‘Oxygen uptake efficiency slope’ in trained and untrained subjects exposed to hypoxia

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Abstract

We assessed the ability of the oxygen uptake efficiency slope, whether calculated on 100 and 80% of maximal exercise test duration (OUES100 and OUES80), to identify the change in cardiorespiratory capacities in response to hypoxia in subjects with a broad range of VO2peak. Four maximal exercise tests were performed in trained (T) and untrained subjects (UT) in normoxia and at 1000, 2500 and 4500 m. The mean reductions in maximal exercise capacities at 4500 m were the same in T subjects for VO2peak but VO2maximal index of cardiorespiratory functional reserve (VO2peak/V̇Epeak), its dependence towards the duration of the test is limited (Baba et al., 1996; Defoor et al., 2006; Hollenberg and Tager, 2000, 2007). The OUES corresponds to the rate of increase in oxygen uptake (V̇O2) in response to ventilation (V̇E) during an incremental exercise test (V̇O2 = OUES × log 10 V̇E + b). Derived from the logarithmic relation between V̇O2 and V̇E, its dependence towards the duration of the test is limited and OUES could be used in subjects unable to perform a really maximal incremental exercise (Van Laethem et al., 2005). This index has been used to assess aerobic fitness and cardiorespiratory function in young healthy subjects (Baba, 2000; Baba et al., 1999; Mourot et al., 2004; Pichon et al., 2002), elderly subjects (Barnes et al., 2003; Hollenberg et al., 2003; Pogliaghi et al., 2007) and in a number of pathologies such as chronic heart failure or ischemia (Baba et al., 1999; Davies et al., 2006; Defoor et al., 2006; Guazzi et al., 2004; Van Laethem et al., 2005, 2006), depression (Hollenberg and Tager, 2000), obesity (Marinov and Kostianev, 2003) or renal deficiency (Tsuyuki et al., 2003). The OUES, even if calculated from only part of the test, is reproducible, reliable and highly correlated with the peak oxygen uptake (VO2peak) or with the ventilatory anaerobic threshold (VAT) (Baba et al., 1999; Defoor et al., 2006; Hollenberg and Tager, 2000). However, the interchangeability of OUES with VO2peak or VAT has been shown to be limited in a large population of healthy (Pichon et al., 2002) or elderly subjects with ischemic heart disease (Van Laethem et al., 2006). Neither the effects of hypoxemia in patients nor the environmental conditions of the test (hypoxia vs. normoxia) on the validity of OUES have been evaluated yet (Agostoni, 2006).

The OUES, as proposed by Baba et al. (1996), represents how efficiently oxygen is extracted and taken into the body from the air. They proposed that OUES would be linked to the develop-
ment of metabolic acidosis and to the physiologic dead space. However, it seems obvious that OUES would be affected by all parameters acting on both $\dot{V}_O_2$ and $V_E$ during incremental exercise. Significant decrements in $V_{O_2,peak}$ have been reported for subjects exposed to acute hypoxia when compared to sea level, mainly because of a decrease in oxygen delivery, caused by a drop in arterial oxygen partial pressure ($P_{O_2}$) that cannot be fully compensated by an increase in $O_2$ extraction (Ferretti et al., 1997; Mollard et al., 2007a,b). Ventilation is also modified in hypoxic conditions at sub-maximal and maximal intensities. Physical training could also enhance the drop in $\dot{V}_{O_2,peak}$ during hypoxia due to a lower mixed venous $O_2$ pressure and a greater diffusion limitation (Woorons et al., 2005). These changes in $V_{O_2,peak}$ and $V_E$ during hypoxia and training could modify extensively the values of OUES. Therefore, hypoxia represents an interesting stimulus to evaluate the responsiveness of OUES in hypoxic subjects with a broad range of $V_{O_2,peak}$.

Hence, we assessed if the OUES calculated on 100 and 80% of the test duration ($OUES_{100}$ and $OUES_{80}$) is able to identify the change in cardiorespiratory capacities in response to hypoxia.

2. Methods

2.1. Subjects

In this study we used data obtained in 10 trained (T) and 14 untrained (UT) men, without known cardiac, respiratory or other disease. The 24 subjects were all sea level natives and residents. None of the subjects were on medication. A physical examination and a 12-lead ECG were performed before the exercise test. The subjects gave their written consent after receiving explanations about the aims and risks of maximal exercise test. This study was approved by Necker’s hospital ethical committee. The T subjects were runners or triathletes with at least four training sessions per week. Subjects were asked to avoid strenuous physical activity 48 h before the tests. Part of the data obtained during this study has already been published (Mollard et al., 2007b; Woorons et al., 2006).

2.2. Protocol

Subjects performed four maximal exercise tests on a cycle ergometer (Jaeger ER 800, Würzburg, Germany) in two different sessions. Each session, composed by two tests and separated by 3 h of rest with a light lunch, was separated by 7 days. The first test of the first session was always carried out in normoxia (inspired oxygen fraction ($F_{I,O_2}$) = 0.209, inspired oxygen pressure ($P_{O_2}$) = 150 mmHg). In the other tests, which were randomly assigned, we used a $F_{I,O_2}$ of 0.187, 0.154, and 0.117 ($P_{O_2}$ of 132, 108, and 81 mmHg, respectively) for the simulated altitudes of 1000, 2500 and 4500 m, respectively. Altitude was simulated using the AltiTrainer200® (S.M. TEC, Geneva, Switzerland) which produces a normobaric hypoxic mixture (reduced oxygen fraction) by addition of nitrogen in ambient air with a short response time (between 15 and 50 s). The gas mixture passes through a 30 L buffer tank before being inhaled by the subjects. An $O_2$ probe (electrochemical $O_2$ probe MOX3, City technology, Portsmouth, UK) continuously controls the $O_2$ partial pressure of the inhaled gas mixture. The maximal difference between the $P_{O_2}$ measured by the AltiTrainer200® $O_2$ probe and the $P_{O_2}$ calculated from the $O_2$ fraction measured by an external probe (Servomex 720A, Geneva, Switzerland) is less than 1 mmHg over the whole range of $P_{O_2}$ (150–69 mmHg). This device is reliable for altitudes below 5500 m and ventilation lower than 200 L min$^{-1}$.

2.3. Incremental exercise test

Before exercise, the subjects breathed the desired gas mixture for at least 5 min. Then the exercise test began with a 3-min warm-up at a power output (PO) of 60 W. Thereafter, PO was increased by 30 W every 2 min, until the subjects could no longer maintain a pedalling frequency of 70 rpm. The subjects were verbally encouraged to continue exercising as long as possible.

We used a rigid mouthpiece connected to a “Y” system fixation with a two-way non-rebreathing valve (Jaeger, Würzburg, Germany). An inspiratory valve, connected to the AltiTrainer200® allowed the subject to inhale the hypoxic mixture. Expired gases were collected into a metabograph (Oxycon, Jaeger, Würzburg, Germany) to measure expired minute volume of gas at body temperature and pressure saturated ($V_{E,TPS}$) and $V_{O_2}$- Electrocardiogram and heart rate ($f_H$) were recorded continuously. Transcutaneous arterial $O_2$ saturation ($S_{PO_2}$) was assessed by an ear pulse oximeter (Ohmeda Biox 3740, Louisville, CO, USA) after ear lobe vasodilation with a capsaicin cream (Disalgyl® Monin). The breath-by-breath measurements and $S_{PO_2}$ were averaged over 30 s intervals. For assessment of $V_{O_2,peak}$, data were averaged over the two highest 30 s periods, and at least two of the classical criteria were met. These criteria were (i) stabilization of $\dot{V}_{O_2}$ despite a further increase in workload (−150 mL increase over 2 min), (ii) lactate concentration at peak exercise >9 mmol L$^{-1}$, and (iii) a $R > 1.1$. The first step reached at $\dot{V}_{O_2,peak}$ was taken as the power at $\dot{V}_{O_2,peak}$ ($P_{\dot{V}_{O_2,peak}}$).

2.4. Cardiovascular parameters

We used a bioimpedance method for determination of stroke volume and heart rate (Physioflow, Manatec Type PF05L1, Paris, France). The theoretical basis for this technique and its application and validity for exercise testing have been previously described (Charloux et al., 2000; Richalet et al., 2005). For this experiment, stroke volume (SV) and $f_H$ were measured continuously during each test with beat-to-beat data smoothed by a 5 s moving averaging algorithm. Cardiac output ($Q$) calculation by the device is based on the following formula: $Q = f_H \times SV_i \times BSA$ where $Q$ is expressed in L min$^{-1}$, the stroke volume index (SVi) in mL m$^{-2}$, and the body surface area (BSA) in m$^2$. The impedance cardiography provides accurate Q measurements during sub-maximal and maximal exercises (Charloux et al., 2000; Richalet et al., 2005; Richard et al., 2004; Welsman et al., 2005). Parameters of convective $O_2$ transport to the tissue were calculated at maximal exercise as follows: arterial $O_2$ content (ml L$^{-1}$):
CaO$_{2\text{max}}$ = [Hb] $\times$ 1.34 $\times$ SaO$_2$/100 (neglecting dissolved O$_2$). Capillary blood from a prewarmed earlobe with a vasodilating capsaicin cream (Disalgyl$^*$ Monin) was sampled at rest and at maximal exercise to measure hemoglobin concentration and other classical blood gases [Radiometer ABL 700, Copenhagen, Denmark]. When associated with V$_O_2$ measurements, it allows the estimation of the arterial-venous O$_2$ difference by the Fick equation (D(a-v)O$_2$ = V$_O_2$/O) and the determination of O$_2$ extraction (D(a-v)O$_2$ = CaO$_2$).

2.5. Determination of sub-maximal indices

The OUES reflects the relationship between oxygen uptake (V$_O_2$ in mL min$^{-1}$) and ventilation (L min$^{-1}$) and is best described by a single exponential function in almost all subjects. Using the values obtained over the entire test except the first 2 min (30 s averaging), the following formula was applied to the data from each subject: $V_{O_2} = a \times 10^{b E}$ where the constant ‘$a$’ was defined as the OUES$_{100}$ (OUES for 100% of the test). The OUES$_{80}$ was calculated using $V_{O_2}$ and $E$ values obtained up to 80% of the duration of the test before the $V_{O_2}$ peak.

The VAT was determined visually by two independent observers as the point at which the ventilatory equivalent for oxygen ($V_{VE}/V_{O_2}$) started to rise nonlinearly while the ventilatory equivalent for carbon dioxide ($V_{VE}/V_{CO_2}$) remained unchanged and the respiratory gas exchange ratio did not exceed 1.0 (Wasserman et al., 1973). VAT was expressed in mL min$^{-1}$ and normed by body mass. The power at VAT was also assessed ($P_{\text{VAT}}$).

2.6. Statistical analysis

The results are expressed as mean values ± S.D. Linear regression was used to fit the curve describing the relation between $V_{\text{O}_2,\text{peak}}$ and VAT in all the subjects, as well as the relations linking $V_{\text{O}_2,\text{peak}}$ to OUES$_{100}$ and to OUES$_{80}$. Pearson’s table was used to assess the significance of these inter-individual relationships. The parallelism of these relationships (slope and intercepts) between training status and altitudes was assessed using the Student ‘$t$’ test. Relationships between $V_{\text{O}_2,\text{peak}}$, OUES$_{100}$ or OUES$_{80}$ with cardiovascular variables (D(a-v)O$_2$, SV, Q, $f_R$), altitude and training status were assessed by regression analyses. Differences between the two groups of subjects (T and UT) and the four altitudes were assessed by using MANOVA with Greenhouse and Geisser adjustments. There is no effect of test order on any variables. The Newman–Keuls post hoc test was used to assess significant differences. Student ‘$t$’ test was used whenever appropriate. A $p$ value smaller than 0.05 was considered statistically significant.

3. Results

3.1. Maximal indices

The characteristics of the subjects were reported in Table 1. The T subjects showed greater values of $V_{\text{O}_2,\text{peak}}$, $P_{\text{O}_2,\text{peak}}$, OUES$_{100}$, OUES$_{80}$ and $P_{\text{VAT}}$ than UT subjects. Hypoxia induced a significant decrease in physical capacities from the simulated altitude of 2500 m (Fig. 1) with a greater decrease in T compared with UT subjects. The mean reductions in maximal exercise capacities at 4500 m were the same in T subjects for $V_{\text{O}_2,\text{peak}}$ ($-$30%), OUES$_{80}$ ($-$26%) and OUES$_{100}$ ($-$26%) whereas in UT subjects only OUES$_{100}$ ($-$14%), but not OUES$_{80}$ ($-$20%), was lower compared with $V_{\text{O}_2,\text{peak}}$ ($-$21%, $p < 0.05$). $V_{E,\text{max}}$ decreased progressively in T and UT subjects with simulated altitude (main effect, $p < 0.05$) whereas it remained significantly greater in T subjects (main effect, $p < 0.05$, Fig. 1).

3.2. Sub-maximal indices

$V_{\text{O}_2}$ and log 10 $V_{E}$ were significantly correlated with each other up to 80% $PV_{\text{O}_2,\text{peak}}$ and 100% $PV_{\text{O}_2,\text{peak}}$ and there was no effect of altitude or training on the coefficients of correlation between these two variables. The OUES$_{80}$ was similar to OUES$_{100}$ for all conditions (Fig. 1). We observed significant correlations ($p < 0.01$) between OUES$_{100}$ or OUES$_{80}$, $V_{\text{O}_2,\text{peak}}$ and VAT for all conditions (Table 2). However, the relation-

### Table 1

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Untrained subjects</th>
<th>Trained subjects</th>
<th>$p$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>27 ± 5</td>
<td>29 ± 5</td>
<td>$p=0.35$</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>178 ± 5</td>
<td>177 ± 9</td>
<td>$p=0.86$</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74 ± 9</td>
<td>72 ± 8</td>
<td>$p=0.69$</td>
</tr>
<tr>
<td>OUES$_{100}$</td>
<td>3233 ± 680</td>
<td>5358 ± 1888*</td>
<td>$p=0.0008$</td>
</tr>
<tr>
<td>OUES$_{80}$</td>
<td>3406 ± 715</td>
<td>5523 ± 1568*</td>
<td>$p=0.0021$</td>
</tr>
<tr>
<td>$V_{\text{O}_2,\text{peak}}$ (mL min$^{-1}$)</td>
<td>3207 ± 531</td>
<td>4718 ± 816*</td>
<td>$p=0.0001$</td>
</tr>
<tr>
<td>$V_{\text{O}_2,\text{peak}}$ (mL min$^{-1}$ kg$^{-1}$)</td>
<td>43 ± 5</td>
<td>65 ± 6*</td>
<td>$p=0.0001$</td>
</tr>
<tr>
<td>$P_{\text{VAT}}$ (W)</td>
<td>241 ± 43</td>
<td>344 ± 46*</td>
<td>$p=0.0001$</td>
</tr>
<tr>
<td>$f_R$ max (bpm)</td>
<td>191 ± 8</td>
<td>182 ± 9*</td>
<td>$p=0.021$</td>
</tr>
<tr>
<td>$R_{\text{max}}$</td>
<td>1.2 ± 0.1</td>
<td>1.2 ± 0.1</td>
<td>$p=0.39$</td>
</tr>
<tr>
<td>$V_{E,\text{max}}$ (L min$^{-1}$)</td>
<td>131 ± 30</td>
<td>147 ± 20</td>
<td>$p=0.17$</td>
</tr>
<tr>
<td>VAT (mL min$^{-1}$ kg$^{-1}$)</td>
<td>23.3 ± 6.2</td>
<td>40.4 ± 8.9*</td>
<td>$p=0.0001$</td>
</tr>
<tr>
<td>$P_{\text{VAT}}$ (W)</td>
<td>114 ± 43</td>
<td>197 ± 66*</td>
<td>$p=0.0008$</td>
</tr>
</tbody>
</table>

