Comparative determination of ventilatory efficiency from constant load and incremental exercise testing

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Abstract: The analysis of the relationships between minute ventilation (\( V_E \)) to CO\(_2\) output (VCO\(_2\)), referred to as ventilatory efficiency, in response to incremental exercise testing, is considered a useful index for assessing the presence and severity of cardiopulmonary and metabolic diseases. The effects of constant load exercise testing performed at work intensity associated with anaerobic threshold (AT) and respiratory compensation points (RCP), on the accurate measurements of ventilatory efficiency are not well known. The aim of this present study was to investigate the reliability of the \( V_E/VCO_2 \) ratio obtained from constant load exercise tests performed with two important metabolic rates (at the AT and RCP) and compare it to that of those of incremental exercise tests. A total of 20 young male (20.8±0.4 yr) subjects initially performed an incremental exercise test and then two constant load exercise tests, on different days. Respiratory and pulmonary gas exchange variables were used to estimate AT and RCP. A paired t-test was used to analyse data. AT and RCP (average) occurred at 60% and at 71% of peak \( O_2 \) uptake, respectively. The lowest \( V_E/VCO_2 \) ratio recorded within the first 2 minutes of constant load exercise tests with a work load of AT (26.4±0.3) and RCP (26.7±0.5) was not statistically different from the lowest ratio obtained from the incremental exercise tests (26.0±0.7). In the constant load exercise test, despite the different metabolic rates, the increase in ventilation corresponded closely with the increase in \( CO_2 \) production, reflecting an optimal ventilation and perfusion ratio. Clinicians should consider the constant load exercise test work load associated with AT and RCP as it provides a meaningful lowest value for ventilatory efficiency.

Key words: Exercise; Anaerobic threshold; Respiratory compensation point; Ventilatory efficiency; Ventilation.

Introduction

Cardiopulmonary exercise testing is an effective tool for evaluating the substantiality of cardiovascular, respiratory, and metabolic systems functions in healthy individuals and patients, including those with acute or chronic illnesses (1, 2). Incremental exercise testing is frequently performed to objectively measure three important parameters: the transition point from aerobic to anaerobic metabolism (i.e. anaerobic threshold, AT), the onset of metabolic acidemia induced hyperventilation (i.e. respiratory compensation point, RCP) and the peak \( O_2 \) uptake (\( VO_2 \text{peak} \)) capacity (2).

The \( VO_2 \text{peak} \) (3) and/or \( VO_2 \) at the AT (4, 5) have been considered valuable indices in determining patients’ prognosis. The RCP is the critical metabolic turning point that reflects the highest tolerated metabolic rate for long durations (6, 7).

In addition, measurement of the slope (or ratio) of ventilation (\( V_E \)) relative to CO\(_2\) output (VCO\(_2\)) during incremental exercise below the respiratory compensation point (RCP) \( V_E/VCO_2 \), called ventilatory efficiency (8), can be used as an important prognostic criteria in patients with heart (9, 10) or lung diseases (11). Ventilatory efficiency reflects the sensitivity of matching of ventilation and perfusion (8) and is possible to be measured across different age groups from pediatrics to adolescents (12).

During an incremental exercise test, there is a gradual increase in metabolic rate and ventilatory response. Ventilation increases in close relationship with the increase in VCO\(_2\) until the RCP is reached. However, above the RCP, \( V_E \) increases rapidly compared to VCO\(_2\) and the \( V_E/VCO_2 \) slope (ratio) becomes steeper (2, 13). During an incremental exercise test, the lowest \( V_E/VCO_2 \) ratio that is generally possible to be achieved in patients with impaired heart or lung functions causes a higher \( V_E/VCO_2 \) slope (or ratio) (9, 14). It has been suggested that the prognostic power of the \( V_E/VCO_2 \) ratio is more powerful than that of peak \( VO_2 \) data in cardiac patients (14, 15).

Constant load exercise testing with two different exercise intensities (AT and RCP) and corresponding metabolic demands may also provide valuable information concerning the response of the \( V_E/VCO_2 \) ratio, when compared to the incremental exercise test. So far, to our knowledge, there is no study that evaluates the \( V_E/VCO_2 \) relationship during constant load exercise testing that corresponded to AT and/or RCP, that then compares the results with those obtained in an incremental exercise test.

The aim of this study was to evaluate the ventilatory
efficiency (i.e. the lowest values of $V_e/VCO_2$) response to constant load exercise tests performed at the AT and RCP, and that then compares the results with the those of obtained from an incremental exercise test.

**Materials and Methods**

Twenty healthy young male subjects (age: 20.8±0.4 yr, height: 184±2 cm, weight: 75.3±1.2 kg and body mass index: 22.2±0.4 kg/m²) agreed to participate in the investigation and signed written informed consent forms, which were approved by the institutional ethics committee.

Testing conditions between experiments were standardised for each subject: tests were conducted at the same time of day (between 08:00 to 10:00); after a period of overnight fasting (or a light meal was taken at a similar time prior to arrival at the laboratory, no sooner than 2 hour before testing). Before the test, the subjects' height and body weight were measured (Tanita, TBF 300 M, Japan). The exercise tests were performed in a climatically controlled laboratory where the temperature was kept at around 22ºC. The subjects were introduced to the laboratory environment and the protocol of experiment they would undergo. The subjects were requested to refrain from smoking, or consuming alcohol or caffeine. They were asked to avoid strenuous exercise or caffeine. They were asked to avoid strenuous exercise for a period of 12 hours prior to testing.

Each subject performed an incremental exercise test to exhaustion (16) on an electromagnetically braked cycle ergometer (VIA sprint TM150/200P). The exercise test consisted of an initial period of 4 minutes of cycling at the 20 W as a warm-up, followed by an increase of power at 15 W/min to the limit of the subject's tolerance. The pedalling frequency was between 50 and 70 rpm (average 60 rpm). Seat and handlebar heights were set for each subject. Prior to the work load application, the subjects were controlled carefully for non-specific hyperventilation to avoid the pseudo-threshold phenomenon (17). Then each subject performed two random constant load exercise tests on different days (with at least three day between each test): these consisted of an initial period of 4 minutes of cycling at the 20 W as a warm-up, followed by an increasing rate of power at the AT and/or RCP. The exercise time for the constant load exercise was a period of 15 minutes to avoid substrate alteration to ventilation and subjects' ventilatory efficiency becoming stable.

The $V_{peak}$ was measured at the highest $O_2$ level attained at the end of the ramp test. The AT was estimated non-invasively, using a cluster of standard gas exchange indices (18): the break-point in the $VCO_2/VO_2$ relationship (the 'V-slope' technique) (19); the increase in ventilatory equivalent for $O_2$ uptake ($V_e/VO_2$) and end-tidal partial pressure of $O_2$ ($P_{ET\ O_2}$) without a corresponding increase in ventilatory equivalent for $CO_2$ ($V_e/VCO_2$) and decrease in end-tidal partial pressure of $CO_2$ ($P_{ET\ CO_2}$) (2, 18). The RCP was determined by observing the point where the increase in ventilatory equivalent for $CO_2$ ($P_{ET\ CO_2}$) and decrease in end-tidal partial pressure of $CO_2$ ($P_{ET\ CO_2}$) occurred (2, 18).

During the test, the subjects breathed through a low dead-space, low-resistance turbine volume transducer (Triple V-Volume Sensor) for continuous measurement of inspired and expired volumes and flows. The ventilatory and gas exchange parameters of minute ventilation ($V_e$ BTPS); $O_2$ uptake ($VO_2$, STPD), $CO_2$ output ($VCO_2$, STPD), end-tidal $O_2$ pressure ($P_{ET\ O_2}$), and end-tidal $CO_2$ pressure ($P_{ET\ CO_2}$) were evaluated breath-by-breath using a gas analyser system (Master Screen CPX, Germany). The system was calibrated before each test for temperature, barometric pressure, and $O_2$ and $CO_2$ concentrations according to the manufacturer’s specifications. Cardiac parameters (including heart rate, ST, T and QT) were followed continuously using a 12 lead ECG. Heart rate was recorded as beat-by-beat throughout the study.

The data are expressed as means (± standard error [SE]). A paired $t$-test was used to analyse the significance of data. A value of $p<0.05$ was accepted as statistically significant.

### Results

Table 1 shows the work rate, heart rate, and ventilatory and pulmonary gas exchange variables of subjects during the warm up period, at the AT, at the RCP and at the end of the ramp test. During incremental exercise testing, aerobic to anaerobic metabolic transition (i.e., AT) occurred at 60% of $VO_2$peak and exercise hyperventilation (i.e., RCP) began at 71% of $VO_2$peak. The work production capacity for each kilogram of body weight was found to be 1.71±0.06 W/min/kg for AT, 2.07±0.07 W/min/kg for RCP and 2.92±0.07 W/min/kg for maximal exercise. $VO_2$ for each kg of body weight was found to be 24.46±0.8 ml/min/kg at the AT 28.62±0.9 ml/min/kg.

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### Table 1.

The mean (±SE) values for work rate ($W$), heart rate ($HR$), $O_2$ uptake for each kilogram of body weight ($VO_2/BW$), minute ventilation ($V_e$), $O_2$ uptake ($VO_2$), $CO_2$ output ($VCO_2$), minute ventilation to $O_2$ uptake ($V_e/VO_2$) ratio, minute ventilation to $CO2$ output ratio ($V_e/VCO_2$) at warm up ($W_{20}$), at the anaerobic threshold ($W_{AT}$), at the respiratory compensation point ($W_{RCP}$), and at the maximal exercise performance ($W_{max}$) during an incremental exercise test.
kg at the RCP and 40.01±1.0 ml/min/kg at the maximal exercise.

During incremental exercise testing, with an increasing work load, \( V_{E}/V_{CO2} \) and \( V_{E}/V_{O2} \) decreased to their lowest values at the AT. Beyond the AT, \( V_{E}/V_{CO2} \) stabilised above the AT until the RCP, whereas \( V_{E}/V_{O2} \) continued to increase (Table 1). The (mean ± SE) \( V_{E}/V_{CO2} \) (Figure 1) and \( V_{E}/V_{O2} \) (Figure 2) relationships are plotted for AT and RCP for the constant work-rate exercise tests. The lowest \( V_{E}/V_{CO2} \) ratio was recorded within 2 minutes of the constant load exercise tests with work load AT (26.4±0.3) and RCP (26.7±0.5). Then they increased and reached the values of 29.1±0.5 (AT) and 32.0±0.8 (RCP).

There was no significant differences in the lowest values of \( V_{E}/V_{CO2} \) observed during the constant load exercise test and in RCP during the incremental test (Figure 3). However, the \( V_{E}/V_{CO2} \) ratio at the end of the constant load exercise test was significantly higher than that obtained from the ramp test (Figure 3).

The \( V_{E}/V_{O2} \) ratio showed different responses to the applied work load intensity. In the constant load exercise performed at the AT, the \( V_{E}/V_{O2} \) ratio varied between 21.8 to 29.7. There was no significantly differences between the lowest value obtained from the constant load exercise test (25.5±0.5) and the lowest value observed in the incremental test (25.5±0.8). However, there were significant differences between the lowest \( V_{E}/V_{O2} \) values obtained at the RCP from constant load exercise (between 17.6 and 27) and from the incremental ramp test (p<0.0001). The significantly difference in lowest \( V_{E}/V_{O2} \) values was observed between the AT (25.5±0.5) and RCP (22.5±0.7) (p < 0.05) in the constant load exercise test. At the end of the constant load testing, \( V_{E}/V_{O2} \) was found to be 29.4±0.6 for the AT and 30.9±0.9 for the RCP.

**Discussion**

The intention of our study was to evaluate the prognostic sensitivity of the lowest \( V_{E}/V_{CO2} \) ratio in constant load exercise testing associated with work load AT (2) and RCP (20) both of which are important set point for exercise. In the present study we used the \( V_{E}/V_{CO2} \) ratio instead of slope that is shown not significantly different (8). The lowest values for \( V_{E}/V_{CO2} \) ratio at two different metabolic rates (i.e. AT and RCP) were similar to the obtained from the incremental ramp exercise test (Figure 3).

The \( V_{E}/V_{CO2} \) ratio in normal subjects is an indicator of ventilatory sensitivity that is influenced by peripheral and central chemoreceptors (21) and changes in dead space (22). Typically, in clinical medicine, a rapid incremental exercise test is the first choice for evaluating...
the $V_e$ and $VCO_2$ ($V_e/VCO_2$) relationship (23). During an incremental exercise test with breathing hypoxic gas, increased ventilatory equivalents have been shown (24). The $V_e/VCO_2$ relationship ratio has not been widely studied in constant load exercise tests associated with AT and RCP in normal subjects.

The work production capacity and VO$_2$ levels for each kilogram of body weight at the AT, at the RCP and at maximal exercise capacity showed the fitness status of the subjects (25). In normal healthy subjects, the $V_e/VCO_2$ ratio (or slope) is usually recorded within a range of approximately 24 to 34 (2). In the study, we have found that the $V_e/VCO_2$ ratio varied between 20 to 30 in both exercise set points (AT and RCP). An important consideration is that a $V_e/VCO_2$ slope above 34 can be used as a prognostic indicator of ventilatory inefficiency.

An increased ratio of dead space to tidal volume (11) and a ventilation perfusion mismatch (9) in patients with impaired heart or lung functions are the main reasons for an increased $V_e/VCO_2$ slope. It is important to emphasise that, many patients with cardiac or pulmonary function disease may not be able to perform an incremental exercise test to maximal effort, and therefore may be unable to achieve an acceptable prognostic $V_e/VCO_2$ slope. In the literature, it has been suggested that an exercise test below the 50% of RCP may provide an adequate, prognostic $V_e/VCO_2$ slope (26). The results of this study suggest that the application of moderate intensity (i.e. intensity corresponded to the AT) constant load exercise testing will provide an adequate data for the $V_e/VCO_2$ ratio (Figure 2). A significant correlation has been shown between $V_e/VCO_2$ slope and ratio (2, 8). A high levels of mortality rate has been reported in patients undergoing major abdominal surgery with a $V_e/VCO_2$ value above 34 and VO$_2$ at the AT below 11 ml/min/kg (4). In addition, a high risk of death in the post-operative period has been reported in patients with a $V_e/VCO_2$ ratio above 42 (27).

At the end of constant load exercise, the $V_e/VCO_2$ ratio is higher in RCP compared to AT. The stable $V_e/VCO_2$ ratio during constant load exercise shows a higher tolerable and sustainable point for ventilation and perfusion matching. This could be another set point for evaluating subjects' fitness status, in addition to the lowest value of $V_e/VCO_2$

The evaluation of ventilatory efficiency from the $V_e/VO_2$ ratio during constant load exercise testing may not indicate an acceptable outcome (Figure 3) (8). The variability of the $V_e/VO_2$ ratio regarding work load intensity showed a significant difference when compared to the ramp test. The regulation of the ventilatory control mechanism is closely associated with arterial blood pH and CO$_2$ levels (21). The decrease in the $V_e/VCO_2$ ratio during the early stage of constant load exercise tests could be the result of a decrease in the dead space to tidal volume ratio that occurs at the AT during incremental exercise testing (28).

The non-invasive measurements of ventilatory efficiency from the $V_e/VCO_2$ relationship during a constant load exercise test of moderate intensity can provide useful information for identifying the severity of heart or lung diseases. To indicate the clinical efficacy of the lowest and most stable $V_e/VCO_2$ ratio during constant load exercise testing performed at the AT, further research is needed to analyse these findings in subjects with impaired lung, heart, or metabolic system functions.

**Author’s contribution**
We gratefully declare that all authors participated in the study design, data collection, data analysis, manuscript preparation and revision and agree to be accountable for all aspects of the work.

**References**
15. Poggio R, Arazi HC, Giorgi M, Miriuca SG. Prediction of severe cardiovascular events by $V_e/VCO_2$, slope versus peak VO$_2$ in systolic


