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Original Article *Özgün Araştırma*

EVALUATION OF THE SUCCESS OF THE SYSTEMIC IMMUNE-INFLAMMATORY INDEX IN DIAGNOSING, PREDICTING COMPLICATIONS AND MORTALITY IN PATIENTS WITH PEPTIC ULCER PERFORATION PRESENTING TO THE EMERGENCY DEPARTMENT

Acil Servise Başvuran Peptik Ülser Perforasyonu Olgularının Tanısında, Komplikasyon ve Mortaliteyi Öngörmede Sistemik İmmün İnflamatuvar İndeksin Başarısının Değerlendirmesi

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ABSTRACT

Objective: Peptic ulcer perforation (PUP) is a severe complication of peptic ulcer disease, characterized by acute abdominal pain and systemic inflammation. The systemic immune-inflammatory index (SIII) has emerged as a promising biomarker for evaluating inflammation in various acute conditions, including PUP. This study investigates the diagnostic and prognostic value of SIII in PUP, focusing on its ability to predict complications and mortality.

Material and Methods: This retrospective, single-center study included 150 PUP patients and 150 control patients who presented between January 2021 and December 2024. Data on the cases' demographics, vital signs, and laboratory findings were collected. Based on clinical and postoperative findings, patients were divided into complicated (CPUP) and non-complicated peptic ulcer perforation (NCPUP) groups. Statistical analyses, including ROC curve analysis, were performed to evaluate the diagnostic accuracy and prognostic value of SIII.

Results: SIII levels were significantly higher in PUP patients than controls ($p<0.001$). In CPUP patients, SIII levels were higher than in NCPUP patients ($p<0.001$). ROC analysis showed high diagnostic performance of SIII in identifying PUP (AUC=0.945, sensitivity=84.7%, specificity=96%). In predicting complications and mortality, SIII demonstrated moderate diagnostic accuracy (AUC=0.693 and AUC=0.745, respectively). In gastric PUP cases, complication rates were higher, and mortality was associated with increased SIII, neutrophil-lymphocyte ratio, and decreased lymphocyte-neutrophil ratio.

Conclusion: SIII is a reliable biomarker for the diagnostic success of PUP and for predicting complications and mortality. Its integration into clinical practice could improve patient management and outcomes. Further studies are needed to validate these findings in larger populations.

Keywords: *Peptic ulcer perforation, systemic immune-inflammatory index, emergency department, complications*

ÖZ

Amaç: Peptik ulkus perforasyonu (PUP), akut karın ağrısı ve sistemik inflamasyonla karakterize peptik ülser hastalığının ciddi bir komplikasyonudur. Sistemik immün-inflamatuvar indeks (SIII), PUP dahil olmak üzere çeşitli akut durumlarda inflamasyonu değerlendirmek için umut verici bir biyobelirteç olarak ortaya çıkmıştır. Bu çalışma, komplikasyonları ve mortaliteyi tahmin etme yeteneğine odaklanarak PUP'ta SIII'in tanısal ve prognostik değerliliğini araştırmaktadır.

Gereç ve Yöntemler: Bu retrospektif, tek merkezli çalışmaya Ocak 2021 ile Aralık 2024 arasında başvuran 150 PUP hastası ve 150 kontrol hastası dahil edildi. Olguların demografi, vital ve laboratuvar bulgularıyla ilgili veriler toplandı. Hastalar klinik ve postoperatif bulgularına göre komplike (KPUP) ve komplike olmayan peptik ulcus perforasyonları (NKPUP) gruplarına ayrıldı. SIII'in tanısal doğruluğunu ve prognostik değerini değerlendirmek için ROC curve analiz de dahil olmak üzere istatistiksel analizler yapıldı.

Bulgular: SIII düzeyleri PUP hastalarında kontrollere kıyasla önemli ölçüde daha yüksekti ($p<0,001$). KPUP hastalarında SIII düzeyleri NKPUP hastalarına kıyasla yüksekti ($p<0,001$). ROC analizi, PUP'u tanımlamada SIII için yüksek tanı performansı gösterdi (AUC=0,945, sensitivite=84,7%, spesifite=96%). Komplikasyonları ve mortaliteyi tahmin etmede SIII, orta düzeyde tanı doğruluğu gösterdi (sırasıyla AUC=0,693 ve AUC=0,745). Gastrik PUP vakalarında komplikasyon oranları daha yüksekti ve mortalite, artan SIII, nötrofil-lenfosit oranı ve azalan lenfosit-nötrofil oranı ile ilişkiliydi.

