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Correlation between aerobic threshold and cardiopulmonary response to exercise onset in patients with myocardial infarction

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Abstract

Purpose: This study aimed to identify the correlation between aerobic threshold (AT) and cardiopulmonary response at the start of exercise in patients with myocardial infarction (MI).

Subjects and Methods: Thirty-one male patients with MI underwent a sub-maximal cardiopulmonary exercise test with expiratory gas analysis to determine their peak oxygen uptake ($\dot{V}O_2$) level, using Ramp protocol.

Results: The patients demonstrated an extended time constant (TC) and decline in AT in this study. Extended TC suggested impaired cardiac function due to reduced left ventricular ejection fraction (LVEF), as well as an LVEF of 59.8% on average. However, there was no significant correlation between TC and AT. Pearson product-moment correlation coefficients were 0.56 between AT and area under the oxygen uptake curve ($\dot{V}O_2$AUC), -0.22 between TC and $\dot{V}O_2$AUC, and -0.23 between AT and TC.

Conclusion: $\dot{V}O_2$AUC is representative of oxygen utilization and is correlated with AT in patients with MI.

Key words: Oxygen uptake, myocardial infarction, aerobic capacity.

INTRODUCTION

It has been demonstrated that a high aerobic capacity leads to a decrease in mortality[1, 2], and that cardiac dysfunction leads to a decrease in aerobic capacity[3]. Oxygen uptake is the product of cardiac output and arterial-mixed venous oxygen difference; therefore, an increase in oxygen uptake during exercise is critical for patients with myocardial infarction (MI). However, it is difficult to attain the maximal exercise level in order to determine the maximal oxygen uptake owing to the lack of muscle strength and development of fatigue, symptoms such as chest pain, or psychological factors such as depression in patients with MI[4, 5]. Moreover, a safe and simple method is required to determine the decrease in aerobic capacity because of aging in patients with MI.

We had earlier attempted to obtain anaerobic threshold as an initial response to exercise. There is little information on how this response changes with different aerobic capacities[3, 6].

The aim of this study was to identify the correlation between aerobic threshold (AT) and cardiopulmonary response to exercise onset in patients with MI.

SUBJECTS AND METHODS

Thirty-one male patients with MI and an average age of 63.1 years (range: 41-79 years) were enrolled in this study. Data on their medical history and physical characteristics such as age, height, and weight were collected, and informed consent was obtained from all patients before their participation in the study. Furthermore, information on the risk factors for coronary stenosis and coronary infarction, such as hypertension, hyperlipidemia, hyperuricemia, diabetes, smoking, and the left ventricular ejection fraction (LVEF) was collected. The number of patients using beta blockers was recorded. The inclusion criteria were diagnosis of MI, participation in cardiac rehabilitation programs, and determination of

the aerobic capacity by cardiopulmonary exercise test (CPET). The exclusion criteria were: lethal arrhythmia, inability to determine AT, and oscillatory ventilation.

The patients underwent a sub-maximal CPET with expiratory gas analysis to determine their peak oxygen uptake ($\dot{V}O_2$) level. The peak $\dot{V}O_2$ was determined during an incremental exercise test conducted at an initial workload of 10 W, which was subsequently increased by 10 W per minute on a cycle ergometer using Ramp protocol. CPET was continued until the patients reported symptoms like chest pain suggestive of a coronary disease, their inability to keep the pedaling frequency under 50 rounds per minute, or on receiving a declaration from the patients. Throughout the test, the patients underwent electrocardiography. The pedaling frequency was monitored to be at least 50 rounds per minute. The pulmonary ventilation and gas exchange parameters were determined with each breath during CPET by AE-300 (MINATO Medical Science Co.). The system was calibrated before each test using gas mixtures of known composition. All CPET underwent immediately followed the instructions from cardiologists.

AT, time constant (TC), and area under the oxygen uptake curve ($\dot{V}O_2$AUC) were determined from pulmonary ventilation and gas exchange parameters. AT was determined from the nonlinearity of carbon dioxide ($\dot{V}CO_2$) and plotted against $\dot{V}O_2$ during the incremental test (V-slope method), in addition to the following convention criteria: Ventilation over oxygen uptake increases or decreases after being stable, whereas ventilation over carbon dioxide remains constant or decreases; further, the gas exchange ratio that was stable or increased gradually, begins to increase more rapidly[3)].