Values are mean ± S.D. OUES$_{100}$ and OUES$_{80}$, oxygen uptake efficiency slope calculated on 100% and 80% of the maximal exercises tests durations; $V_{\text{O}_2,\text{peak}}$, peak oxygen uptake; $PV_{\text{O}_2,\text{peak}}$, power at $V_{\text{O}_2,\text{peak}}$; $f_R$ max, maximal heart rate; $R_{\text{max}}$, maximal respiratory exchange ratio; $V_{E,\text{max}}$, maximal minute ventilation; VAT, ventilatory anaerobic threshold; $P_{\text{VAT}}$, power at the ventilatory anaerobic threshold. *Significantly different from untrained subjects.

### Table 2

<table>
<thead>
<tr>
<th>OUES$_{100}$</th>
<th>Untrained</th>
<th>0.825$^*$</th>
<th>0.759$^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trained</td>
<td>0.890$^*$</td>
<td>0.779$^*$</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OUES$_{80}$</th>
<th>Untrained</th>
<th>0.825$^*$</th>
<th>0.834$^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trained</td>
<td>0.854$^*$</td>
<td>0.702$^*$</td>
<td></td>
</tr>
</tbody>
</table>

*$^{p<0.05} ; ^{*p<0.01}$. 

### References

ship between $V_{O_2}^{\text{peak}}$ and OUES was highly influenced by the decrease in $P_{O_2}$ and this effect was more important in T subjects (Fig. 2). We observed that the slope of this relationships did not change significantly with the decrease in $P_{O_2}$ from 0 to 4500 m in UT subjects, whereas it decreased significantly in T subjects ($p < 0.05$).

### 3.3. Cardiovascular parameters

Hypoxia induced a decrease in D(a-v)$_{O_2}$ and Ca$_{O_2}$max in both UT and T subjects (Fig. 3). These changes were greater and appeared at a lower altitude in T subjects (2500 m) compared with UT ones (4500 m). Moreover, the D(a-v)$_{O_2}$/Ca$_{O_2}$max was significantly higher in T than in UT men whatever the simulated altitude. We also observed a main effect of altitude on the D(a-v)$_{O_2}$/Ca$_{O_2}$max which increased significantly at 4500 m. However, this rise compared with sea level values was mainly due to UT subjects (+14.7%) and only for a little part to T subjects (+3.7%). The $f_H^{\text{max}}$ was higher in UT than in T subjects ($p < 0.01$) and $f_H^{\text{max}}$ decreased with altitude in both groups by 5 and 8% at 2500 and 4500 m, respectively ($p < 0.001$) but remained significantly greater in UT subjects ($p < 0.001$). The maximal cardiac output and SV$_{\text{max}}$ were not significantly modified by simulated altitude.

