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The effect of percutaneous transluminal coronary angioplasty on anaerobic threshold in patients with angina pectoris

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Summary

The anaerobic threshold (AT) is regarded an objective parameter for evaluating exercise tolerance, but its relationship to the improvement of myocardial ischemia remains uncertain. To investigate this relationship, submaximal treadmill exercise tests were performed for 15 consecutive patients with angina pectoris who had undergone successful percutaneous transluminal coronary angioplasty (PTCA). Before and after PTCA, the AT was determined using cardiorespiratory monitoring, while the patients were receiving their usual vasodilator medications. 1) Before PTCA, the minute oxygen uptake ($\dot{V}O_2$) at the AT correlated well with the peak $\dot{V}O_2$ ($r=0.92$, $p<0.002$). The $\dot{V}O_2$ at the AT, however, showed less correlation ($r=0.71$, $p<0.002$) with the $\dot{V}O_2$ at ST segment depression, while the latter parameter correlated closely with the peak $\dot{V}O_2$ ($r=0.91$, $p<0.002$). 2) After PTCA, exercise time, peak $\dot{V}O_2$, and the double product at peak exercise increased significantly (from 640.1 ± 212.2 to 772.9 ± 230.3 sec, $p<0.001$, from 19.1 ± 5.2 to 22.4 ± 4.9 m*l*/min/kg, $p<0.05$, and from $19.7\pm5.0\times10^3$ to $23.7\pm4.5\times10^3$, $p<0.001$, respectively). However, the $\dot{V}O_2$ at the AT did not increase significantly (from 15.8 ± 4.1 to 16.6 ± 3.5 m*l*/min/kg, p=NS). The heart rate, systolic blood pressure, and double product at the

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AT did not change significantly.

In conclusion, in patients with angina pectoris, the AT is apparently related to the onset of myocardial ischemia. However, the AT does not necessarily reflect acute improvement of myocardial ischemia immediately after PTCA.

Key words

Anaerobic threshold Myocardial ischemia Percutaneous transluminal coronary angioplasty (PTCA)

Introduction

Objective evaluation of exercise tolerance is essential for appropriate treatment of patients with congestive heart failure (CHF). Parameters commonly used, including peak exercise time and peak oxygen uptake, are readily influenced by subjective factors, such as the patient's will to continue exercise and the physician's decision to terminate the exercise test. Maximal oxygen uptake is a parameter which is not influenced by such subjective factors[1,2], but its measurement requires much effort on the part of the subject and is sometimes dangerous for CHF patients. The anaerobic threshold (AT) is parameter[3,4], which shows whether the exercise is carried out at moderate intensity during the rehabilitation of CHF patients[5,6]. However, the correlation of the AT with the improvement in myocardial ischemia remains obscure. In patients with ischemic heart disease, the increase in cardiac output during exercise is thought to be suppressed after the onset of myocardial ischemia, which may influence the AT. To elucidate the relationship between the AT and myocardial ischemia during exercise and to explain the obscure correlation between the AT and improvement of myocardial ischemia, we studied patients with angina pectoris who had undergone successful percutaneous transluminal coronary angioplasty (PTCA).

Methods

Subjects

Fifteen consecutive patients with angina pectoris (mean age: 57.2±10.0 years, 13 men and 2 women) who had undergone PTCA were selected. Despite treatment with vasodilators, 14 of them experienced chest pain during their usual daily activities. All of the patients had definite coronary stenosis consisting of at least 75% luminal stenosis. By PTCA, their lesions were adequately dilated. None of the patients had evidence of myocardial infarction. Echocardiography at rest showed no asynergy of the left ventricular wall motion. In the patients who had exhibited diagnostic ST segment depression during submaximal treadmill exercise testing before PTCA, the ST segment depression was resolved after PTCA. Before PTCA, exercise ^{201}thallium scintigraphy demonstrated exercise-induced defects with redistribution, but after PTCA, scintigraphy showed no such defects. The patients were not receiving either beta-blocking agents or digitalis, and had no evidence of pulmonary or peripheral vascular disease. In each of 10 patients, a single vessel was involved, in 4, 2 vessels, and in one, all 3 vessels. The sites of the stenotic lesions responsible for the ST segment depressions were the left anterior descending artery in 11 patients, the left circumflex artery in one, and the right coronary artery in 3. Patients with several stenotic lesions were included in the present study if the lesion responsible for the ST segment depression was dilated, irrespective of the presence of other lesions.