TC was determined from the initial increase in $\dot{V}O_2$ on exercise onset in the warm-up phase. $\dot{V}O_2$AUC was calculated from oxygen uptake between exercise onset and the initial 4-min period of warm-up phase (Fig. 1). $\dot{V}O_2$ and $\dot{V}O_2$AUC were calculated during the warm-up phase for 4 min. $\dot{V}O_2$AUC was the product of measured $\dot{V}O_2$ and periods. This calculation excluded the influence of the resting state (Fig. 2).

Data are reported as mean (SD) values of age, body mass index (BMI), LVEF, TC, $\dot{V}O_2$AUC, and AT. The statistical significance of the correlation between TC, $\dot{V}O_2$AUC, and AT was expressed as the Pearson product-moment correlation coefficient, and p-values <0.05 were considered significant. All statistical analyses were performed using IBM SPSS statistical software (version 24).

The study was approved by the ethics committee of Tokyo Metropolitan University (approval number: 13099) and Ukima Central Hospital (approval number: H25-1) and was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

Patients' mean (SD) age was 63.1 (10.0) years; mean BMI, 22.9 (2.5) kg/m^2; mean LVEF, 59.8 (2.2) %; mean TC, 44.7 (29.3) seconds; $\dot{V}O_2$O2AUC, 12.6 (1.4) mL/kg; and AT, 10.4 (2.2) mL/kg/min (Table 1).

Risk factors for coronary diseases were hypertension in 19 (61.3%) cases, hyperlipidemia in 24 (77.4%) cases, hyperuricemia in 9 (29.0%) cases, diabetes in 1 (3.2%) case, and smoking in 29 (93.5%) cases.

Main coronary stenosis was located in the right coronary artery in 10 (32.3%) cases, left anterior descending artery in 17 (54.8%) cases, and left circumflex artery in 4 (12.9%) cases.

Fifteen (48.4%) cases were under treatment with beta blockers (Table 2).

Pearson's product-moment correlation coefficients were 0.56 ($p<0.05$) between AT and $\dot{V}O_2$AUC, -0.22 ($p=0.42$) between TC and $\dot{V}O_2$AUC, and -0.23 ($p=0.21$) between AT and TC (Fig.3-5).

DISCUSSION

Our study suggests a correlation between $\dot{V}O_2$AUC and AT. AT has been shown to be correlated with oxygen transport[7] as a component of the exercise capacity. Cardiac function plays a considerable role in regulating human fitness along with pulmonary ventilation or muscle function[8]. Oxygen uptake response, particularly, TC of oxygen uptake, at exercise onset is remarkable [9, 10] because of correlation with aerobic capacity or cardiac output. Furthermore, cardiac function had distracted a decline in LVEF and stroke volume at AT[11]. We considered the effect of impaired cardiac function in patients with MI in order to predict AT at exercise onset in this study. AT is the level of exercise $\dot{V}O_2$ above which aerobic energy production is supplemented by anaerobic mechanism, and it is reflected by an increase in lactate/pyruvate ratio in the muscle or arterial blood; therefore, consideration of oxygen transport and oxygen utilization is required to predict AT at the exercise onset.

The patients demonstrated an extended TC and decline in AT in this study. Extended TC suggested impaired cardiac function due to reduced LVEF, and an LVEF of 59.8% on average. However, there was no significant correlation between TC and AT. We considered that declined oxygen transport led to oxygen utilization in this study. MI resulted in the lack of capacity to repair cardiac dysfunction and oxygen utilization. $\dot{V}O_2$AUC was representative of oxygen application, and was correlated with AT in people with cardiac dysfunction such as MI.

Moreover, some other factors were correlated with AT, such as ventilation, lactic acid metabolism, muscle function, and mitochondrial function.

These were measured from exercise onset; however, no significant correlation was found between them in this study. Our results suggest that $\dot{V}O_2$AUC had been influenced by oxygen application rather than oxygen transport, unlike TC. These two values were independent and mutually compensated.

