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Diagnostic Accuracy of D-Dimers in Patients with Non-ST-Segment Elevation Myocardial Infarction Using Troponin-I as the Gold Standard.

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Abstract

Background: Non-ST segment elevation myocardial infarction (NSTEMI) is defined as a clinical syndrome characterized by symptoms of myocardial ischemia and the release of biomarkers of myocardial necrosis in the absence of electrocardiographic ST-segment elevation. Biomarkers play a pivotal role in both the early diagnosis and prognosis of myocardial infarction. Among them, D-dimer has been proposed as a potential diagnostic marker. This study aimed to determine the diagnostic accuracy of D-dimer in patients with NSTEMI, using Troponin-I as the gold standard.

Methodology: Following approval from the College of Physicians and Surgeons Pakistan (CPSP), a cross-sectional validation study was conducted in the Department of Cardiology, Hayatabad Medical Complex, Peshawar, from March 7 to September 7, 2019. Patients aged 18 to 80 years presenting with suspected NSTEMI were enrolled after providing written informed consent. Each participant underwent a detailed history, physical examination, and 12-lead electrocardiography (ECG). Troponin-I was measured prior to administration of anticoagulant therapy in the emergency department, while D-dimer was tested concurrently. Diagnostic accuracy was assessed using Troponin-I as the reference standard.

Results: A total of 275 patients were included, of whom 69.81% were male. The mean age was 62 ± 10.79 years. The majority of patients were non-smokers (81.45%), non-diabetic (86.55%), and normotensive (86.55%). When compared with Troponin-I, D-dimer showed a sensitivity of 38.68%, specificity of 47.38%, positive predictive value (PPV) of 14.91%, negative predictive value (NPV) of 76.36%, and an overall diagnostic accuracy of 45.64%.

Conclusion: Although D-dimer alone demonstrated limited sensitivity and specificity, its relatively high negative predictive value suggests potential utility as a supportive biomarker in ruling out NSTEMI. Incorporating D-dimer testing into the routine chest pain unit protocol, alongside established biomarkers such as Troponin-I, may aid in early risk stratification and clinical decision-making.

Keywords

Myocardial Infarction, Non-ST Elevated, D-dimer, Troponin I, Biomarkers, Diagnostic Accuracy.

Introduction

Acute coronary syndrome (ACS) encompasses a spectrum of clinical conditions, including ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UA)[1]. STEMI is characterized by symptoms of myocardial ischemia, persistent electrocardiographic ST-segment elevations, and subsequent release of biomarkers of myocardial necrosis[2]. In contrast, NSTEMI is distinguished from UA by the rise of cardiac biomarkers, which are absent in UA[3]. Approximately one in four patients presenting to the emergency department with ACS are diagnosed with NSTEMI[4].

Troponin-I has emerged as the most reliable biomarker for diagnosing myocardial infarction and is widely regarded as the gold standard[5]. The underlying pathophysiology of myocardial infarction involves atherosclerotic plaque rupture or erosion with superimposed intracoronary thrombosis, leading to myocardial cell necrosis and release of troponins into the bloodstream[6]. Simultaneously, activation of the coagulation and fibrinolytic systems results in plasmin-mediated degradation of fibrin clots, releasing D-dimers into circulation[7].

Evidence suggests that D-dimers may serve as an early diagnostic marker for myocardial infarction in patients with suspected ACS[8]. Beyond their diagnostic role, D-dimers have also demonstrated prognostic value in patients with myocardial infarction[9]. In one study, D-dimers showed a prevalence of 15.3% for NSTEMI, with reported sensitivity and specificity of 58% and 62%, respectively[10].

Despite these findings, no local study has yet been conducted in Peshawar, Pakistan, to evaluate the diagnostic utility of D-dimers in patients with NSTEMI. Generating such local evidence is crucial to guide clinical decision-making and optimize the use of diagnostic resources. This study, therefore, aimed to assess the diagnostic accuracy of D-dimers in comparison with Troponin-I as the gold standard.

The results are expected to strengthen the existing body of knowledge and provide locally relevant evidence for clinicians, researchers, and healthcare policymakers.

Methodology

Study Design

A descriptive cross-sectional validation study was conducted over a six-month period, from March 7 to September 7, 2019. The study was designed to assess the diagnostic accuracy of D-dimer testing for non-ST elevation myocardial infarction (NSTEMI) in comparison with troponin-I levels.

Ethics

Ethical clearance was obtained from the Research Ethics Committee of Hayatabad Medical Complex (HMC), Peshawar, prior to the initiation of the study. Written informed consent was taken from all participants. Patient confidentiality was strictly maintained, and all procedures were carried out in accordance with the principles outlined in the Declaration of Helsinki.