Sonuç: SIII, PUP'un tanısal başarısı, komplikasyonları ve mortaliteyi öngörmesi açısından güvenilir bir biyobelirteçtir. Klinik uygulamaya entegrasyonu hasta yönetimini ve sonuçlarını iyileştirebilir. Bu bulguları daha geniş popülasyonlarda doğrulamak için daha fazla çalışma yapılması gerekmektedir.

Anahtar Kelimeler: *Peptik ülser perforasyonu, sistemik immün inflamatuvar indeks, acil servis, komplikasyon*

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INTRODUCTION

Peptic ulcer perforation (PUP) is one of the most serious complications of peptic ulcer disease and usually presents with acute abdominal pain, shock, and abdominal tenderness. Peptic ulcer is a condition in which a wound occurs in the gastric or duodenal mucosa, and a perforation occurs when this wound perforates the stomach or intestinal wall.[1] This condition is a clinical emergency requiring immediate surgical intervention. Factors such as Helicobacter pylori infection, NSAID use, and smoking play an essential role in the etiology of PUP.[2]

The systemic immune-inflammatory index (SIII) is increasingly gaining attention as a biomarker that evaluates the degree of inflammation. The systemic immune-inflammatory index (SII) reflects the level of systemic inflammation in the body. Especially after acute illnesses and surgical interventions, monitoring inflammation is reported to be an important tool for evaluating the prognosis and response to treatment of patients.[3-6] Monitoring the course of inflammation in PUP is important to guide patients' treatment response more accurately.

Systemic inflammation may affect the prognosis of peptic ulcer perforations and its early detection may help optimize the treatment process. In this context, the role of SIII in determining inflammation associated with PUP is being investigated increasingly in clinical practice. In our study, we aimed to investigate the value of SIII in determining PUP and predicting complications and mortality and to contribute to the literature with our results.

MATERIALS AND METHODS

Study setting

Our study was conducted retrospectively between January 1, 2025, and February 1, 2025. The study was conducted with 150 patients who applied to our hospital's emergency department with abdominal pain and were subsequently diagnosed with PUP and met the study inclusion criteria, and 150 control group cases.

Study Population

Our study was conducted retrospectively and single-centered in the emergency department of a tertiary hospital. Our hospital has an average of 560 patient applications to our emergency department per day, has a bed capacity of 510, and is one of the largest hospitals in our province.

Patients presenting with abdominal pain between January 1, 2021, and December 31, 2024, who were subsequently diagnosed with peptic ulcer perforation were included in the study. Among these patients, patients whose outcomes could not be tracked, patients whose PUP was not detected during the operation, pregnant and pediatric patients, and patients with missing data were excluded from the study. In addition, only the first application of patients with repeated applications was used.

Furthermore, patients with a history of hematological disease were excluded from the study due to the use of neutrophil, lymphocyte, and platelet parameters in the calculation of the systemic immune-inflammatory index. Similarly, patients with signs of active infection other than PUP at the time of admission -such as pneumonia, urinary tract infection, or soft tissue infections- were also excluded, as these conditions could affect systemic inflammatory parameters. The presence of such infections was evaluated using clinical findings, radiological imaging, and laboratory markers, including elevated procalcitonin and/or other infection indicators.

Data collection

Patients were detected by scanning the automation system (PANATES®) during the study. For PUP, the ICD10 diagnosis codes "K27.0, K27.1, K27.4, K27.5, K27.6" were used from the automation system. Three hundred forty-two patients were detected with the scan. Some of the 342 cases identified were not included in the study. Those not included in the study were: those without PUP, those with incomplete data, those who did not accept surgery, those who were discharged at their request, and those whose outcome could not be followed up because they were referred to another center due to the need for an intensive care unit (ICU), and the entries of patients with repeated applications in their subsequent applications.

In total, 192 eligible cases remained after exclusions. From these, 150 patients were randomly selected based on the order of presentation. For the control group, patients of similar age and gender who applied to the general surgery clinic and were planned to undergo endoscopy imaging and had no suspicion of perforation were included.

