CARDIAC TROPONIN-T AND CK-MB (MASS) LEVELS IN CARDIAC AND NON CARDIAC DISEASE

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ABSTRACT

Serum cardiac troponin T (cTnT) and CKMB (mass) were analysed in three groups of patients. The first group (n=32) were patients with acute coronary syndromes including myocardial infarction. The second group (n=35) were patients with hypertension. The third group (n=24) were patients who had succumbed to non cardiac diseases. In all 3 groups, cardiac troponin T was elevated when compared with controls ($p < 0.001$). However, CKMB elevation was not significant in all groups. CKMB levels correlated well with troponin T levels only when CKMB was greater than 50 ng/ml ($r=1.00$). Small elevations of troponin T identifies minimal cardiac necrosis and patients can benefit from early invasive therapy.

KEY WORDS

Troponin-T, CK-MB (mass), hypertension, acute coronary syndromes.

INTRODUCTION

The earliest clinical use of troponin -T levels was in the diagnosis of myocardial infarction (MI) where in it was found to be highly specific with a positive predictive value higher than CK-MB (1). Emerging studies are using elevated levels of troponin-T to indicate mild cardionecrosis in conditions other than MI. These include cardiotoxic chemotherapy (2), uremia (3), cardiogenic pulmonary edema in patients without MI (4) and following stent implementation (5).

In preliminary observations, we found that the quantum of increase in CK-MB (mass) was disproportionate to that of troponin-T. This study was conducted in 3 different groups of patients to determine the difference in the quantum of troponin-T and CKMB (mass) elevations. The first group of patients were those with acute coronary syndrome. This is defined as a spectrum of clinical presentations ranging from unstable angina through a non Q MI and Q wave MI (6). In a second group of patients, troponin-T and CK-MB (mass) were determined in patients with a clinical history of hypertension, without a previous history of acute coronary syndrome. The possibility of troponin-T and CK-MB (mass) elevations as an index of myocardial

dysfunction was studied retrospectively in a third group of patients who succumbed to non-cardiac diseases. The aim of studying this group was to determine the use of troponin-T to identify patients at risk of developing cardionecrosis secondary to metabolic changes occurring in non-cardiac terminal events following septicemia, chronic renal failure and diabetes mellitus.

METHODS

Patients presenting to the Kamineni Hospital with suspected acute coronary syndromes with a history of one or more episodes of angina and ECG confirmation of MI by the cardiologist comprised the Group I patients (n=32). Venous blood samples were drawn, using a tourniquet, immediately on admission and serum was analysed within 30 min. Persons presenting for a routine, general health check-up with normal ECG pattern were taken as the control group, (n=15). Patients with a history of primary hypertension (n=22) and patients who were diagnosed with primary hypertension at admission (n=13) comprised the second group of patients. The details of these patients is given in Table 1.

The third groups of patients were those who succumbed to non-cardiac diseases like septicemia, renal failure or metabolic complications arising from diabetes mellitus in whom troponin-T and CKMB (mass) had been analysed before the terminal event (n=24).

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Table 1. Details of patients in Group II (n = 35)

Age	: 39 ± 6.3 years
Male : Female	: 24 : 11
Diastolic pressure	: 115 ± 17 mm Hg
Systolic Pressure	: 198 ± 23 mm Hg

Estimation of troponin-T and CK-MB (mass)

Troponin-T was determined by means of a third generation assay (sandwich immuno assay) based on electrochemiluminescence (Elecsys, Roche Diagnostics) which uses recombinant human cardiac troponin-T as a reference standard. CK-MB (mass) was also determined on Elecsys (Roche Diagnostics) (7)

In all 3 groups, the objective was to determine the quantity of troponin-T raised in proportion to the CKMB (mass). This would identify CKMB (mass) levels which correspond to clinically significant troponin-T levels in case the laboratory has access to performing only CKMB tests. Another objective of the study was to determine whether the clinical use of troponin T levels alone would serve as an indicator of myocardial dysfunction in acute coronary syndromes, hypertension and non-cardiac diseases.

RESULTS

In Group1, patients with symptoms of angina had significantly higher CK-MB (mass) and troponin-T levels when compared to healthy controls ($p < 0.001$, Table 2)

The correlation coefficient (r) between CK-MB (mass) and troponin-T was 0.81 in controls and 0.75 in the patient group. These patients were subdivided into 4 subgroups (A,B,C,D) based on the levels of serum CK-MB (mass). The results

are shown in Table 3. In subgroup A, when CK-MB (mass) levels were less than 15 ng/ml, CK-MB(mass) levels did not correlate with troponin-T levels and were not proportionately elevated ($r = -0.13$), although troponin-T was still significantly elevated from the control. Higher CK-MB (mass) levels which indicates greater severity of cardiac damage correlated better with troponin-T. (Subgroup C, $r = 1.0$; subgroup D, $r = 0.76$). When compared to subgroup A, subgroup C had an 18 fold increase in CK-MB (mass) and a 4.5 fold increase in troponin-T levels. This indicates that small elevations of troponin-T are as significant as large elevations of CK-MB (mass).

In the second group, patients with a previous history of hypertension, ($n = 22$) had mild elevations of troponin-T, (0.024 ± 0.013). Patients who did not have a history of hypertension but were found to be hypertensive on admission ($n = 13$) also had similar elevations of troponin-T (0.023 ± 0.013). While this is significantly altered from controls, ($p < 0.01$), it is below the clinically significant level of 0.1 ng / ml for myocardial infarction. CKMB (mass) levels were not significantly different from controls in these patients.

In third group of patients who succumbed to septicemia ($n = 6$), chronic renal failure ($n = 8$) and complications of diabetes mellitus ($n = 10$) the levels were mean = 0.303, 0.694 and 0.75 ng/ml respectively. In these groups there was no significant correlation between troponin-T and CK-MB (mass) levels and CK-MB (mass) elevation was not significantly different from the control population. However, the elevation of troponin-T in non cardiac diseases is an indicator that metabolic complications unrelated to MI can bring about cardionecrosis, resulting in cardiac dysfunction.

DISCUSSION

Small elevations of cardiac troponin-T can identify high risk patients who derive a large clinical benefit from an early invasive strategy. A number of

Table 2. Troponin-T (cTnT) and CK-MB(mass) values in control group and in patients with acute coronary syndromes

Parameter	Control (n=15)	Patients (n=32)	Significance
CK-MB (mass) (ng/ml)	3.09 ± 1.2	118.3 ± 14.6	$P < 0.001$
cTnT (ng/ml)	< 0.010	4.7 ± 2.09	$P < 0.001$
According to the methods employed, control population should have CKMB (mass) levels < 5 ng/ml and troponin-T levels < 0.010 ng/ml.			

Table 3. Comparison of CKMB (mass) and troponin-T levels in sub-group of patients with acute coronary syndromes

Sub-Group	A (n=8)	B (n=13)	C (n=14)	D (n=7)
CKMB (ng/ml) mean $\pm$ SD (comparison with control)	6.01 $\pm$ 2.8 NS	33.4 $\pm$ 14.0 P<0.001	108.7 $\pm$ 36.13 p<0.001	358.5 $\pm$ 100.4 p<0.001
Troponin-T (ng/ml) mean $\pm$ SD (comparison with control)	1.6 $\pm$ 0.8 P<0.001	3.7 $\pm$ 1.5 P<0.001	6.11 $\pm$ 2.4 P<0.001	7.9 $\pm$ 5.6 P<0.001
Correlation between CKMB and Troponin-T	r = -0.13	r = 0.14	r = 1	r = 0.76
Patients were subdivided into 4 groups based on their CKMB (mass) values. Subgroup A: <15 ng/ml, subgroup B: between 15-50 ng/ml, subgroup C: between 50-200 ng/ml, subgroup D: between 200-500 ng/ml.				

treatment strategies, such as low molecular weight heparins, glycoprotein 2b/3a inhibitors, and aggressive treatment with cardiac catheterization are emerging as particularly beneficial for patients who present with elevated levels of cardiac troponins (8). Enzyme diagnosis is interfered by non specific elevation unrelated to permanent myocardial injury. Sustained release of troponin-T is a marker of permanent myocardial injury. It is released considerably longer than cytosolic CKMB(5). In a study by Kliemam S *et al.*, 31% of the patients with normal CKMB (mass) had elevated troponin-T levels (9). Zurich SW *et al.* (10) found using a single troponin T determination, that 46% of patients with confirmed MI had an abnormal cTnT and normal CKMB initially. Both studies concluded that an initial troponin-T determination drawn at the time of the patients' presentation is a powerful diagnostic tool for a rapid diagnosis rather than serial CKMB determination. In our study, 25% of patients who had AMI had CKMB levels not significantly different from controls. All these patients had elevated troponin-T levels (subgroup A). Hence troponin-T is more specific for confirming the diagnosis of AMI. With lower CKMB (mass) levels, the insignificant correlation with troponin-T as in subgroups A and B may indicate minimal myocardial cell injury. Hence if CKMB (mass) is used as the single diagnostic criteria of myocardial cell injury, several cases may be missed. The enhanced sensitivity of troponin-T (0.1 ng/ml) as the marker of cardiac dysfunction is best evident in these cases. With further elevations of CKMB (mass), indicating severe myocardial cell injury troponin-T has a better correlation with CKMB (mass). (subgroups C and D, $r=1$ and 0.76 respectively). Here, an average of 38 fold elevation of CKMB (mass) corresponded to

an average of 6 fold elevation of troponin-T. Hence, a smaller elevation of troponin-T has greater sensitivity and specificity than larger elevation of CKMB (mass).

In group 2, patients with hypertension showed minimal but definite elevation of troponin-T ($p<0.01$) but not CKMB. In another study (11), a low but significant troponin-T elevation supported the hypothesis that troponins may be used as markers of microembolization from thrombus formation on a disrupted atherosclerotic plaque. The occurrence of visible thrombus increases with rising levels of cardiac troponin-T and highest levels of troponin-T was more associated with occlusion of the left circumflex artery (12). In these patients, CKMB (mass) is not a sensitive enough parameter to detect minimal cardiac damage.

In group 3, patients succumbing to non-cardiac events also showed significant elevations of troponin-T but not CK-MB. Hence even in non-cardiac illness, troponin-T can be used as an indicator of cardiac necrosis for risk stratification and predicting outcome.

Studies have shown that cardiac troponin T levels predict short term prognosis in renal failure as an independent risk factor across the entire spectrum of renal function (3).

In conclusion, CK-MB (mass) is not sensitive enough to diagnose minimal myocardial cell injury. However, in severe myocardial injury, CKMB levels correlate with troponin-T levels. Troponin-T levels can be used to detect early and minimal myocardial cell injury even in the presence of normal CKMB levels in acute myocardial infarction. It is also an

indicator of minimal myocardial necrosis secondary to some non-cardiac illness.

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