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Original article

Usefulness of anaerobic threshold to peak oxygen uptake ratio to determine the severity and pathophysiological condition of chronic heart failure

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ABSTRACT

Background: Anaerobic threshold (AT) and peak oxygen uptake (VO_2) are well known as indicators of severity and prognosis of heart failure. Since these parameters are regulated by many factors, multiple organ dysfunction may occur in chronic heart failure, and these two parameters would vary among patients. However, it is not clear whether AT and peak VO_2 deteriorate similarly. Therefore, we planned to compare the degree of deterioration of these two parameters using a ratio of AT and peak VO_2 (%AT/peak), and evaluated its significance in heart failure subjects.
Methods: One hundred ninety-four stable heart failure patients who had optimal medical treatment for at least 3 months were enrolled. Cardiopulmonary exercise testing, echocardiography, and blood sampling were examined within one week. Since %AT/peak varied from 50.3% to 108.5%, we divided patients into tertiles of %AT/peak [Group A, 50.1–70.0 (n = 112), Group B, 70.1–90.0 (n = 64), Group C, 90.1–110.0 (n = 18)], and compared factors relating with skeletal muscle and heart failure among these 3 groups.
Results: In Group A, ratio of measured AT against predicted value (%AT) and measured peak VO_2 against predicted value (%peak VO_2) were similar (80.3 ± 19.0% and 80.4 ± 17.1%, respectively). Peak VO_2 became lower as %AT/peak increased (Group B; 65.6 ± 14.8%, $p < 0.01$ vs. Group A, Group C; 38.3 ± 9.7%, $p < 0.01$ vs. Group B). On the other hand, %AT in Group B (77.1 ± 18.5%) was similar to Group A, and diminished in Group C (58.0 ± 8.2%, $p < 0.05$ vs. Group B). Peak work rate and lean body mass were smaller in Group B than those in Group A. Although, left ventricular ejection fraction and E/E' deteriorated in Group B compared with Group A, plasma B-type natriuretic peptide and estimated glomerular filtration rate stayed constant in Group B and deteriorated in Group C.
Conclusions: %AT/peak showed negative correlation with peak VO_2. In chronic heart failure, muscle weakness occurs at an early stage, and this can be evaluated using %AT/peak.

Introduction

Both anaerobic threshold (AT) and peak oxygen uptake (VO_2) are established parameters of exercise tolerance. AT [1,2] and peak VO_2 [3,4] are well documented indicators of severity and prognosis of heart failure. This is because these parameters are regulated by many factors that affect mortality such as cardiac function [5,6], skeletal muscle function [7,8], endothelial cell function [9,10], autonomic nerve function [11] and others, each of which are essential factors to determine patients' prognosis.

Usually, AT appears to be 50–60% of peak exercise during an incremental exercise protocol [12–14]. Exercise intensity at AT is the moderate intensity at which stroke volume nearly reaches plateau [15], where sympathetic nerve function becomes active [16], and participation of type 2 fiber in skeletal muscle starts to increase. At the intensity of AT, maximal muscle strength is not required. On the other hand, at the peak exercise, it is necessary to use these functions, including muscle strength, enough to achieve

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the maximum performance. Therefore, it is supposed that regulatory mechanism of AT and peak VO_2 would be different, and that the ratio of AT against peak VO_2 (%AT/peak) would not be constant among patients.

In aged subjects, %AT/peak is reported to be greater [12]. However, as for chronic heart failure, there is no report to evaluate how AT and the peak VO_2 decreases, and how %AT/peak changes as heart failure exaggerates. Therefore, we planned to clarify the relationship between AT and peak VO_2 in stable chronic heart failure and related factors that regulate %AT/peak.

Methods

Subjects

Chronic heart failure patients who were admitted to our hospital from 2004 to 2014 were enrolled. Patients who did not receive optimal medical treatment, treated less than 5 months, in decompensated stage, and had severe other diseases were excluded as shown in Table 1. Finally, 194 patients were enrolled.

All patients performed cardiopulmonary exercise test (CPX) and echocardiography and blood sampling within a week without any problems. Patients were divided into three groups according to %AT/peak. Since %AT/peak varied from 50.3% to 108.5% in this study, we divided patients into tertiles of %AT/peak as follows: Group A, 50.1–70.0% (n = 112), Group B, 70.1–90.0% (n = 64), Group C, 90.1–110.0% (n = 18).

This study was approved by the Ethics Committee of Gunma Prefectural Cardiovascular Center and was conducted in accordance with the Declaration of Helsinki.

