Original Research Article

The significance of lipid profile and positive troponin-I in predicting cardiac event

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ABSTRACT

Background: Diagnosis of acute cardiac event in the early stage of its onset is important in the treatment process. The development of highly sensitive and specific immunoassays for myocardial proteins such as cardiac troponin-I had made it possible. However troponin indicates cardiac events only after its onset or after cardiac tissue necrosis. Traditionally such high risk subjects were identified using lipid profiles. The identification of subjects with high risk of developing cardiac event in the future is more significant as it will provide time to prevent such incidents.
Methods: In this retrospective study data of the 250 patients presented to the emergency department with symptoms of cardiac ischemia who underwent both troponin-I and lipid profiles tests were compared with the lipid profiles of 100 normal healthy subjects (controls). The troponin-I was detected quantitatively when a specimen contains troponin-I above the 99th percentile (TnI >0.3 ng/ml). The total cholesterol, high density lipoproteins cholesterol, very low density lipoproteins cholesterol and triacylglycerol levels were also analyzed and low density lipoprotein cholesterol level was calculated using Friedewald's formula.
Results: Patients with chest pain and positive troponin-I test (with confirmed cardiac event) were found to have significantly elevated levels of total cholesterol, triacylglycerols, low density lipoprotein cholesterol level and significantly reduced high density lipoproteins cholesterol levels when compared to the patients who experienced only chest pain with (negative troponin-I) and healthy controls.
Conclusions: An acute cardiac event is best diagnosed by highly sensitive and specific positive troponin-I test (by quantitative method). However, traditional lipid profile levels still can be used in screening the populations to identify those subjects with high risk of developing cardiac event, in those centres where troponin-I test facility is unavailable.

Keywords: Troponin-I, Chest pain, Cardiac event, Lipid profile

INTRODUCTION

Cardiovascular disease (CVD) is still the leading cause of morbidity and mortality globally. There is general consensus that prevention is the key to address the CVD burden, however identifying high-risk individuals in the community who may benefit from more aggressive preventive treatment remains a challenge. Risk prediction algorithms such as the Australian absolute cardiovascular disease risk calculator, the New Zealand cardiovascular risk charts and Euro-score are currently the accepted means of doing this, but all of them still have limitations in sub-optimal sensitivity, specificity, and poor accuracy in certain sub-populations including diabetics, renal disease, and those with a family history of premature CVD.[1-4] Biomarkers may increase the accuracy of these

