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The Relationship between D-Dimer Levels and Coronary Lesion Severity in Patients with Acute Myocardial Infarction with ST-Segment Elevation at Haji Adam Malik Hospital Medan

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ABSTRACT

Introduction: Acute coronary syndrome results from rupture or erosion of an atherosclerotic plaque. D-dimer is a direct marker of fibronolysis events and an indirect marker of hypercoagulable state associated with atherosclerotic plaque formation and acute coronary syndrome. The purpose of this study was to determine the relationship between D-dimer levels and the severity of coronary lesions in ST Elevation Myocardial Infarction patients at H. Adam Malik Hospital Medan.
Method: This study was conducted with a cross-sectional method on 72 ST Elevation Myocardial Infarction patients at H. Adam Malik Medan Hospital who underwent coronary angiography from December 2022 to May 2023. Definition of ST Elevation Myocardial Infarction followed the definition of Universal Definition of Myocardial Infarction and the severity of coronary lesions was calculated based on syntax score. Data were analyzed univariately and bivariately using SPSS to assess the association of D-dimer levels with syntax score with $p<0.05$ considered statistically significant.
Results: The total study subjects were 72 people with an average age of 56,54±10,84years. Most of the study samples were male 56 people (77.8%). The median D-dimer level was 605 and mean syntax score 22.027±14.61. There is a significant relationship between D-dimer levels and the severity of coronary lesions based on the syntax score (p: <0.001).
Conclusion: There is a significant relationship between D-dimer and severity of coronary lesions in patients with acute myocardial infarction with ST segment elevation at H. Adam Malik General Hospital, Medan.

Keywords

D-dimer, ST Elevation Myocardial Infarction, SYNTAX score

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INTRODUCTION

Coronary heart disease (CHD) is the leading cause of death worldwide, especially acute myocardial infarction (AMI).[1] Almost one-fifth of patients with AMI require re-hospitalisation within 1 year and 10% of patients will experience recurrent AMI. IMA plays a role in 2.4 million deaths in the United States and more than 4 million deaths in European and North Asian countries.[1] IMA is characterised by an increase in cardiac enzymes and is divided based on electrocardiographic (ECG) images into Acute Myocardial Infarction with ST Segment Elevation (IMA-EST) and Acute Myocardial Infarction without ST Segment Elevation (IMA-NEST).[2] In Indonesia, heart disease is still the highest cause of death based on RISKESDAS in 2018 with a prevalence of cardiovascular disease in Indonesia of 1.5% or around 4.2 million Indonesians.[3]

IMA occurs due to thrombosis of an atherosclerotic plaque that has ruptured or eroded triggering platelet aggregation followed by fibrin formation and thrombus formation.[4] The process of thrombosis, activation of the coagulation process and fibrinolysis plays a role in the pathogenesis of coronary heart disease. D-dimer is

a specific product of fibrin degradation resulting from the activation of thrombin, factor XIII, and plasmin. Higher D-dimer levels in plasma are one of the useful biomarkers in patients with IMA.[5]

The severity of coronary lesions can be assessed using the SYNTAX (SYNergy between PCI with TAXUS™ and Cardiac Surgery) scoring system.The SYNTAX score is a comprehensive scoring system to assess the complexity of coronary artery lesions based on angiography and predict the outcome of percutaneous coronary intervention or coronary artery bypass surgery (CAD).[6,7] It assesses coronary artery lesions by combining the number of significant lesions and the location and complexity of each lesion independently. Higher SYNTAX scores indicate greater complexity and poorer prognosis.[8]

Recent studies have shown that elevated D-dimer levels are associated with coronary lesion severity based on SYNTAX score and SYNTAX score II in IMA-EST patients undergoing primary percutaneous coronary intervention. D-dimer levels > 260 ng/ml correlated with greater coronary lesion severity as measured by SYNTAX Score II (sensitivity 69.8% and specificity 65.6% with area under the ROC curve: 0.725 (CI: 95%: 0. 667-0.782, P<0.001).[5] Research by Zhao et al in 2021 examined the relationship of D-dimer combined with creatinine (D-dimer/creatinine ratio) with coronary lesion severity based on the Gensini score in IMA-EST patients. The results showed that patients with D-dimer/creatinine ratio >14.2 had a positive correlation with increased Gensini score (r: 0.493, p<0.001).[4]

In Indonesia, there are no studies that discuss the relationship between D-dimer and the severity of coronary lesions, especially in patients with acute myocardial infarction with ST segment elevation (IMA-EST). Based on these data, researchers are interested in examining whether there is a relationship between D-dimer levels and the severity of coronary lesions in IMA-EST patients at the Haji Adam Malik (HAM) Central General Hospital in Medan.

