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Exercise Capacity and Quality of Life after Total Cavopulmonary Connection at Adults

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Abstract

Objective: The aim of this study was to evaluate the clinical and psychological profile of after total cavopulmonary connection procedure and to identify the significant determinants of quality of life.

Methods: Data from 21 patients underwent total cavopulmonary connection procedure from January 2001 to December 2015 were retrospectively analyzed. Patients underwent an echocardiography and cardiopulmonary exercise testing. Used ST-36 questionnaire to perceived health status. The NT-pro BNP levels was test.

Results: 21 patients aged between 19 to 36 years (mean 26.6 years) were enrolled. The mean follow-up time was 44.2 ± 29.9 months. The mean EF was 59.4 ± 6.2%, and the mean maximal oxygen consumption was 19.9 ± 3.6 ml/kg/min, predict value was 52.5 ± 8.9%. SF-36 score was well. Independent risk for impaired exercise capacity was interval time from surgery.

Conclusions: The exercise capacity of total cavopulmonary connection patients was impaired. Identify more predict factors of the quality of these patients need further study.

Keywords: Total cavopulmonary connection; Cardiopulmonary exercise testing; Follow-up study quality of life adults

Introduction

Since the first successful Fontan procedure was performed in 1971 [1], this technique has become the standard procedure for palliation of functionally univentricular hearts (UVH). Many innovative modifications have refined the operation, the total cavopulmonary connection (TCPC) was introduced by De Leval and his colleagues in 1988 [2] and has a good clinical result. Now, a large number of patients with functionally univentricular hearts (UVH) have reached adulthood [3]. With survival time extended, physiology, psychosocial and behavioral issues emerget [4]. There are many studies of quality of life (QOL) in congenital heart diseases (CHD) [5-7], and patients after TCPC surgery [8-17]. Because of the economic and social reasons, some of complex CHD patients missed the surgical treatment during their childhood. Until adult underwent TCPC surgery, and but there are none reports of such patients' QOL and exercise tolerance after TCPC. The aim of this study is first to provide an overview of the clinical and psychosocial profile of adult patients after TCPC procedure.

Methods

Study subjects

The study cohort consisted of from 21 patients (age ≥ 16 years) underwent total cavopulmonary connection procedure in Beijing Fuwai hospital from January 2008 to December 2015. The hospital records, operative reports, cardiac catheterization date, and echocardiography date were reviewed and analysed. All patients manifested with exercise tolerance impairment and cyanosis, 5 cases had syncope, 2 cases had aquatting phenomenon, 4 cases had palpitation. Mean ages were 22.7 ± 4.3 (16-32) years. Preoperative diagnosis included 7 cases of single ventricle (SV), 5 cases of congenitally corrected transposition of the great arteries (cc-TGA), 2 cases of double outlet right ventricle (DORV), 2 cases of tricuspid atresia (TA). The mean McGoon ratio was 2.0 ± 0.4, 1.52-3.01, Nakata index was 310.2 ± 111.9 mm^2/m^2 (146.9-542.8 mm^2/m^2).

The surgical procedures were performed with cardiopulmonary bypass (CPB). TCPC was completed with a means age of 22.7 ± 4.3 (16-32) years. A lateral tunnel was performed in 10 cases (47.6%) and an extra-cardiac conduit was performed in 11 cases (52.4%). Among the 21 patients, 6 cases (28.6%) had received Bidirectional Glenn shunt (BDG) before the TCPC. A fenestration procedures were created at 19 cases (90.5%). Complications included 2 cases of pleural effusion, 3 cases of secondary thoracotomy surgery and 3 cases of hemodialysis. A summary of the patients' data is shown in Table 1.

Characteristic	n (%)		Mean ± SD
Primary diagnosis		-	-
SV		7 (33.3)	-
DORV		7 (33.3)	-
cc-TGA		5 (23.8)	-
TA		2 (9.5)	-
Gender (male)		7 (33.3)	-
Age (years)		-	22.7 ± 4.3
Weight (Kg)		-	48.5 ± 6.8
SPO_2 (%)		-	74.0 ± 9.4
HGB (g/L)		-	210.3 ± 40.0
NYHA		-	-
I		0	-
II		10 (47.6)	-
III		10 (47.6)	-
IV		1 (4.8)	-
EF (%)		-	60.1 ± 6.4
Mean PAP (mmHg)		-	12.7 ± 3.1
MoGoon ration		-	2.0 ± 0.4
Nakata index (mm^2/m^2)		-	310.2 ± 111.9
Intraoperative			-
CPB duration (min)			178.1 ± 67.0
Cross-clamp time (min)			62.0 ± 69.5
ET-TCPC		11 (52.4)	-
Fenestrated		19 (90.5)	-
By staging TCPC		6 (28.6)	-
Prior BDG interval (mon)			57.8 ± 49.1
Postoperative			-
Mechanical ventilation (h)			32.7 ± 11.9
ICU stay (d)			5.3 ± 4.8
Postoperative hospital stay (d)			21.2 ± 11.9
Post-SPO_2 (%)			93.2 ± 4.7
HGB (g/L)			137.0 ± 24.9
Duration of chest tube drainage (d)			5.3 ± 4.8
Postoperative complication			-
Secondary thoracotomy		3 (14.3)	-
Hemodialysis		3 (14.3)	-
Pleural effusion		2 (9.5)	-
Sum		8 (38.1)	-

Table 1: Baseline characteristics of the cohort; SD: Standard Deviation; Single Ventricle; DORV: Double Outlet Right Ventricle; cc-TGA: congenitally corrected Transposition of the Great Arteries; TA: Tricuspid Atresia; SPO_2: Transcutaneous Oxygen Saturation; HGB: Hemoglobin; CPB: Cardiopulmonary Bypass; BDG: Bidirectional Glenn Shunt; NYHA: New York Heart Association; EF: Ejection Fraction; PAP: Pulmonary Artery Press; CPB: Cardiopulmonary Bypass; ET-TCPC: Extracardiac Conduit Total Cavopulmonary Connection; ICU: Intensive Care Unit.

Echocardiography

Each patient underwent echocardiography examination regularly at the department of Pediatric ultrasound. Regular examine data of ejection fraction (EF), atrioventricular valve regurgitation, vena cava blood flow velocity, thrombogenesis or not, fenestration condition were recorded close or not.

Blood routine, Coagulation function, haemoglobin, NT-Pro BNP, Liver and kidney function were tested. All patients received standard 6 MWT(6-minute walk test).

Perceived health status

Perceived health status was assessed with the Short Form 36 (SF-36), which include 36 items, divided into eight domains: physical functioning (PF), role-physical function (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional functioning (RE) and mental health (MH). PF, RP, BP, GH belongs to physical health, VT, SF, RE, MH belongs to the mental health field. A score ranging from 0 to 100 is generated for each domain.

Cardiopulmonary exercise test (CPET)

All patients underwent a symptom-limited cardiopulmonary exercise test on the power bicycle CPET system (Italian COSMED). The test was under supervision of a physician. After a 3 min rest to examine baseline values, patients had a 3 min warm-up without load, follow by a ramp-wise increase of load with 15, 20, 25 W/min depending on the individual physical capacity estimated by the investigator. The aim was to reach peak exercise load at 5 to 8 min [18-20]. The end of the CPET was marked by symptom limitation and was followed by a 5 min recovery period. Carbon dioxide elimination, VO_2, and minute ventilation were measured with a computerized breath-by-breath analyser. A 12 lead electrocardiogram (ECG), blood pressure and transcutaneous oxygen saturation (SPO_2) were continuously monitored.

Statistical analysis

Comparisons between subgroups were performed by chi-square test. Continuous variables are expressed as means ± standard deviation, comparisons between subgroups were performed by unpaired t-test and Non-parametric U tests. The Spearman's correlation test was used to evaluate correlations between the CPET value and clinical records such as age at repair, EF, SPO_2. Risk factor analysis was performed by logistic regression analysis. All analyses were performed using SPSS 19.0 software (SPSS, Inc. Chicago, IL,

USA). For all analyses, a two tailed and P values <0.05 were considered significant.

Results

The mean follow-up time was 44.2 ± 29.9 months. All the patients daily life is not limited, according to New York Heart Association (NYHA) grade, I, II was 20 cases (95.2%), compared with preoperative (42.9%) improved significantly (p<0.001). Six cases required re-hospital including 4 cases of arrhythmias, 1 case of pleural effusion and 1 case of wound healing adverse.

The mean SPO_2 was 88.8%, compared with preoperative (74.0%) improved significantly (p<0.001). The mean haemoglobin was 169.3 g/l, compared with preoperative (210.3 g/l) decreased significantly (p<0.001) (Table 2).

	Preoperative	Postoperative	Follow up	P1	P2
SPO_2 (%)	74.0 ± 9.4	93.2 ± 4.7	89.0 ± 7.2	<0.001	<0.001
HGB (g/L)	210.3 ± 40.0	137.0 ± 24.9	168.4 ± 23.3	<0.001	0.01

Table 2: SPO_2 and HGB (P1 Follow *vs.* Preoperative, P2 Follow *vs.* Postoperative); SPO_2: transcutaneous oxygen saturation; HGB: Hemoglobin.

Echocardiographic data are list in table 3. Mean EF was 59.4 ± 6.2%, and 2 cases emerge atrioventricular valve regurgitation moderate or more.

Variable	n (%)	Mean ± SD
Echocardiography date		
atrioventricular valve regurgitation	13 (61.9)	
Mild	11 (52.4)	
Moderate	1 (4.8)	
Moderate to severe	1 (4.8)	
EF (%)		59.4 ± 6.2
SVC blood flow velocity (cm/s)		30.0 ± 8.9
IVC blood flow velocity (cm/s)		29.1 ± 5.0
Fenestration reserve	10 (7.6)	
Fenestration diameter (mm)		4.3 ± 1.6
Cardiopulmonary exercise test data		
Exercise tolerance decreased		
Mild	1 (4.8)	
Moderate	14 (66.7)	
Severe	6 (28.6)	
Pulmonary function		
Mild restrictive ventilator dysfunction	10 (47.6)	
peak VO_2 (ml/kg/min)		19.9 ± 3.6
% predicted peak VO_2		52.5 ± 8.9
AT (ml/kg/min)		13.4 ± 6.3
CO max (L/min/m^2)		4.5 ± 0.9
% predicted VE		38.1 ± 9.6
% predicted HR		77.2 ± 9.7
VO_2/VE max		39.6 ± 5.7
VE/VCO_2 min		30.3 ± 4.2
VE/VCO_2 slope		27.0 ± 5.5
Maximal workload (W)		93.6 ± 26.0
% predicted Maximal workload		59.1 ± 12.5
Peak HR (bpm)		150.1 ± 18.5
Resting HR (bpm)		91.0 ± 8.8
HR reserve (bpm)		59.1 ± 18.7
score of SF-36		
Physical functioning		85.5 ± 8.9
Role-physical function		71.4 ± 35.6
Role-emotional functioning		67.5 ± 35.9
Social functioning		80.4 ± 19.6
Bodily pain		79.4 ± 16.6
Mental health		73.1 ± 14.3
Vitality		73.6 ± 9.9
General health		61.3 ± 16.4

Table 3: Echocardiography, Cardiopulmonary exercise test date and score of SF-36; SD: Standard Deviation; EF: Ejection Fraction; SVC: Superior Vena Cava; IVC: Inferior Vena Cava; SD: Standard Deviation; peak VO_2: peak Oxygen Consumption; AT: Anaerobic Threshold; CO: Cardiac Output; VE: Minute Ventilation; HR: Heart Rate, bpm: beats per minute.

The mean six-minute walk distance (6 WMD) was 514.1 ± 76.6 (415-755) meters. There are 4 cases exceed 550 meters, 16 cases between 425 to 550 meters, and 1 case under 425 meters.

The mean NT-Pro BNP was 203.9 ± 159.8 pg/ml, and 3 patients above 450 pg/ml.

Exercise tolerance declines at all the patients including 6 cases of severe decline, 14 cases of moderate decline decreased, and 1 case of slight decline. The means peak VO_2 was 19.9 ± 3.6 (ml/kg/min), and 52.5 ± 8.9% of predicted value (Table 3).

Self-estimated life quality was fairly good. SF-36 physical health mean score was 74.4 ± 23.2, and mental health score was 73.6 ± 22.3 (Table 3).

The peak VO_2 was correlated with heart rate reserve (R 0.790 P<0.001), and 6WMD (R 0.520 P=0.016). However, we failed to find correlation among with NT-Pro BNP (P=0.059), EF (P=0.250), SPO_2 (P=0.947), age (P=0.120), age at repair (P=0.689); the peak VO_2 had no

statistic difference between different groups (fenestration or no fenestration, LT-TCPC or ET-TCPC, by stage TCPC or not). There is an inverse correlation between interval times after operation and percent predicted (R 0.510 P=0.018) (Table 4).

As for Risk factor analysis, logistic regression analysis showed that only interval times after operation was risk factor for predict Exercise tolerance severe decreased (HR 1.663, 95% CI 1.109-2.715, P=0.042).

All domains of score of SF-36 were not correlation with NT-Pro BNP (P=0.059), EF (P=0.250), SPO_2 (P=0.947), age (P=0.120), age at repair (P=0.689) (Table 4).

There are 19 (90.5%) cases received fenestration procedure intraoperatively. Among these patients, 3 cases underwent percutaneous transcatheter closure of the fenestration, 6 cases closed spontaneously and 10 cases still keeped fenestration till the lastest follow-up. The mean SPO_2 for fenestration keeping group was 85.5%, compared with fenestration closure group at 91.7%, which is significant lower (P=0.038). The CPET parameter and SF-36 score had no statistic difference between two groups (Table 5).

Discussion

In this study cohort, most patients underwent TCPC have now reached adulthood, their life quality of life needs close attention of physicians. Therefore, we report the results of the first study of adult patient's quality of life after TCPC and the first study of a China TCPC population. The mean age of our patients was 26.6 ± 4.5 years, and the follow up was 44.2 ± 29.9 month.

This study shows the mean peak VO_2 was 19.9 ± 3.6 (ml/kg/min), and percent predict peak VO_2 was 52.5 ± 8.9%, which are significantly lower than healthy population, and is consistent with the previously reports [10-17]. Exercise capacity decreases obviously, 14 (66.7%) cases of moderate decline, and 6 (28.6%) cases of severe decline. The correlation analysis shows peak VO_2 are related with heart rate reserve (R 0.790 P<0.001) and 6 MWD (R 0.520 P=0.016), but not related with NT-Pro BNP (p=0.059), EF (p=0.25), SPO_2 (p=0.685), age (p=0.521), and age at TCPC (p=0.673). About the age, Bordin [15]Muller [16] and Idorn [17] report there are a negative correlation between age and peak VO_2, but we have no relevant conclusion, perhaps because our patients are adults and our follow-up period was relatively short. The percent predict peak VO_2 was negative correlated with interval repair time (R-0.510 P=0.018)which shows the exercise capacity tend to decrease with time. Heart rate reserve is an important component of cardiac function reserve Bordin [15] report heart rate reserve is significantly predict factor correlated with rehospitalization cardiac transplantation and mortality. We found that a strong corralation between heart rate reserve and peak VO_2 (R 0.790 P<0.001), heart rate reserve maybe can help predicting the outcome of complex CHD. Fenestration or not, and ET-TCPC or LT-TCPC have no corralation with Peak VO_2, which is consistent with findings reported by Bordin [15] and Muller [16].

Exercise capacity declines obviously, 14 (66.7%) cases of moderate decline, and 6 (28.6%) cases of severe decline. Logistic regression analysis showed only interval times after operation was risk factor for predict Exercise tolerance severe decreased (HR 1.663, 95% CI 1.109-2.715, P=0.042). The exercise tolerance and interval times ROC curve take cut point 52 months (Sensitive 0.833 and specificity 0.8 P=0.029) (Figure 1). The % predicted peak VO_2 of group interval times after operation above 52 months significantly lower than under 52 months (56.15 ± 7.9% *vs.* 46.5 ± 7.4% P=0.012). The HGB of cases of severe decline was significantly higher than of moderate decline (241.5 ± 54.9 g/L *vs.* 197.8 ± 25.1 g/L p=0.019). Microthrombus caused by increased hemoglobin and sticky blood may be harm to patients in a long term.

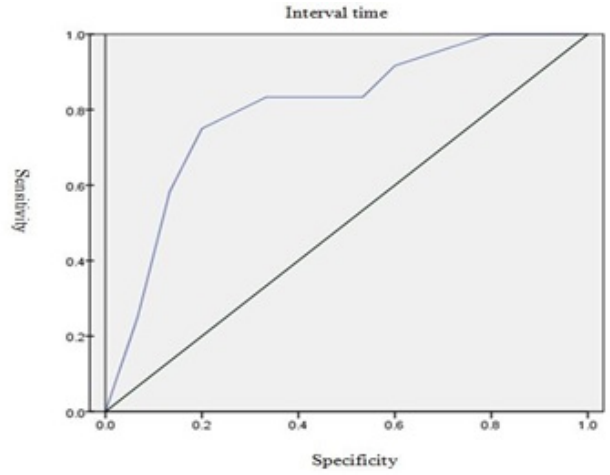

Figure 1: Operation interval time prediction of severe exercise tolerance ROC curve ROC-AUC (95% CI=0.811 (0.607-1.000), P=0.029.

Quality of life scale is widely used in the choice of clinical treatment, comprehensive evaluation of the prognosis of disease. There are include of QWB scale, NHP scale and so on. The SF-36 scale has a good reliability and validity of the application of the most widely. This group of patients with physical health 74.4 ± 23.2, mental health 73.6 ± 22.3, and Pan Yanfang et al. [21] reported 6 provinces and cities in China the average score is similar to this cohort, physical and psychological condition is good, probably because although the patients' postoperative exercise tolerance decreased significantly , But the patient has long been aware of their own physical illness and accept the deficiencies, and improved physical condition after surgery was obvious, so that their body is generally better, score higher, but the emotional function scores lower, indicating that TCPC surgery Mental health issues need attention. There were no significant correlations between SF-36 scores and age, oxygen saturation, surgical modality, windowing, EF, peak VO_2 and heart and lung motion, which was consistent with d'Udekem [13], Bordin [15] had reported.

Postoperative ultrasound showed good cardiac systolic function, EF 59.4 ± 6.2%, and Bordin [15] reported the similar results, no upper and lower chamber thrombosis. 2 patients with moderate to severe reflux, were severe exercise tolerance decreased, suggesting that valve regurgitation is the impact of long-term activity tolerance and prognosis of the important factors.

With the problem of TCPC postoperative pregnancy, with the increase in adult patients underwent TCPC, as well as many female children during the survival of TCPC surgery reaching to the age of pregnancy, pregnancy problems can't be ignored. However, whether the single-ventricular circulation after TCPC can bear the needs of maternal and child circulation of pregnancy is a major challenge, the maximum cardiac output during pregnancy than usual doubled and myocardial oxygen consumption increased by 20%, heart rate increased by 15-20%. It is reported that Fontan postoperative infertility

was significantly higher than normal age women [22], and like other cyanotic heart disease, abortion rate was significantly higher than normal [23]. Abortion rate in the first three months of was 2 times of ordinary congenital Heart disease 2 times [24], is 3 times of normal same age women [25]. Second Affiliated Hospital of Sichuan University has reported three cases of uncontrolled single ventricle successful delivery of the report [26], there are also relevant case reports abroad [27,28]. Theoretically, after functional single ventricle treated by TCPC, cyanosis was significantly improved, cardiac function, exercise tolerance will be improved, the probability of successful pregnancy delivery is significantly higher than the untreated patients.

At present, fontan postoperative pregnancies are mostly found in small cases reported [26-30]. Gouton [30] reported 13 cases of French Fontan operation (84% of TCPC) after the pregnancy data, 37 patients a total of 59 pregnancies, including 13 cases of women twice and above, up to 5 times. The mean age of the pregnancy was 27 ± 5 years, with an average age of 13 ± 7 years. 36 infants (including 1 twin) were successfully born with a miscarriage rate of 27%, with a preterm delivery rate of 69%. One patient had a single ventricle in the fetus and one had left superior vena cava. No maternal deaths occurred, but 6 had Cardiac adverse events like the arrhythmia; bleeding. 10 cases had embolism, 5 cases before delivery, 5 cases after delivery. Although the risk of mother and child pregnancy was significantly higher than normal women, but to strengthen the management during pregnancy, there are still the majority of women can be pregnant and fertile. 2 patients in our group had pregnancy. Their preoperative, intraoperative, postoperative had no significant difference with other female patients, and postoperative review cardiopulmonary exercise in one case peak VO_2 16 ml/kg/min, the percentage of 43%. Below the mean peak VO_2 19.9 ± 3.6 (ml/kg/min) Percentage predicted 52.5 ± 8.9%. Another case is in the peak VO_2 of 20.2 ml/kg/min, the percentage of 52% predicted, is also in the average level. Therefore, we believe that this group of adult patients with TCPC surgery should be available to pregnancy and childbirth. Of course, this requires further follow-up and management during pregnancy.

Conclusions

The survival rate of patients with TCPC was significantly lower than that of the control group. The scores of SF-36 were good and the patients had good physiological and psychological health. With the increase of survival rate of TCPC, more and more patients survived. Some patients with good quality of life need attention. This study initially explored the quality of life of patients with TCPC after surgery, the choice of TCPC surgery, prognosis can provide a reference. To find out more predictors of long-term survival after TCPC and quality of life indicators is the key in future research.

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