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Significance of Cardiac Troponin T Release in Detecting Minor Myocardial Injury After Percutaneous Transluminal Coronary Angioplasty

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Abstract: Cardiac Troponin T (TnT) is a regulatory contractile protein not normally found in blood. Its detection in the circulation has been shown to be a sensitive and specific marker for myocardial cell damage. This study was designed to evaluate the diagnostic efficiency of TnT enzyme immunoassay in detecting myocardial damage in patients with stable angina pectoris undergoing visually successful percutaneous transluminal coronary angioplasty (PTCA) and to compare this newly developed test with the conventionally used cardiac enzyme tests. The study population consisted of 24 patients (3 females and 21 males) with a mean age of 55±9 years. Serial blood samples were drawn for measurement of serum Tn T, CPK and CK-MB activities before the PTCA procedure and at the 4th, 8th and 16th hours thereafter. At the same time, ECG was also recorded. We used an enzyme immunologic assay for the quantitative determination of serum Tn T and enzymatic methods for CPK and CK-MB.

Tn T levels >0.2 ng/ml, CPK levels >190 U/L and CK-MB levels >24 U/L were assumed to be an abnormal increase and indicative of myocardial injury. None of the patients showed either ECG evidence of myocardial infarction or CPK elevation. However, Tn T was elevated in 15 of 24 patients (62.5%) while CK-MB was elevated in only 6 of them (25%), whose Tn T levels were also elevated. Patients with elevated Tn T and CK-MB did not differ from the others with respect to demographic data or in the PTCA procedure. Serum Tn T and CK-MB levels were more elevated in patients with type C (morphologically complex) and multivessel lesions.

The results of this study demonstrate the high diagnostic sensitivity of Tn T versus CK-MB and CPK in detecting minor myocardial damage after successful PTCA.

Key Words: Troponin T, percutaneous transluminal coronary angioplasty

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Introduction

Percutaneous transluminal coronary angioplasty (PTCA) is a well-established technique for myocardial revascularization (1, 2). The duration of coronary occlusion and subsequent myocardial ischemia in uncomplicated PTCA is brief and usually well tolerated by myocardium (3). There is controversy as to the source and significance of mild elevations of CPK and CK-MB activities in patients undergoing PTCA (1, 4-6). This is mainly the result of a lack of cardiac specificity of these biochemical markers and the presence of CPK and CK-MB release in reversible ischemia (1, 7, 8).

Recently, Katus et al. developed an enzyme immunoassay for the cardiac Tn T isoform which has proved useful as a diagnostic tool in detecting minor ischemic myocardial damage in unstable angina pectoris

not detected by measurements of CK-MB activity (1, 9-11).

TnT is the tropomyosin-binding protein of the troponin regulatory complex located on the thin filament of the contractile apparatus of the myocyte (11). The advantages of TnT are its cardiospecificity (caused by a cardiac isoform), a measurable ongoing release from necrotizing myocytes and a sensitive immunoassay (1, 9-11).

The purpose of the present study was therefore to investigate the diagnostic efficiency of TnT enzyme immunoassay in detecting minor myocardial injury in patients with stable angina pectoris undergoing visually successful PTCA and to compare this newly developed test with the conventionally used cardiac enzyme tests.

Material and Methods

In this study conducted in the hospital of Ege University School of Medicine, the procedures followed were in accord with the ethical standards of the committee on human experimentation of the hospital of Ege University Medical Faculty.

The study population consisted of 24 patients (3 females and 21 males) with a mean age of 55±9, who were hospitalized in Cardiology Department for the PTCA procedure. Serial blood samples were drawn for measurement of serum TnT, total CK activity (CPK) and CK-MB activity before the PTCA procedure and at the 4th, 8th and 16 th hours thereafter. At the same time, 12 lead ECG was also recorded.

Blood samples were stored at room temperature for 30 minutes to allow clotting. After centrifugation at 5000g for 10 minutes, the serum samples were stored frozen at -10°C as aliquots for a maximum of two months until the analysis.

For the quantitative determination of serum TnT, an enzyme immunoassay (ELISA Troponin T; Boehringer Mannheim) was used. Based on a technique using streptavidin, this single step sandwich assay allows serial determination of blood samples to be made within two hours (9-13).

Commercially available kits were used for the determination of serum CPK and CK-MB levels (CK-NAC activated, CK-MB NAC activated, Boehringer-Mannheim).

For TnT, the reference interval (0.0-0.2 ng/ml) was established from samples of ten healthy blood donors from laboratory staff. Values greater than 0.20 ng/ml for TnT, 190 U/L for CPK and 24 U/L for CK-MB were

assumed to be an abnormal increase and indicative of myocardial injury.

Statistics: Comparison was made between the group with normal TnT and CK-MB values versus the group with increased TnT or CK-MB values using Student's *t* test. A *p* value <0.05 was considered statistically significant.

Results

In our study all patients had normal values for all cardiac markers before PTCA. After angioplasty, none of the patients had chest pain suggestive of ongoing ischemia and also none of them showed either ECG evidence of myocardial infarction or CPK elevation. However, TnT was determined to be elevated in 15 of 24 patients (62.5%) while CK-MB was elevated in only 6 of these patients (25%) within 16 hours after the PTCA procedure.

The demographic data are listed in Table 1. Patients with elevated TnT and CK-MB values did not differ from the others with respect to demographic data or in the PTCA procedure (Table 1). According to ACC/AHA classification of lesion type morphologically (14), type C lesions were the complex lesions with low success (<60%) and high risk for PTCA. Serum TnT and CK-MB levels were more elevated in patients with type C and multivessel lesions. The relative increase of TnT and CK-MB values after the PTCA with respect to the mean values prior to PTCA are shown in Figure 1. The mean±SD values of cardiac marker proteins before and after the PTCA procedure are presented in Figures 2 and 3, respectively.

	Total	Normal CK-MB/TnT	Increased CK-MB	Increased TnT
Number of patients	24	9	6	15
Male/Female ratio	3/21	2/7	0/6	7/8
Median age, years	55±9	54±7	54±6	57±9
Cardiac risk factors				
* Previous AMI	12	5	7	2
* Systemic hypertension	1	0	1	0
* Diabetes mellitus	1	0	1	0
* Hyperlipidemia	9	4	5	3
* Family history	6	1	5	1
* Cigarette smoker	18	7	11	3

Table 1. Demographic data of the patients with stable angina pectoris undergoing visually successful PTCA.

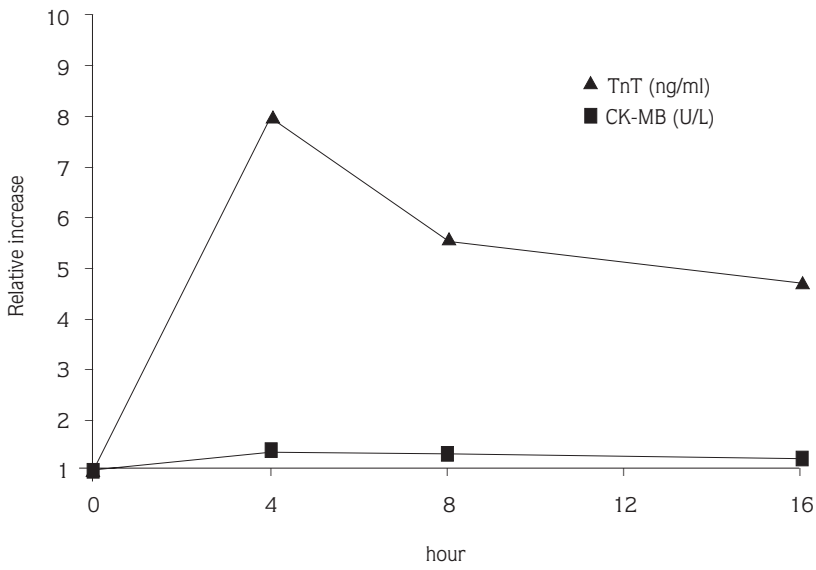


Figure 1. Relative increase of TnT and CK-MB values after the PTCA with respect to the mean values before the PTCA procedure.

n: 24	CPK (U/L)	CK-MB (U/L)	TnT (ng/ml)
Before PTCA	71.2±20	17±5.7	0.07±0.04
After PTCA			
* At the 4th hour	102±53	24±10	0.56±0.89
* At the 8th hour	81±33	23±11	0.36±0.35
* At the 16 th hour	74±24	21±10	0.33±0.34

Table 2. Cardiac marker proteins before and after the PTCA procedure (mean±SD values)

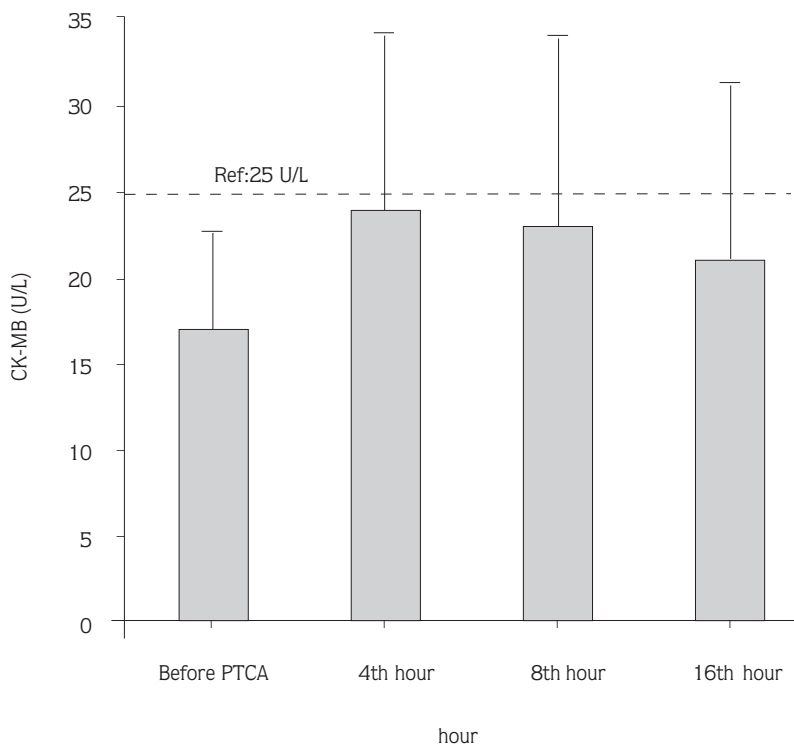


Figure 2. Mean±SD values of CK-MB before and after PTCA procedure.

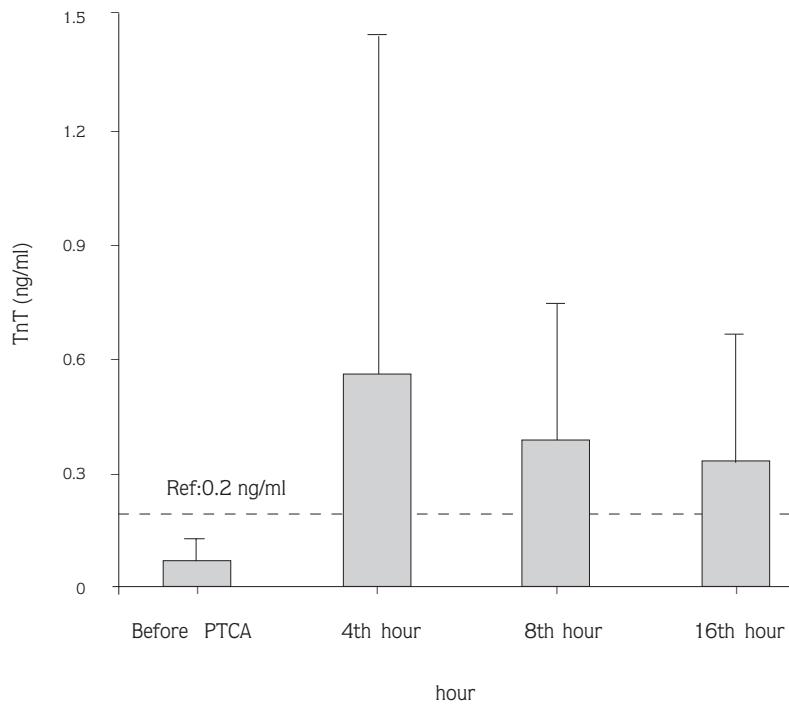


Figure 3. Mean±SD values of TnT before and after PTCA procedure.

Discussion

Elevation of CPK or CK-MB activity is seen in 15% to 20% of successful angioplasties. There is controversy as to the source and significance of mild elevations of CK-MB activity in patients undergoing PTCA (4-6). The duration of coronary occlusion and subsequent myocardial ischemia in uncomplicated PTCA is brief and usually well tolerated by myocardium (3).

Biochemical marker release may or may not reflect irreversible ischemia. In a cell culture of adult heart cells, Piper HM et al. (8) showed a gradual release of cytosolic enzymes from reversibly injured myocardial cells subjected to anoxia. These findings were supported by those of Heyndrickx GR et al. (7) who with their conscious baboon model showed that CPK and CK-MB release may occur after short periods of coronary occlusion without myocardial necrosis. Whether these cardiac marker elevations reflect reversible or irreversible ischemia is not clear, as this study provides no histological evidence.

In our study comprised of 24 patients TnT levels >0.2 ng/ml were detected in 15 of 24 patients (62.5%) within 16 hours after the PTCA procedure while only 6 patients (25%) all of whom TnT levels were also elevated had increased CK-MB activity and none had CPK elevation (Table 1).

Our results are in concordance with Karim MA et al. (3) who reported that TnT levels >0.2 ng/ml were detected in 11 of 25 patients (44%) while only 4 patients (16%) had CPK elevation 24 hours after the PTCA procedure which was diagnostic for acute injury. As to Ravkilde J. et al. (1), they found CPK to be elevated in 9% of their series, with no CK-MB elevation in any of their cases and TnT to be elevated in 13% of their patients within 10 to 24 hours.

Meanwhile, Talasz H. et al (15) found TnT elevated in 14% (3 of 21) of their patients. However it must be pointed out that this percentage is not directly comparable to ours, as these investigators used a higher discriminator value (0.50 µg/L).

In our study, comparative analysis of TnT and CK-MB as markers of minor myocardial injury after PTCA clearly indicated that TnT had a significantly higher sensitivity with respect to CK-MB ($p < 0.05$). Our results also reflect that PTCA frequently produces measurable levels of TnT. The lack of diagnostic sensitivity of conventional CPK and CK-MB activity assays makes it almost impossible to determine whether minor myocardial damage has occurred during episodes of unstable angina or PTCA. In our study in patients with type C and multivessel lesions more elevated serum TnT and CK-MB levels were observed.

Diagnostic sensitivity defines the probability of a positive test result for myocardial damage in patients with stable angina pectoris undergoing visually successful PTCA and calculated by dividing no. of PTCA subject with positive test result to no. of all PTCA subjects tested and therefore indicates how surely patients with PTCA would produce a positive test result. This study demonstrates a very high diagnostic sensitivity of TnT versus CPK and

CK-MB in the detection of minor myocardial injury after PTCA.

TnT uncovers severe myocardial ischemia/minor myocardial damage even in patients with inapparent clinical and electrocardiographic evidences after visually successful PTCA. For determining the efficacy of coronary angioplasty the application of TnT may be of considerable value in the future.

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