SILENT MYOCARDIAL ISCHAEMIA: THE TAN TOCK SENG EXPERIENCE

K H Mak, E K Tan, L Chew, S H Gan, A L K Chan

ABSTRACT

The results of treadmill exercise stress test (TMX) for ischaemia is based on ST-segment depression. Patients with positive test may or may not be symptomatic. This study examines if there are any differences between these two groups of patients.

A total of thirty-nine patients with coronary artery disease and positive TMX results in 1988 was studied. There were 16 patients with chest pain and 23 without. They were followed-up for a mean period of 16.9 and 15.2 months respectively. The following factors were found not to be statistically significant between these two groups of patients: age, sex, race, height, weight, history of hypertension, diabetes mellitus or smoking, indication for the test, use of drugs, total and HDL-cholesterol, exercise duration and the initial double product. The difference between the maximal double product of the two groups was statistically significant (p=0.004).

In the follow-up period, in the group of patients with silent myocardial ischaemia, one had a cardiac event and one underwent revascularisation. While in the symptomatic group, two had cardiac events and seven underwent revascularisation. There were no deaths in either group. The difference in overall outcome was significant statistically (p=0.002).

Therefore, patients with silent myocardial ischaemia have a higher maximal double product in TMX; hence a higher maximal workload and a less adverse outcome compared to symptomatic patients.

Keywords: Coronary artery disease, Outcome, Prognosis, Treadmill exercise stress test.

INTRODUCTION

Silent myocardial ischaemia was once thought to be an uncommon feature of coronary artery disease (CAD). Lately, it was recognised as a common clinical entity. It has been estimated that probably millions of persons have silent ischaemia in the asymptomatic patients[1]. Initially, about one-third of ischaemic patients with CAD are silent[2]. Subsequently, with increasing awareness, some reported that figure to be as high as 87%[3,4].

The exact reason as to why certain ischaemic episodes are silent is unclear. On the one hand, it may represent the earliest or mildest form of coronary disease. On the other hand, it could mean a more ominous sign as a predictor for sudden death as the anginal warning system is defective[2,5,6]. Various methods have been used to detect ischaemia in patients. Treadmill exercise stress test (TMX) is the commonest method em-

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ployed in our unit. This study describes our local experience in the cardiological unit of a peripheral general hospital. The results would be relevant to practitioners who diagnose and treat patients with coronary artery disease based on clinical history and basic investigations.

MATERIALS AND METHOD

Patients with a history for coronary artery disease, after myocardial infarction or revascularisation surgery were included in the study. Those with positive TMX in 1988 were entered into the study. TMX was carried out based on the Bruce protocol using 12 lead electrocardiographic monitoring. The test was positive when the ST segment was depressed at least 2 mm measured at 80 milliseconds from the J-point during exercise or recovery.

The age, sex, race, height, weight, indication for TMX, drugs that the patient was on prior to the TMX, history of hypertension, diabetes mellitus and smoking, fasting cholesterol and HDL-cholesterol levels (which were obtained from the case-notes based on a blood sample nearest to the date of the TMX), the initial and maximal double products and the duration of exercise were compared between the groups of patients with and without pain during TMX.

Long term follow-up information was available by telephone interviews or the last clinic visit. It was eventful when the patient sustained a myocardial infarct, underwent any form of revascularisation procedures (including angioplasty) or death.

The student's unpaired t-test was used to analyse the differences in means (for quantitative variables) and proportions. For categorical variables, the Chi-square test for association and the Fisher's exact test were used. Data management and statistical analysis was assisted by dBase IV, EPISTAT and SPSS (ver 3.1).

RESULTS

There were 39 patients of which 23 had silent myocardial ischaemia (SMI) and 16 were symptomatic. There were 36 (92%) men and 3 (8%) women. The various epidemiological characteristics of the patients are listed in Table I. Race distribution is found in Table II. When these parameters were compared, between the two groups of patients, none of them were found to be statistically significant.

Table I
Characteristics of Patients

Parameter	Silent	Symptomatic	p-value
No. of patients	23	16	
Age (years)	54.1± 8.1	50.1±7.3	NS#
Sex (M/F)*	21/2	15/1	NS
Race (C/NC)+	18/5	12/4	NS
Height (metres)	1.66 ± 0.06	1.64 ± 0.07	NS
Weight (kg)	68.0 ± 11.3	68.0 ± 10.7	NS
Hypertension (Y/N)@	10/1	7/9	NS
Diabetes mellitus (Y/N)	5/18	3/13	NS
Smoking (Y/N)	14/9	10/6	NS
Cholesterol (mg/dl)	242.2 ± 35.4	235.1 ± 41.9	NS
HDL-cholesterol (mg/dl)	45.6 ± 7.1	42.0 ± 7.9	NS

\# not significant
* male/female
+ Chinese/non-Chinese
@ Yes/No

Table II
Race Distribution

Race	Silent	Symptomatic
Chinese	18	12
Malay	2	3
Indian	3	1

Table III
Indication for TMX

Indication	Silent	Symptomatic
Coronary artery disease (%)	14 (60.9)	9 (56.2)
Post-infarct	6 (26.1)	4 (25.0)
Post-surgery	3 (13.0)	3 (18.8)
Total	23 (100)	16 (100)

Table IV
Use of Drugs

No. of drugs used	Types of drugs	Silent	Symptomatic
None		3 (13.0)	0
One only	(a) beta-blockers	4	2
	(b) calcium antagonist	2	1
	(c) nitrates	2	5
Subtotal		8 (34.8)	8 (50.0)
Two	(a) and (b)	4	1
	(a) and (c)	4	3
	(b) and (c)	4	2
Subtotal		12 (52.2)	6 (37.5)
All three	(a), (b) and (c)	0	2 (12.5)
Total		23 (100)	16 (100)
Mean number of drugs used		1.4 ± 0.7	1.6 ± 0.7

Chi-square (df=1) p>0.05
unpaired t-test (df=37) p=0.326

The indications for TMX are shown on Table III. We did not find that the difference in the proportion of patients in each category to be significant statistically. The use of drugs was also assessed. From Table IV, it appears that the group of patients who were symptomatic were placed on more drugs than the group of patients who had silent ischaemia. However, the difference in the mean number of drugs used was not statistically significant. Due to the small numbers of patients, the patients who were placed on one drug or none at all were grouped together for the purpose of comparison.

The mean duration of exercise for the symptomatic group (1.5 to 18.0 minutes) was 1.8 minutes shorter than the silent group (4.5 to 15.5 minutes). This was also not significant statistically.

Though the initial double product was higher in the silent group than the symptomatic group, it was not significant (Table V). On the other hand, the maximal double product was significantly higher in the silent group.

Table V
Characteristics at TMX

Parameter	Silent	Symptomatic	p-value
Exercise duration (mins)	12.2 ± 4.0	10.4 ± 3.2	NS
Initial double product*	10240.7 ± 2502.0	9882.5 ± 1645.6	NS
Maximal double product*	25220.3 ± 5632.8	19707.5 ± 5312.1	0.004

* mmHg.beats/min

Table VI
Results of Follow-up

Parameter	Silent	Symptomatic	p-value
Follow-up duration (mths)	15.2 ± 6.2	16.9 ± 6.2	NS
Eventful outcome	2/23	9/16	0.001
Types of Event			
infarction	1	1	NS
revascularisation	1	7	<0.05
death	0	0	NS

Of the 23 patients with SMI, 13 (51%) had coronary angiography. On the other hand, 12 (75%) of the patients who had symptoms had the same test. The mean number of diseased vessels in the silent group was 1.6 ± 0.3 and the symptomatic group was 2.4 ± 0.2 (p=0.04).

After a mean period of 15.2 months and 16.9 months of follow-up for the silent and symptomatic groups respectively, there were more patients with an eventful outcome for the symptomatic group. Two of them had myocardial infarction and seven had revascularisation procedures. Whilst only one patient had myocardial infarction and another had revascularisation in the silent group. There were no deaths in either group for the duration of follow-up.

DISCUSSION
TMX is a common means of assessment of patients with coronary artery disease. Its value in identifying a high risk subset of patients with positive low level exercise is used for risk stratification in the post-infarction period. This is independent of chest pain[9,10]. It was later found that prognosis was dependent on the extent of coronary artery disease, left ventricular function and exercise duration[11,12]. Similarly, Weiner[13,14] showed that prognosis after coronary artery surgery did not depend on symptoms but on extent of disease. On the other hand, from the Duke-Harvard Collaborative Coronary Artery

Disease Data Bank[5], in a 4-year follow-up period, the mortality was 2.7% for the asymptomatic and 5.4% for the symptomatic group in exercise-induced ST segment depression every year. The mortality was also higher in patients with triple vessel disease for the symptomatic group (8.7 versus 4.7%). The mean number of diseased vessels were less in the silent group compared to the symptomatic group. This accounts for the use of greater number of drugs and also the greater number of patients who underwent revascularisation procedures. Furthermore, there was a larger proportion of patients in the symptomatic group who underwent coronary angiography. This could also mean that there were more difficulties in controlling angina compared to patients with SMI.

Though our patients were heterogenous, there was no significant difference in each of the subgroups for indication for the TMX (Table III). It is interesting to note that there were no deaths in either group in the follow-up period. There was no difference in the proportion of patients with subsequent infarcts in both groups. The difference came from those who required revascularisation. A review of these group of patients actually showed that most of them had pain which was not adequately controlled by anti-anginal drugs. Though patients in the symptomatic group had more diseased vessels, could this also mean that symptomatic patients have a lower threshold for pain and hence more of them were subjected to revascularisation procedures since the eventual end-points like death and infarction are the same?

Droste[15] studied the pain threshold and tolerance in 20 patients with asymptomatic ischaemia and 22 patients with reproducible angina. He found that all the patients with silent ischaemia had a higher threshold for electrical and forearm ischaemic pain and a higher tolerance for cold pressor and forearm ischaemia. The psychological make-up of such patients was also found to be different using the Freiberger Personality Inventory Test[16]. This difference in pain perception may be mediated by endorphins[15,17-19]. Contrarily, using similar methods of study, other authors could not reproduce the results[21-24]. This confusion is brought about by the discrepant or insensistive radioimmunoassay methods with cross-reactivity to non-opoids and considerable overlap of levels. There is also variation between individuals and the time of day the blood was assayed.

Our asymptomatic patients had a higher exercise capacity compared to the symptomatic group. This may be due to the differences in the amount of myocardium at jeopardy. The painless episodes could mean less severe ischaemia and hence the patients can tolerate a higher workload. Studies had shown that electrical, perfusion defects in radionuclide scans and wall motion abnormalities occurred before the onset of pain[25-27]. This theory is further substantiated by the fact that painless ischaemic episodes were shorter in duration and had less left ventricular abnormalities[28-32]. But, there were overlaps and should be interpreted with caution. Nevertheless, these studies suggest a better outcome for the silent group compared to the symptomatic group.

CONCLUSION
We found that patients with silent myocardial ischaemia have a higher maximal workload and a better prognosis in terms of subsequent revascularisation procedures compared to the symptomatic group. The number of patients in the study was small and hence caution has to be exercised in interpreting the results. But this finding was consistent with other studies. Patients who are symptomatic may have more severe disease than those who are not. The patient's perception of pain may also play a role in symptomatology.

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