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Estimating Equations for Cardiopulmonary Exercise Testing Variables in Fontan Patients: Derivation and Validation Using a Multicenter Cross-Sectional Database

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Abstract

Cardiopulmonary exercise testing (CPET) is a common method of evaluating patients with a Fontan circulation. Equations to calculate predicted CPET values are based on children with normal circulation. This study aims to create predictive equations for CPET variables solely based on patients with Fontan circulation. Patients who performed CPET in the multicenter Pediatric Heart Network Fontan Cross-Sectional Study were screened. Peak variable equations were

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calculated using patients who performed a maximal test (RER > 1.1) and anaerobic threshold (AT) variable equations on patients where AT was adequately calculated. Eighty percent of each cohort was randomly selected to derive the predictive equation and the remaining served as a validation cohort. Linear regression analysis was performed for each CPET variable within the derivation cohort. The resulting equations were applied to calculate predicted values in the validation cohort. Observed versus predicted variables were compared in the validation cohort using linear regression. 411 patients underwent CPET, 166 performed maximal exercise tests and 317 had adequately calculated AT. Predictive equations for peak CPET variables had good performance; peak VO_2, $R^2 = 0.61$; maximum work, $R^2 = 0.61$; maximum O_2 pulse, $R^2 = 0.59$. The equations for CPET variables at AT explained less of the variability; VO_2 at AT, $R^2 = 0.15$; work at AT, $R^2 = 0.39$; O_2 pulse at AT, $R^2 = 0.34$; VE/VCO_2 at AT, $R^2 = 0.18$; VE/VO_2 at AT, $R^2 = 0.14$. Only the models for VE/VCO_2 and VE/VO_2 at AT had significantly worse performance in validation cohort. Of the 8 equations for commonly measured CPET variables, six were able to be validated. The equations for peak variables were more robust in explaining variation in values than AT equations.

Keywords

Fontan; Cardiopulmonary exercise testing; Congenital heart disease

Introduction

Cardiopulmonary exercise testing (CPET) is a long established means of evaluating patients with heart disease providing invaluable diagnostic, physiological, and prognostic information [12, 18, 23]. CPET has been used in the clinical management of congenital heart disease as well as endpoint for therapeutic clinical trials, especially in patients with single ventricles who have had a Fontan surgery [13, 20, 28]. This has led to an ever growing knowledge of the factors that influence CPET variables in the Fontan population [10]. Despite the growing knowledge regarding CPET in Fontan patients, it is frequent for authors to use calculated predicted CPET variables using formulas developed for children without heart disease [6].

The aim of this study was to develop predictive equations for CPET variables specific for patients with Fontan circulation.

Methods

The study was approved by the Institutional Review Board of the Medical University of South Carolina. Data from the multi-institutional NIH/NHLBI Pediatric Heart Network (PHN) Fontan Cross-Sectional Study was downloaded from the PHN website (www.pediatricheartnetwork.org). The methods and results of PHN Fontan study have been previously reported [1]. Briefly, 7 US and Canadian centers recruited 546 Fontan survivors between ages 6 and 18.

Exercise Testing

The exercise protocols employed during the study have been previously published [26]. Patients underwent maximal exercise testing using a cycle ergometer with a ramp protocol. Peak oxygen consumption (peak VO_2) was defined as the maximal oxygen consumption obtained during exercise. Anaerobic threshold (AT) was calculated by the V-slope method. Ventilatory equivalents for carbon dioxide production (VE/VCO_2) and oxygen consumption (VE/VO_2) were measured at the AT. O_2 pulse at peak exercise and AT was calculated by dividing VO_2 at each time point by heart rate. Work measured by Watts was recorded at AT and peak exercise.

Equation Development

Linear regression was performed to create predictive equations for the following CPET variables at peak exercise: peak VO_2, O_2 pulse, and work; and the following variables at AT: VO_2, O_2 pulse, work, VE/VCO_2 and VE/VO_2. The patient characteristics and anatomical variables used for analysis were chosen due to previously reported or likely association with CPET variables (Table 1) [9, 10, 21, 24–26]. For categorical variables, the key denotes the value for a variable given when developing the equation. Peak VO_2 was similar between the left and mixed ventricular morphology patients; therefore, these two groups were combined.

