Incidence and Predictors of Cardiac Markers Elevation after Coronary Intervention

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Abstract

Objectives-This study evaluated the incidence and predictors of CK-MB and troponin elevation after successful coronary intervention.

Background- CK-MB and troponin elevation after coronary intervention correlate with late cardiac events and survival.[1,2,19,24] We investigated the incidence and predictors of CK-MB and troponin elevation in patients who underwent percutaneous coronary intervention in Rajaie Cardiovascular, Medical and Research Center.

Results CK-MB and troponin elevation was detectable in 203 (70%) patients. Predictors of cardiac enzyme elevation were hyperlipidemia, functional class, and smoking. There were no in-hospital adverse events in the CK-MB and troponin elevation group.

Conclusion- Cardiac enzyme elevation after coronary intervention was detected in 70% of all our patients and was more common in diffuse atherosclerosis hyperlipidemia, smoking, and high functional class. Enzyme elevation was observed even in the absence of discernible procedural complications, and early discharge of patients with CK-MB and troponin elevation is safe. Mid-term survival of patients with CK-MB and or troponin elevation was similar to those with normal enzymes ***(Iranian Heart Journal 2011; 12 (1):27 -34).***

Key words: percutaneous coronary intervention (PCI)■ cardiac enzyme (CK-MB and troponin) ■ coronary lesion types

After successful percutaneous coronary intervention (PCI), CK-MB and troponin elevation occurs in 6-30% of patients.[4,5,6] Recently, controversy has arisen regarding minor elevation of CK-MB and troponin influence on the short- and long-term prognoses.[1] Numerous reports have demonstrated high risk of subsequent events and death.[3-7,8,9,10,22] In these studies, the risk of adverse outcomes increased proportionally to the magnitude of CK-MB elevation.[11,22]

Previous reports have revealed higher incidence of cardiac markers elevation after stenting[13,14,15] and other devices such as the DCA[15] and rotablater.[16] Studies have also shown that there is no correlation between enzyme elevation and mid-term cardiac events and survival.[9,10,12]

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substantiated on enhanced cardiac magnetic resonance imaging. Myocardial necrosis may be due to the distal embolization of clot or debris. Other causes of cardiac markers elevations are transient vessel closure, slow flow, side branch occlusion, and hypotension.[10,17,19] Moreover, it is unclear whether CK-MB elevation after a successful procedure is a reflection of the procedure itself or a marker of diffuse atherosclerosis embolization or atheroma burden, which causes worse long-term prognosis. because it is more frequent in coronary artery disease (CAD) accompanied by peripheral vascular disease[3,7,10,26] or is due to arterial inflammation

with predilection to This prospective study was conducted with the following objectives:

1) To evaluate the incidence of CK-MB and troponin elevation after PCI,
2) To identify clinical and angiographic predictors of CK-MB elevation, and
3) To appraise the effect of enzyme elevation on short- and mid-term survival.

Methods

All patients undergoing PCI in Rajaiee Cardiovascular, Medical and Research Center between May 2009 and June 2010 were included in the study. Patients with acute myocardial infarction, non-ST-segment elevation myocardial infarction, and unstable angina were excluded. The study population consisted of 300 consecutive patients with stable angina pectoris. Prior to the procedure and eight and sixteen hours after the procedure, CK-MB and troponin values were measured. After the procedure, the patients were admitted to the coronary care unit.

Protocol

All the patients had a baseline ECG and enzyme measurement twenty-four hours before the procedure and received Aspirin 325mg and Clopidogrel 300mg two-three days before the procedure. The stents utilized were bare metal stents (BMS) and drug-eluting stents (DES) at the discretion of the operator. Blood samples were drawn eight and sixteen hours after the procedure for cardiac enzymes. ECGs were routinely recorded after the procedure and the following morning.

If there was CK-MB or troponin elevation, the ECG was analyzed for ST-segment and T wave changes and new Q waves.

If there were no complications, the patients were discharged two days after the procedure in spite of cardiac enzyme elevation.