algorithms in predicting risk. Cardiac troponins (cTn) are specific biomarkers of myocardial injury and have a well established role in guiding the management of chest pain.[5,6] An elevated troponin-I (cTnI) has also been associated with a poor prognosis in critical illness, pulmonary embolism, cardiac and non-cardiac surgery, stroke, and end-stage renal disease.[7-14] The assessment of patients with acute chest pain of possible cardiac cause continues to be a challenge and positive diagnosis has psychological, social and legal implications.[15,16] The presence of ST segment elevation in the ECG is highly specific (but only about 50% sensitive) for acute myocardial infarction (MI).[15] However, many patients presenting to coronary care units have chest pain without ST elevation in the ECG. The diagnostic possibilities in these cases include: acute coronary syndrome in evolution, or 'non-ischaemic' chest pain. The world health organization defines for diagnosing acute myocardial infarction (AMI), the presence of two of the three enlisted features namely, symptoms of myocardial ischemia, elevated levels of cardiac marker (protein or enzyme) concentrations in the blood, and a typical electrocardiographic pattern involving the development of Q waves or persistent T wave changes.[17] Further the American heart association case definition for acute myocardial infarction (AMI) requires an "adequate set" of biomarkers: two measurements of the same marker at least 6 hours apart.[18-20] Cardiac troponin concentration is the preferred marker of myocardial necrosis.[21] Elevated concentrations of cTnI have a strong association with an adverse prognosis in patients with acute coronary syndromes and are used to identify patients who are likely to benefit from an early invasive management strategy.[22-24] Traditionally the cardiac enzymes used in the assessments for the detection of MI includes the triad of lactate dehydrogenase, aspartate transaminase (serum glutamate oxaloacetate transaminase) and creatine kinase-MB (CKMB) which is of heart origin. However the use of biochemical 'gold-standard' CK-MB levels has limited prognostic power compared to the serum troponins (both I and T) which are considered to be more specific and sensitive over CK-MB in the setting of acute coronary syndromes and have been validated for post operative risk stratification for noncardiac surgical procedures.[15,16] With CK-MB being used as a marker, it has limitations to identify the future risk of acute coronary syndromes hence, many of the patients are kept in ICCU and occupy beds unnecessarily, and other who are presumed to be safe and are discharged, returns to ICCU with recurrent coronary events.[15,16] Highly sensitive and specific immunoassays for myocardial proteins, such as troponins T and/or I which are components of the thin filaments of the sarcomere are used in the identification of subjects with small areas of myocardial necrosis.[17] Troponin-I testing had better sensitivity, specificity and prognostic value than troponin T testing. A positive troponin-I result was a strong predictor of cardiac events (death from cardiac causes or MI) in the next 30 days. The predictive value of a negative troponin-I result was also high, with a total 30 days event rate of 0.3%, regardless of the admission ECG.[15,16] The assessment of smaller molecular mass proteins such as myoglobin (1600 kD) derived from the cytosol of both skeletal and cardiac muscle, heart type fatty acid binding protein (hF-ABP) are considered to be more cardio specific, are promising novel markers for early detection of acute or persistent myocardial damage. However in clinical practice neither of these proteins is considered as cardiac markers.[17] The new diagnostic criteria include a characteristic rise and fall in blood concentrations of cardiac troponins and/or CK-MB in the context of spontaneous ischemic symptoms or coronary intervention.[17] Cardiac troponin-I and T are highly sensitive and highly specific and may be elevated when CK-MB concentrations are not even mildly elevated. In addition, they may predict recurrent cardiac events in patients with acute coronary syndromes. However, use of troponin-I testing has been limited by availability of laboratory based diagnostic techniques and by relatively long processing times.[15,16] Even minor elevations of troponin-I concentrations in the blood are indicative of myocytes necrosis and not due to leakage of proteins through the myocyte cell membrane. The current immunoassay assays for troponins T and I reliably detect cardiac (as distinct from skeletal muscle) forms of these proteins.[25] Furthermore, troponins have greater sensitivity and specificity for the diagnosis of MI in acute myocardial ischemia. In this study we proposed to evaluate the association between lipid profile levels of the subjects with chest pain with positive or negative troponin-I test.

METHODS

This retrospective study is conducted at department of biochemistry of Gayatri Vidya Parishad institute of health care and medical technology, Visakhapatnam, India. Study includes 250 patient records presenting to the emergency department with symptoms of cardiac ischemia. The study is accepted by ethical committee of the college, the study includes the patient records from January 2018 to March 2019. The inclusion criteria was the records of subjects (n=250) who were admitted to the intensive care unit of the hospital complaining with severe chest pain and estimation of both troponin-I and lipid profiles were done. In addition to that, reports of 100 healthy subjects who had got their lipid profiles checked were taken as controls.

The troponin-I was quantitatively estimated in the patient samples using the fluorescence immunoassay chroma analyzer. A cut off of 0.3 ng/ml which is the 99th percentile of population is recommended for probable diagnosis. The total cholesterol (TC), high density lipoproteins cholesterol (HDL) and triacylglycerol levels (TG) were analyzed. All the estimations were done using Medica Easy RA fully automated analyzer using the kits from Medica. The very low density lipoprotein cholesterol (VLDL) was derived from triglyceride values (VLDL-C is TG/5). The low density lipoprotein cholesterol (LDL-C) was calculated using Friedewald's

formula.[26] Data was analysed using EpiInfo windows version and applying paired/unpaired t-test.

RESULTS

Out of the 250 subjects with the chest pain and tested for the presence of troponin in the serum qualitatively, only 79 subjects were detected positive. The larger proportion of the subjects154 with severe chest pain was found to be troponin negative. Initially, the differences in various lipid parameters among the subjects with chest pain and with or without a troponin were compared (Table 1).

Table 1: Comparison of lipid parameters of the subjects with chest pain and troponin-I positive vs. chest pain and troponin-I negative patients.

Variables	Subjects with chest pain (n=250)		
	Troponin-I negative mean±SD (n=154)	Troponin-I positive mean±SD (n=96)	P value
Age (years)	47.16±6.75	59.34±12.73	<0.01 (S)
Total cholesterol (TC) mg/dl	144.54±23.96	210.89±18.11	<0.01 (S)
Triglycerides (TG) mg/dl	85.75±21.25	174.62±17.53	<0.01 (S)
High density lipoprotein (HDL) mg/dl	44.22±4.11	37.1±3.34	<0.01 (S)
Low density lipoprotein (LDL) mg/dl	83.19±23.63	138.7±19.46	<0.01 (S)
Very low density lipoprotein (VLDL) mg/dl	17.14±4.31	35.09±3.48	<0.01 (S)

(S): significant

Table 2: The comparison of lipid profiles of the controls with the patients with chest pain and troponin-I positive and chest pain and troponin-I negative groups.

Variables	Control (n=100)	Chest pain (n=250)		P value
		Troponin	Mean±SD	
Age (years)	48.76±7.2	P (96)	59.34±12.73	<0.01 (S)
		N (154)	47.16±6.75	0.07 (NS)
Total cholesterol (mg/dl)	149.6±14.6	P (96)	210.89±18.11	<0.01 (S)
		N (154)	144.54±23.96	0.06 (NS)
Triglycerides (mg/dl)	89.4±12.5	P (96)	174.62±17.53	<0.01 (S)
		N (154)	85.75±21.25	0.12 (NS)
LDL (mg/dl)	87.6±17.8	P (96)	138.7±19.46	<0.01 (S)
		N (154)	83.2±23.63	0.11 (NS)
HDL (mg/dl)	45.4±3.96	P (96)	37.10±3.34	< 0.01 (S)
		N (154)	44.22±4.11	0.02 (S)
VLDL (mg/dl)	18.27±4.68	P (96)	35.09±3.48	<0.01 (S)
		N (154)	17.14±4.31	0.04 (S)

Values in the parenthesis indicated the number of subjects, P=subjects with chest pain and troponin-I positive, N=subjects with chest pain and troponin-I negative, S=significant, NS=non significant.

In addition to that these two groups were compared for the same parameters with those levels of normal healthy subjects (controls), the data shows significant difference was observed for age among the two groups of subjects. The subjects with chest pain (n=250) among which troponin-I negative (n=154), troponin-I positive (n=96) were observed, variables were compared and significant p<0.01 was observed. Among these subjects with chest pain troponin-I positive variables were increased except high density lipoprotein. Hence all other parameters of the lipid profiles were significantly different in two groups. Among the subjects with chest pain total cholesterol, triacyl glycerol, low density lipoproteins levels were higher in the subjects with troponin positive

than the subjects with a negative troponin. Further HDL levels in the subjects with troponin positive were lower than troponin negative. Of the subjects with chest pain, a significantly (p<0.001) higher levels of TC, LDL and TG, have been observed in subjects with positive troponin test, when compared to the healthy subjects (Table 2) and the subjects with a negative troponin test (Table 1). The data (Table 2) shows the comparison of biochemical parameters of the subjects with chest pain and with or without a positive test for troponin against the healthy controls.

Further HDL level of the subjects with chest pain and positive troponin was significantly lower than the HDL

levels of controls (Table 2) and that of the subjects with a negative troponin test (Table 1). The effect of sex on having only chest pain (when troponin is negative) was evaluated and data are given in (Table 3).

Table 3: The effect of sex on the variables in subjects only with chest pain with troponin-I negative.

	Females (n=63)		Males (n=91)		P value
	Mean	SD	Mean	SD	
Age	46.58	7.08	47.59	6.54	0.36 (NS)
Troponin-I	0.07	0.04	0.07	0.03	<0.001 (S)
Total cholesterol	141.88	26.80	146.46	21.81	0.24 (NS)
Triglycerides	82.30	21.41	88.22	21.01	0.09 (NS)
HDL	43.30	3.68	44.87	4.31	0.02 (S)
LDL	82.06	27.60	84.00	20.59	0.62 (NS)
VLDL	16.52	4.34	17.59	4.29	0.13 (NS)

Table 4: The effect of sex on the variables in subjects only with chest pain with troponin-I positive.

	Females (n=32)		Males (n=64)		P value
	Mean	SD	Mean	SD	
Age	58.71	11.41	59.54	13.98	0.7 (NS)
Troponin-I	13.96	9.65	11.17	9.56	0.08 (NS)
Total cholesterol	208.84	19.45	211.80	17.56	0.33 (NS)
Triglycerides	177.55	19.48	173.33	16.58	0.15 (NS)
HDL	36.58	3.35	37.33	3.33	0.17 (NS)
LDL	136.58	20.52	139.64	19.05	0.34 (NS)
VLDL	35.68	3.93	34.83	3.25	0.14 (NS)

In the subjects with chest pain which is not due to cardiac event as indicated by negative troponin test a significantly greater levels were observed for TG and for VLDL in males than in females. However all these parameters were within the normal levels. The all other parameters including TC, LDL and HDL levels were the same for both sexes. The effect of sex on having only chest pain (when troponin is positive) was evaluated and data are given in (Table 4). In the subjects with chest pain due to cardiac event as determined by positive troponin-I test is closely associated with elevated levels of TC, LDL, and TG and also with significantly reduced HDL. However the comparison of lipid parameters of males and females in the sub group of positive troponin-I tests revealed (Table 4) that there was highly significant difference in parameters due to difference in sex.

DISCUSSION

In a previous study of subjects with chest pain it was reported that troponin was positive in 160 subjects (31.9%) and negative in 323 (64.3%) subjects.[18] Dyslipidemia and obesity pose a serious public health concern in view of the rapid changes in lifestyle with processed foods increasingly replacing traditional foods. In the present study of subjects with chest pain it is reported that troponin-I was positive in 96 subjects and negative in 154 subjects. They also reported higher incidence of acute myocardial infarction, acute heart failure, and death due to cardiac event in the subjects with chest pain and positive troponin I confirming that it

is a powerful, independent and valuable tool for risk stratification in patients with acute chest pain.[27]

The present study indicates that, of the subjects with chest pain (250) only (96) were detected positive and a larger proportion of subjects (154) were detected negative for troponin I. Accordingly, those 250 subjects with chest pain are at high risk of developing cardiac event though the cardiac event occurring in only (96). It is well known that increased levels of low density lipoproteins (LDL), triacylglycerides (TG) and total cholesterol (TC) and decreased levels of high density lipoproteins (HDL) are also indicative of increased incidence of cardiac events and are considered as risk factors.[27] Therefore in this retrospective study the relationship between levels of lipid profile parameters and the results of troponin-I test in predicting cardiac events is evaluated.

Present study data indicated that mean TC level (210.89±18.11 mg/dl) of the subjects with positive troponin-I (96) was well above the recommended desirable level (<200 mg/dl) thus indicating those subjects are susceptible to develop cardiac event.[27] The level of total cholesterol of the subjects with negative troponin test (144.54±23.96 mg/dl) but with chest pain (154). In previous studies the mean TC level of the subjects (38) with positive troponin (221±35.8 mg/dl) was well above the recommended desirable level (<200 mg /dl) thus indicating those subjects are susceptible to develop cardiac event.[27] The level of total cholesterol of the subjects (221) with negative troponin test but with chest pain (176±46.17) was significantly lower than that