METHOD

This study is an observational analytic study with a cross-sectional research design to examine the relationship between D-dimer and the severity of coronary lesions in IMA-EST patients at the Hajj Adam Malik Hospital Medan. Sampling was conducted at H. Adam Malik Hospital Medan from December 2022 and continued until May 2023. The target population was patients with a diagnosis of IMA-EST. The target population is patients with a diagnosis of IMA-EST who seek treatment at H. Adam Malik Hospital Medan.

Inclusion criteria were patients with a diagnosis of IMA-EST who were treated at the Hajj Adam Malik Hospital Medan, had complete clinical data and supporting examinations in the medical record, patients who had undergone coronary angiography examination, willing to become research subjects by signing a consent form. Patients were included in the exclusion criteria if patients with a history of major surgery or trauma in the last 6 months, patients who received previous fibrinolysis therapy, patients with a history of malignancy, congenital heart defects, a history of coagulation factor disorders, taking anticoagulant drugs or already receiving anticoagulant drugs at admission, suffering from COVID-19, and severe renal impairment.

The diagnosis of IMA-EST was made based on guidelines from ESC and PERKI. The sample collection used the quota method where each subject who met the inclusion criteria was sampled until the total sample size was at least 62 patients. Subjects who became research samples were all patients with a diagnosis of IMA-EST in the emergency department who then received therapy and performed coronary angiography where before the action had signed a letter of consent to patients who met the inclusion criteria. Basic data, subject identity (age, gender, history of hypertension, history of diabetes, history of smoking and history of diseases related to D-Dimer such as malignancy, congenital heart disease, coagulation factor disorders, kidney or liver disease and COVID-19) and previous treatment history were recorded. Blood collection for laboratory examination (D-dimer) was carried out when the patient first came to the emergency department of HAM Hospital. Venous blood was placed in a tube containing 9:1 sodium citrate and sent to the laboratory without special treatment. This sample was centrifuged to obtain the supernatant and then D-dimer examination was performed with a Sysmex CS 2500 Coagulometer using the latex agglutination method to obtain quantitative plasma D-dimer levels. This method is based on covalent binding between monoclonal antibodies and D-

dimer-specific epitopes. The results will be printed automatically. This study will use the D-dimer cut-off point according to previous research conducted by Turkoglu et al in 2020 where this study found that D-dimer cut-off points > 260 ng/ml were associated with high SYNTAX scores (> 23) while D-dimer < 260 ng/ml was associated with low SYNTAX scores (< 23). Coronary angiography examination to measure SYNTAX score was performed at the catheterisation room of RSUP Haji Adam Malik Medan. Coronary angiography with or without percutaneous coronary intervention was performed according to the clinical judgement of the doctor in charge. After coronary angiography was performed, the SYNTAX score was assessed by viewing the recorded results of coronary angiography by 2 interventional consultant cardiologists who did not know the patient's D-dimer value.

Categorical variables are presented with number or frequency (n) and percentage (%). Numerical variables were presented with mean (average) and standard deviation for normally distributed data, while numerical data that were not normally distributed used the median (minimum - maximum), which was then compared with Student's t-test or Mann Whitney U. The normality test for numerical variables in all research subjects used the Kolomogorov Smirnov test (n>50) or Shapiro Wilk (n<50). For assessment of interobserver agreement on the examination of SYNTAX scores, the Bland Altman test will be carried out which is presented in tabular form and concluded that agreement or reliability is good when the value of the limit of agreement is between -5 and 5. SYNTAX scores were determined by two interventional consultant cardiologists who did not know the patient's D-dimer.

To determine the association of D-dimer with coronary lesion severity in IMA-EST patients if the data were normally distributed, the chi square test was used and if the data were not normally distributed, the Fisher exact test was used. For samples that were found to be significant in the bivariate analysis test, they were included in the multivariate test with logistic regression. Statistical data analysis using computer statistical tools, p value <0.05 was said to be statistically significant.

RESULT

This study was conducted at the Department of Heart and Vascular Diseases, Integrated Heart Centre, H. Adam Malik Hospital, Medan, by sampling a total of 72 patients with a diagnosis of IMA-EST within the data collection period in accordance with the inclusion and exclusion criteria. Data were collected from the patients' clinical condition at admission, laboratory examination results, electrocardiography and coronary angiography.

The study sample consisted of 17 subjects with inferior IMA-EST, 28 subjects with anterior IMA-EST, and 27 subjects with anteroseptal IMA-EST. Of the 72 samples in this study, there were 29 subjects with high SYNTAX scores and 43 subjects with low SYNTAX scores. The mean age of the sample in this study was 56.54±10.84 years, where patients with high SYNTAX scores had an older mean age. This study population was dominated by male gender as many as 56 patients (77.8%), with a female to male ratio of 1:3. In the group with high SYNTAX scores, the most common risk factors were smoking and hypertension.

All samples of this study were collected data in the form of physical examination (blood pressure, pulse frequency, respiratory frequency, weight and height), routine laboratory examination (Hb, haematocrit, leucocytes, platelets), renal function examination (ureum and creatinine and creatinine clearance), electrolyte examination (Na, K, Cl), diabetes examination (KGD, HbA1C), Cholesterol (HDL, LDL, triglyceride), cardiac enzyme (CKMB, Troponin I), electrocardiography, CXR, ejection fraction and coronary angiography.

On physical examination, the mean blood pressure and pulse frequency were higher in the group with high SYNTAX score. Routine blood tests showed that the high SYNTAX group had lower haemoglobin, haematocrit and platelet levels, and higher leucocytes. Renal function tests showed high ureum and creatinine levels in the high SYNTAX group, resulting in lower mean creatinine clearance in this group. The lipid profile examination showed high total cholesterol, LDL and triglycerides in the high SYNTAX group.

Table 1 . Characteristics of research subjects

Parameter	SYNTAX Score (n=7 1)		Total	p value
	≥ 23 (n= 29)	<23(n= 42)		
Age, years	59 , 97 ± 10 , 14	53, 48 ±10.4 6	56, 13 ±10, 75	0.01*
Gender (%)				
Man	2 3 (79 , 3)	34 (81)	5 7 (80.3)	1,000+ -
Female	6 (20 , 7)	9 (19)	1 4 (19.7)	
Onset				
<24 hours	1 8 (62 , 1)	2 6 (61 , 9)	4 4 (62)	0.682 ++
24-48 hours	5 (17 , 2)	10 (23 , 8)	15 (2 1 , 1)	
>48 hours	6 (20 .7)	6 (14 , 3)	1 2 (1 6 , 9)	
Hypertension				
Yes	7 (24.1)	24 (57 , 1)	3 1 (43 , 7)	0.01+ -
No	22 (75.9)	18 (42 , 9)	40 (56 , 3)	
DM				
Yes	1 0 (34 , 5)	8 (19)	2 8 (2 5 , 4)	0.233+ -
No	1 9 (65.5)	34 (81)	5 3 (7 4 , 6)	
Dyslipidemia				
Yes	3 (10 , 3)	2 (4, 8)	5 (7 , 0)	0.393 ++
No	2 6 (89 .7)	40 (95 , 2)	6 6 (9 3 , 0)	
Smoke				
Yes	21 (72.4)	3 0 (71 , 4)	51 (71 , 8)	1,000+ -
No	8 (27 , 6)	12 (28 , 6)	2 0 (28 , 2)	
Hb	1 3.5 (9-1 7)	1 4 , 0 5 (7 - 19)	13, 8 (7 - 19)	0.071 ++
Ht	40 (2 6 -52)	41 .7 (29-5 4)	40, 4 (2 2 - 54)	0.137 ++
Leukocytes	12 895 , 52 ± 3940 .6 9	1 2882.86 ±41 , 95	12 883 , 03 ±4 5 , 43	0.990*
Platelets	2 81624 , 14 ± 72670 3, 026	2 52452 , 38 ±7 2775 , 365	364 . 098±71 . 452.44	0.101 *
Urea	39 (18-1 03)	30 (13- 78)	3 1 (13-1 03)	0.045 ++
Creatinine	1, 39 (1 - 4)	1 (1 - 2)	1.0 7 (1 - 4)	0,041++
CrCl	73,90±37,38	82,93±26,05	79,24±31,25	0,234*

The results of blood sugar examination in the high SYNTAX group showed higher fasting blood sugar levels. The average SYNTAX score in this study was 22.027 + 14.61. SYNTAX score measurement results are numerical data from coronary angiography results, measured twice by 2 experienced observers. Intraobserver reliability assessment was carried out with the Bland Altman test and the measurement difference between the two observers did not exceed 5 so that the results obtained were quite reliable for the SYNTAX score.