For the study, demographic data (age and gender), clinical data (vital findings, laboratory test results, neutrophil-lymphocyte ratio (NLR), lymphocyte-neutrophil ratio (LNR) obtained from these results, and systemic immune-inflammatory index (SIII)), location of peptic ulcer in cases (stomach, prepyloric, duodenum), presence of complications, patient outcomes (ward admission and intensive care unit admission), length of stay, and mortality status were scanned retrospectively. The obtained data were entered into the previously prepared case form and archived by assigning a case number. Additionally, C-reactive protein (CRP) levels were retrospectively obtained and recorded as a supporting inflammatory marker. These values were used in the general evaluation of the systemic inflammatory response and were taken into consideration in the interpretation of SIII values and clinical progression.

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Splenectomy due to inflammatory conditions seen during the operation or sepsis seen after surgery were considered complications. The cases were then classified into two groups as complicated peptic ulcer perforation (KPUP) and non-complicated peptic ulcer perforation (NKPUP).

SIII was calculated using the following formula: SIII = (neutrophil x platelet) / lymphocyte formula was calculated.[7,8]

Statistical Analyses

Data were analyzed with SPSS Package Program version 24.0. Number, percentage, mean, standard deviation, median, minimum, and maximum were used in the presentation of descriptive data. The conformity of the data to normal distribution was evaluated with Kolmogorov-Smirnov Test. In univariate analysis, continuous variables showing normal distribution were expressed as Mean±ss and compared using t-test. Pearson chi-square test was used in the analysis of categorical variables. Fisher's exact test was used in the presence of less than 5 variables in categorical variables. A t-test was used for the comparison of two independent numerical data. Spearmen's correlation test was used in the correlation analysis of multiple variables. Diagnostic accuracy was assessed using ROC (receiver operating characteristic) curve analysis. Appropriate cut-off values were determined, and sensitivity and specificity values were calculated for parameters with an area under the curve (AUC) above 0.600. $p<0.05$ was accepted as the statistical significance level.

Ethics committee approval was obtained from the ethics committee of our third-level hospital (Ethics committee decision numbered 2024-155)

Our study was conducted following the Declaration of Helsinki and the principles of good clinical practice.

RESULTS

Our study included 150 patients and 150 controls. The patients included in the control group were randomly created in a way that their age and gender were similar. The mean age was 53.29±16.17 years in the patient group and 52.11±13.43 years in the control group. No significant difference was found between the patient and control groups in terms of vital parameters. In laboratory tests, WBC, neutrophil, platelet, and CRP levels were found to be significantly higher in the patient group than in the control group ($p<0.001$ for each parameter); while the lymphocyte level was significantly higher in the control group ($p<0.001$) (Table 1).

When the laboratory parameters of the cases were compared; the mean NLR and SIII in the patient group with peptic ulcer perforation were significantly higher than in the control group, while the LNR was significantly lower (Table 1) ($p<0.001$ for each parameter).

Table 1: Comparison of demographic and clinical data of case and control groups

Parameter	Sub-parameter	Patient group n (%), mean±sd	Control group n (%), mean±sd	p*
Age		53.29±16.17	52.11±13.43	0.492
Gender	Male	77 (51.3)	76 (50.7)	0.908
	Female	73 (48.7)	74 (49.3)	
Vital Parameters	Systolic BP (mmHg)	126.63±28.41	131.79±21.87	0.884
	Diastolic BP (mmHg)	76.52±16.69	78.42±14.28	0.924
	Pulse (Beats/min)	94.03±19.71	92.79±17.82	0.864
Laboratory Values	WBC ($x10^9$/L)	13.37±7.64	7.37±1.56	**<0.001**
	Neutrophil ($x10^9$/L)	11.40±7.13	4.53±1.18	**<0.001**
	Lymphocyte ($x10^9$/L)	1.18±0.89	2.16±0.59	**<0.001**
	Platelet ($x10^9$/L)	307.18±108.65	264.37±66.35	**<0.001**
	CRP	89.91±77.36	3.63±5.71	**<0.001**
Ratios	NLR	15.97±18.22	1.24±0.84	**<0.001**
	LNR	0.13±0.10	0.50±0.16	**<0.001**
	Sİİ	4935.90±6069.98	600,12±305.80	**<0.001**

sd: Standard deviation, BP: Blood pressure, NLR: Neutrophil-lymphocyte ratio,LNR: Lymphocyte neutrophil ratio, SIII: Systemic immune-inflammatory index

