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Relation between D-Dimer Level and Coronary Artery Disease Severity in Patients with ST Segment Elevation Myocardial Infarction

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ABSTRACT

Background: The breakdown of cross-linked fibrin by plasmin results in D-dimer. The production of fibrin and its subsequent breakdown by the endogenous fibrinolytic system are prerequisites for the plasma concentrations of D-dimer, a coagulation marker. Numerous studies have revealed a link between poor outcomes for individuals hospitalized for myocardial infarction and increased D-dimer levels.

Objective: The current work aimed to detect the association between the serum level of D-dimer upon admission and the severity of coronary artery disease (CAD) in patients with ST-elevation myocardial infarction (STEMI).

Patients and methods: This prospective observational study included 120 patients with STEMI who were recruited from the Cardiology Department, Menoufia University Hospital and Banha Teaching Hospital.

Results: in the current study, the mean syntax II score was 27.82 ± 5.20 and there were 63 cases (52.5%) with High syntax II score (syntax II score ≥ 25). The D-dimer level was statistically significantly higher in the cases with high syntax II score compared to the cases with low syntax II score ($p< 0.001$). The best cutoff point of D-dimer level to identify cases with high syntax II score was > 1.75 ng/ml with 73.5% sensitivity and 64.5% specificity. The area under the curve was 0.701 and this value showed a statistically significant value ($p = 0.001$).

Conclusion: Serum level of D-dimer could be used as a non-invasive biomarker for detection of the disease severity in cases with acute STEMI.

Keywords: D-dimer, CAD severity, STEMI.

INTRODUCTION

A potentially fatal consequence of CAD, STEMI is one of the main causes of mortality worldwide. In patients with STEMI, primary percutaneous coronary intervention (P-PCI) of the responsible artery is conventional therapeutic practice [(1)].

40–65% of patients had one or more concurrent coronary lesions at the time of P-PCI, often known as multivessel disease (MVD). It has been proposed that one characteristic linked to poor clinical outcomes in individuals with STEMI is the existence of constricted coronaries other than those caused by index ischemia [(2)]. When compared to single-vessel CAD, the presence of MVD is significantly linked to increased 30-day mortality, a higher reinfarction ratio, a worse success rate for myocardial reperfusion, and a greater incidence of major adverse cardiac events (MACE) at one year [(3)].

The most widely used anatomical grading system in the world, the SYNTAX score, has been linked to the prognosis of STEMI patients. A new grading system called SSII incorporates clinical factors [(4)]. Fibrinolytic enzyme breaks down cross-linked fibrin to generate D-dimer [(5)]. Numerous illnesses, including aortic dissection, pulmonary embolism, myocardial infarction, disseminated intravascular coagulation, tumors, and sepsis, have been linked to significantly increased D-dimer levels. The diagnosis and prognosis of MI are also influenced by the D-dimer's capabilities [(6)].

The purpose of this study was to detect the association between the serum Level of D-dimer upon admission and the severity of CAD in patients with STEMI.

PATIENTS AND METHODS

This prospective observational study included a total of 120 patients with STEMI, attending at Department of Cardiology, Menoufia University Hospital and Banha Teaching Hospital, Egypt, during the period from June 2023 to December 2023.

Inclusion criteria: The patients with STEMI who were admitted to Menoufia University Hospital or Banha teaching hospital and eligible for primary PCI.

Exclusion criteria: Patients with history of coronary artery bypass graft (CABG) surgery, patients with previous PCI, patients with previous admission with ACS, Recent admission with pulmonary embolism or DVT or any other venous thromboembolism, Recent admission with stroke or PVD, Malignancy, Significant hematologic disorder (anemia, thrombocytopenia, leukocytosis, leukemia) and Patients presented with NSTEMI.

All patients were subjected to:

Complete history taking, including demographic data (age, sex, and residence), general medical history and associated comorbidities, History of risk factors for CAD as DM, hypertension, smoking and symptoms suggestive of cardiac disease e.g. CAD, current medications, family history and other co-morbidities e.g. previous cerebrovascular disease, chronic

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obstructive pulmonary disease, chronic kidney disease, peripheral vascular disease. As well as degree of physical activity and daily life activities.

Systemic hypertension is defined as SBP of 140 mm Hg or more and/or DBP of 90 mm Hg or more, measured on three different occasions with or without therapy before admission.

Patient classified as having diabetes if he has a past history or a current diagnosis of DM (By measuring random, fasting, 2-hour postprandial blood sugar & HbA1c).

- **Dyslipidemia** was defined as serum T. cholesterol level over 200 mg /dl or TG more than 150 mg /dl or current treatment with lipid lowering medication.
- **Current smoking** an adult who presently smokes cigarettes and has smoked 100 cigarettes in their lifetime.
- **Clinical examination:** Vital signs: HR, BP and RR.
- **General examination**: was done with special attention to signs of HF.
- **Local cardiac examination:** abnormal pulsation, heart sounds & murmurs and **Resting 12 leads ECG.**
- **Laboratory tests:** including D-dimer, CBC, lipid profile, HbA1c, uric acid, creatinine, cardiac troponin I (conventional or high-sensitivity), estimated eGFR using the Cockroft-Gault formula [(7)].

Serum D-dimer was measured by using human enhanced immuno-turbidimetric test kits (Catalog No. CSBA082431 America, USA).

Results of cardiac catheterization that was conducted through PCI. Routine transthoracic echocardiography was conducted prior to initial PCI. The infarct-related artery (IRA) was discovered. An interventional cardiologist determined the culprit lesion based on the infarct site on the admission ECG and the angiographic data (target vessel, lesion characteristics). Multi-vessel disease was characterized as having ≥ 1 lesion with >50% stenosis in ≥ one main epicardial coronary artery or its major branches far from the IRA.

Calculation of syntax score

The Judkins approach was used to perform selective coronary angiography on each patient. Before the intervention and throughout it, all patients will receive 300 mg of acetylsalicylic acid and a P2Y12 inhibitor (either 180 mg of ticagrelor as a loading dose or 600 mg of clopidogrel). Unfractionated heparin will also be administered to all patients. After stent implantation and balloon angioplasty were used to treat the culprit lesions, the SYNTAX II score was determined using the SYNTAX Score Calculator online tool. This score takes into account six clinical variables as well as two anatomical variables: age, creatinine clearance, LVEF, sex, COPD, and peripheral arterial disease [(8)].

The following factors are used to calculate the score of each lesion: dominant coronary artery, diseased segments, total occlusion, trifurcation or bifurcation, lesions leading to severe tortuosity, lesion with aorto-ostial site, lesion longer than 20 mm, severe calcification of the lesion, presence of thrombus, and diffusely diseased and narrowed segment.

Patients with CAD were separated into two groups based on their SYNTAX II scores. Patients in the first group had a low syntax II score (< 25), whereas those in the second group had a high syntax II score (≥ 25).

Outcomes: The incidence of MACE were evaluated including AF, cardiac arrest, cardiogenic shock, mortality, and duration of hospital stay **[(9)].**

Ethical consideration

Menoufia University Faculty of Medicine's local ethics committee authorized the study design (IRB approval number: 4/2023CARD28). Prior to their involvement in the study, all participants (or their family) provided written informed consent in which the purpose and the procedures of the study were explained. At every stage of the study, personal privacy and confidentiality were upheld. Patients have no repercussions if they decide to stop participating in the study at any time. The Helsinki Declaration was adhered to at every stage of the investigation.

Statistical method

With SPSS V. 22.0, the results were statistically evaluated. The continuous data may be summarised using descriptive statistics as mean±SD for normally distributed data or median (Med) and range for skewed data. To show the qualitative data, frequency was expressed as a percentage (%). When comparing two or more groups with respect to a single qualitative variable, the Pearson $\chi 2$-test was employed. When comparing two or more groups on a single qualitative variable and one cell has a frequency less than five (more than two X two tables), the Monte-Carlo test was utilised as an alternative. Fischer's exact test: When comparing two or more groups on a single qualitative variable and one cell has a frequency of less than five (2X2 tables), this test was employed as a substitute. separate examples T-test: The exam is parametric and should be compared to groups that have quantitative parametric data. additionally, to the ROC analysis for the case-specific marker prediction level. A significant level is defined as P-values < 0.05.

RESULTS

The current study included 120 patients with STEMI. The mean age of the cases was 52.28 ± 10.37 years, and the mean BMI was 27.08 ± 1.85 kg/m^2. Among the cases there were 97 males (80.8%) and 23 females (19.2%) **(Table 1).**

Table (1): Demographic data in the study.

Variables		Study cases N = 120	
Age (years)	Mean ± SD	52.28 ± 10.37	
	Median	63 (49 – 75)	
		Number	Percent
Sex			
Male		97	80.8
Female		23	19.2
BMI (Kg/m2)	Mean ± SD	27.08 ± 1.85	
	Median	27 (22 – 31.5)	

In the current study, patients were subdivided into two groups according to SYNTAX II score. There were 63 cases (52.5%) with High syntax II score (syntax II score ≥ 25) and 57 cases (47.5%) with low SYNTAX II score (SYNTAX II score < 25). The mean syntax score was 27.82 ± 5.20, **(Table 2).**

Table (2): The syntax II score in the cases of the study.

Variables		Study cases N = 120	
Syntax II score	Mean ± SD	27.82 ± 5.20	
	Median (Range)	24.5 (19 – 42)	
		Number	Percent
Syntax II score grading			
Low syntax II score (< 25)		57	47.5
High syntax II score (≥ 25)		63	52.5

In the current study, D-dimer level was statistically significantly higher in the cases with high syntax II score (p< 0.001), **(Table 3).**

Table (3): Analysis of the laboratory data according to the syntax score.

Variable	Group 1 (Low syntax II score) (N= 57)	Group 2 (High syntax II score) (N= 63)	Test of sig.
D. dimer (ng/l)	1.8 (0.02 – 3)	2.5 (0.3 – 4.60)	z = - 3.800 P < 0.001*

Median and range: non parametric test, *: Significant

In the current study, patients were classified according to ejection fraction into normal ejection fraction (50%-70%) and mildly reduced ejection fraction (41%-49%). We found that the ejection fraction was statistically significantly lower in the cases with high syntax II score (p= 0.022), **(Table 4).**

Table (4): Analysis of the ejection fraction according to the syntax score.

Variable	Group 1 (Low syntax II score) (N= 57)	Group 2 (High syntax II score) (N= 63)	Test of sig.
Ejection fraction (%)	53.11 ± 5.41	48.79 ± 4.96	t = 3.542 P = 0.022*
Grading of LV according to EF			
Normal (50% - 70%)	35 (61.4%)	26 (41.3%)	
Mildly reduced LV ejection (41%- 49%)	22 (38.6%)	37 (58.7%)	χ^2= 4.845 P = 0.028*

In the current study, the duration of hospital stay didn't show a statistically significant difference between the two groups. However, the overall incidence of MACE in the form of (AF, Cardiac arrest, Shock and Mortality) was statistically significantly higher in the cases with high syntax II score (p= 0.001) **(Table 5).**

Table (5): Analysis of the outcomes according to the syntax score

Variable	Group 1 (Low syntax II score) (N= 57)	Group 2 (High syntax II score) (N= 63)	Test of sig.
Duration of hospital stay (Days)	6 (1 – 13)	7 (1 – 13)	z = - 0.656 P = 0.506
Complications			
Overall MACE in the form of (AF, Cardiac arrest, Shock and Mortality)	17 (29.8%)	37 (58.7%)	χ2= 10.102 P = 0.001*

Figure 1 and table 6 show that the best cutoff point of D-dimer level to identify cases with high syntax II score was > 1.75 ng/ml with 73.5% sensitivity and 64.5% specificity. The area under the curve was 0.701 and this value showed a statistically significant value (p = 0.001), **(Table 6, Figure 1).**

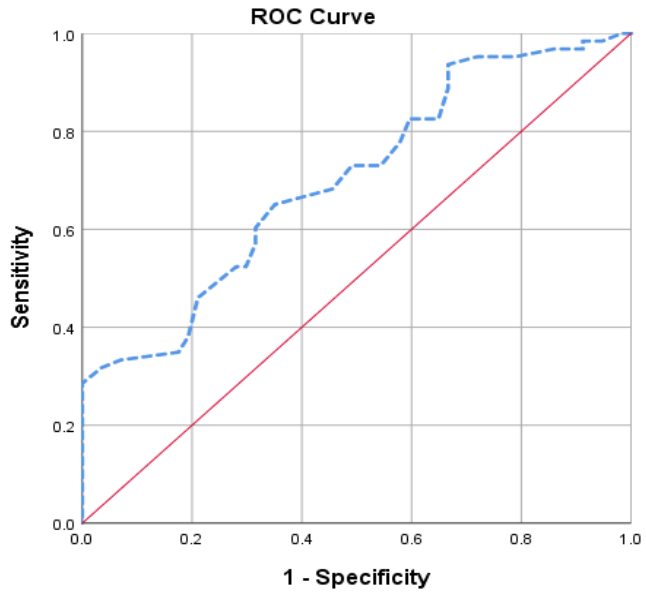

Figure (1): ROC curve of Diagnostic value of d dimer (ng/ml) to differentiate of the cases with high SYNTAX score.

Table (6): Diagnostic value of D-dimer (ng/ml) to differentiate of the cases with high syntax II score.

Diagnostic criteria	High syntax II score
AUC	0.701
Cut off point	> 1.75
Sensitivity	73.5 %
Specificity	64.5 %
NPV	76.3 %
PPV	60.4 %
Accuracy	68.6 %
P value	0.001*

AUC: area under the curve. NPV: Negative predictive value, PPV: Positive predictive value, *: significant

DISCUSSION

In the current study, patients were divided into two groups according to SYNTAX II score. There were 63 cases (52.5%) with High syntax II score (syntax II score ≥ 25) and 57 cases (47.5%) with low SYNTAX II score (SYNTAX II score < 25). The mean syntax score was 27.82 ± 5.20. The present findings were consistent with the research conducted by **Türkoğlu *et al.*** [4], which comprised 300 STEMI patients who had primary PCI. SSII<25 was classified as a low syntax group (n = 151), whereas SSII≥25 was classified as a high syntax group (n = 149). Patients were split into these two groups based on their median SSII.

In the current investigation, subjects with high syntax II scores had an ejection percent that was statistically substantially lower. This was consistent with the findings of **Türkoğlu *et al.*** [4], who found that a high syntax II score was linked to a higher thrombus score, a lower LVEF, and a greater prevalence of the no-reflow phenomenon.

In the current investigation, instances with high syntax had a statistically significant higher total incidence of MACE, which includes the incidence of AF, cardiac arrest, shock, and death. This was in line with **Safarian *et al.*'s** [10] findings, which demonstrated that patients in the highest SYNTAX score tertile (21.6%) had a substantially higher risk of MACE than patients in the lowest (7.5%) or intermediate (9.9%) tertiles. Without taking into account in-hospital events, the rates of mortality, TVR, and MI also significantly correlated with SYNTAX score.

A research by **Bundhun *et al.*** [11] states that sixteen trials with 19,751 people overall—8589 with a low SYNTAX score and 11,162 with a high score—were included. A higher SYNTAX score was associated with a considerably higher death rate (RR 2.09, 95% CI 1.78–2.46), according to the data. Likewise, there was a substantial increase in myocardial infarction, MACE, stent thrombosis, and recurrent revascularization with a high SYNTAX score.

In a more recent study, 2364 individuals with unstable angina were included by **Xu *et al.*** [12]. 1346 patients had PCI, 1018 patients got medicinal treatment, and 1695 patients had low SYNTAX scores (≤ 22), 432 patients had medium SYNTAX scores (23–32), and 237 patients had high SYNTAX scores (≥ 33). 95 individuals experienced long-term MACEs during the course of the 3.38 ± 0.99-year follow-up. Patients with high SYNTAX scores (7.4% vs. 16.7%, P = 0.048; 3.7% vs. 14.6%) had fewer MACEs and cardiac deaths in the PCI group than in the medical treatment group, but there was no decrease in patients with low and medium SYNTAX scores [12].

According to **Brown *et al.*** [13] raising the SYNTAX score was a reliable indicator of MACEs (HR: 1.61, 95% CI 1.05–2.47). According to **Eickhoff *et al.*** [14] the 1-year and 2-year mortality in individuals under 75 years of age were independently predicted by the SYNTAX score (HR: 1.43, 95% CI 1.03–2.00, P = 0.034; and HR: 1.33, 95% CI 1.01–1.76).

An independent predictive predictor of in-hospital outcomes in patients with ST STEMI, a pilot investigation found that a high SYNTAX score was linked to a 6.2-fold hazard of in-hospital mortality (OR 6.2, 95% CI 2.6–14.1) [15]. 834 patients who had pPCI were included in **Li *et al.*'s** [16] research, and 778 individuals were ultimately included. 539 (69.3%) and 239 (30.7%) of the 778 patients, respectively, had normal D-dimer values (≤0.5 mg/L and >0.5 mg/L). They stated that patients with elevated D-dimer levels had a greater overall risk of death.

In the current investigation, the patients with high syntax II scores [2.5 (0.3 – 4.60)] had a statistically significant greater D-dimer level than the cases with low syntax II scores [1.8 (0.02 – 3). This was consistent with the findings of **Türkoğlu *et al.*** [4], who demonstrated that patients in the high SSII group had greater D-dimer levels than those in the low SSII group.

According to a study by **Biccirè *et al.*** [17], D-dimer level was positively correlated with higher in-hospital

and short- and long-term complications in patients with acute coronary syndrome (ACS), as well as with the no-reflow phenomenon. These findings suggest that D-dimer is a useful marker to identify patients with residual thrombotic risk after ACS.

With 73.5% sensitivity and 64.5% specificity, the optimal D-dimer level cutoff point in the current investigation was > 1.75 ng/ml for identifying subjects with high syntax II scores. With an area under the curve of 0.701, the result indicated a level of statistical significance. The findings of the ROC curve analysis in the study by **Türkoğlu *et al.*** [(4)] showed that D-dimer s could predict the severity of CAD with 69.8% sensitivity and 65.6% specificity at a cutoff value of 0.26 µg/ml; the area under the ROC curve was 0.725 (CI 95%: 0.667-0.782).

Zorlu *et al.*'s [(18)] study from revealed that >1435 ng/ml was the ideal cut-off level of D-dimer to predict cardiovascular death. D-dimer levels were favorably connected with left ventricular diastolic diameter and left atrium size, and adversely linked with ejection fraction. In univariate studies, D-dimer >1435 ng/ml, age, diabetes mellitus, atrial fibrillation, and creatinine level were revealed to have predictive relevance.

ROC curves were used in the study by **Li *et al.*** [(16)] to assess the D-dimer's possible predictive value for in-hospital HF in all patients. D-dimer's AUC values for HF prediction were 0.657, with 79.3% specificity and 50.9% sensitivity .

CONCLUSION

Acute STEMI is a serious condition associated with relatively high incidence of major adverse cardiovascular events. Although Syntax II score is a reliable assessment tool for detection of disease severity in cases with acute STEMI, Serum level of D-dimer could be used as a non-invasive biomarker for detection of the disease severity in cases with acute STEMI.

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