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Original Research Paper

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EVALUATION OF RAPID D DIMER TEST IN CONJUNCTION WITH CKMB FOR TRIAGING THE PATIENTS WITH ACUTE CORONARY SYNDROME

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ABSTRACT

Background: In ER, one of the most common-critical conditions requiring rapid assessment is Acute Coronary Syndrome. Triage should be ideally done to minimize time to treatment for ACS. This study was done to determine the role of rapid D-dimer test in conjunction with CKMB in the diagnosis of Acute Myocardial Infarction in patients with Acute Coronary Syndrome. **Methods:** Patients with acute coronary syndrome who visited our ER were taken as the subjects of this cross-sectional investigation. This study comprised a total of 50 patients. At the time of admission, the entire study group underwent a routine 12-lead ECG as well as D-dimer and CKMB tests. Based on the patient's history of chest pain, ECG results, and CKMB, the patients were divided into two groups: MI patients, and unstable angina (UA) patients. Using SPSS version 17, the chi-square test and Pearson correlation test were performed. Receiver operating characteristic (ROC) curve analysis was used to assess the cut-off point of D-dimer for MI diagnosis. **Results:** A total of 50 individuals were evaluated, with a mean age of 55.6 11.75 years. Of these, 35 patients had MI, and 15 had UA. Patients with MI had proportionately greater D-dimer and CKMB levels than patients with UA (P = 0.001). A D-dimer value of more than 500 ng/ml was strongly linked to MI. D-dimer had a 510 ng/mL cut-off point that had a sensitivity of 90% and a specificity of 70% for the diagnosis of MI. The sensitivity was increased to 98.4% by using both CKMB and D-dimer, which helps in early triage of patients. **Conclusions:** This study demonstrates that, with high sensitivity and moderately good specificity, D-dimer and CKMB levels can be used to differentiate MI from UA in individuals with ACS. D-Dimer is a sign of active thrombus lysis and formation. When utilised in conjunction with CKMB for the early identification of acute coronary syndrome manifesting as chest discomfort, it offers a significant added benefit. Additionally, it offers independent data to supplement the conventional myocardial infarction assessment. Hence, clinical diagnostic models for the identification of MI in the ER can include D-Dimer.

KEYWORDS : Myocardial infarction; Unstable angina; Acute coronary syndrome; D-dimer; CKMB-creatine kinase iso-enzyme MB; Troponin.

INTRODUCTION

Acute coronary syndrome (ACS) is one of the important cause of death worldwide and also the major cause of morbidity and mortality in India. So, there has been an increasing need for rapid diagnosis and emergency interventional procedures like Thrombolysis, PCI and CABG, as there has been an increasing incidence of complex cardiovascular lesions necessitating CCU admissions[3]. The diagnostic criteria for Acute Coronary syndrome is based on clinical history, ECG and serum cardiac bio-markers like CKMB and Troponin. Due to the rise in cardiac enzymes 3–4 hours after the start of symptoms, these criteria, however, have limited diagnostic utility in the early stages of MI[4]. Therefore, these markers should be evaluated consecutively in most centres. And in this instance, there is uncertainty surrounding their use in the quick triage of MI patients. Since many patients won't experience the typical anginal chest pain, and other patients may present in the emergency room with an initial non-diagnostic ECG. Previous studies reported approximately 2–4% of patients with chest pain presentation discharged from the ER was later diagnosed to have MI within 24 h. Hence, there is a need for more accurate diagnostic tool for MI in the ER. Searching a biomarker that indicates early stage of acute coronary syndrome is a reasonable way to improve the diagnostic efficiency. CKMB and Cardiac troponin becomes elevated approximately 4h to 6 h after the onset of MI and peaks around 24 h and 24-48 hrs respectively[5,6]. At present they are the most established biomarkers for MI.

The major drawback of these tests, despite its excellent sensitivity and specificity, is its delayed response time, as CKMB and Troponin levels may not be measurable for the first four to six hours following the initiation of myocardial cell injury. CKMB and cTnI test findings are frequently normal in MI patients when they are admitted to the emergency room. Measurements must be taken repeatedly, with a 6–9-hour gap between each measurement, which significantly lowers the accuracy of MI diagnosis. On the other hand, as coronary artery thrombosis is a precursor to MI, D-dimer may be a useful marker for early identification of MI. Previous studies have demonstrated that the elevation of several markers of thrombin generation and clot lysis are associated with MI and proved to increase the diagnostic sensitivity for MI[7]. However, little is known of their potential role in the triage and risk stratification of patients with ACS in the ER. Therefore the aim of this study is (1) to evaluate the diagnostic value of serum D-dimer concentration obtained from patients with acute MI upon ER admission[1], and (2) to evaluate the clinical role of combined CKMB and D-dimer tests in the diagnosis of MI.

METHODS

Research design and setting

This cross-sectional study was carried out in the emergency room of Raja Muthiah Medical College and Hospital in Chidambaram, Tamil Nadu, India, from November 2020 to October 2022.

Inclusion Criteria

were, Patients of both gender presenting with new onset Typical chest pain (sub-sternal chest discomfort) lasting for >20minutes, provoked by exertion and relieved by rest or nitro-glycerine, with age >20years, Onset of symptoms within 12 hours at the time of presentation.

Exclusion Criteria

were, patients admitted >12 h after the onset of chest pain, age <20 years, patients with ECGs showing evidence of LBBB (Left bundle branch block), RBBB (Right bundle branch block), LVH (Left ventricular hypertrophy) and old myocardial infarction, patients who had undergone thrombolysis,

coronary angiography, coronary artery bypass grafting, angioplasty or open-heart surgery, patients admitted with other causes of a raised D-dimer level (e.g. upper gastrointestinal bleeding, acute intestinal ischemia, ischemic and haemorrhagic stroke, deep vein thrombosis, pulmonary thrombo-embolism, sepsis, Disseminated intravascular coagulation (DIC), Malignancy, liver illness, post-surgical care, trauma, pregnancy, snake venom poisoning), use of cytotoxic medications, beta blockers, nitrate and aspirin, antiplatelets, anticoagulants including warfarin and heparin, and individuals with CORADS-4 and above who tested positive for COVID-19 infection using RT-PCR/CT-THORAX.

Sampling

Sample size and method

Three groups of patients - ST-Elevation MI, Non-ST-Elevation MI, and Unstable Angina - were studied using purposeful random sampling. Based on a 0.05 alpha and a 20% beta, the sample size was estimated.

Data collection

The patients who presented to the emergency room (ER) with characteristic chest pain for ACS within 12 hours of the onset of the pain and who also underwent physical examination were included in the study. Other information, such as the subject's age, sex, location, onset, quality, and radiation of their pain as well as any accompanying symptoms and ACS risk factors such diabetes, hypertension, and dyslipidemia were gathered. All the study population underwent ECG and blood was drawn to determine the levels of serum D dimer, CKMB, and troponin at the time of presentation. Based on the results of the ECG, the levels of CKMB and troponin, the patients were then divided into three groups: ST-Elevation MI, non-ST-Elevation MI and Unstable angina.

Measurement tool

Prior to administering heparin and at the time of ER presentation, a 2ml serum sample was collected to assess D-dimer levels. Enzyme-linked immunosorbent assay was used to determine the serum D-dimer level (ELISA).

Diagnosis of MI

According to ECG changes and cardiac biomarkers like CKMB and Troponin, patients with the diagnosis of AMI were divided into two groups: STEMI and non-STEMI. If there was no MI, other trial participants were assigned to the UA group.

Ethical consideration

This was approved by the Ethical Committee of Rajah Muthiah Medical College and Hospital, Chidambaram. The patients involved in the study were informed about the study and written consent was obtained.

Statistical analysis

SPSS 17.0 for Windows was used to statistically analyse the demographic and paraclinical data that was collected from the patients. p-value of 0.05 was considered significant, and data were presented as mean ±SD. Initial analysis focused on the data distribution. The homogeneity of the comparison groups (MI and UA) was next investigated with regard to age, sex, and risk factors for diabetes, hypertension, and dyslipidemia. ANOVA test was used to compare the data across the three groups of STEMI, NSTEMI, and UA, as well as to compare quantitative data (serum D-dimer level and CKMB) between the MI and UA groups. The cut-off threshold for D-dimer in diagnosis of MI was established using the ROC curve. Using the MedCalc 15 programme, the sensitivity, specificity, and positive and negative predictive values of D-dimer in the diagnosis of MI were determined.

RESULTS

Baseline characteristics

50 patients were enrolled in the 24-month study, and nobody was turned away. The patients included in the study have a mean age of 55.2 11.5 years. Age, gender, diabetes, hypertension, dyslipidemia, smoking, and alcoholism were not substantially different in the three groups of patients with STEMI (n = 24), NSTEMI (n = 11), and UA (n = 15). (Table 1).

Table 1: Univariate comparison of clinical characteristics between STEMI, NSTEMI and Unstable angina patients

Characteristics	STEMI (n=24)	NSTEMI (n=11)	UA (n=15)	p-value
Age (mean±SD)	57±12.4	53±11.6	50±8.3	0.712
Sex Male, n(%) Female, n(%)	 17(71%) 7(29%)	 5(46%) 6(54%)	 6(40%) 9(60%)	0.123
Diabetes Mellitus, n(%)	15(62.5%)	7(63.6%)	9(60%)	0.980
Hypertension, n(%)	13(54.2%)	7(63.6%)	10(66.7%)	0.712
Dyslipidemia, n(%)	5(20.8%)	2(18.2%)	5(33.3%)	0.591
Smoking, n(%)	13(54.2%)	1(9.1%)	2(13.3%)	0.05*
Alcoholism, n(%)	7(29.2%)	0	2(13.3%)	0.09
CKMB (Mean±SD)	75.5±41.5	64.5±28.2	23.3±10.7	0.001*
Troponin (Mean±SD)	1.98±0.28	1.09±0.3	0.02±0.01	0.001*
D Dimer (Mean±SD)	892±234.5	714±152	554.9±186	0.001*

CKMB and D-dimer level

All patients had an average CKMB of 55 26.8 IU/L. At the time of admission, the serum CKMB level in the STEMI group was higher (75.5 41.5 IU/L), followed by NSTEMI (64.5 28.2 IU/L), and UA (23.3 10.7 IU/L) (P = 0.001). Additionally, all patients had a mean serum D-dimer level of 720.3 190.8 ng/ml, with STEMI patients having a mean of 892 234.5 ng/ml, NSTEMI patients having a mean of 714 152 ng/ml, and UA patients having a mean of 554.9 186 ng/ml (P = 0.001). (Table 1)

Table 2: Comparing Serum Level of CKMB, D-Dimer and Troponin in Three Groups of Patients With Myocardial Infarction With ST Segment Elevation, Without ST Segment Elevation, and Unstable Angina

Parameter	Unstable Angina N=15	STEMI N=24	NSTEMI N=11	P value
	Mean ± SD	Mean ± SD	Mean ± SD	
CKMB (IU/L)	23.3 ± 10.7	75.5 ± 41.5	64.5 ± 28.2	0.001*
TROPONIN	0.02 ± 0.01	1.98 ± 0.28	1.09 ± 0.3	0.001*
D Dimer (ng/ml)	554.9 ± 186	892 ± 234.5	714 ± 152	0001*

Subgroup analysis

Furthermore, this study's findings revealed that, the three groups of STEMI, NSTEMI, and UA are significantly different in terms of CKMB levels (P = 0.001) and D-dimer levels (P = 0.001), based on ANOVA. (Table 2)

D-dimer and correlated factors

According to the results of the chi-square test and Pearson correlation analysis, there is a moderate to good link between D-dimer and smoking (P = 0.05) (Table 3), the duration of chest discomfort (P = 0.03) (Table 4), and CKMB (P = 0.001; Table 5).

Table 3: Comparison of Smoking vs D dimer

	Normal	Abnormal	p P value
	n (%)	n (%)	
Yes	5 (83.3)	10 (23)	0.05*
No	1 (16.7)	34 (77)	
Total	6	44	

Table 4: Comparison of Duration of chest pain VS D dimer

	Normal <500	Abnormal		P value
		500-999	>999	
	n (%)	n (%)	n (%)	
0-3 hrs	1 (16.7)	2 (5)	2 (50)	0.03*
3-6 hrs	2 (33.3)	27 (67.5)	1 (25)	
>6hrs	3 (50)	11 (27.5)	1 (25)	
Total	6	40	4	

Table 5: Correlation of CK-MB with D dimer

	D dimer	
	Pearson corrleation	P value
CK-MB	0.624	0.001*

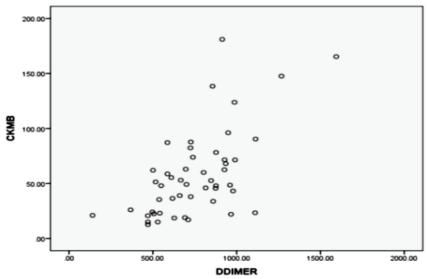

Figure 1: Scatter plot showing the correlation between serum levels of d-dimer and CKMB among patients with MI and non-MI on ED admission

Diagnostic value of D-dimer

The D-dimer serum level cut-off point with the best sensitivity and specificity for the diagnosis of MI was determined using the ROC curve. The optimal D-dimer cut-off point for MI is 510 ng/ml, according to the results of the ROC curve. In patients who present with ACS, this point's sensitivity and specificity in distinguishing MI from UA are 90% and 70%, respectively. The early triaging of patients is made possible by the use of both CKMB and D-dimer, which increased sensitivity to 98.4%.

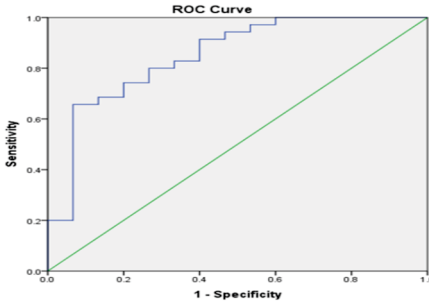

Figure 2: Receiver operating characteristic curve on the diagnostic value of D-dimer in diagnosis of acute myocardial infarction

Area Under the Curve				
Test Result Variable(s): DDIMER				
Area	Std. Errora	Asymptotic Sig.b	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.850	.062	.000	.728	.971

Table 6: Operative Characteristics of D-Dimer for the Diagnosis of Myocardial Infarction

Discriminate level (ng/ml)	Sensitivity (%)	Specificity (%)
484	100	80
510	90	70
540	80	72

DISCUSSION

Only a small number of studies have been conducted to establish the significance of D-dimer in the diagnosis of MI[9]; it was previously employed as a marker of venous thromboembolism and aortic dissection. Our study evaluated the role of the rapid D-dimer test in conjunction with CKMB for triaging patients with acute coronary syndrome, and the findings demonstrated that D-dimer can also be used as a diagnostic marker in conjunction with CKMB for the early diagnosis of acute myocardial infarction in patients with acute coronary syndrome with the appropriate sensitivity and specificity. CKMB and Troponin measurements are currently regarded as two of the most accurate markers for determining myocardial injury. However, a rise in their serum level 3 to 4 hours after the start of symptoms is their main disadvantage. Therefore, it is important to review these markers repeatedly. And in such a situation, their use in the quick triage of MI patients is unclear. Additionally, more haematological biomarkers are still thought to be necessary for a quicker detection of coronary artery thrombosis, which is a characteristic of ACS[4]. One of these is the D-dimer, which is created when plasmin breaks down a fibrin clot at the site of an injury. This process symbolises the production of active thrombosis and subsequent lysis. Because D-dimer is produced more quickly than other markers during ACS pathophysiology, it is anticipated that D-dimer levels will rise in acute ischemic episodes earlier than other cardiac biomarkers. Previous research has demonstrated a clear correlation between D-dimer levels and the development or recurrence of cardiovascular disorders. As a result, people with D-dimer levels in the higher one-third of the range are 70% more likely to develop coronary artery disease. According to research by Baya-Genis et al, patients with MI and UA have higher plasma levels of D-dimer than patients with ischemic event-free status. Additionally, individuals with MI had serum D-dimer levels that were greater than those with UA[10]. This study also showed that D-dimer levels larger than 500 ng/mL, together with ECG results and patient history, can enhance the diagnosis of MI (sensitivity increases from 73% to 92%). The optimum cut-off point in our investigation, which had a sensitivity of 90% and a specificity of 70%, was attained in discriminating MI from UA at 510 ng/ml. Additionally, our study's results show that reducing the cut-off point to 484 ng/mL increased D-dimer sensitivity to 100% and raising it to 540 ng/mL increased specificity of the test by up to 72%. (Table 6). When comparing the results of this investigation with the Bayes-Genis study, it appears that a serum level of 500–550 ng/mL or greater can be used as a valid cut-off point to distinguish MI from UA. Our study's major goal is to identify patients with ACS who have MI or non-MI so that the most effective cardiovascular therapies can be started as soon as possible. However, some research has looked at the diagnostic use of D-dimer in predicting ACS from pains of non-cardiac origin.

In Orak et al's study, the D-dimer sensitivity and specificity in the differentiating ACS from non-ACS was specified as 95.4% and 83.7%, respectively. D-dimer hasn't been reported to have a high positive predictive value, nevertheless, in any of these studies. If a group of normal subjects were enrolled in this study, we could evaluate the diagnostic power of D-dimer in differentiating ACS from non-ACS events.

CONCLUSION

According to the study results, measuring the serum D-dimer level may be a useful way to distinguish STEMI and NSTEMI from UA in patients with ACS. This marker has a high sensitivity and a moderately good specificity. It appears that D-dimer in combination with CKMB can be used to appropriately triage patients and quickly refer them to cardiologists for more specialised therapies. This is especially true given the greater sensitivity of this marker and its availability in most ERs. This study recommends using CKMB in addition to D-dimer measurements to increase the diagnostic accuracy of D-dimer.

Conflict of Interest

The author declare that there is no conflict of interest regarding the publication of this paper.

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