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 $74\% \pm 14\%$, peak heart rate was $90\% \pm 8\%$, peak workload was $62\% \pm 13\%$, and slope of ventilation versus carbon dioxide elimination (VE/VCO₂ slope) was $127\% \pm 30\%$ 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 ($70\% \pm 12\%$ vs $77\% \pm 15\%$; $P = .040$), and the percentage of predicted VE/VCO₂ slope was greater in the ILT group ($123\% \pm 36\%$ vs $108\% \pm 14\%$; $P = .015$). 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/VCO₂ 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)

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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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 ₂ peak	= 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 (VO₂peak) 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/VCO₂ 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 VO₂ 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 VO₂/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 VCO₂ increased out of proportion compared with VO₂, was determined using the ventilatory equivalent method and expressed in VO₂.¹²

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 single ventricular volumes and mass to compare the different cardiac configurations possible.¹⁵

Statistical Analysis

The data are presented as frequencies, mean $\pm$ 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 VO₂peak and the percentage of the predicted VE/VCO₂ 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

FIGURE 1. Flow chart showing patient enrollment. *RERpeak*, Peak respiratory exchange rate.

of ventricular morphology ($P = .768$). The inclusion rate was greater for the ILT group (73% for ILT vs 49% for ECC; $P \leq .001$).

The 30-day postoperative and long-term survival after TCPC has been previously reported for most of our patients in a recent retrospective study demonstrating the absence of a difference in mortality for ILT and ECC in 3 of the 4 surgical groups participating in the current evaluation of Fontan survivors.¹⁶

Exercise testing failed in 8 patients because of a mismatch between patient height and the ergometer or patient noncompliance with the protocol. One patient was excluded from the analysis because of respiratory dysfunction caused by primary ciliary dyskinesia.

A total of 101 patients successfully underwent bicycle exercise testing. Of the 101 patients, 82 reached a *RERpeak* of ≥ 1.00 . The patient characteristics are listed in Table 1.

No significant difference was found in the distributions of ventricular morphology between the 2 TCPC groups (chi-square, $P = .151$).

Maximal Exercise Parameters

The results of the maximal exercise parameters for the total group and stratified by TCPC type are listed in Table 1. No differences were found in the baseline characteristics between the ILT and ECC groups.

The 81 patients who had performed maximally had a *RERpeak* of 1.09 ± 0.06 . For these patients, the $\text{VO}_{2\text{peak}}$ was 33.5 ± 6.8 mL/kg/min or $74\% \pm 14\%$ of the predicted values. The maximum heart rate (*HRmax*) was $91\% \pm 9\%$ of the predicted value. The $\text{VO}_{2\text{peak}}$, as the percentage predicted, was significantly lower for the ILT patients ($P = .040$). The other maximal exercise parameters showed no significant differences between the 2 groups.

Comparing the left and right ventricular morphology, no differences were found in the baseline parameters. The absolute value for the peak O_2 pulse ($\text{VO}_{2\text{peak}}/\text{HRmax}$) was significantly greater in the patients with a morphologically left dominant ventricle (8.4 ± 2.6 for left vs 7.3 ± 1.8 for right; $P = .032$). No significant differences were found for the other exercise parameters.

Submaximal Exercise Parameters

The results of the submaximal exercise testing are also listed in Table 1. These values were calculated for all 101 patients. The mean absolute VE/VCO_2 slope was 34.5 ± 8.1 , $127\% \pm 30\%$ of the predicted value. The patients with an ILT Fontan procedure had a greater absolute VE/VCO_2 slope ($P = .047$) and percentage of predicted ($P = .015$). The percentage of the predicted oxygen uptake efficiency slope and change in $\text{VO}_2/\text{workrate}$ slope were lower for the ILT patients.

Comparing the left and right ventricular morphology showed a difference in the absolute value for the VE/VCO_2 slope (median, 32.0; interquartile range, 30.0-34.8, for left vs 36.6 ± 7.6 for right; $P = .016$).

Patients With Pacemakers

We included 5 patients who had a pacemaker. Of these 5 patients, 4 reached a *RERpeak* of ≥ 1.00 . The absolute values and percentage of predicted *HRmax*, $\text{VO}_{2\text{peak}}$, and VE/VCO_2 slope were comparable between the patients with a pacemaker and those without.

