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Original Research Article

A Study on Clinical Application of High-Sensitivity Cardiac Troponin I Assay in Individuals with Suspected Myocardial Infarction

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Abstract

Introduction: The prevalence of chest pain and its admission to the emergency department is quite high and it is a need of the hour that a simpler diagnostic or prognostic index be found in the prediction of acute myocardial infarction (AMI). There are many diagnostic pathways available but the current pathway is unable to confirm AMI during the presentation and the occurrence of hospital admissions are high among the geriatric population with chest pain. In Europe and America alone, there are more than 20 million cases annually which indicate a possible occurrence of AMI but cannot be diagnosed on a confirmed basis. This either causes repeated admission or deaths due to a lack of proper management.

Aims and Objectives: This current study intends to find out the efficacy of quantifying high sensitivity cardiac Troponin I (hs-cTnI) to predict AMI.

Materials and Methods: This current prospective study is of cohort type which has obtained medical records of the patients including the level of hs-cTnI at presentation. After 6 months of presentation, the follow-up study was conducted to predict the efficacy of having AMI. The study also analyzed several risk factors and other baseline characteristics with the occurrence of AMI. The statistical analysis was conducted to highlight the significance.

Results: The study has found that the patients had shown significant differences in ECG characteristics, creatinine clearance and few medication history like ACE inhibitor or ARB, aspirin and statin ($p<0.05$) when patients with AMI and Non-AMI were compared. It was shown that the concentration of hs-cTnI is found to be significantly more ($p<0.05$) at the beginning of the study in those patients who finally had AMI during the follow-up study, as compared to the patients who did not show AMI during the follow-up study.

Conclusion: The study concluded that the efficacy of using hs-cTnI in the clinical setting can be considered to be the guideline of AMI diagnosis in the emergency department. The study also highlighted the significant characteristics which can be used as the predictor of AMI in the future.

Keywords: AMI, cardiactroponin, troponin, troponin T, troponin I, cardiovascular

Introduction

Chest pain is a prevalent reason for hospital admission all over the world and is a significant drain on medical resources [1]. Every year, about 1 million people in the UK visit emergency rooms because of chest pain [2]. Even though many of these patients might be eligible for immediate discharge from the emergency room [3], current care pathways are unable to rule out myocardial infarction at presentation, and guidelines advise serial troponin tests necessitating hospital admission in the majority of patients [4]. This method results in a high number of possibly needless hospital admissions because the majority of these patients don't have myocardial infarction [2,5,6].

Each year, almost 20 million individuals in America and Europe visit emergency rooms (EDs) with symptoms that could indicate a myocardial infarction (MI) [7]. It can be challenging to diagnose MI in patients because they can exhibit a wide range of symptoms, including chest discomfort, shortness of breath, weakness, nausea, and exhaustion [8,9]. Although they can help with treatment choices, demographics, conventional cardiac risk factors, symptoms of chest pain, and physical examination are insufficient on their own to distinguish between those with and without MI [10]. Although the majority of patients lack a definite diagnosis, certain patients may have concrete proof [10].

The medical and financial necessity of rapid rule-out is highlighted by the fact that only a minority of MI cases will be discovered, with the majority of cases having symptoms brought on by non-cardiac and frequently benign disorders like pleuritis, gastroesophageal reflux, or musculoskeletal pain (9,10). Additionally, an early MI diagnosis is essential for the quick start of an evidence-based course of treatment. Missed MI has significant medical and legal ramifications because it is the most expensive single diagnosis in terms of money spent and the third most common cause of malpractice claims made against emergency physicians [11].

In the emergency room, clinical evaluation, 12-lead electrocardiography, and cardiac troponin are crucial diagnostic tests for the early diagnosis of acute coronary syndrome. The primary diagnostic tool for acute coronary syndrome is now cardiac troponin levels [12]. Early risk classification for acute myocardial infarction (AMI) using the 0-hour/1-hour (0-/1-h) algorithm with high-sensitivity cardiac troponin (hs-cTn), which has been recommended as class A and evidence level B, was endorsed by the European Society of Cardiology (ESC) in 2015 [12]. Only Abbott Architect hs-cTnI, Siemens Vista hs-cTnI, and Roche Elecsys hs-cTnT are available as hs-cTn assay systems.

The definition of a high-sensitivity system has changed over the last 20 years, and an updated version was released in 2018 [13]. The troponin assay system must be improved for this upgrade. In response, the International Federation of Clinical Chemistry (IFCC) established the following criteria for what constitutes a high-sensitivity assay: (1) the 99th percentile for hs-cTn assays must be established in a healthy population of at least 300 male and female subjects; (2) the 99th percentile for hs-cTn assays must be measured with an analytical imprecision of 10% of the coefficient of variation (CV); and (3) the assays must measure cardiac troponin Therefore, a novel assay system should fulfil the recommendation of IFCC [12, 13] for the detection of cardiac troponin. Recently, the Japanese company Fujirebio Inc. developed Lumipulse Presto hs Troponin I, which satisfies the IFCC's requirements.

Accurate detection of troponin in the majority of healthy individuals is made possible by high-sensitivity cardiac troponin tests with good precision at very low concentrations [14]. Through the creation of secure and efficient methods to

rule out myocardial infarction in the emergency room, these assays potentially revolutionize the evaluation of patients who are experiencing chest discomfort. 9 Some studies contend that patients with undetectable troponin concentrations are at low risk [16], even though worldwide recommendations [15] advise using cardiac troponin concentrations above the 99th centile for the diagnosis of myocardial infarction.

We aimed to promote a threshold that would distinguish individuals with the suspected acute coronary syndrome (myocardial infarction) at presentation who are at low risk of myocardial infarction and may be eligible for rapid release in this study using a high-sensitivity cardiac troponin I assay.

Materials and Methods

Study Design

This current prospective study is of cohort type which was conducted during the period of seven months. Medical records of the patients were obtained from the concerned hospital. The history and details of the patients like impressions of the physical examinations were taken. Laboratory testing was done including clinical high sensitive cardiac Troponin (hs-cTnI and hs-cTnT) concentrations, radiological examination, electrocardiogram, echocardiography, coronary angiography and cardiac MRI. Study specific characteristics were assessed which include chest pain characteristics, and quantification of hs-cTnI and hs-cTnT. The follow-up study was carried out based on the outcome of the patients whether they had AMI. If AMI is positive in the follow-up study, then, the particular patient is marked as AMI while patients who were not found with AMI, were classified as Non-AMI. The latter includes patients of unstable angina, cardiac disease without coronary artery disease, non-cardiac disease and unknown causes. Finally, the laboratory result of Troponin I and other findings was analyzed with respect to the outcome of the patients during the follow-up study.

Inclusion and Exclusion Criteria

The patients who were suspected of AMI based on radiological examination, laboratory examination, cardiac exercise test and the pattern of morphology in coronary angiography, were included. This suspicion was confirmed by 2 cardiologists and 1 radiologist separately. The patients who come under the geriatric population (age more than 55 years old) and gave consent to share the hospital records, were included. The patients who had shown ST-elevation MI were excluded and those who did not cooperate till the end of the study were also excluded. The study authors initially considered 100 patients and after applying inclusion and exclusion criteria, the study finally considered 70 patients.

Ethical Approval

The study made each of the patients understand the whole process and also obtained consent from each of them for sharing the information, and results, and cooperate with the tests and follow-up study. The whole study was conducted according to the Declaration of Helsinki (World Medical Association).

Statistical Analysis

The study has effectively used SPSS 25 and excel software for statistical analysis and other calculations, respectively. Continuous variables were expressed as mean±standard deviation. The study used Mann-Whitney U-test for analyzing the baseline characteristics and while ANOVA was used for the analysis of Troponin levels in AMI and non-AMI conditions. Chi-square was used for categorical variables. The level of significance was considered to be $\alpha = 0.05$.

Results

The study found the baseline characteristics of the study population and analyzed them separately based on the outcome of the

patients during follow-up, namely, diagnosed AMI or Non-AMI.

The study found that there is a statistically significant difference in many of the characteristics between the two groups of patients. Table 1 shows the detailed finding.

Table 1: The baseline characteristics of the patients in this study

Characteristic	Diagnosed AMI (n=40)	Confirmed Non-AMI (n=30)	*p*-value
Age	69.25±3.66	59.12±3.22	$p<0.05$
Males, n (%)	33	25	$p>0.05$
Females, n (%)	7	5	$p>0.05$
Body Mass Index	27.87±1.99	25.18±0.95	$p>0.05$
Risk Factors			
Diabetes, n (%)	6 (15)	2 (6.67)	$p<0.05$
Currently smoking, n (%)	25 (62.5)	12 (40)	$p>0.05$
Hypercholesterolemia n (%)	20 (50)	8 (26.6)	$p<0.05$
Hypertension, n (%)	34 (85)	12 (40)	$p<0.05$
History			
Smoking, n (%)	29 (72.5)	15 (50)	$p>0.05$
Past MI, n (%)	14 (35)	9 (30)	$p<0.05$
Past revascularization, n (%)	21 (52.5)	12 (40)	$p<0.05$
Peripheral Artery Disease, n (%)	15 (37.5)	9 (30)	$p<0.05$
Past stroke, n (%)	9 (22.5)	2 (6.67)	$p<0.05$

Again, the patients were found to have significant differences of ECG characteristics, creatinine clearance and few medication history like ACE inhibitors or ARB, aspirin and statin ($p<0.05$), between the two groups.

Table 2: The ECG characteristics, Laboratory findings and drug history of the patients in this study

ECG characteristics			
ECG characteristics	**Diagnosed AMI (n=40)**	**Confirmed Non-AMI (n=30)**	***p*-value**
ST- depression, n (%)	7 (23.34)	8 (26.67)	$p<0.05$
T-wave inversion, n (%)	3 (10)	1 (3.34)	$p<0.05$
Insignificant abnormalities, n (%)	21 (70)	16 (53.34)	$p<0.05$
Left Bundle Branch Block (LBBB), n (%)	8 (26.67)	7 (23.34)	$p<0.05$
Laboratory Findings			
Laboratory findings	**Diagnosed AMI (n=40)**	**Confirmed Non-AMI (n=30)**	***p*-value**
Creatinine clearance (mL/min/m^2)	75±2.3	87.5±3.5	$p<0.05$
Medication History			
Medication History	**Diagnosed AMI (n=40)**	**Confirmed Non-AMI (n=30)**	***p*-value**
Vitamin K antagonists, n (%)	3 (10)	2 (6.67)	$p>0.05$

Beta-blockers, n (%)	7 (17.5)	5 (16.67)	$p>0.05$
ACE inhibitor or ARB, n (%)	15 (37.5)	12 (40)	$p<0.05$
Calcium antagonists, n (%)	9 (22.5)	11 (36.67)	$p>0.05$
Nitrates, n (%)	12 (30)	13 (43.37)	$p>0.05$
Aspirin, n (%)	20 (50)	16 (53.37)	$p<0.05$
Statins, n (%)	18 (45)	16 (53.37)	$p<0.05$

The main objective of the study was to evaluate the efficiency of predicting AMI by quantification of hs-cTnI. It was shown that the concentration of hs-cTnI is found to be significantly more ($p<0.05$) at the beginning of the study in those patients who finally had AMI during the follow-up study, as compared to the patients who did not show AMI during the follow-up study. Figure 1 shows the boxplot diagram of quantification of hs-cTnI at the beginning of the study for each group of patients.

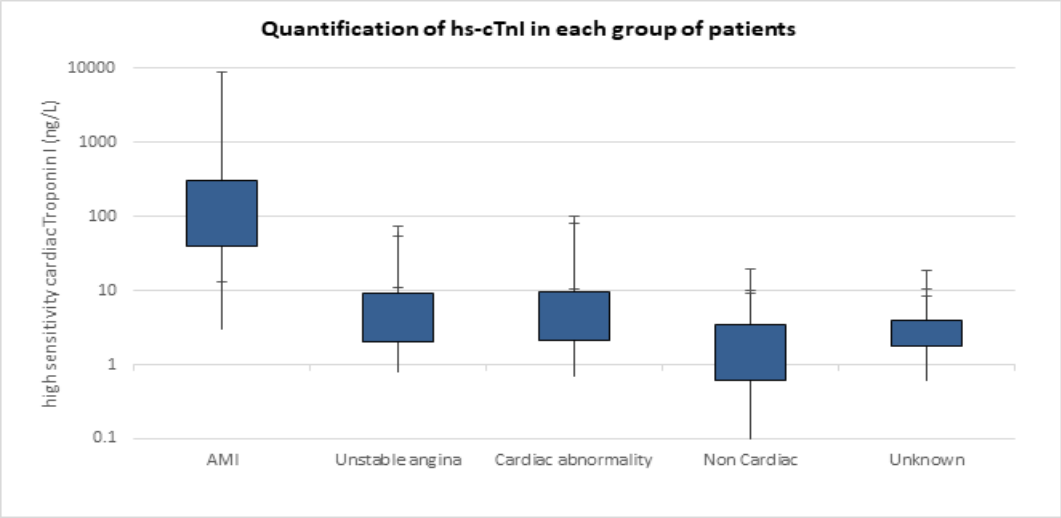

Figure 1: Concentration of high sensitivity cardiac Troponin I during initial study

Discussion

According to Shah et al study, [16] which involved over 6000 patients with the suspected acute coronary syndrome, we have established a cardiac troponin threshold at the presentation that identifies nearly two-thirds of patients as having a very low risk of myocardial infarction or cardiac death and who may be capable of being safely discharged from the emergency room. The use of this strategy would decrease needless hospital admissions and have significant advantages for both patients and healthcare professionals.

We defined a negative predictive value of at least 99.5% as a troponin I concentration less than 5ng/L. Nearly two-thirds of patients with suspected acute coronary syndrome may have been released with relatively few cardiac events if they had reached this criterion. The number of patients discharged straight from the emergency room could double in the application of this criteria. Lower thresholds would identify fewer individuals who were eligible for release while doing nothing to increase the negative predictive value. The number of adverse events would double if the threshold was raised to fewer than 6ng/L, but it would also identify an additional 6% of patients who may be discharged. Additionally, we have evaluated this threshold both internally and externally, and a troponin concentration of less than 5ng/L appears to be the ideal threshold for study populations.

To ensure reliable case ascertainment in their analysis, we evaluated the final diagnosis using a high sensitivity assay. Our investigation was the first to use a high-sensitivity cardiac troponin I assay, which has better precision and repeatability at low concentrations and the suggested threshold, in contrast to other studies of the cardiac troponin T assay. For this method to be used in clinical practice, it must be applied consistently across sites, analyzers, and reagent batches. Additionally, two to three times as many low-risk patients are identified using cardiac troponin I at our threshold as opposed to using earlier methods [17, 18].

Shiozaki et al reported study [12] examined whether the LumipulsePresto hs-cTnI novel hs-cTnI test system is useful for the diagnosis of AMI on admission and risk stratification using the 0-/1-h algorithm. This global multicenter cohort was created prospectively for AMI utilizing the widely accepted hs-cTnT test method, which has been approved by the US Food and Drug Administration. The LumipulsePresto hs-cTnI met the IFCC requirements for a high-sensitivity system. In inference, the hs-cTnI assay system from LumipulsePresto offers similar capabilities to the hs-cTnT system. In conclusion, the hs-cTnI assay system from LumipulsePresto offers similar capabilities to the hs-cTnT system.

This extensive multicenter study was conducted to evaluate the clinical utility and diagnostic performance of the hscTnI-VITROS assay for the early detection of AMI. In conclusion, the hscTnI-VITROS assay for AMI has a high diagnostic accuracy that is at least on par with that of other recently developed and well-established hs-cTnT/I assays. The majority of patients presenting with chest pain to the ED can be triaged toward safe rule-out and accurate rule-in of AMI using a straightforward method that takes into account hs-cTnIVITROS concentrations at presentation and absolute changes during the first 1 h.

Acute myocardial infarction (AMI) can be ruled out in patients coming to the emergency room using a baseline high sensitivity cardiac troponin (hs-cTnI) result below the limit of quantification, according to research by Cook et al (ED). 46 (8.1%) of the 567 people had AMI, which was diagnosed in these individuals. The presenting hs-cTnI findings for 202 (40.9%) patients were below <4.0 ng/L. None of the patients with baseline hs-cTnI <4.0ng/L experienced an AMI, resulting in a favourable prognosis with a negative predictive value of 100.0 % and a sensitivity of 100% (no AMIs or cardiac-related deaths at 30 days). In this single-center ED investigation, 40.9 % of all patients presenting with any symptoms suggestive of AMI had their AMI effectively ruled out by a baseline presenting a new hs-cTnI value of <4.0ng/L.

According to Kavasak et al study [20], hs-cTnI and clinical chemistry score (CCS) are compared to predict myocardial infarction in emergency rooms. Using the CCS split instead of the established cutoffs for hs-cTnI alone provides better sensitivity and specificity with low and high mortality rates. 5974 patients were included in their cohort analysis, with a death rate of 1 year of 17.2% (95%CI). The mortality rate was considerably lower for patients with CCS1 (95%CI) compared to patients with hs-cTnI 5ng/L (95%CI) at one year. [21] In contrast to the hs-cTnI 5ng/L cutoff sensitivity of 88.4%, a CCS 1 produced a sensitivity of 99.2% (95 % CI). With no change in fatality rates (37.4% vs 36.3%), a CCS of 5 also produced a greater specificity of 88.5 % (95 % CI) compared to hs-cTnI >26ng/L (83.9 %; 95% CI). This pattern persisted at the 3-month and 5-year mortality rates.

It was established that the Troponin-I assay is much superior to the Troponin assay, as per all previously reported studies. This test can be used to control myocardial infarction in patients in emergency rooms and normal people. Low and high-risk death rates can

be easily predicted from the emergency department population concerning good clinical research with the aid of the CCS cut-off.

Conclusion

The study has concluded that the diagnostic efficiency of hs-cTnI assay was statistically significant for predicting the probability of AMI and hence, can be used in the clinical setting. The study also found several baseline characteristics including risk factors, patient's history, ECG characteristics, laboratory findings, and medication history, to be significant between AMI and Non-AMI patients. The authors suggest that there should more studies be conducted in analyzing the significance of hs-cTnI in the prediction of AMI among the varied population.

The conclusion of this study would benefit the clinical diagnostic of AMI and would contribute to the management of Acute Myocardial Infarction.

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