Should Troponin-T Be Assessed During Exercise Stress Testing in Patients with Stable Angina Pectoris?

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Objective: This study was planned to investigate whether or not troponin-T positivity has occurred during exercise stress testing in patients with stable angina pectoris and if yes, its relationship with the severity of the disease.
Methods: One hundred patients with stable angina pectoris who presented with typical chest pain were included in this study. They were subjected to the exercise stress testing according to Bruce protocol. Troponin-T was studied 3 times: immediately before, 6 and 24 hours after the exercise testing. Coronary angiography was performed two hours after the last blood sampling.
Results: Exercise stress test was found positive in 67 (67%) and negative in 33 (33%) patients. Coronary artery disease was present in 47 (70.1%) of those with positive and in 17 (51.5%) with negative test results. Troponin-T was negative in all the patients before the stress test. Troponin-T was found positive in readings taken 6 and 24 hours after the test in 4 patients (6.2%) with coronary artery disease. Of these patients, 2 had positive and the remaining 2 had negative stress test results. Troponin-T was found negative in readings after the stress test in all the patients without coronary artery disease. The duration of the exercise stress test was found to be significantly shorter in patients with troponin positivity than their counterparts with negativity (277.5±81 sec vs. 428.8±195 sec, p=0.024). Troponin-T positivity after the stress test was found considerably higher in patients with three-vessel disease (p=0.021).
Conclusions: Heavy exercises like stress test may severely lead to myocardial damage. The study of post-stress test troponin T readings, in patients with stable angina pectoris and with negative stress test result, may be of great help in detecting especially the patients with multiple vessel disease. *(Ana Kar Der, 2002;2: 132-7)*
Key Words: Exercise stress testing, troponin-T, stable angina pectoris

Introduction

Exercises stress testing is a diagnostic method frequently employed in patients with chest pain (1), however, the probability of the test to be negative is rather high in patients with coronary artery disease. The test may prove negative even in three-vessel disease. In recent years, as an indication of myocardial damage, troponin-T has begun to be used. It is known that cardiac events occur more often in unstable angina in case of troponin-T positivity (2-6). While it is reported that the elevation of troponin-I during the stress test in patients with unstable angina may be an indication of ischemia (7), literature lacks information as to whether troponin-T rises during exercise stress testing in patients with stable angina. For this reason, we planned this study to investigate whether or not troponin-T increases after exercise stress testing in patients with stable angina, and if yes, its relationships with the severity of the disease.

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Material and Methods

Study patients

Patients with stable angina pectoris diagnosed during clinical examination in the outpatient clinic of

cardiology department were included in the study. First exercise stress testing, and then coronary angiography were planned. The following were accepted as the exclusion criteria of the study: being taken antihistaminic agents or digitalis, the presence of a non-cardiac reason for angina, severe aortic stenosis, hypertension, cardiac failure, anaemia, right or left bundle block on ECG, unstable angina, and presence of contraindications to exercise stress testing. One hundred patients, 64 (64%) male and 36 (36%) female, were taken into the study. The mean ages of the male and female patients were 53±11 years and 52±8 years, respectively. All the patients had the typical chest pain.

Study protocol and procedures

After written consent had been obtained, all the patients were subjected to exercise stress testing according to Bruce protocol. A record was kept of the duration, workload, and the negativity or positivity of the test. The test was considered positive in cases of typical chest pain, aggravation of the pain during the testing and/or occurrence of ST depression over 1 mm in at least 2 deviations [horizontal or downsloping ST-segment depression of 0.10mV (1.0mm) or more for 80 msec in at least three consecutive 'isoelectric' or level complexes] or a fall of 10 mmHg or more from the initial systolic blood pressure.

Venous blood samples were taken for the study of troponin-T levels immediately before, 6 and 24 hours after the test. Troponin measurements were done using the cardiac troponin strips (Roche Diagnostics, Cardiac Troponin T Quantitative), and the troponin level over 0.1 ng/dl was considered positive.

At most 2 hours after the completion of blood sampling, coronary angiography was done. Coronary artery disease was defined by the presence of angiographically detectable lesions of any severity and graded in 5 groups according to off-line quanti-

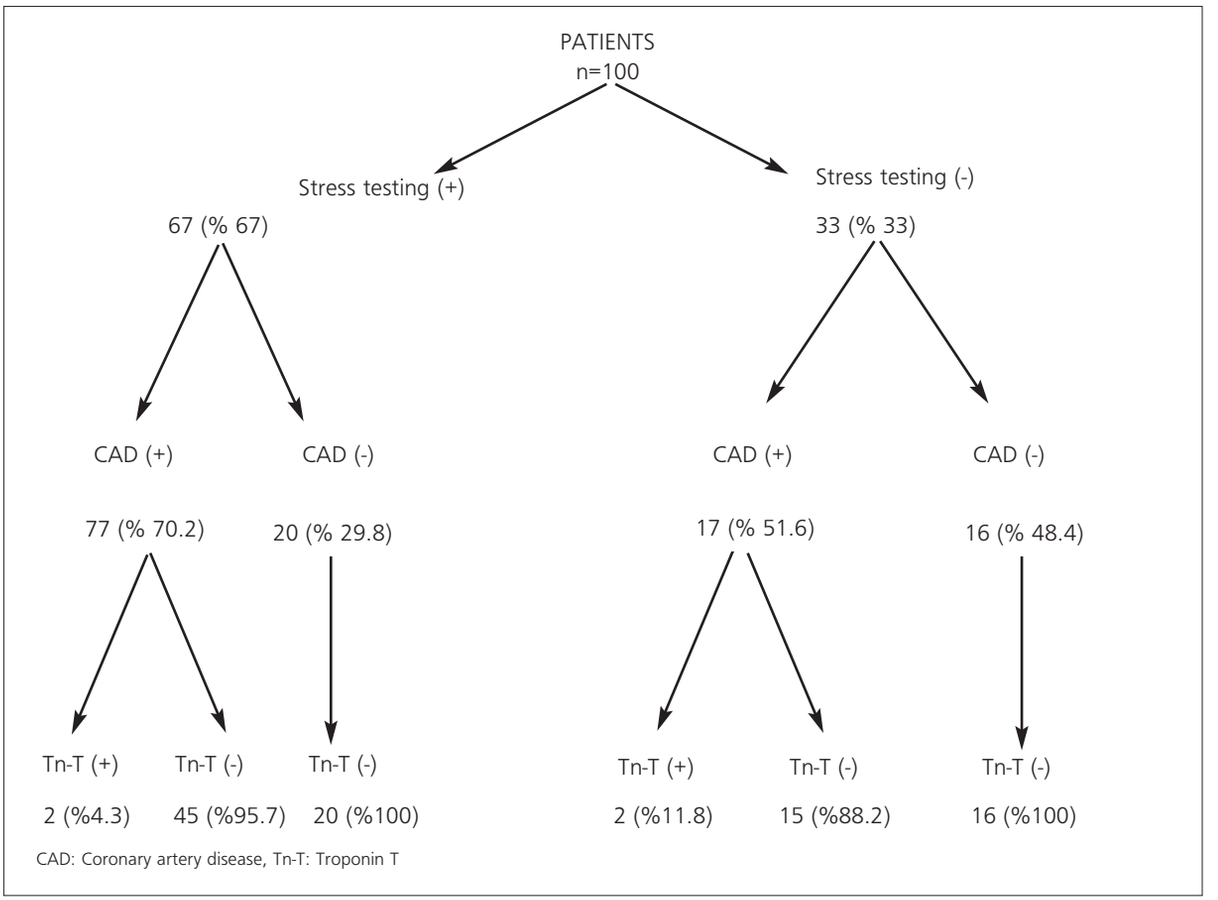

Figure I: Schematic depiction of patients

tative angiographic analysis; normal: no vessel alterations, non critical: vessel alterations with no lesions >70%, one vessel: significant lesions >70% in one major vessel, two vessels: significant lesions >70% in two major vessels, and three vessels: significant lesions >70% in three major vessels. The number of the vessels with critical lesions and the absence or presence of wall movement disorder on ventriculography were recorded. Left ventriculography was evaluated at 5 different segments on right anterior oblique plane: posterobasal, inferior, apex, anterolateral and anterobasal. Scoring was as follows: normal wall movement=1, mild or moderate hypokinesia=2, severe hypokinesia=3, akinesia=4 and dyskinesia=5 (8).

For all statistical analyses, a P value of less than 0.05 was considered to indicate a significant difference. All calculations were performed with IBM compatible SPSS (version 8.0) and two-tailed Student's t-test for continuous variable, chi-square test for categorical data and Fisher exact test for small samples were used to make comparison between the groups.

Results

The study diagram of the patients and their main characteristics are presented in Fig. 1 and Table 1. Exercise stress testing was found positive in 67 patients (67 %) and negative in 33 (33%) patients. Coronary angiography was normal in 20 (29.8%) of the 67 patients with the positive test results. Coronary angiography was abnormal in 17 (51.5%) of the 33 patients with negative test results, and 5 of these patients had three vessels disease. While troponin-T was found negative in all the patients before the test, it was found positive 6 and 24 hours after the test in four patients (6.2%) with coronary artery disease. The exercise stress testing was positive in 2 of these patients and negative in the other two (p>0.05). Three vessels disease was detected angiographically in all patients with troponin-T positivity. When compared with the other patients, troponin-T positivity in patients with 3 vessels disease was found statistically significant (p=0.02). The duration of the test in those with troponin-T positivity was meaningfully shorter (277.5±81 sec, 428.8±195 sec, (p=0.024). Troponin-T was found positive in no patients with normal coronary angiography regardless of their positive or negative exercise stress test results.

Table 1: Baseline and clinical characteristics of study patients

			Tn-T(+)	Tn-T (-)	P
Age (year)			61.7±6.1	52.9±9.1	0.060
Sex					NS
	Male		4	60	
	Female		-	36	
Test duration (sec)			277.5±81	428.8±195	0.024
Angiography					
	Normal		-	36	NS
	Abnormal				
		Non critical	-	11	NS
		One vessel	-	24	NS
		Two vessels	-	13	NS
		Three vessels	4	12	0.021
Stress testing					
	Positive				NS
		CAD (+)	2	45	
		CAD (-)	-	20	
	Negative				NS
		CAD (+)	2	15	
		CAD (-)	-	16	
Wall motions abnormalities					NS
	Yes		3	42	
	No		1	54	

Tn-T: Troponin-T, CAD: Coronary Artery Disease, NS: p>0.05

Three of the 4 patients with troponin-T positivity had wall movement disorder, unlike the remaining one.

Discussion

On account of its being noninvasive and of low cost, exercise stress test is a frequently employed diagnostic method in patients suspected of coronary artery disease. However, its probability of proving false positive and negative is high. In our study population, coronary arteries were found normal in 29.9% of those with positive exercise stress test results. The proportion of coronary artery disease in those with negative test results, on the other hand, was 51.5 %. Such a high incidence of coronary artery disease in patients with negative test results can be explained with the fact that those patients are mostly the ones with single vessel disease.