No significant correlation was found between AT and TC in this study, although TC of oxygen uptake has been remarkably correlated with cardiac output at exercise onset[10]. Unlike cardiac output, stroke volume and LVEF have been reported to decline after AT[9]. Previous reports have discussed several complex mechanisms that are involved in the transport and utilization of oxygen for human physical fitness. Cardiac function may be improved via cardiac rehabilitation because oxygen transport has been associated with cardiac output, expansion of blood vessels[12], and blood pressure, even though it cannot improve LVEF. $\dot{V}O_2$AUC could reflect value of $\dot{V}O_2$. Fig. 6. showed that $\dot{V}O_2$AUC was different from TC (Fig. 6). $\dot{V}O_2$AUC could make determination easily compared with TC in the case who had difficulty to determine TC. β -blockers were not necessarily enough to affect heart rate just because fifteen subjects took them. However, several cases had a likelihood that β -blockers affect heart rate and $\dot{V}O_2$ in this study. This study has a few limitations. First, there was no evidence on the correlation between $\dot{V}O_2$AUC and oxygen application in muscle mass, muscle fiber type, and mitochondrial function. Second, the study was conducted in male patients only, since morbidity due to MI is reported as higher in men than women. To better understand the influence of sex differences on human physical fitness and aerobic capacity of patients with cardiac dysfunction, further studies including female participants should be conducted.

In conclusion, area under the oxygen uptake curve between exercise onset and initial 4-min period during warm-up phase is a reliable measure of physical fitness and could be a predictor of aerobic capacity in patients with MI.

Funding and Conflict of interest: None

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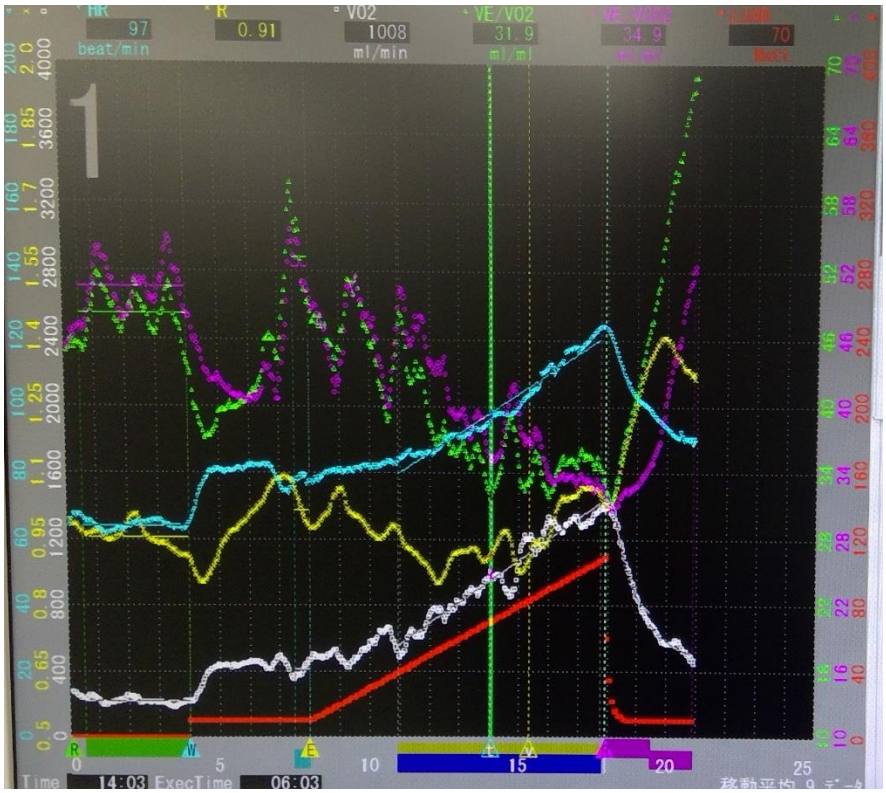
Table 1. Characteristics for subjects in this study (n=31).