Multiple regression analyses showed a significant link between the D(a-v)$_{O_2}$ and $V_{O_2}^{\text{peak}}$ ($r^2 = 0.97$, $dl = 6.42$, $F = 115.56$, $p < 0.001$), OUES$_{100}$ ($r^2 = 0.91$, $dl = 6.41$, $F = 31.6$, $p < 0.001$) and OUES$_{80}$ ($r^2 = 0.89$, $dl = 6.41$, $F = 25.98$, $p < 0.001$) but not to the other cardiovascular variables when all simulated altitudes were pooled. Simple regression analyses between D(a-v)$_{O_2}$ and OUES$_{100}$, OUES$_{80}$ and $V_{O_2}^{\text{peak}}$ are plotted in Fig. 4.

### 4. Discussion

Our study was designed to assess the responsiveness of the OUES to hypoxia in subjects with a broad range of cardiorespiratory fitness. We observed, with our model of maximal exercise in hypoxia, that OUES was highly influenced by $O_2$ availability and $O_2$ utilisation by active tissues. The lesser decrease of $V_E$ and $V_{O_2}^{\text{peak}}$ observed in untrained subjects in hypoxia compared with trained subjects is confirmed by changes in OUES values calculated on only 80% of the whole test duration. Therefore OUES could be considered as a sensible sub-maximal index to assess cardiorespiratory fitness in subjects with arterial hypoxemia.

There was no difference between OUES$_{100}$ and OUES$_{80}$ in T and UT subjects showing the utility of OUES as sub-maximal index of cardiopulmonary performance. As previously observed (Pichon et al., 2002), the regression coefficients between $V_{O_2}$ and log $V_E$ were higher for OUES$_{80}$. Indeed, the hyperpnoea observed during the last minute of maximal exercise could
Fig. 2. Relationships between $\dot{V}_O_2^{\text{peak}}$ and the oxygen uptake efficiency slope calculated on 80% of the maximal exercises tests (OUES$_{80}$) in untrained and trained subjects at simulated altitudes of 0 m (A), 1000 m (B), 2500 m (C) and 4500 m (D). Regression equations and coefficients of regression were reported.

Mourot et al. (2004) proposed that OUES is not sufficiently sensitive to assess training adaptation after 6 weeks of training in young and fit women (+7% for OUES$_{100}$, +9.1% for OUES$_{90}$ and +13.9% for OUES$_{75}$) but they observed a significant increase of $\dot{V}_O_2^{\text{peak}}$ despite a mean change of only 6.4%, quite similar to the variability of the measurement (Kuipers et al., 1985). More recently and in unfit subjects with cardiac heart failure Van Laethem et al. (2007) observed that OUES (+13.9% for OUES$_{100}$ and +16.2% for OUES$_{90}$) and $\dot{V}_O_2^{\text{peak}}$ (+15.7%) improves significantly after long term exercise training (6 months) with strength and aerobic exercise. Even if the type of subject and the training duration were different between both...
studies, the changes and coefficient of variation of OUES and $V_{O_2}$ peak were quite comparable. Therefore, it seems that OUES and $V_{O_2}$ peak could reflect similarly the improvement in aerobic fitness. In our study, OUES$_{80}$ decreases in the same extent as $V_{O_2}$ peak during artificial physiological limitations induced by the hypoxic conditions (Fig. 1). Therefore, OUES$_{80}$ could be valuable to identify training and detraining in healthy subjects or to classify subjects according to their aerobic fitness, even though $V_{O_2,\max}$ is reached in most cases. Hypoxia induces a decrease in $P_{O_2}$, and therefore a significant hypoxemia in healthy subjects. As OUES$_{80}$ is validated to assess cardiorespiratory fitness in acute hypoxia, we validate its potential usefulness in subjects with pathological hypoxemia. This could be the case in a number of pathologies as severe cardiac heart failure, chronic obstructive pulmonary disease or interstitial lung disease. However, hypoxemia induced by hypoxia cannot completely reflect the adaptation observed in pathological subjects and further studies should be conducted to confirm the clinical usefulness of OUES in this kind of subjects.