Exercise protocol

Submaximal treadmill exercise tests were performed on all patients 3–10 days before and after PTCA using the same protocol each time. The exercise protocol was based on Bruce's protocol, the modified Bruce's protocol and the ramp protocol, and was tailored to the level of each patient's daily activity. The tests were performed on the patients taking vasodilators within 2 hours after meals. The patients were monitored throughout the test using 12-lead electrocardio-

grams (Stress System ML-8000, Fukuda Denshi, Tokyo). The ST segment amplitude was measured 80 msec after the J point in all 12 leads at 10-sec intervals by computer analysis. A down slope or horizontal ST segment depression of 0.1 mV or more was considered positive, and the first point at which the ST segment depression became positive was defined as the onset of the ST segment depression. Cuff blood pressure was measured at one-min intervals using an automatic indirect manometer (Stress Test Blood Pressure Monitor STBP-780, Collin Denshi, Aichi).

Gas analysis

The respiratory indices were measured by the breath-by-breath method using an RM-300 (Minato Medical Science Co, Ltd), or an MMC-4400tc (Nihon Koden Co, Ltd) and were recorded at 10 to 30 sec intervals. The measured variables were minute oxygen uptake ($\dot{V}O_2$ ml/min/kg), minute carbon dioxide production ($\dot{V}CO_2$ ml/min/kg), and minute ventilation ($\dot{V}E$ *l*/min). The AT point was determined visually when the initial breakpoint at which $\dot{V}E/\dot{V}O_2$ began to increase without an increase in $\dot{V}E/\dot{V}CO_2$. The $\dot{V}$-slope method was used to confirm the AT[7]. Peak oxygen uptake during the exercise test is termed peak $\dot{V}O_2$ in the present study.

Study protocol

Using the data obtained before PTCA, linear regression analysis was performed for the $\dot{V}O_2$ at the AT, peak $\dot{V}O_2$, and the $\dot{V}O_2$ at ST segment depression. In addition, the exercise parameters (i.e., $\dot{V}O_2$, heart rate, systolic blood pressure, and double product) at the AT before and after PTCA were compared.

Table 1. Coronary stenosis and exercise time before and after PTCA

	Stenosis (%)	Ex time (sec)
Before PTCA	94.6±4.6	640.1±212.2
After PTCA	34.0±14.6	772.9±230.3
p value	<0.001	<0.001

Stenois=coronary stenosis; Ex time=exercise time; p value=before PTCA vs after PTCA by Student's paired t-test.

Statistical analysis

Statistical analysis was performed using the Student's t-test for paired data, and a p value of <0.05 was considered statistically significant. Data are shown as means±SD.

Results

Before PTCA

The degree of coronary stenosis at the sites of the lesions responsible for the ST segment depression was 94.6±4.6%. Exercise duration was 640.1±212.2 sec, and the end points were the onset of chest pain in 8 patients, the attainment of ST segment depression greater than 0.2 mV in 3, the occurrence of leg fatigue in 3, and a short run of ventricular tachycardia in one (**Table 1**). Peak $\dot{V}O_2$, heart rate, systolic blood pressure, and the double product at peak exercise were 19.1±5.2 m*l*/min/kg, 117.1±17.2/min, 167.0±30.5 mmHg, and 19.7±5.0×10^3, respectively (**Table 2**).

After PTCA

Coronary stenosis decreased to 34.0±14.6% ($p<0.001$). The $\dot{V}O_2$, heart rate, systolic blood

Table 2. Peak $\dot{V}O_2$, heart rate, systolic blood pressure, and the double product at peak exercise before and after PTCA

	$\dot{V}O_2$ (m*l*/min/kg)	HR (beats/min)	sBP (mmHg)	DP ($\times10^3$)
Before PTCA	19.1±5.2	117.1±17.2	167.0±30.5	19.7±5.0
After PTCA	22.4±4.9	132.7±14.3	178.5±28.9	23.7±4.5
p value	<0.05	<0.001	<0.01	<0.001

$\dot{V}O_2$=minute oxygen consumption; HR=heart rate; sBP=systolic blood pressure; DP=double product; p value=before PTCA vs after PTCA by Student's paired t-test.

Table 3. Exercise parameters at rest before and after PTCA

	$\dot{V}O_2$ (ml/min/kg)	HR (beats/min)	sBP (mmHg)	DP ($\times 10^3$)
Before PTCA	3.3±0.4	68.1± 9.8	124.5±22.2	8.5±2.0
After PTCA	3.4±0.5	70.7±10.2	125.8±22.7	8.9±1.9
p value	NS	NS	NS	NS

NS=no significant difference. Other abbreviations: see Tables 1 and 2.

pressure, and the double product did not change significantly at rest (**Table 3**). Exercise duration increased to 772.9±230.3 sec ($p<0.001$) (**Table 1**), and the end point was the occurrence of leg fatigue in 9 patients and attainment of the target heart rate [(220−the patient's age)×0.9)] in 6. Peak $\dot{V}O_2$, heart rate, systolic blood pressure, and the double product at peak exercise were 22.4± 4.9 ml/min/ kg ($p<0.05$), 132.7±14.3 beats/min ($p<0.001$), 178.5±28.9 mmHg ($p<0.01$) and 23.7±4.5×10^3 ($p<0.001$), respectively (**Table 2**).

1. Correlations between the $\dot{V}O_2$ at the AT, the peak $\dot{V}O_2$, and the $\dot{V}O_2$ at ST segment depression before PTCA (**Figs. 1–3**)

There was good positive correlation ($r=0.92$) between the $\dot{V}O_2$ at the AT and the peak $\dot{V}O_2$. The $\dot{V}O_2$ at the ST segment depression and the peak $\dot{V}O_2$ also correlated well ($r=0.91$). Although there was a positive correlation between the $\dot{V}O_2$ at the AT and the ST segment depression, the correlation coefficient was relatively low ($r=0.71$).

2. Comparison of exercise parameters at the AT before and after PTCA (**Figs. 4, 5**)

$\dot{V}O_2$ increased markedly in some cases, but there was no significant overall change in the $\dot{V}O_2$ at the AT after PTCA (from 15.8±4.1 to 16.6±3.5 ml/min/kg, p=NS). Heart rate, systolic blood pressure, and the double product did not change significantly (from 100.8±13.1 to 106.8±15.7 beats/min, from 156.7±28.5 to 157.9±28.5 mmHg, and from 15.8±3.6×10^3 to

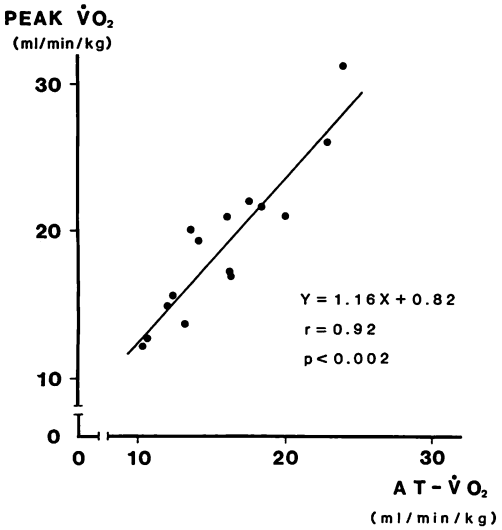

Fig. 1. Correlation between the $\dot{V}O_2$ at the AT and the peak $\dot{V}O_2$.
AT-$\dot{V}O_2$=$\dot{V}O_2$ at the AT.

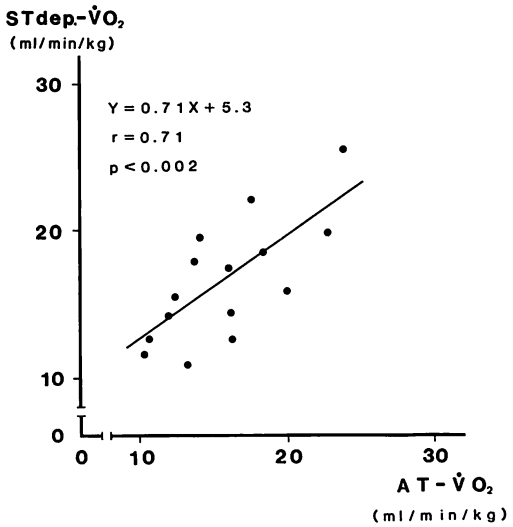

Fig. 2. Correlation between the $\dot{V}O_2$ at the AT and the ST segment depression.
ST dep.-$\dot{V}O_2$=$\dot{V}O_2$ at the ST segment depression.

