Exercise capacity in children after total cavopulmonary connection: Lateral tunnel versus extracardiac conduit technique

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Objectives: In patients with univentricular heart disease, the total cavopulmonary connection (TCPC) is the preferred treatment. TCPC can be performed using the intra-atrial lateral tunnel (ILT) or extracardiac conduit (ECC) technique. The purpose of the present study was to evaluate exercise capacity in contemporary TCPC patients and compare the results between the 2 techniques.

Methods: A total of 101 TCPC patients (ILT, n = 42; ECC, n = 59; age, 12.2 ± 2.6 years; age at TCPC completion, 3.2 ± 1.1 years) underwent cardiopulmonary exercise testing. The patients were recruited prospectively from 5 tertiary referral centers.

Results: For the entire group, the mean peak oxygen uptake was 74% ± 14%, peak heart rate was 90% ± 8%, peak workload was 62% ± 13%, and slope of ventilation versus carbon dioxide elimination (VE/VCO_2 slope) was 127% ± 30% of the predicted value. For the ILT and ECC groups, patient age, age at TCPC completion, body surface area, peak workload, and peak heart rate were comparable. The percentage of predicted peak oxygen uptake was lower in the ILT group (70% ± 12% vs 77% ± 15%; $P = .040$), and the percentage of predicted VE/VCO_2 slope was greater in the ILT group (123% ± 36% vs 108% ± 14%; $P = .015$). In a subgroup analysis that excluded ILT patients with baffle leak, these differences were not statistically significant.

Conclusions: Common exercise parameters were impaired in contemporary Fontan patients. Chronotropic incompetence was uncommon. The peak oxygen uptake and VE/VCO_2 slope were less favorable in ILT patients, likely related to baffle leaks in some ILT patients. These results have shown that a reduced exercise capacity in Fontan patients remains an important issue in contemporary cohorts. The ECC had a more favorable exercise outcome at medium-term follow-up. (J Thorac Cardiovasc Surg 2014;148:1490-7)

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In patients with univentricular types of congenital heart disease, total cavopulmonary connection (TCPC), a modification of the original Fontan operation, has been the preferred procedure for surgical palliation for >20 years.[1,2] Since the introduction of the TCPC, the functional state of patients who have undergone the Fontan operation has vastly improved.[3,4] The TCPC has usually been performed as a staged procedure, using either an intra-atrial lateral tunnel (ILT) or an extracardiac conduit (ECC) to connect the inferior caval vein to the pulmonary arteries. However, various studies have shown decreased ventricular function and impaired exercise capacity.[3-6]

Previous studies of adults with congenital heart disease have shown that patients with poor exercise capacity have an increased risk of mortality. It is, therefore, important to identify patients with a poor exercise capacity and to know the factors that could affect this capacity.[7]

Mid- to long-term follow-up data from modern Fontan patients are scarce. The study populations of patients with a contemporary TCPC have been small or the studies have combined the exercise data from these patients with the exercise data from patients who had undergone surgery with an older technique (eg, single-stage TCPC or atriopulmonary connection [APC]).[5,6] Also, many studies have been performed retrospectively, which could have introduced a selection bias.[8,9]

Furthermore, most studies have used data attained at maximal exercise. In younger children, and in Fontan patients in particular, maximal exercise levels have been difficult to achieve. Therefore, the results of submaximal exercise should be a part of the evaluation of exercise tests in Fontan patients.[10]

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This work was supported by the Dutch Heart Foundation (grant 2008T037).

Disclosures: Authors have nothing to disclose with regard to commercial support.

Received for publication Oct 1, 2013; revisions received Dec 20, 2013; accepted for publication Dec 24, 2013; available ahead of print Feb 9, 2014.

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0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2013.12.046

Abbreviations and Acronyms

APC	= atriopulmonary connection
ECC	= extracardiac conduit
HRmax	= maximum heart rate
ILT	= intra-atrial lateral tunnel
MRI	= magnetic resonance imaging
RERpeak	= peak respiratory exchange rate
TCPC	= total cavopulmonary connection
VCO_2	= carbon dioxide elimination
VE/VCO_2 slope	= slope of ventilation versus VCO_2
VO_2	= oxygen uptake
VO_2peak	= peak oxygen uptake

The purpose of the present study was to evaluate the exercise capacity in a relatively large cohort of contemporary Fontan patients in terms of maximal and submaximal parameters. We aimed to determine the predictors for impaired exercise capacity and compare the results of the 2 different surgical techniques.