*: Pearson χ^2 Test and T-Test were used

Complications were observed in 37 cases in our study. These cases were included in the complicated peptic ulcus perforation (KPUP) group, while 113 cases were evaluated as the non-complicated peptic ulcus perforation (NKPUP) group. The mean age in KPUP cases was found to be statistically significantly higher than that of NKPUP cases ($p=0.012$). There was no significant difference between KPUP and NKPUP cases in terms of gender ($p<0.05$). No significant difference was found between the two groups in terms of vital parameters. In KPUP cases, when compared to NKPUP cases, the mean values of platelet and CRP levels were significantly higher ($p<0.001$ and $p<0.001$, respectively); no significant difference was found

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between the mean neutrophil and lymphocyte levels. Again, in KPUP cases, SIII was significantly higher than in NKPUP cases (p<0.001); and no significant difference was found between the mean NLR and LNR (Table 2).

When the location of the lesions detected in the cases was examined, it was determined that complications were more common in PUP cases seen in the stomach and this situation was statistically significant (p=0.001).

No significant relationship was found between the complication status and the size of the lesion. When the outcome of the cases was evaluated according to the complication status, it was seen that the intensive care unit stay level was significantly higher in KPUP cases (p<0.001); and mortality was significantly higher (p=0.004). There was no significant difference between the two groups in terms of hospitalization duration (Table 2).

Table 2: Comparison of demographic and laboratory data of KPUP and NKPUP cases

Parameter	Sub Parameter	CPUP (n=37) n (%), mean±sd	NCPUP (n=113) n (%), mean±sd	p*
Age (years)		59.08±15.21	51.40±16,09	**0.012**
Gender	Male	20 (26.0)	57 (74.0)	0.704
	Female	17 (23.3)	56 (76.7)	
Vital parameters	Systolic BP (mmHg)	120.59±21.68	123.66±22.42	0.304
	Diastolic BP (mmHg)	74.46±11.52	76.18±16.41	0.283
	Pulse (Beats/min)	91.16±20.58	94.66±18.72	0.925
	Temperature (°C)	36.57±0.51	36.58±0.49	0.913
Laboratory parameters	Neutrophil ($x10^9$/L)	11.77±10.67	11.28±5.57	0.717
	Lymphocyte ($x10^9$/L)	0.92±0.90	1.27±0.87	0,040
	Platelet ($x10^9$/L)	391.86±105.32	297.45±94.84	**<0.001**
	CRP	144.14±74.47	72.16±69.92	**<0.001**
Ratios	NLR	19.61±16.83	14.78±18.56	0.162
	LNR	0.10±0.08	0.14±0.11	0.052
	SIII	8052.37±9040.72	3915.47±4299.48	**<0.001**
Lesion Site	Stomach	4 (10.8)	0 (0.0)	**0.001**
	Prepyloric	0 (0.0)	6 (5.3)	
	Duodenum	33 (89.2)	107 (94.7)	
Lesion width (mm)		6.57±2.15	5.82±3.47	0.221
Finalization	Hospital ward admission	12 (32.4)	78 (69.0)	**<0.001**
	ICU Admission	25 (67.6)	35 (31.0)	
Hospitalization duration		9.57±5.83	8.14±3.39	0.069
Mortality	No	22 (59.5)	93 (82.3)	**0.004**
	Yes	15 (40.5)	20 (17.7)	

Sd: standart deviation, BP: blood pressure, NLR: Neutrophil-lymphocyte ratio, LNR: Lymphocyte neutrophil ratio, SIII: Systemic immune-inflammatory index
*: Pearson χ^2 Test and T-Test were used

Mortality due to PUP was observed in 35 cases in our study. No significant difference was found in terms of age and gender in cases with mortality. In vital parameters, systolic and diastolic blood pressures were significantly lower in cases with mortality than in living cases; pulse was significantly higher. No significant difference was found in terms of fever. In laboratory tests performed on the cases; it was determined that platelet and CRP levels were significantly higher in cases with mortality; there was no significant difference in terms of lymphocytes and neutrophils. The NLR and SIII parameters of the cases were significantly higher in cases with mortality (p=0.005 and p<0.001, respectively); while the LNR level was significantly lower (p=0.001). While mortality was significantly higher in cases hospitalized in the ICU, no significant difference was found between the two groups in terms of hospitalization time, lesion size and outcome (Table 3).

