Clinical Significance of Symptom-limited Exercise Test to Evaluate the Coronary Narrowings in Patients with Effort Angina Pectoris

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EXERCISE electrocardiography has been commonly used as a screening procedure to detect the ischemic heart disease^{1,2} and to predict the severity of coronary artery lesions from the ST-segment changes,³⁻⁹ since the basic premise of exercise testing is to increase the myocardial oxygen requirement to unmask a reduced, coronary blood flow.

The exercise tolerance (external work capacity) and maximal double product during exercise which reflects maximal oxygen consumption, have been also used to estimate myocardial oxygen supply-demand balance, and to evaluate the therapeutic interventions for effort angina pec-

toris.¹⁰⁻¹² These parameters, however, were not extensively studied in relating to the severity of coronary artery disease.

The present study demonstrated the correlations between coronary arteriographic findings and exercise tolerance, double product change until onset of angina, and electrocardiographic response to exercise in 74 patients with effort angina pectoris.

MATERIALS AND METHODS

1) Materials

Seventy-four patients with effort angina pectoris were studied. They were 60 males and

TABLE I SUBJECTS

<i>The Number of Vessels Involved</i>	<i>MI (-)</i>	<i>MI (+)</i>	<i>Total</i>
<i>SVD</i>	25	6	31
<i>DVD</i>	14	8	22
<i>TVD</i>	3	6	9
<i>LMCAD</i>	4	8	12
<i>Total</i>	46	28	74

Effort Angina Pectoris: 74 Pts. (35-73 yrs.)
Male 60 pts.
Female 14 pts.

Abbreviations: SVD; Single Vessel Disease, DVD; Double Vessel Disease, TVD; Triple Vessel Disease, LMCAD; Left Main Coronary Artery Disease, MI; Prior Myocardial Infarction

Key Words:

Effort angina pectoris
Symptom-limited exercise test
CAG
Exercise tolerance
Double product
ST-T change

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14 females, and average age was 60 years old. Twenty-eight of these patients had previous history of myocardial infarction (Table I). The patients with variant form of angina, unstable angina, and cardiac failure were excluded from

this study. In our series the patients with acid-base imbalance or serum electrolyte disorder were not included.

2) Exercise Test

Multistage ergometer exercise test was performed in semi-Fowler's position (30°C) at least two hours after meal or in the fasting state. All patients had three exercise tests: one with small load as a trial test to minimize the emotional intervention during exercise test, and other two tests with symptom-limited maximal load were performed. In these tests work load was initially 150 kpm and increased by 150 kpm every three minutes until chest pain was induced. Serial changes of arterial blood pressure and standard 12-lead electrocardiograms were recorded every one minute during the procedure (Fig. 1). All tests were done under hospitalization at least 12 hours after withdrawal of coronary vasodilators and three days after withdrawal of β -blockers.

In our study (1) exercise tolerance (total load until chest pain is induced), (2) maximal double product (blood pressure $\times$ heart rate), (3) the extent of increase of double product (Δ DP), and (4) the summed ST-segment depression (Σ ST) and the total number of leads (nST) in which the significant ST-segment depression was observed (leads II, III, and aVF for inferior region, and leads I, aVL and V_1-V_6 for anterior region) were obtained. Ischemic ST-segment

Method

Multistage Exercise Test on a Bicycle Ergometer
Standard 12-lead ECG Monitoring
End Point: Onset of Anginal Attack

Parameters

Exercise Tolerance (Total Exercise Load: kpm)
Double Product Change
ST Change in Exercise ECG

Fig. 1. The protocol of exercise test.

Fig. 2. Relationship between the exercise tolerance (total exercise load) and the severity of coronary artery disease (coronary index) in all 74 patients with effort angina pectoris (EA).

Fig.3. Relation between the total exercise load and the coronary index in 46 patients with effort angina pectoris excluding 28 patients with prior myocardial infarction.

Fig.4. Relationship between the exercise tolerance (total exercise load) and the number of involved vessels in 46 patients without prior myocardial infarction.

deviation was defined as horizontal or downward sloping ST-segment depression of 0.1 mV or more for at least 0.08 msec beyond J point.

3) Selective Coronary Arteriography

Right and left heart catheterization and selective coronary arteriography were performed within one month after exercise tests. Coronary arteriography was done with the Phillips 6 inch cesium iodide image amplifier system. To evaluate the severity of coronary artery narrowings quantitatively, the coronary index which represents the summed score of coronary narrowings in each major coronary vessel was obtained: score 0 with normal coronary artery to score 300 with complete obstructions of three vessels. The patients were divided into four groups according to the number of involved vessels ($\geq 50\%$ narrowing).

Group 1: 31 patients with single vessel disease

Group 2: 22 patients with double vessel disease

Group 3: 9 patients with triple vessel disease

Group 4: 12 patients with left main coronary artery disease

The collateral and its distribution was also evaluated.

Electrocardiographic changes on exercise and coronary arteriographic findings were interpreted by three special cardiologists independently and agreed interpretation at least by two were

Fig. 5. Relationship between the exercise tolerance and the degree of coronary narrowing in 21 patients with a single vessel lesion in left anterior descending artery (left), and in 14 patients with multiple vessel lesions (right).

adopted.

RESULTS

1) Exercise Tolerance

Exercise tolerance was obtained as a total work load until chest pain was induced by multi-stage exercise test in 74 patients with effort angina. Good reproducibility was obtained in two maximal exercise tests.^{14,15}

Figures 2 and 3, represent the coronary index and the total exercise load in all 74 patients and 46 patients without prior myocardial infarction, respectively. Although no significant correlation was observed between these two parameters in 74 patients, a significant inverse correlation ($r = -0.59$) was obtained in 46 patients excluding 28 patients with prior myocardial infarction, see Fig. 3.

In these 46 patients the relationship between the number of involved vessels and the total exercise load was investigated. The mean total exercise loads were 1690 ± 180 kpm in SVD (single vessel disease), 850 ± 120 kpm in DVD (double vessel disease), 660 ± 200 kpm in TVD (triple vessel disease), and 400 ± 120 kpm in LMCAD (left main coronary artery disease). The

mean total exercise load in SVD was significantly higher than those in other groups, although the standard deviation was large in SVD (Fig. 4).

In 21 patients with significant coronary narrowing in left anterior descending artery, the relationship between the degree of narrowing and the total exercise load was investigated. There was a clear difference in exercise tolerance between in 10 patients with narrowing less than 75% in diameter and in 7 patients with severe (75%–99%) narrowing: 2190 ± 260 kpm and 680 ± 80 kpm, respectively (Fig. 5). This indicates that the degree of coronary narrowing is also one of the determinants of exercise tolerance. Unexpectedly, however, 4 patients with complete obstruction in left anterior descending artery showed the higher exercise tolerance than that in patients with narrowing of 75%–99%. These patients received good collaterals from right coronary artery and this may contribute the higher exercise tolerance.

2) Double Product

In our exercise test, a good reproducibility of double product (blood pressure $\times$ heart rate) obtained at the time of chest pain was observed. This suggests that the chest pain is induced at the

Fig.6. Relationship between the extent of increase of double product until chest pain is induced (ΔDP) and the number of involved vessels in 46 patients without prior myocardial infarction.

Fig.7. Relationship between ΔDP and the degree of coronary artery narrowing in 21 patients with a single lesion in left anterior descending artery.

Fig.8. Relationship between electrocardiographic changes (nST & ΣST) at the end-point of exercise test and the number of involved vessels.

Fig.9. Serial ST-segment change during exercise test.

same individual level of myocardial oxygen demand because double product represents the myocardial oxygen consumption (MVO_2).¹³ In this study, we also obtained the change of double product (ΔDP) as an index of the maximal reserve of myocardial oxygen consumption, which was compared with the severity of coronary artery disease in 46 patients without prior myocardial infarction.

Figure 6 shows the relationship between ΔDP and the number of involved vessels. The mean values of ΔDP were 12000 ± 900 , 8200 ± 700 , 5400 ± 1300 , and 4900 ± 1300 mmHg·beat·min⁻¹ in SVD, DVD, TVD, and LMCAD respectively, indicating that the ΔDP becomes smaller with the number of involved vessels. The mean ΔDP in SVD was significantly greater than those in other groups (Fig. 6).