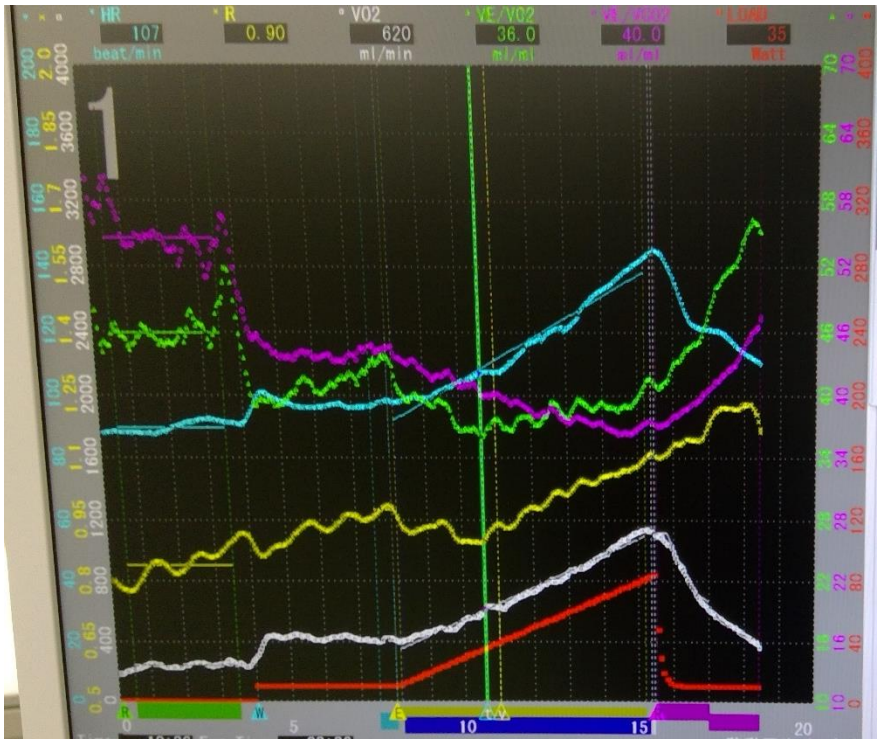
		Average（SD）	
Age	［years］	63.1	(10.0)
Hight	［cm］	165.9	(5.2)
Weight	［kg］	63.3	(8.6)
BMI	［kg/m^2］	22.9	(2.5)
AT	［ml/kg/min］	10.4	(2.2)
Peak $\dot{V}O_2$	［ml/kg/min］	14.3	(3.2)
TC	［sec］	44.7	(29.3)
$\dot{V}O_2$AUC	［ml/kg］	12.6	(1.4)
LVEF	［%］	59.8	(12.2)

Table 2. Prevalence of risk factors for coronary diseases, main coronary infarction, and mediation with β-blocker on people with myocardial infarction in this study. (n=31)

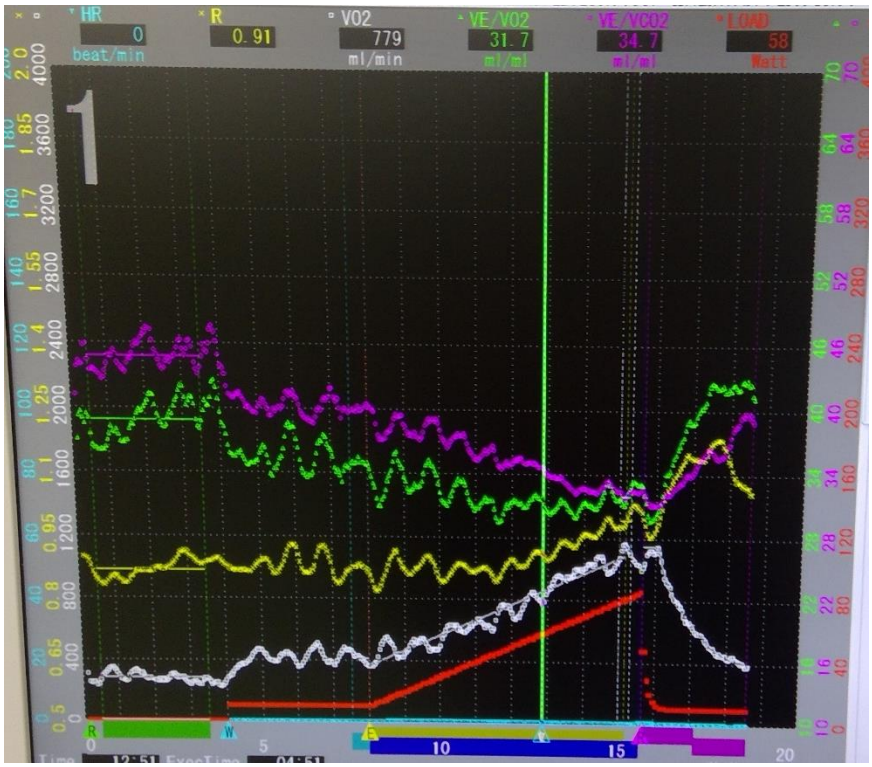
	Number of cases ［cases］
Risk factors for coronary diseases	
-hypertension	19
-hyperlipidemia	24
-diabetes	9
-hyperuricemia	1
-smoking	29
Main coronary infarction	
-RCA	10
-LAD	17
-CX	4
Mediation with β-blocker	15



