The Time From Anaerobic Threshold (AT) to Respiratory Compensation Point Reflects the Rate of Aerobic and Anaerobic Metabolism After the AT in Chronic Heart Failure Patients

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The significance of the time from anaerobic threshold to respiratory compensation point (RCP-AT time) in patients with chronic heart failure was investigated. Thirty-seven patients with chronic heart failure (New York Heart Association class II or III) were enrolled into the study. Cardiopulmonary exercise testing was performed using breath-by-breath gas sampling. A bicycle ergometer was used, and incremental exercise testing was carried out. Anaerobic threshold, respiratory compensation point (RCP), and the slope of oxygen uptake (\(\Delta VO_2/\Delta WR\)) as a function of work rate were measured. A positive correlation (r=0.53) between RCP-AT time and \(\Delta VO_2/\Delta WR\) was found. RCP-AT time was corrected for the whole exercise period (ramp exercise-RCP point), and the correlation between corrected RCP-AT time and \(\Delta VO_2/\Delta WR\) was still present (r=0.46). There was no correlation between RCP-AT time and anaerobic threshold. These findings suggest that RCP-AT time is a new parameter that reflects the rate of the aerobic and anaerobic metabolism after AT. (Jpn Circ J 1999; 63: 274–277)

Key Words: \(\Delta VO_2/\Delta WR\); Anaerobic threshold (AT); Respiratory compensation point (RCP)

When a subject performs incremental exercising testing, exercise hyperpnea increases toward the end of the exercise. This is due to an increase in acidosis, which is caused by accumulating lactic acid. Lactic acid is produced once the working skeletal muscle cells reach the anaerobic threshold (AT). Usually circulating bicarbonate compensates for this lactic acidosis to begin with. This period is called the isocapnic buffering stage. However, beyond a certain point work intensity becomes so great that lactic acid production can no longer be compensated by circulating bicarbonate and hyperventilation begins. This point is called the respiratory compensation point (RCP).

We have previously reported that in heart failure the ability of skeletal muscle to utilize oxygen is increased during mild exercise by increasing the arteriovenous oxygen difference. However, there are few reports of aerobic metabolism after AT. The time from AT to the RCP (RCP-AT time), ie, the duration of isocapnic buffering, varies from subject to subject, although the normal value is believed to be approximately 2 min. RCP-AT time depends on the rate of aerobic and anaerobic metabolism after AT, and for subjects with reduced exercise tolerance, such as chronic heart failure patients, this period seems to be shorter. However, the significance of this period is not yet fully understood, and it has not been determined whether the duration of this period is correlated with any indicators of exercise tolerance, such as the anaerobic threshold.

Thus, we studied the correlation between the RCP-AT time and the anaerobic threshold and also investigated the correlation between RCP-AT time and the \(\Delta VO_2/\Delta WR\), which is thought to indicate the peripheral blood flow and also the aerobic exercise tolerance. We hypothesized that RCP-AT time may be a new indicator that shows the rate of aerobic and anaerobic metabolism after the AT point.

Methods

Study Patients

We studied 37 patients with chronic heart failure (19 men and 18 women); all patients were in New York Heart Association functional class II or III. Their diagnoses were dilated cardiomyopathy and coronary artery disease, and their mean age was 57.8±6.3 years. The nature and the purpose of the study and the risks involved were explained, and informed consent was obtained from each subject before his or her voluntary consent to entry into the study.

Ventilatory Parameters

Patients performed the cardiopulmonary exercise test under expired gas analysis. Expired gases were monitored continuously in all patients by a breath-by-breath expired gas analyzer (AE280S, Minato Ikagaku, Tokyo, Japan). Oxygen uptake (\(VO_2\)), carbon dioxide output (\(VCO_2\)), and minute ventilation (\(VE\)) were measured. Anaerobic threshold (AT) was determined as the break point in the V-slope method! The respiratory compensation point (RCP) was determined as the point at which the ratio of minute venti-
lation to carbon dioxide output (\(\dot{V}E/\dot{V}CO_2\)) starts to increase. \(\Delta \dot{V}O_2/\Delta WR\) was calculated by least squares liner regression from data obtained between 100 s after the start to 20 s before the end of the ramp test, from a plot of \(\dot{V}O_2\) vs work rate as described previously by Beaver et al.\(^1,2\)

**Exercise Testing**

Patients performed a symptom-limited exercise test on an electromagnetically braked upright cycle ergometer (CPE2000 MedGraphics, St Paul, MN) at least 3 h postprandially. Exercise protocol and gas exchange analyses were performed according to the method previously described by Itoh et al.\(^6\) In brief, after a 4-min rest on the ergometer, exercise was started at 20 W for a 4-min warming-up period, and was increased by a 10-W incremental loading every 60 s. Patients stopped exercise because of leg fatigue or dyspnea.

During exercise testing, expired gases were continuously collected through the tubing, and respiration rate, tidal volume, oxygen uptake (\(\dot{V}O_2\)), and carbon dioxide production (\(\dot{V}CO_2\)) were measured on a breath-by-breath basis. A facemask was used to collect gas samples, which were analyzed by gas analyzer.

Patients’ electrocardiograms were monitored throughout the test by the stress test system (MAT2100, Fukuda Densi, Tokyo). Blood pressure was also measured every minute with an automatic sphygmomanometer (STB-780, Collin Densi, Aichi, Japan).

**Results**

Fig 1A shows that there was no correlation (\(r=0.32\)) between RCP-AT time and \(\dot{V}O_2\) at the anaerobic threshold.

