

# Oxygen Uptake Efficiency During Cardiopulmonary Exercise Testing in Adolescents with Cystic Fibrosis

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## ABSTRACT

**Background** A high level of aerobic fitness, typically characterized by peak oxygen uptake (VO<sub>2</sub> peak), is associated with significant clinical benefits in young people with Cystic fibrosis. Higher VO<sub>2</sub> peak is linked to improved quality of life, reduced risk of hospitalization due to pulmonary exacerbations, and lower mortality risk. Consequently, regular cardiopulmonary exercise testing (CPET) is recommended by the European Cystic Fibrosis Society and endorsed by the European Respiratory Society to monitor aerobic fitness and guide clinical decision-making. Oxygen Uptake Efficiency (OUE) parameters have been proposed as potential submaximal surrogates for VO<sub>2</sub> peak; however, their clinical utility in pediatric cystic fibrosis remains unclear.

**Methods** Cardiopulmonary exercise test (CPET) data were collected from 72 children (36 with cystic fibrosis and 36 age- and sex-matched controls). OUE was assessed at three time points highest 90-second average (OUE plateau; OUEP), gas exchange threshold (OUEGET), and respiratory compensation point (OUERCP). Pearson's correlation coefficients, independent t-tests, and factorial ANOVAs were used to evaluate group differences and determine the suitability of OUE measures as surrogates for allometrically scaled VO<sub>2</sub> peak.

**Results** Children with cystic fibrosis demonstrated significantly lower ( $p < 0.05$ ) allometrically scaled VO<sub>2</sub> peak and all OUE parameters compared with controls. Significant moderate correlations ( $p < 0.05$ ) were observed between OUE parameters and allometrically scaled VO<sub>2</sub> peak in both cystic fibrosis ( $r = 0.49-0.52$ ) and control groups ( $r = 0.46-0.52$ ). In the cystic fibrosis group, OUE parameters were also significantly correlated with pulmonary function (FEV<sub>1</sub> % predicted;  $r = 0.38-0.46$ ), whereas no such relationship was observed in controls ( $r = -0.20-0.14$ ). OUEP differentiated aerobic fitness tertials in controls but not in participants with cystic fibrosis.

**Conclusion** Oxygen Uptake Efficiency parameters are reduced in children and adolescents with cystic fibrosis but do not represent suitable surrogates for VO<sub>2</sub> peak. Where feasible, clinical teams should continue to prioritise maximal CPET-derived parameters to assess aerobic fitness. Future research should explore the prognostic value of OUEP, as it appears sensitive to disease status and severity.

**Keywords** Adolescence; Aerobic fitness; Cardiopulmonary exercise testing; Paediatrics; Respiratory disease.

**INTRODUCTION** Cystic fibrosis (CF) is one of the most common life-limiting autosomal recessive disorders, affecting approximately 1 in 2,500 live births in populations of European descent. It is caused by mutations in the CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) gene located on chromosome 7q31.2. The CFTR protein functions as a chloride and bicarbonate channel in epithelial cells lining the airways, pancreas, intestines, hepatobiliary system, sweat glands, and reproductive ducts.<sup>1</sup>

Defective or absent CFTR protein results in impaired chloride secretion and increased sodium and water reabsorption, leading to dehydrated, thick, and viscous secretions. In the respiratory system, accumulation of thick mucus causes airway obstruction, chronic infection, inflammation, and progressive airflow limitation. These pulmonary complications remain the leading cause of morbidity and mortality in individuals with CF. Although advances such as CFTR modulators, improved antimicrobial therapy, and airway clearance techniques have significantly increased survival, preserving pulmonary function and aerobic fitness remains central to long-term health and quality of life.<sup>2</sup>

Aerobic fitness reflects the integrated function of the respiratory, cardiovascular, and muscular systems to transport and utilize oxygen during exercise. It is commonly measured as peak oxygen uptake ( $\text{VO}_2$  peak) during cardiopulmonary exercise testing (CPET) and is considered the gold standard indicator of aerobic capacity.<sup>3</sup> Higher  $\text{VO}_2$  peak values in CF are associated with slower pulmonary decline, fewer exacerbations, improved quality of life, and greater survival. For this reason, the European Cystic Fibrosis Society and European Respiratory Society recommend routine CPET assessment to monitor disease progression and therapeutic response.<sup>3</sup>