Cardiopulmonary exercise testing

AT and peak VO_2 were evaluated using a symptom-limited cardiopulmonary exercise testing on an upright, calibrated cycle ergometer (StrengthErgo 8, Mitsubishi Electric Engineering, Tokyo, Japan) with electrocardiograph (ML-9000, Fukuda Denshi Ltd., Tokyo, Japan). CPX was performed 2–4 h after a light meal. This test began with three minutes of rest and three minutes of warm-up at 0 W followed by continuous increasing of work rate by 1 W every 6 s until exhaustion, as recommended by Buchfuhrer et al. [17], and previously reported by us [18]. It was determined whether exercise load was taken enough or not by the gas exchange ratio (R) and/or rating of perceived exertion. When R is more than 1.1 and/or perceived exertion was more than Borg 17, we judged enough exercise load was taken as previously reported [19]. Work rate increase levels were chosen on the basis of fitness of the subjects to keep the exercise period between 8 and 15 min [17]. VO_2, carbon-dioxide production (VCO_2), and minute ventilation (VE) were measured on a breath-by-breath basis using a gas analyzer (MINATO 300S, Minato Science Co. Ltd., Osaka, Japan). Peak VO_2 was determined as the highest VO_2 achieved during exercise. The AT was measured by the V-slope method [20]. In group C, because the size of the change of VO_2 is small, and moreover because the latter part of V-slope is short, it is difficult to determine the AT. However, in such cases zooming the X-axis helps us to recognize the breaking point at the end of V-slope. Breaking point of VE/VO_2 in trend graph is also helpful to determine the AT.

Echocardiography

Cardiac function at rest was evaluated using echocardiography within a week of cardiopulmonary exercise testing by a standard procedure for recording images and making measurements [21,22]. Ultrasound equipment used was either Vivid 5 or 7 (General Electric Medical Systems, Milwaukee, WI, USA). Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson method. Diastolic function was evaluated using pulsed Doppler recordings of mitral inflow velocities of E and A waves, deceleration time (DcT), and tissue-Doppler derived early diastolic mitral annular motion at septum (E'), and the ratio of E and E' (E/E'). In patients with pulmonary regurgitation, end-diastolic velocity of pulmonary regurgitant flow was measured by continuous-wave Doppler echocardiography, and the Doppler-determined pressure gradient at end-diastole was added to right atrial pressure estimated by inferior vena cava morphology [23].

Data analysis

All data are expressed as mean ± standard deviation. Differences between the three groups were assessed by one-way analysis of variance with Bonferroni analysis as post hoc analysis. Chi square analysis was also used where applicable. These analyses were performed using SPSS version 18 (SPSS Inc., Chicago, IL, USA). A value of $p < 0.05$ was considered significant.

Results

As shown in Table 1, there were no differences in age, body weight, basal disease, and use of pharmaceutical agents among the three groups. The ratio of females gradually increased as %AT/peak increased (Group A, 14.3%, Group B, 31.2%, Group C, 38.9%, $p < 0.01$).

A representative case of each group is shown in Fig. 1. The value of peak VO_2 and AT is shown to get closer in order of A, B, C. The relationship between %AT/peak and peak VO_2 is shown in Fig. 2A. There was a negative relationship ($r = -0.590$) between them. When %AT/peak was above 90%, peak VO_2 of all patients was below 15 mL/min/kg. The relationship between AT and %AT/peak is shown in Fig. 2B. There was not a strong relationship between them. Parameters of exercise tolerance of the 3 groups are shown in Table 2. Average peak R was above 1.15, from which it can be decided that exercise test was performed strenuously enough. Peak VO_2 and peak work rate significantly decreased in Group B compared with Group A ($p < 0.01$, 0.05, respectively). It decreased more in Group C than Group B ($p < 0.01$ both). On the other hand, AT stayed constant in Group B, and decreased in Group C compared with Group B ($p < 0.01$).

Parameters relating to skeletal muscle strength and cardiac function in heart failure in the 3 groups are also shown in Table 2. Peak work rate and lean body mass (LBM) in Group B were smaller than those in Group A ($p < 0.01$, both). Fig. 3 is a graph showing the relationship between %AT/peak and peak work rate. There was a negative relationship between them ($r = -0.591$).

Table 1
Patients' profiles.

	Group A	Group B	Group C
Age (years)	59.1 ± 13.8	62.7 ± 14.0	68.2 ± 10.5
BH (cm)	166.0 ± 8.0	160.4 ± 12.4	159.6 ± 8.4
BW (kg)	67.4 ± 15.0	61.4 ± 18.7	56.9 ± 10.1
BMI	24.3 ± 4.2	23.6 ± 4.4	22.3 ± 3.5
Cardiomyopathy (%)	22.3	25.0	27.8
Coronary heart disease (%)	31.3	32.8	38.9
HHD (%)	24.1	21.9	22.2
BB (%)	92.9	89.0	88.9
ACEi/ARB (%)	86.6	82.8	83.3

BH, body height; BW, body weight; BMI, body mass index; HHD, hypertensive heart disease; BB, beta blocker; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker.