Prevalence and Clinical Significance of Silent Myocardial Ischemia in Exercise Test

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Prevalence of silent myocardial ischemia in exercise test was retrospectively reviewed from 749 tests performed for 513 patients with definite evidence of ischemic heart disease. The clinical significance was studied and absence of transient ischemia, occurrence of transient ischemia with and without pain were observed in 48%, 30%, and 22% of the tests, respectively. Anginal pain was frequently observed in exercise tests for patients with severe coronary artery disease and low exercise tolerance. A large number of tests showing ischemic response were discontinued due to symptoms other than anginal pain and hence silent myocardial ischemia could be thought to be a result of ischemic state which does not reach the angina threshold. Silent myocardial ischemia was frequently observed during usual daily life. However, a definite correlation between severity of transient ischemia and presence or absence of chest pain in the same individuals was not obtained in the study. A day to day variation in the angina threshold might be responsible. In general, silent myocardial ischemia was not rare. However, the consistent condition was very unusual. In angina of effort (EA) and old myocardial infarction (OMI), 3.7% and 12.3% were silent, respectively. A higher incidence was obtained in OMI than in EA. This is important for the management of these patients. The mechanism of silent myocardial ischemia and the cause of the different incidence of this state between EA and OMI were not defined and remained to be further studied.

Silent myocardial ischemia is defined as a transient ischemic alteration of the myocardium in the absence of chest pain or its equivalents. It is widely known that asymptomatic ischemic ST changes are frequently observed on Holter ECG monitoring. Painless ST depression is also frequently observed in exercise tests performed to detect ischemic heart disease. However, diagnostic accuracy is not high unless chest pain is accompanied with ST depression. In other words, exercise test becomes a reliable tool for diagnosing ischemic heart disease only when ST depression is accompanied with chest pain. In this sense, two different situations are involved in painless ST depression induced by exercise: one is of non-ischemic etiology and the other is of ischemic origin, called silent myocardial ischemia.

This paper did not aim to study the former situation, but it considers the latter one, especially its prevalence and clinical significance.

SUBJECTS AND METHODS

Subjects were retrospectively selected from a continuous series of exercise tests performed for patients having definite evidence of ischemic heart disease. These included 513 patients with stable angina of effort (EA) or old myocardial infarction (OMI). A total of 749 exercise tests including repeated tests for the same individuals

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were used for this study. Subjects taking digitalis or showing intraventricular conduction disturbance were excluded because of misinterpretation of exercise-induced ST depression. But those taking usual doses of antianginal drugs were included.

EA was diagnosed by an evident past or present history of EA, organic coronary arterial stenosis of 75% or more on coronary arteriography (CAG) or transient defect on exercise thallium scintigraphy. Subjects showing no significant lesion on CAG yet in whom vasospastic angina was suspected were excluded. OMI was diagnosed by a documented history of acute myocardial infarction and abnormal Q wave on recent resting ECG.

Exercise test was performed with Bruce’s protocol using a treadmill up to the symptom-limited maximal level. Horizontal or downsloping ST depression of 0.2 mV or more measured at 0.04 sec after J point was defined as ischemic. Further, tests showing ST depression on the opposite leads to the infarcted site, supposedly the reciprocal change of ST elevation, were excluded.

Items of the study included (1) how frequently silent myocardial ischemia was observed in exercise test, (2) how exercise tolerance differed among subjects showing different endpoint symptoms, (3) what CAG findings were observed in subjects showing silent myocardial ischemia, (4) how reproducibly silent myocardial ischemia was induced and (5) how the severity of ischemia differed between these two states. Further, Holter ECG was recorded in 59 cases showing exercise-induced ischemia accompanied with pain and 430 recordings were used to study (6) how ST depression with or without pain occurred during usual daily life. Horizontal or downsloping ST depression of 0.1 mV or more measured at 0.06 sec from the nadir of S wave on CM5 was defined as ischemic after posture-induced changes were excluded.

A mean value ± 1 SD was calculated for com-
comparison between groups. Statistical analysis was performed by Student's t-test and a p value of less than 0.01 was assessed as significantly different.

RESULTS

(1) Of a total of 749 tests, 360 (48%) showed no significant ST depression and their endpoints symptom was severe shortness of breath or fatigue (SOB tests). The remaining 389 tests showed ischemic ST depression, of which 168 (22%) were accompanied with pain (pain (+) tests) and 221 (30%) without pain (pain (−) tests).

(2) Exercise tolerance time at the endpoint of test and the peak stage of Bruce's protocol are shown in Fig. 1. Exercise endurance time was significantly higher in SOB tests than in other groups of tests. Between the latter two tests, that was significantly higher in pain (−) tests than in pain (+) tests. A ratio of pain (−) to pain (+) tests at each peak stage of Bruce's protocol is also shown in Fig. 1. The incidence of occurrence of pain decreased as exercise tolerance was increased. A comparison of the heart rate (HR), systolic blood pressure (SBP) and their products (DP) between pain (+) and pain (−) tests is shown in Fig. 2. These were all significantly higher in pain (−) tests than in

Fig.3. CAG findings in subjects showing ischemic response with and without pain.

- pain (−): Subjects showing ischemic response without pain
- pain (+): Subjects showing ischemic response with pain
- vessel 1: Single vessel disease
- vessel 2: Double vessel disease
- vessel 3: Triple vessel disease
- LMT: Left main trunk lesion

pain (+) tests. This result also indicated that pain (−) tests showed a higher exercise tolerance than pain (+) tests.

(3) CAG findings in subjects showing ischemic ST depression are shown in Fig. 3. In this study, classification of pain (+) or pain (−) subjects was performed by results obtained from exercise tests and those showing inconsistent results of pain (+) or pain (−) test were classified as pain (+) subjects. Among 76 pain (−) subjects, single and multi-vessel disease including left main trunk lesion were observed in 27 and 49, respectively (a ratio of 1:1.8). Among 101 pain (+) subjects, such disease was observed in 24 and 77, respectively (1:3.2). A higher incidence of multi-vessel disease was observed in pain (+) than in pain (−) subjects.

(4) Precise incidence of chest pain in 266 subjects showing ischemic ST depression is shown in Table I. These subjects were divided into two groups: one of 199 subjects in whom exercise test was performed only once and the other of 67 subjects in whom consistent ST depression was observed in more than two tests. Among the former group, 99 subjects showed pain and 100 did not. Among the latter group, 9 (5 with EA and 4 with OMI) consistently showed pain, 27 (11 with EA and 16 with OMI) consistently did not and the remaining 31 (21 with EA and 10 with OMI) showed inconsistent results. Among 27 subjects with consistent pain (−) tests, 21 were always examined having taken medication. If these cases were

![Control and Bruce protocol stage II (2 min 55 sec)](image)

Fig. 4. An example of exercise-induced silent myocardial ischemia in 58 years old male with inferior old myocardial infarction.

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excluded, only 5 cases with EA showed consistently reproducible pain(−) ischemia. These five included three with single- used disease, one with double-vessel disease and one with left main trunk lesion. The incidence of consistent pain(−) ischemia among ischemic exercise tests in patients having taken no medication was 3.7% (5/136) in EA and 12.3% (16/130) in OMI.

Figure 4 shows an example of exercise-induced pain(−) ischemia. This case was a 58-year-old male with inferior OMI. While performing exercise at stage II of Bruce's protocol, marked ST depression exceeding 0.3 mV developed without pain and was followed by ventricular fibrillation initiated from short runs of ventricular premature contractions. He was successfully resuscitated with DC countershock. This patient has had no chest pain during his recent daily life.

(5) The results obtained from repeated tests in 31 subjects showing inconsistent responses of pain are shown in Table II. Maximal grade of ST depression, numbers of leads showing ST depression of 0.1 and 0.2 mV, exercise endurance time, HR, SBP and DP at the endpoint were no difference between pain(+) and pain(−) tests.

(6) The results obtained from Holter ECG study are shown in Table III. Among 430 ischemic episodes, 76 (17.7%) were accompanied with pain, as contrasted to 354 (82.3%) without pain. The grade of maximal ST depression, persistence of ST depression exceeding 0.1 mV, peak HR at the moment when maximal ST depression occurred and the HR change from the control state were all significantly higher in pain(+) than in pain(−) episodes.

