRQoL) [6]. In fact, neurodevelopment is impaired in all kinds of children with CHD already in infancy [7]. But those early neurological limitations, especially in severe CHD, are tracked from infancy into childhood and adolescents where they also become obvious as limitations in motor development, motor skills and health-related physical fitness (HRPF) [8–10]. In addition to the single ventricle morphology, neurodevelopmental and motoric impairments contribute to the diminished exercise capacity of these patients [11]. Those physical limitations may also affect the HRQoL since some studies report lower HRQoL [6,12], whereas others show equal or even better HRQoL outcomes [5].

In front of this background the aim of this study was to investigate HRPF as a further evidence for motor development of children with

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TCPC, their exercise capacity and present HRQoL in comparison to healthy counterparts.

## 2. Patients and methods

### 2.1. Study subjects

We included 78 children and adolescents (12.0 ± 3.2 years, 21 female) between 6 and 18 years with an univentricular heart after TCPC who had a routine follow-up appointment in our department between July 2014 and October 2016. All of them were free from syndromes, acute infects and able to exercise.

Patients' age at TCPC surgery was 2.3 ± 1.5 years. 69 patients had an extracardial connection and 9 a lateral tunnel. Their general type of CHD was hypoplastic left heart (27 patients), double inlet left ventricle (12 patients), tricuspidal atresia (13 patients), malposition of the great arteries (10 patients), atrioventricular anomaly (5 patients), hypoplastic right heart (4 patients) and miscellaneous (7 patients). 34 TCPCs had a right systemic ventricle, 37 a left one and in 7 a dominant ventricle could not be defined.

Healthy controls (n = 1650, 12.6 ± 2.4 years, 49% female) were obtained from studies recently conducted in several Bavarian schools. Several data from the reference studies has already been published elsewhere [13,14]. With respect for participation in the investigation the inclusion in each analyses can be seen in Fig. 1. Not all of included participants finished all tests. This was because of lack of time, fully booked capacity (outpatient) or further appointments. Written informed consent was obtained from all participants and their guardian. The study was approved by the local ethical board of the Technical University of Munich (project number: 314/14).

### 2.2. Health-related physical fitness (HRPF)

Patients and healthy controls performed a motor test with five tasks. To asses upper-body strength they performed maximum repetitions in curl-ups and push-ups. Complete sitting up in curl-ups and at least 90° flexion in elbows in push-ups were required to be counted. The exercise was stopped after the second invalid execution. Flexibility was tested by shoulder stretch (distance between pointers' knuckles behind the back having a fist) and sit and reach (distance fingertips to toes, sitting), whereas trunk lift (distance chin to the ground) measured trunk extensor strength and flexibility. Shoulder stretch, as well as sit and reach, were performed separately for each side. Trunk lift was performed twice and the best value was recorded. The test battery was based on the Fitnessgram® [15]. More detailed instructions can be accessed from the Online Supplement. For analyses the mean of the left and right-sided test in shoulder stretch and sit and reach were used.

### 2.3. Cardio-pulmonary exercise test (CPET)

Exercise capacity was assessed with a symptom-limited cardio-pulmonary exercise test (CPET) on a bicycle in upright position with a rampwise protocol as it is routine in our institution [16]. Subjects' peak oxygen uptake ($\dot{V}O_2$ peak) was defined as the highest mean uptake of any 30 s time interval during exercise. Peak workload was described as maximum value in watt which the subjects reached when terminating the test. The estimated ventilatory efficiency ($\dot{V}_E/\dot{V}CO_2$ slope) represents how much liter of air patients have to exhale (volume of expiration $\dot{V}_E$) to eliminate one liter of $CO_2$ ($\dot{V}CO_2$). The slope was calculated manually with the V-slope method according to Beaver et al. [17] and corrected by the $\dot{V}_E/\dot{V}CO_2$ curve. Ventilatory efficiency was displayed as $\dot{V}_E/\dot{V}CO_2$ slope confined to the linear part of the curve, excluding values beyond the respiratory compensation point [18].

### 2.4. Health-related quality of life (HRQoL)

To estimate the HRQoL we used the KINDL-R since it is a common used questionnaire and sufficiently validated [19,20]. It has 24 items, four for each of the six domains inquiring for the behavior and feelings during the last week's period. The questions can be answered on a 5-point Likert scale (never, seldom, sometimes, often and always). The results in the 24 items are summed up and calculated into a total score. The finally converted HRQoL scores range from 0 (worst) to 100 (best) whereas higher value indicates a better HRQoL.