We also showed that OUES can be a useful sub-maximal index to determine the efficiency of oxygen uptake during maximal exercise tests both in normoxia and hypoxia. At a simulated altitude of 1000 m we did not observe a reduction of OUES in both groups because $V_{O_2}$ and $V_E$ declined similarly. However, with lower $P_{O_2}$, the decrease in $V_{O_2}$ during exercise was much greater than the decrease in $V_E$ in T subjects compared with UT. These results demonstrate that the OUES and therefore the efficiency of oxygen uptake declines faster in T than in UT subjects during exercise in hypoxia. These results confirmed the ability of OUES$_{80}$ to reflect the traditional decrease of aerobic performance in hypoxia (Woorons et al., 2005; Mollard et al., 2007b).

The relative hypoventilation observed in trained subjects comparatively to the $V_{O_2}$ (Woorons et al., 2006) could be due to the possible decrease in chemosensitivity (Ohyabu and Honda, 1990) and a better matching of ventilation to CO$_2$ production rate for a given work rate. This relative hypoventilation observed during maximal exercise in T subjects compared with UT ones in normoxia (Prefaut et al., 1994) was progressively reduced with altitude ($V_{E,max}/V_{O_2,peak} = 22$ vs 30 at 0 m and 27 vs. 33 at 4500 m for T and UT, respectively). This interesting finding shows that respiratory adaptation to hypoxia is significantly modified in T but not in UT subjects, to reach a quite similar point at 4500 m. This result suggests that for the same change in $V_{O_2}$ peak the change of OUES is lower in hypoxia only in trained subjects, probably because of the decrease in $V_{E,max}$. This relationship between OUES$_{80}$ and $V_{O_2}$ peak could allow identifying good or bad responders to exercise in hypoxia. Indeed, Bernardi et al. (2006) showed that successful extreme altitude climbers have a greater ventilatory efficiency and a less sensitive hypoxic response allowing an increase in ventilatory reserve at very high altitude.

Baba et al. (1996, 1999) proposed that the physiological basis of OUES is the development of metabolic acidosis, the physiologic dead space, and the arterial CO$_2$ partial pressure. OUES, which represents the slope of the relationship between $V_{O_2}$ and $\log_{10} V_E$ during an incremental exercise, also integrates cardiovascular factors like $Q$ or O$_2$ extraction from the muscles as well as pulmonary factors, like lung diffusion or lung perfusion. Multiple regression analyses, taking into account cardiovascular variables, training status and effect of hypoxia, showed that the OUES and the $V_{O_2}$ peak were similarly and principally affected by $D(a-v)O_2$. This result suggests that both oxygen diffusion in the lung and oxygen utilisation by active muscles, decreasing arterial and venous oxygen content, respectively, could influence these variables of aerobic fitness. Therefore, OUES$_{80}$ could be used instead of $V_{O_2}$ peak to assess cardiorespiratory fitness during sub-maximal tests in subjects with different fitness levels and in hypoxemic conditions. However the lack of references values for OUES to characterise exercise maladjustment, the necessity

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Fig. 4. Simple regression analyses between $O_2$ arterial-venous difference ($D(a-v)O_2$) and OUES$_{100}$ (A), OUES$_{80}$ (B) and $V_{O_2,peak}$ (C) for all altitudes ($p<0.01$ for all).
to establish equation to predict $\dot{V}_{O_2\text{peak}}$ from OUES in different populations, as well as the moderate sensitivity of this index, could limit the utility of OUES in clinical practice.

In conclusion, the OUES$_{80}$, calculated from only 80% of the test duration, is influenced in the same extent as $\dot{V}_{O_2\text{peak}}$ during exercise performed in hypoxia. Therefore, OUES$_{80}$ is useful to assess cardiorespiratory capacities in a population with a broad range of $\dot{V}_{O_2\text{peak}}$ and could be considered as an interesting sub-maximal index of cardiorespiratory fitness in normal and hypoxemic subjects unable to reach $\dot{V}_{O_2\text{peak}}$.

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References