Results

There were 300 patients and 350 lesions. Angiographic success was attained in all the lesions. CK-MB elevation occurred in 85 (41.4%) patients, troponin in 64 (31.5%), and both CK-MB and troponin in 54 (26.6%) (totally, 203 patients). (Fig.1)

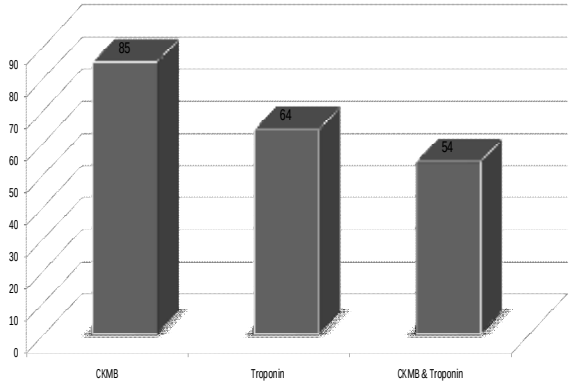


Fig. 1. Frequency of CK-MB and troponin elevation in enzyme elevated group

and Table II. Maximum CK-MB was 95 IU/l, and maximum troponin was 2.8 mc.g/l.
The baseline and clinical characteristics of the normal and elevated enzyme groups are presented in Table I.

Table I. Baseline characteristics (n = 295)

Age (year)	58 ± 9.9
Female/Male	69/226
Diabetes	222 (75.3%)
Positive Family History	242 (82%)
Smoking	231 (78.3%)
Hypertension	232 (78.6%)
Hyperlipidmia	50 (16.9%)
Previous Myocardial Infarction	215 (72.5%)
Angina Pectoris	133 (45.1%)
NYHA Function Class	
Class I	5 (1.7%)
Class II	260 (88.1%)
Class III	30 (10.2%)
Class IV	0
Coronary Artery Significant Stenosis	
LAD	169 (57.3%)
RCA	100 (33.9%)
LCX	47 (15.9%)
Left Main	1 (0.3%)
Diagonal	16 (5.4%)
OM	15 (5.1%)
Multi-Vessel Disease	
No Vessel	27 (9.2%)
Single Vessel	224 (75.9%)
Two Vessels	40 (13.6%)
Three Vessels	4 (1.4%)
Clinical Symptom	
Chest Pain	27 (9.2%)
Dyspnea	13 (4.4%)
Management	
Medical Treatment	291 (98.6%)
Re-PCI	4 (1.4%)

Table II. High serum enzyme levels in patients, during the study (n = 295)

	Before PCI	After PCI		P value
		8 Hours	16 Hours	
High Troponin I and CK-MB	0	203 (68.8%)	203 (68.8%)	<0.001

Te mean age of the group was 59 years, with 23% being women. Variables correlating with enzyme elevation were the male gender, angina class III-IV, smoking, hyperlipidemia (Table III), diabetes, hypertension and multi-vessel disease.

Table III. Associations between Increase of serum enzymes and patients' characteristics

	Serum Troponin (8 hours)		P value
	Normal (n = 92)	High (n = 203)	
Age (years)	57 ± 9.8	58 ± 10	0.201
Sex (F/M)	27/65	42/161	0.104
Diabetes	80 (87%)	142 (70%)	0.002
Positive Family History	80 (87%)	162 (79.8%)	0.138
Smoking	80 (87%)	151 (74.4%)	0.015
Hypertension	79 (85.9%)	153 (75.4%)	0.041
Hyperlipidemia	34 (37%)	16 (7.9%)	<0.001
Chest Pain	0	27 (13.3%)	<0.001
Dyspnea	0	13 (6.4%)	0.011
NYHA Function Class			<0.001
Class I	0	5 (2.5%)	
Class II	92	168 (82.8%)	
Class III	0	30 (14.8%)	
Coronary Artery Significant Stenosis			
LAD	53 (57.6%)	116 (57.1%)	0.940
RCA	27 (29.3%)	73 (36%)	0.266
LCX	15 (16.3%)	32 (15.8%)	0.906
Diagonal	6 (6.5%)	10 (4.9%)	0.575
OM	7 (7.6%)	8 (3.9%)	0.184
Multi-Vessel Disease			0.701
Single Vessel	74 (80.4%)	150 (73.9%)	
Two Vessels	9 (9.8%)	31 (15.3%)	
Three Vessels	1 (1.1%)	3 (1.5%)	
Re-PCI	0	4	0.314

There was no difference between the normal enzyme and elevated enzyme groups in terms of hypertension and diabetes. Multivariable logistic regression showed that hyperlipidemia, angina (Table IV) functional class III-IV, and smoking were highly correlated with CK-MB and troponin elevation. Maximum CK-MB was 95i.u/lit., and maximum troponin was 2.8 mic/lit.