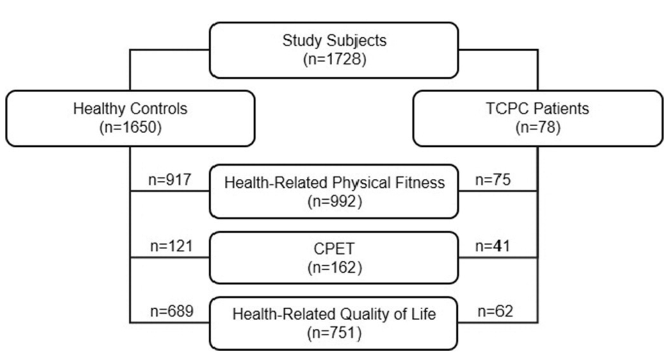


**Fig. 1.** Subjects inclusion. TCPC: total cavopulmonary connection, CPET: cardio-pulmonary exercise test.

### 2.5. Data analyses

Descriptive data was expressed in mean values and standard deviation (mean ± SD). Means' differences between the patients and healthy controls were first analyzed via Student's *t*-test for independent samples. Second, since TCPC and healthy controls differ in anthropometrics (Table 1), multivariable regression was used to adjust for sex, age and BMI.

All analyses were performed using SPSS 23.0 software (IBM Corp., Armonk, NY, USA). Two-sided p-values < 0.050 were considered significant.

## 3. Results

Crude comparison of patients with TCPC and healthy controls is outlined in Table 2.

Of all TCPC patients 96.2% (n = 75) finished the test battery for HRPF, 52.6% (n = 41) completed a CPET and 79.5% (n = 62) filled in the KINDL-R questionnaire.

In multivariable regression (Table 3), adjusted for sex, age and BMI, the impairments in all domains of HRPF became obvious. In terms of strength TCPC achieved just 45.4% of the mean curl-ups of healthy controls (Beta = −12.4, p < 0.001) and 71.7% in push-ups (Beta = −2.6, p = 0.010). In flexibility TCPCs' results were 7.5 cm worse in shoulder stretch (p < 0.001), 4.7 cm worse in sit and reach (p < 0.001) and they reached 65.5% of controls' mean in trunk lift (Beta = −8.5, p < 0.001).

Peak oxygen uptake was limited to 77.7% (Beta = −9.4; p < 0.001) compared to healthy peers. TCPC reached 34.8 ± 7.5 ml/min/kg whereas controls had 42.1 ± 8.4 ml/min/kg (p < 0.001). Also in peak workload TCPC achieved only 68.9% (Beta = −51.5, p < 0.001). Ventilatory efficiency, measured as $\dot{V}_E/\dot{V}CO_2$ slope, was impaired (healthy: 27.5 ± 2.9 vs. TCPC: 31.6 ± 3.3, p < 0.001) and after correction 4.4 points higher on average.

Regarding HRQoL the adjusted regression showed no difference (p = 0.184) between TCPC and healthy peers. There were no significant different in all functional parameters when comparing patients with a systemic right ventricle to those with a left one.

## 4. Discussion

This study showed that children and adolescents after TCPC still have functional limitations with regards to HRPF and exercise capacity. Their HRQoL, on the other hand, does not differ from healthy subjects.

### 4.1. Health-related physical fitness (HRPF)

Already in infancy fine and gross motor skills of patients with CHD are insufficiently developed and the degree of impairment worsens with the severity of the defect [21]. Contributing factors for this early impairment are among other open heart surgery [7], time of deep hypothermic circulatory arrest, number of hospitalizations and time spent in the intensive care unit [22]. Patients with TCPC comprise more or less all of those factors. But also inborn neurological defects are associated with

**Table 1**
Study characteristics.

| | Healthy controls (n = 1650) | TCPC patients (n = 78) | p-Value* |
|---|---|---|---|
| Sex (female) | 807 (48.9%) | 21 (27.0%) | <**0.001** |
| Age (years) | 12.6 ± 2.4 | 12.0 ± 3.2 | 0.078 |
| Body weight (kg) | 47.0 ± 14.2 | 39.1 ± 14.5 | <**0.001** |
| Body length (cm) | 155.0 ± 13.6 | 145.2 ± 18.7 | <**0.001** |
| Body mass index (z-score) | 0.04 ± 1.05 | −0.27 ± 0.86 | **0.003** |

* Chi-Square test or Student's *t*-test for independent samples, significant with p < 0.050.