In the ROC curve analysis performed for the diagnostic value of SIII in the diagnosis of PUPs; it was determined that it was a successful marker with a sensitivity of 84.7% and a specificity of 96% (AUC=0.945; 95% CI: 0.917-0.972; p<0.001) for a cut-off value of 1201.52. In the ROC curve analysis, we performed to determine the value of SIII in predicting complication status and mortality in PUPs; For the distinction between KPUP and NKPUP, it was found that the sensitivity was 62.2 and the specificity was 71.7% (AUC=0.693; 95% CI: 0.597-0.790; p<0.001) for the SIII cut-off value of 4105.21; and for mortality, it was found that the sensitivity was 91.4 and the specificity was 53.9% (AUC=0.745; 95% CI: 0.655-0.835; p<0.001) for the SIII cut-off value of 2373.36 (Figure 1 and Table 3).

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Table 3: Comparison of demographic and laboratory data of PUP cases according to mortality status

Parameter	Sub-parameter	Exitus cases (n=35) n (%), mean±sd	Living cases (n=115) n (%), mean±sd	p*
Age (years)		57.74±18.51	51.94±15.22	0.063
Gender	Male	19 (54.3)	58 (50.4)	0.690
	Female	16 (45.7)	57 (49.6)	
Vital parameters	Systolic BP (mmHg)	106.95±18.72	128.76±21.22	**0.038**
	Diastolic BP (mmHg)	58.63±10.57	77.61±15.48	**0.028**
	Pulse (Beat/min)	101.62±23.85	92.60±19.27	**0.014**
	Temperature (°C)	37.13±0.68	36.68±0.53	0.082
Laboratory parameters	Neutrophil ($x10^9$/L)	12.03±9,28	11.21±6.37	0.553
	Lymphocyte10^9/L)	0.63±0.31	1.35±0.94	**<0.001**
	Platelet ($x10^9$/L)	360.54±92.87	290.94±108.25	**0.001**
	CRP	110.63±79.72	83.61±75.86	0.070
Ratios	NLR	23.56±21.79	13.66±16.40	**0.005**
	LNR	0.08±0.07	0.14±0.11	**0.001**
	Sİİ	8648.11±8545.94	3806.10±4566.87	**<0.001**
Lesion site	Stomach	2 (5.7)	2 (1.7)	0.119
	Prepyloric	3 (8.6)	3 (2.6)	
	Duodenum	30 (85.7)	110 (78.6)	
Lesion width (mm)		6.69±2.72	5.80±3.32	0.153
Finalization	Hospital Ward Admission	15 (42.9)	75 (65.2)	**0.018**
	ICU Admission	20 (57.1)	40 (34.8)	
Hospitalization duration		9.31±5.33	8.24±3.71	0.182

sd: Standard deviation, BP: Blood pressure, NLR: Neutrophil-lymphocyte ratio, LNR: Lymphocyte neutrophil ratio, SIII: Systemic immune-inflammatory index
*: Pearson χ^2 Test and T-Test were used