Troponin-T has been used frequently in recent years both to diagnose coronary artery disease and to determine its prognosis. Troponin-T is a sensitive marker of myocardial injury and prolonged ischemia has been associated with detectable blood levels of troponin-T in patients with unstable angina pectoris without clinical findings for acute myocardial infarctions (9,10). Troponin-T has been found positive in 16% of the 773 patients who presented themselves to the emergency clinic with chest pain and this proportion in those with myocardial infarction has been reported to be 94%. Troponin-T has been found positive in 22% of the 315 patients with unstable angina pectoris and it has been noted that the cardiac complications in these patients were greater than in the others (11). Collinson et al. have reported that troponin-T in patients with myocardial damage was positive by as high as 97.6 % (12). It has been reported that, in patients with high troponin-T levels, both the number of diseased arteries and lesions in the arteries were greater (13). Furthermore, high troponin levels have been reported to be able to indicate even the minor cardiac damages (14) and to rise in laboratory animals even after cardiac punction (15). It has been reported that the strips analysis may reliably be performed by doctor and nurses outside the laboratory and that its diagnostic value is the same as that done in the laboratory (16,17). We, too, used strips in our study since they were reliable and practical.

The elevation of enzymes in marathon runners and those who do heavy exercises has aroused interest and the answer has been sought to the question of whether or not cardiac damage has occurred. It has been reported that the rises in creatine kinase (CK) and CK-MB are due to skeletal muscles during the marathon (18) and also it has been demonstrated through myocardial perfusion scintigraphy that ischaemia does not occur in those with elevated enzyme levels (19). Collinson et al have studied CK, CK-MB and troponin-T levels in 219 soldiers with no cardiac disease after subjecting them to vigorous exercise and reported that CK and CK-MB have increased 22.6 and 6.6 fold, respectively. They maintained that these elevations stemmed from non-cardiac factors, and reported that the troponin-T elevations were noteworthy only in 2 soldiers (20). However, these soldiers were not scanned scintigraphically for myocardial ischemia nor did they undergo coronary angiography. Therefore, it is hardly easy to say that they had cardiac ischemia. Cummins et al. have studied the pre- and post-race troponin-I, CK, CK-MB, myoglobin, tropomyosin and C-reactive protein levels in marathon runners, and reported that CK, CK-MB, myoglobin and tropomyosin levels, unlike troponin-I and C-reactive protein levels, have risen significantly after the race. Judging from the relationship between the enzyme levels, they proposed that the increase resulted from the skeletal muscles, not from the cardiac muscle (21). In a similar study, Siegel et al, too, reported that no elevation in troponin-T and -I occurred (22). All the subjects in these studies were young and/or sportsmen; therefore they could not be expected to have cardiac damage, unless they had coronary artery disease, even after vigorous exercise. Nevertheless, such damage is more likely to occur in those suspected of coronary artery disease. But it is clear that there is hardly any information in the literature to show whether troponin-T rises during the exercise test in such patients. In our study troponin-T was found positive in 4 (6.2%) patients with coronary artery disease, two of whom had negative results of exercise tests and these four patients had also three vessels disease. This situation suggests the probability of myocardial damage, slight as it is, during the pain in patients with multiple vessel disease. Furthermore, the meaningfully short length of exercise test, and again the meaningfully low workload in patients with troponin-T positivity may be an early indication of myocardial damage. However, it may be helpful to study troponin-T

especially in order to detect the three-vessel disease in patients with stable angina pectoris, particularly in those who have completed the exercise test earlier than others, even if their exercise tests are negative.

Limitations

Since the proportion of the patients whose troponin-T level rose during the exercise test was low, it was impossible to study the relationship between the known risk factors for coronary artery disease and troponin-T elevation. This would be studied more appropriately in series with greater number of cases.

Though it has been found reliable to study troponin-T levels using strips, quantifications in a laboratory may be thought to be more accurate. However, since troponin-T measurements in emergency units and clinic are done by means of strips, the findings in our study may be closer to those in real life.

Conclusion

In conclusion, though the proportion of the myocardial damage during the exercise test is 6.2 % in patients with coronary artery disease, this should be considered important. It may be helpful to study post-test troponin-T in order to detect the patients with multiple vessel disease, especially those with stable angina pectoris and negative exercise test results.

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