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Relationship between Cardiac myosin binding protein–C with traditional risk factors in early diagnosis of acute coronary syndrome patients

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Abstract

Background: *Coronary heart disease (CHD) is primarily caused by atherosclerotic lesions within the intima of coronary arteries and acute coronary syndrome (ACS) is the main acute clinical manifestation of CHD. The ACS is manifested in one of three subtypes and is still one of the main causes of morbidity and mortality worldwide. Early diagnosis of ACS and of MI, in particular, is important in decreasing mortality in ACS patients. Few risk factors were established as factors that increase risk of CHD while many have emerged and need to be established.*

Objective: *To investigate relationship between cardiac myosin binding protein–C with traditional risk factors for acute coronary syndrome patients in early diagnosis.*

Subjects & Methods*:One hundred twenty patients (72 males and 48 females), aged ≥ 30 years were consecutively selected from those who were admitted to emergency department (ED) of Al-Yarmouk teaching hospital and diagnosed as ACS by specialist cardiologists. The ACS patients constituted three subgroups according to the subtype of ACS; namely the STEMI, NSTEMI and UA group.The duration between onset of chest pain and admission to ED should not exceed three hours in any selected patient. Apparenty healthy subjects as controls group. For each study subject, cMybp-C serum levels was measured using enzyme linked immunosorbent assay kits. For each ACS patient, serum level of FBS,GOT and cholesterol were measured by COBAS 111fully automated device.*

Results:*The cMybp-C serum level remained significant higher level in presence or absence of any of the studied risk factors in (STEMI and NSTEMI) subgroups,while non-significant increase in UA subgroup with or without risk factors .The cMybp-C mean level showed an overall significant difference among study groups, cMybp-C mean level was significantly higher in each ACS subgroup than in controls group (P < 0.001).*

Conclusion:*The study found that risk factors do not have an effect on the biochemical marker cMybp-C,but they do have an effect on increasing the prospect of coronary heart disease, which will lead to change in the concentrations of the biochemical marker.That is, the effect is indirect. So cMybp-C serum level remained significant higher level in presence or absence of any of the studied risk factors*

Keywords: *Acute coronary syndrome, high sensitivity cardiac troponin I, cardiac myosin binding protein I.*

Introduction

Coronary heart disease (CHD) is a condition in which there is an inadequate supply of blood to the myocardium that is primarily caused by a formation of atherosclerotic plaques within the intima of coronary arteries. The plaque may erode or rupture resulting in thrombosis and partial or total closure of a coronary artery that imped blood flow and manifested acutely as acute coronary syndrome (ACS) [1, 2]. The ACS could be manifested as one of three subtypes. These subtypes of ACS include myocardial infarction (MI) with the electrocardiogram (ECG) is showing ST-segment elevation (STEMI), the another is MI with the ECG is showing no ST-segment elevation (NSTEMI) and the third type is unstable angina (UA) [3].

Certain risk factors lead to increase occurrence of acute coronary syndrome like : Age , Being overweight or obese , Diabetes , Smoking , High blood pressure , High cholesterol , Family history of heart disease , chest pain, or stroke and Not being physically active may be modified through changes in behavior or by pharmacological therapy so may be appropriate targets for interventional efforts to decrease the probability of developing or to slow the progression of CHD.[4,5]

Although some risk factors cannot be modified, a person who have high risk for developing CHD may still benefit from more aggressive effective interventions for other risk factors [6].

Cardiac myosin-binding protein c (cMybp-C)"Myosin-binding protein C has been recently described as a new candidate biomarker of cardiac injury and it was shown in small group studies that its serum concentration increases and decreases faster than that of troponin T and I". [7] "Cardiac myosin-C binding protein (cMybp-C) is a cardio-specific regulatory protein that plays a role in regulating of cardiac contraction and diastolic relaxation of cardiomyocytes"."As with cTn-T and cTn-I, cMybp-C expression is restricted to the heart but in higher concentrations.[8]

It is released more rapidly into the circulation than cardiac troponins T or I following MI due to its higher concentration in myocardiocytes [9]. The change in its serum level especially in patients with an onset of chest pain of < 3 hours has been shown to have a higher diagnostic accuracy for MI than that of cT-I or T and and so may help in early diagnosis of patients with MI and may help in their early management [10]

Materials and Methods

Study patients were recruited from the coronary care unit at "Al-Yarmouk Teaching Hospital" during the period among the "1st of November 2022 to the 1st of September 2023". 120 patients "72 males and 48 females", aged ≥ 30 years were consecutively selected from those who were admitted and diagnosed as "ACS" by specialist cardiologists. The diagnosis of ACS was based on the presence of two out of three criteria:

- Clinical presentation of the patient
- ECG changes
- A positive troponin test

Based on the same adopted criteria, ACS patients comprised three subgroups; namely, STEMI, NSTEMI and UA. The apparently healthy subjects as a controls group were recruited from those who had no current illness with consideration of age and sex matching with the ACS patients. They had no history of CHD or other

systemic diseases and have had normal ECG recording.

