The Role of Troponin I as A Predictor of Early Left Ventricular Systolic Dysfunction in Acute ST Segment Elevation Myocardial Infarction

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Abstract

Background and Objectives:
The cardiac troponin provides useful information for the extent of injury suffered by the myocardium and left ventricular systolic dysfunction. We sought to assess the role of admission troponin I level in patients with acute ST-elevation myocardial infarction to predict early Left Ventricle systolic dysfunction and regional wall motion abnormality diagnosed by Transthoracic Echocardiography.

Patients and Methods
In a cross sectional study of 52 consecutive patients (37 male, 15 female), their mean age (60.6 + 13.3) years with acute ST elevation myocardial infarction who had been admitted to the Coronary Care Unit at Hawler Teaching Hospital from October 2016 to April 2017 were enrolled in this study. Patients were classified according to their initial troponin I level in to: Normal troponin I (< 0.5 ng/ml), Medium troponin I (1 to 3 times the upper normal level) and high troponin I (3 times the upper normal level). Transthoracic echocardiography was done to assess the left ventricular systolic function and regional wall abnormalities.

Results
High troponin I level was associated with high Global Registry for Acute Coronary Events (GRACE) score (p = 0.002), and high frequency rate of left ventricular regional wall abnormalities (p=0.025). Patients with higher troponin I has higher frequency of left ventricular systolic dysfunction but without statistical significant value.

Conclusion
Elevated troponin I values may predict early left ventricular systolic dysfunction, regional wall motion abnormality as well as high GRACE score.

Key words: Troponin I, STEMI, AMI

Introduction

Cardiovascular disease (CVD) is now the most common cause of death worldwide[1]. The global burden of IHD deaths has shifted to low-and-middle income countries as lifestyles approach those of high income countries[2]. Ischemic heart disease is the leading cause of death in Iraq, it kills 27.5 thousand people annually. Iraq is in rank 22 among other country in which there is highest mortality related to coronary artery disease and the second in Arab countries[3]. According to the 2016 Iraq profile in the institute of health metrics and evaluation IHD is the first cause of premature death[4].

ST segment elevation myocardial infarction (STEMI) usually occurs when coronary blood flow stopped abruptly after a thrombotic occlusion of a coronary artery previously affected by atherosclerosis[1].

Cardiac troponin I (cTnI) is a component of the contractile apparatus of myocardial cells and is expressed almost exclusively in the heart[5]. it has N-terminal extension (amino acids 1–30) that is not present in fast Troponin I and slow Troponin I[6].

Cardiac troponin has been proven to be a potent, independent indicator of recurrent ischemic events, and an estimate for the risk of death among patients presenting with acute coronary syndrome (ACS) [7]; it has not only diagnostic, but prognostic importance as well[8]. The troponin provides a window into the heart by allowing the physician to track the extent of injury suffered by the myocardium. It provides useful information for early risk assessment that is complementary to the determination of cardiac function and volumes especially in (STEMI) patients[9].

Serum troponin I concentration has a strong negative correlation with left ventricular ejection fraction after first acute myocardial infarction, and hence can be used to assess the left ventricular ejection fraction (LVEF) in patients with first myocardial infarction (MI)[10].

Echocardiography is an important tool for assessment of acute MI because of their ability to detect wall motion abnormalities or loss of viable myocardium in the presence of elevated cardiac biomarker values[11]. the measurement of LVEF has prognostic implications[12] ; Reduced LVEF is associated with greater mortality among patients with coronary artery disease[13].

The Global Registry of Acute Coronary Events (GRACE) investigators have published models derived from the GRACE registry to predict mortality in-hospital as well as at six months[14]. The use of the GRACE risk score for predicting in-hospital mortality was validated in a contemporary cohort of patients with STEMI[15].

The GRACE registry data set has been harnessed to develop a simple, accurate, and widely used risk-prediction tool, which has been validated in multiple populations. The value of the GRACE risk score is supported by its inclusion in European and American clinical guidelines on the management of ACS[16].

We sought to assess the role of admission troponin I level on the development of early Left Ventricle systolic dysfunction (LVSD) and regional wall motion abnormality (RWMA) diagnosed by Transthoracic Echocardiography in patients with acute STEMI.

Patients and methods

This is a cross sectional study done on patients with first time STEMI who had been admitted to the coronary care unit (CCU) at Hawler Teaching Hospital from October 2016 to April 2017.

A total 52 consecutive Patients with first attack STEMI of both gender and ages more than 18 years who presented within 24 hours from onset of symptoms and have had no chance to do percutaneous coronary intervention (PCI) were included in this study.

The following patients were excluded: Patients who had ischemic heart diseases, heart failure, left bundle branch block, Wolf Parkinson White syndrome, rheumatic heart diseases, congenital heart diseases, valvular heart diseases, myocarditis, sepsis, anemia, pulmonary embolus, arrhythmias, stroke, and renal failure.

The term STEMI used when the following criteria meets the diagnosis: detection of a rise of cardiac troponin I, with Symptoms of ischemia and new ST elevation at the J-point in two contiguous leads with the cut off points ≥ 0.1 mV in all leads other than leads V2-V3where the following cut off apply: ≥ 0.2 mV in men or ≥ 0.15 mV in women in the absence of Left ventricular hypertrophy or Left bundle branch block[5].

The risk factors for ischemic heart disease where recorded including diabetes mellitus either diagnosed on admission by plasma glucose in a random venous sample ≥ 200 mg/dl or fasting plasma glucose ≥126 mg/dl[17], or patient already on oral hypoglycemic agents or using insulin.

Hypertension defined as patients already diagnosed or on treatment for hypertension or hospital reading of systolic blood pressure ≥140 mmHg and diastolic blood pressure ≥ 90mmHg were regarded as hypertension[18,5].

Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared, over weight was defined as BMI of 25–30; obesity was defined as a BMI of 30 or higher[19].

Smoking, family history of ischemic heart disease (IHD) in first-degree relatives was recorded, a proper history taking, physical and systemic examination had been done for all the patients.

The patients with STEMI who admitted to the CCU within 12 hours of onset of symptoms were received thrombolytic therapy unless there were an obvious contraindication or patient refused to be thrombolysed.

Resting electrocardiogram and laboratory studies had been done for all patients, including, random blood sugar on admission, complete blood count , serum electrolytes, and renal function test.

Venous blood was withdrawn from patients at the time of admission, the blood sample was tested for Troponin I using Nano-CheckTM AMI Cardiac Test which is an immune chromatography assay for the quantitative/qualitative determination of the three cardiac markers (cTnl, CK-MB, and Myoglobin), the normal cut off value for troponin I in our center is <0.5ng/ml according to the kit reference value with Sensitivity and Specificity of 96.1% and 97.8%.

The time from onset of symptoms to blood sampling for troponin was recorded and Patients were classified according to their initial troponin I level in to three groups: normal troponin(had no elevation ,Tn-I < 0.5 ng/ml), Medium troponin(had Tn-I levels between 1 to 3 times the upper normal level, 0.5– 1.5 ng/ml) and high troponin (had more than 3 times the upper normal level, >1.5ng/ml)[20].

Our patients were Also had estimated risk of in hospital death according the GRACE risk score system were eight factors used to calculate the score: age, heart rate, systolic blood pressure, renal function, congestive heart failure, ST-segment deviation, cardiac arrest, elevated cardiac biomarkers , The patients are classified in to low (score 49-125), intermediate (score 126- 154), and high (score 155-319) risk groups[21].

Transthoracic two-dimensional Color Doppler Echocardiography had been performed for all patients within 3 days of admission to the CCU using Vivid E9 GE (2015). Ejection fraction was determined by 2D guided M-mode approach[22]. The data gathered for ejection fraction and regional wall abnormality if present. Left ventricular ejection fractions of ≤40% are suggestive of heart failure

with reduced ejection fraction[23]; regional myocardial function is assessed on the basis of the observed wall thickening and endocardial motion of the myocardial segment[22].

The three groups were evaluated and compared according to the baseline characteristics of the study populations (demographic and risk factors), the mean time from onset of symptoms to blood sampling for troponin level, early in hospital outcome for arrhythmias (ventricular tachycardia, ventricular fibrillation, atrial fibrillation), cardiogenic shock, pulmonary edema, syncope, bleeding, mortality, GRACE risk score for in hospital outcome, and echocardiographic findings.

Verbal and written consent obtained from all patients, and this study is approved by the ethical committee of Kurdistan Board for Medical specialties.

Statistical analysis:

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 22). Chi square test of association was used to compare between proportions. When the expected count of more than 20% of the cells of the table was less than 5, Fisher's exact test was used. Analysis of variance (ANOVA) was used to assess the variability between and within the three groups. A post hoc test (LSD) was used to compare each two groups. A p value of ≤ 0.05 was considered statistically significant.

Results

Fifty-two patients with acute STEMI had been included in the study. Their mean age were 60.6 ±13.3 years, ranging from 23 to 86 year. The median was 60 years (4 patients ,7.7%) were less than 45 years old, and more than half (29 patients,55.8%) aged 45-64 years. The majority (37 patients, 71.2%) were males and (15 patients, 28.8%) were female, (59.6%) of patients had hypertension, (51.9%) were smoker, (38.5%) were diabetics and (26.9%) had positive family history of IHD, as shown in table 1.

Table 1. Demographic and clinical characteristics of patients with acute coronary Syndrome

Variables	**No.(52)**	**(%)**
Ages		
<45	4	(7.7)
45-64	29	(55.8)
≥65	19	(36.5)
Gender		
Male	37	(71.2)
Female	15	(28.8)
Smoking	27	(51.9)
Family history	14	(26.9)
Hypertension	31	(59.6)
Diabetes Mellitus	20	(38.5)

The association between BMI and troponin I was significant (p = 0.004), but in spite of that, the pattern was not consistent where high proportions of the normal weight and obese had high troponin, while none of the over-weight patients had high troponin. No significant association was detected between troponin I level with age, gender, hypertension, smoking and family history of ischemic heart disease, as shown in table 2.

Table 2. Correlation of risk factors with troponin I level.

Risk Factors		**Troponin I level ng/ml**						**P**
		<0.5		**0.5-1.5**		**>1.5**		
		No.18		**No.9**		**No.25**		
		N0	**(%)**	**No.**	**(%)**	**No.**	**(%)**	
Age	**<45**	2	(50)	0	(0)	2	(50)	0.173*
	45-64	12	(41.4)	7	(24.1)	10	(34.5)	
	≥65	4	(21.1)	2	(10.5)	13	(68.4)	
Gender	**Male**	14	(37.8)	7	(18.9)	16	(43.2)	0.549
	Female	4	(26.7)	2	(13.3)	9	(60)	
BMI	**<25**	5	(27.8)	1	(5.6)	12	(66.7)	0.004*
	25-29	7	(77.8)	2	(22.2)	0	(0)	
	≥30	6	(240	6	(24)	13	(52)	
Smoking		12	(44.4)	6	(22.2)	9	(33.3)	0.089*
Family history		6	(42.9)	1	(21.1)	7	(50)	0.546*
Hypertension		12	(38.7)	3	(9.7)	16	(51.6)	0.207
Diabetes mellitus		4	(20)	3	(15)	13	(65)	0.133

*****Fisher's exact test. **BMI**: Body mass index

The associations between troponin I level and almost all early in-hospital outcomes were not significant as shown in table 3.

Table 3. Correlation of in-Hospital outcomes with troponin I level.

IN-HOSPITAL OUTCOMES	**Troponin I level ng/ml**						**P**
	<0.5		**0.5-1.5**		**>1.5**		
	N0	**(%)**	**No.**	**(%)**	**No.**	**(%)**	
Ventricular tachycardia	2	(11.1)	0	(0)	0	(0)	0.143*
Ventricular fibrillation	0	(0)	0	(0)	0	(0)	NA
Atrial fibrillation	0	(0)	0	(0)	0	(0)	NA
Ventricular ectopic beat	2	(11.1)	4	(44.4)	4	(16)	0.144*
Pulmonary edema	0	(0)	0	(0)	5	(20)	0.077*
Bleeding	2	(11.1)	0	(0)	0	(0)	0.143*
Cardiogenic Shock	0	(0)	1	(11.1)	3	(12)	0.371*
Syncope	2	(11.1)	0	(0)	3	(12)	0.698*
Death	0	(0)	1	(11.10	1	(4)	0.434*

*****By Fisher's exact test

High troponin I level (>1.5ng/ml) was associated with high GRACE score (≥155) were (11 patients, 44%) of those with high troponin level, had high GRACE score, compared with (3 patients, 33.3%) of those of medium troponin level (0.5-1.5ng/ml), and (4patients, 22.2%) of those with low troponin level (<0.5ngm/ml) (p = 0.002). as shown in table 4.

Table 4. Correlation of GRACE mortality score with troponin I level.