However, achieving maximal effort during CPET can be challenging, particularly in children and adolescents due to dyspnea, fatigue, anxiety, or advanced lung disease. These limitations may compromise the accuracy of  $\text{VO}_2$  peak measurement and highlight the need for reliable submaximal exercise parameters.<sup>4</sup>

Oxygen Uptake Efficiency (OUE), defined as the ratio of oxygen uptake ( $\text{VO}_2$ ) to ventilation (VE), has emerged as a promising submaximal marker of cardiopulmonary performance. Unlike the Oxygen Uptake Efficiency Slope (OUES), OUE preserves the natural curvilinear  $\text{VO}_2$ –VE relationship and does not require logarithmic transformation. OUE demonstrates lower variability, good reproducibility, and can be measured at any stage of incremental exercise.<sup>5</sup>

The oxygen uptake efficiency plateau (OUEP), calculated as the highest 90-second average of  $\text{VO}_2/\text{VE}$ , typically occurs near the ventilatory or gas exchange threshold. This submaximal region reflects optimal oxygen extraction before the onset of metabolic acidosis. While OUEP has demonstrated prognostic value in cardiac populations, its clinical relevance in CF—particularly in pediatric patients—remains insufficiently explored.<sup>6</sup>

Children with CF frequently exhibit ventilatory inefficiency due to airway obstruction and ventilation–perfusion mismatch, making OUE a potentially sensitive indicator of disease severity.<sup>7</sup> Furthermore, with increasing use of CFTR modulator therapies, sensitive and non-invasive submaximal tools are needed to detect subtle improvements in aerobic function.<sup>7</sup>

CF is a multisystem disorder primarily affecting the respiratory and digestive systems. The airways are lined by ciliated epithelium and mucus-producing goblet cells that normally clear inhaled particles via the muco-ciliary escalator. In CF, thick secretions impair ciliary function, leading to mucus plugging, bronchiectasis, recurrent infections, fibrosis, and progressive destruction of lung parenchyma.<sup>8</sup> Pancreatic ducts become obstructed by thick secretions, causing exocrine insufficiency, malabsorption, steatorrhea, and failure to thrive. Progressive fibrosis may result in CF-related diabetes. Bile duct obstruction can lead to biliary cirrhosis and portal hypertension. Intestinal complications include meconium ileus in neonates and distal intestinal obstruction syndrome in older patients. Males commonly exhibit congenital bilateral absence of the vas deferens, resulting in obstructive azoospermia. Females may experience reduced fertility due to thick cervical mucus. Failure of chloride reabsorption leads to elevated salt concentration in sweat, a diagnostic hallmark of CF.<sup>9</sup>

CF follows an autosomal recessive inheritance pattern; affected individuals inherit two mutated CFTR alleles. Mutations may result in absent, misfolded, dysfunctional, or unstable CFTR protein, ultimately disrupting epithelial ion transport. The resulting dehydrated secretions underlie the multisystem clinical manifestations of the disease.<sup>10</sup>

CF presents as a multisystem disorder, Chronic cough, sputum production, recurrent infections (commonly *Staphylococcus aureus* and *Pseudomonas aeruginosa*), bronchiectasis, wheezing, dyspnea, nasal polyps, and progressive respiratory failure. And Pancreatic insufficiency, steatorrhea, malnutrition, fat-soluble vitamin deficiencies, distal intestinal obstruction syndrome. Hepatobiliary include Focal biliary cirrhosis and potential portal hypertension. Metabolic includes CF-related diabetes mellitus. And Other like Digital clubbing, osteopenia/osteoporosis, and electrolyte imbalance due to excessive salt loss.<sup>11</sup>

**Aim of the study** Is To evaluate oxygen uptake efficiency parameters as indicators of cardiopulmonary function in young people with Cystic fibrosis and to determine their relationship with disease severity and selected physiological variables.

**Objectives of the study** Is To assess oxygen uptake efficiency parameters — including Oxygen Uptake Efficiency Slope (OUES), Oxygen Uptake Efficiency Plateau (OUEP), and peak oxygen uptake ( $VO_2$  peak) — in young individuals with cystic fibrosis. Is To compare these parameters between young people with cystic fibrosis and age- and sex-matched healthy controls. Is To examine the relationship between oxygen uptake efficiency parameters and pulmonary function indices ( $FEV_1$ , FVC, and  $FEV_1/FVC$  ratio). Is To determine the association between oxygen uptake efficiency parameters and anthropometric or nutritional variables (e.g., BMI and body composition). Is To evaluate whether oxygen uptake efficiency parameters can serve as reliable submaximal indicators of exercise capacity and disease severity in young people with cystic fibrosis.

