ORIGINAL ARTICLE

Correlation of Troponin Rapid Test and Severity of Coronary Artery Disease in patients with chest pain

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ABSTRACT

Background: Many patients in emergency are admitted with chest pain, whether typical or atypical. They undergo varieties of tests to diagnose whether they are suffering from ischemic heart disease or not. One of the tests performed in the emergency is Troponin T rapid test.

Study design: This is an observational study of 100 patients who presented with chest pain from January 2013 to June 2013.They were all admitted in the hospital.50% of the patients were troponin T rapid test positive and 50% of them were negative. All of them underwent coronary angiogram. A coronary angiography severity criterion was defined as significant coronary artery disease with more than 50% diameter stenosis in vessels more than 1.5mm diameter.

Result: The average age of patients in the study is 55 years. The average age of troponin positive patient is 56+/-14 years with male average age of 55years and female average age of 58 years. The male average age in this group was slightly lower than female. The average age in troponin negative group is 55 years both in male and female. In patients who were troponin rapid test positive, the coronary artery disease was found severe in 47(94%) patients, 2 patients (4%) had moderate disease and one patient (2%) had mild disease. Whereas 23(46%) had triple vessel disease, 17(34%) double vessel disease and 10(20%) had single vessel disease. The main vessel involved in this group was LAD which was found diseased in 44(88%) of patients. In patients who had troponin rapid test negative, disease was mild in 35(70%) of patients, 8(16%) had moderate disease and 7(14%) had severe disease. The predominantly involved vessel was LCX in 47(94%) of cases.

Conclusion: Our study revealed that the patients with troponin rapid test positive were having severe coronary artery disease involving multiple vessels mainly the LAD in about 88% of patients. Where as in patients with negative troponin rapid test the disease was mild in majority of cases and predominantly involved vessel was LCX. The disease was found severe in only 14% of patients in this group and this small group must be looked after properly and must receive aggressive medical treatment and must be considered for revascularization.

Keywords: Chest pain, Troponin rapid test, coronary artery disease

INTRODUCTION

Troponin is a complex of three regulatory proteins (troponin I, troponin T and troponin c) that is integral to the muscle contraction in skeletal and cardiac muscle but not in smooth muscle. The increased levels of cardiac troponins circulating in the blood have been shown to be biomarker of heart disorder, the most important of which is myocardial infarction. The raised troponin levels indicate cardiac muscle cell death as the enzyme is released in to the circulation upon injury to the heart.

The cardiac troponin is sensitive and specific indicator of damage to the myocardium and it is raised in all the heart damage and not just the myocardial infarction. The diagnosis of acute myocardial infarction is generally based upon WHO criteria and consists of the presence of at least two of three classic findings; clinical symptoms, diagnostic ECG and serological findings of abnormal finding of CK, LD or their isoenzymes[12]. Troponin is also raised in supraventricular tachycardia, heart failure myocarditis, pericarditis, cardiomyopathy, left ventricular hypertrophy, peripartum cardiomyopathy, takotsuo cardiomyopathy, amyloidosis, ASD closure, PCI, radiofrequency ablation. Troponin is also raised in non cardiac conditions like sepsis ,gastrointestinal bleeding, chemotherapeutic agents like cyclophosphamide, cicplatin, anthracycline, several toxins and venoms ,carbon monoxide poisoning, cyanide poisoning, dissection or hemorrhage, stroke, seizure, patients with end stage renal disease, strenuous endurance exercise, polymyositis, dermatomyositis and preeclamsia.

The testing for cardiac troponins in the clinical setting of acute coronary syndrome is considered a class 1 indication for early risk stratification as per American College of Cardiology /American Heart Association (ACC/AHA) guidelines as improves

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clinical outcome in these patients[1]. Cardiac troponin elevation following cardiac cell necrosis starts within 2-3 hours and peaks in approximately in 24 hours and persists for one to two weeks.

TROPNIN T is a part of troponin tropomyosine complex .It binds to tropomyosine, interlocking them and form troponin tropomyosine complex. There are three tissue specific subtype. Slow skeletal troponin T1, cardiac troponin T2, fast skeletal troponin T3. Tropnin binds to tropomyosine and help position it on Actin and with the rest of the troponin complex and modulates contraction of skeletal muscle.

New generation high sensitivity cardiac troponin (hs-cTn) has recently been developed which allows for the detection of even minor myocardial necrosis with high precision. Increased diagnostic and prognostic accuracy of hs-cTnT has been recently reported in many studies and it allows risk stratification in patients with ischemic heart disease both in chronic and acute events. The Trop T Sensitive rapid assay provides qualitative analytical test result and is designed to yield a positive result for cardiac troponin T concentration >0.08ng/ml[13].

Significant Coronary artery disease was defined as a 50% or greater luminal diameter stenosis of a major epicardial artery or its branches of more than 1.5mm diameter. A left main stenosis of 50% or more was regarded as equivalent to two vessel disease.

METHODS

Study population: One hundred patients of chest pain who were admitted in hospital (70 of them were male and 30 were female. Mean age is 55 years.) Patients were divided in to two groups. One group was Tropnin T Sensitive Rapid Test (Cobos Roche) positive and other was negative .All the patients with atypical chest pain presenting in the emergency were included in the study .No age limit was defined and there was no gender discrimination. Coronary angiography was performed for the investigation of ischemic heart disease based upon atypical central chest pain. ECG was nondiagnostic in all the patients. Troponin T rapid test was positive in 50% of patients, whereas it was negative in 50% of patients. The patients with coronary lesion of a diameter stenosis of >50% in >1.5mm vessel were included in the study. All patients were clinically stable. Exclusion criteria were presence of acute myocardial infarction, new ST segment elevation or depression, alteration of the previous ischemic symptoms, new development of Q wave, neoplastic disease, heart failure, recent trauma or surgery, liver or kidney disease, previous MI, previous PCI or CABG, valvular or myocardial disease, or pericardial disease.

Blood sample: The test is based upon the dual monoclonal antibody “sandwich” principle using a poly (streptavidin) biotin capture system with gold sol particle label as described by the manufacturer. The test is initiated by addition of whole blood to the TROP T Sensitive Rapid Assay, which separate red blood cells from plasma .Cardiac troponin T in plasma combine with both boitinylated. Anticardiac troponin T antibody conjugated to gold sol particle, to form a ‘sandwich’. This ‘sandwich’ combine with poly (strepteavidin),which is immobilized in a stripe or a line across the read window of the TROP T Sensitive Rapid Assay, producing a radish purple line .The intensity and the speed at which the color forms are related to the concentration of cardiac troponin T in blood .The test is taken as positive even if the line is very faint .Venous whole blood anticoagulated with EDTA or heparin is collected with standard veinipuncture technique or arterial whole blood anticoagulated with heparin .150 micro liter anticoagulated blood is taken in a specially designed syringe to transfer blood from sample collection tube to the Rapid Assay .If the test line is positive ,it is read immediately or after 15-20 minutes or when red-brown discoloration appear in the read window, whichever come first record the time and result is read. The Trop T Sensitive Rapid Assay is designed to yield a positive result for cardiac troponin T concentration >.08ng/ml and it is a qualitative test.

Coronary angiography: All patients under went coronary angiography with judkins technique. Coronary angiograph y was performed with standard femoral or radial approach. Coronary angiography was analysed independently by two experienced interventional cardiologists who had no knowledge of the patients clinical status and cTnT status. Luminal diameter stenosis of more than 50% was taken as significant coronary artery disease in 1.5 mm or more vessels. The vessel was taken as single, double, or triple vessel disease if one, two or three vessels were involved. Left main was taken as separate entity. The mild disease is defined as luminal diameter stenosis of 20-50%, moderate disease is 50-70% stenosis and severe is more than 70% stenosis.

RESULT

Average age of the patients in the study is 55 years. 10% of patients are between the age of 30-40 years, 30% The age of 40-50 years, 25% between 50-60 years, 20% between 60-70 years and 15% were more than 70 years of age (Table 1). The average age of troponin positive patients is 56.5 years and male average age is 55 years and female average age is 58 years and male average age in this group is slightly lower than female. The average age in troponin negative group is 55 years in both male and

female. In the study 70% are male and 30% are female (Table 2). Among the patients 65(65%) patients were diabetic, 40(40%) hypertensive, 30(30%) patients had hyperlipidemia, 37(37%) were smokers and 60(60%) patients were having BMI more than 25(Table 3). Among the patients many had more than one risk factor. Among the patients 50(50%) were troponin positive and 50(50%) were troponin negative (Table 4). In the troponin positive patients, 3 patients (6%) had mild CAD, 4 patients (8%) had moderate CAD, 43 patients (86%) had severe disease .Single vessel disease was found in 10(20%) of patients, double vessel disease was found in 17(34%) and triple vessel disease was present in 26(46%) of patients. Left main stem disease was found in 6(12%), left anterior descending artery (LAD) disease was present in 42(84%), 30(60%) of patients had left circumflex disease and 36(72%) of patients had right coronary artery disease (Table 5). In the Tropnin T Rapid Test negative group, 35(70%) patients had mild disease 9(18%) moderate disease and severe disease was found in only 6(12%) patients. Single vessel disease was found in 35(70%) of patients ,double vessel in 5(10 %) patients and triple vessel disease was found in 10(20%) patients .Left main disease was present in 2(4%) patients, LAD disease in 25(50%), LCX disease in 38(76%) and 20(40%) patients had RCA disease.

Table 1 (n=100)

Age (years)	n	%age
30-40	10	10
40-50	30	30
50-60	25	25
60-70	20	20
More than 70	15	15

Table 2 (n=100)

Gender	n	%age
Male	70	70
Female	30	30

Table 3: Conventional cardiac risk factors(n=100)

Risk Factors	n
Diabetes mellitus	65
Hypertension	40
Hyperlipidemia	30
Smoking	37
Obesity	60

Table 4: Troponin t sensitive rapid test (n=100)

Tests	n	%age
Troponin Positive	50	50
Troponin Negative	50	50

Table 5: Cad in troponin positive group (n=100)

CAD Severity	n	%age
Mild (20-50 %)	3	6
Moderate (50-70 %)	4	8
Severe (> 70%)	43	86
Single Vessel Disease	10	20
Double Vessel Disease	17	34
Triple Vessel Disease	23	46
Left Main Disease	6	12
LAD Disease	42	84
LCX Disease	30	60
RCA Disease	36	72

Table 6: CAD in Troponin negative group

CAD Severity	n	%age
Mild (20-50 %)	35	70
Moderate (50-70%)	9	18
Severe (>70%)	6	12
Single Vessel Disease	35	70
Double Vessel Disease	5	10
Triple Vessel Disease	10	20
Left Main Disease	2	4
LAD Disease	25	50
LCX Disease	38	76
RCA Disease	20	40

CAD- Coronary Artery Disease, LAD- Left Anterior Descending Artery, LCX- Left Circumflex Artery, RCA- Right Coronary Artery.

DISCUSSION

The diagnostic criteria for acute myocardial infarction is mainly based upon, history of chest pain , ECG and laboratory test like cardiac enzymes and troponins. Many times patient is presenting with atypical history of chest pain especially in patients with diabetes and in female where the symptomatology is very deceptive. Similarly the ECG may be equivocal and have nonspecific changes for diagnosis of ischemic heart disease and in the end, the laboratory test may or may not be available .Further more they take few hours to become detectable and especially cardiac troponins start rising after 3-4 hours of cardiac insult. In the light of all above mentioned difficulties, which tool may be more important to diagnose and not miss any patient of impending ischemic heart disease.

In the light of above mentioned facts we tried to correlate the symptomatology with laboratory data and extent of CAD .This is one of the few studies that investigated the correlation of TROPONIN T Sensitive Rapid Test which is freely available in our hospitals and even clinics. This is a spot test, the result of which is instantly available to the treating physician to forecast the extent and severity of the CAD in patient with chest pain.

The main finding of our study is that, the patients presenting with chest pain and who are Troponin T rapid test positive, they have more extensive and severe disease in about 86% of cases. Among those cases 84% were having left anterior descending artery disease which supplies the major part of myocardium, 60% had LCX(Left circumflex artery) disease and 72% had RCA (Right coronary artery). 46% of patient had triple vessel ,34% double vessels, and 20% had only single vessel disease .Severe disease was found in 86% of patient whereas only 8% had moderate and only 6% were having mild disease .

Whereas the negative group had mild disease in 70% of cases, 18% had moderate and 12% had mild disease. In contrast to the positive group, the negative group had LCX disease in 76% of cases, 40% RCA, and 50% LAD disease. 70% had single vessel disease, 10% double vessel and only 20% had severe triple vessel disease. The above mentioned facts revealed that Troponin T rapid test positivity in patients with chest pain had CAD which is more severe and complex. Whereas negative group do not exclude the CAD but smaller percentage have still severe disease but majority of them had mild disease and this is the group which must be looked after properly.

Recent studies have demonstrated that hs-cTnT assay increases the accuracy of diagnosis in the early period of acute myocardial infarction and hs-cTnT allows the detection of even minor myocardial necrosis with precision .The elevated levels of hs-cTnT in patient with stable or unstable angina presenting with undetectable conventional cardiac troponin are significantly associated with decreased survival. Omland et al[2], also reported that cardiac troponin concentration as measured with high sensitive assay are significantly associated with the incidence of heart failure as well as cardiovascular death in patients with CAD.

SYNTEX Score and diabetes are independently associated with hs-cTnT. The cut off value of hs-cTnT obtained by ROC curve analysis is 9.69ng/l for prediction of higher SYNTEX Score .hs-TnT, age diabetes, creatinine and hs-CRP are independent predictor for higher syntax score.

The present study showed that Trop T Sensitive rapid test performed in emergency and even clinics in patients with chest pain, the positivity is directly associated with extent and severity of CAD. Those patients who are Troponin T sensitive rapid test negative majority of them have mild disease but small number of patients has severe disease.

N Drepepa et al[3] investigated to study the factors that are associated with increase in high sensitive troponin T in patients with stable or unstable angina undergoing revascularization .They found that patients with upper tertile of hs-cTnt have higher incidence of multi vessels disease compared with low tertile. They also reported that, the elevated levels of hs-cTnt in patients with stable or unstable angina are significantly associated with reduced survival. In another study N Drepepa et al[5]. demonstrated that in patients with stable and angiographically proven CAD, hs-TnT level is increased compared to subjects without CAD and correlate angiographic atherosclerotic extent and burden . These findings are consistent with our study which also revealed that hs-cTnT positivity is associated with more severe CAD as compared with hs-cTnT negative group. Omland et al[2] also reported that cardiac Troponin T concentration as measured with high sensitive assay are significantly associated with increased incidence of heart failure as well as cardiovascular death in patients with stable CAD .

The pathophysiological mechanism underlying the association between hs-cTnT with extent and complexity of CAD is still unclear .Traditionaly it was thought that release of cTnT is equivalent to myocardial necrosis .However in previous studies even mild stable CAD was associated with quantifiable circulating levels of hs-cTnT in patients without acute coronary syndrome[2,3,11].

Recently Sabatine et, al[4] shown that transient stress test induced ischemia is associated with increased cTnt as detected by ultrasensitive cTnI assay. Hickman et al[11] reported that cardiac troponins may be released by ischemia alone without necrosis. In this, he has suggested that, the presence of membranous blebs in cardiac myosites is enabling troponins to be released from cardiac cells due to ischemia without necrosis .Moreover some animal studies have suggested that short episodes of ischemia may result in release of cTnT without demonstration of cell death because more complex and severe lesions at the site of more complex atherosclerosic lesion may be responsible for higher hc TnT release .

N Drepepe at al[5] showed that hs-c TnT can reliably stratify the risk of mortality in patients with stable or unstable angina .In our study, we demonstrated that in patients with chest pain and Trop T Sensitive rapid test positive is the predictor of more severe and complex CAD disease and negative result is associated with mild disease in majority of cases but small percentage of patients have severe disease and this group of patients must be looked after and undergo revascularization .Thus our result suggests that Trop T Sensitive Rapid Test in addition to clinical evaluation can be supplementary for further management of patients with chest pain. James et; al in their study has shown that among low to

intermediate risk patients with chest pain hsTnT provides good sensitivity and specificity for acute coronary syndrome. Elevation of hsTnT identifies patients with myocardial injuries and significant structural heart disease irrespective of the diagnosis of acute coronary syndrome. These findings are consistent with our study as far as the sensitivity and the severity of the coronary heart disease is concerned in relation to the elevation of cardiac troponin T. deFilippi et al[8] conducted a similar study in chest pain unit in patients of chest pain without ischemic electrocardiographic changes and they demonstrated that in a group of patients with chest pain anticipated to have a low prevalence of CAD and a good prognosis, cTnT identifies a sub group with high prevalence of extensive and complex CAD and increased risk for long term adverse outcome. The cTnT positive patients had a significantly higher percent diameter stenosis and a greater frequency of calcified; complex and occlusive lesions. These findings are very similar to our study, which also demonstrated the greater severity of disease in cTnT positive patients as compared to cTnT negative patients. Christain et al[9] in their study of patients of chest pain they demonstrated that the bed side test for cardiac specific troponins are highly sensitive for the early detection of myocardial cell injury in acute coronary syndrome. Negative test results are associated with low risk and allow rapid and safe discharge of patients with an episode of acute chest pain from the emergency room. These findings are consistent with our study however, our study revealed that a small group of patients with chest pain do have severe coronary heart disease and they should be kept for further observation and revascularization.

CONCLUSION

Trop T Sensitive Rapid Test performed in emergency is an important toll to predict the severity and complexity of CAD in patients with chest pain and even if it is negative with typical history of chest pain and equivocal ECG, must be evaluated for CAD because minor percentage of patients may have severe CAD. For patients who had short term observation for chest pain in the absence of ischemic ECG changes, cTnT elevation had a strong association with presence of severe and complex CAD. Prognostically, a positive a positive cTnT test is an independent and powerful predictor of future adverse cardiac events. Therefore, cTnT measurement should be an integral part of diagnostic work up in these patients with chest pain ,as it provides a simple method to identify those at risk of future ischemic complications that otherwise would not differentiated by clinical history or CK-MB result. Further studies are needed to clarify whether patient with chest pain and positive hs-cTnT and non diagnostic ECG will benefit from early and aggressive medical therapy, as is now being administered to patients with ischemic ECG changes.

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