DISCUSSION

Selection of subjects is important for the study of silent myocardial ischemia, because painless exercise-induced ST depression includes a high incidence of phenomena of non-ischemic origin. Subjects selected for this study were limited to patients having definite evidence of organic coronary arterial lesion or myocardial infarction and having had tests strongly suggestive of transient ischemia. Strictly, exercise study tests should be performed without medication. However, the purpose of this study was not
to evaluate the precise pathophysiology of ischemia but to assess the state of routine exercise tests and thus subjects taking usual doses of antianginal drugs were included. The results should be evaluated with these limitations in mind.

In the general sense, silent myocardial ischemia is not rarely observed in exercise test. From the retrospective study, 168 of 389 ischemic tests (56.8%) were painless. Two different types of silent myocardial ischemia should be distinguished among these tests.

One is the situation in which the test is discontinued before the angina threshold is reached. Exercise test usually involves a symptom-limited method in which the endpoint of the test is subjectively determined by occurrence of any symptom which makes it necessary. If a test is discontinued because of shortness of breath or fatigue at a load which does not reach the angina threshold, this test is assessed as painless. So, the presence or absence of pain would be reflected from poor or good exercise tolerance. From this study, anginal pain seems to be easily developed in a test of low exercise tolerance. In contrast, shortness of breath or fatigue increased in a test of moderate to high exercise tolerance. This result could be supported by the finding of a high incidence of severe coronary artery disease among subjects showing ischemic response with pain.

A considerable number of patients showed inconsistent results with or without pain in repeated tests. However, significantly different results could not be obtained concerning the severity of transient ischemia between these two tests. This result can not be well explained by the concept mentioned above. Perception of pain might not be expressed in the same manner by the same individuals, or a day to day variation of pain threshold might exist. However, this explanation is conceptual and further study is required.

The other situation was consistent silent myocardial ischemia. This kind of ischemia was rather rare, especially among patients with EA. An incidence of 3.7% was found in this study. Even in these patients, there is a past or present history of EA. Nevertheless, anginal pain could not always be induced by repeated tests. Its cause is not clear. EA might have been unstable angina in the past and might have stabilized to the mild or low grade, not reaching the exercise test angina threshold. However, this explanation is not satisfactory, because subjects with severe coronary arterial lesion such as double vessel or left main trunk disease were included among those showing consistent silent myocardial ischemia. It is well known that silent myocardial ischemia occurs more frequently in a diabetic state than in a non-diabetic one. No conclusion was possible on this point, because of the limited numbers of subjects complicated with diabetes mellitus. In discussing this problem, silent myocardial ischemia incidentally discovered in exercise tests for health check-ups should be analyzed.

In contrast to the low incidence of consistent silent myocardial ischemia in EA, a considerably higher incidence was obtained in OMI. This would be noteworthy in the clinical setting. As shown in Fig. 4, severe ischemia may occur painlessly and sudden death may occur.

Lastly, ischemic episodes during daily life were studied in subjects showing ischemia with pain in exercise test. A large number of ischemic episodes (82.8%) occurred without pain and the remaining small number (17.7%) were accompanied with pain during daily life. Another study from our laboratory revealed that 59.8% and 40.2% of vasospastic angina occurred with and without pain, respectively. Silent myocardial ischemia occurred more frequently in EA than in vasospastic angina during daily life. EA is thought to be induced by increasing cardiac work and presence or absence of chest pain is dependent on the severity of ischemia determined by the grade of cardiac work. A high incidence of silent myocardial ischemia in EA could indicate that the grade of daily life activities were mostly within the range not reaching the angina threshold. By contrast, most vasospastic angina occurred spontaneously and the severity of occurring ischemia could not be controlled by the grade of physical activity.

It was concluded from this study that occurrence of silent myocardial ischemia in the general sense is not rare, but its consistent occurrence in the same individual is rare among subjects with EA as contrasted to rather high incidence among those with OMI. The mechanism of silent myocardial ischemia and the cause of the different incidence between EA and OMI remains to be determined and further cautious study is required.

REFERENCES

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