〈A〉 A case just started $\dot{V}O_2$ increasing at the beginning of warm-up phase.



〈B〉 A case $\dot{V}O_2$ increasing started just before warm-up phase.



〈C〉 A case had difficulty to determine steady state.

Fig. 1. Method to calculate TC

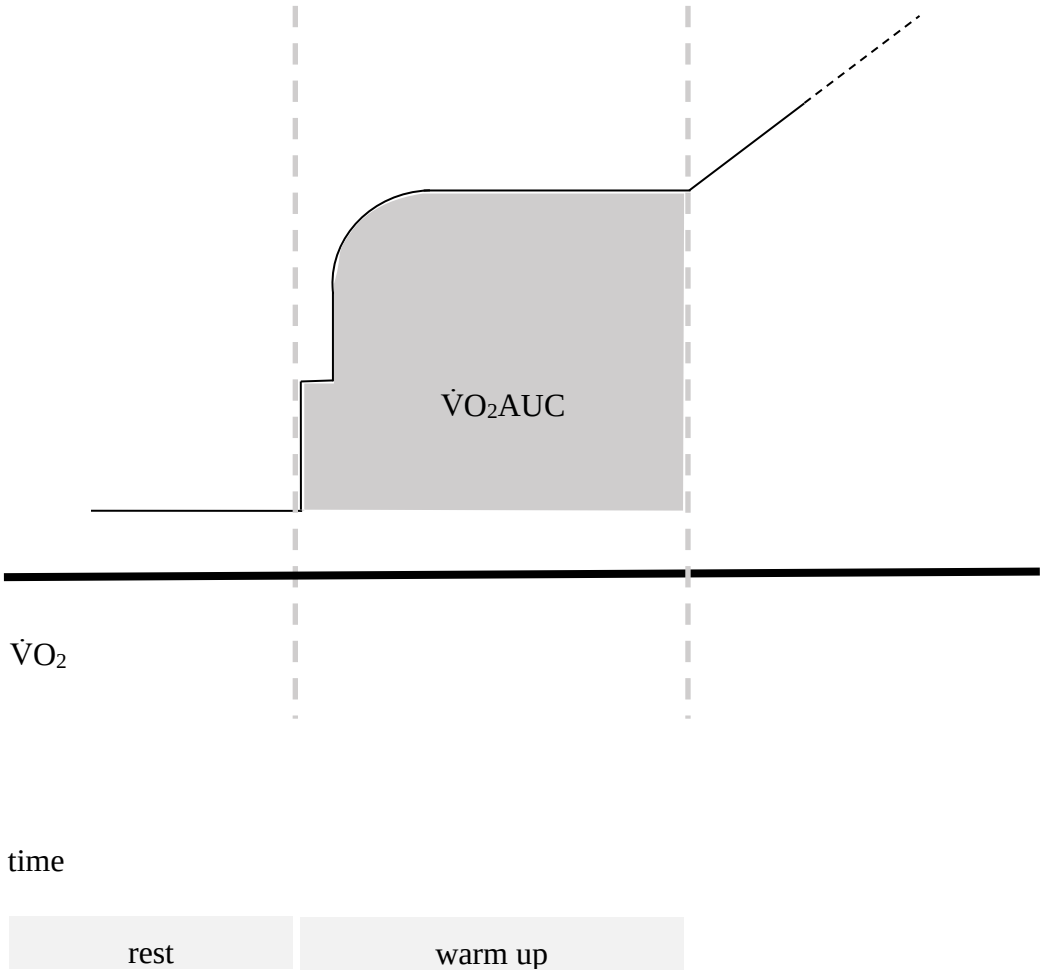


Fig. 2. Method to calculate $\dot{V}O_2AUC$

$\dot{V}O_2AUC$ were calculated during the warm-up phase for 4 min. This calculation excluded the influence of the resting state.

