THE OXYGEN UPTAKE EFFICIENCY SLOPE IS NOT A VALID SURROGATE OF AEROBIC FITNESS IN CYSTIC FIBROSIS

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ABSTRACT

Background

Maximal cardiopulmonary exercise testing is recommended on an annual basis for children with cystic fibrosis (CF), due to a clinically useful prognostic information provided by maximal oxygen uptake ($\dot{V}O_{2max}$). However, not all patients are able, or willing, to reach $\dot{V}O_{2max}$, and therefore submaximal alternatives are required. This study explored the validity of the oxygen uptake efficiency slope (OUES) as a submaximal measure of $\dot{V}O_{2max}$ in children and adolescents with CF.

Methods

Data were collated from 72 cardiopulmonary exercise tests (36 CF, 36 controls), with OUES determined relative to maximal and submaximal parameters of exercise intensity, time and individual metabolic thresholds. Pearson's correlation coefficients, independent t-tests and factorial ANOVAs were used to determine validity.

Results

Significant ($p < 0.05$) correlations with $\dot{V}O_{2max}$ were observed for most expressions of OUES, but were consistently weaker in CF ($r = 0.30 – 0.47$) when compared to CON ($r = 0.58 – 0.89$). Mean differences for all OUES parameters between groups were not significant ($p > 0.05$). When split by $\dot{V}O_{2max}$ tertiles, minimal significant differences were found between, and within, groups for OUES, indicating poor discrimination of $\dot{V}O_{2max}$.

Conclusions

The OUES is not a valid (sub)maximal measure of $\dot{V}O_{2max}$ in children and adolescents with mild-to-moderate CF. Clinicians should continue to use maximal markers (i.e. $\dot{V}O_{2max}$) of exercise capacity.

KEYWORDS

Oxygen uptake, exercise testing, adolescence, respiratory disease.

ABBREVIATIONS

Body surface area (BSA), cardiopulmonary exercise test (CPET), control (CON), cystic fibrosis (CF), effect size (ES), oxygen uptake efficiency slope (OUES), forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), gas exchange threshold (GET), respiratory compensation point (RCP), time to exhaustion (TTE), maximal oxygen uptake (VO_{2max})

1. INTRODUCTION

Previous research indicates the benefit of high levels of cardiorespiratory fitness, as characterised by maximal oxygen uptake ($\dot{V}O_{2max}$), for young people with cystic fibrosis (CF). A high $\dot{V}O_{2max}$ is associated with an improved quality of life [1], reduced risk of hospitalisation for pulmonary exacerbations [2] and reduced mortality risk [3]. Consequently, individuals with CF are advised to increase their exercise and habitual physical activity levels, with regular maximal cardiopulmonary exercise testing (CPET) also recommended and endorsed by the European CF Society [4] and European Respiratory Society, to monitor changes in their aerobic fitness status.

However, assessing $\dot{V}O_{2max}$ requires patients to provide a maximal physical effort and is thus considered an ‘effort dependent’ test. Motivation, discomfort, excessive dyspnoea, chronic fatigue and naivety towards protocols may make patients with CF more unwilling or unable to reach volitional exhaustion and their $\dot{V}O_{2max}$. Therefore, physiological markers of aerobic fitness that can be attained during submaximal regions of a CPET can be particularly useful [5].

One such marker is the oxygen uptake efficiency slope (OUES), a submaximal, effort-independent parameter describing the relationship between $\dot{V}O_2$ and the common logarithm of minute ventilation ($\dot{V}_E$) [6]. Given the curvilinear relationship between ventilation and oxygen uptake during incremental exercise, it is difficult to model and therefore normalisation of ventilation (i.e. $\log V_E$) allows for direct comparison between tests (and groups). A higher value for the OUES indicates a greater ventilatory efficiency. The OUES has been shown to significantly and positively correlate with $\dot{V}O_{2max}$ in healthy children [7] and children with heart disease [6], indicating its potential as a submaximal surrogate of aerobic fitness in paediatric groups.