For linear regression analysis of peak exercise CPET variables only patients who reached peak exercise, defined as respiratory exchange ratio (RER) greater than 1.1 at peak exercise, were included. For analysis of AT variables only patients who were reported to have an identifiable AT were included.

In each analysis, a derivation and validation cohorts were created randomly. The derivation cohort consisted of 80 % of the study population; the validation cohort was the remaining 20 %. Random selection was performed by the statistical program, IBM SPSS® v. 21 (New York, USA). Covariates associated with the CPET variable in univariate analysis ($p \leq 0.1$) were placed into the linear multivariable regression analysis. In order to create an efficient as well as accurate equation, covariates were removed in a stepwise fashion from the multivariable regression analysis if the partial R^2 for the covariate was less than 0.01 or covariate p value was > 0.05.

Linear regression was then performed between the predicted CPET variables and observed values in validation cohort. To determine the performance of the equation in the validation cohort, two statistical tests were performed. First, the difference between R^2 (R^2 difference) between the both cohorts was calculated (R^2 of derivation cohort— R^2 of validation cohort). A priori, a difference between R^2 of ≤0.05 was set as acceptable, i.e., the R^2 of the validation cohort could be no more than 0.05 lower than the R^2 of the derivation cohort to be acceptable, but could be higher. Secondly, to determine if there was a significant tendency in the equation to over or under estimate variables, a single sample T test was performed to see if the mean difference in the entire validation cohort between predicted and observed variables differed significantly ($p < 0.05$) from zero.

All statistical analysis was performed using IBM SPSS® v.21 (New York, USA).

Results

Of the 546 patients who were recruited, 411 underwent exercise testing, in which 166 (40 %) had maximal exercise tests and 317 (77 %) had adequate AT calculated. The patient characteristics of each group are listed in Table 2.

For the maximal exercise cohort, 136 (82 %) cases were randomly selected for the derivation cohort of peak exercise variables. Associations between covariate and peak variables using univariate statistics for the derivation cohort are shown in Table 3. Table 4 outlines how the final estimating equations were created. The final models yielded the equations outlined in Table 5.

Comparisons between the validation and derivation (n = 30) cohort are shown in Table 6. The cohorts were similar in possible covariates as well as peak CPET variables except that the validation cohort was younger at time of Fontan (2.7 ± 1 0.2 vs. 3.7 ± 2.3, p = 0.04). For all three peak variable equations the R^2 difference was <0.05 and showed no bias toward over or underestimated peak variable. Predicted peak VO_2 correlated well with observed peak VO_2 in the derivation cohort, R^2 = 0.67, SEM = 0.26, p < 0.01, with a R^2 difference of −0.06, and the mean difference between predicted and observed did not differ from zero (p = 0.59), 0.02 L/min ± 0.25. Predicted maximal work showed good correlation with observed maximum work, R^2 = 0.61, SEM = 21.2, p < 0.01 when comparing the predictive equation to observed work. The mean difference between observed and predicted peak work was 4.3 ± 21.1 W and did not differ from zero (p = 0.27) and R^2 difference was 0. There was significant correlation between predicted peak O_2 pulse and observed O_2 pulse in the derivation cohort (R^2 = 0.79, p < 0.01), observed 0_2 pulse did not differ from zero (−0.07 ± 1.62, p = 0.81), and the R^2 difference was −0.2. Therefore, all three equations for maximal CPET variables were validated (Fig. 1).

For the group with adequately calculate AT, 246 (78 %) were randomly selected for the derivation cohort. Univariate statistics between possible covariates and AT CPET variables are shown in Table 7. The initial models and steps to reach final models are outlined in Table 4. Of note, model explanation of variation of AT variables was lower than peak CPET variables, with R^2 ranging from 0.13 to 0.39. The final equations are shown in Table 5.

The validation and derivation cohort were similar in patient characteristics except that the derivation cohort were more likely to be male (71 vs. 54 %, p = 0.04) and had slightly higher VE/VCO_2 at AT (44.5 vs. 42.8, p = 0.03). Linear regression comparing calculated VO_2 at AT versus observed values showed similar model performance as the derivation cohort, R^2 = 0.18, SEM = 0.43, p < 0.01. The mean difference between observed and peak values did not differ from zero (−0.23 ± 0.43, p = 0.35). R^2 difference was −0.02. Similarly, calculated predicted work and 02 pulse at AT correlated with observed variables in similar fashion in the validation cohort as the derivation cohort, and the mean difference between calculated and observed values did not differ from zero; (Watts; R^2 = 0.42, SEM = 18.6, p < 0.01, mean difference 0.9 ± 18.8, p = 0.40, R^2 difference = −0.03) (02 pulse, R^2 = 0.38, SEM = 2.7, p < 0.01, mean difference −0.04 ± 2.6, p = 0.90, R^2 difference = −0.04). However, the correlation between predicted VE/VCO_2 and VE/VO_2 at AT and observed values was lower

in the validation cohort; VE/VCO_2, $R^2 = 0.10$, $p = 0.01$, R^2 difference = 0.08; and VE/VO_2, $R^2 = 0.04$, $p = 0.09$, R^2 difference = 0.09. Therefore, the equations for VO_2 at AT, Work at AT and O_2 pulse at AT were validated; however, VE/VCO_2 and VE/VO_2 at AT were not validated.

Discussion

To the authors' knowledge, this study represents the first development and validation of predictive equations for CPET variables specific for patients with Fontan physiology. The data used to derive the equations are from a multicenter database with a heterogeneous group of Fontan patients. Therefore, the equations that showed good performance in the validation cohort are applicable to routine clinical practice. These equations will help the congenital cardiologist interpret the results of CPET testing in Fontan patients by benchmarking the CPET results to other Fontan patients while taking into account relevant patient characteristics, such as height, weight, and gender. The equations can be easily added to existing CPET software, and therefore, the clinician can quickly compare a Fontan patient's performance to normal children (using previous published equations) as well as other Fontan patients.

The equations can be used in clinical practice to help identify patients who may benefit from therapeutic interventions. Low skeletal mass has been associated with poorer worse exercise performance in Fontan patients and exercise training programs have been associated with improved exercise capacity [2, 7, 8]. However, referring all Fontan patients for exercise training programs is unfeasible in clinical practice. Using the Fontan CPET equations, pediatric cardiologists could easily identify those Fontan patients who have significantly reduced exercise capacity, and make selective referral for exercise training. Secondly, phosphodiesterase 5 inhibitors have been associated with improved exercise capacity in Fontan patients with the best benefit seen in patients with the lowest exercise capacity [11, 15]. Therefore, by comparing CPET results to other patients with similar circulation and adjusting for height, weight, and gender, clinicians can use the equations to easily identify patients who would theoretically most likely benefit from phosphodiesterase 5 inhibitors.

The predictive equations predict lower VO_2 at peak and AT, as well as work and 0_2 pulse when compared to standard pediatric formulas derived from normal children [6]. This is consistent with previous reports, and not surprising given that the Fontan patient have decreased skeletal muscle, lower lean body mass, and no subpulmonary ventricle to help augment systemic ventricular stroke volume during exercise [3, 8, 14, 19]. The equations developed incorporate both height and weight in predicting peak VO_2, while other commonly used pediatric equations only use height or weight [5, 6, 17]. In the equations to predict peak VO_2, O_2 pulse, and Watts, height is given more influence on predicted peak VO_2 than body weight. Two commonly used pediatric predictive equations rely solely on height to calculate predicted peak VO_2, supporting the correlation between height and peak CPET variables [5, 17]. However, our equation does incorporate weight as well. Since weight does influence lean body mass, and lean body mass is associated with maximal exercise capacity, the incorporation of body mass is physiologically appropriate [4, 16].

Of the eight equations, only VE/VCO_2 and VE/VO_2 at AT did not show similar performance in validation cohort as the derivation cohort and, therefore, may not be applicable. However, in both VE/VCO_2 and VE/VO_2 at AT equations, fenestration was a significant covariate. Persistent fenestration was not associated with peak exercise variables. This is consistent with previous reports that showed a decrease in VE/VCO_2 slope after fenestration closure and, therefore, removal of a significant right to left shunt, but no change in peak exercise variables [25]. Patients with elevated VE/VCO_2 at AT may have a residual right to left shunt. Therefore, the equations give a benchmark which the clinician can help determine when VE/VCO_2 at AT is elevated in the Fontan population.

The peak exercise predictive equations had a higher R^2 than the equations for AT variables. This is likely from multiple etiologies. First, the peak variable cohort was smaller and only consisted of patients who participated and reached maximal exercise (RER > 1.1 at maximal exercise). Fontan patients who were able to perform maximal exercise testing are more likely to be healthier and, therefore, may have less variability than patients who only reach AT. However, when we performed linear regression on just participants who performed maximal exercise tests, resulting models showed similar R^2 values. Given that it was a multicenter database, there is possible practice variation in determining AT that would lead to variability that could not be accounted for in the multivariable model.

The equations that showed similar performance in the validation cohort, consistently only required the following covariates: gender, height, weight, and fenestration. While this makes the equations more practical to implement, it does leave out covariates that have been previously associated with CPET variables. Specifically, age and age at Fontan completion were not used in the final equations despite being associated with peak VO_2 in previous reports [10, 22]. Unlike Giardini et al. and Fernandes et al., who reported an association between age and decreasing peak VO_2, the current database was from a cross-sectional study, while the previous studies were longitudinal studies. Secondly, Giardini's study included Fontan patients into their third decade of life, where as the database only included patients into their second decade. Therefore, it is possible that equations derived from a longitudinal database that included patients into their third decade of life would include the covariate of age. A previous study by Madan et al. [22] showed that age at time of Fontan is independently associated with CPET results. However, that study utilized percent of predicted VO_2 as the primary outcome, while our study investigated absolute peak VO_2. The difference in primary outcome between studies is the likely etiology for the differing results in regard to age at Fontan surgery.

Limitations

The dataset only included Fontan patients into their second decade of life, therefore, the developed equations may not be applicable to older patients. The equations developed for VE/VCO_2 and VE/VO_2 at AT did not show similar R^2 in the validation cohort and, therefore, may not be applicable to wide population. There is significant variation not explained in the AT equations. Lastly, due to a lack of collected information or in order to derive equations that are clinically relevant, patient specific factors that have been associated with exercise performance were not included [27]. The analysis of peak variables is based

upon the 166 patients who were able to perform maximal exercise tests. Therefore, more than half of the patients enrolled in the study were not included in this analysis. The equations are derived from patients with ages that ranged from 7 to 18 years, weight range of 23–97 kg and height range of 126–183 cm. Therefore, the equations may not be applicable to Fontan patients who fall within these ranges.

Conclusion

Using multivariable analysis, equations to predict CPET variables specific for Fontan population were derived. Six of the eight equations showed similar performance in a validation cohort. Only, VE/VCO_2, and VE/VO_2 equations may not be applicable. These equations can assist the pediatric cardiologist in interpreting CPET results for patients with Fontan circulation. These equations should further be refined as this cohort of patients continues to age through the current PHN Fontan 3 longitudinal study.

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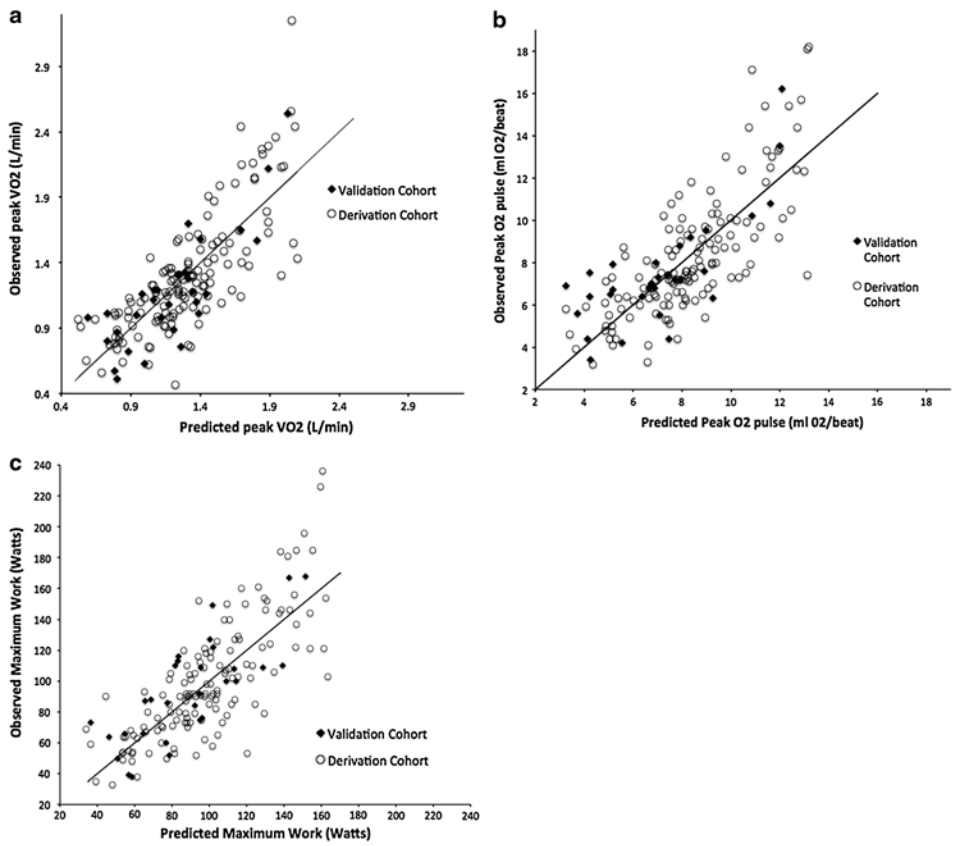

Fig 1.

Graphs depicting correlation between predicted CPET variables and observed values of both cohorts. The validation cohort is noted by *closed diamonds*, the derivation cohort by *open circles*. Reference line shows 1:1 correlation

Table 1

Variable evaluated in the multivariable model

Categorical variables
Gender (0 = female, 1 = male)
Ventricular looping (0 = d-loop, 1 = l-loop)
Dominant ventricle (0 = left and mixed, 1 = right)
Rhythm at rest (0 = non-sinus rhythm, 1 = sinus rhythm)
Fenestration present at study (0 = no, 1 = indeterminate, 2 = yes)
Continuous variables
Age at exercise testing
Age at Fontan
Height
Weight

Table 2

Patient characteristics in each cohort

Characteristic	Total (*n* = 411)	Maximal exercise (*n* = 166)	Adequate anaerobic threshold (*n* = 317)
Age			
At Fontan	3.4 ± 2.0	3.4 ± 2.1	3.5 ± 2.2
At exercise test	12.4 ± 3.2	13.9 ± 2.9	12.9 ± 3.1
Height (cm)	146.9 ± 16	154.5 ± 14	150 ± 15
Weight (kg)	42.5 ± 16	48.5 ± 16	44.9 ± 16
Male, *n* (%)	242 (59)	94 (57)	190 (60)
Dominant ventricle, *n* (%)			
Right	126 (31)	51 (30)	99 (31)
Left and mixed	211 (68)	115 (69)	216 (69)
Sinus rhythm at rest, *n* (%)	283 (69)	116 (70)	216 (69)
Fenestration present at time of study, *n* (%)			
Not present	327 (80)	127 (77)	244 (78)
Indeterminate	46 (11)	21 (13)	40 (13)
Present	37 (9)	15 (9)	29 (9)
L-loop, *n* (%)	79 (19)	41 (25)	66 (21)