Echocardiographic examination showed a lower mean ventricular ejection fraction in the group with a SYNTAX score ≥ 23. The D-dimer level was higher in the group with a high SYNTAX score.

Analysis of the Relationship between D-Dimer and Coronary Lesion Severity in IMA-EST Patients

In this study, D-dimer values were grouped into D-dimer levels < 260 ng/ml and D-dimer levels > 260 ng/ml in accordance with previous research by Turkoglu et al 2020 where D-dimer levels > 260 ng/ml were associated with more severe SYNTAX score severity (> 23) so that it became a guide for this study.

Table 2 shows in the group with high SYNTAX scores, dominated by subjects with high D-dimer levels, namely, there were 26 subjects with D-dimer > 260. Based on bivariate analysis, there was a significant relationship between D-dimer levels and the severity of coronary lesions with a p value of 0.001.

Table 1. *Continuous*

Parameter	Skor SYNTAX (n=71)		Total	Nilai p
	≥ 23 (n=29)	<23(n= 42)		
Sodium	139.6 9 ±6, 39	1 40 , 64 ±7, 07	1 40 , 25 ±6, 77	0.563*
Potassium	4, 2 ±0.7 1	4.04 ± 0.57 _	4.1 1 ±0.6 3	0.310*
Chloride	104 (94-112)	105 (90-110)	104 (90-112)	0,293**
GDP	128 (89-261)	117 (66-424)	122 (66-424)	0,029**
KGD2PP	157 (103-312)	125 (86-439)	146 (86-439)	0,017**
HbA1C	6,7 (5-13)	5.9 (5-1 6)	6.2 (5 -16)	0.108 **
Total cholesterol	195.24 ± 47 .7 5	1 67 , 55 ±4 2 , 93	1 78 , 86 ± 46 , 69	0.013 *
HDL	3 6 (21 - 56)	38 (24 -56)	36.94 (21 -56)	0.197 **
LDL	13 6 , 94 ±5 1 , 561	11 3 , 71 ±3 7 , 02	12 3 , 20 ±4 4 , 70	0.030 *
Triglycerides	13 1 (36-260)	10 7 (52-789)	1 37.38 (36-789)	0.109 **
Troponin I	15 (0-15)	15 (0-4 4)	15 (0 - 44)	0.753 **
EF	4 0 , 90 ±1 3 , 27	4 6 , 55 ±12, 49	44, 2 4±13, 02	0.072 *
RWMA				
Ya	23 (79 , 3)	37 (88 , 1)	60 (8 4 , 5)	0.338 ++
Tidak	6 (20 , 7)	5 (11 , 9)	11 (15,5)	
KILLIP				
I	18 (62,1)	38 (90,5)	56 (78,9)	0,01*
II	5 (17,2)	4 (9,5)	9 (12, 7)	
III	4 (13 , 8)	0 (0)	4 (5,6)	
IV	2 (6 , 9)	0 (0)	1 (2 , 8)	
CRUSADE	3 2,9 ± 15 , 95	2 5 , 43 ±11, 29	30,06±14,82	0.0001 *
TIMI	5 (1-10)	4 (1-7)	3,96 (1-10)	0,035**
GRACE Score	119,28±20,78	100,12±21,94	108,25±22,83	0,024*
D-dimer	830 (200-2300)	250 (100- 1570)	330 (100- 2300)	0.0001 **

Table 2 . Bivariate analysis of D-dimer on SYNTAX scores in IMA-EST patients

D-dimer	SYNTAX Score (n=71)		Total	p value
	≥ 23 (n=31)	<23(n=40)		
>260	26 (36.6)	14 (19.4)	40 (56.3)	<0.0001+
≤ 260	5 (7)	26 (37)	31 (43,7)	

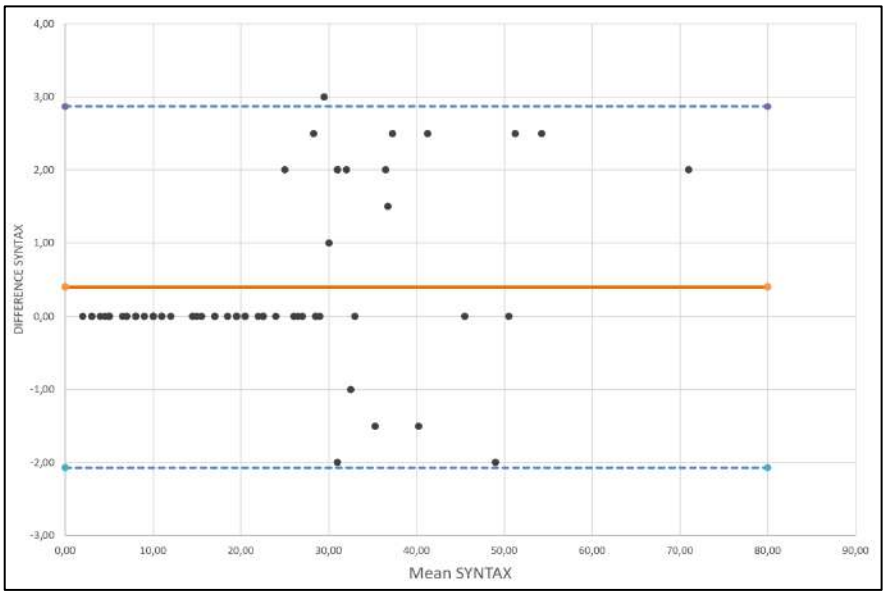

Figure 1. Bland-Altman graph of SYNTAX scores in the intraobserver reliability test

DISCUSSION

Coronary heart disease is the leading cause of death worldwide, and IMA is a clinical condition with high morbidity and mortality. Various reperfusion methods, increased effective pharmacological therapies and improved management of acute cardiovascular disease have improved the prognosis in patients with myocardial infarction. However, there is an increasing need for more accurate risk stratification to identify high risk of major cardiovascular events as well as poorer prognosis in patients with myocardial infarction.[9] This study was conducted to assess the association of D-dimer with coronary lesion severity as measured by SYNTAX score in 72 patients with IMA-EST at H. Adam Malik Hospital, Medan. In this study 29 subjects (40.2%) had high SYNTAX score. This result was lower when compared to the previous study, which found high SYNTAX scores in 149 subjects (49.6%) out of a total of 300 subjects with IMA-EST.

In this study, there was an association between the risk factor of hypertension and the severity of coronary lesions (p=0.002). Hypertension is also an independent risk factor of coronary lesion severity, where subjects who have a history of hypertension have a 4.7-fold risk of more complex coronary lesions (p=0.014; OR=4.723, IK 95% 1.367-16.319). A previous study in 462 patients with coronary heart disease showed the mean SYNTAX score was higher in the hypertensive group and hypertension was an independent predictor of coronary lesion complexity. Mohammed et al reported more complex coronary lesions in patients with hypertension (p<0.005). The mean SYNTAX score in patients with hypertension was higher than those without hypertension (279 vs 184, p=0.006). However, hypertension was not a predictor of coronary lesion severity. This could be due to the presence of undiagnosed hypertension during sampling. Blood pressure plays a role in atherosclerotic plaque growth and is associated with arterial stiffness and coronary perfusion.[9]

Bicciré et al revealed that D-dimer levels can help identify myocardial infarction patients who are at high risk of complications and worse outcomes. Pharmacological management (use of glycoprotein IIb/IIIa inhibitors and higher doses of heparin) and specific technical procedures can reduce the likelihood of no flow in myocardial infarction patients with high D-dimer.[1,10]

Based on this description, D-dimer value can be used as an auxiliary tool in the assessment of coronary lesion severity in patients with acute myocardial infarction. D-dimer can also be used by clinicians in considering therapeutic strategies as well as estimating the prognosis of patients with myocardial infarction.

CONCLUSION

There is a significant relationship between D-dimer and severity of coronary lesions in patients with acute myocardial infarction with ST segment elevation at H. Adam Malik General Hospital, Medan.

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and Haji Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or

critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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