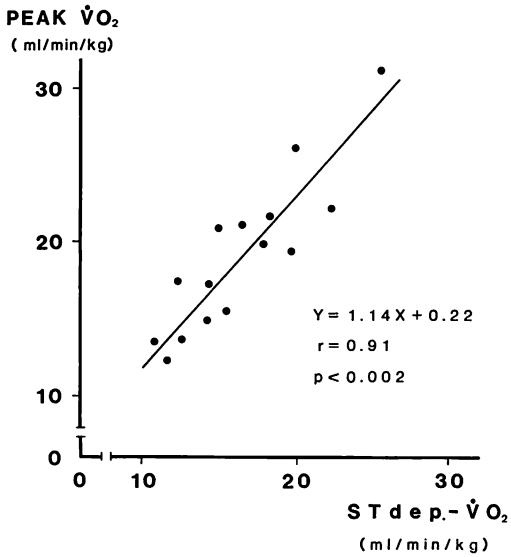

Fig. 3. Correlation between the $\dot{V}O_2$ at the ST segment depression and the peak $\dot{V}O_2$.

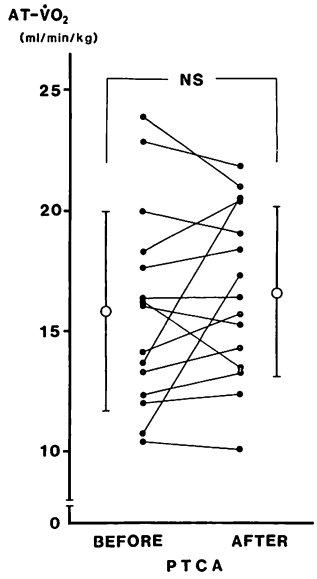

Fig. 4. Individual $\dot{V}O_2$ values at the AT before and after PTCA.

NS=no significant difference between before and after PTCA by Student's paired t-test.

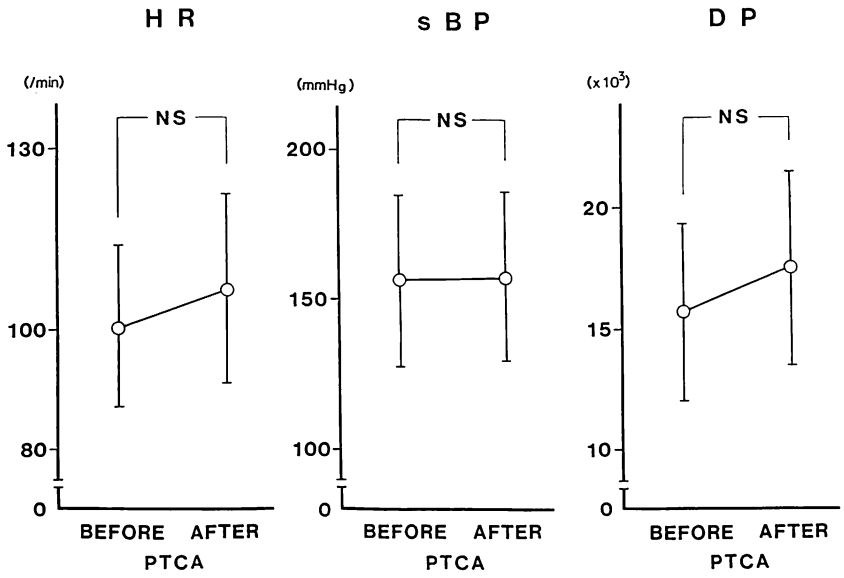

Fig. 5. Heart rate, systolic blood pressure, and the double product at the AT before and after PTCA.

Abbreviations: see Table 2.

$17.5 \pm 4.0 \times 10^3$, respectively; all p=NS).

Discussion

In working skeletal or cardiac muscle, energy (ATP) is supplied with the TCA cycle and glycolysis[8,9]. At a low-level workload, ATP is supplied with the TCA cycle alone, but when the workload surpasses the level at which the oxygen demand exceeds the oxygen supply available, anaerobic glycolysis is activated and the blood lactate level begins to increase. This results in additional carbon dioxide production, which augments the ventilatory drive. Wasserman defined the AT as "the level of $\dot{V}O_2$ above which aerobic energy production is supplemented by anaerobic mechanisms, causing a sustained increase in lactate and metabolic acidosis"[3], and reported that the AT could be used as an objective parameter for evaluating exercise tolerance in patients with CHF. There have also been some reports that the $\dot{V}O_2$ at the AT correlates well with the maximal $\dot{V}O_2$[4,10].

The AT, which is the breakpoint of blood lactate accumulation, has recently been used to determine a safe and effective exercise level for patients' rehabilitation.

The AT, with this clinical value, has been widely used for patients with various diseases. However, in patients with ischemic heart disease, the relationship between the AT and myocardial ischemia during exercise remains unclear.

Cardiopulmonary exercise testing was performed before and after PTCA. Resolution of ST segment depression and of exercise defects on ^{201}thallium scintigraphy, prolonged exercise duration and increased double product at peak exercise after PTCA showed that myocardial ischemia was alleviated by PTCA. The major determinants of $\dot{V}O_2$ are thought to be cardiac output and peripheral oxygen uptake efficiency. $\dot{V}O_2$ changes with the change in the cardiac output or the peripheral oxygen uptake efficiency or both. In patients with CHF, peripheral oxygen uptake efficiency is improved by rehabilitation in 3 to 6 months[11,12]. In the present study, follow-up tests were performed only 3 to 10 days after the initial tests to permit an increase of peripheral oxygen uptake efficiency. Furthermore, since no rehabilitation was accomplished in these patients, the increase in $\dot{V}O_2$ after PTCA depended mainly on increased cardiac output.

In some cases, the $\dot{V}O_2$ at the AT increased markedly immediately after PTCA. $\dot{V}O_2$ is known to increase with the increase in the AT because of the increased cardiac output at the AT due to the improvement of myocardial ischemia.

However, in most cases, the $\dot{V}O_2$ at the AT did not increase after the prompt improvement in myocardial ischemia immediately after PTCA. Although cardiac output during exercise usually increases after rapid improvement in myocardial ischemia when cardiac output is not appreciably increased by PTCA during exercise, hibernating myocardium is suspected. However, since echocardiography showed no asynergy before PTCA, hibernating myocardium being unlikely. The increase in cardiac output during exercise after PTCA does not correlate with the increase in the AT.

Yamabe also reported that prompt improvement in myocardial ischemia following the oral administration of isosorbide dinitrate did not increase the $\dot{V}O_2$ at the AT[13].

Before PTCA, the $\dot{V}O_2$ at the AT correlated well with the peak $\dot{V}O_2$. The $\dot{V}O_2$ at the AT also correlated with the $\dot{V}O_2$ at the ST segment depression, the onset of myocardial ischemia, with the correlation coefficient being lower than that between the peak $\dot{V}O_2$ and ST segment depression.

Since the influence of suppressed increase in cardiac output during exercise on the AT was ruled out, the mechanism that causes obscure correlation between the $\dot{V}O_2$ at the AT and the $\dot{V}O_2$ at ST segment depression may be related to peripheral oxygen uptake efficiency. Most patients experienced chest pain during their daily activities, which also limited the exercise intensity below the level where chest pain occurred. Such limitations may be responsible for the decrease in peripheral oxygen uptake efficiency. Decrease in peripheral oxygen uptake efficiency,

according to its degree, lowered the $\dot{V}O_2$ at the AT, therefore, there may be a positive correlation between the $\dot{V}O_2$ at the AT and the $\dot{V}O_2$ at ST segment depression, the onset of myocardial ischemia. Decreased oxygen uptake efficiency did not recover immediately after PTCA, and the $\dot{V}O_2$ at the AT did not increase. If the limitations in daily activities are eliminated, the peripheral oxygen uptake efficiency may improve, and the $\dot{V}O_2$ at the AT may increase in the long run.

Apparently, the AT is not a sensitive parameter for reflecting prompt improvement in myocardial ischemia. However, the $\dot{V}O_2$ at the AT correlated with the peak $\dot{V}O_2$ before PTCA and did not change immediately after PTCA. Therefore, we can speculate that there is previous exercise tolerance in patients with ischemic heart disease even after prompt improvement in myocardial ischemia using the AT. Further investigations are therefore needed.

In conclusion, in patients with angina pectoris, the AT is apparently related to the onset of myocardial ischemia. However, the AT does not necessarily reflect prompt improvement in myocardial ischemia immediately after PTCA.

要　約

労作性狭心症患者における嫌気性代謝閾値の検討：PTCA による虚血改善の効果

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嫌気性代謝閾値 (AT) は運動耐容能評価の客観的指標と考えられているが，AT と心筋虚血との関係は不明である．両者の関係を検討するために，PTCA が成功した連続 15 名の狭心症患者に対し，亜最大負荷 treadmill 運動負荷試験を施行した．AT 測定は日常の冠血管拡張剤内服の状態で，PTCA 前後，呼気ガス分析にて行なった．

1. PTCA 前，AT 時の酸素摂取量 ($\dot{V}O_2$) は peak $\dot{V}O_2$ と良く正相関した ($r=0.92$, $p<0.002$)．AT 時の $\dot{V}O_2$ は ST 低下時の $\dot{V}O_2$ とも正相関したが，peak $\dot{V}O_2$ に比し粗であった ($r=0.71$, $p<0.002$)．一方，ST 低下時の $\dot{V}O_2$ は peak $\dot{V}O_2$ と良く相関した ($r=0.91$, $p<0.002$)．

2. PTCA 後，運動時間は延長し，peak $\dot{V}O_2$，亜最大負荷時の二重積も有意に増加した (640.1 ± 212.2 対 772.9 ± 230.3 sec, $p<0.001$, 19.1 ± 5.2 対 22.4 ± 4.9 m*l*/min/kg, $p<0.05$, $19.7\pm5.0\times10^3$ 対 $23.7\pm4.5\times10^3$, $p<0.001$)．しかし AT 時の $\dot{V}O_2$ は，著明な増加例もみられたが，全体としては有意の増加を示さなかった (15.8 ± 4.1 対 16.6 ± 3.5 m*l*/min/kg, $p=NS$)．AT 時の心拍数，収縮期血圧，二重積も有意には変化しなかった．

以上の結果から，AT は労作誘発性心筋虚血の出現と関連があると考えられた．しかし必ずしも PTCA 直後における心筋虚血の急速な改善を反映するものではなかった．

References

1) Taylor HL, Buskirk E, Henschel A: Maximal oxygen intake as an objective measure of cardio-respiratory performance. J Appl Physiol **8**: 73-80, 1955
2) Astrand PO, Rodahl K: Textbook of Work Physiology, 3rd ed. McGraw-Hill, New York, 1986, pp 354-390
3) Wasserman K, Whipp BJ, Koyal SH, Beaver WL: Anaerobic threshold and respiratory gas exchange during exercise. J Appl Physiol **35**: 236-243, 1973
4) Davis JA, Vodak P, Wilmore JH, Vodak K, Kurtz P: Anaerobic threshold and maximal aerobic power for three modes of exercise. J Appl Physiol **41**: 544-550, 1976
5) Gibbons ES: The significance of anaerobic threshold in exercise prescription. J Sports Med **27**: 357-361, 1987
6) Katch V, Weltman A, Sady S, Freedson P: Validity of the relative percent concept for equating training intensity. Eur J Appl Physiol **39**: 219-227, 1978
7) Beaver WL, Wasserman K, Whipp BJ: A new method for detecting anaerobic threshold by gas

exchange. J Appl Physiol **53**: 1184–1189, 1982
8) Wasserman K, Whipp BJ: Exercise physiology in health and disease. Am Rev Resp Dis **112**: 219–249, 1975
9) Ivy JL, Withers RT, Handel JV, Elger DH: Muscle respiratory capacity and fiber type as determinants of lactate threshold. J Appl Physiol **48**: 523–527, 1980
10) Matsumura N, Nishijima H, Kojima S, Hashimoto F, Minami M, Yasuda H: Determination of anaerobic threshold for assessment of functional state in patients with chronic heart failure. Circulation **68**: 360–367, 1983
11) Sullivan MJ, Higginbotham MB, Cobb FR: Exercise training in patients with severe left ventricular dysfunction. Circulation **78**: 506–515, 1988
12) Sullivan MJ, Higginbotham MB, Cobb FR: Exercise training in patients with chronic heart failure delays ventilatory anaerobic threshold and improves submaximal exercise performance. Circulation **79**: 324–329, 1989
13) Yamabe H, Kobayashi K, Fukuzaki H: The effect of nitrate on the oxygen availability during exercise in effort angina pectoris. Jpn Heart J **25**: 1019–1028, 1984