Table IV. Multivariable logistic regression analysis to predict the increase of cardiac enzymes after PCI

	Coefficient ± SE	P value	Odds Ratio [CI95%]
Diabetes	-0.589 ± 0.394	0.135	0.56 [0.26 – 1.20]
Smoking	-0.783 ± 0.385	0.042	0.46 [0.22 – 0.97]
Hypertension	-0.362 ± 0.399	0.365	0.70 [0.317 – 1.52]
Hyperlipidemia	-1.687 ± 0.360	<0.001	0.19 [0.09 – 0.38]
Chest Pain	20.242 ± 749	0.998	-
NYHA Function Class	1.417 ± 0.537	0.008	4.12 [1.44 – 11.81]
P value for Hosmer and Lemeshow goodness of fit test = 0.186			

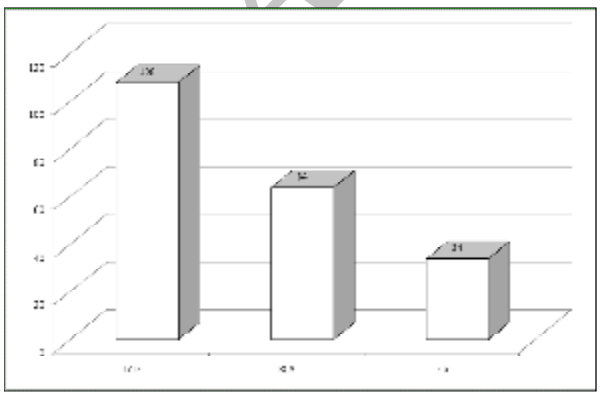
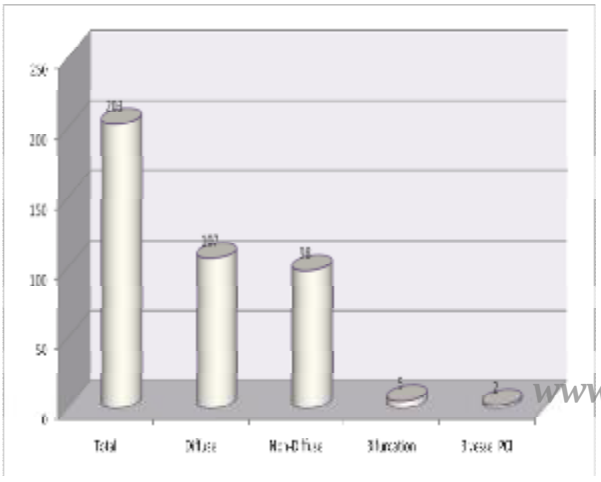


Fig 3. Frequency of lesion types in patients with Ck-MB and troponin elevation

Fig. 2. Vessel location in enzyme elevated group



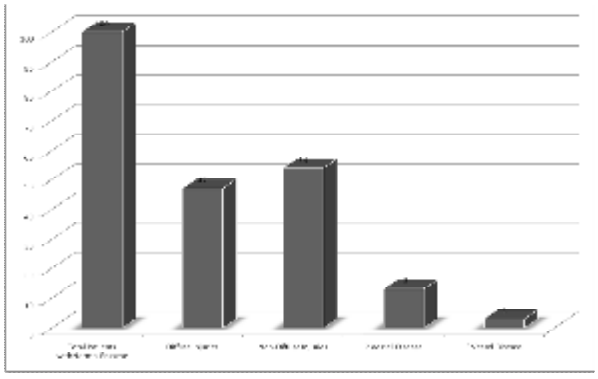


Fig 4. Frequency of lesion types in patients with normal CKMB and troponin after PCI

Vessel Location

With respect to the location of the vessel in the 203 patients, who underwent intervention and developed enzyme elevation, 108 cases were in the LAD, 64 in the RCA, and 34 in the LCX (Fig.2). Additionally, amongst these patients, lesions were diffuse in 107 and non-diffuse in 98. Five patients had bifurcation lesions and 3 patients had three-vessel disease (Fig. 3). In patients with normal enzyme post procedure, only 47 patients had diffuse lesions, 54 had non-diffuse lesion, 13 had two-vessel disease, and 3 had three-vessel disease (Fig.4). An analysis of the cardiac markers showed elevation of CK-MB in 85 (43%) patients, elevation of troponin in 64 (32%), and elevation of both troponin and CK-MB in 54 (26.6%) (Fig.1). In the normal enzyme patients, the mean lesion length was 21.6mm in the LAD, 20mm in the RCA, and 20mm in the LCX (Fig.5).

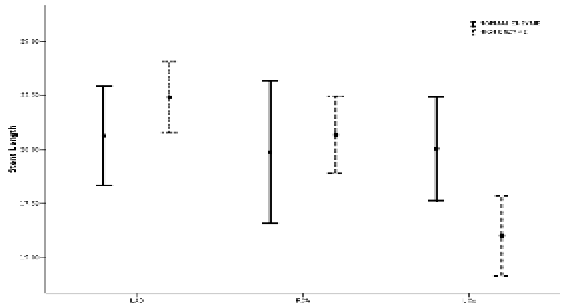


Fig .5. Mean Stent length in patients with and without enzyme elevation

In the CK-MB and troponin elevated group, the mean lesion length was 22mm in the LAD, 20.5mm in the RCA, and 17.8mm in the LCX (Fig.6).

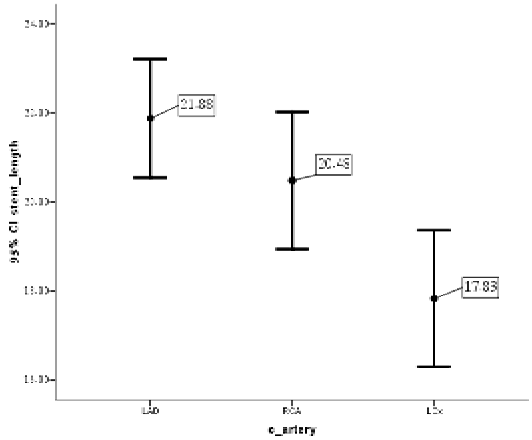


Fig. 6. Mean stent length in patients with CK-MB and troponin elevation in different coronary vessels

A comparison of the stent length between the normal enzyme group and high enzyme group showed that the mean stent length was 0.6 mm longer in the high enzyme group, but the difference was highly significant (Fig.7) and, therefore, there was no significant difference in the lesion length between the normal enzyme group and the elevated enzyme group (Fig.5).

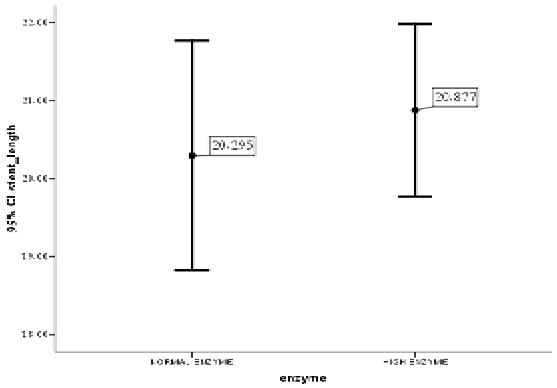


Fig.7. Mean Stent length in patients with normal enzyme and elevated enzyme group

Characteristics such as eccentricity, calcification, ostial, and total or subtotal occlusion did not correlate with CK-MB release. Most often, there was no apparent cause for CK-MB and troponin elevation. It is worthy of note that although troponin is much more sensitive than CK-MB for minor necrosis, [26] some patients have only elevation of CK-MB without apparent troponin elevation.[12]
None of the patients with enzyme elevation had clinical events in hospital and were discharged two days after PCI.

Statistical Analysis

For the description of the quantitative variables, the results were expressed as mean ± SD; and for the qualitative variables, frequency and relative frequency were used as percentages. For the analysis of the results, a two-tailed Student test and one way ANOVA accompanied by the Bonferrani post-hoc test were conducted to compare the quantitative variables between the subgroups. The Mann-Whitney U test was done to compare the ordinal variables, and the Chi-square test and the Fisher exact test were carried out to compare the nominal variables between the subgroups. Statistical significance was defined at the level of 0.05 or less. The results in the multiple regression model were reported as odds ratios and 95% confidence intervals.