of the subjects with positive troponin I above confirming the importance of maintaining total cholesterol levels below the recommended level.[27] Similarly the mean TG level of the subjects (96) with positive troponin-I (174.62±17.53 mg/dl) was well above the both the recommended desirable level (<150 mg/dl), and the level of TG of the subjects (154) with negative troponin I test but with chest pain (85.75±21.25 mg/dl). Previous reported studies shows that the mean TG level of the subjects with positive troponin (163.74±48.22 mg/dl) was well above the both the recommended desirable level (<150 mg/dl), and the level of TG of the subjects with negative troponin test but with chest pain (148.20±54.79 mg/dl). Further the TG level of the subjects with only chest pain was slightly lower than the recommended safe level. Increased level of LDL is highly atherogenic as it could get oxidized and initiates the atheroma formation. Thus it is believed that increased level of LDL than the recommended level is a high risk factor in the development of cardiac event. The mean LDL level of the subjects (96) with positive troponin I (138.7±19.46 mg/dl) was well above the recommended desirable level (<130 mg/dl).[27] Further the mean LDL level of the subjects (154) with negative troponin I test but with chest pain (83.19±23.63 mg/dl). In previous studies the mean LDL level of the subjects (38) with positive troponin (152.26±39.41) was well above the recommended desirable level (<130 mg/dl) the mean LDL level of the subjects (221) with negative troponin test but with chest pain (102.49±44.29 mg/dl) was well below the recommended level and confirmed the importance of maintaining lower levels of LDL in preventing future cardiac event. Thus present study data indicated that the subjects who developed chest pain due to cardiac event as confirmed by positive troponin-I test had significantly greater levels of TC. TG, LDL when compared to those levels in subjects without cardiac event as indicated by negative troponin I test. On the other hand lower HDL level (<40 mg/dl) is also regarded as a cardiac risk factor and the mean HDL level of the subjects (96) with positive troponin-I (37.1±3.34 mg/dl) is lower than the recommended safe level. In previous studies lower HDL level (<40 mg/dl) is consider as cardiac risk factor, and the mean HDL level of the subjects (38) with positive troponin (36.82±5.29 mg/dl). This also indicates that the development of cardiac event was associated with reduced levels of HDL than the recommended level. Further the subjects (154) with negative troponin-I test (no cardiac event) had a mean HDL level above the cut off value suggestive of safe levels and that value was (44.22±4.11 mg/dl) significantly (p<0.001) greater than the mean HDL levels of the subjects who had a cardiac event. These lipid parameters to be compared with the values of age matched hundred (100) healthy subjects without any known disease condition. All the values of lipid parameters are within the safe levels for healthy subjects indicating they were having a minimum possibility of developing any cardiac event. Only the mean TG level was slightly higher (89.4±12.5 mg/dl) than the risk level of 150 mg/dl in some subjects (100).

The total cholesterol level and LDL levels of the subjects with positive troponin-I was significantly (p<0.01) greater than the healthy subjects and no significant difference was observed for TC between healthy subjects and subjects with a negative troponin-I test but with chest pain. However no significant differences were observed for TG and VLDL between these groups.

Significantly lower (p<0.01) mean HDL level is observed in the subjects with positive troponin I when compared to healthy subjects and the subjects only with chest pain but with negative troponin-I test. These data indicated that the chest pain due to cardiac event as determined by negative troponin-I test is closely associated with elevated levels of TC, LDL, and TG and also with significantly reduced HDL. However the comparison of lipid parameters of males and females in the sub group of negative troponin-I tests revealed (Table 3) that there were no major significant difference of those parameters due to differences in sex. These data indicated that the chest pain due to cardiac event as determined by positive troponin-I test is closely associated with elevated levels of TC, LDL, and TG and also with significantly reduced HDL. However the comparison of lipid parameters of males and females in the sub group of positive troponin-I tests revealed (Table 4) that there is highly significant difference in parameters due to difference in sex.

Limitations

As this is not a prospective study hence the inference derived from the study need to be tested by prospective study.

CONCLUSION

The present study shows in the patients who developed chest pain due to cardiac event as confirmed by positive troponin-I test were having lipid parameters in the risk level as suggested by ATP III. The subjects who had lipid profile levels within risk level were at a greater risk of developing chest pain due to cardiac event. Therefore it is essential to and measure screen to identify those subjects with a risk levels of lipid profile parameters and advise them to control their lipid profiles to maintain within the normal levels as per recommendation of ATP III guide-line.

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