Table 3

Univariate statistics for derivation cohort of peak CPET variables (*n* = 136)

Covariate	Peak VO_2 (L/min)		Peak work (W)		Peak 02 pulse (mL O_2/beat)	
Age						
At Fontan	$r = -0.07$	$p = 0.41$	$r = -0.08$	$p = 0.35$	$r = -0.33$	$p = 0.70$
At exercise	$r = 0.51$	$p < 0.01$	$r = 0.60$	$p < 0.01$	$r = 0.52$	$p < 0.01$
Height	$r = 0.72$	$p < 0.01$	$r = 0.73$	$p < 0.01$	$r = 0.72$	$p < 0.01$
Weight	$r = 0.69$	$p < 0.01$	$r = 0.70$	$p < 0.01$	$r = 0.67$	$p < 0.01$
Gender						
Male	1.45 ± 0.52	$p < 0.01$	110 ± 42	$p < 0.01$	9.24 ± 3.36	$p < 0.01$
Female	1.11 ± 0.27		85 ± 27		7.12 ± 1.79	
Rhythm at rest						
Sinus	1.31 ± 0.48	$p = 0.74$	99 ± 39	$p = 0.91$	8.20 ± 3.02	$p = 0.33$
Non-sinus	1.29 ± 0.42		100 ± 36		8.74 ± 2.87	
Fenestration						
Present	1.01 ± 0.31		80 ± 30		6.58± 2.54	
Indeterminate	1.23 ± 0.24	$p = 0.02$	88 ± 22	$p = 0.07$	7.73 ± 1.42	$p = 0.32$
Not present	1.35 ± 0.48		103 ± 40		8.67 ± 3.12	
Dominant ventricle						
Left and mixed	1.35 ± 0.48	$p = 0.09$	103 ± 39	$p = 0.11$	8.71 ± 3.08	$p = 0.04$
Right	1.21 ± 0.39		92 ± 34		7.60 ± 2.63	
Ventricular looping						
d-loop	1.29 ± 0.45	$p = 0.21$	98 ± 37	$p = 0.34$	8.24 ± 2.95	$p = 0.38$
l-loop	1.40 ± 0.47		105 ± 42		8.78 ± 3.10	

Table 4

Derivation of predictive equations

	Peak variables		
	Peak VO_2	**Maximum work**	**Max O_2 pulse**
Initial model	Age at exercise, height, weight, gender, fenestration, dominant ventricle	Age at exercise, height, weight, gender, fenestration, dominant ventricle	Age at exercise, weight, height, gender, dominant ventricle
Covariate removed			
Step 1	Dominant ventricle*	Dominant ventricle*	Age at exercise*
Step 2	Age at exercise*	Fenestration*	Dominant ventricle*
Step 3	Fenestration*	Age at exercise*	
Covariates in final model	Gender, height, weight	Gender, height, weight	Gender, height, weight
	Anaerobic threshold variables		
	VO_2 at AT	Work at AT	O_2 pulse at AT
Initial model	Age at exercise, height, weight, gender	Ventricular looping, gender, weight, height, age at exercise, dominant ventricle, fenestration	Ventricular looping, gender, weight, height, age at exercise, dominant ventricle, fenestration
Covariate removed			
Step 1	Weight*	Dominant ventricle*	Ventricular looping*
Step 2	Age at exercise*	Age at exercise*	Age at exercise*
Step 3		Weight*	Fenestration*
Step 4		Ventricular looping**	Dominant ventricle*
Covariates in final model	Gender, height	Height, gender, fenestration	Gender, height, weight
	Ventilatory equivalents at anaerobic threshold		
	VE/VCO_2 at AT	VE/VO_2 at AT	
Initial model	Ventricular looping, weight, height, age at exercise, dominant ventricle, fenestration	Ventricular looping, weight, height, age at exercise, dominant ventricle, fenestration	
Covariate removed			
Step 1	Height*	Height*	
Step 2	Dominant ventricle*	Age at exercise*	
Step 3	Age at exercise*	Dominant ventricle*	
Covariates in final model	Weight, ventricular looping, fenestration	Weight, ventricular looping, fenestration	