Despite OUES appearing to be a valid determinant of exercise tolerance in adults with CF [8], evidence for its use in children and adolescents with CF requires further verification. Only one study has previously sought to validate the OUES as an effort-independent marker of $\dot{V}O_{2max}$ in a paediatric population with mild-to-moderate CF [9]. This study calculated OUES at 100%, 75% and 50% of the test duration and concluded it invalid, due to the observed moderate positive correlations between the OUES and $\dot{V}O_{2max}$ (r = 0.41 – 0.54). Furthermore, despite decreased $\dot{V}O_{2max}$ in children with CF, the OUES was unable to differentiate fitness status between children with, and without CF; leading authors to conclude the invalidity of OUES in this patient group. However, there are multiple methodological weaknesses to this study. Firstly, utilising CPET time to exhaustion (TTE) as a measure of intensity may be flawed, as it does not account for variances in individual metabolic thresholds. As the presence of reduced maximal capacity [10] and an altered oxygen cost of exercise [11] have been demonstrated in individuals with CF, it is conceivable that patients in this previous study [9] may be exercising at differing relative exercise intensities (i.e. as a percentage of $\dot{V}O_{2max}$), and even within differing intensity domains, despite being matched for exercise duration. Secondly, there was a lack of appropriate normalisation for the influence of body size, with authors utilising ratio-standard scaling, whereas previous research has shown this to be insufficient at removing residual effects of body size from OUES [12].

Given aforementioned issues associated with previous research [9], OUES should instead be assessed at individually determined parameters of relative exercise intensity (%$\dot{V}O_{2max}$) and domain thresholds, such as the gas exchange threshold (GET) and respiratory compensation point (RCP) [13], alongside utilising allometric scaling protocols to ensure a size-free analysis of OUES [12].

Therefore, the purpose of this study was to examine correlates of allometrically-scaled OUES with $\dot{V}O_{2max}$, and to systematically investigate differences in the OUES between children with CF and healthy controls (CON) at appropriately matched parameters of relative exercise intensity (%$\dot{V}O_{2max}$), TTE and individual metabolic boundaries (GET and RCP). In addition, the study will examine whether the OUES can differentiate between patients of differing aerobic fitness statuses vs. healthy matched controls and, therefore, its suitability as a submaximal surrogate for $\dot{V}O_{2max}$.

2. MATERIALS AND METHODS

2.1 Participants

Data from 45 children and adolescents with CF were considered for inclusion in the current retrospective analysis. Nine children were excluded due to inadequate data (insufficient, or missing data, *n* = 7; insufficient test length, *n* = 2). Remaining data were subsequently age- and gender-matched from existing exercise databases of healthy children, resulting in a final sample of *n* = 72 (36 CF, 36 CON; 21 males per group; mean age 13.3 ± 2.8 years). All CON children were screened for contraindications to exercise prior to CPET participation, including pulmonary disorders and unstable co-morbid asthma.

As the study was a retrospective analysis of existing data, additional ethics approval was not required. Ethics approval for data collected was originally approved by South West NHS Research Ethics and local institutional ethics committees, whereby fully informed written consent and assent were obtained from parents/guardians and paediatric participants, respectively.

2.2 Data Collection

All participants undertook a CPET to volitional exhaustion on an electronically braked cycle ergometer, to determine $\dot{V}O_{2max}$ and submaximal measures of cardiorespiratory fitness. If required by patients with CF, bronchodilators were administered prior to CPET. Pulmonary function was assessed using a hand-held spirometer, with maximal values of forced expiratory volume in one-second (FEV_1) and forced vital capacity (FVC) compared to normative values [14-16]. Pubertal status of children was determined as age from peak height velocity (aPHV), using published equations [17].

2.3 Data Analysis

Pulmonary gas exchange and ventilation data were collected breath-by-breath, and subsequently averaged to 10 second time intervals. Previously described techniques were utilised to ascertain $\dot{V}O_{2max}$ [18], GET and RCP [13]. To ascertain OUES values, linear regressions were obtained between $\dot{V}O_2$ and the logarithmic transformation of $\dot{V}_E$ ($\log\dot{V}_E$), using data up to the following boundaries: 100%, 75% and 50% of TTE (100_{TTE}, 75_{TTE}, 50_{TTE}), 100%, 75% and 50% of $\dot{V}O_{2max}$ ($100_{\dot{V}O2max}$, $75_{\dot{V}O2max}$, $50_{\dot{V}O2max}$), GET and RCP. The time point of $100\%_{\dot{V}O2max}$ also describes $100\%_{TTE}$ – providing eight OUES parameters per participant.

2.4 Scaling of Data

All OUES values were allometrically scaled to BSA [19], in line with recent recommendations [12]. An allometric model was applied to remove residual effects of body size, with OUES scaled to $BSA^{1.40}$. $\dot{V}O_{2max}$ was not scaled using allometric procedures as ratio-standard scaling sufficiently removed residual effects of body size.

2.5 Statistical Analyses

Descriptive data are reported as mean (± standard deviation (SD)) unless otherwise stated. Pearson's correlation coefficients were calculated between $\dot{V}O_{2max}$ and each of the eight normalised OUES values, to identify if the two variables are significantly related. Independent samples *t*-tests were also performed to identify differences between CF and CON for all variables, and identify the impact of disease status upon OUES. Finally, factorial ANOVAs were conducted to identify the interaction between $\dot{V}O_{2max}$ status, split by tertile [3], and disease status upon $\dot{V}O_{2max}$ and $OUES/BSA^{1.40}$. Where main or interaction effects were found, pairwise comparisons using Bonferroni corrections were applied to identify where relationships existed.

Statistical significance was set at an alpha of 0.05 and Cohen’s thresholds are used to report effect sizes (ES) and illustrate the magnitudes of the mean difference [20].

3. RESULTS

3.1 Participant characteristics

Participant characteristics and mean differences between groups are presented in Table 1. Significant differences were observed between CF and CON for pulmonary function and the absolute $\dot{V}O_2$ at the GET.

3.2 Correlation between OUES and $\dot{V}O_{2max}$

All OUES/BSA$^{1.40}$ variables significantly correlated with body mass relative $\dot{V}O_{2max}$, apart from 50%$_{TTE}$ within the CF group (Table 2).

3.3 Difference in OUES between CF and CON

Mean values for BSA corrected OUES values were lower, but not significantly, in CF compared to CON at each threshold (50$_{\dot{V}O2max}$: 923 ± 273 vs. 992 ± 290; 75$_{\dot{V}O2max}$: 1088 ± 224 vs. 1153 ± 293; 50$_{TTE}$: 1019 ± 219 vs. 1091 ± 273; 75$_{TTE}$: 1101 ± 225 vs. 1182 ± 284; 100$_{\dot{V}O2max}$ and 100$_{TTE}$: 1141 ± 257 vs. 1206 ± 267; GET: 958 ± 296 vs. 996 ± 361; RCP: 1148 ± 251 vs. 1189 ± 297; $p > 0.05$ for all comparisons (range = 0.18 – 0.63); units for all parameters: $mL \cdot min^{-1} \cdot logL^{-1} \cdot m^{-2.8}$). Figure 1 represents the data for OUES relative to BSA, according to categories of duration, intensity and the metabolic thresholds.

3.4 OUES and fitness tertiles

When the data were split by tertiles according to $\dot{V}O_{2max}$ (Figure 2), a significant difference was observed between tertiles within both CF (45.7 ± 4.8 vs. 38.0 ± 2.0 vs. 29.5 ± 4.6 $mL \cdot kg^{-1} \cdot min^{-1}$, respectively) and CON (51.9 ± 5.6 vs. 38.9 ± 2.5 vs. 29.0 ± 6.3 $mL \cdot kg^{-1} \cdot min^{-1}$, respectively) groups with regards to aerobic fitness ($p < 0.001$ for all pairwise comparisons, *ES*

= 2.07 – 3.84). However, there was only a significant difference in $\dot{V}O_{2max}$ between CF and CON in the highest aerobic fitness tertile ($p < 0.001$, *ES* = 1.19).

When split by $\dot{V}O_{2max}$ tertiles, there was no significant difference in OUES/BSA$^{1.40}$ at 100%TTE ($p > 0.05$). In CF, at 100%TTE, OUES/BSA$^{1.40}$ was significantly higher in the highest (1271 ± 241) relative to the lowest (1020 ± 281) fitness tertile ($p = 0.016$, *ES* = 0.96). The middle tertile (1131 ± 198) was not significantly different between either the highest ($p = 0.34$, *ES* = 0.63) or lowest tertile ($p = 0.62$, *ES* = 0.46). By comparison, in the CON group significant differences were found between the highest (1441 ± 211) and lowest (957 ± 206; $p < 0.001$, *ES* = 2.32), between the middle (1219 ± 108) and the lowest ($p = 0.011$, *ES* = 1.59) and middle and highest ($p = 0.041$, *ES* = 1.32; Figure 3) tertiles.

There was no significant difference in $OUES_{GET}$/BSA$^{1.40}$ between the groups ($p > 0.05$). When $OUES_{GET}$/BSA$^{1.40}$ was split by aerobic fitness tertiles, a significant difference was only found within the CON group between the highest (1221 ± 336) and lowest tertiles (798 ± 273, $p = 0.005$, *ES* = 1.38). The middle tertile (952 ± 356) was not significantly different to either the highest ($p = 0.114$, *ES* = 0.78) or lowest tertile ($p = 0.712$, *ES* = 0.49). In the CF group, no significant differences were found between any tertiles (highest: 1017 ± 273; middle: 1006 ± 324; lowest: 854 ± 290, all $p > 0.61$, *ES* = 0.04 – 0.58). No significant differences between groups were observed for each tertile (all $p > 0.11$, *ES* = 0.16 – 0.64; Figure 3).