GRACE mortality score	**Troponin I level ng/ml**						**P**
	<0.5		**0.5-1.5**		**>1.5**		
	No. 18		**No.9**		**No.25**		
	N0	**(%)**	**No.**	**(%)**	**No.**	**(%)**	
<126	10	(5.6)	0	(0)	2	(8)	0.002
126-154	4	(22.2)	6	(66.7)	12	(48)	
>155	4	(22.2)	3	(33.3)	11	(44)	

GRACE: Global Registry of Acute Coronary Events

The higher the troponin level, the higher the frequency rate of LVSD was observed, but the difference between the proportions was not significant. The association between troponin level and RWMA was significant, where it is evident that all of those with medium (9 patients, 100%) and high troponin level (25 patients, 100%) had RWMA compared with (14 patients, 77.8%) of low troponin level (p = 0.025). table 5.

Table 5. Correlation of left ventricular systolic dysfunction with troponin I level.

	Troponin level ng/ml						**P**
	<0.5		**0.5-1.5**		**>1.5**		
	N0	**(%)**	**No.**	**(%)**	**No.**	**(%)**	
LVSD	4	(22.2)	3	(33.3)	9	(36)	0.617
RWMA	14	(77.8)	9	(100)	25	(100)	0.025*

* By fisher's exact test

LVSD: Left ventricular systolic dysfunction. RWMA: Regional wall motion abnormalities

Disscusion

This study was done as an attempt to evaluate the role of troponin I to predict the development of early LVSD diagnosed by Transthoracic Echocardiography in patients with first STEMI.

Results showed that the majority of patients (71.2%) were males and (28.8%) were female, this is consistent with Andreotti et al[24]who demonstrated that the incidence of ACS is lower in women than men in all ages and Rosengren et al[25] who found that women presented more often with AMI without ST elevation or unstable angina and less often with STEMI compared to men.

The most common risk factor in the present study was hypertension (59.6%), Smoking (51.9%), Diabetes mellitus was (38.5 %) while family history of ischemic heart disease was (14 %), which was similar to El-Menyar et al[26]. in regard to smoking 52%, and family history (13 %.) While hypertension and diabetes was lower than this study (33 %, 32%).

No significant association was detected between troponin I level with age, gender, hypertension, diabetes mellitus, family history of IHD, and smoking; this is in parallel with Matetzky et al[27]. and Bhatt et al[28].

The association between BMI and troponin was significant (p = 0.004), but in spite of that, the pattern was not consistent where high proportions of the normal weight and obese had high troponin, while none of the over-weight patients had high troponin. While Cepeda-Valery et al[29] demonstrated that obesity was associated with lower peak troponin I as an estimation for infarction size in STEMI but Bhatt et al[28] and Chia et al[30].found no association between troponin I and BMI.

In contrary to other studies, no significant association was found between early in-hospital outcomes with troponin I level[26, 29], this may be explained by small number of patients in this study, but it's worth to mention that higher rate of pulmonary edema, syncope, cardiogenic shock were observed in patients with high troponin level and all deaths (two cases) were of high and medium troponin level.

High GRACE score was found in 44% of those with high troponin level, compared with 33.3% of those of medium troponin level, and 22.2% of those with low troponin level which was statistically significant (p = 0.002).this is in agreement with Baptista et al[31]. who found high correlation between GRACE score and troponin I level (p=<0.001).

This study revealed the higher the troponin level, the higher the frequency rate of LVSD, but the difference between the proportions was statistically not significant ,while Matetzky et al[27] found that

the pre discharge LVEF determined by using Simpson's biplane method was significantly lower in patients with elevated admission cTnI (p=0.04) This can be explained by the difference in sample size and the way of estimation of the ejection fraction were we depended on the 2D M-mode method for the calculation of ejection fraction.

The association between troponin level and RWMA was significant (p = 0.025), where it is evident that all of those with medium and high troponin level had RWMA compared with 77.8% of those with low troponin level. This is consistent with Battioni et al[32], and with a study done in Iran by Hajsadeghi S. et al[33] were Cardiac Troponin I Level and regional wall motion score index was Positively Correlated (P= < 0.001).

Limitations

The main limitation of our study is it's a small size sample with short duration of follow up.

Conclusion

Elevated troponin I values may predict early left ventricular systolic dysfunction, regional wall motion abnormality as well as high GRACE risk score in the early phase of admission.

Recommendations : Large-scale multicenter prospective studies needed to farther evaluate the role of troponin I on early left ventricular systolic dysfunction and farther study to evaluate the role of BMI on troponin level.

Conflicts of Interest

The authors report no conflicts of interest.

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