Setting

The study was conducted in the Department of Cardiology at Hayatabad Medical Complex, a tertiary care hospital in Peshawar, Pakistan. This hospital caters to a large population and receives a significant number of patients with suspected acute coronary syndromes, making it an appropriate setting for this study.

Participants

All patients aged between 18 and 80 years who presented to the emergency department with a possible NSTEMI were evaluated for inclusion. Patients were excluded if they had conditions known to elevate D-dimer levels independent of myocardial infarction, including upper gastrointestinal bleeding, acute intestinal ischemia, ischemic or hemorrhagic stroke, deep vein thrombosis, sepsis, and malignancy. Those who had received anticoagulant therapy such as heparin, warfarin, or novel oral anticoagulants prior to blood sampling were also excluded from the study.

Variables

The main outcome variable was the diagnosis of NSTEMI, established using troponin-I as the gold standard. The predictor variable was D-dimer level, measured at the time of presentation. Additional demographic and clinical variables such as age, sex, comorbidities, and ECG findings were also recorded.

Data Sources and Measurement

Each participant underwent a detailed medical history and physical examination on presentation. A standard 12-lead electrocardiogram (ECG) was performed. Troponin-I was measured before the administration of anticoagulants and served as the reference diagnostic test for NSTEMI. D-dimer levels were measured simultaneously using standardized laboratory procedures, and interpretation was made in accordance with operational definitions.

Bias

Potential sources of bias included misclassification bias due to false-positive or false-negative biomarker results. To minimize this risk, standardized laboratory protocols were used for all biochemical analyses, and investigators assessing troponin-I levels were blinded to the D-dimer results. Selection bias was reduced by including consecutive eligible patients who presented within the study period.

Study Size

The sample size was calculated as 275 patients, based on a 95% confidence level, an expected sensitivity of 58%, an expected specificity of 62%, an estimated prevalence of 15.3% for NSTEMI diagnosed by D-dimers, and an absolute precision of 15%.

Statistical Methods

All data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistics were applied for baseline characteristics. Frequencies and percentages were calculated for categorical variables, while means and standard deviations were computed for continuous variables. The diagnostic accuracy of D-dimers in detecting NSTEMI was assessed by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), using troponin-I as the reference standard (Table 1).

Table 1: Diagnostic accuracy of D-dimers.

		Status of a patient according to Trop I (Gold standard)	
		Positive	**Negative**
D-dimer test (Screening test)	Positive	True positive (TP)	False-positive (FP)
	Negative	False-negative (FN)	True negative (TN)

Results

Participants

A total of 275 patients presenting with suspected NSTEMI were included in the study. The mean age of the study population was 62 ± 10.79 years.

Of the total participants, 100 patients (36.36%) were in the age group of 18–50 years, while 175 patients (63.63%) were between 51 and 80 years of age.

There were 192 male patients (69.81%) and 83 female patients (30.19%), reflecting a male predominance in the study population.

Descriptive Data

Among the 275 patients, 51 (18.55%) were smokers, whereas 224 (81.45%) were nonsmokers. The prevalence of diabetes mellitus was 13.45% (n=37), and the prevalence of hypertension was also 13.45% (n=37). Detailed baseline characteristics of the participants are summarized in Table 2.

Outcome Data

The diagnostic accuracy of D-dimers was assessed against troponin-I, which served as the gold standard for NSTEMI diagnosis. The cross-tabulation of results is presented in Table 3.

Main Results

Based on the cross-tabulated findings, the diagnostic performance of D-dimer for detecting NSTEMI was calculated. Sensitivity was 38.68%, specificity was 47.38%, positive predictive value (PPV) was 14.91%, and negative predictive value (NPV) was 76.36%. The overall diagnostic accuracy was 45.64%.

Table 2: Characteristics of patients (n=275).

Variables		N(%)
Gender	Male	192 (69.81)
	Female	83 (30.19)
Age (Years); Mean ± SD		62.00±10.79
Smoking status	Smokers	21 (18.55)
	Non-smokers	224 (81.45)
Diabetes mellitus	Yes	37 (13.45)
	No	238 (86.55)
Hypertension	Yes	37 (13.45)
	No	238 (86.55)

Table 3: Diagnostic accuracy of D-dimers (n=275).

Findings on D-Dimers	Findings on Troponin-I		Total
	Positive	Negative	
Positive	41	234	275
Negative	65	210	275
Total	106	447	550

Discussion

Acute coronary syndrome (ACS), encompassing ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UA), remains a major cardiac emergency associated with high morbidity and mortality worldwide. Early detection and timely management are critical to improving patient outcomes[11]. NSTEMI is often challenging to distinguish from UA because both conditions present without ST-segment elevation; however, the presence of elevated cardiac biomarkers differentiates NSTEMI[3]. Established risk factors for NSTEMI include diabetes, tobacco use, hypertension, physical inactivity, dyslipidemia, family history of cardiovascular disease, and obesity[12].

Epidemiological data highlight the growing burden of NSTEMI, which accounts for more than 60% of myocardial infarction cases in Southern Europe, particularly among the elderly[13]. Male patients are affected more commonly than females, with a ratio of approximately 3:2[12]. Cardiac troponin remains the biomarker of choice in ACS, given its superior sensitivity and specificity compared to earlier biomarkers[12]. Nevertheless, D-dimer, a fibrin degradation product released during plasmin-mediated fibrinolysis, has been proposed as an additional diagnostic and prognostic marker in ACS[7,8]. D-dimer reflects cross-linked fibrin turnover and has been associated not only with acute events but also with long-term ischemic heart disease risk, even in individuals without baseline vascular disease[14–17].

In our study, the mean age of participants was 62 ± 10.79 years, with a majority (63.63%) aged 51–80 years. Male patients predominated (69.81%), while comorbidities such as smoking (18.55%), diabetes mellitus (13.45%), and hypertension (13.45%) were also prevalent. These findings are consistent with

established demographic and clinical risk patterns reported in NSTEMI populations[12,13].

When diagnostic accuracy was assessed, D-dimers demonstrated a sensitivity of 38.68%, specificity of 47.38%, positive predictive value of 14.91%, negative predictive value of 76.36%, and an overall accuracy of 45.64% when compared with troponin-I. These findings indicate that, while D-dimers have some utility in ruling out disease due to their relatively high NPV, their diagnostic accuracy remains limited. Comparable findings have been reported in international studies. For example, Volschan et al. observed a diagnostic accuracy of 51.4% for D-dimers in NSTEMI patients, which aligns closely with our results[10].

Several studies further support the dual diagnostic and prognostic role of D-dimers. Gosai et al. demonstrated that elevated D-dimer levels correlated with disease severity in NSTEMI patients[18]. Kim et al. reported that 49.5% of NSTEMI patients had elevated D-dimers, alongside a 38% rise in troponin levels[19]. Satilmisoglu et al. identified a significant positive correlation between D-dimer levels and TIMI scores ($r=0.253$, $p<0.001$), highlighting their role in risk stratification [20]. Similarly, Nichenametla et al. reported significantly higher D-dimer levels in ACS patients compared to controls ($p<0.001$), reinforcing its diagnostic relevance[21]. Orak et al. further demonstrated sensitivity and specificity values of 83.7% and 95.4% for D-dimers in ACS diagnosis, with significant differences observed between NSTEMI patients and controls ($p<0.05$)[22].

Beyond diagnosis, D-dimers have prognostic implications. Mjelva et al. identified elevated D-dimer levels as an independent predictor of mortality in patients presenting with chest pain suggestive of myocardial infarction (HR: 1.26)[23]. Lu et al. reported that increased D-dimer levels were significantly associated with higher mortality and cardiovascular event risk (HR: 2.2, $p<0.001$)[24]. Collectively, these findings emphasize that while D-dimers may have limited standalone diagnostic value for NSTEMI, they provide important prognostic information and may enhance risk stratification when used alongside established biomarkers such as troponin.

Our study contributes to the limited body of local evidence regarding the role of D-dimers in NSTEMI diagnosis. Although D-dimers showed moderate utility in ruling out disease due to their negative predictive value, their poor sensitivity and specificity limit their effectiveness as a sole diagnostic tool. Nevertheless, their role as an adjunctive biomarker, particularly for prognosis and risk stratification, remains promising and warrants further investigation in larger, multicenter studies.

This study has several limitations that should be acknowledged. First, it was conducted at a single tertiary care center in Peshawar, which may limit the generalizability of the findings to other populations and healthcare settings. Second, the study design was cross-sectional, restricting the ability to establish causal relationships or assess the long-term prognostic value of D-dimers. Third, the relatively small sample size may have influenced the precision of sensitivity, specificity, and predictive value estimates. Fourth, although major confounding conditions associated with elevated D-dimer levels were excluded, other subclinical factors may still have affected biomarker levels. Finally, diagnostic accuracy was assessed only against troponin-I as the reference standard, without the incorporation of advanced imaging or long-term follow-up, which may have provided additional diagnostic and prognostic insights.

Conclusion

D-dimer demonstrated value as a supportive biomarker in the evaluation of patients with suspected NSTEMI. While its limited sensitivity and specificity restrict its role as a standalone diagnostic test, its relatively high negative predictive value suggests that it may be useful for ruling out NSTEMI when incorporated into routine chest pain unit protocols. Integrating D-dimer measurement alongside established biomarkers such as troponin-I could enhance early decision-making and risk stratification in emergency settings. Further large-scale, multicenter studies are

warranted to validate these findings and refine its role in clinical practice.

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