Discussion

CK-MB isoenzyme and troponin can be released from myocardial necrosis or profound ischemic injury.[2,11] Several reports has shown that enzyme elevation following angioplasty is associated with higher later cardiac events and death.[8,11,22] Correlation of troponin elevation after PCI and late mortality has been an inconsistent finding.[23,24] Enzyme elevation during coronary intervention is device-dependent and enzyme release is higher for non-balloon modalities such as atherectomy and stent use.[15,14] The cause of markers release is multifactorial and includes transient abrupt vessel closure, dissection, spasm, slow flow, distal embolization and side branch occlusion, plaque volume, and plaque vulnerability and specially patient specific characteristics such as arterial inflammation, elevation of CRP, and aspirin resistance. The use of stenting and antithrombotics such as Clopidogrel, GPIIb/IIIa inhibitors and embolic protection devices has decreased the incidence of periprocedural myocardial infarction. Side branch occlusion has been one of the most frequent procedural complications noted in the enzyme elevation groups and has been significantly higher after stent use and in thrombotic lesions.[3,28] CK-MB and troponin elevation has been shown to occur even in the absence of complications. In the present study, procedure complication, prolonged recurrent chest pain, and ECG changes were infrequent in the group with enzyme elevation. In most of our patients, CK-MB and troponin elevation was unsuspected and could not have been predicted after the procedure.
In our study, CK-MB and troponin I elevation was seen in 70% of the procedures, which is similar to similar figures in other published studies.[3, 7, 10] In a report,[12] minor enzyme elevation in patients with a mean follow-up of 36±22 months

had a worse long-term prognosis and most of theses patients had undergone angioplasty with directional coronary atherectomy.

In a large study, side branch occlusion was one of the most frequent procedural complications. Enzyme elevation post angioplasty of the saphenous vein graft has a negative influence on survival.[18] On the other hand, numerous recent studies have reported a lack of correlation between CK-MB release and survival.[27]

Long-term data will be required to establish a lack of correlation between mortality and low to medium enzyme elevation (1-5×normal). In one study, patients with low (1-3×normal) to medium (3-5×normal) CK-MB elevation had no higher in-hospital adverse cardiac events compared with normal CK-MB patients.[28] Callif et al.[6] suggested that patients with elevated CK-MB of three times the normal value after intervention be managed like non-ST-segment elevation myocardial infarction patients. In our study, stable patients with low to medium CK-MB and troponin elevation were routinely discharged two days after intervention without apparent short-term adverse events. In a report,[25-28] multivariate predictors of CK-MB elevation were diffuse coronary atherosclerosis, multi-vessel disease, and systemic atherosclerosis. Other reported causes of CK-MB and troponin elevation are side branch occlusion, flow-limiting dissection, abrupt closure, embolization, no reflow, DCA, stents, large thrombus burden, plaque and atheroma volume, plaque vulnerability, arterial inflammation, aspirin resistance,[36] and genetic predisposition.[11,28] Periprocedural antithrombotic therapy may ameliorate periprocedural myocardial infarction. The EPISTENT trial demonstrated a reduction in periprocedural myocardial infarction and one-year mortality with the use of glycoprotein IIb/IIIa, especially in acute coronary syndromes.[20] Baseline inflammatory markers can predict the occurrence of periprocedural myonecrosis[32,33] and studies have established the prognostic value of baseline hs CRP in patients undergoing PCI.[31] Thus, arterial inflammation may be a cause of embolization and pretreatment with statins is associated with a decreased rate of ischemic events.[32,33,34]

These data suggest that cardiac markers elevation may be due to the distal micro embolization of clot or atheromatous debris by high pressure balloons or stents.[35]

Study limitation

The fact that CK-MB and troponin were measured two times after the procedure is the most notable limitation of the present study because enzymes might elevate after twenty-four hours in some patients. Another important limitation is our short follow-up (6-10 months), which precludes the determination of late major adverse cardiac events.

Conclusion

In this study, we showed that enzyme elevation after intervention is common and occurs in 70% of patients mostly due to diffuse disease. Moreover, low to medium elevation of CK-MB and troponin has no adverse effect in hospital course and in short and medium term. Finally, early discharge of patients with mild to moderate enzyme elevation is safe.

Conflict of Interest

No conflicts of interest have been claimed by the authors.

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