4. DISCUSSION

The primary purpose of this study was to investigate the validity of the OUES as a submaximal alternative to $\dot{V}O_{2max}$ in young people with CF – utilising a larger CF cohort than previous research [9,21]. Specifically, we comprehensively compared differences in the OUES, when appropriately normalised for BSA [12], between children and adolescents with mild-to-moderate CF and their healthy peers, at parameters of time and relative exercise intensity. Although OUES was associated with $\dot{V}O_{2max}$ in both CF and CON groups, coefficients were consistently smaller in CF. Despite differences in these correlations, statistically significant differences in OUES could not be found between groups, regardless of whether it was standardised to percentage of $\dot{V}O_{2max}$, test duration or submaximal metabolic thresholds. Furthermore, OUES could not discriminate fitness status within, and between, groups. Taken collectively, these observations suggest OUES does not provide a valid surrogate of $\dot{V}O_{2max}$ in children and adolescents with CF, supporting previous findings [9].

In this present study, significant correlations were observed between body-mass relative $\dot{V}O_{2max}$ and the majority of BSA corrected OUES thresholds, except at $50\%_{TTE}$ in the CF group. The locations of significance are identical to the only previous OUES study in children with a similar severity of CF during incremental cycling exercise, with magnitudes of correlations in the CF and CON groups corroborating previous work [9] as CON shows larger effect sizes (r = 0.58 – 0.89) in comparison to the medium effect sizes (r = 0.30 – 0.47) of the CF cohort. As the correlation coefficients in the CF groups suggest a shared variance (R^2) of between 9 and 22% (unlike 34 – 79% in CON), these results suggest that despite their association, OUES may not be a viable surrogate for $\dot{V}O_{2max}$.

Despite positive correlations with $\dot{V}O_{2max}$, no mean differences in OUES were observed between CF and CON at each parameter (of intensity, time and metabolic thresholds) – a finding contrasting previous adult and paediatric studies assessing OUES in independent groups [6-8,22,23]. However, it could be argued that since a significantly lower $\dot{V}O_{2max}$ was not observed in CF versus CON in the present study, in contrast to previous findings [10,21], a recruitment bias may be present. The lack of differences between groups may be due to deconditioning of control participants (as opposed to increased fitness in CF), with $\dot{V}O_{2max}$ being 10 $ml \cdot kg^{-1} \cdot min^{-1}$ lower in the current study, when compared to previous research [9]. Consequently, it would also be expected that no differences in OUES would be observed. However, factorial ANOVAs sought to identify the sensitivity of the OUES measurement in discriminating between children of differing fitness. As the OUES supposedly represents $\dot{V}O_{2max}$ when maximal exercise efforts cannot be reached [6], it is assumed that the OUES should follow a similar profiling pattern to $\dot{V}O_{2max}$ and differentiate between patients of differing clinical and aerobic fitness states.

When data were categorised into fitness based upon aerobic fitness tertiles, a division shown to predict mortality in CF [3], a significant difference in $\dot{V}O_{2max}$ was clearly evident both within and between the groups, but the former was only seen at the highest fitness level. This observation identifies that differences in aerobic fitness ($\dot{V}O_{2max}$) can be isolated within children with CF. However, when represented as aerobic fitness tertiles, differences in the OUES and $OUES_{GET}$ (Figure 3) were not clearly defined, with a difference only evident between high-fit and low-fit children and adolescents with CF for OUES at 100%TTE. In contrast, better discriminatory sensitivity was evident in the CON group, showing differences in OUES between all tertiles for aerobic fitness. Thus, even though some discriminatory power may be evident between children and adolescents with CF for high and low aerobic fitness, this was only found for OUES at 100%TTE. This suggests that to isolate individuals of differing fitness status, a measurement of OUES would need to be taken at maximal exercise, as opposed to a submaximal parameter which can be identified in real-time during a CPET, such as the GET (characterised by a disproportionate increase in $\dot{V}CO_2$ relative to $\dot{V}O_2$). However, if participants would be required to reach volitional maximum to produce a maximal OUES value, clinicians would benefit from utilising $\dot{V}O_{2max}$ as opposed to OUES from peak exercise.

Since the purpose of the OUES is to provide a measure that is useful in lower functioning patients, i.e. those unable/unwilling to reach volitional exhaustion, differentiation between these patients is a key requisite of this CPET parameter, especially at submaximal thresholds. Unfortunately, this study demonstrates that the OUES does not provide such sensitivity in children and adolescents with CF. Therefore, despite the OUES showing potential as a clinical outcome in other paediatric cohorts [6,23], its use as a surrogate of $\dot{V}O_{2max}$ in children and adolescents with CF is doubtful.

Previous studies have assessed the validity of the OUES in clinical populations, such as congestive heart failure [24] and congenital heart disease [25], finding it, to an extent, to be a suitable, effort-independent, parameter of aerobic fitness. Moreover, two previous studies have assessed the applicability of the OUES in individuals with CF. One, conducted in 31 adults and 34 healthy controls, concluded that OUES at 80% of test duration is a valid predictor of maximal aerobic fitness, due to high correlation (r = 0.91) with VO_{2peak} – and therefore may be a clinically useful submaximal exercise parameter [8]. In addition, Bongers *et al.* [9] sought to validate the OUES at 50%, 75% and 100% of test duration in 22 children and adolescents with CF and 22 healthy controls. In contrast to earlier findings in adults, it was concluded to be an invalid measure, due to limited distinguishing properties and moderate correlations with

$\dot{V}O_{2max}$. However, previous studies have analysed OUES at submaximal parameters of time, without attempts to standardise and individualise exercise intensity, meaning participants may be exercising in differing metabolic domains, despite matching for exercise duration. Hence, the current study accounted for these factors, by analysing OUES at submaximal parameters of intensity, time and individual metabolic thresholds. Furthermore, the groups in the existing paediatric study [9] were poorly matched, with a significant difference in age evident between children with CF and healthy counterparts. As previous work has identified age- and sex-related differences in the OUES [7], this may have inadvertently affected results. In addition, inappropriate ratio-standard scaling methods were utilised, whereas previous research has shown that allometric procedures are required to remove residual effects of body size from OUES [12]. In order to solely isolate the effects of disease status, the current study deliberately age- and gender-matched participants, utilising allometric scaling to ensure all influencing factors were controlled for.

Given that the OUES is physiologically dependent on metabolic CO_2 production ($\dot{V}CO_2$) and the ratio of pulmonary dead space to tidal volume (V_D/V_T) [6], it is prudent to examine which factors are altered in CF which may account for its weaker relationship with $\dot{V}O_{2max}$ compared to their healthy counterparts. Whilst a reduced $\dot{V}O_{2max}$ has been reported in children with CF [10,21], no differences exist between CF and CON for the percentage of $\dot{V}O_{2max}$ at which GET (an indication of the onset of metabolic acidosis [13]) occurs [9,10,21,26], suggesting metabolic development of CO_2 is not impaired in CF, and it may be the V_D/V_T ratio responsible for reduced OUES – a suggestion proposed, and supported by, previous research [9]. Given the progressive decline in lung function with age in CF, due to bronchiectasis and airway obstruction [27], such pulmonary impairments may contribute towards elevated dead space ventilation in CF [28], thus impacting upon OUES. As this decline in lung function is observed with age [29], this may account for the discrepancy observed between the current research and previous OUES analyses in adults with CF [8]. Furthermore, given that the majority of patients in this study had mild-to-moderate CF (FEV_1 > 70% predicted in 31/36 patients), it is unclear if the OUES will display a differing profile in patients with severe CF (FEV_1 < 40% predicted).

In conclusion, the OUES is not a valid submaximal surrogate of aerobic fitness in children and adolescents with CF. This research subsequently provides clinical teams with the clear evidence that only maximal markers of prognostic value (i.e. $\dot{V}O_{2max}$) should continue to be measured in patients with CF. Furthermore, continued research is required to identify submaximal variables that may hold clinical utility in this patient population when unable or unwilling to exercise to volitional exhaustion.

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CONFLICT OF INTEREST

The authors declare they have no conflict of interest.

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IMAGE LEGENDS

Figure 1. Comparison of OUES/BSA$^{1.40}$ values between children and adolescents with CF (black bars) and healthy age- and gender-matched controls (white bars) at different exercise thresholds.

Figure 2. Comparison of $\dot{V}O_{2max}$, split by $\dot{V}O_{2max}$ tertile (black bars = highest tertile, white bars = middle tertile, grey bars = lowest tertile), within the CF and healthy control groups. * Significant ($p < 0.01$) difference from highest tertile. † Significant ($p < 0.01$) difference from middle tertile. § Significant ($p < 0.05$) difference between groups.

Figure 3. Comparison of OUES/BSA$^{1.40}$ at 100% TTE and $OUES_{GET}$/BSA$^{1.40}$ split by $\dot{V}O_{2max}$ tertile (black bars = highest tertile, white bars = middle tertile, grey bars = lowest tertile), within the CF and healthy control groups. * Significant ($p < 0.05$) difference from highest tertile. † Significant ($p < 0.05$) difference from middle tertiles.

Table 1. Anthropometric, pulmonary function and exercise-related differences between CF and CON groups.

Variable	CF	CON	*p* value	Effect Size
Stature (cm)	155.6 (13.5)	159.1 (15.2)	0.32	0.24
Body mass (kg)	50.15 (15.46)	51.15 (14.49)	0.78	0.07
BMI ($kg·m^{-2}$)	20.28 (3.67)	19.91 (4.18)	0.70	0.09
BSA (m^2)	1.46 (0.28)	1.49 (0.28)	0.65	0.11
aPHV	0.27 (2.70)	0.65 (2.44)	0.89	0.15
FEV_1 (L)*	2.46 (0.97)	2.96 (0.86)	0.07	0.53
FEV_1 (% Predicted)*	88.0 (19.6)	101.9 (12.2)	**0.002**	0.79
FVC (L)*	3.10 (1.14)	3.44 (1.02)	0.30	0.31
FVC (% Predicted)*	94.8 (15.9)	100.2 (12.5)	0.21	0.36
$\dot{V}O_{2max}$ ($L·min^{-1}$)	1.74 (0.57)	2.03 (0.88)	0.093	0.39
$\dot{V}O_{2max}$ ($mL.kg^{-1}·min^{-1}$)	37.74 (7.74)	39.93 (10.70)	0.32	0.23
GET ($L·min^{-1}$)	0.91 (0.28)	1.12 (0.54)	**0.035**	0.49
GET (% $\dot{V}O_{2max}$)	53.4 (9.3)	55.0 (8.0)	0.42	0.18
HR_{max} ($beats·min^{-1}$)	182 (8)	185 (14)	0.30	0.26
$\dot{V}_{Emax}$ ($L·min^{-1}$)	74.66 (35.62)	69.18 (33.45)	0.50	0.16
RER_{max}	1.27 (0.23)	1.21 (0.13)	0.22	0.32

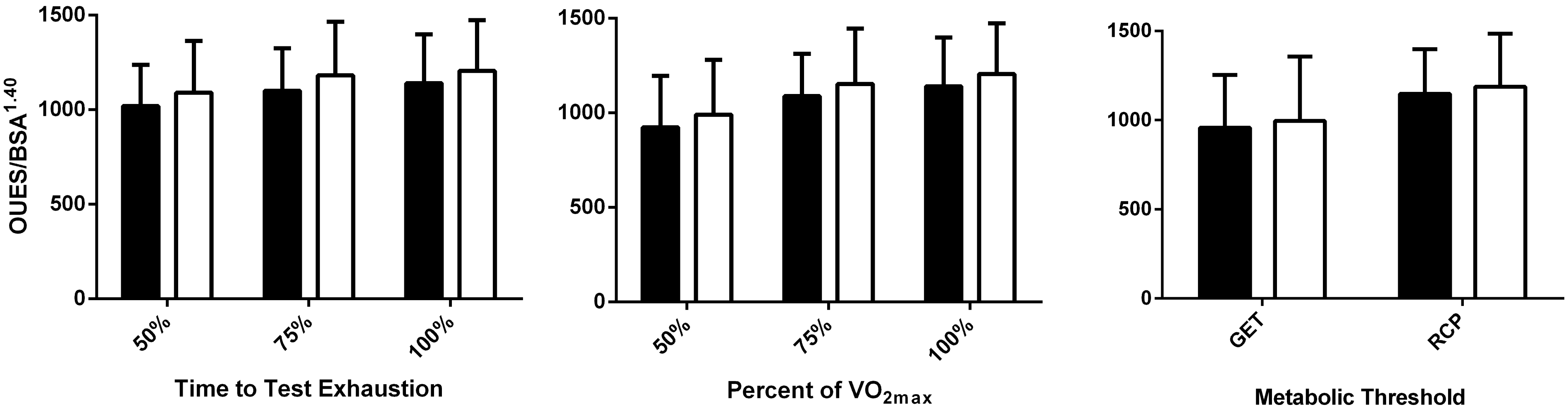
Measures are presented as mean (± SD). Significant mean diffeences are denoted by a bolded p vlaue. * Unequal groups for pulmonary volumes (CF, *n* = 36; CON, *n* = 18).

BMI: body mass index; BSA, body surface area; aPHV, age from peak height velocity; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; $\dot{V}O_{2max}$, maximal oxygen uptake; GET, gas exchange threshold; HR, heart rate; $\dot{V}_E$, minute ventilation; RER, respiratory exchange ratio.

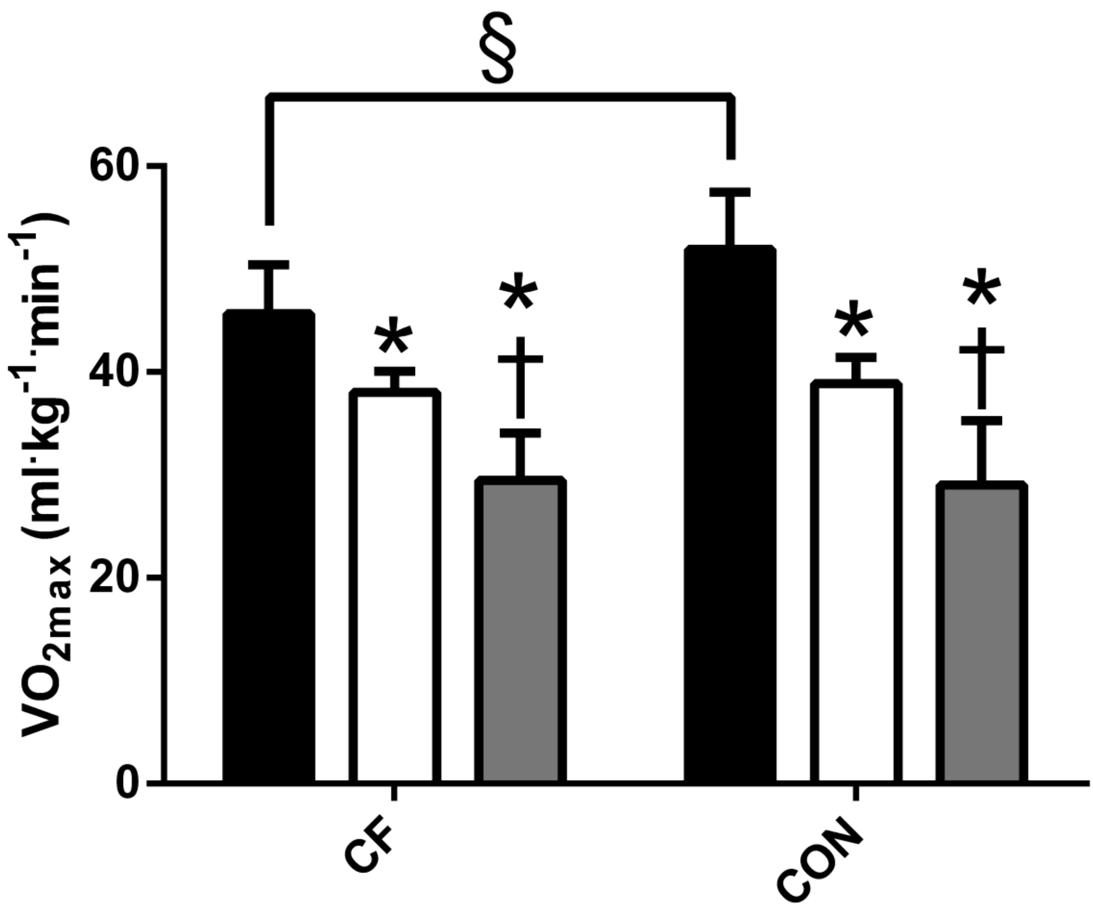
Table 2. Correlations at different thresholds between parameters of oxygen uptake and ventilatory efficicency and $\dot{V}O_{2max}$ relative to body mass.

Oxygen Uptake Parameter	CF	CON
OUES/$BSA^{1.40}$ @ 50% $\dot{V}O_{2max}$	0.36 (0.040)	0.75 (< 0.001)
OUES/$BSA^{1.40}$ @ $50\%_{TTE}$	0.30 (0.071)	0.76 (< 0.001)
OUES/$BSA^{1.40}$ @ 75%$\dot{V}O_{2max}$	0.33 (0.049)	0.85 (< 0.001)
OUES/$BSA^{1.40}$ @ $75\%_{TTE}$	0.38 (0.023)	0.87 (< 0.001)
OUES/$BSA^{1.40}$ @ 100%$\dot{V}O_{2max}$ & $_{TTE}$	0.47 (0.004)	0.89 (< 0.001)
OUES/$BSA^{1.40}$ @ GET	0.35 (0.042)	0.58 (< 0.001)
OUES/$BSA^{1.40}$ @ RCP	0.45 (0.007)	0.88 (< 0.001)