Fig. 3. Correlation coefficient between AT and $\dot{V}O_2AUC$.

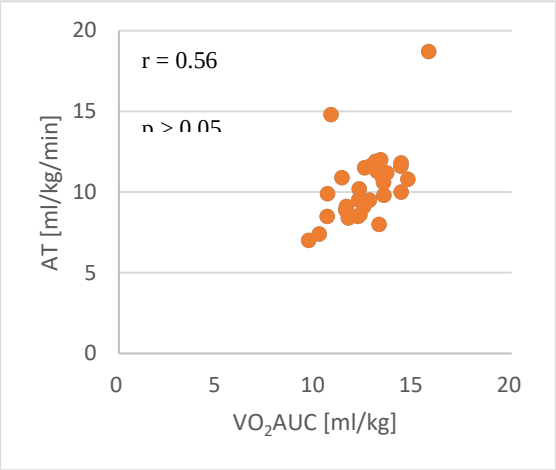


Fig. 4. Correlation coefficient between TC and $\dot{V}O_2AUC$.

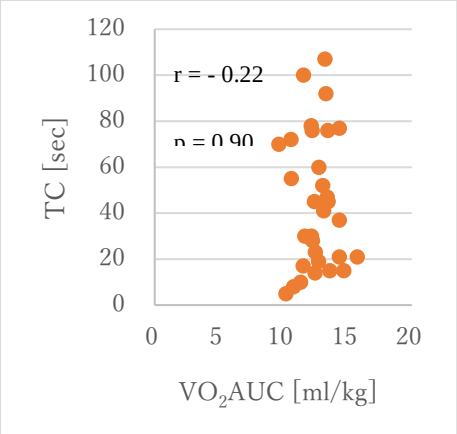
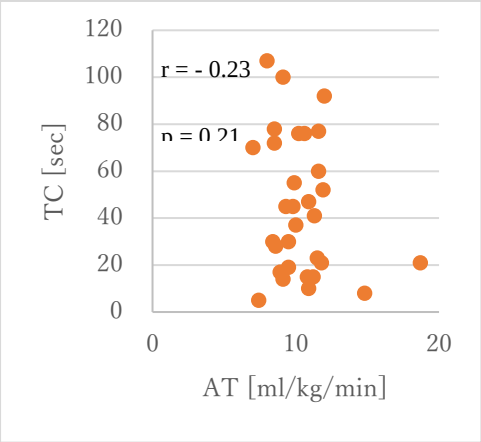
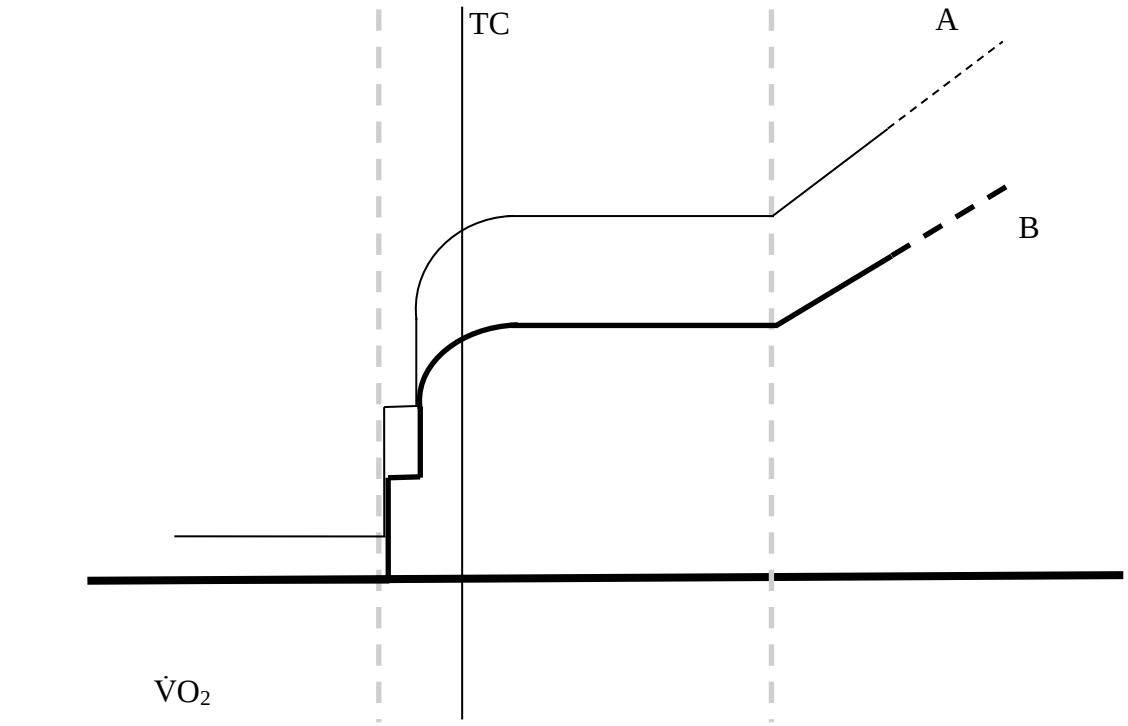
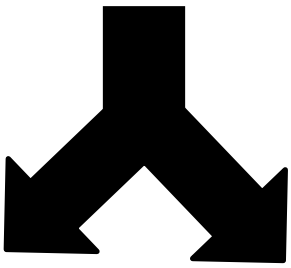
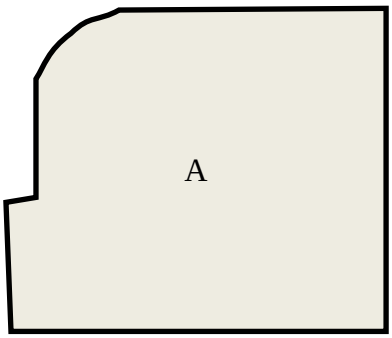