**Hypothesis**, Alternate Hypothesis ( $H_1$ )- There is a significant difference in oxygen uptake efficiency parameters (OUES, OUEP, and  $VO_2$  peak) between young people with cystic fibrosis and age- and sex-matched healthy controls. And Oxygen uptake efficiency parameters are significantly correlated with pulmonary function indices and anthropometric variables in young people with cystic fibrosis.

Null Hypothesis ( $H_0$ )- There is no significant difference in oxygen uptake efficiency parameters (OUES, OUEP, and  $VO_2$  peak) between young people with cystic fibrosis and age- and sex-matched healthy controls. And Oxygen uptake efficiency parameters are not significantly correlated with pulmonary function indices or anthropometric variables in young people with cystic fibrosis.

**Materials And Methodology** Study Design Simple Randomized Controlled Trial (RCT) to analyze oxygen uptake efficiency parameters in young individuals with Cystic fibrosis. A total of 72 participants were recruited based on predefined inclusion and exclusion criteria. In which 36 participants diagnosed with cystic fibrosis and 36 age- and sex-matched healthy controls. Study Setting- The study was conducted at the Outpatient Department of MNR Sanjeevani College of Physiotherapy. The duration of the study was 3 months.

**Inclusion Criteria** Age: 10–25 years, **Diagnosis:** Clinically confirmed cystic fibrosis (positive sweat chloride test and/or CFTR gene mutation), **Clinical Stability:** No acute pulmonary exacerbation within 4 weeks prior to testing, **Pulmonary Function:** Mild to moderate disease severity ( $FEV_1 \geq 40\%$  predicted), **Informed Consent with Participant Information Sheet:** Written informed consent from participants (and parental/guardian consent for minors), **Exercise Capability:** Physically able and willing to perform incremental exercise testing. **Exclusion Criteria** Severe Pulmonary Disease:  $FEV_1 < 40\%$  predicted or resting  $SpO_2 < 90\%$ , **Recent Exacerbation:** Respiratory infection requiring antibiotics within the past 4 weeks, **Cardiovascular Contraindications:** Known cardiac disease, arrhythmias, or contraindications to exercise testing, **Musculoskeletal/Neurological Disorders:** Conditions limiting exercise performance, **Other Chronic Illnesses:** Significant comorbidities affecting exercise tolerance, **Medication Interference:** Use of drugs significantly altering heart rate or ventilatory responses (e.g., beta-blockers)

**Materials Used** were Stadiometer, Digital weighing scale, BMI calculator, Measuring tape, Skinfold calipers, Spirometer, Mouthpiece with bacterial filter, Nose clip, Pulse oximeter, Cycle ergometer or treadmill, Metabolic cart (breath-by-breath analysis system), Heart rate monitor / ECG, Face mask or mouthpiece with flow sensor.

Outcome Measures, Primary Outcomes were Oxygen Uptake Efficiency Slope (OUES), Oxygen Uptake Efficiency Plateau (OUEP) and Peak Oxygen Uptake ( $\text{VO}_2$  peak). Secondary Outcomes Were Body Mass Index (BMI), Pulmonary Function Test parameters ( $\text{FEV}_1$ , FVC,  $\text{FEV}_1/\text{FVC}$  ratio), Quality of Life Assessment – SF-36 Questionnaire.

## Research Protocol/ Procedure

### Step 1: Participant Identification

Participants were identified through referrals to the outpatient department.

### Step 2: Screening

Eligibility was assessed according to inclusion and exclusion criteria.

### Step 3: Informed Consent

Written informed consent was obtained from all participants (and guardians where applicable).

### Step 4: Baseline Assessment

- Demographic data collection
- Anthropometric measurements (Height, Weight, BMI)
- Pulmonary Function Testing ( $\text{FEV}_1$ , FVC,  $\text{FEV}_1/\text{FVC}$  ratio)

### Step 5: Cardiopulmonary Exercise Testing (CPET)

Participants performed an incremental exercise test on a cycle ergometer or treadmill following standardized CPET protocol.

#### Parameters recorded:

- $\text{VO}_2$  (oxygen uptake)
- $\text{VCO}_2$  (carbon dioxide output)
- VE (minute ventilation)
- Heart rate
- $\text{SpO}_2$
- Blood pressure

Breath-by-breath gas exchange analysis was conducted using a calibrated metabolic cart.

### Step 6: Data Processing

The following parameters were calculated from CPET data:

- **OUES:** Derived from the linear regression of  $\text{VO}_2$  against  $\log_{10}\text{VE}$
- **OUEP:** Highest 90-second averaged  $\text{VO}_2/\text{VE}$  ratio
- **$\text{VO}_2$  peak:** Highest oxygen uptake achieved during exercise

### Step 7: Statistical Analysis

- Independent t-tests used to compare groups
- Pearson correlation coefficients to assess relationships

- ANOVA where appropriate
- Statistical significance set at  $p < 0.05$

**Statistical Analysis** Data was analyzed using appropriate statistical software. Descriptive statistics were presented as mean  $\pm$  standard deviation (SD). Normality of distribution was assessed prior to inferential testing. Independent sample t-tests were used to compare differences between the cystic fibrosis (CF) and control (CON) groups. Pearson's correlation coefficients ( $r$ ) were calculated to determine relationships between oxygen uptake efficiency (OUE) parameters, peak oxygen uptake ( $VO_{2\text{peak}}$ ), and pulmonary function ( $FEV_1$ ). Factorial ANOVA was performed to examine differences across aerobic fitness tertiles and disease groups. Effect sizes (ES) were calculated to determine the magnitude of differences. Statistical significance was set at  $p < 0.05$ . Unequal sample sizes were noted for certain pulmonary variables (CF = 36, CON = 18 where applicable).

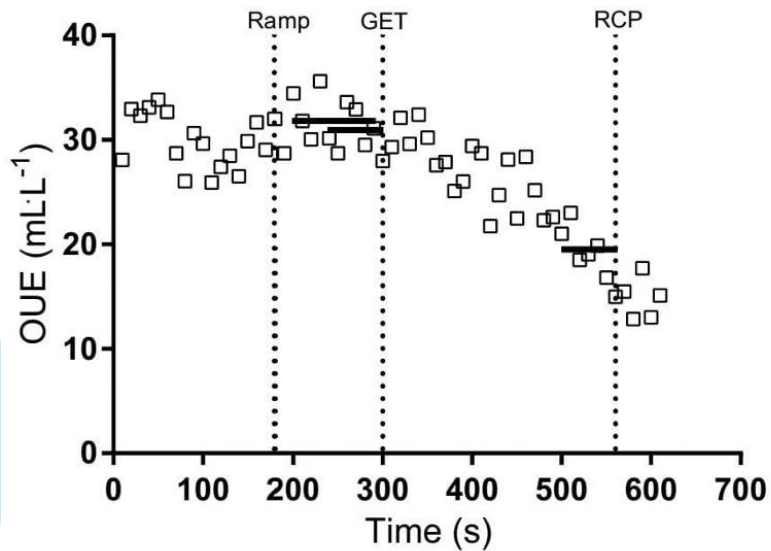
**Table 1** Correlations between OUE parameters,  $VO_{2\text{peak}}$ , and  $FEV_1$  in CF, CON, and Combined Groups. Values are presented as correlation coefficients ( $r$ ) with corresponding p-values in parentheses. Bold values indicate statistically significant correlations ( $p < 0.05$ ).

	CF	CON	Combined
Absolute $VO_{2\text{peak}}$ (L $\text{min}^{-1}$ )	0.22	0.40	0.41
OUE <sub>GET</sub>	0.36	0.29	0.28
OUE <sub>RCP</sub>	0.12	0.42	0.44
OUEP	0.43	0.12	0.24
OUEP(%predicted)			
Allometrically scaled $VO_{2\text{peak}}$ ( $\text{mL} \cdot 0.86 \cdot \text{min}^{-1}$ )			
OUE <sub>GET</sub>	0.49	0.46	0.51
OUE <sub>RCP</sub>	0.31	0.24	0.35
OUEP	0.52	0.52	0.54
OUEP(%predicted)	0.49	0.38	0.47
$FEV_1$ (%predicted)			
OUE <sub>GET</sub>	0.38	-0.06	0.44
OUE <sub>RCP</sub>	0.07	0.14	0.24
OUEP	0.43	-0.20	0.43
OUEP(%predicted)	0.46	-0.19	0.44

