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Research Article

EXAMINING THE ROLE OF SUPAR AND HS-CRP LEVELS IN PREDICTING CORONARY ARTERY DISEASE SEVERITY IN ACUTE MYOCARDIAL INFARCTION: AN AGE-STRATIFIED ANALYSIS INCORPORATING SYNTAX SCORE

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ABSTRACT

Objective: This study examines the association between traditional inflammatory biomarkers, soluble urokinase plasminogen activator receptor (suPAR) levels in elderly and young myocardial infarction patients, and coronary artery disease severity.

Materials and Methods: In this study, 332 participants, including 227 acute myocardial infarction (AMI) patients and 107 controls, underwent evaluation through Syntax Score analysis, suPAR, and high-sensitivity C-reactive protein (hs-CRP) level assessments. AMI patients were divided into young and elderly groups based on age. Syntax Score was utilized to ascertain the severity of coronary artery disease.

Results: suPAR plasma concentrations were significantly higher in AMI patients compared to controls, with values of 2.76 (2.32-3.56) in the young MI group and 3.33 (2.43-4.41) in the elderly MI group, versus 2.33 (1.94-3.11) in the control group ($p<0.001$). Additionally, hs-CRP levels were notably elevated in the elderly MI groups ($p<0.001$). The ROC analysis identified threshold values for suPAR at 3.10 pg/mL and hs-CRP at 6.5 mg/dL to predict a Syntax Score of 23 or higher, with suPAR showing 74.7% sensitivity, 69.9% specificity, and an area under the curve (AUC) of 0.811 ($p<0.001$). The sensitivity of hs-CRP was 65.8%, the specificity was 60.2%, and the AUC was 0.700 ($p<0.001$).

Conclusion: Our study reveals a pivotal relationship between inflammatory markers, particularly suPAR, and Syntax Score in MI patients, suggesting its potential in refining cardiovascular risk assessment and informing future diagnostic and therapeutic approaches for coronary artery disease management.

Keywords: suPAR, hs-CRP, Young myocardial infarction, Elderly myocardial infarction

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INTRODUCTION

The complex pathophysiology of acute myocardial infarction (AMI); includes inflammation, myocardial structural change, and myocardial injury as a result of myocardial stress (1). Biomarkers involved in this complex process help infarct size, myocardial dysfunction, identification of risky patients, treatment and follow-up (2).

In particular, traditional biomarkers reflecting inflammatory processes, such as high-sensitivity C-reactive protein (hs-CRP) and erythrocyte sedimentation rate (ESR), have been associated with an increased risk of cardiovascular disease and AMI (3). Known to be involved in the inflammatory process, soluble urokinase plasminogen activator receptor (suPAR) has been associated with newly discovered cardiovascular disease risk and all-cause mortality (4,5).

SuPAR can be found in a variety of cell types, including monocytes, endothelial cells, activated T lymphocytes, macrophages, fibroblasts, megakaryocytes, smooth muscle cells, keratinocytes, and some tumor cells (6,7). uPAR consists of three sites and is involved in immune system activation. The release of suPAR occurs when the membrane-bound uPAR is cleaved, leading to its presence in various bodily fluids such as plasma, cerebrospinal fluid, serum, blood, and urine. The concentration of suPAR in bodily fluids can vary depending on the level of immune system activation (8).

Recent studies have revealed that patients with AMI have significantly higher suPAR levels which can be used as a predictor of cardiac events (9-11). It is also known that the suPAR level increases with age (12). The risk of AMI also increases with age. However, it is still unknown about suPAR values based on the age of the patients who have AMI.

The main objective of this study was to compare the traditional inflammatory biomarkers and suPAR levels in elderly and young myocardial infarction (MI) patients with those in patients who had been determined not to have coronary artery disease (CHD). Furthermore, this research aimed to investigate the correlation between suPAR concentrations and the extent of CHD severity.

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MATERIALS AND METHODS

This study encompassed 243 patients admitted to the intensive care unit with an initial diagnosis of AMI, who were scheduled for coronary angiography between April 2019 and January 2020. Of these, 14 patients, initially diagnosed and set to partake in the study, declined to undergo coronary angiography, leading to their exclusion. Furthermore, two individuals from the control group were also excluded on account of rheumatological diseases. The study further categorized patients based on age: those 55 years and younger were classified as the 'young' group, while those older than 55 years were designated as the 'elderly' group. The control group consisted of patients who underwent coronary angiography for indications other than AMI and had less than 50% coronary artery stenosis.

The study excluded patients presenting with active infections, malignancies, autoimmune disorders, hyperthyroidism, or those on immunosuppressive medication. Additionally, individuals with chronic kidney disease, rheumatological conditions, those who had undergone revascularization with fibrinolytic therapy, or had a history of pulmonary embolism were also excluded.

The study's intended participants were given information about the study and given the option to volunteer for it after receiving their consent. Ethical clearance was granted by Selçuk University's Ethics Committee (Decision No: 2019/92, Date: 08.05.2019). The study received funding support from the Selçuk University Scientific Research Projects Coordinatorship, under the project identifier 19102049.

Blood samples

At the time of hospitalization, 5 ml of blood were drawn from the patients upon admission to the intensive care unit with the diagnosis of AMI, and from the control group after coronary angiography. Then, those blood samples were placed in eppendorf tubes to study the suPAR level and stored at -80°C after centrifugation at 4000 rpm for 5 minutes.

In the biochemistry laboratory, blood samples such as creatinine, HDL cholesterol, triglyceride, LDL cholesterol, sodium, potassium, and hs-CRP in the BECKMAN COULTER AU5800 autoanalyzer, complete

blood count (hemoglobin, platelet, leukocyte) in the COULTER DXH 800 blood count device. Sedimentation was measured in the ALIFAX device, and the results were recorded separately for each patient.

Plasma suPAR levels were measured on an automated BMG LABTECH CLARIOSTAR instrument utilizing the suPARnostic AUTO Flex ELISA kit for determination, based on the instructions provided by the manufacturer (ViroGates A/S, Birkerød, Denmark).

Syntax score analysis

Catheterization images were evaluated using the Syntax Score system. All lesions causing a reduction in luminal diameter of 50% or more in coronary vessels with a diameter equal to or greater than 1.5 mm were accounted for in the Syntax Score computation. For this calculation, we utilized the dedicated software available at http://www.syntaxscore.com (13). The evaluation of the Syntax Score was independently conducted by two interventional cardiologists who were not informed of the study protocol or the patient demographics. Intermediate-high risk was determined as 23 and above.

Statistical analysis

Statistical analyses were conducted using SPSS version 29.0 (SPSS Inc., Chicago, IL, USA). The normality of distribution for numerical variables was verified through the Kolmogorov-Smirnov test. These variables were presented as mean ± standard deviation and median (with interquartile range from the 25th to 75th percentile). Categorical variables were expressed in terms of frequencies and percentages. The comparison of numerical variables among the three study groups was performed using either one-way ANOVA or the Kruskal-Wallis test, depending on the suitability for parametric analysis. The chi-square test was applied for the assessment of categorical variables. For the analysis of bivariate relationships among continuous variables, Spearman's rank correlation coefficient was employed. The efficacy of the Syntax Score in predicting the severity of coronary artery disease was evaluated using Receiver Operating Characteristic (ROC) curve

analysis, with a particular focus on establishing a diagnostic threshold for a Syntax Score greater than 23 and above. Two-sided p values less than 0.05 were considered statistically significant.

RESULTS

Basic characteristics of patients

This investigation included a total of 332 participants, who were allocated into three groups: a young myocardial infarction (MI) group with 100 patients, an elderly MI group encompassing 127 patients, and a control group consisting of 105 individuals, as outlined in Table 1.

The median age in the group of young patients with MI was 49 years (44.2–53), in the group of elderly patients with MI the median age was 66 years (62–74), and in the control group the median age was 59 years (53 -66), showing a statistically significant difference ($p<0.001$). Compared to the control group, both groups of AMI patients had a higher proportion of men (88% in the young MI group, 65.4% in the older MI group, 45.7% in the control group, $p<0.001$). However, there was no statistically significant difference in body mass index (BMI) between the groups ($p=0.77$).

Diabetes Mellitus (DM) appears to be homogeneously distributed in all three groups ($p=0.07$). Among the young MI group, 52% presented with ST-segment elevation MI (STEMI), and in the elderly MI group, 41.7% had STEMI. In the AMI population compared to the control group, left ventricular ejection fraction as determined by Simpson's formula in echocardiography was significantly lower (49.68±9.84 for the young MI group, 44.84±9.58 for the elderly MI group, 54.27±7.35 for the control group, $p<0.001$).

Laboratory findings

The laboratory test results of patients participating in this study are presented in Table 1. The suPAR plasma concentration value was 2.76 (2.32~3.56) for the young MI group, 3.33 (2.43~4.41) for the elderly MI group, and 2.33 (1.94~3.11) for the control group. In comparison to the control group, a significant increase was seen in the AMI population ($p<0.001$). In the elderly MI group, hs-CRP and ESR were

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significantly higher (p<0.001). In comparison to the control group, the AMI population had significantly higher levels of syntax score, white blood cell, triglycerides, and LDL-C (p<0.001).

Table 1. Patient characteristics and serum parameters

Variable	Young MI n=100	Elderly MI n=127	Control n=105	p value
Age, year	49(44.2~53)	66(62~74)	59(53~66)	<0.001
Sex (male), n (%)	88/88	83/65.4	48/45.7	<0.001
Body Mass Index (kg/m2)	27.6(26.1~29.4)	27.5(25.4~29.8)	28.4(24.9~31.2)	=0.774
DM n (%)	19/19	41/32.3	31/29.5	=0.07
STEMI n (%)	52/52	53/41.7		<0.001
LVEF %	52(45~58)	46(38~54)	58(54.25~58)	<0.001
suPAR	2.76(2.32~3.56)	3.33(2.43~4.41)	2.33(1.94~3.11)	<0.001
Hs-CRP	5(2.6~9.2)	8.7(3.6~21)	3.66(1.57~6.94)	<0.001
ESR	8(4~12.7)	13(7.5~23.5)	9(4.5~15)	<0.001
Syntax Score	12(8~18.75)	22(19~28)		<0.001
Hgb, g/dl	14.7(13.7~15.5)	12.7(11.1~14.2)	13.6(12.3~15)	<0.001
White Blood Cell, 10^3/µl	10.8(9.2~12.9)	10.4(7.7~11.5)	7.3(6~8.4)	<0.001
Platelet, 10^3/µl	227(185~262)	213(163~253)	239(207~286)	=0.001
Creatinine, mg/dl	0.74(0.67~0.86)	0.81(0.67~0.99)	0.72(0.63~0.84)	=0.003
HDL, mg/dl	38(31.2~43)	38(33~44)	43(38~51)	=0.015
LDL, mg/dl	130±39.2	119.70±39.15	112.56±32.80	<0.001

The values are presented as n (%), mean ± standard deviation, or median (25th and 75th percentiles). LDL: low-density lipoprotein, HDL: high-density lipoprotein, Hgb: hemoglobin, Na^+: sodium, K^+: potassium, suPAR: soluble urokinase plasminogen activator receptor, Hs-CRP: high-sensitivity C-reactive protein, ESR: erythrocyte sedimentation rate, LVEF: left ventricular ejection fraction, STEMI: ST-segment elevation myocardial infarction, DM: diabetes mellitus

The assessment of all three groups within the analyzed patient cohort is summarized in Table 2. Significantly higher suPAR plasma concentrations were observed in the elderly MI group compared to the young MI group (p=0.002). Additionally, in the elderly MI group, both hs-CRP and ESR values were significantly elevated when compared to the young MI group (p=0.003, p<0.001, respectively). In contrast, the young MI group exhibited significantly higher suPAR plasma concentrations than the control group (p=0.008). However, no significant differences were observed in the concentration of Hs-CRP and ESR between the group with young MI and the control group (p=0.725, p=0.658, respectively).

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When the elderly MI group was compared to the control groups, in the elderly MI group, the suPAR plasma concentration was significantly higher (p<0.001). In the elderly MI group, Hs-CRP and sedimentation values were significantly higher when both groups were compared (p<0.001 for both).

Table 2. Comparison of groups

	Young MI n=100	**Elderly MI n=127**	**Control n=105**	**p value[a]**	**p value[b]**	**p value[c]**
suPAR	2.76(2.32~3.56)	3.33(2.43~4.41)	2.33(1.94~3.11)	**0.002**	**0.008**	**<0.001**
Hs-CRP	5(2.6~9.2)	8.7(3.6~21)	3.66(1.57~6.94)	**0.003**	0.725	**<0.001**
ESR	8(4~12.7)	13(7.5~23.5)	9(4.5~15)	**<0.001**	0.658	**<0.001**

The values are presented as medians (25th and 75th percentiles). suPAR: soluble urokinase plasminogen activator receptor, Hs-CRP: high-sensitivity C-reactive protein, ESR: erythrocyte sedimentation rate, [a] p value for comparison of young MI and elderly MI, [b] p value for comparison of young MI and control groups, [c] p value for comparison of elderly MI and control groups

Table 3. Correlations of suPAR with other parameters

	suPAR	
	Coefficient(r)	p value
Hs-CRP	0.291	<0.001
ESR	0.234	<0.001
Syntax Score	0.533	<0.001
Age	0.157	=0.004
LV EF %	-0.336	<0.001
Hgb, g/dl	-0.127	0.023
White Blood Cell, $10^3/\mu l$	0.338	<0.001
Creatinine, mg/dl	0.209	<0.001
HDL, mg/dl	-0.262	<0.001
LDL, mg/dl	-0.087	0.118

LDL: low-density lipoprotein, HDL: high-density lipoprotein, Hgb: hemoglobin, suPAR: soluble urokinase plasminogen activator receptor, Hs-CRP: high-sensitivity C-reactive protein, ESR: erythrocyte sedimentation rate, LVEF: left ventricular ejection fraction

Table 3 summarizes the correlation analysis between suPAR and commonly used clinical biomarkers. The results revealed several important relationships. Notably, suPAR was significantly correlated with hs-CRP (r=0.291, p<0.001), grammar score (r=0.533, p<0.001), white blood cell count (r=0.338, p<0.001) and ESR (r= 0.234, p<0.001), age (r=0.157, p=0.004) and creatinine (r=0.209, p<0.001). On the other hand, negative correlations were observed between suPAR and hemoglobin (r=-0.127, p=0.023), left ventricular ejection fraction (LVEF) (r=-0.336, p<0.001) and high-density lipoprotein (HDL) . (r=-0.262, p<0.001).

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In the logistic regression model assessing age, SuPAR, and Hs-CRP as predictors of intermediate-high Syntax Scores (≥23), all three variables showed a significant association in the univariate analysis with a p-value of <0.001. In the multivariate analysis, age remained significant with a p-value of 0.002, Hs-CRP with a p-value of 0.003, and SuPAR with a p-value of <0.001. ESR had a significant association in univariate analysis (p<0.001), but it had no significant association in multivariate analysis (p=0.424). WBC had a significant univariate effect (p=0.038), but it had no significant impact on the multivariate analysis (p=0.146). The association between DM, gender and obesity was considered, but this did not have a significant impact on the statistics (Table 4).

Table 4. Binary logistic regression analysis aiming to determine independent variables associated with intermediate-high SYNTAX score (≥23)

	Univariate Analysis			**Multivariate Analysis**		
Variable	OR	95% CI	P	OR	95% CI	P
SuPAR	3.134	2.219-4.428	<0.001	2.436	1.508-3.937	<0.001
Hs-CRP	1.067	1.036-1.099	<0.001	1.025	1.025-1.122	0.003
ESR	1.043	1.018-1.069	0.001	1.007	0.972-1.040	0.424
Age	1.107	1.048-1.170	<0.001	1.160	1.057-1.273	=0.002
DM status	0.952	0.447-2.028	0.899			
Gender	1.679	0.900-3.130	0.103			
BMI	1.070	0.994-1.153	0.073			
WBC	1.104	1.005-1.213	0.038	1.146	0.953-1.378	0.146
HDL	0.961	0.929-0.994	0.023	0.978	0.921-1.037	0.454
LDL	1.002	0.995-1.009	0.552			

LDL: low-density lipoprotein, HDL: high-density lipoprotein, suPAR: soluble urokinase plasminogen activator receptor, Hs-CRP: high-sensitivity C-reactive protein, ESR: erythrocyte sedimentation rate, DM: Diabetes mellitus

Table 5: Assessing the predictive value of SuPAR and Hs-CRP in determining the severity of coronary artery disease: An evaluation of intermediate-high syntax scores (≥23)

	p	**AUC**	**Cutoff**	**Sensitivity**	**Specificity**
suPAR	<0.001	0.811	3.10	74.7%	69.9%
Hs-CRP	<0.001	0.700	6.5	65.8%	60.2%

suPAR: soluble urokinase plasminogen activator receptor, Hs-CRP: high-sensitivity C-reactive protein,

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In the ROC analysis, the established threshold values for suPAR and hs-CRP for forecasting a Syntax Score of 23 or higher were identified as 3.10 pg/mL and 6.5 mg/dL, respectively. These thresholds exhibited sensitivities of 74.7% for suPAR and 69.9% for hs-CRP, and specificities of 65.8% and 60.2%, respectively.

The respective area under the curve (AUC) metrics were calculated as 0.811 ($p<0.001$) for suPAR and 0.700 ($p<0.001$) for hs-CRP, as depicted in Figure 1 and Table 5.

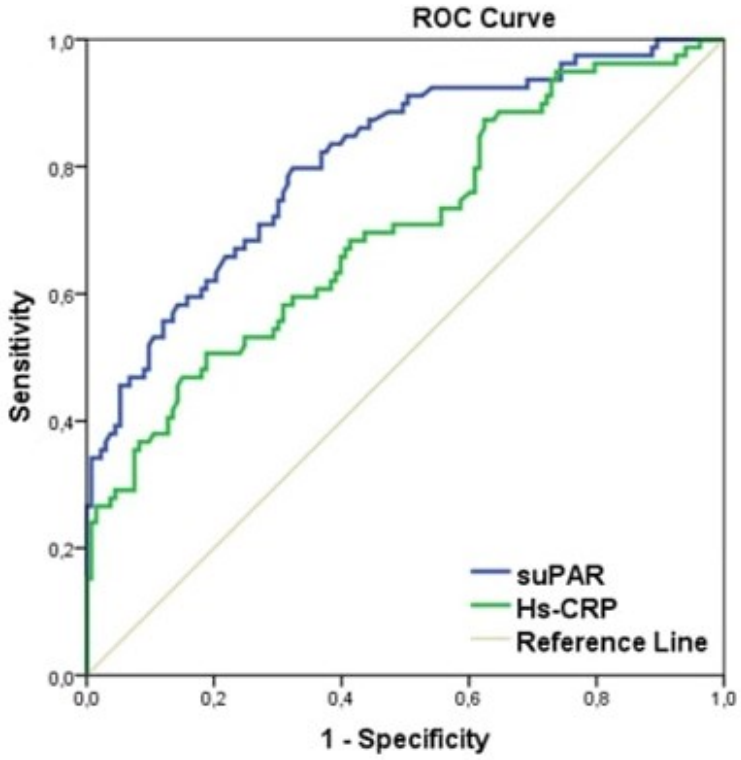

Figure 1. Assessing the predictive value of SuPAR and Hs-CRP in determining the severity of coronary artery disease: An evaluation of intermediate-high syntax scores (≥23)

DISCUSSION

Our main findings from this study indicate that suPAR levels were significantly higher in patients with MI compared to healthy controls. Additionally, it was observed that suPAR concentrations were notably higher in the elderly MI group in comparison to the younger MI group. In a similar vein, Hs-CRP levels demonstrated an increase in the elderly MI group. However, the comparison between the young MI group and the control group did not reveal any statistically significant rise in Hs-CRP levels. A strong positive

correlation was observed with the suPAR syntax score. Levels of suPAR and hs-CRP have been associated with predicting intermediate and high Syntax scores. In this context, ROC analysis revealed that new threshold values of suPAR and Hs-CRP could be useful in predicting an intermediate-high syntax score (≥23), suggesting their potential as simple and repeatable diagnostic tools for assessing the severity of coronary artery disease. Therefore, our findings contribute further to the existing literature on the relationship between suPAR, syntax score, and AMI patients. To our knowledge, this is the first study examining the relationship between suPAR levels and syntax scores in patients with AMI.

An increased syntax score is a globally applied and well-established scoring system that indicates the severity of coronary artery disease. Previous studies have shown that an elevated syntax score is associated with increased cardiovascular mortality and morbidity (14,15). Chronic inflammatory processes have also been shown to contribute to the increase in Syntax Score (16). Chronic inflammation is linked to endothelial dysfunction, vasculopathy, and atherosclerosis (17). In a study by Corban et al., a relationship between suPAR and endothelial dysfunction was established (18). Another study by Hindy et al. demonstrated that suPAR triggers monocyte modulation, thereby inducing atherosclerosis (19). In research conducted by Goodchild et al., suPAR plays a key role in the pathophysiology of atherosclerosis by stimulating pro-inflammatory cytokines and activating neutrophils, monocytes, and endothelial cells (20).

Similarly, previous studies involving hs-CRP have also established its association with endothelial dysfunction, vasculopathy, and atherosclerosis. Research conducted by Zaghloul et al and Mario et al demonstrated the relationship between endothelial dysfunction and hs-CRP (21,22). Additionally, studies by Niknezhad et al, Yu et al, and Swastini et al have linked hs-CRP with the development of atherosclerosis (23-25).

Previous studies have examined the relationship between hs-CRP and the syntax score. In the studies by Rezk et al. and Karadeniz et al., increased hs-CRP levels have been associated with an elevated syntax score in patients with ACS (26,27). Karadeniz et al. found that in patients with ACS, hs-CRP at a cut-off value of 5.77 mg/dL predicted an intermediate-high risk syntax score (≥23) with 75% sensitivity and 69% specificity (27). In our study, similarly, hs-CRP at 6.5 mg/dL was found to predict an intermediate-high syntax score,

demonstrating 65.8% sensitivity and 60.2% specificity ($p<0.001$). However, SuPAR levels were superior to Hs-CRP in both regression and ROC analyses for predicting moderate-to-high Syntax Scores.

In contrast to hs-CRP, it has been demonstrated that the level of suPAR in plasma is not influenced by circadian rhythms and remains more stable under acute stress conditions (8,28). Additionally, suPAR has been shown to be superior to hs-CRP in predicting in-hospital mortality in patients with severe sepsis and septic shock (29).

Numerous studies involving coronary artery disease have emphasized the significance of suPAR. Persson et al.'s research found that elevated plasma suPAR levels are linked to a higher incidence of cardiovascular disease (30). Lyngbæk et al. demonstrated that in patients with AMI, plasma suPAR levels are predictive of all-cause mortality and recurrent MI (28). Furthermore, Eapen et al. revealed that plasma suPAR levels are indicative of the presence of Coronary Artery Disease and can predict future adverse events (31). Importantly, this study also established that in predicting MI and mortality, suPAR operates independently of hs-CRP.

Botha et al. observed a significant increase in suPAR levels over a five-year follow-up in South African black individuals who developed hypertension, indicating an independent association of baseline suPAR levels with the hypertensive group (32). Tahhan et al. found that individuals with peripheral artery disease have higher plasma suPAR levels compared to those with only coronary artery disease, correlating the prevalence of the disease with increased suPAR levels (33). Persson et al. also noted an increase in plasma suPAR levels in patients with carotid plaque, significantly elevating the risk of ischemic stroke and coronary artery disease (34).

In our study, we examined the relationship between suPAR and SYNTAX score. Although it has been shown that suPAR triggers endothelial dysfunction, stimulates pro-inflammatory cytokines, and ultimately leads to atherosclerosis, to our knowledge, there are no studies demonstrating a relationship between suPAR levels and the SYNTAX score, which is used to indicate the severity of coronary artery disease. In this study, suPAR was found to be a strongly independent predictor of an intermediate-high syntax score (≥23). The cut-off for suPAR was identified at 3.10 pg/dl, demonstrating a sensitivity of 74.7% and specificity of 69.9%.

Our study has several limitations. Firstly, its cross-sectional design suggests a need for larger, more comprehensive studies in the future to expand upon our results. Secondly, the age cutoff of 55 years used for grouping patients, while not a definitive boundary, has been utilized in some studies (35-38). The median age in the young MI group was 49, and in the elderly MI group, it was 66, indicating a significant age difference between the two groups. Thirdly, we recognize a major limitation in the gender distribution within the groups, particularly the predominance of male patients in the young MI group. This imbalance is a concern, though it is well-known that the incidence of AMI in younger ages is much higher in males (39,40).

The principal strength of our research, likely to be of significant interest to clinical practitioners, lies in its provision of novel evidence concerning the pronounced impact of suPAR on the syntax score in predicting intermediate-high risk scenarios. This finding introduces a critical line of inquiry in the realm of cardiovascular risk assessment and management.

CONCLUSION

Our study contributes valuable insights into the relationship between inflammatory markers and the syntax score in MI patients. The strong correlation of suPAR with intermediate-high syntax scores offers a novel perspective in cardiovascular risk assessment. Despite its limitations, this research paves the way for future investigations, emphasizing the need for larger, more diverse cohorts to fully elucidate these relationships. Ultimately, these findings could have significant implications for the development of more nuanced diagnostic tools and targeted therapeutic strategies in the management of coronary artery disease.

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Authorship contributions

Concept: M.S.A, A.T. Design: M.S.A, A.T., B.B.A, Data Collection or Processing:M.S.A., A.T.,M.U.Y., K.D. N.A., B.B.A., H.T., O.C.P., A.M.T., Analysis or Interpretation: M.S.A., A.T.,M.U.Y., K.D., H.T., O.C.P., A.M.T., B.Ö., Literature Search: M.S.A., A.T., N.A., B.B.A. B.Ö., Writing: M.S.A, A.T., B.B.A.

Declaration of competing interest

No conflict of interest was declared by the authors.

Ethics

Ethical clearance was granted by Selçuk University's Ethics Committee (Decision No: 2019/92, Date: 08.05.2019).

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REFERENCES

1. Ong S-B, Hernández-Reséndiz S, Crespo-Avilan GE, Mukhametshina RT, Kwek X-Y, Cabrera-Fuentes HA, et al. Inflammation following acute myocardial infarction: multiple players, dynamic roles, and novel therapeutic opportunities. Pharmacol Ther 2018; 186: 73-87.

2. Arbel Y, Strauss BH. suPAR: A cardiac biomarker with a future? Can J Cardiol 2015; 31: 1223-4.

3. Baghai TC, Varallo-Bedarida G, Born C, Häfner S, Schüle C, Eser D, et al. Classical risk factors and inflammatory biomarkers: one of the missing biological links between cardiovascular disease and major depressive disorder. Int J Mol Sci 2018; 19: 1740.

4. Li Y, Ding Y, Zhao Y, Gui Y, Shen Y, Xiang Q. Prognostic value of soluble urokinase-type plasminogen activator receptor in coronary artery disease: A meta-analysis. Eur J Clin Invest 2022; 52: e13867.

5. Torino C, Pizzini P, Cutrupi S, Postorino M, Tripepi G, Mallamaci F, et al. Soluble urokinase plasminogen activator receptor (suPAR) and all-cause and cardiovascular mortality in diverse hemodialysis patients. Kidney international reports 2018; 3: 1100-9.

6. Rasmussen LJH, Petersen JEV, Eugen-Olsen J. Soluble urokinase plasminogen activator receptor (suPAR) as a biomarker of systemic chronic inflammation. Front Immunol 2021; 12: 780641.

7. Estreicher A, Mühlhauser J, Carpentier J-L, Orci L, Vassalli J-D. The receptor for urokinase type plasminogen activator polarizes expression of the protease to the leading edge of migrating monocytes and promotes degradation of enzyme inhibitor complexes. The Journal of cell biology 1990; 111: 783-92.

8. Thunø M, Macho B, Eugen-Olsen J. suPAR: the molecular crystal ball. Dis Markers 2009; 27: 157-72.

9. Wang X-Y, Zhang F, Zhang C, Zheng L-R, Yang J. The biomarkers for acute myocardial infarction and heart failure. BioMed research international 2020; 2020.

10. Sörensen NA, Nikorowitsch J, Neumann JT, Rübsamen N, Goßling A, Hartikainen TS, et al. Predictive value of soluble urokinase-type plasminogen activator receptor for mortality in patients with suspected myocardial infarction. Clin Res Cardiol 2019; 108: 1386-93.

11. Pan Y, Wang L, Xie Y, Tan Y, Chang C, Qiu X, et al. Characterization of differentially expressed plasma proteins in patients with acute myocardial infarction. J Proteomics 2020; 227: 103923.

12. Wlazel RN, Szwabe K, Guligowska A, Kostka T. Soluble urokinase plasminogen activator receptor level in individuals of advanced age. Sci Rep 2020; 10: 15462.

13. Serruys PW, Onuma Y, Garg S, Sarno G, van den Brand M, Kappetein A-P, et al. Assessment of the SYNTAX score in the Syntax study. EuroIntervention 2009; 5: 50-6.

14. Kul S, Akgul O, Uyarel H, Ergelen M, Kucukdagli OT, Tasal A, et al. High SYNTAX score predicts worse in-hospital clinical outcomes in patients undergoing primary angioplasty for acute myocardial infarction. Coron Artery Dis 2012; 23: 542-8.

15. Girasis C, Garg S, Räber L, Sarno G, Morel M-A, Garcia-Garcia HM, et al. SYNTAX score and Clinical SYNTAX score as predictors of very long-term clinical outcomes in patients undergoing percutaneous coronary interventions: a substudy of SIRolimus-eluting stent compared with pacliTAXel-eluting stent for coronary revascularization (SIRTAX) trial. Eur Heart J 2011; 32: 3115-27.

16. Altunova M, Karakayalı M, Kahraman S, Avcı Y, Demirci G, Sevinç S, et al. Systemic Immune-inflammatory index is associated with residual SYNTAX score in patients with st-segment elevation myocardial infarction. Anatolian Journal of Cardiology 2023; 27: 472.

17. Castellon X, Bogdanova V. Chronic inflammatory diseases and endothelial dysfunction. Aging Dis 2016; 7: 81.

18. Corban MT, Prasad A, Nesbitt L, Loeffler D, Herrmann J, Lerman LO, et al. Local production of soluble urokinase plasminogen activator receptor and plasminogen activator inhibitor-1 in the coronary circulation is associated with coronary endothelial dysfunction in humans. Journal of the American Heart Association 2018; 7: e009881.

19. Hindy G, Tyrrell DJ, Vasbinder A, Wei C, Presswalla F, Wang H, et al. Increased soluble urokinase plasminogen activator levels modulate monocyte function to promote atherosclerosis. The Journal of clinical investigation 2022; 132.

20. Goodchild TT, Li Z, Lefer DJ. Soluble urokinase plasminogen activator receptor: From biomarker to active participant in atherosclerosis and cardiovascular disease. The Journal of Clinical Investigation 2022; 132.

21. Zaghloul A, Al-Bukhari TA, Al-Pakistani HA, Shalaby M, Halawani SH, Bajuaifer N, et al. Soluble endothelial protein C receptor and high sensitivity C reactive protein levels as markers of endothelial dysfunction in patients with type 1 and type 2 diabetes mellitus: their role in the prediction of vascular complications. Diabetes Res Clin Pract 2014; 106: 597-604.

22. Maio R, Perticone M, Suraci E, Sciacqua A, Sesti G, Perticone F. Endothelial dysfunction and C-reactive protein predict the incidence of heart failure in hypertensive patients. ESC Heart Failure 2021; 8: 399-407.

23. Niknezhad N, Haghighatkhah HR, Zargari O, Ghalamkarpour F, Younespour S, Niknejad N, et al. High-sensitivity C-reactive protein as a biomarker in detecting subclinical atherosclerosis in psoriasis. Dermatol Ther 2020; 33: e13628.

24. Swastini DA, Wiryanthini IAD, Ariastuti NLP, Muliantara A. Atherosclerosis prediction with high sensitivity C-reactive protein (hs-CRP) and related risk factor in patient with dyslipidemia. Open access Macedonian journal of medical sciences 2019; 7: 3887.

25. Yu H, Rifai N. High-sensitivity C-reactive protein and atherosclerosis: from theory to therapy. Clin Biochem 2000; 33: 601-10.

26. Rezk A, Sarhan M, Elmoghl A. Highly-Sensitive C-reactive Protein Level and its Association with Intermediate and High Syntax Score in cases of Acute Coronary Syndrome. The Egyptian Journal of Hospital Medicine 2019; 75: 2064-70.

27. Karadeniz M, Duran M, Akyel A, Yarlıoğlueş M, Öcek AH, Çelik İE, et al. High sensitive CRP level is associated with intermediate and high syntax score in patients with acute coronary syndrome. Int Heart J 2015; 56: 377-80.

28. Lyngbæk S, Marott JL, Møller DV, Christiansen M, Iversen KK, Clemmensen PM, et al. Usefulness of soluble urokinase plasminogen activator receptor to predict repeat myocardial infarction and mortality in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous intervention. The American journal of cardiology 2012; 110: 1756-63.

29. Suberviola B, Castellanos-Ortega A, Ruiz Ruiz A, Lopez-Hoyos M, Santibañez M. Hospital mortality prognostication in sepsis using the new biomarkers suPAR and proADM in a single determination on ICU admission. Intensive Care Med 2013; 39: 1945-52.

30. Persson M, Engström G, Björkbacka H, Hedblad B. Soluble urokinase plasminogen activator receptor in plasma is associated with incidence of CVD. Results from the Malmö Diet and Cancer Study. Atherosclerosis 2012; 220: 502-5.

31. Eapen DJ, Manocha P, Ghasemzadeh N, Patel RS, Al Kassem H, Hammadah M, et al. Soluble urokinase plasminogen activator receptor level is an independent predictor of the presence and severity of coronary artery disease and of future adverse events. Journal of the American heart association 2014; 3: e001118.

32. Botha S, Fourie CM, Schutte R, Eugen-Olsen J, Schutte AE. Soluble urokinase plasminogen activator receptor and hypertension among black South Africans after 5 years. Hypertens Res 2015; 38: 439-44.

33. Tahhan AS, Hayek SS, Sandesara P, Hajjari J, Hammadah M, O'Neal WT, et al. Circulating soluble urokinase plasminogen activator receptor levels and peripheral arterial disease outcomes. Atherosclerosis 2017; 264: 108-14.

34. Persson M, Östling G, Smith G, Hamrefors V, Melander O, Hedblad B, et al. Soluble urokinase plasminogen activator receptor: a risk factor for carotid plaque, stroke, and coronary artery disease. Stroke 2014; 45: 18-23.

35. Yusuf S, Hawken S, Ôunpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. The lancet 2004; 364: 937-52.

36. Pilote L, Karp I. GENESIS-PRAXY (GENdEr and Sex determInantS of cardiovascular disease: From bench to beyond-Premature Acute Coronary SYndrome). Am Heart J 2012; 163: 741-6. e2.

37. Spatz ES, Curry LA, Masoudi FA, Zhou S, Strait KM, Gross CP, et al. The variation in recovery: role of gender on outcomes of young AMI patients (VIRGO) classification system: a taxonomy for young women with acute myocardial infarction. Circulation 2015; 132: 1710-8.

38. Lichtman JH, Lorenze NP, D'Onofrio G, Spertus JA, Lindau ST, Morgan TM, et al. Variation in recovery: role of gender on outcomes of young AMI patients (VIRGO) study design. Circ Cardiovasc Qual Outcomes 2010; 3: 684-93.

39. Gao H, Wang Y, Shen A, Chen H, Li H. Acute myocardial infarction in young men under 50 years of age: clinical characteristics, treatment, and long-term prognosis. Int J Gen Med 2021: 9321-31.

40. Peters SA, Muntner P, Woodward M. Sex differences in the prevalence of, and trends in, cardiovascular risk factors, treatment, and control in the United States, 2001 to 2016. Circulation 2019; 139: 1025-35.