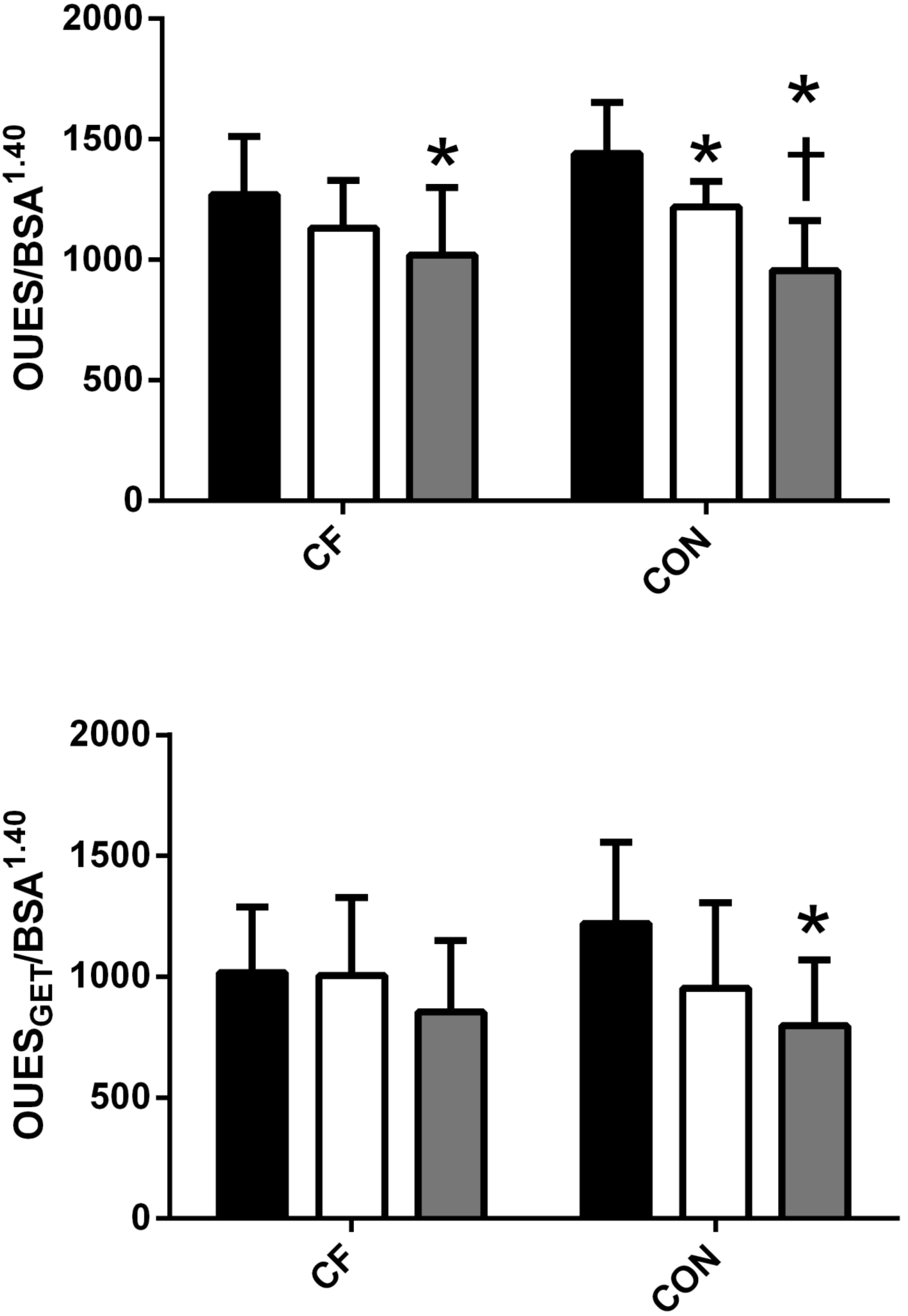
Values are presented as correlation coefficients (*r*) with *p* vlaues in parentheses.


OUES/BSA^1.40
1500
1000
500
0
50%
75%
100%
Time to Test Exhaustion
Percent of VO2max
GET
RCP
Metabolic Threshold

575



576


OUES/BSA^1.40
2000
1500
1000
500
0
CF
CON
*
*
*
†
OUES_GET/BSA^1.40
2000
1500
1000
500
0
CF
CON
*