METHODS

Patients

We performed a cross-sectional, multicenter study of patients after TCPC completion. The inclusion criteria were TCPC, a staged approach with a bidirectional Glenn procedure before TCPC completion using a current technique (ie, the ILT technique or ECC technique), TCPC completion before 7 years of age, study inclusion at ≥8 year old, and ≥4 years of follow-up after TCPC completion. The medical records were reviewed for the presence of pacemakers and significant baffle leaks or fenestrations. These were defined as a right to left shunt at the atrial level as assessed by echocardiography, magnetic resonance imaging (MRI), or catheterization and an arterial oxygen saturation at rest <90%. The patients with contraindications for exercise and those with severe mental retardation or syndromes were excluded from the present study.

The patients were recruited from 5 tertiary referral centers in The Netherlands (Erasmus Medical Centre – Sophia Children's Hospital, Rotterdam; Academic Medical Centre – Emma Children's Hospital, Amsterdam; Leiden University Medical Centre – Willem-Alexander Child and Youth Centre, Leiden; University Medical Centre Utrecht – Wilhelmina Children's Hospital, Utrecht; Radboud University Medical Centre – Radboud University Medical Centre Children's Hospital, Nijmegen).

The institutional medical ethical review boards of the different centers approved the present study. All patients and/or their parents provided written informed consent.

All patients underwent a routine physical examination before testing. The physical examination included measuring the weight, height, blood pressure, and arterial oxygen saturation. The resting heart rate was determined using a standard 12-lead electrocardiogram with the patient in the supine position.

Cardiopulmonary Exercise Testing

The patients underwent exercise testing in the outpatient clinic of their own medical center. All the centers were located at sea level. The exercise tests were performed using an upright (Rotterdam, Leiden, Utrecht) or semirecumbent (Amsterdam, Nijmegen) bicycle ergometer. Breath-by-breath gas exchange analysis was performed continuously to measure the respiratory parameters. The heart rate and rhythm were continuously monitored using 12-lead electrocardiography. The blood pressure was measured every 2 minutes, and the oxygen saturation was measured continuously using pulse oximetry. The patients were encouraged to perform to exhaustion. Each test consisted of a 1-minute resting phase, a test phase with stepwise increments of 10 to 15 W/min, and a 3-minute recovery phase. Exercise tests with a peak respiratory exchange rate (RERpeak) of ≥1.00 during the test phase were considered maximally performed tests. The parameters of maximal exercise were assessed for those patients with a maximal test, and the submaximal parameters were determined for all patients.

The peak oxygen uptake (VO_2peak) and peak minute ventilation were averaged for the final 30 seconds of the test, and the peak workload was averaged for the final 60 seconds of the test. The slope of ventilation versus carbon dioxide elimination (VE/VCO_2 slope) was determined using measurements from the second minute of the test phase until the respiratory compensation point had been reached. The oxygen uptake efficiency slope was calculated from the linear relation of VO_2 versus the logarithm of minute ventilation using data from the second minute of the test phase until 90% of the test phase had been reached.[11] The VO_2/workrate slope was assessed using data from the second minute of the test phase until the peak of the test phase had been reached.

The ventilatory anaerobic threshold, the moment that the VCO_2 increased out of proportion compared with VO_2, was determined using the ventilatory equivalent method and expressed in VO_2.[12]

To calculate the predicted values, we used normal values derived from 214 healthy children who had undergone testing at 2 of the participating centers.[13]

MRI Studies

All patients underwent cardiac MRI. The ventricular volumes were imaged using a multislice, multiphase, steady-state, free precession sequence. The technical details of the sequences have been previously reported.[14] Volume analysis was performed using an Advanced Windows workstation (GE Medical Systems, Milwaukee, Wis) using MASS software (Medis Medical Imaging Systems, Leiden, The Netherlands). The endo- and epicardial contours were manually drawn in the end-diastole and end-systole phases. The volumes and mass of the left and right ventricle were added to calculate the singe ventricular volumes and mass to compare the different cardiac configurations possible.[15]

Statistical Analysis

The data are presented as frequencies, mean ± standard deviation in the case of a normal distribution, or median and interquartile range in the case of a non-normal distribution. Comparisons between groups were made using an independent *t* test in the case of a normal distribution and the Mann-Whitney *U* test in the case of a non-normal distribution.

The dichotomous data are presented as counts, and differences between the groups of patients were evaluated using the chi-square test or Fisher's exact test.

To identify the predictors for the percentage of the predicted VO_2peak and the percentage of the predicted VE/VCO_2 slope, linear regression analysis was performed. The variables that showed a significant ($P \leq .05$) association on univariable linear regression analysis were entered in the multivariable model. $P \leq .05$ was required for a variable to be retained in the final model.

RESULTS

A total of 110 patients <18 year old were enrolled in the present study (Figure 1). The patients enrolled in the present study were comparable to the total group of eligible patients in terms of age ($P = .181$), age at Fontan completion ($P = .360$), gender distribution ($P = .185$), and distribution

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