Fig. 5. Correlation coefficient between AT and TC.




TC
A
B
V̇O2
time




A

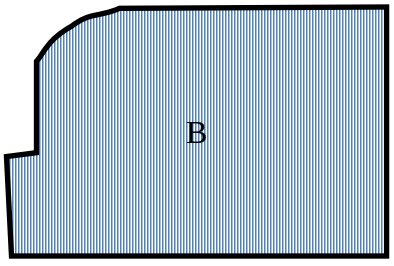

B

Fig. 6. $\dot{V}O_2$AUC was different from TC

List

$\dot{V}O_2$ increasing started just before the warm-up phase in several cases. TC was calculated from $\dot{V}O_2$ increasing lasted. Steady state estimated at the end of warm-up phase.

$\dot{V}O_2$AUC was calculated from oxygen uptake between exercise onset and the initial 4-min period of warm-up phase. $\dot{V}O_2$ and ($\dot{V}O_2$AUC) were calculated during the warm-up phase for 4 min. $\dot{V}O_2$AUC was the product of measured $\dot{V}O_2$ and periods. This calculation excluded the influence of the resting state.

Pearson's product-moment correlation coefficient between AT and $\dot{V}O_2$AUC in people with MI.

AT; aerobic threshold, $\dot{V}O_2$AUC; area of under oxygen uptake curve, MI; myocardial infarction.

Pearson's product-moment correlation coefficient between TC and $\dot{V}O_2$AUC in people with MI.

TC; time constant, $\dot{V}O_2$AUC; area of under oxygen uptake curve, MI; myocardial infarction.

Fig. 5. Correlation coefficient between AT and TC.

Pearson’s product-moment correlation coefficient between AT and TC in people with MI.

AT; aerobic threshold, TC; time constant, MI; myocardial infarction.

Fig. 6. $\dot{V}O_2$AUC was different from TC

Case A showed large $\dot{V}O_2$AUC compared with case B, in case A and B showed equally TC.