Conflicting Interest: no conflict of interest was declared by the authors

Ethics approval: the scientific committees of the local health care department at al-karkh of Baghdad province the at to allow this research .research goals were explained for each patient to obtain their approval to involve in it

Blood analysis

Blood samples were collected from patients and controls. Serum was separated, divided into aliquots, and used for measurement of cMybp-C. The assays of cMybp-C depended on use of enzyme linked immune sorbent assay kits that were supplied by MyBioSource Company, USA. Serum cholesterol, glutamate oxaloacetate transaminase (GOT), and fasting blood sugar (FBS) were measured by fully automated cobas c111 analyser.

Statistical analysis

Data were analyzed by the statistical package of SPSS-24. After assuring that the data was normally distributed, data presentation was done by mean, standard error or standard deviation of the mean, and percentage. LSD test was used for the difference between two means. A P-value of "< 0.05" was measured as statistically significant.

Results

The clinical characteristics of study subjects are shown in table 1. The patients and the control subjects had a similar sex distribution (60 % males, 40% females). The study patients who were ≤ 50 years in age constituted 33.3% and persons were > 50 years constituted 66.66%. In regard to BMI, 20% normal weight of patients, "47.5%" overweight and "32.5% "were within the obese. The ACS patients included those with STEMI (40 patients), NSTEMI (40 patients) and UA (40 patients).

Table 1: Clinical characteristics of study subjects

Characteristic	**Patients** **N= 120**	**Controls** **N=80**
Age (years)		
≤ 50 y	N= 40 (33.3%)	N = 27 (33.75%)
> 50 y	N= 80 (66.66%)	N = 53 (66.2%)
BMI (kg/m^2)		
Normal weight	N=24 (20%)	N=16 (20%)
Over weight	N= 57 (47.5%)	N= 38 (47.5%)
Obese	N= 39 (32.5%)	N= 26 (32.5%)
Sex		
Male	N= 72 (60%)	N= 48 (60%)

Female	N= 48 (40%)	N= 32 (40%)
ACS subgroups		
STEMI	N= 40 (33.3%)	80 (100%)
NSTEMI	N= 40 (33.3%)	
UA	N= 40 (33.3%)	

"N: Number, BMI: Body mass index, STEMI: ST-elevation myocardial infarction, NSTEMI: non ST-elevation myocardial infarction, UA: Unstable angina".

The result of comparison of levels of study parameters among subgroups of ACS patients (STEMI, NSTEMI and UA) and controls is shown in table 2. The comparison revealed significant differences among the study groups or subgroups in regard to the cMybp-C mean level as well as to the mean levels of cholesterol, GOT, and FBS.

Table 2: Demographic, clinical Characteristics, baseline laboratory tests and copeptin level in subgroups of ACS patients and controls

Characteristic	STEMI N= 40	NSTEMI N = 40	UA N= 40	Controls N= 80	P-value
	Mean ± S.E.				
Age (years)					
Range	45-75 years	45-78 years	47-80 years	34-77 years	0.065
Mean	59 ± 2	60 ± 3	61 ± 3	57 ± 2	NS
BMI (kg/m^2)	28.53±0.57	28.17±0.53	27.53±0.57	23.37±0.46	0.032 Sig.
FBS (mg/dl)	194.27 ± 8.78	173.79 ± 11.32	152.77 ± 6.81	92.67 ± 2.37	<0.001 Sig.
Cholesterol (mg/dl)	211.42 ± 5.2	173.87 ± 5.93	153.18 ± 4.58	141.64 ± 2.73	<0.001 Sig.
GOT (IU/l)	146.1 ± 14.86	58.69 ± 3.17	15.74 ± 1.2	14.42 ± 0.56	<0.001 Sig.
cMybp-C (ng/ml)	3.11 ± 0.21	1.36 ± 0.11	0.6 ± 0.05	0.53 ± 0.04	<0.001 Sig.

ANOVA test was performed, STEMI: ST-segment elevation myocardial infarction, NSTEMI: non ST-segment elevation myocardial infarction, UA: unstable angina, BMI: body mass index, FBS: fast blood sugar, GOT:

glutamate oxaloacetate transaminase

Effect of some CHD risk factors on cardiac myosin binding protein-C between ACS subtypes and controls

The effect of traditional CHD risk factors (age, BMI, hypertension, smoking and diabetes mellitus) on (cMybp-C) in patients and controls is shown in tables (3-7).

Table 3: Comparison of myosin binding protein –C between ACS patients and controls according to age

	Age (years)	Groups	N	Mean ± S.E. cMybp-C (ng/ml)	P value
STEMI	**≤ 50 years**	**Patients**	**12**	3.22 ± 0.4	**<0.001**
		Control	**28**	0.5 ± 0.06	
	> 50 years	**Patients**	**28**	3.06 ± 0.24	**<0.001**
		Control	**52**	0.54 ± 0.05	
NSTEMI	**≤ 50 years**	**Patients**	**8**	1.36 ± 0.21	**0.004**
		Control	**28**	0.5 ± 0.06	
	> 50 years	**Patients**	**32**	1.36 ± 0.12	**<0.001**
		Control	**52**	0.54 ± 0.05	
UA	**≤ 50 years**	**Patients**	**8**	0.64 ± 0.1	**0.223**
		Control	**28**	0.5 ± 0.06	
	> 50 years	**Patients**	**32**	0.59 ± 0.05	**0.541**
		Control	**52**	0.54 ± 0.05	

Table 4: Comparison of myosin binding protein-C of ACS patients and controls according to hypertension

		Groups	N	Mean ± S.E. cMybp-C (ng/ml)	P-value
STEMI	**HT**	**Patients**	**20**	3.17 ± 0.3	**<0.001**
		Control	**80**	0.53 ± 0.04	
	Non-HT	**Patients**	**20**	3.05 ± 0.29	**<0.001**
		Control	**80**	0.53 ± 0.04	
NSTEMI	**HT**	**Patients**	**30**	1.37 ± 0.12	**<0.001**

		Control	**80**	0.53 ± 0.04	
	Non-HT	**Patients**	**10**	1.33 ± 0.21	**<0.001**
		Control	**80**	0.53 ± 0.04	
UA	**HT**	**Patients**	**20**	187.16 ± 8.12	**0.876**
		Control	**80**	162.65 ± 3.19	
	Non-HT	**Patients**	**20**	184.48 ± 8.17	**0.876**
		Control	**80**	162.65 ± 3.19	

Table 5 : Comparison of myosin binding protein – C between STEMI patients and controls according to diabetic

		Groups	**N**	**Mean ± S.E. cMybp-C (ng/ml)**	**P value**
STEMI	**DM**	**Patients**	**24**	3.1 ± 0.26	**<0.001**
		Control	**80**	0.53 ± 0.04	
	Non-DM	**Patients**	**16**	3.11 ± 0.34	**<0.001**
		Control	**80**	0.53 ± 0.04	
NSTEMI	**DM**	**Patients**	**16**	1.33 ± 0.14	**<0.001**
		Control	**80**	0.53 ± 0.04	
	Non-DM	**Patients**	**24**	1.38 ± 0.15	**<0.001**
		Control	**80**	0.53 ± 0.04	
UA	**DM**	**Patients**	**18**	0.59 ± 0.08	**0.294**
		Control	**80**	0.53 ± 0.04	
	Non-DM	**Patients**	**22**	0.6 ± 0.06	**0.294**
		Control	**80**	0.53 ± 0.04	

Table 6 : Comparison of myosin binding protein – C level between of STEMI patients and controls according to smoking

		Groups	**N**	**Mean ± S.E. cMybp-C (ng/ml)**	**P value**
STEMI	**SMO**	**Patients**	**16**	3.1 ± 0.35	**<0.001**
		Control	**80**	0.53 ± 0.04	
	Non-SMO	**Patients**	**24**	3.11 ± 0.26	**<0.001**

		Control	**80**	0.53 ± 0.04	
NSTEMI	**SMO**	**Patients**	**20**	1.33 ± 0.14	**<0.001**
		Control	**80**	0.53 ± 0.04	
	Non-SMO	**Patients**	**20**	1.39 ± 0.16	**<0.001**
		Control	**80**	0.53 ± 0.04	
UA	**SMO**	**Patients**	**12**	0.58 ± 0.08	**0.294**
		Control	**80**	0.53 ± 0.04	
	Non-SMO	**Patients**	**28**	0.6 ± 0.06	**0.243**
		Control	**80**	0.53 ± 0.04	

Table 7: Comparison of myosin binding protein -C of STEMI patients and controls according to body mass index

		Groups	**N**	**Mean ± S.E. cMybp-C (ng/ml)**	**P value**
STEMI	**Normal weight**	**Patients**	**8**	3.21 ± 0.56	**0.002**
		Control	**19**	0.53 ± 0.1	
	Over weight	**Patients**	**18**	3.16 ± 0.32	**<0.001**
		Control	**25**	0.55 ± 0.05	
	Obese	**Patients**	**14**	2.98 ± 0.31	**<0.001**
		Control	**36**	0.48 ± 0.05	
STEMI	**Normal weight**	**Patients**	**8**	1.37 ± 0.22	**0.002**
		Control	**19**	0.53 ± 0.1	
	Over weight (25-29.9)	**Patients**	**21**	1.45 ± 0.14	**0.001**
		Control	**25**	0.55 ± 0.05	
	Obese (> 30)	**Patients**	**11**	1.17 ± 0.23	**0.014**
		Control	**36**	0.48 ± 0.05	
UA	**Normal weight (18-24.9)**	**Patients**	**8**	0.68 ± 0.15	**0.419**
		Control	**19**	0.53 ± 0.1	
	Over weight (25-29.9)	**Patients**	**18**	0.64 ± 0.06	**0.275**

		Control	**25**	0.55 ± 0.05	
	Obese (> 30)	**Patients**	**14**	0.49 ± 0.06	**0.908**
		Control	**36**	0.48 ± 0.05	

Discussion

Early identification of ACS patients among those presenting with acute chest pain to the ED in the real-life daily clinical practice is important. Patients with ACS can benefit from rapid and aggressive medical and interventional treatment.

Laboratory investigation of certain biomarker, principally the cardiac troponins, is complementary to the clinical evaluation and ECG in the steps of diagnosis, triage, and management of patients with suspected ACS. The interval of 1–2 hours which allows for ruling out of acute myocardial infarction or its early diagnosis is currently the most significant clinical hurdle to overcome. The release of cardiac troponin I (cTn-I) is relatively delayed after onset of myocardial infarction. The rule out of AMI by using ECG and troponins is time-consuming owing to the need for serial blood sampling to determine changes in troponin concentrations, especially in patients with non-ST elevation ACS. It is crucial to conduct successive assessments during the downtime for AMI diagnosis and during the extended monitoring of patients in emergency medical and/or cardiology centers to drive the development of fresh rule-in and rule-out tactic for the timely identification of AMI [(11)].

The study finding that STEMI subgroup of ACS patients had the highest level of cMybp-C, compared with other subgroups NSTEMI & UA, and reflects its role as a biomarker of cardiac necrosis [(12)]. This agree with a study by Nappi, F and et al [(7)] because a more dynamic increase in cMybp-C in the early stages of myocardial infarction than hscTn-I. The finding may be due to cMybp-C in higher concentrations in myocardial cells or to presence of a different mechanism for protein release from damaged myocardial cells. The study finding that serum level of cMybp-C increases and then decreases faster than serum level of hscTn-I as revealed in patients with MI on admission and at three hours after admission, is also consistent with the finding of studies that described a faster release of cMybp-C into the circulation than hscT-I following MI and attribute it to its higher concentration in myocardiocytes [(13)].

Traditional risk factor and their influence on cMybp-C level in ACS patients

When the major conventional risk factors were examined for their impact on the significant effect in cMybp-C levels between ACS patients and controls, the results remained significant whether any of the risk factors under study was present or not in (STEMI and NSTEMI) subgroups , while non-significant increase in UA subgroup with or without risk factors . Nevertheless, this does not rule out the possibility that these risk factors have an impact on cMybp-C levels. Then there are circumstances other than ACS presentation; these pertain to a predominance of alterations brought on by the existence of ACS and its underlying disease or effects.

In the present study, there was a significantly high level of cMybp-C levels in ACS patients with presence or absence of any of the studied risk factors when compared with controls in the first few hrs. after onset of chest pain (by LSD TEST) [(14)]. cMybp-C level may even be raised within ≤ 3 hrs. after the onset of chest pain in patients with AMI as a this marker is more abundant than cTn, then it is released into the bloodstream faster

during MI and it is useful to evaluate the accuracy of cMybp-C as useful biomarker in the early diagnosis of MI patients , the finding of no significant difference in cMybp-C between UA & controls is something that is expected due to no presence of myocardial necrosis in UA patients. This finding is consistent with many previous studies such as that by [15].

The study found that risk factors do not have an effect on the biochemical marker, but they do have an effect on increasing the likelihood of coronary heart disease, which will lead to changes in the concentrations of the biochemical marker. That is, the effect is indirect.

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