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Predictive value of platelet/albumin ratio in coronary slow-flow patients

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ABSTRACT

Aims: The pathophysiology of coronary slow flow is not yet fully understood, and it is thought to be related to multiple mechanisms such as endothelial dysfunction, microvascular disorder, and atherosclerosis. In this study, we aimed to investigate the predictive value of platelet/albumin ratio (PAR) in coronary slow flow patients (CSF). In addition, we compared it with other current parameters containing albumin.

Methods: The study was designed retrospectively. The study population included a review of the medical records of 260 people who underwent coronary angiography from 2020 to 2023. The study groups consisted of 108 patients with coronary slow flow and 101 patients with normal coronary arteries who met the inclusion criteria. Various parameters such as demographic data, Platelet/Albumin Ratio and prognostic nutritional index were compared between these two groups. ROC analysis was performed on these parameters.

Results: There was no significant difference between the coronary slow flow and control groups in terms of basic demographic characteristics such as age, gender and smoking, but BMI (p<0.001), LDL (p:0.026) and total cholesterol (p:0.041) ratios were higher in the coronary slow flow group. PAR showed a significant difference between the coronary slow flow group and the control group (p:0.022). Prognostic nutritional index was not significant (p:0.142). ROC curve analysis for the PAR showed a moderate discriminatory ability with an area under the curve (ROC) of 0.592 (95% CI: 0.517-0.667). Conversely, the prognostic nutritional index exhibited limited diagnostic performance with an AUC of 0.441 (95% CI: 0.365-0.522).

Conclusion: These findings suggest that easily measurable PAR may be a valuable biomarker in assessing coronary slow flow, especially in resource-limited settings. Not only does PAR demonstrate a discriminatory ability, but it also outperforms other traditional biomarkers like the prognostic nutritional index (PNI) in this specific patient population.

Keywords: Coronary angiography, blood platelets, albumin, coronary slow flow

INTRODUCTION

Coronary slow flow (CSF) is a condition in which there is a delay in the visualization of the distal blood vessels in the heart, despite the arteries appearing normal in an angiogram. This condition can lead to serious health concerns such as angina, acute coronary syndrome, and sudden death. It is more commonly seen in young male smokers and has a prevalence of 1-5% on coronary angiograms. This condition is linked to microvascular disease and increased resting coronary vasomotor tone.[1-4]

There is no evidence of obstruction in the coronary arteries; however, a delay in the contrast flow is observed in the distal blood vessels. This delay is identified in at least one major coronary artery or confirmed by a TIMI-2 flow (requiring at least three cardiac beats for complete vessel opacification) or a corrected myocardial infarction (TIMI) frame count exceeding 27 frames.[5,6] After excluding other potential etiologies, a diagnosis of CSF should be established.

Patients with CSF experience impaired endothelium-dependent flow-mediated dilatation and resting coronary vasomotor tone, which indicate the presence of microvascular spasm and endothelial dysfunction.[7,8] Furthermore, CSF could potentially lead to atherosclerosis, as it is often linked with elevated resistance in the coronary arteries due to widespread atherosclerotic disease and a greater frequency of metabolic syndrome, which can cause microvascular dysfunction.[9]

Some studies conducted in the past have indicated a potential association between inflammation and serum albumin.[10,11] In a study in which ischemia-modified albumin (IMA) was evaluated in patients with CSF, it was concluded that serum IMA levels increased in the CSF group and IMA may be related to the pathogenesis of CSF.[12] Abnormalities in platelet function may be pathogenetically important in patients with coronary artery disease. Functional abnormalities such as increased spontaneous aggregation and increased release of

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beta-thromboglobulin, fibrinopeptide A, and platelet factor 4 have been described in these patients.[13]

Platelet/albumin ratio (PAR), which stands for platelet and serum albumin ratio, has been proposed as a dependable index for assessing systemic inflammation and immune nutrition status.[14] The reason behind choosing PAR as a marker is that it provides greater consistency in physiological and/or disease types compared to its individual components, namely platelet and serum albumin. In another recent study, PAR independently predicted the risk of MACE in PCI-treated NSTE-ACS patients.[15]

Ultimately, the precise mechanism behind CSF phenomena remains unclear, although inflammation and endothelial dysfunction are believed to be significant factors contributing to its development. In this phenomenon, which cardiologists now encounter more frequently, the PAR can predict important outcomes. In this study, the effects and potential predictive value of PAR on CSF were investigated, which had not been examined before in this patient group.

METHODS

This study is a single-center retrospective study. The ethical guidelines of the 1975 Declaration of Helsinki were followed to prepare the study protocol. The study received ethical approval from the Siirt Training and Research Hospital Ethics Committee (Date: 14.12.2023, Decision No: 2023/12/01/12). Experimental group; 2000 patients who applied to the cardiology outpatient clinics of Siirt Training and Research Hospital between January 2020 - December 2023 and underwent coronary angiography were retrospectively screened and 260 patients were included in the study. Then, the PAR was measured in patients with a coronary slow flow. The study included 108 patients who were diagnosed with CSF and 101 control groups who had normal coronary blood flow, after applying the exclusion criteria.

The study recorded the basic demographic, clinical, and angiographic characteristics of the patients. Hypertension was defined as having a blood pressure of at least three measurements of ≥140/90 mm/Hg or taking antihypertensive drugs. A diagnosis of diabetes was determined by either knowing the diagnosis or having a fasting blood glucose level of ≥126 mg/dl. Smoking status was considered positive for current smokers and those who quit smoking in the last year with a history of smoking more than ten packs of cigarettes.

The study examined various basic biochemical tests and whole blood values of patients who underwent coronary angiography. Lymphocyte, leukocyte, monocyte, platelet, albumin, hemoglobin, creatinine, eGFR, triglyceride, and high-density lipoprotein, total cholesterol, low-density lipoprotein, plasma atherogenic index, systemic inflammatory index, and PAR ratios were recorded. To determine PAR, the study evaluated the platelet count (×109/L) and serum albumin (mg/dL) levels. The calculation involved dividing the platelet count by the serum albumin level and then dividing it by 10 to derive the PAR value. Prognostic nutritional index (PNI) was calculated as follows. PNI=serum albumin (g/L)+0.005×total lymphocyte count (109/L).

The decision to perform coronary angiography was based on the presence of unstable angina and coronary ischemia that were confirmed through an exercise stress test or myocardial perfusion imaging. During the procedure, a standard Judkins technique was used with a 6 Fr Judkins diagnostic catheter and iopromide contrast agent. The coronary arteries were viewed from different angles and positions, ensuring that a standardized dye injection rate was maintained for all patients. At least two angles for the right coronary system and four angles for the left coronary system were recorded on cine using the resulting images.

Three invasive cardiologists evaluated coronary angiograms blindly. The measurement of the sluggish movement in the coronary arteries was accomplished via the Thrombolysis in TIMI flow method. The TIMI value recommended by Gibson et al. for diagnosing CSF was accepted as >27. For every coronary vessel, TIMI values were quantified. To find the corrected TIMI value, the number of TIMI values attributed to the left anterior descending (LAD) artery was divided by 1.7. The control group included patients with stenosis of 10% or less in one or more coronary arteries. Thus, the participants of the study were split into two categories, namely the group with slow flow in the coronary artery and the group with normal flow in the same artery.

The study excluded individuals who had previously experienced undergone percutaneous coronary intervention, acute myocardial infarction, had moderate or low ejection fraction heart failure, hereditary hyperlipidemia, severe kidney or liver dysfunction, severe valvular heart disease, congenital heart disease or pulmonary HT.

Statistical Analysis

The SPSS 22.0 program, created by SPSS Inc. in Chicago, IL, USA, was used to conduct statistical analysis on the data. The dispersion of the data was examined using the Kolmogorov-Smirnov test. Numerical data that had a normal distribution were presented as the mean±standard deviation, while data that did not follow a normal distribution were presented as the median and 25-75% range. Categorical data were expressed as numbers and percentages. Spearman correlation analysis was used to determine the correlation between PAR, SII, and AIP. To evaluate the sensitivity and specificity of PAR and to determine the optimal cut-off point for predicting CSF, the receiver operating characteristic (ROC) curve was utilized. A statistically significant result was considered when the p value was less than 0.05.

RESULTS

The baseline characteristics of the CSF and control groups were compared; there was no significant difference in terms of baseline demographics such as age, gender, and smoking, but the CSF group had higher BMI (p<0,001), LDL (p:0,026), and total cholesterol (p:0,041) ratios. Other data and their results are shown in **Table**.

Our study results revealed that the PAR value significantly differed between the normal coronary and the CSF groups (p: 0.022) (**Figure 1**). PNI showed no significant differences between the CSF group and normal group (p:0.142) (**Table**).

Table. Main demographic, clinical and laboratory characteristics of the coronary slow flow and control group

	Normal group (n=108)	Slow flow (n=101)	p value
Age	56.3 (±9)	57.1 (±10.7)	0.196
Sex (female)	44 (%40)	47 (%46)	0.163
BMI	27.5 (20.5-37.5)	30.5 (18.4-42)	**<0.001**
DM	26 (%25)	31 (%28)	0.740
HT	42 (%41.5)	48 (%44)	0.783
Smoker	26 (%25)	33 (%30)	0.536
Creatinine (mg/dl)	0.86 (0.58-1.6)	0.82 (0.46-1.45)	0.053
Na (mmol/L)	140.0 (131.0-146.0)	139.0 (133.0-145.0)	0.077
K (mmol/L)	4.25 (±0.36)	4.29 (±0.42)	0.532
Albumin	41.5 (34.0-50.0)	43.0 (35.0-48.0)	0.163
Hgb (g/dl)	13.75 (±1.55)	13.35 (±1.46)	0.054
Wbc (10^3/µl)	7.25 (4.13-14.74)	7.3 (4.05-16.2)	0.711
Lymphocyte (10^3/µl)	4.62 (±1.55)	4.62 (±1.55)	0.997
Neutrophil (10^3/µl)	4.55 (2.19-8.6)	4.3 (2.42-9.9)	0.586
Platelet (10^3/µl)	259.5 (147.0-534.0)	249.0 (102.0-409.0)	0.052
LDL (mg/dl)	104.0 (43.5-238.0)	113.6 (49.0-268.0)	**0.026**
HDL (mg/dl)	45.3 (±10.9)	46.4 (±11)	0.469
Total cholesterol	181.0 (112.0-349.0)	173.0 (112.0-304.0)	**0.041**
Triglyceride	156.5 (75.7-399.0)	165.0 (91.0-369.0)	0.359
PAR	6.32 (3.06-12.71)	5.77 (2.35-9.29)	**0.022**
PNI	41.5 (34.0-50.0)	43.0 (35.0-48.0)	0.142

The student t test was applied to those who showed normal distribution, and the Mann Whitney U test was applied to those who did not distribute. The mean standard deviation of the normally distributed and the median min-max values of the non-dispersive ones are given. A p-value< of 0.05 indicates statistical significance.
Abbreviations: PAR: Platelet/albumin ratio, PNI: Prognostic nutritional index, BMI: Body-mass index

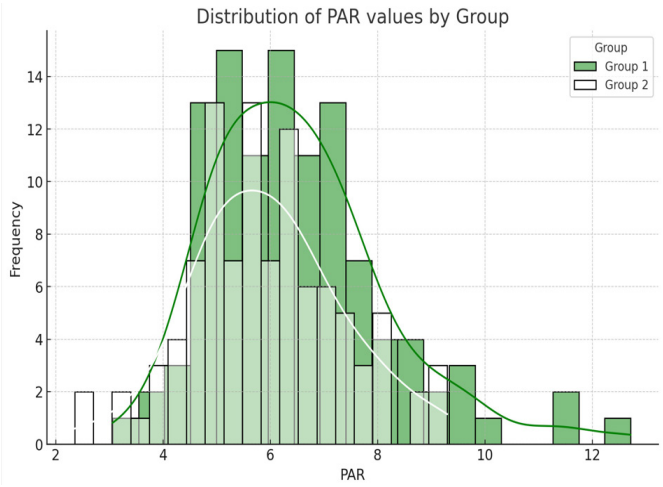

Figure 1. Distribution of the platelet/albumin ratio value in both groups.

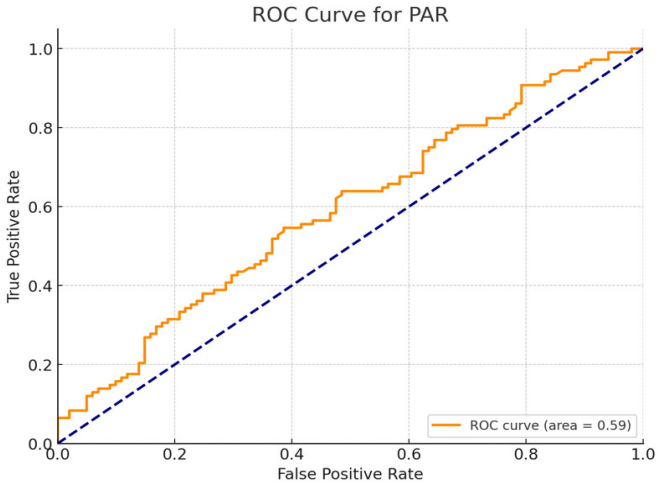

Figure 2. Receiver operating characteristic curve plotted for platelet/albumin ratio

The ROC curve analysis for PAR demonstrated a moderate discriminatory ability with an area under the curve (AUC) of 0.592 (95% CI: 0.517-0.667) (Figure 2). Conversely, PNI displayed limited diagnostic performance with an AUC of 0.441 (95% CI: 0.365-0.522) (Figure 3).

DISCUSSION

In our study, we investigated the predictive value of PAR in CSF patients who had not been previously examined in this patient group. In the literature, it was stated that the PAR is associated with inflammation and thrombosis and can be used as a prognostic indicator in various cardiovascular conditions. The results of our study show that PAR shows a significant difference among CSF patients, which may be a useful biomarker for the understanding and management of

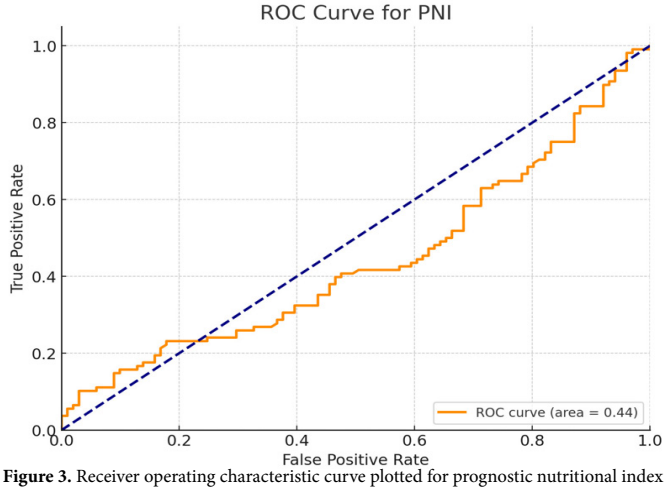

Figure 3. Receiver operating characteristic curve plotted for prognostic nutritional index

CSF. In addition, the difference between the two groups was not observed in the PNI value, which is a relatively new index containing the albumin.

Mean platelet volume (MPV) reflects platelet size and is an indicator of platelet function. High MPV levels may reflect the presence of platelets, which are larger and have a higher tendency to aggregate. In one study, high MPV in patients with stable coronary artery disease (CAD) was associated with chronic inflammation, diabetes, and aortic distenciability.[16] Another study examined the relationship between platelet distribution width and coronary slow flow. CSF was associated with increased PDW, neutrophil-lymphocyte ratio (NLR), hemoglobin (Hb), and red cell distribution width (RDW).[17] In another study investigating the relationship between albumin and CSF, a high uric acid/albumin ratio was found to be an independent predictor of CSF.[18] Some parameters, such as platelet/lymphocyte ratio, have been frequently investigated in non-cardiac conditions and significant results have been obtained.[19] Our study was inspired by these studies and investigated the PAR value in coronary slow flow.

When we look at the latest current studies with PAR, the platelet-albumin ratio has been shown to have a predictive value for cardiac surgery-associated acute kidney injury and in-hospital mortality in intensive care patients.[20] In another study, a higher platelet-albumin ratio was associated with increased rates of adverse cardiovascular events in patients with acute coronary syndrome without ST-segment elevation who underwent percutaneous coronary intervention. It was concluded that the PAR value was directly associated with an increased risk of adverse cardiovascular events, that PAR has moderate capacity as a predictor of MACE incidence, and that PAR can be used as an appropriate and ready prognostic factor for patients with ASCVD, especially patients with ACS.[15] In some non-cardiac conditions, ischemia-modified albumin value was investigated, and significant results were obtained.[21,22]

In our study, PNI was calculated and evaluated to see other outcomes that may be affected by albumin. The PNI has been extensively studied in the context of CAD and prognostic value.[23] Studies show that low levels of PNI are associated with increased mortality and major adverse cardiac events in CAD patients.[24] In addition, in patients with acute myocardial infarction, PNI has been shown to be an independent predictor of all-cause mortality, especially in critical patients admitted to intensive care.[25] Overall, PNI serves as a valuable tool in assessing the nutritional and inflammatory status of CAD patients, helping with risk stratification, and predicting negative outcomes. In our study, PNI did not give significant results in patients with coronary slow flow. It is important that this coronary slow current shows its versatile nature, unlike coronary artery disease.

The pathophysiology of CSF is not yet fully understood, and it is thought to be related to multiple mechanisms such as endothelial dysfunction, microvascular disorder, and atherosclerosis. PAR has not been previously investigated in the group of patients with CSF. It can be hypothesized that PAR may reflect these aspects of CSF, as it is associated with platelet function and inflammation, and this may explain why PAR appears as a potential indicator. In our study, PAR was statistically higher in the coronary slow-flow group. The PAR, composed of two simple measurements, is a valuable prognostic tool for clinicians working with CSF patients. When assessed together, these parameters yield significant and robust results. In conclusion, PAR plays a pivotal role in the diagnosis and management of CSF, reflecting the combined effect of inflammation and platelet activation, and is thus a significant indicator that will guide future research in this area. These findings shed light on how PAR could be integrated into clinical practices and utilized in the management of CSF, providing direction for future studies to better understand its application.

Limitations

This study has some limitations. First of all, since it is a retrospective study, there are restrictions such as choice bias and lack of knowledge. Secondly, the study population is specific to a specific geographic region, and the generalization of the findings to other populations is limited. Third, the role of other potential biomarkers other than PAR and PNI was not studied in this study. Finally, long-term clinical results and their relationship with PAR were excluded from the scope of this study.

CONCLUSION

The findings of this study highlight that the PAR, although composed of a combination of two simple measurements, stands as a valuable prognostic tool for clinicians dealing with CSF patients. Individually, these parameters do not provide meaningful insights into the complex nature of CSF, yet when assessed together, they yield significant and robust results. Furthermore, the lack of a significant difference between the two groups in another albumin-based index, the PNI, underscores the specificity of PAR and its potential importance in the evaluation of albumin in CSF patients.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study received ethical approval from the Siirt Training and Research Hospital Ethics Committee of (Date: 14.12.2023, Decision No: 2023/12/01/12).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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