Because the exercise tolerance of the individual patients differed, the exercise time varied. The RCP-AT time also varied according to the intensity of incremental ramp exercise, and there was a possibility that the RCP-AT time was influenced by the total exercise time in heart failure patients. For this reason, we corrected the RCP-AT time by the total exercise time (from the start of ramp exercise to the RCP point) and expressed this as percent RCP-AT time; there was still no correlation between percent RCP-AT time and anaerobic threshold. Percent RCP-AT time was calculated as follows:

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\text{Percent RCP-AT Time} = \left( \frac{\text{RCP-AT time}}{\text{Whole exercise time}} \right) \times 100
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Fig 1B shows the plot of percent RCP-AT time vs anaerobic threshold.

Next, we compared the RCP-AT time and \(\Delta \dot{V}O_2/\Delta WR\). As shown in Fig 2A and B, RCP-AT time has a significant positive correlation with \(\Delta \dot{V}O_2/\Delta WR\) (\(r=0.53, p<0.05\)). Also, there was a significant positive correlation (\(r=0.46,\))
p<0.05) between percent RCP-AT time and ∆VO₂/∆WR.

Discussion

We report here that the time from anaerobic threshold to the respiratory compensation point (RCP-AT time) is closely related to the slope of VO₂ as a function of work rate (∆VO₂/∆WR), although there was no correlation between the RCP-AT time and the anaerobic threshold. The RCP-AT time is a new indicator of aerobic metabolism after AT.

After the anaerobic threshold (AT), lactate (pK 3.9) increases in muscles, but it is soon buffered by HCO₃⁻. This period of metabolic buffering by HCO₃⁻ is called the isocapnic buffering stage and lasts almost 2 min in normal subjects. After the isocapnic stage, stimulation of the carotid body by lactic acid and potassium ions from skeletal muscles induces excessive hyperventilation. The point at which hyperventilation begins is called the respiratory compensation point (RCP). The duration of isocapnic buffering depends on the production of lactate and the buffering ability. After the AT, production of lactate increases significantly. Because aerobic metabolism cannot produce enough energy for a higher work rate, anaerobic metabolism that produces energy and lactate is used for extensive exercise. Astrand and Rodahl reported that work efficiency (caloric equivalent of the measured work + caloric equivalent of the O₂ consumed for the measured work) varies only slightly from one individual to another. In addition, Hansen et al. reported that the slope of VO₂ as a function of work rate (∆VO₂/∆WR) is constant in normal subjects of different gender, age, and training status. In contrast, ∆VO₂/∆WR decreases in ill patients because of inadequate O₂ uptake and reduced O₂ diffusion from capillaries to mitochondria in muscles. Thus, this marker is important because it measures aerobic work efficiency. Patients with chronic heart failure exhibit a low ∆VO₂/∆WR. An increase in anaerobic metabolism within the muscle cells in chronic heart failure has been demonstrated during static exercise by nuclear magnetic resonance spectroscopy. An increase in ∆VO₂/∆WR suggests a high blood flow to the whole body during exercise. In patients with severe heart failure, because blood perfusion to the skeletal muscle is limited, ∆VO₂/∆WR decreases. When blood acidosis increases slowly, the RCP-AT time is longer. This is due to a low rate of anaerobic metabolism and a high rate of aerobic metabolism after the AT point. The high rate of aerobic metabolism is most probably due to good oxygen transport to the peripheral muscle. Thus, ∆VO₂/∆WR is an indicator of peripheral blood flow. A high ∆VO₂/∆WR shows a high rate of aerobic metabolism after the AT point, and consequently the RCP-AT time is closely related to the ∆VO₂/∆WR. When the rate of aerobic exercise is high, the RCP-AT time is longer, and the RCP-AT time could be an indicator of aerobic metabolism after the AT point.

An additional factor is differences in the types of muscle fibers used. Human skeletal muscles consist of 2 basic fiber types (types I and II). Type II fibers, whose aerobic efficiency is lower than that of type I fibers, are recruited at higher work rates. In chronic heart failure patients, the number of type II fibers is increased, resulting in higher lactate production than in normal subjects. The buffering ability of HCO₃⁻ is influenced by renal function. Among the patients in this study, renal function was within normal limits (data not shown).

Above the RCP, stimulation of the carotid body by lactic acidosis and potassium ions from skeletal muscles induces excessive hyperventilation. Below the AT, increasing ventilation maintains homeostasis of the blood (H⁺, K⁺, etc), with no leg fatigue, hyperventilation, or shortness of breath. During exercise above the AT, if lactic acid production is low or the metabolism of lactic acid is rapid enough (because the increase in H⁺ and K⁺ is slow), the RCP-AT time will be longer. When the RCP-AT time is long, shortness of breath appears slowly after the AT. In contrast, when the RCP-AT time is shorter, patients experience shortness of breath soon after the AT and the workload is lower. RCP-AT time shows total exercise ability without exhaustion after the AT.

RCP-AT time varies according to the intensity of incremental ramp exercise. To estimate the RCP-AT time without the influence of exercise intensity, we calculated the RCP-AT time/total exercise time (from the start of ramp exercise to RCP time) × 100 (percent RCP-AT time). Percent RCP-AT time is also positive correlated with ∆VO₂/∆WR (r=0.46).

There was a significant positive correlation between the AT and the ∆VO₂/∆WR! When aerobic work efficiency is low, the AT is also low. In this study, there was no correlation between RCP-AT time and AT. RCP-AT time is an indicator of aerobic metabolism after the AT, this is partly because of a low correlation between RCP-AT time and AT.

RCP-AT time is closely related to ∆VO₂/∆WR as an indicator of aerobic metabolism after the AT. In chronic heart failure, RCP-AT time could be useful to estimate the rate of aerobic and anaerobic metabolism after the AT.

References

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