The ΔDP also decreased with the degree of coronary artery narrowing in 21 patients with a single lesion in left anterior descending artery,

except 4 patients with complete obstruction in proximal portion but with good collaterals from right coronary artery (Fig. 7).

3) Electrocardiographic Response to Exercise

In 45 out of 48 patients with effort angina pectoris but without prior myocardial infarction, the significant ST-segment depression (≥ 0.1 mV) was observed in at least one lead of standard 12 leads. This means that the sensitivity of exercise electrocardiography was 94% in our series. Three patients with negative response were all with isolated left circumflex disease.

The total number of leads which showed the significant ST-segment depression (nST) and the summed ST-segment depression (ΣST) in 11 leads (see Method) were obtained at the end-point of exercise. Although large deviation of nST was observed in each group, nST increased with the increase of the number of involved vessels. ΣST was also greater in patients with multiple vessel disease than that in patients with single vessel

Fig.10. Relationship between the exercise tolerance and the extent of increase of double product (Δ DP) until the appearance of a significant ST-segment depression (0.1 mV or more) and the number of involved vessels.

disease (Fig. 8).

Serial electrocardiographic changes in leads V_4 – V_6 demonstrated that ST-segment depression occurred during early phase of exercise and its recovery to the control level was significantly delayed in patients with multiple vessel disease (Fig. 9). Total exercise load to induce the ST-segment depression of 0.1 mV and Δ DP during this period was depicted in Fig. 10. These parameters demonstrated significantly smaller values in patients with multiple vessel disease than in patients with single vessel disease.

DISCUSSION

Our study demonstrated that the total exercise tolerance which represents the external exercise capacity inversely correlated with both the coronary index, the number of involved coronary vessels, and the degree of coronary narrowings except for the isolated left coronary artery obstruction with good collaterals. The change of double product (Δ DP) also inversely correlated with the number of involved coronary vessels. These results indicate that the extent and degree of coronary narrowings directly reflect the decrease of external exercise capacity

and cardiac functional reserve in patients with effort angina.

Previous studies suggested that exercise tolerance^{10,14,15,19} and maximal double product in symptom-limited maximal exercise test^{11,13,19} are useful indices to evaluate functional coronary reserve. Ellstad and Wan,¹⁶ and Goldschlager et al¹⁷ have reported that the patients who demonstrated ST-segment depression with low exercise load had higher incidence of coronary events and more extensive coronary artery disease than those with higher exercise tolerance. Sheffield et al¹⁸ also reported that the exercise tolerance time was closely correlated to the severity of coronary narrowings compared with the degree of ST-segment depression in postexercise electrocardiograms. Although the total exercise tolerance also inversely correlated with the degree of coronary narrowing in patients with a single lesion in left anterior descending artery in our series, 4 patients with a complete obstruction in left anterior descending artery with good collaterals showed relatively high tolerance. In patients with multiple vessel lesions, however, this preferable effect of collaterals was not observed. The cause of discrepancy of the function of

collaterals between in single vessel disease and in multiple vessel disease was not elucidated by our data but the coronary lesions of donor vessels may directly reflect the blood supply to the involved vessels.

The clinical value of exercise electrocardiography to predict the coronary artery disease has been reported by many investigators.^{3-9,16-19} In our study using 12 lead monitoring system, 93% of 48 patients without prior myocardial infarction showed positive exercise response. Three patients with negative response had isolated left circumflex disease. McHenry et al²⁰ reported that 83% of 85 patients who had significant ($\geq 75\%$) narrowings of one or more major coronary arteries had positive exercise response and 73% of the patients with negative response had isolated right coronary artery or left circumflex artery disease. Although their data were similar to ours, they did not investigate the relationship between the severity of coronary lesions and electrocardiographic response. In our study both nST and Σ ST at the end-point in exercise test showed the significant correlation with the number of involved vessels.

These results strongly suggest that the total exercise tolerance and the change of double product obtained in the exercise test could represent the physical and cardiac functional reserve and reflect the resultant coronary blood supply modified by collaterals. The extent and the degree of ST-segment depression in exercise test could also reflect the coronary narrowing and these parameters obtained during the exercise test should be of great value to evaluate the coronary artery disease.

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