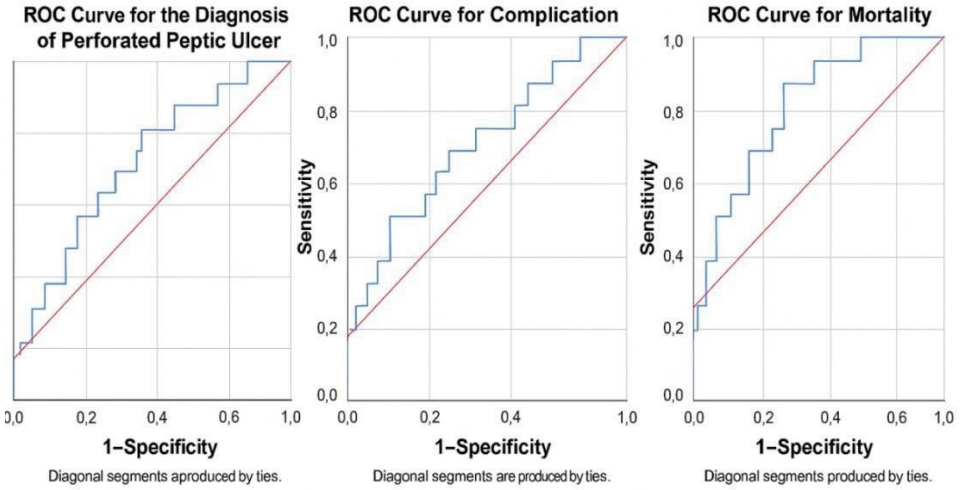

Figure 1: SIII ROC Analysis in diagnostic evaluation and prediction of complications and mortality in peptic ulcer perforation

DISCUSSION

PUP is one of the most common complications of peptic ulcer disease and is frequently seen in individuals between the ages of 40-50. PUP is a cause of acute abdomen and can result in clinical conditions such as peritonitis, sepsis, and mortality.[9] Although gender distribution is equal; mortality and morbidity increase with age.[10,11]

In our study, the success of SIII in predicting complications and mortality in the diagnosis of PUP was evaluated and our results showed that SIII was a successful parameter both in determining PUP patients and in predicting complications and mortality. We saw that it had high levels of AUC, sensitivity, and specificity (0.945, 84.7% and 96%, respectively), especially in determining PUP cases. In this context, we thought that SIII would be beneficial in clinical use in the diagnosis of PUP.

It is seen that many parameters have been investigated in the literature regarding the diagnosis and progression of PUP. In the study conducted by Bilge et al.; in the diagnosis of PUP, the diagnostic value of platelet/albumin was investigated, and it was stated that it was significant as a diagnostic biomarker.[12] Jafarzadeh

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et al. suggested the usability of the correlation between Helicobacter pylori positivity, WBC and NLR for the diagnosis of PUP.[13] Kondo et al. also showed in their study that Helicobacter pylori eradication in PUP cases reduced blood neutrophil and monocyte counts.[14] Again, some studies in the literature investigated some biomarkers to predict PUP-related mortality. In the study conducted by Aydın et al., they evaluated several parameters in predicting mortality in PUP cases and reported that platelet-lymphocyte ratio, neutrophil-lymphocyte ratio, and lymphocyte level were usable markers in predicting the risk of postoperative mortality.[15] In another study in the literature, Seow et al. investigated the success of low serum albumin level in predicting gastric resection in PUP cases and reported that it was a significant biomarker in their study results.[16] In our results, it was found that NLR and LNR parameters showed significant differences in PUP diagnosis and mortality prediction.

In the study conducted by Taş et al.; it was seen that the average age of PUP cases was 51.7 years; in the study conducted by Ugochukwu et al.; it was 39.5 years; in the study conducted by Bilge et al.; it was 46.3 years.[12,17,18] In our study, the average age in PUP cases was found to be 53.29±16.17 years. While our results were similar to the study conducted by Taş et al.; it was found to be higher than the results of Ugochukwu et al. and Bilge et al. We think that this difference is due to the elderly population in the region where our study was conducted. While gender was previously a predisposing factor for peptic ulcer disease; the widespread eradication of Helicobacter pylori, changes in socioeconomic income levels in countries, and the introduction of proton pump inhibitors in 1989 have both increased the age of PUP and equalized the gender distribution.[19,20] In our study, while the ratio of women and men was similar, no significant difference was found between complications and mortality and gender. Our results are similar to the literature. One of the factors that most affect mortality in PUP cases is complications. In our study, complications were seen in 24.7% of the cases. Sepsis constitutes a large portion of these complications.[21] In PUP cases, there is a variability in abscess formation and sepsis severity according to the perforation location. In the literature, Fong's study reported that postoperative abscess formation and sepsis development were higher in cases with gastric PUP than in cases with duodenal PUP.[21] In our study, it was observed that the complication rate was significantly higher in cases where the PUP site was the stomach compared to other lesion sites (prepyloric and duodenum). Our results support Fong's results in this context. However, in our study, there was no significant relationship between lesion size and complications and mortality. