ORIGINAL RESEARCH

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Role of Platelet Indexes, Neutrophil Lymphocyte Ratio, and Platelet Lymphocyte Ratio in Determining Mortality in Mesenteric Ischemia

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Abstract

Objective: Here is no disease-specific marker that gives a definite result in the diagnosis of mesenteric ischemia (MI). However, high-intensity inflammation and infection are observed in the presence of MI, and there are studies on the subject by evaluating routine Complete blood count examinations. The objective of this study is to present the relationship between platelet indices (PI), platelet/lymphocyte value (PLR), and neutrophil-lymphocyte ratios (NLR) parameters in patients with a diagnosis of MI and the morbidity and mortality of the disease.

Materials and Methods: The study was carried out retrospectively with the information of 59 patients whose data were fully accessible by scanning the patient files. The primary endpoint of the study was the mortality association of PI, PLR, and NLR.

Results: A total of 59 patients with a mean age of 72.5±13.8 (min-max: 39-96) and 44.1% (n=26) female were included in the analysis. While 23.7% of the patients had more than one vascular thrombus, the most common (61.0%) involvement was spinal muscular atrophy. It was observed that the patients underwent surgery at a rate of 39.0%, and the 1-month and 12-month mortality rates were 37.3% and 67.2%, respectively. When 1-month and 1-year periods were evaluated, age was found to be significantly higher in the mortal groups. Other demographic characteristics appear to be statistically similar. In the multiple logistic regression analysis performed for 1-month and 1-year mortality prediction, no statistically significant parameter that could predict 1-month mortality was found. For 1-year mortality, age was found to be an independent predictor.

Conclusion: PI, PLR, and NLR values are not statistically significant in predicting 1-month and 1-year mortality of the disease.

Keywords: Mesenteric ischemia, lymphocytes, neutrophils, platelet activation

Introduction

Mesenteric ischemia (MI) is an inflammatory condition that often comes to the fore in the elderly population, is secondary to the deterioration of the nutrition of the mesenteric visceral organs, and leads to necrosis in the intestinal wall if not treated [1]. Patients are at a higher risk of complications such as peritonitis or sepsis. Although mortality is high, early diagnosis and surgical treatment are lifesaving. However, patients are usually diagnosed late, and the most important reasons for this are delayed admission, the absence of typical disease-specific findings, and the lack of disease-specific and lack of parameters in laboratory evaluations [2,3]. There is no sensitive and specific marker specific to the disease that gives a definite result in the diagnosis of MI. However, high-intensity inflammation and infection are observed in the presence of MI, and there are studies on the subject by evaluating routine complete blood count (CBC) examinations [4,5].

In addition to hemostasis or the inhibition of bleeding, platelets assist the inflammatory process, host-microbial defense, wound healing, angiogenesis, and remodeling. In addition, although there are many pathophysiological pathways in which platelets are involved, the oxidative stress state seen in inflammation can also activate platelets. This shows that platelets can undertake many basic tasks in revealing the pathophysiology of diseases,

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considering the ability of platelets to affect other cells. Platelet indices (PI) are markers that show platelet activation. Thrombocytocrit, mean platelet volume (MPV), and platelet distribution width (PDW) are values that can be measured free of charge in hemogram tests [6].

It has been shown that high platelet/lymphocyte value (PLR) and distribution red cell distribution width (RDW), white blood cells (WBC), neutrophil-lymphocyte ratios (NLR), and advanced age and female gender are associated with the risk of postoperative complications of acute MI [7]. In addition, PLR is a measure of inflammation that correlates with adverse outcomes [8,9]. The NLR value, on the other hand, shows an increased value in patients with diabetes mellitus (DM) in autoimmune inflammatory disease states such as impaired glucose metabolism, ulcerative colitis attacks, hashimoto and euthyroid and/or chronic autoimmune thyroiditis, and this is directly proportional to the strength of autoimmune diseases [10].

The objective of our study was to determine the relationship between PI, PLR, and NLR in patients with MI and their mortality and morbidity.

Materials and Methods

This study was conducted retrospectively by scanning the files of the patients. The study was initiated after ethical approval was obtained from the Ankara City Hospital Ethics Committee (decision no: E2-21-432, date: 21.04.2021). The study was conducted in accordance with the Declaration of Helsinki. Study patients with a diagnosis of MI who were admitted to the emergency department between May 2019 and December 2020 were included in the study. Fifty-nine patients whose data were fully accessible were included in the study. Because the study was conducted as a retrospective file review, informed consent was not obtained from the patients.

A form was prepared for the patient data records. Demographic data [gender, age, comorbid diseases (DM, coronary artery disease (CAD), hypertension (HT))] and history of smoking, blood cell counts, biochemistry, and blood gas parameters of the samples were recorded. Two groups of mortal end-surviving patients were compared.

The devices used in the laboratory for CBC, blood analysis, blood gas, and coagulation parameters were studied on Advia 2120 (Simens/Germany), Siemens atellica solution device (Simens/Germany), RAPIDLAB 1200 Series (Simens/Germany), and Sysmex cs-5100 (Simens/Germany) devices, respectively. MI diagnoses of the patients were made with contrast-enhanced abdominal computed angiography arterial phase 64 slide spiral GE/Revolution CT (General Electric/USA) tomography device.

The data obtained from the patients were compared with their 30-day and 1-year mortality rates. Patients were divided into two groups: deceased (group 1) and alive (group 2). Demographic data, comorbidities, hemogram, biochemistry, blood gas results, and coagulation parameters of the patients in groups 1 and 2 were analyzed by comparing them.

The hospital automation system [Health Integrated Campus (HiCamp)] and national health database (e-pulse) were used to access and record the available data. The data were recorded by 2 emergency specialists, and another emergency medicine specialist checked.

Outcome

The primary outcome of the study was the PI, NLR, and PLR values for the prediction of 1-month and 1-year mortality. The second endpoint was whether demographic data and other blood parameters increased with mortality.

Statistical Analysis

Statistical analysis of the study was performed using the IBM SPSS Statistics 20.0 for the Windows package program. The Shapiro-Wilk test and histogram graphs were used for normality analysis of continuous data. Assuming that the parameters with $p<0.05$ do not satisfy the assumption of normality, these data are presented with median and interquartile ranges. Data that were considered to be normally distributed are presented as mean and standard deviation. The mean and median comparisons between the two independent groups were performed using the independent samples-t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Ratio comparisons in categorical data were performed using Pearson's chi-square test and Fisher's exact test. Multiple logistic regression analysis was used to determine mortality predictors. The level of $p<0.05$ was set as statistically significant.

Results

A total of 59 patients with a mean age of 72.5 [13.8 (min-max: 39-96)] and 44.1 percent (n=26) female were included in the analysis. Although 23.7% of the patients had more than one vascular thrombus, the most common (61.0%) involvement was spinal muscular atrophy). The patients underwent surgery at a rate of 39.0%, and the 1-month and 12-month mortality rates were 37.3% and 67.2%, respectively. When the 1-month and 1-year periods were evaluated, age was found to be significantly higher in the mortal groups. Other demographic characteristics appear to be statistically similar (Table 1).

The distribution of laboratory parameters according to 1-year and 1-month mortality is given in Table 2.

In the multiple logistic regression analysis performed for 1-month and 1-year mortality prediction, no statistically significant parameter that could predict 1-month mortality was found (Table 3). For 1-year mortality, age was found to be an independent predictor (Table 3). Prognostic accuracy statistics are presented in Table 4 to reveal the value of age as a mortality indicator. In addition, the receiver operating characteristic curve for "age" in terms of 1-year mortality estimation is also given (Figure 1).

Discussion

MI is a disease that can progress to necrosis in the intestinal wall and has a high mortality (40-70%). Its causes include embolism in mesenteric vascular structures, thrombosis, and thrombosis of the mesenteric vein [2,11]. Definitive diagnosis is made by methods such as computed tomography or angiography, but sometimes difficulties can be encountered in emergency cases [6].

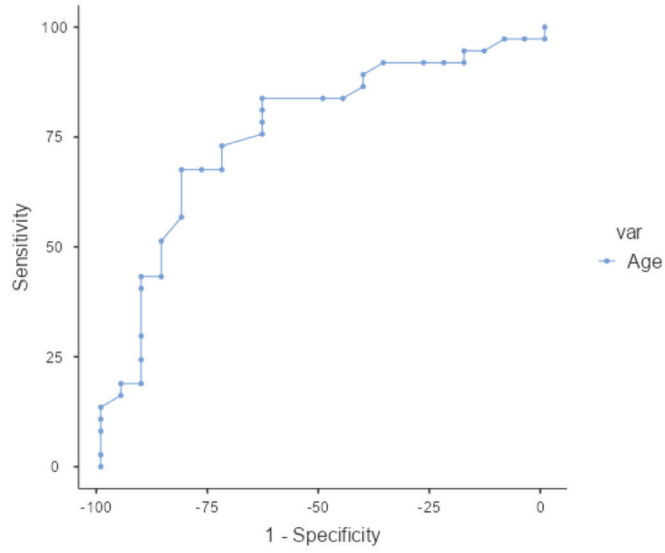

Figure 1. ROC curve for "age" in terms of 1-year mortality prediction

ROC: Receiver operating characteristic

Table 1. Distribution of demographic parameters according to one-month/year mortality

Variables		Survival-1 month			Survival-1 year		
		Survived	Mortal	p value	Survived	Mortal	p value
		n (%)	n (%)		n (%)	n (%)	
Total		37 (62.7)	22 (37.3)	-	22 (37.3)	37 (62.7)	-
Age-mean ± SD		69±12	78±14	0.019*	65±12	77±13	0.001
Gender	Male	22 (66.7)	11 (33.3)	0.479*	12 (36.4)	21 (63.6)	0.869*
	Female	15 (57.7)	11 (42.3)		10 (38.5)	16 (61.5)	
DM		4 (50)	4 (50)	0.455**	2 (25)	6 (75)	0.697**
COPD		4 (57.1)	3 (42.9)	1.000**	3 (42.9)	4 (57.1)	1.000**
CAD		23 (63.9)	13 (36.1)	0.815*	13 (36.1)	23 (63.9)	0.815*
HT		17 (58.6)	12 (41.4)	0.523*	10 (34.5)	19 (65.5)	0.661*
Malignancy		7 (70)	3 (30)	0.729**	1 (10)	9 (90)	0.074**
Blood type-AB0	A	17 (63)	10 (37)	0.133†	13 (48.1)	14 (51.9)	0.259†
	B	6 (85.7)	1 (14.3)		3 (42.9)	4 (57.1)	
	AB	1 (20)	4 (80)		1 (20)	4 (80)	
	0	10 (66.7)	5 (33.3)		3 (20)	12 (80)	
Blood type-Rh	Positive	31 (63.3)	18 (36.7)	1.000**	18 (36.7)	31 (63.3)	1.000**
	Negative	3 (60)	2 (40)		2 (40)	3 (60)	
Localisation-2 or more vascular		7 (50)	7 (50)	0.260*	4 (28.6)	10 (71.4)	0.440*
Localisation	SMA	20 (55.6)	16 (44.4)	0.155*	12 (33.3)	24 (66.7)	0.432*
	IMA	10 (62.5)	6 (37.5)	0.984*	5 (31.2)	11 (68.8)	0.559*
	SMV	9 (100)	0 (0)	0.020**	6 (66.7)	3 (33.3)	0.066**
	TC	6 (42.9)	8 (57.1)	0.079*	3 (21.4)	11 (78.6)	0.160*
Surgery		13 (56.5)	10 (43.5)	0.432*	8 (34.8)	15 (65.2)	0.750*

Age: independent samples t-test (mean ± SD), †The analysis is not reliable due to insufficient expected and observed sample numbers in this parameter. *Pearson chi-square test; n (%), **Fisher's exact test; n (%),

SD: Standard deviation, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, CAD: Coronary artery disease, HT: Hypertension, SMA: Spinal muscular atrophy, IMA: Internal mammary artery, SMV: Superior mesenteric vein, TC: Truncus celiacus

Table 2. Distribution of laboratory parameters according to one-month/year mortality

Variables	Survival-1 month			Survival-1 year		
	Survived	Mortal	p value	Survived	Mortal	p value
	Mean ± SD or med (25-75%)	Mean ± SD or med (25-75%)		Mean ± SD or med (25-75%)	Mean ± SD or med (25-75%)	
WBC	10.7 (8.93-15.11)	16.99 (9.55-28.18)	0.067*	10.6 (8.93-14.28)	15.53 (9.4-21.18)	0.128*
Neu	8.22 (5.8-13.38)	13.4 (7.06-21.53)	0.117*	7.7 (5.1-12.31)	12.34 (7.06-19.09)	0.105*
Lymph	1.23 (1.13-1.77)	1.04 (0.86-1.87)	0.225*	1.45 (1.17-2.04)	1.09 (0.87-1.76)	0.035*
NLR	6.58 (4.3-10.68)	12.97 (3.81-21.01)	0.148*	5.33 (2.62-8.67)	10.13 (4.93-19.98)	0.043*
PLR	202.88 (151.96-313.11)	242.2 (126.87-329.11)	0.633*	185.21 (141.24-277.3)	242.95 (162.2-330.41)	0.158*
Hb	12.98±2.05	12.2±1.95	0.153**	13.41±1.78	12.26±2.08	0.033**
Htc	39.74±6.06	39.44±5.73	0.848**	40.88±6.11	38.88±5.71	0.210**
RDW	15.5 (13.9-16.5)	15.85 (15.1-17.1)	0.249*	15.6 (13.5-16.5)	15.7 (14.7-17)	0.319*
Plt	292 (243-373)	262 (217-340)	0.297*	300 (248-373)	272 (211-340)	0.372*
MPV	8.5 (7.8-9.3)	8.9 (8.6-9.6)	0.022*	8.3 (7.5-8.7)	8.8 (8.3-9.6)	0.021*
PCT	0.26±0.09	0.26±0.13	0.946**	0.26±0.07	0.26±0.12	0.783**
PDW	55.22±8.22	60.78±8.49	0.016**	51.6 (49.9-59.6)	57.9 (55.7-62.5)	0.034*
LUC	0.15 (0.12-0.19)	0.11 (0.08-0.21)	0.257*	0.15 (0.12-0.19)	0.14 (0.09-0.21)	0.619*
NRBC	0.00 (0.00-0.00)	0.00 (0.00-0.00)	0.184*	0.00 (0.00-0.00)	0.00 (0.00-0.00)	0.165*
DNI	0 (0-2.2)	1.7 (0-4.6)	0.123*	0.2 (0-2.2)	1.1 (0-5.25)	0.285*
Urea	39.5 (30-51.5)	71 (47-87)	0.001*	34 (28-43)	52 (45-75)	0.001*
Cre	0.88 (0.72-1.21)	1.24 (1.02-1.64)	0.006*	0.92 (0.74-1.21)	1.12 (0.86-1.53)	0.213*
T-prot	63.42±7.18	62.36±8.97	0.624**	64.38±6.04	62.24±8.7	0.323**
Alb	39.5 (35-42.5)	35.5 (32-38)	0.185*	39.33±4.6	35.92±6.52	0.039**
AST	26 (16.5-34.5)	63 (40-146)	<0.001*	20.5 (16-32)	58 (28-79)	<0.001*
ALT	20 (16-28)	33.5 (25-46)	0.002*	18 (15-25)	28 (17-41)	0.017*
LDH	259 (198-341)	523 (341-852)	<0.001*	222.5 (196-286)	394 (303-708)	<0.001*
Na	138 (135-140)	139 (137-143)	0.137*	138 (135-141)	138 (137-141)	0.441*
K	4.17±0.42	4.55±1.12	0.150**	4.1±0.36	4.43±0.93	0.065**
Cl	103.69±5.73	104.63±7.94	0.625**	106 (104-108)	103 (100-109)	0.643*
PT	13.4 (12.4-14.8)	16.9 (13.1-22.5)	0.020 *	13 (12.1-15.1)	14.3 (13.1-17.6)	0.032*
INR	1.1 (1.1-1.2)	1.4 (1.1-1.7)	0.195 *	1.1 (1.1-1.2)	1.2 (1.1-1.5)	0.128*
D-dimer†	3.28 (1.12-8.1)	13.91 (12.11-15.7)	0.178†	1.97 (1.15-10.66)	5.54 (4.59-12.11)	0.690†
Fibrinojen†	3.01 (2.99-7.57)	5.86 (1.01-6.41)	1.000†	5.28 (2.99-7.57)	4.44 (2.01-6.14)	0.800†
Proc†	0.06 (0.03-0.44)	0.93 (0.16-4.31)	0.008†	0.06 (0.04-0.38)	0.49 (0.15-1.06)	0.087†
CRP	0.06 (0.02-0.14)	0.18 (0.06-0.21)	0.045*	0.05 (0.02-0.11)	0.14 (0.05-0.2)	0.061*
pH	7.4 (7.34-7.46)	7.38 (7.21-7.43)	0.078*	7.38 (7.34-7.44)	7.41 (7.28-7.46)	0.891*
HCO_3	22.19±4.52	19.85±6.39	0.128**	21.44±4.3	21.21±5.89	0.891**
Lct	2.12 (1.48-3.6)	2.97 (2.36-6)	0.005*	2.04 (1.33-3.55)	2.52 (2.08-4.83)	0.103*
BE	-1.8±4.19	-6.01±8.15	0.042**	-2.1 (-5.5-0.5)	-3.1 (-5.6-1.3)	0.868*

†The reliability of the analysis is limited due to the redundancy of missing data, *Mann Whitney-U test, **Independent samples t-test, SD: Standard deviation, WBC: White blood cell, Neu: Neutrophil, Lymph: Lymphocyte, NLR: Neutrophil-lymphocyte ratios, PLR: Platelet/lymphocyte value, Hb: Hemoglobin, Htc: Hematocrit, RDW: Distribution diameter of red blood cells, Plt: Platelet, MPV: Mean platelet volume, PCT: Thrombocytocrit, PDW: Platelet distribution width, LUC: Large unstained cells, NRBC: Nucleated red blood cell, DNI: Do-not-intubate, Cre: Carbapenem-resistant Enterobacteriaceae, Alb: Albumin, AST: Aspartat aminotransferaz, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, PT: Prothrombin time, INR: International normalized ratio, CRP: C-reactive protein, Lct: Lactase, BE: Base excess, T-prot: Total protein, Proc: procalcitonin

Considering the demographic data of the studies conducted by Klar et al. [2] and Acosta [12], it has been reported that its incidence and mortality increase with advanced age. The data of this study are statistically similar to those in the literature. While Acosta [12], reported that the female-male ratio was equal, there was no statistical difference in our study, which is similar to the literature.

In a review by Klar et al. [2], they stated that heart failure, atrial fibrillation, CAD, and primary HT are among the predisposing factors of the disease. The most common chronic and serious diseases of the patients included in the study, such as DM, chronic obstructive pulmonary disease, CAD, HT, and malignancy, were recorded, and it was concluded that it was not statistically significant at this stage.

In a study conducted by Kisaoglu et al. [5], it was reported that RDW, WBC, lactate dehydrogenase (LDH), and blood urea nitrogen values increased significantly. RDW, WBC, LDH, and urea values obtained in this study were statistically inconsistent.

There are many studies in the literature suggesting that high MPV values are associated with mortality and reporting that mortality is higher in patients with patients [13-16]. In this study, however, MPV values did not show compatibility in predicting both 1-month and 1-year mortality. Wang et al. [17], reported in a study that high PLR, NLR, and concomitant coronary heart disease were associated with poor outcomes in the prognosis of patients. In a retrospective study conducted by Karadeniz et al. [18], they showed that PLR, NLR, PDW, and RDW values were significantly higher in MI, but lymphocyte values were significantly lower. In another study, it was reported that PLR and PDW values showed a positive correlation in recognizing MI [19]. It was also revealed that the NLR value was also diagnostically significant [20]. However, the values recorded in this study were statistically insignificant. There is a study in the literature reporting that PLR is a significant predictor of 1-month mortality in patients who come to the emergency department with acute MI, but NLR is not as significant as PLR [21]. The results of this study are inconsistent in terms of PLR and support the literature in terms of NLR.

In a retrospective study, Toptas et al. [4], reported that the neutrophil and lymphocyte levels were significantly higher in the control group, but the platelet count was similar between the two groups. Although the data of this study do not support the data of the current study in terms of neutrophil and lymphocyte counts, they are similar in that the platelet count was also insignificant in our study. In the same study, it was found that PLR, NLR, and C-reactive protein (CRP) values were higher than those in the control group, and there was a

Table 3. Regression model for 1-month and 12-months mortality

Model coefficients-survival-1 month					Model coefficients-survival-12 months				
			95% Confidence interval					95% Confidence interval	
Predictor	**p**	**Odds ratio**	**Lower**	**Upper**	**Predictor**	**p**	**Odds ratio**	**Lower**	**Upper**
Intercept	0.117	2525.720	0.142	4.50E+07	**Intercept**	0.334	295.073	0.003	3.02E+07
Age	0.340	0.962	0.889	1.040	**Age**	0.011	0.888	0.809	0.974
Cre	0.453	0.480	0.071	3.260	**Lymph**	0.529	1.466	0.446	4.824
ALT	0.782	0.996	0.968	1.020	**Hb**	0.260	1.347	0.803	2.259
PT	0.434	0.970	0.899	1.050	**MPV**	0.610	0.788	0.316	1.964
CRP	0.440	0.007	2.78E-08	1935.77	**Alb**	0.290	1.092	0.928	1.286
Lct	0.075	0.610	0.354	1.050	**AST**	0.111	0.926	0.843	1.018
PDW	0.979	1.002	0.886	1.130	**ALT**	0.389	0.954	0.858	1.062
					PT	0.734	1.011	0.949	1.078
Note: Estimates represent the log odds of "survival" vs. "mortal"					Note: Estimates represent the log odds of "survival" vs. "mortal"				

Cre: Creatin, ALT: Alanine aminotransferase, PT: Prothrombin time, CRP: C-reactive protein, Lct: Lactase, PDW: Platelet distribution width, Lymph: Lymphocyte, Hb: Hemoglobin, MPV: Mean platelet volume, Alb: Albumin, AST: Aspartat aminotransferaz

Table 4. Diagnostic statistics for "age" in terms of 1-year mortality prediction

Scale: age					
Cutpoint	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**Youden's index**
66	83.8	63.6	79.5	70.0	0.474
72	73.0	72.7	81.8	61.5	0.457
77	67.6	81.8	86.2	60.0	0.494

AUC: 0.763 (95% CI: 0.635-0.891); p=0.001, PPV: Positive predictive values, NPV: Negative predictive values, AUC: Area under the curve, CI: Confidence interval

positive correlation between PLR and CRP and between NLR and CRP [4]. However, this study is not similar to other studies.

When we look at the above studies, it is seen that there are contradictory results in studies with PI in the literature. Therefore, it is difficult to establish a meaningful and precise link between diseases and PI. Significant values are likely to occur in these values in the chronic inflammatory processes of the patients. However, because the activation of platelets varies in acute inflammatory events, it is not reflected in the laboratory with meaningful results. In addition, the development of MI on a background such as atherosclerosis and atrial fibrillation suggests that these patients may receive antiaggregant and anticoagulant therapy. This situation causes variability in platelet count and activation. Therefore, PI may not have shown effective results in acute inflammatory and thromboembolic conditions. As a result, PI, PLR, and NLR values are suspicious of the diagnosis of MI, and their relationship with mortality was significant in some of the previous studies, whereas it was insignificant in others. None of the parameters included in our study, except advanced age, were statistically significant in predicting mortality.

Study Limitations

Among the limitations of the study, it is of great importance that it is retrospective. In addition, it is not known how the blood is taken from the patients and the current conditions, the way and time of blood reaching the laboratory is not known, and it is not known whether all these are fully in accordance with the standards.

Conclusion

It is significant in 1-month and 1-year mortality in advanced age patients in MI patients. However, PI, NLR, and PLR values have no clinical or statistical significance in predicting the mortality of patients.

Ethics

Ethics Committee Approval: The study was initiated after ethical approval was obtained from the Ankara City Hospital Ethics Committee (decision no: E2-21-432, date: 21.04.2021).

Informed Consent: Informed consent was not obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.D., A.B.E., A.Ş., G.K.Ç., Concept: S.D., A.B.E., A.Ş., G.K.Ç., Design: S.D., A.B.E., A.Ş., G.K.Ç., Data Collection or Processing: S.D., A.B.E., A.Ş., G.K.Ç., S.Ö., B.I., Analysis or Interpretation: S.D., A.B.E., A.Ş., S.Ö., B.I., Literature Search: S.D., A.B.E., A.Ş., S.Ö., B.I., Writing: S.D., A.B.E., A.Ş., S.Ö., B.I.

Conflict of Interest: No conflicts of interest were declared by the authors.

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