*Removed due to partial $R^2 < 0.02$ and p value > 0.05

**Removed due to p value > 0.05

Table 5

Final predictive equations

CPET variable	Constant	Height (cm)	Weight (kg)	Gender	Fenestration	Ventricular looping	R^2	Standard error of estimate
Peak VO_2 (L/min)	−1.71	0.016	0.008	0.243			0.61	0.29
Maximum O_2 pulse (mL O_2/beat)	−11.89	0.111	0.043	1.51			0.59	1.92
Maximum work (W)	−153.47	1.35	0.66	17.72			0.61	24.2
VO_2 at AT (L/min)	−0.933	0.011		0.218			0.15	0.46
Work at AT (W)	−3.97	0.926	9.976		−4.762		0.39	18.9
O_2 pulse at AT (mL O_2/beat)	−9.581	0.088	0.044	1.271			0.34	2.8
VE/VCO_2 at AT	50.91		−0.169		1.851	−4.784	0.18	8.21
VE/VO_2 at AT	48.04		−0.134		2.086	−5.164	0.18	9.01

Final equations are: CPET variable = constant + [Coefficient1*Covariate1] + [Coefficient2*Covariate2]… Example: For a 170 cm and 70 kg male, fenestration present and l-looped ventricle: predicted peak VO_2 (L/min) ± one SD = −1.71 + [0.016*170 cm] + [0.008*70 kg] + [0.243*1] = 1.813 L/min ± 0.29. Predicted VE/VCO_2 at AT ± one SD = 50.91 + [−0.169*70 kg] + [1.851*2] + [−4.784*1) = 38 ± 9. For categorical variables: gender (0 = male, 1 = male); fenestration (0 = no, 1 = indeterminate, 2 = yes); Ventricular looping (0 = d-loop, 1 = l-loop)

All constant and coefficients of covariates were significant ($p < 0.05$), blank fields represent covariates not in final equation *CPET* cardiopulmonary exercise testing, *AT* anaerobic threshold

Table 6

Comparisons between derivation and validation cohorts

	Peak CPET			Anaerobic threshold		
Variable	**Derivation cohort (*n* = 136)**	**Validation cohort (*n* = 30)**	***p* value**	**Derivation cohort (*n* = 246)**	**Validation cohort (*n* = 69)**	***p* value**
Patient characteristics						
Height (cm)	155.3 ± 13.1	151.1 ± 15.5	0.13	149.7 ± 14.5	151.3 ± 15.7	0.64
Weight (kg)	49.3 ± 15.9	44.2 ± 13.9	0.11	45.0 ± 15.8	44.6 ± 16.6	0.6
Age at exercise (years)	13.9 ± 2.9	13.9 ± 2.9	0.92	12.9 ± 3.0	13.1 ± 3.3	0.24
Age at Fontan (years)	3.7 ± 2.3	2.7 ± 1.2	0.04	3.5 ± 2.2	3.3 ± 2.0	0.44
Male, *n* (%)	78 (57)	16 (53)	0.69	141 (57)	49 (71)	0.04
d-looped ventricles, *n* (%)	104 (77)	20 (67)	0.23	190 (77)	59 (86)	0.14
Right dominant ventricle, *n* (%)	44 (32)	8 (17)	0.09	81 (33)	18 (26)	0.28
Sinus rhythm at rest, *n* (%)	98 (72)	18 (60)	0.19	164 (67)	52 (75)	0.17
Fenestration present, *n* (%)	14 (10)	1 (3)	0.22	22 (9)	7 (10)	0.78
CPET variables						
Peak VO_2 (L/min)	1.31 ± 0.46	1.17 ± 0.44	0.13			
Maximum work (W)	99.6 ± 38	93.5 ± 34	0.42			
Maximum O_2 pulse (mL 02/min)	8.35 ± 2.98	7.52 ± 2.63	0.16			
VO_2 at AT (L/min)				0.82 ± 0.50	0.83 ± 0.34	0.83
Work at AT				48.9 ± 24.0	55.0 ± 26.7	0.64
02 pulse at AT				6.23 ± 3.4	6.56 ± 3.7	0.63
VE/VCO_2 at AT				42.8 ± 3.9	44.5 ± 12.3	0.03
VE/VO_2 at AT				41.5 ± 9.6	43.0 ± 11.3	0.19