Patients With Baffle Leaks or Fenestrations

No significant right-to-left shunts were present in the ECC group. However, 4 ILT patients had a significant baffle leak, of whom, 2 reached a peak *RER* of ≥ 1.00 . These patients had a comparable *HRmax*, lower percentage of predicted $\text{VO}_{2\text{peak}}$, and greater VE/VCO_2 slope. When these 4 patients were removed from the analysis, the differences in the percentage of predicted $\text{VO}_{2\text{peak}}$ ($71\% \pm 12\%$ for ILT vs $77\% \pm 15\%$ for ECC; $P = .082$) and VE/VCO_2 slope ($128\% \pm 29\%$ for ILT vs $121\% \pm 16\%$ for ECC; $P = .121$) were no longer statistically significant.

MRI Results

The single ventricular end-diastolic volume index was 89 ± 20 mL/m², the single ventricular end-systolic volume index was 43 ± 15 mL/m², the single ventricular stroke

TABLE 1. Patient characteristics and exercise test results

Parameter	Total	ILT	ECC	P value
Baseline				
Total patients	101	42	59	
Male gender	61	32	29	.134
Age at study (y)	12.2 ± 2.5	12.6 ± 2.9	11.8 ± 2.1	.126
Age at TCPC (y)	3.2 ± 1.1	3.1 ± 1.3	3.3 ± 1.1	.481
BSA (m ²)	1.31 ± 0.25	1.31 ± 0.27	1.31 ± 0.24	.968
Resting heart rate (beats/min)	70 ± 16	72 ± 17	69 ± 14	.309
Resting SaO ₂ (%)	95 ± 3	94 ± 5	96 ± 2	.748
Dominant ventricle				.171
Left	60	22	38	
Right	39	20	19	
Indifferent	2	0	2	
Cardiac diagnosis				.150
Tricuspid atresia	28	6	22	
Hypoplastic left heart syndrome	18	7	10	
Pulmonary atresia	15	6	9	
Double inlet left ventricle	13	7	6	
Double outlet right ventricle	13	8	5	
Other	14	7	7	
Pre-TCPC operations	2.2 ± 0.8	2.1 ± 0.7	2.3 ± 0.8	.271
Post-TCPC operations	0.3 ± 0.7	0.4 ± 0.9	0.2 ± 0.4	.455
Pacemaker	5	4	1	.157
Significant baffle leak or fenestration	4	4	0	.027*
Maximal exercise				
Total patients	81	30	51	
HRmax (beats/min)	171 ± 17	168 ± 13	173 ± 18	.137
RERpeak	1.09 ± 0.06	1.07 ± 0.04	1.10 ± 0.06	.064
VO ₂ peak (mL/min/kg)	33.5 ± 6.8	32.0 ± 6.8	34.4 ± 6.8	.137
VO ₂ peak (% of predicted)	74 ± 14	70 ± 12	77 ± 15	.040*
Peak O ₂ pulse (% of predicted)	77 ± 15	73 ± 15	79 ± 14	.073
VEpeak (% of predicted)	73 ± 16	72 ± 16	73 ± 16	.887
Wpeak (% of predicted)	62 ± 13	59 ± 13	64 ± 13	.146
Wpeak/kg (% of predicted)	67 ± 13	65 ± 13	69 ± 13	.243
Submaximal exercise				
Total patients	101	42	59	
VE/VCO ₂ slope	34.5 ± 8.1	34.0 (31.6-41.7)	33.0 ± 4.6	.047*
VE/VCO ₂ slope (% of predicted)	127 ± 30	137 ± 40	121 ± 16	.015*
OUES (% of predicted)	79 ± 20	75 ± 21	83 ± 18	.028*
VO ₂ /WR slope (mL/min/W)	9.0 ± 1.9	8.4 ± 1.9	9.5 ± 1.7	.005*
VO ₂ at VAT (mL/min/kg)	23.7 ± 6.6	23.0 ± 6.6	24.2 ± 6.5	.361

Data presented as n or mean ± standard deviation, or median (range). *ILT*, Intra-atrial lateral tunnel; *ECC*, extracardiac conduit; *TCPC*, total cavopulmonary connection; *BSA*, body surface area; *SaO₂*, arterial oxygen saturation; *HRmax*, maximum heart rate; *RERpeak*, peak respiratory exchange rate; *VO₂peak*, peak oxygen uptake; *VEpeak*, peak minute ventilation; *Wpeak*, peak workload; *VE/VCO₂ slope*, slope of ventilation versus carbon dioxide elimination; *OUES*, oxygen uptake efficiency slope; *VO₂/WR slope*, oxygen uptake to work rate slope; *VO₂*, oxygen uptake; *VAT*, ventilatory anaerobic threshold. *Statistically significant.

volume index was 46 ± 11 mL/m², and the single ventricular ejection fraction was $53 \pm 8\%$. These values were the similar between the ILT and ECC groups.

Predictors

Univariable linear regression analysis (Table 2) showed a strong positive relation between the percentage of predicted VO₂peak and the HRmax. A negative relation was found between the percentage of predicted VO₂peak and the body surface area, body mass index, patient age, and

interval since Fontan completion. The ejection fraction and single ventricular end-systolic volume index showed a significant relationship with the percentage of predicted VO₂peak. No relationship was found with the resting heart rate, age at Fontan completion, number of pre- and post-Fontan surgical procedures, single ventricular end-diastolic volume index, single ventricular stroke volume index, and ventricular mass.

The variables that showed a significant ($P \leq .05$) association on univariable linear regression analysis were entered in the

TABLE 2. Significant univariable predictors for VO₂peak and VE/VCO₂ slope (percentage of predicted)

Variable	R ²	P value	β
Predictor of VO ₂ peak			
%predicted			
HRmax (beats/min)	0.115	.002	0.291
BSA (m ²)	0.128	.001	−20.212
BMI (kg/m ²)	0.149	<.001	−1.873
SVESVi (mL/m ²)	0.072	.027	−0.237
SVEF (%)	0.082	.018	0.465
Age (y)	0.050	.045	−1.277
Interval since Fontan (y)	0.084	.009	−1.616
ECC type Fontan	0.053	.040	6.692
Predictor of VE/VCO ₂ slope			
%predicted			
HRmax (beats/min)	0.090	.003	−0.363
ECC type Fontan	0.078	.005	−16.807

VO₂peak, Peak oxygen uptake; VE/VCO₂ slope, slope of ventilation versus carbon dioxide elimination; HRmax, maximum heart rate; BSA, body surface area; BMI, body mass index; SVESVi, single ventricular end-systolic volume index; SVEF, single ventricular ejection fraction; ECC, extracardiac conduit.

multivariable model (Table 3). In the multivariable model, the significant predictors for the percentage of predicted VO₂peak were HRmax, body mass index, and single ventricular ejection fraction.

The same variables were tested in a univariable analysis for the percentage of predicted VE/VCO₂ slope. This resulted in 2 significant predictors (Table 2). On multivariable regression analysis (Table 4), HRmax and the TCPC technique were significant predictors.

In univariable and multivariable regression analysis, the type of ergometer (upright or semirecumbent) was not a significant predictor for the percentage of predicted VO₂peak, VE/VCO₂ slope, or HRmax.

DISCUSSION

Our results have shown that Fontan patients treated according to current surgical strategies will have a moderately decreased exercise capacity. This was observed for both the maximal and the submaximal parameters.

The patients who had been treated using the ILT technique had a lower percentage of the predicted VO₂peak than those who had the ECC technique. The most important submaximal parameter, the VE/VCO₂ slope, was also more favorable in the ECC group.

TABLE 3. Multivariable prediction model for VO₂peak (%predicted) (R² = 0.300)

Predictor VO ₂ peak %predicted	β	P value
Constant	18.051	.088
HRmax (beats/min)	0.281	.002
BMI (kg/m ²)	−1.747	.002
SVEF (%)	0.456	.009

VO₂peak, Peak oxygen uptake; HRmax, maximum heart rate; BMI, body mass index; SVEF, single ventricular ejection fraction.

TABLE 4. Multivariable prediction model for VE/VCO₂ slope (%predicted) (R² = 0.125)

Predictor VE/VCO ₂ -slope %predicted	β	P value
Constant	193.619	.000
HRmax (beats/min)	−0.307	.011
ECC type of Fontan	−10.240	.050

VE/VCO₂ slope, Slope of ventilation versus carbon dioxide elimination; HRmax, maximum heart rate; ECC, extracardiac conduit.

In contrast, no differences relating to the anatomic type of systemic ventricle were found. In multivariable analysis, the HRmax, body size, and ejection fraction were related to the percentage of the predicted VO₂peak.

Patients with a univentricular type of congenital heart disease have been among those with the greatest risk of late attrition.¹⁷ Our data set provided an opportunity for a head-to-head comparison of both current TCPC techniques. The surgical technique used in our patients depended on the preference of the operating surgical team. In The Netherlands, the referral patterns for congenital heart disease have mainly followed a geographic pattern. Therefore, the ILT and ECC groups can be considered “random samples” of patients with univentricular heart disease.

The exercise capacity of patients after Fontan operation has been extensively studied.^{6,18,21} Compared with previous studies, our study is one of the few with prospective data collection, reducing the likelihood of an inclusion bias. Furthermore, compared with other studies with similar goals, our study population was relatively large, young, homogeneous, and in accordance with current techniques.

In general, the results in our patients for the VO₂peak, HRmax, and peak workload were better than those in most previous reports.^{6,18,21} This most likely reflected differences in the study populations but has also demonstrated that with current surgical strategies, the exercise capacity in Fontan patients can be relatively well preserved at midterm follow-up. As such, our data provide reference for other and younger populations of Fontan patients.

Cardiopulmonary exercise testing can provide data on the maximal exercise capacity, such as VO₂peak and HRmax, but also on submaximal values, including the VE/VCO₂ slope and VO₂ efficiency slope. These values have been shown to be an important part of the clinical assessment, because young children and patients with Fontan circulation might have difficulties performing a maximal exercise test in terms of reaching a peakRER of ≥1.00.²² Our results have shown the feasibility and usefulness of determining the submaximal exercise parameters in children after the Fontan operation. Moreover, submaximal exercise might be more in line with the children’s daily exercise levels.

Recently, Diller and colleagues¹⁹ showed a strong relationship between exercise capacity and the risk of hospitalization

but no relationship with the risk of death or transplantation in Fontan patients.

Exercise performance in Fontan patients can be limited by various factors. These can relate to the surgical technique, state of pulmonary vasculature, ventricular morphology, patient age, and duration of follow-up after completion of the Fontan circulation.^{18,23,24} Other factors that have been identified include intrinsic ventricular function, impaired ventriculoarterial coupling, and chronotropic competence.^{18,25}

Regarding the surgical technique, Müller and colleagues²⁶ did not find a significant difference in exercise capacity between ILT and ECC patients in a group of 57 TCPC patients. In the study by Diller and colleagues,¹⁹ it was shown that patients who had undergone an APC-Fontan procedure had a 3.7-fold increased risk of death or transplantation compared with TCPC patients. However, that study did not show differences between the 2 TCPC techniques.¹⁹ Other studies also did not describe differences between the 2 TCPC techniques.^{4,23}

Our results showed a lower exercise capacity in the ILT patients than in the ECC patients. This was observed in the maximal and submaximal exercise parameters. The effect of the surgical technique can likely be explained in part by the presence of significant right-to-left shunts, which were only present as baffle leaks in the ILT group. A right-to-left shunt in the Fontan circulation will result in a greater VE/VCO₂ slope. A study comparing exercise capacity in 20 Fontan patients before and after fenestration closure showed a significant decrease in the VE/VCO₂ slope after closure, but the VO₂peak had not changed.²⁷ Baffle leaks are sometimes difficult to close in ILT patients, and can be considered a disadvantage of this technique. We chose not to exclude patients with right-to-left shunts from our analysis, because they are an integral part of the Fontan population. An analysis excluding the patients with a baffle leak showed that the difference between ILT and ECC in the VO₂peak and VE/VCO₂ slope disappeared, and the difference in VO₂peak decreased slightly, to a nonsignificant value, demonstrating the effect of this type of residual lesion. Considered the limited number of patients with a significant right-to-left shunt, we did not include this in our multivariable regression models. Another possible explanation could be that the ECC patients have a more efficient TCPC geometry compared with ILT patients, in whom increasing dilatation of the baffle is often seen. This could lead to lower power loss in the ECC patients.²⁸ Computational fluid dynamics studies have shown that the energy loss inside the TCPC increased in a nonlinear fashion during exercise conditions. In “inefficient” TCPC geometries, the energy loss might be greater than in more favorable anatomic situations.²⁸

Ventricular morphology was not a predictor of the VO₂peak or the VE/VCO₂ slope in our patients. This was

in accordance with the findings from other studies, which could not establish a difference in exercise capacity for single ventricles of the left or right ventricular morphology.^{4,26} In adult Fontan patients, Giardini and colleagues⁵ described a steeper decline in exercise capacity with age in those with a single ventricle of the morphologically right ventricular type.

In our study, the percentage of the predicted VO₂peak showed a decline with age. In their longitudinal follow-up study of Fontan patients aged 6 to 50 years, Fernandes and colleagues,²³ in 2010, showed that the VO₂peak decreased over time with an annual decline of 1.25% annually. The strongest decline occurred in patients <18 year old.²³ We found a comparable rate of decline in our cross-sectional study (Table 2). Giardini and colleagues⁵ also assessed the longitudinal exercise capacity in 53 patients (33 APC and 22 TCPC). They found a greater rate of decline in the VO₂peak (2.6% annually). Compared with APC patients, the rate of decline was less in the TCPC patients.

MRI studies have shown that most young TCPC patients have a relatively normal, preserved ventricular function at rest.^{3,14} However, during pharmacologic stress, signs of diastolic dysfunction and preload impairment became evident.^{3,14} This combination will cause an abnormal decrease in the end-diastolic volume during exercise, preventing an increase in the stroke volume.²⁰ Another potential limiting factor for exercise is chronotropic impairment, which is common in Fontan patients.^{18,29} Combined with the inability to increase the stroke volume, chronotropic impairment can have detrimental effects on cardiac output and exercise parameters.¹⁴ Remarkably, chronotropic impairment was not an important issue in our study. Our subjects reached 91% of their predicted HRmax. This was greater than that reported in previous studies.^{6,18} In our study population, we did not observe a decline in the HRmax with age. However, because the decline in the HRmax with age is a normal phenomenon in adulthood, the combination of an impaired stroke volume increase and chronotropic limitation might, in part, explain the decline in exercise performance with age demonstrated in earlier studies.^{5,23,30} This provides support for guidelines advocating continued long-term follow-up of all Fontan patients.³¹ Not surprisingly, because this follows from the Fick equation predicting the cardiac output, the HRmax and stroke volume were significant predictors of the VO₂peak in the patients with a Fontan circulation.

No relationship was found between the percentage of predicted VO₂peak or VE/VCO₂ slope and age at Fontan completion or the number of surgical procedures. This was probably because the population was uniform—all the patients had undergone 2-stage TCPC before 7 years of age, and the number of reoperations after Fontan completion was low (Table 1).

Clinical Implications

Our results have shown that the exercise performance is relatively good in young Fontan patients. Our ILT patients had lower exercise performance at medium-term follow-up after TCPC, likely because of the presence of baffle leaks. Decreased exercise performance in the presence of a baffle leak might be an indication for baffle leak closure. The negative association between the body mass index and VO_2peak indicates that unnecessary weight gain should be prevented. Stefan and colleagues³² have shown that activity restriction is the most important predictor for an increase in body mass in children with congenital heart disease. Exercise performance can be improved by exercise training. However, hardly any data exist on the cardiac effects of exercise training in these patients.³³

A well-known link exists between exercise performance and activity level. Müller and colleagues²⁶ have shown that TCPC patients have a fairly normal activity pattern. They also demonstrated a negative correlation between age and activity.²⁶ This means that various factors convene to increase the risk of a decline in exercise performance with age in Fontan patients. Active counseling concerning physical activity for these patients might be beneficial.^{34,35}

Our study was performed in adolescents. Whether the fixed diameters of the ECC will result in comparable findings with long-term follow-up remains a matter of close surveillance.

Study Limitations

Because of the multicenter nature of our study, the patients were tested using different exercise equipment. Although all equipment had been thoroughly calibrated, small differences might have been present among the centers. However, earlier studies have demonstrated that the results of exercise testing are not center specific.²¹ Furthermore, all tests were supervised by 1 of 2 investigators, and the same standardized operating procedure was followed at all centers. The arterial oxygen saturation measurements during maximal exercise were often unreliable and therefore were not reported.

CONCLUSIONS

The results of our study have shown that exercise capacity is impaired in contemporary adolescent Fontan patients. Chronotropic incompetence was uncommon in our patients. Comparing the outcomes of the 2 common surgical modifications of the TCPC technique, the VO_2peak was significantly lower and the VE/VCO_2 slope was significantly greater in patients who had undergone an ILT TCPC procedure. This was likely caused by the presence of significant baffle leaks in some ILT patients.

Although the exercise performance in our cohort was better than previously reported data, these results showed

that a reduced exercise capacity in Fontan patients remains an important issue, even with contemporary treatment strategies.

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