



The role of erythrocyte distribution width in predicting poor outcomes in geriatric patients with acute pancreatitis

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ABSTRACT

Introduction and aim. In our study, our aim was to evaluate the relationship between red cell distribution width (RDW) values and prognosis in geriatric patients with acute pancreatitis.

Material and methods. Patients over the age of 65 and diagnosed with acute pancreatitis who applied to the Emergency Department of Ümraniye Training and Research Hospital between 16.07.2021 and 15.05.2022 were included in our retrospective study. RDW levels were recorded using the hospital data system.

Results. Our study included 184 patients, 19 (10.3%) of which died. Sixty-five percent of our patients were women. The mean hospital stay was 5 days (from 3 to 9). A statistically significant relationship was also observed between high RDW and mortality ($p=0.006$). The diagnostic test performance analyses of CRP, and RDW in predicting mortality revealed that they were statistically significant in predicting mortality, with the AUC value being calculated as 0.66 (0.6061–0.7368) for CRP, with a cut-off value of 22; and 0.69 (0.6909–0.7368) for RDW, with a cut-off value of 14.5 ($p=0.019$, $p=0.006$, respectively).

Conclusion. Hematological parameters can help predict a prognosis in patients with acute pancreatitis. Although RDW is not statistically more significant than CRP, it can be used as a prognostic marker in patients with acute pancreatitis.

Keywords. acute pancreatitis, CRP, RDW

Introduction

Acute pancreatitis is a sudden onset inflammatory disease of the pancreas that can develop due to many illnesses, especially gallstones and alcohol use.^{1,2} In the inflammatory process, an increase in the number of neutrophils may be expected, as well as a decrease in lymphocytes in conjunction with physiological disorders.²⁻⁴ Acute pancreatitis can occur locally or cause widespread organ dysfunction. Mortality can reach up to 50% in patients with severe acute pancreatitis. The reason for this is multiple organ dysfunction syndrome (MODS).^{5,6} It is possible, however, to prevent

organ failure and mortality with early and effective treatment.⁶

In order to predict the prognosis, studies on albumin, white blood cell (WBC), and C-reactive protein (CRP) were performed in patients with pancreatitis.⁷⁻⁹ Hematological parameters have been the subject of studies on acute pancreatitis and many other inflammatory diseases.^{2,9} Red cell distribution width (RDW), which may increase due to inflammation, ischemia, and hypoxia, is a measure of the mean corpuscular/erythrocyte volume calculated using the standard deviation of erythrocyte volume heterogeneity.^{10,11} Some studies have

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previously been conducted to evaluate the association of RDW with a poor prognosis in patients with pancreatitis, mostly comparing patients with pancreatitis with patients without pancreatitis.^{2,6,9,12-14} The relationship of RDW with mortality was also investigated in patients with acute coronary syndrome, acute appendicitis with inflammation similar to acute pancreatitis, infective diseases such as COVID-19, and malignancies.^{11,15-17}

It can be quite difficult to predict the prognosis of acute pancreatitis, which has many causes, including idiopathic, especially in geriatric patients. Geriatrics may not be able to apply to the hospital with common symptoms, and this may prolong the clinician's time to make the diagnosis. In studies investigating the relationship of RDW with prognosis in patients with acute pancreatitis, the geriatrics group was not evaluated separately.¹⁵ In addition, we found that CRP, an inflammatory parameter, was investigated in patients with acute pancreatitis, and again, it was not evaluated separately in the geriatric patient group.⁹

Although it has been predicted that RDW may be effective in ischemic diseases and inflammatory processes, we think that evaluating the relationship of RDW with a prognosis in geriatrics with acute pancreatitis and its comparison with CRP in the same study will contribute to the literature.

Aim

In our study, our primary aim was to evaluate the relationship between RDW and prognosis in geriatric patients diagnosed with acute pancreatitis, and our secondary aim was to compare the relationship between RDW and CRP and prognosis in geriatric patients diagnosed with acute pancreatitis.

Material and methods

Ethical approval

The instant study was carried out with the permission of the University of Health Sciences, Ümraniye Education and Research Hospital Ethics Committee (Date: 23/06/2022, Decision No: B.10.1.TKH.4.34.H.GP.0.01/215).

Study design

Patients who applied to the Emergency Department of Ümraniye Training and Research Hospital between 16.07.2021 and 15.05.2022 were included in our retrospective study.

Study population

The study included patients over the age of 65 who were admitted to the emergency department and were considered to have acute pancreatitis, who were confirmed clinically and via laboratory and radiologically, whose hemogram parameters were measured and registered in

the emergency department. Those with acute pancreatitis findings on tomography were included in the study, while those with only clinical findings and only elevated amylase and/or lipase parameters but no findings on tomography were excluded from the study. Patients with incomplete data on mortality, with chronic pancreatitis, under 65 years of age, and who refused to participate in the study were excluded.

Data collection

Age (year), comorbid diseases, WBC count, neutrophil count, monocyte count, lymphocyte count, platelet count, hemoglobin, hematocrit count, RDW, mean platelet volume (MPV), platelet distribution width (PDW), and sodium, potassium, glucose, blood urea nitrogen (BUN), creatinine, albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), CRP, amylase, lipase levels were recorded. Length of hospital stay, ward, intensive care stays, and 30-day mortality rates were also recorded. Length of hospital stay, and intensive care unit admission rates were recorded using the hospital data system. According to their survival status, the patients were divided into two groups – survivors and those who died – according to the National death notification system in Turkey. The examinations and data of patients who attended the emergency department were used.

Statistical analysis

The categorical data was done using the fisher exact test and chi-square test. Quantitative variables were presented as median and interquartile range (IQR, 25th-75th percentile) values, and the Mann-Whitney test was used in analyzing the paired groups. During this analysis, the area under the curve (AUC) values were calculated, and the sensitivity, specificity, accuracy, and 95% confidence interval (CI) data were analyzed. The AUC values of the parameters were calculated and tested mutually for significance with the DeLong quality test. Statistical analysis was performed using SPSS v. 26.0 (IBM, Chicago, IL, USA). Statistical significance was accepted as $p < 0.05$.

Results

Our study included 184 patients, 19 (10.3%) of which died. Sixty-five percent of our patients were women. The mean hospital stay was 5 days (between 3 and 9). There was a statistically significant correlation between hospitalized patients and mortality ($p=0.001$). Comorbid disease was present in 84% of the patients. While age values were found to be higher in the non survivor group ($p=0.023$), there was no statistically significant relationship between comorbidity and mortality ($p=0.19$). Amylase and lipase values were higher in living patients ($p=0.039$, $p=0.01$, respectively). A statistically significant correlation was observed between high BUN and

creatinine and mortality ($p=0.004$, $p=0.001$, respectively) (Table 1).

Table 1. The relationship of demographic characteristics of geriatric patients with acute pancreatitis with mortality*

Characteristic	n=184	Survivor n=165 (89.7%)	Non-Survivor n=19 (10.3%)	p-value
Age	76 (70, 83)	75 (70, 82)	83 (78, 86)	0.023
Gender, n (%)				0.026
Female	120 (65%)	112 (68%)	8 (42%)	
Male	64 (35%)	53 (32%)	11 (58%)	
LOHS	107 (54, 206)	112 (54, 204)	91 (60, 218)	0.78
Length of Stay Days	5 (3, 9)	5 (3, 9)	4 (3, 10)	0.72
LOHS_Dicotom, n (%)				0.6
<= 7 Days	126 (68%)	114 (69%)	12 (63%)	
> 7 Days	58 (32%)	51 (31%)	7 (37%)	
ED Outcome, n (%)				0.001
Disposition	25 (14%)	25 (15%)	0 (0%)	
Admission to Services	146 (79%)	134 (81%)	12 (63%)	
Admission to ICU	13 (7.1%)	6 (3.6%)	7 (37%)	
Comorbidities, n (%)				0.19
Hypertension	132 (72%)	120 (73%)	12 (63%)	0.38
Diabetes mellitus	65 (35%)	62 (38%)	3 (16%)	0.06
Malignancy	25 (14%)	22 (13%)	3 (16%)	0.73
Hyperlipidemia	88 (48%)	81 (49%)	7 (37%)	0.31
Alzheimer	13 (7.1%)	11 (6.7%)	2 (11%)	0.63
COPD	27 (15%)	23 (14%)	4 (21%)	0.49
Ischemic heart disease	66 (36%)	59 (36%)	7 (37%)	0.93
Asthma	28 (15%)	27 (16%)	1 (5.3%)	0.32
Heart failure	24 (13%)	22 (13%)	2 (11%)	>0.99
Chronic renal failure	22 (12%)	19 (12%)	3 (16%)	0.71
Cerebrovascular disease	19 (10%)	18 (11%)	1 (5.3%)	0.7

* LOHS – length of hospital stay; ED – emergency department; ICU – intensive care unit; COPD – chronic obstructive pulmonary disease

There was a statistically significant relationship between low hemoglobin and hematocrit and mortality ($p=0.012$, $p=0.005$, respectively). A statistically significant relationship was also observed between high RDW and mortality ($p=0.006$). No statistically significant correlation was observed between hematological parameters other than hemoglobin, hematocrit and RDW, and mortality. A statistically significant correlation was found between low albumin and high CRP and mortality ($p=0.001$, $p=0.019$, respectively) (Table 2).

The diagnostic test performance analyses of albumin, CRP, and RDW in predicting mortality revealed that they were statistically significant in predicting mortality, with the AUC value being calculated as 0.78 (0.5789–0.8606) for albumin, with a cut-off value of 35.8; 0.66 (0.6061–0.7368) for CRP, with a cut-off value

of 22; and 0.69 (0.6909–0.7368) for RDW, with a cut-off value of 14.5 ($p=0.001$, $p=0.019$, $p=0.006$ respectively) (Table 3, Fig. 1, Fig. 2).

Table 2. Relationship between laboratory parameters and mortality in geriatric patients with acute pancreatitis*

Characteristic	n=184	Survivor n=165 (89.7%)	Non-Survivor n=19 (10.3%)	p-value
Median (IQR); n (%)				
ALT (IU/L)	80 (26, 202)	82 (27, 201)	62 (22, 308)	0.94
Albumine (g/dL)	40.1 (36.9–42.3)	40.7 (37.3–42.7)	35.2 (33.1–38.5)	0.001
Amylase (U/L)	712 (299–1.502)	741 (324–1.545)	348 (209–878)	0.039
AST (IU/L)	130 (40–277)	133 (42–253)	125 (28–511)	0.87
CRP (mg/L)	13 (4–47)	11 (3–44)	37 (16–58)	0.019
Glucose (mmol/L)	137 (110–181)	137 (111–181)	133 (108–174)	0.55
BUN (mg/dL)	41 (33–62)	40 (32–60)	62 (51–126)	0.004
Creatinine (mg/dL)	0.96 (0.77–1.42)	0.93 (0.76–1.27)	1.80 (1.02–2.57)	0.001
Lipase (U/L)	1.437 (606–3.566)	1.698 (641–4.123)	696 (409–1.364)	0.01
Potassium (mEq/L)	4.4 (4.1–4.72)	4.4 (4.1–4.7)	4.5 (4.2–5.1)	0.22
Sodium (mEq/L)	138 (136–140)	138.9 (136–140)	137 (133.8–138)	0.063
Total bilirubin (mg/dL)	1.29 (0.63–2.78)	1.27 (0.62–2.59)	1.58 (1.00–3.66)	0.38
Direct bilirubin (mg/dL)	0.63 (0.22–1.44)	0.62 (0.24–1.42)	0.71 (0.13–2.2)	>0.99
Indirect bilirubin (mg/dL)	0.56 (0.28–1.01)	0.56 (0.28–1)	0.81 (0.28–1.46)	0.32
WBC ($10^3/\mu\text{L}$)	10.7 (8–13.9)	10.5 (8.0–13.3)	12.4 (8.5–16)	0.3
Neutrophil ($10^3/\mu\text{L}$)	8.6 (6.1–12.1)	8.5 (6.1–11.5)	10.7 (6.1–15.3)	0.31
Monocyte ($10^3/\mu\text{L}$)	0.48 (0.33–0.65)	0.48 (0.32–0.65)	0.47 (0.36–0.69)	0.66
Lymphocyte ($10^3/\mu\text{L}$)	1.11 (0.66–1.64)	1.15 (0.68–1.64)	0.87 (0.5–1.5)	0.17
Hemoglobin (g/dl)	12.60 (11.3–13.60)	12.70 (11.5–13.70)	11.20 (9.55–12.9)	0.012
Hematocrit (%)	38.5 (34.8–41.6)	38.9 (35.5–41.6)	33.5 (29.6–39)	0.005
RDW (fl)	14.05 (13.50–14.93)	14.00 (13.50–14.60)	15.30 (14.25–15.95)	0.006
Platelet ($10^3/\mu\text{L}$)	251 (194–308)	251 (194–304)	253 (214–317)	0.29
MPV (fl)	9.5 (8.8–10.6)	9.5 (8.8–10.6)	9.10 (8.55–10.9)	0.61
Pct ($\mu\text{g/L}$)	0.24 (0.19–0.29)	0.24 (0.19–0.29)	0.23 (0.21–0.31)	0.31
PDW (fl)	16.1 (15.9–16.5)	16.1 (15.9–16.5)	16.2 (15.95–16.45)	0.87

* ALT – alanine aminotransferase; AST – aspartate aminotransferase; CRP – C-reactive protein; BUN – blood urea nitrogen; WBC – white blood cell; RDW – red cell distribution width; MPV – mean platelet volume; PDW – platelet distribution width

Table 3. ROC analysis for laboratory parameters for 30-day mortality

	Cut-off point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	p-value
Albumin (g/dL)	35.8	86.06%	57.89%	94.67%	32.35%	0.78	0.001
Amylase (U/L)	482	63.64%	68.42%	94.59%	17.81%	0.64	0.039
Lipase (U/L)	871	69.7%	63.16%	94.26%	19.35%	0.68	0.01
Hemoglobin (g/dl)	10.5	91.52%	42.11%	93.21%	36.36%	0.68	0.012
Hematocrit (%)	34.9	78.79%	63.16%	94.89%	25.53%	0.7	0.005
RDW (fl)	14.5	73.68%	69.09%	21.54%	95.8%	0.69	0.006
Creatinine (mg/dL)	1.78	52.63%	86.06%	30.30%	94.04%	0.74	0.001
BUN (mg/dL)	49.22	78.95%	63.03%	19.74%	96.30%	0.7	0.004
CRP (mg/L)	22	73.68%	60.61%	17.72%	95.24%	0.66	0.019

* RDW – red cell distribution width; BUN – blood urea nitrogen; CRP – C-reactive protein

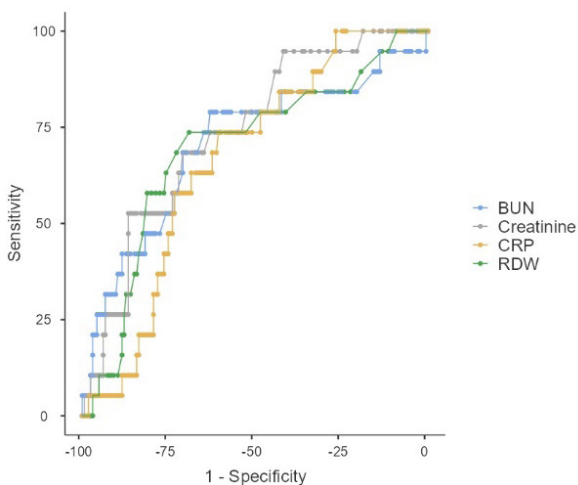


Fig. 1. Parameters associated with mortality as their values increase

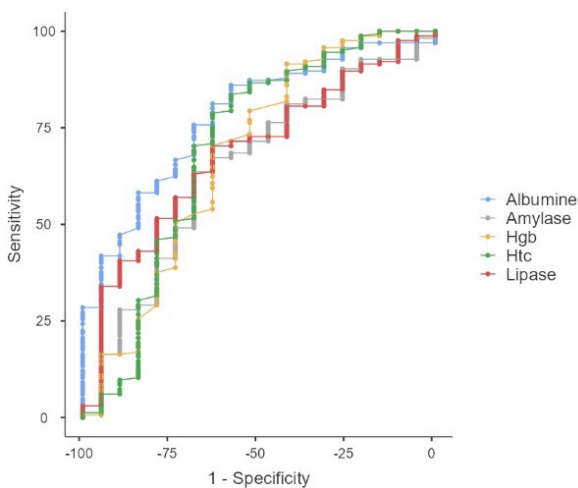


Fig. 2. Parameters associated with mortality as their values decrease

The effect of laboratory parameters on mortality according to cut-off values was also evaluated separately and is shown in Table 4.

In the cox regression analysis performed with age and laboratory parameters, there was a statistically significant relationship between albumin, hemoglobin, hematocrit, RDW and BUN and mortality in the univariate analysis (p=0.002, p=0.026, p=0.036, p=0.028, p=0.004 respectively) (Table 5).

Table 4. Comparison of the effects of laboratory values on cut-off values and mortality*

	n=184	Survivor n=165 (89.7%)	Non-Survivor n=19 (10.3%)	Odds Ratio	95% CI		p-value
					Lower	Upper	
Albumine < cut-off point (g/dL)	45 (24.5%)	33 (20%)	12 (63.15%)	6.86	2.5	18.77	<0.001
Amylase < cut-off point (U/L)	74 (40.2%)	61 (37%)	13 (68.42%)	3.69	1.34	10.22	0.008
Lipase < cut-off point (U/L)	63 (34.23%)	51 (31%)	12 (63.15%)	3.83	1.43	10.30	0.005
Hemoglobin < cut-off point (g/dl)	48 (26.08%)	38 (23%)	10 (52.63%)	3.71	1.41	9.80	0.005
Hematocrit < cut-off point (%)	39 (21.2%)	28 (16.9%)	11 (57.9%)	6.73	2.48	18.24	<0.001
RDW > cut-off point (fl)	58 (31.5%)	45 (27.27%)	13 (68.42%)	5.78	2.07	16.12	<0.001
Creatinine > cut-off point (mg/dL)	61 (33.15%)	48 (29.09%)	13 (68.42%)	5.28	1.90	14.70	<0.001
BUN > cut-off point (mg/dL)	76 (41.3%)	61 (37%)	15 (78.94%)	6.39	2.03	20.14	<0.001
CRP > cut-off point (mg/L)	64 (34.78%)	52 (31.51%)	12 (63.15%)	3.73	1.39	10.01	0.006

* RDW – red cell distribution width; BUN – blood urea nitrogen; CRP – C-reactive protein

Table 5. Cox regression analysis of age and laboratory parameters*

	Univariate			Multivariate				
	Hazard Ratio	95% CI Lower	95% CI Upper	p value	Hazard Ratio	95% CI Lower	95% CI Upper	p value
Age	1.04	0.985	1.099	0.16	1.008	0.948	1.073	0.798
Albumin (g/dL)	0.863	0.785	0.948	0.002	0.899	0.792	1.02	0.098
Amylase (U/L)	0.999	0.999	1	0.125	1	0.999	1.001	0.727
Lipase (U/L)	1	0.999	1	0.078	1	0.999	1	0.399
Hemoglobin (g/dl)	0.748	0.579	0.966	0.026	0.639	0.215	1.905	0.422
Hematocrit (%)	0.912	0.838	0.994	0.036	1.089	0.755	1.572	0.648
RDW (fl)	1.202	1.02	1.415	0.028	1.142	0.917	1.423	0.236
Creatinine (mg/dL)	1.137	0.958	1.35	0.142	0.74	0.471	1.162	0.191
BUN (mg/dL)	1.005	1.002	1.009	0.004	1.008	1	1.017	0.061
CRP (mg/L)	1.004	0.997	1.012	0.259	1	0.989	1.011	0.968

* RDW – red cell distribution width; BUN – blood urea nitrogen; CRP – C-reactive protein

Discussion

In our study, we found that RDW with CRP can predict a prognosis in patients with acute pancreatitis. When we looked at the AUC values, we found that RDW was superior to CRP in predicting mortality. There was no statistically significant relationship between neutrophil and lymphocyte mortality, which are inflammatory markers. In the Cox regression analysis, which included age and laboratory parameters, RDW and CRP were not statistically significant in the multivariate analysis; We observed that RDW can be used as a mortality marker in univariate analysis. CRP was not statistically significant in the univariate analysis. As far as we could detect, there was no study comparing RDW and CRP in predicting mortality. Since acute pancreatitis is an inflammatory disease, CRP; albumin and kidney function tests because it can cause fluid and electrolyte disorders, and AST, ALT, bilirubin and amylase, lipase values due to biliary tract diseases were examined in our study. While hemoglobin and albumin were significantly lower in non-survivors; BUN and creatinine were significantly higher as we expected. Many studies have been conducted to investigate the effect of RDW on prognosis in acute pancreatitis.^{2,6,8} In a study examining patients with acute pancreatitis due to gallstones, it was found that the RDW level was statistically significantly higher in patients with severe acute pancreatitis.² A study in which Pian et al. examined 169 acute pancreatitis patients showed that, in addition to high neutrophils and low lymphocyte levels in patients with severe acute pancreatitis, high RDW values also creates a statistically significant difference in mild acute pancreatitis. In the same study, low albumin was also found to be associated with a poor prognosis.⁶ In another retrospectively planned study, low albumin, high WBC, and high RDW were associated with a poor prognosis.⁸ Hao et al., in an acute pancreatitis study of 210 patients, showed that high RDW and low albumin may be indicators of a poor prognosis.¹² Another meta-analysis stated that RDW could be used as an easily measurable parameter in predicting the prognosis of acute pancreatitis.¹³ In another study examining hematological parameters and inflammatory markers, neutrophil RDW and CRP were statistically significantly higher in patients with severe acute pancreatitis with a poor prognosis.⁹ This is different than our study as it found that CRP was more determinative than RDW in severe acute pancreatitis. Lymphocytes and albumin were statistically significantly lower.⁹ In another study investigating the effect of CRP on prognosis in acute pancreatitis, it was found that CRP was higher in patients with local complications present on computed tomography, but it was not statistically significant.¹⁴ In our study, there was a statistically significant relationship between high RDW and CRP and mortality, but although high neutrophil and

low lymphocyte levels were evident in non-surviving patients, there was no statistically significant relationship between high neutrophil levels and low lymphocytes and mortality. There was a statistically significant correlation between low albumin and mortality.

We thought that the rate of comorbid disease had an important place in geriatric patients, but our study found no statistically significant relationship between comorbidity and mortality.

In the literature, there were studies investigating the relationship of RDW with prognosis in different diseases.^{11,15-17} In a study conducted in patients with acute coronary syndrome, there was no statistically significant difference between RDW and mortality.¹¹ A meta-analysis found that there was no statistically significant difference in RDW level in patients with acute appendicitis compared to patients without a diagnosis of acute appendicitis.¹⁵ In a study conducted in patients with a diagnosis of COVID-19, there was a statistically significant relationship between high RDW and mortality.¹⁶ In a study conducted in patients with colorectal cancer, the rate of development of infectious complications was statistically significantly higher in patients with high RDW.¹⁷ In a meta-analysis conducted in psoriasis patients, it was observed that the RDW level was significantly higher in patients with psoriasis, but no statistically significant correlation was found between disease severity and RDW.¹⁸ Considering the results obtained in previous studies in inflammatory diseases and acute pancreatitis, we think that studies should be conducted in which RDW is compared with different parameters.

Limitations of the study

In our study, application data of acute pancreatitis patients were obtained, laboratory data were not obtained during follow-up, and re-admission evaluations could not be made. Since chronic pancreatitis patients who have not been diagnosed yet are not known were evaluated as having acute pancreatitis.

Conclusion

Hematological parameters can help predict a prognosis in patients with acute pancreatitis. High CRP together with low hemoglobin and hematocrit can predict the prognosis of patients with acute pancreatitis. Although RDW is not statistically more significant than CRP, it can be used as a prognostic marker in patients with acute pancreatitis.

Declarations

Funding

Authors have no commercial interest and financial interest. The costs of the research were covered by the researchers.

Author contributions

Conceptualization, H.Ş.A. and A.Ö.; Methodology, H.Ş.A.; Software, A.Ö.; Validation, H.Ş.A. and A.Ö.; Formal Analysis, A.Ö.; Investigation, H.Ş.A.; Resources, H.Ş.A.; Data Curation, A.Ö.; Writing – Original Draft Preparation, H.Ş.A.; Writing – Review & Editing, H.Ş.A.; Visualization, A.Ö.; Supervision, H.Ş.A.; Project Administration, H.Ş.A.; Funding Acquisition, A.Ö.

Conflicts of interest

All authors declare that there are no conflicts of interest.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

The instant study was carried out with the permission of the University of Health Sciences, Ümraniye Education and Research Hospital Ethics Committee (Date: 23/06/2022, Decision No: B.10.1.TKH.4.34.H.GP.0.01/215).

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