Table 7

Univariate statistics for derivation cohort of AT CPET variables (*n* = 246)

Covariate	AT VO_2 (L/min)		AT work (W)		AT 02 pulse (mL O_2/beat)		AT VE/VCO_2		AT VE/VO_2	
Age										
At Fontan	*r* = 0.04	*p* = 0.58	*r* = 0.32	*p* = 0.61	*r* = 0.06	*p* = 0.35	*r* = -0.02	*p* = 0.74	*r* = -0.06	*p* = 0.36
At exercise	*r* = 0.17	*p* < 0.01	*r* = 0.46	*p* < 0.01	*r* = 0.41	*p* < 0.01	*r* = -0.27	*p* < 0.01	*r* = -0.21	*p* < 0.01
Height	*r* = 0.32	*p* < 0.01	*r* = 0.57	*p* < 0.01	*r* = 0.55	*p* < 0.01	*r* = -0.32	*p* < 0.01	*r* = -0.23	*p* < 0.01
Weight	*r* = 0.31	*p* < 0.01	*r* = 0.52	*p* < 0.01	*r* = 0.52	*p* < 0.01	*r* = -0.33	*p* < 0.01	*r* = -0.25	*p* < 0.01
Gender										
Male	0.92 ± 0.61	*p* < 0.01	53.4 ± 25	*p* < 0.01	6.76 ± 3.8	*p* < 0.01	42.8 ± 10	*p* = 0.98	41.6 ± 10	*p* = 0.94
Female	0.70 ± 0.23		42.9 ± 21		5.51 ± 2.7		42.8 ± 9		41.5 ± 8	
Rhythm at rest										
Sinus	0.85 ± 0.57	*p* = 0.33	49.3 ± 24	*p* = 0.73	6.24 ± 3.0	*p* = 0.95	42.8 ± 9	*p* = 0.92	41.8 ± 10	*p* 0.54
Non-sinus	0.78 ± 0.32		48.2 ± 24		6.20 ± 4.1		42.8 ± 9		41.0 ± 8.9	
Fenestration										
Present	0.91 ± 1.3		36.6 ± 22		5.13 ± 1.7		47.3 ± 10		46.1 ± 11	
Indeterminate	0.73 ± 0.2	*p* = 0.38	43.1 ± 21	*p* = 0.08	5.21 ± 4.0	*p* = 0.04	43.8 ± 7	*p* = 0.03	42.9 ± 10	*p* = 0.03
Not present	0.83 ± 0.34		51.3 ± 24		6.53 ± 3.4		42.1 ± 9		40.7 ± 9	
Dominant ventricle										
Left and mixed	0.80 ± 0.32	*p* = 0.35	50.3 ± 23	*p* = 0.18	6.47 ± 3.3	*p* = 0.11	42.2 ± 9	*p* = 0.13	40.6 ± 9	*p* = 0.04
Right	0.87 ± 0.74		46.0 ± 26		5.73 ± 3.7		44.1 ± 10		43.3 ± 11	
Ventricular looping										
d-loop	0.81 ± 0.53	*p* = 0.61	46.7 ± 22	*p* = 0.02	6.01 ± 3.5	*p* = 0.07	44.0 ± 9	*p* < 0.01	42.8 ± 10	*p* < 0.01
l-loop	0.85 ± 0.37		55.7 ± 28		6.97 ± 3.1		38.7 ± 6		37.2 ± 7	