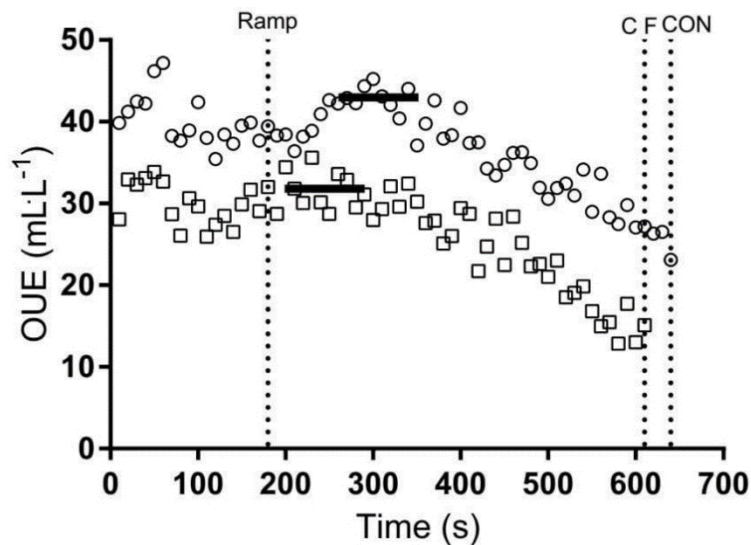
**Table 2** Anthropometric, Pulmonary Function, and Exercise-Related Differences Between CF and CON Groups. Data are presented as mean  $\pm$  SD. Significant differences are indicated by bold p-values. ES = Effect Size.

Variable	CF	CON	p value	ES
Age (years)	13.4 (2.7)	13.2 (2.9)	0.77	0.08
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)	20.28 (3.67)	19.91 (4.18)	0.7	0.09
BSA (m <sup>2</sup> )	1.46 (0.28)	1.49 (0.28)	0.65	0.11
FEV <sub>1</sub> (L)*	2.46 (0.97)	2.96 (0.86)	0.07	0.55
FEV <sub>1</sub> (% <sub>predicted</sub> ) *	85.0 (20.0)	97.5 (10.6)	<b>0.004</b>	0.71
FVC (L)*	3.10 (1.14)	3.44 (1.02)	0.3	0.31
FVC (% <sub>predicted</sub> ) *	92.7 (16.6)	98.6 (11.0)	0.18	0.39
MVV (L min <sup>-1</sup> ) *	86.2 (34.0)	103.6 (30.0)	0.07	0.53
V'O <sub>2</sub> peak (L min <sup>-1</sup> )	1.74 (0.57)	2.03 (0.88)	0.09	0.39
V'O <sub>2</sub> peak (mL kg <sup>-1</sup> min <sup>-1</sup> )	37.74 (7.74)	39.93 (10.70)	0.32	0.23
V'O <sub>2</sub> peak (mL kg <sup>-0.86</sup> min <sup>-1</sup> )	74.62 (15.21)	84.94 (23.51)	<b>0.031</b>	0.52
Relative V'O <sub>2</sub> peak (% <sub>predicted</sub> )	83.3 (16.8)	87.8 (20.8)	0.32	0.24
GET (L min <sup>-1</sup> )	0.91 (0.28)	1.12 (0.54)	0.035	0.49
GET (% V'O <sub>2</sub> peak)	53.4 (9.3)	55.0 (8.0)	0.42	0.18
HR <sub>max</sub> (beats min <sup>-1</sup> )	182 (8)	185 (14)	0.3	0.26
V'E <sub>max</sub> (L min <sup>-1</sup> )	74.66 (35.62)	69.18 (33.45)	0.5	0.16
V'E <sub>max</sub> (% MVV) *	88.3 (30.4)	60.9 (23.3)	0.001	0.97
OUEP (mL L <sup>-1</sup> )	35.58 (5.40)	45.09 (5.78)	< 0.001	1.7
OUE <sub>GET</sub> (mL L <sup>-1</sup> )	34.08 (5.40)	43.24 (5.08)	< 0.001	1.75
OUE <sub>RCP</sub> (mL L <sup>-1</sup> )	29.49 (4.95)	35.15 (4.52)	< 0.001	1.19
OUEP (% <sub>predicted</sub> )	83.2 (13.9)	105.7 (13.0)	< 0.001	1.68

**Results** Detection of OUE Parameters. All OUE outcomes were successfully identified in 68 of 72 participants (94%). In the CF group: OUEGET and OUERCP were detected in 35/36 participants (97%). In the CON group: OUEGET was detected in 36/36 participants (100%). OUERCP was detected in 34/36 participants (94%). A representative CPET profile illustrating OUEP, OUEGET, and OUERCP in a participant with CF is shown below.

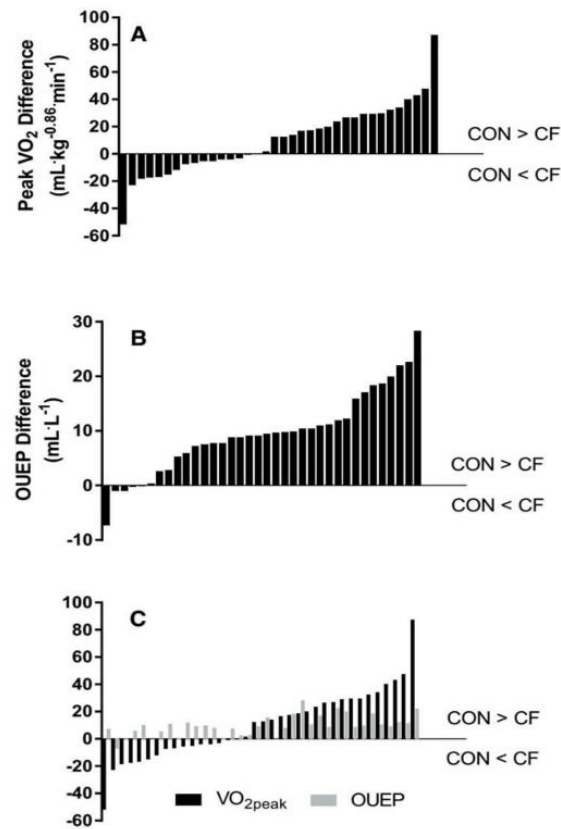


A representative comparison of OUEP between CF and CON participants is shown below.



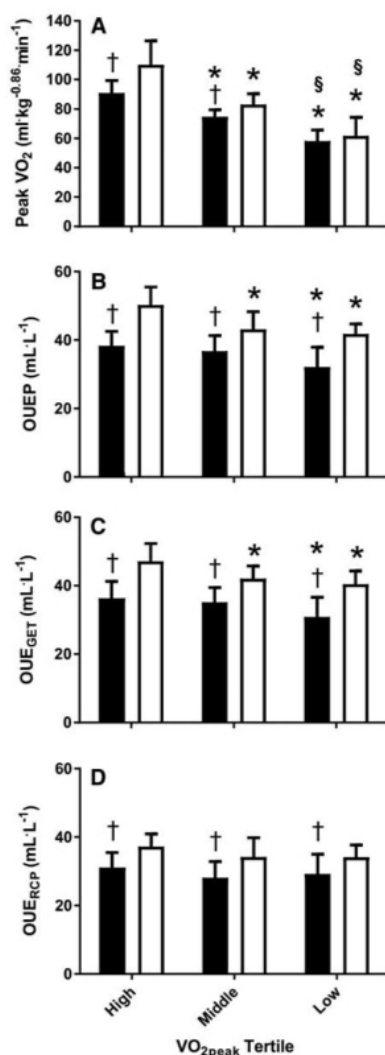
Differences in OUE Between Groups Significant differences were observed between groups for: Pulmonary function, Absolute Gas Exchange Threshold (GET), OUEGET, OUE<sub>RCP</sub>, OUE<sub>P</sub>, in all cases, the CON group demonstrated significantly higher values than the CF group. No significant difference was observed for absolute  $\dot{V}O_2$  peak ( $L \cdot \text{min}^{-1}$ ). However, when  $\dot{V}O_2$  peak was expressed using allometric scaling ( $\text{mL} \cdot \text{kg}^{-0.86} \cdot \text{min}^{-1}$ ), the CON group demonstrated significantly higher values ( $p < 0.05$ ). (Refer to Table 2)

Individual paired differences in allometrically scaled  $\text{VO}_2$  peak and OUEP are illustrated below.



Correlation Between OUE and  $\text{VO}_2$  peak- OUEP and OUEGET showed significant positive correlations with, Absolute  $\text{VO}_2$  peak in both CF and CON groups, Allometrically scaled  $\text{VO}_2$  peak in both CF and CON groups, OUEP did not demonstrate consistent correlation with  $\text{VO}_2$  peak in either group. (Refer to Table 1)

Differences Between Aerobic Fitness Tertiles- Participants were divided into tertiles based on allometrically scaled  $\text{VO}_2$  peak. Significant differences in aerobic fitness were observed between tertiles within both CF and CON groups ( $p < 0.05$ ). Between-group comparisons revealed: Significant differences in the high and middle tertiles and No significant difference in the lowest tertile. When assessing OUEP: Significant main effects were found for group ( $p < 0.001$ ), Significant main effects were found for fitness tertile ( $p < 0.001$ ), No significant interaction effect between group and fitness tertile. Pairwise comparisons demonstrated significantly lower OUEP values in CF compared to CON across all fitness tertiles.



For OUEGET: Significant main effects for group and fitness tertile were observed. For OUE<sub>RCP</sub>: Significant group differences were observed. No significant fitness tertile effect was detected. Relationship with Disease Severity (FEV<sub>1</sub>) Within the CF group: OUEP and OUEGET were significantly correlated with FEV<sub>1</sub> (% predicted). OUE<sub>RCP</sub> was not significantly correlated with FEV<sub>1</sub>. Allometrically scaled VO<sub>2</sub> peak was significantly correlated with FEV<sub>1</sub> ( $r = 0.46$ ,  $p = 0.004$ ). Within the CON group: No significant correlations were observed between OUE parameters and FEV<sub>1</sub>. (Refer to Table 1)

**Discussion** This study examined oxygen uptake efficiency (OUE) parameters in children and adolescents with Cystic fibrosis (CF) and compared them with healthy controls. The main finding was that all OUE measures were significantly lower in the CF group. Although OUE parameters showed moderate positive correlations with peak oxygen uptake (VO<sub>2</sub>peak), they could not fully replace VO<sub>2</sub>peak as a direct surrogate of aerobic fitness. However, OUE—particularly the oxygen uptake efficiency plateau (OUEP)—demonstrated important clinical value as an independent marker of ventilatory efficiency and disease severity.<sup>12,13</sup>

A key observation was that OUEP was reduced in most individuals with CF, even in cases where VO<sub>2</sub> peak was similar to or higher than matched healthy peers. This indicates that oxygen uptake efficiency is impaired in CF regardless of overall aerobic fitness level. In other words, even when children with CF achieve comparable peak performance, their bodies may use oxygen less efficiently during exercise. This highlights that OUE reflects underlying physiological limitations rather than just performance capacity.<sup>14,15</sup>

The study also found significant relationships between OUE (especially OUEP and OUE at the gas exchange threshold) and lung function (FEV<sub>1</sub>%) within the CF group. Children with lower lung function had poorer oxygen uptake efficiency. This suggests that OUE is sensitive to disease severity and may provide additional

clinical insight beyond traditional pulmonary measures. Importantly, this relationship was not seen in healthy controls, reinforcing that OUE impairment is linked to CF-related pathophysiology.<sup>16,17</sup>

Although OUE parameters were moderately correlated with  $VO_2$ peak, their ability to distinguish between different aerobic fitness levels within the CF group was limited. While healthy controls with higher fitness had clearly higher OUEP values, this pattern was less consistent in the CF group.<sup>17,18</sup> Therefore, despite its association with aerobic fitness, OUEP cannot fully substitute  $VO_2$ peak for evaluating maximal exercise capacity.  $VO_2$ peak remains the gold standard for assessing aerobic fitness. One practical advantage of OUEP is its feasibility. It was successfully identified in nearly all participants and does not require maximal effort. Since  $VO_2$ peak testing depends on full exhaustion—which may not always be achievable due to fatigue, dyspnoea, or low motivation—OUEP provides a reliable submaximal alternative.<sup>19,20</sup> This makes it particularly useful in pediatric CF populations, where achieving true maximal effort can be challenging.

The findings also contribute to the limited body of research on oxygen uptake efficiency in young clinical populations. While OUE has been studied in adults with cardiac and pulmonary conditions, data in pediatric CF are scarce.<sup>21</sup> This study expands current knowledge by demonstrating that OUE parameters are reduced in CF and are meaningfully associated with both fitness and lung function.<sup>22</sup> However, some considerations are important. The study focused primarily on individuals with mild-to-moderate CF, so results may not apply to those with severe disease. Additionally, aerobic fitness in the control group was slightly lower compared to values reported in some previous studies, which may have influenced comparisons. Sample size and cross-sectional design also limit conclusions about long-term prognostic value.<sup>23,24</sup>

**Summary** Cystic fibrosis (CF) is a genetic condition that mainly affects the lungs and digestive system. It causes thick mucus buildup in the airways, leading to breathing difficulties, repeated infections, and gradual loss of lung function. Although medical treatment has improved survival, many young people with CF still experience reduced exercise capacity and lower aerobic fitness. Aerobic fitness is important because it is closely linked to overall health, disease progression, and long-term outcomes.<sup>26</sup> Aerobic fitness is usually measured using peak oxygen uptake ( $VO_2$  peak) during a cardiopulmonary exercise test (CPET).  $VO_2$  peak is considered the gold standard measure of fitness. However, it requires maximal effort, which can be difficult for children and adolescents with CF. Breathlessness, fatigue, anxiety, or lack of motivation may prevent them from reaching true maximal effort.<sup>27</sup> As a result,  $VO_2$  peak may sometimes underestimate their actual fitness level.

Because of these challenges, researchers are interested in submaximal exercise measures that do not require full exhaustion. One such measure is Oxygen Uptake Efficiency (OUE). OUE looks at how effectively the body uses oxygen compared to the amount of air being breathed (ventilation).<sup>28</sup> Related measures include Oxygen Uptake Efficiency Plateau (OUEP) and Oxygen Uptake Efficiency Slope (OUES). These values are calculated during exercise but do not depend on achieving maximum effort.<sup>29,30</sup>

This study aimed to examine OUE parameters in children and adolescents with mild-to-moderate CF and compare them with healthy individuals of similar age and sex. It also investigated whether OUE measures could act as substitutes for  $VO_2$  peak and whether they were related to disease severity, measured by lung function ( $FEV_1\%$ ).<sup>31,32</sup> The results showed that OUE, OUEP, and other oxygen uptake efficiency parameters were significantly lower in young people with CF compared to healthy controls. This indicates that children with CF have reduced ventilatory efficiency, meaning their bodies must work harder to use oxygen during exercise.<sup>33</sup>

OUEP and OUE showed moderate positive correlations with  $VO_2$  peak. This means that individuals with higher aerobic fitness generally had better oxygen uptake efficiency. However, OUE could not fully replace  $VO_2$  peak as a direct substitute for measuring aerobic fitness.<sup>34</sup> While related, the two measures are not identical. Importantly, OUEP and OUE were significantly associated with lung function ( $FEV_1\%$ ) in the CF group. Children with poorer lung function tended to have lower oxygen uptake efficiency. This suggests that OUE reflects disease severity and may provide useful clinical information beyond simple fitness measurement.<sup>35</sup>

Another important finding was that OUEP could be identified in almost all participants, making it a practical and reliable measure. Unlike VO<sub>2</sub> peak, it does not require maximal effort. This makes it especially useful in clinical settings where some patients may not be able or willing to exercise to exhaustion.<sup>36</sup> Overall, the study suggests that oxygen uptake efficiency parameters—particularly OUE and OUEP—are valuable submaximal indicators of aerobic performance in young people with CF.<sup>37</sup> Although they cannot completely replace VO<sub>2</sub> peak, they provide meaningful information about ventilatory efficiency, fitness level, and disease severity. In clinical practice, OUE measures could help monitor disease progression, evaluate response to treatment, and guide exercise prescription without requiring maximal testing.<sup>38,39</sup> This is especially important in pediatric populations, where comfort, safety, and cooperation are key considerations.

In conclusion, oxygen uptake efficiency analysis offers a practical, safe, and informative approach to assessing exercise capacity in young individuals with cystic fibrosis. By focusing on submaximal performance rather than maximal exhaustion, healthcare professionals can obtain reliable physiological information while reducing strain on patients. Integrating OUE measures into routine assessment may improve long-term monitoring and support better health outcomes for young people living with CF.

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