Cardiopulmonary exercise testing in children with Cystic Fibrosis: One centre's experience

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ABSTRACT

Background

Exercise testing is increasingly being used as a prognostic indicator in Cystic Fibrosis (CF) but it is reported to be underutilised in UK CF centres, particularly in children. Here, we evaluated the CPET results of our children with CF at the CF annual review and its possible clinical value.

Method

A pilot observational study comparing CPET results using a cycle ramp test (peak oxygen uptake - VO_{2peak}) and pulmonary function (forced expiratory volume in 1 second – FEV_1) was performed. Body mass index (BMI) was used as a marker of disease severity. Data were identified from clinical case notes and our CF database.

Results

Thirty-eight children (mean age 11±2.4; range 7-14 years; sex 17M: 21F) completed at least one CPET with 95% achieving technically satisfactory tests allowing measurement of VO_{2peak}. Mean VO_{2peak} was 105±18; range 74 - 150 % predicted with 8 % of children having a reduced VO_{2peak} of < 85 % of predicted. Mean FEV_1 z-score was -0.77±1.24, range -4.42 – 2.24. We did not demonstrate a significant correlation between VO_{2peak} and FEV_1 or BMI (r = 0.25, -0.05). Twenty-eight of 38 children completed a second CPET the following year with 71 % showing a decline in VO_{2peak}, (mean decline of 8 % of predicted value, equivalent to 3.8 $ml \cdot kg^{-1} \cdot min^{-1}$.

Conclusion

CPET is feasible with 95 % of children achieving technically satisfactory assessments starting from age 7. In this group of children with relatively mild CF, mean VO_{2peak} was normal with no significant correlation between VO_{2peak} and FEV_1 or BMI, as markers of disease severity. The majority of children demonstrated a normal VO_{2peak}. However, 71 % showed a downward trend on repeat testing 12-18 months later.

What is already known on this topic

- Exercise testing is not widely used in CF centres in the UK.
- VO_{2peak} and FEV_1 are independent predictors of mortality in Cystic Fibrosis.

What this study adds

- We demonstrate that it is feasible to include a CPET as part of annual review in children from 7 years and upwards.
- CPET provides information additional to pulmonary function tests.
- In milder disease there is no significant correlation between FEV_1 and aerobic capacity.
- Annual review assessments of exercise capacity may identify declining levels of fitness and allow early physiotherapy intervention.

INTRODUCTION

Objective assessment and monitoring of lung health in Cystic Fibrosis (CF) has traditionally relied on radiographic and pulmonary function measures. In CF, pulmonary function, commonly measured as FEV_1, was noted to be a strong prognostic indicator of mortality,[1]. However, with advances in care, abnormal spirometry is becoming a later disease marker with UK registry data showing that median (IQR) % predicted FEV_1 in children > 6 years attending UK paediatric CF centres is 86 % predicted (73-97 %),[2]. Nixon et al in 1992, Pianosi et al in 2005 and more recently, Hulzebos in 2015, showed that aerobic fitness is an independent predictor of mortality and morbidity in patients with CF,[3,4 5].

The UK CF trust guidelines recommend exercise testing at the CF annual review when clinically indicated,[6]. Additionally, the European Cystic Fibrosis Exercise Working Group recommend that full CPET should be performed routinely in children aged 10 years and over,[7]. However, it has been reported that exercise testing is underused in CF centres in the UK. Of the tests reported to be used, field based walking tests such as the six-minute self-paced walking test (6MWT) and incremental shuttle walk test were most common,[8]. To the best of our knowledge there are no studies assessing the prognostic value of the 6MWT in children with CF. Indeed, there are limited reports on its prognostic value in adults with CF; for example, Martin et at found that a reduced 6 minute walking distance of ≤ 475 m and desaturation to SpO2 ≤ 90 % during the test were independent predictors of death without transplantation,[9]. An incremental shuttle test is a reproducible and valid

alternative to CPET,[10] but there have been no studies to investigate its prognostic value in children with CF. The use of other exercise tests in predicting mortality in children has been investigated. Aurora et al reported that a low minimum oxygen saturation (Sa,O_2min) during a 12-minute walk test was a poor predictor of mortality in 181 children with severe CF lung disease referred for lung transplantation,[11]. In contrast, VO_{2peak} during CPET has been shown to predict mortality in children with CF,[3,4].

VO_{2peak} represents the maximal amount of oxygen that can be delivered by the cardiovascular system and utilised at the muscles, therefore defines a person's functional aerobic capacity,[12]. The correlation between exercise limitation assessed by VO_{2peak} and lung high resolution computed tomographic (HRCT) abnormalities has been reported to be stronger than that between spirometry, or BMI and exercise limitation,[13].In view of the potential usefulness of measuring VO_{2peak} as a guide to understanding the causes and extent of any exercise limitation and for guiding the prescription of individualised exercise programmes,[14], our centre introduced CPET as a replacement to the 6MWT. This has been offered to all patients aged over 7 years on a yearly basis at their CF annual review from May 2013. Here, we review our experience of measuring VO_{2peak} using CPET in this context. We were interested to assess whether in clinical use, there were correlations with other more commonly used outcome measures such as pulmonary function test result and/or nutritional status measured as BMI. We also investigated whether there was a difference in mean VO_{2peak} depending on sex, the presence of at least one DF508 mutation and a history of intravenous antibiotic treatment in the

preceding year. Finally, we were interested to investigate whether there were annual changes in aerobic capacity over time.

MATERIALS AND METHODS

Study participants

We retrospectively analysed 18 months of data for each child attending the CF clinic at the Royal Hospital for Sick Children in Glasgow, who performed CPET between May 2013 to April 2016. The study cohort comprised of children over 7 years who regularly attended the CF clinic and who had completed at least one CPET. They all were clinically stable at the time of testing with disease severities ranging from mild through to severe. Treatment routines remained unchanged during the study period.

Anthropometry

Before CPET, height was recorded without shoes to the nearest 0.1 cm using a fixed stadiometer (Holtan Limited UK),[15]. Weight was measured with minimal clothing to the nearest 0.1 kg (Seca 704).

Pulmonary function testing

Before CPET, spirometry and lung volumes were measured using a Jaeger Masterscreen Body Plethysmograph (Jaeger V5.4, Germany). All pulmonary function measurements were carried out by an experienced physiologist according to American Thoracic Society (ATS)/European Respiratory Society (ERS) standards,[16,17,18].

Cardiopulmonary Exercise Testing

A symptom limited CPET was performed using an electronically-braked cycle ergometer (Ergoline, Netherlands) with an incremental ramp protocol. Before each test, the metabolic cart (Jaeger, CPX, Germany) was calibrated following the manufacturer's protocol using gases of known concentration, and an automatic volume calibration was performed on the turbine volume transducer. We used a Godfrey exercise protocol,[19] modified by our centre to minimise large increments in work load. The bicycle ramp ranged between 6.5 – 25 Watts·min^{-1} with fixed increments of 6.5, 7.5, 8.5, 10, 12, 15, 20 and 25 Watts·min^{-1}. The ramp was increased every 10 s to minimise load perception for the patient. To achieve an optimal test duration of 8-12 min, the child's predicted power output based on weight,[20] was divided by 10 to give the rate of ramp increase. Patients received verbal encouragement to achieve as near to a maximal test as possible. The test was stopped once the cadence could not be maintained > 60 rpm and the patient could not be verbally encouraged to do so. VO_{2peak}, peak oxygen pulse (VO_2/HR_{peak}) and peak ventilation (VE_{peak}) were averaged over the last 30 s of the test. The gas exchange threshold was non-invasively identified using a combination of the 'V slope' method and ventilatory equivalents,[12].

We considered a CPET technically satisfactory if one of the following 3 criteria were achieved at the end of the test: (1) HR_{peak} within 15 bpm of predicted maximum based on age; (2) respiratory exchange ratio (RER) > 1.1; or (3) plateau in VO_2.

Consent

This study was a retrospective review of results from our standard clinical practice. As such, we did not seek informed consent for review of the data. All patient data were anonymised.

Statistical Analysis

Demographic data (age, sex, genotype and intravenous antibiotic use) were retrieved from case notes and our CF database and were expressed as means and standard deviations. FEV_1 was expressed in absolute terms and as z-scores using all age reference ranges,[21]. Static lung volumes were expressed in absolute values and as z-scores using UK derived paediatric reference ranges,[22]. VO_{2peak} was expressed in $L \cdot min^{-1}$, $ml \cdot kg^{-1} \cdot min^{-1}$and as percent predicted using a paediatric reference range,[20].

The relation between disease severity and VO_{2peak} was assessed in two ways. We assessed the relation between VO_{2peak} and body mass index (BMI) since it is well recognized that poor nutritional status has a negative impact on pulmonary disease,[23,24]. We also examined whether there was a correlation between VO_{2peak} and intravenous antibiotic use in the preceding year. We included children treated both for CF exacerbations as well as those receiving routine treatment as part of their CF management.

Relationships between VO_{2peak} with FEV_1, BMI z-score and age were studied using Pearson's Correlation Coefficient. Differences between mean VO_{2peak} with sex and

intravenous antibiotic use were studied using a Two-sample T-Test. A one-way ANOVA was conducted to compare the effect of genotype (DF508 homozygous, DF508 heterozygous and 'other' genotypes) on $VO_{2peak.}$

We used a paired T-test to check for statistically significant differences between initial and consecutive CPET parameters of aerobic fitness. This included absolute VO_{2peak} ($L \cdot min^{-1}$), relative VO_{2peak} ($ml \cdot kg^{-1} \cdot min^{-1}$), VO_{2peak} % predicted and finally VO_{2peak} allometrically scaled ($ml \cdot kg^{2/3} \cdot min^{-1}$).

RESULTS

Genotype.

Nineteen children with DF508 homozygous, 16 children DF508 heterozygous and 3 children with 'other' genotypes.

Pulmonary function & anthropometry.

Anthropometry and pulmonary function are summarised in tables 1 & 2. We analysed results from 38 children (17 male and 21 female). Seven children had an FEV_1 consistently below the lower limit of normal,[22].

Table 1

Table 2

CPET parameters are summarised in table 3. We were able to perform technically satisfactory assessments on 36/38 (95 %) of children. In 2 young children (both 7 years old) the CPET was technically unsatisfactory due to poor cooperation and effort. Aerobic capacity in children with CF was within a range consistent with a normal, healthy population (VO_{2peak} of ≥ 85 % predicted,[25]). Only 5 children (13 %) had VO_{2peak} of < 85 % predicted. Two children desaturated to SpO_2 < 95 % at peak exercise. No ECG arrhythmias were detected in any of the patients.

Table 3

Using Pearson's Correlation Coefficient, we found no significant correlation between VO_{2peak} and FEV_1 (r =0.25, p=0.13), VO_{2peak} and age (r =-0.24, p=0.15) or between VO_{2peak} and BMI z-score (r =-0.05, p=0.77). Using a Two-sample T-Test, we found no significant differences in mean VO_{2peak} between males (107.9±19.1) vs females (107.1±17.0), p=0.90. Fourteen of 38 child received intravenous antibiotic treatment in the preceding year. We found no significant differences in mean VO_{2peak} if the child had received intravenous antibiotics (103.0±18.5) vs no intravenous antibiotics (110.1±17.1), p=0.23. Nineteen children were DF508 homozygous, 16 were DF508 heterozygous and 3 had 'other' genotypes. We found no significant effect of genotype on VO_{2peak} (p=0.24).

Figure 1. Change in VO_{2peak} % predicted in 28 children with CF measured between 12-18 months apart

Consecutive annual CPET data were available for 28/38 (74 %) children (Figure 1). These were performed up to 18 months after the initial CPET due to timings of the CF annual review appointment. Ten children did not perform a repeat CPET: 3 transitioned to adult services; 4 did not attend their annual review appointment; 1 had a CF exacerbation at the time of annual review; 1 had an unsatisfactory test due to submaximal patient effort and there was insufficient staffing for 1 patient.

VO_{2peak} decreased in 71 % of the subjects. The mean change in VO_{2peak} parameters are shown in table 4. Overall, there was no significant difference in mean change of absolute VO_{2peak} ($p > 0.05$). However, there was a statistically significant decline in VO_{2peak} when it was related to body weight, or to % predicted VO_{2peak} (which includes sex and body weight in the predicting equation) or when using allometrical scaling ($ml \cdot kg^{-2/3} \cdot min^{-1}$), p= 0.001, 0.003 and 0.03 respectively. The mean decline relative to body weight was 3.8 $ml \cdot kg^{-1} \cdot min^{-1}$equivalent to an 8 % from baseline value. An 8% change is greater than the normal coefficient of variation reported in the literature for VO_{2peak} (4.8%) when looking at biological quality control,[26] although the normal variability for young CF patients is likely to be greater,[27].

DISCUSSION

We found that the majority of our CF patients had normal BMI and pulmonary function in keeping with data in the UK CF registry,[2]. In this relatively mild group of children with CF, the majority of our VO_{2peak} results were also normal suggesting that we have an aerobically fit group of children. This may partly reflect our Centre's focus on promoting a healthy diet, regular physical activity and physiotherapy in our CF patients.

We found no significant correlation between FEV_1 and VO_{2peak}. This could be explained by the relatively small sample size and the majority having normal lung function and aerobic capacity. However, it is also recognized that FEV_1 has to be significantly reduced to affect exercise capacity,[28]. Previously, FEV_1 has been shown to correlate with VO_{2peak} in children,[29]. McBride et al investigated 64 children with CF aged 8-11 years and found a statistically significant but weak correlation between FEV_1 % predicted and VO_{2peak} % predicted with an R^2 value of 0.14. The most likely explanation for the differences observed in our study is a combination of a larger sample with a wider range of lung function and fitness. However, the low R^2 in the study by McBride and the absence of any correlation in our data suggest there is not a strong relationship between FEV_1 and VO_{2peak}. As only 7 of our patients had an FEV_1 below the lower limit of normal, it is perhaps not surprising that we did not see a relationship in a relatively mildly affected population,[30]. However, there is also a debate about the factors which limit aerobic function in CF with both suggestions of central such as impaired stroke

volume,[31] and/or peripheral mechanisms such as impaired muscle metabolism being involved, apart from changes in lung function[32].

In our mild to moderate CF children, the majority did not demonstrate any evidence of ventilation limitation at maximal exercise, as would be expected in healthy children. There are varying reports in the literature on the aerobic fitness of CF children. Nixon et al were one of the first groups to investigate VO_{2peak} and its prognostic value. Their group included 40 adults and 68 children and adolescents. They found a range of lung function impairment with 65 % of their study population having an FEV_1 of < 65 % predicted. They found generally a low aerobic capacity with a mean VO_{2peak} of 70 % predicted (35 $ml \cdot kg^{-1} \cdot min^{-1}$),[3]. More recently, Hulzebos et al investigated 127 adolescents with CF with a mean FEV_1 of 77.7±15.6 % predicted and a $VO_{2peak/kg}$ 93.3±17.9 % predicted,[5].

Pianosi et al exclusively investigated children with CF and reported an initial VO_{2peak} of 41.2 $ml \cdot kg^{-1} \cdot min^{-1}$,[4]. This would be classed as 'fair' aerobic fitness according to published reference values for children and adolescents,[28]. More recent studies have included control groups and showed that CF children and adolescents had a significantly reduced VO_{2peak} when compared to healthy children. For example, Bongers et al found their CF group of 22 children was within the normal range although the values for VO_{2peak} were significantly lower than the controls,[33]. Saynor et al also found a reduced aerobic capacity (mean VO_{2peak} 36.3 $ml \cdot kg^{-1} \cdot min^{-1}$) in subjects with CF compared to controls,[34].

Other studies have reported that nutritional status affects exercise capacity,[35,36] but since very few of the children in our study had either an abnormal BMI or an abnormal VO_{2peak} ≤ 84 % predicted (range 64 – 84),[25] we were unable to demonstrate a significant a correlation. On reviewing the 3 children with an abnormal $VO_{2peak,}$ all had normal BMI z-scores -0.57, 1.13, 1.83. One child with a BMI z-score of 1.83 (98^{th} percentile) and VO_{2peak} 74 % predicted, had poor exercise activity. His low VO_{2peak} may be a reflection of deconditioning as well as high fat rather than muscle mass.

Whilst the majority of our patients had normal CPET results, 71 % demonstrated a decline in VO_{2peak} on repeat testing 12- 18 months later. There is little reported data about what constitutes a significant decline in VO_{2peak} in CF patients. There are a number of cross sectional and longitudinal studies investigating the trend in VO_{2peak} in healthy children. In a review by Krahenbhul et al, mean values of VO_{2peak} relative to body weight from several longitudinal and cross sectional studies were plotted against age in males and females to investigate the relationship over the age range 6-16 years,[37]. They found that males had an unchanged VO_{2peak} corrected for body weight over time, whereas females showed a decline from 52.0 $ml \cdot kg^{-1} \cdot min^{-1}$ to 40.5 $ml \cdot kg^{-1} \cdot min^{-1}$. However, it is recognized that correcting VO_{2peak} for body mass has limitations and does not normalize the data,[38,39]. Ratio scaling of VO_{2peak} by body mass (as opposed to fat free mass) penalizes females and those that are heavier than their aged match peers and it has been reported that allometric scaling of VO_{2peak} is a more reliable method to interpret changes in $VO_{2peak,}$[40]. The Amsterdam Growth and Health Longitudinal Study recently published data on changes in aerobic fitness

for approximately 650 adolescents over a 25 year period. VO_{2peak} was presented in absolute values, relative to body weight and allometrically scaled. They found that from 12-17 years in both males and females, there was a downward trend in VO_{2peak} relative to body weight. However, when allometrically scaled, VO_{2peak} in males did not decrease whereas females did demonstrate a decline,[41]. In our data, aerobic fitness declined significantly, irrespective of whether it was related to body weight, or to sex and body weight using the predicted values or using allometric scaling (table 4), although the deterioration was least using allometric scaling.

Pianosi et al looked at annual CPET over a 5 year period in CF children and found that VO_{2peak} decreased in 70 % of the subjects with a mean annual decline of 2.1 $ml \cdot kg^{-1} \cdot min^{-1}$,[4]. These results show similarity to our results, albeit over a much shorter period. We can only speculate on the reasons for the decline in some children. Although changes in lung function itself may not have caused changes in aerobic fitness, acute exacerbations as well as disease progression may have resulted in these patients participating in less physical activity with a consequent reduction in fitness. In others, the increase fitness may represent the effects of interventions such as planned exercise prescription.

Pianosi also showed that initial VO_{2peak} did not affect the rate of decline and this highlights that longitudinal assessments of aerobic capacity are important,[4]. Further work will be required to investigate the place of repeated CPET tests in assessing exercise capacity in CF patients over time. Identifying a downward trend in a child's exercise capacity may allow early physiotherapy intervention and

encouragement to increase physical activity to prevent ongoing decline in exercise capacity. Regardless of the definition of a 'clinically significant decline' in VO_{2peak}, we consider any fall in exercise capacity to be important as small declines in VO_{2peak} may cumulatively result in a clinically significant reduction in aerobic capacity. Pianosi at al showed that patients with VO_{2peak} < 32 $ml \cdot kg^{-1} \cdot min^{-1}$exhibited a dramatic increase in mortality,[4]. This may highlight those who would benefit from additional encouragement to increase their physical activity and prevent de-conditioning.

We had previously used the 6 Minute Walk Test (6MWT) to assess exercise performance at annual review but in the light of the evidence about VO_{2peak} as a strong predictor of mortality, we replaced the 6MWT with CPET. Whilst the initial cost for CPET equipment is significant, the cost for consumables is minimal and our respiratory laboratory already had dedicated time allocated for the assessments. Performing an annual CPET in place of 6MWT added minimal time to the CF annual review visit. We found that it was feasible to include CPET as part of the annual review. Ninety-five % of our children achieved technically satisfactory assessments starting from an age of 7 years. In our centre, children under 7 years of age are not routinely offered CPET or field exercise test due to difficulties in performing them in this age group. However, we would attempt CPET if clinically indicated and at the discretion of the referring clinician. For the duration of this study, no children under 7 years of age were referred for exercise testing. Whilst we have demonstrated that CPET is a feasible and achievable investigation in children 7 years and older at the CF annual review, it is a technically demanding assessment and can only be performed in a centre with the necessary equipment and appropriately trained staff.

Although we have no formal feedback, the majority of our patients and their parents have engaged well with the introduction of CPET at annual reviews. The children reported that they enjoy the challenge of CPET. Importantly, our respiratory physiotherapists have found CPET clinically beneficial in identifying those children needing more specific exercise advice, particularly for children with stable lung function but declining VO_{2peak}. Of the 5 patients who had an abnormal $VO_{2peak} \leq 84$ % predicted, none had reduced lung function. Whilst our centre encourages all our patients to undergo regular physical activity, the declines in VO_{2peak} highlighted the need for additional physiotherapy intervention to increase their physical activity and prevent ongoing decline. This emphasizes the value of using CPET as an assessment tool to guide counseling about exercise and the prescription and monitoring of exercise programmes,[42].

Study limitations

This was a retrospective review and we had no control group, relying instead on published normal data. We recognise that our numbers were small, only 74 % completed a second CPET during the study period, and our patients were only followed up for one year. We continue to collect data as longer follow up will give a more informative assessment of extent and value of changes in aerobic capacity. In this case, the predicted values for VO_{2peak} are based on a limited number of North American children. Future research should focus on providing suitable reference data for UK children. In the context of our paediatric clinical population, it was not feasible to perform a supramaximal test on each patient to verify a 'true' VO_{2peak} as demonstrated by a plateau in VO_2. Our use of secondary criteria of HR_{peak} and RER

may therefore underestimate the 'true' VO_{2peak},[43]. We also did not routinely take body fat measurements but recognise that this may affect the VO_{2peak} % predicted which uses body weight in the predictive equation. Finally, we had no standardised recording of physical activity levels of the children in the 12-18 month interval between the first and second tests which might have been informative in assessing the effect of regular activity and/or exercise on aerobic capacity.

CONCLUSION

CPET is feasible as a test of aerobic function at the CF annual review. It offers additional prognostic information to routine pulmonary function tests and allows identification of de-conditioned patients who may need to increase their physical activity. In our population with relatively mild CF, most children had normal VO_{2peak} when compared with reference data. However, a large majority showed significant declines in VO_{2peak} the following year highlighting the importance of serial aerobic fitness measurements to help identify patients who may benefit from additional physiotherapy support and intervention.

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Contributorship.

AD instigated, designed and supervised the study. EW and PB contributed to the design of the study, collected the data and analysed results with DY. EW and PB wrote the article. JYP reviewed and commented on the article.

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Competing interests

None declared

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Table 1

Variable	mean	SD	Min, max Range
Age (years)	11.0	2.39	7.3, 15.7
Height (cm)	145.3	16.48	115, 180.8
Body mass (kg)	39.2	13.18	20.2, 69.5
BMI z-score	0.1	1.00	-2.2, 2.5

Table 2

Variable	mean	SD	Min, max Range
FEV_1 (L)	2.07	0.75	0.98, 4.06
FEV_1 z-score	-0.77	1.24	-4.42, 2.24
FEV_1/FVC (%)	81	8	57, 96
FEV_1/FVC (%) z-score	-0.99	1.24	-3.64, 1.55
TLC (L)	3.67	1.15	2.04, 7.01
TLC z-score	0.70	1.04	-1.08, 3.17
RV (L)	1.07	0.49	0.58, 2.58
RV z-score	0.59	1.75	-1.48, 6.61

Table 3

Variable	Mean	SD	Min, Max Range
Maximal Exercise parameters			
Absolute VO_{2peak} ($L \cdot min^{-1}$)	1.58	0.52	0.88, 3.01
Relative VO_{2peak} ($ml \cdot kg^{-1} \cdot min^{-1}$)	42.0	7.7	29.2, 62.3
VO_{2peak} (% predicted)	105	18	74, 150
VE max ($L \cdot min^{-1}$)	64	24	28, 137
Breathing reserve (%)	19	20	-36, 54
Heart Rate max ($Beats \cdot min^{-1}$)	188	10	160, 208
Oxygen Pulse max ($ml \cdot beat^{-1}$)	8.6	2.8	4.0, 16.0
End test SpO_2 (%)	97	2	89, 100
Peak power Output (Watt)	97	42	41, 212
Relative Peak power output $Watt \cdot kg^{-1}$)	2.5	0.6	1.6, 3.8
Submaximal Exercise			
VO_2 at GET ($ml \cdot min^{-1}$)	826	215	415, 1455
GET (% of VO_{2peak})	53	7	38, 70
VO_2/Work Rate ($ml \cdot watt^{-1} \cdot min^{-1}$)	10.6	0.9	9.1, 12.3
VE/VCO_2 Slope	30.9	3.8	22.4, 44.0

GET - Gas exchange Threshold

Table 4

Variable	$Mean_{1st\ CPET}$	$Mean_{2nd\ CPET}$	Absolute Difference	% Difference
VO_{2peak} ($L \cdot min^{-1}$)	1525 ± 480	1539 ± 420	14	1
VO_{2peak} Relative to bodyweight ($ml \cdot kg^{-1} \cdot min^{-1}$)	42.7 ± 7.0	38.9 ± 8.2	-3.8	-9
VO_{2peak} % Predicted (includes sex and body weight)	107 ± 17	99 ± 17	-8	-8
VO_{2peak} Allometrically scaled ($ml \cdot kg^{-2/3} \cdot min^{-1}$)	137 ± 22	130 ± 22	-7	-6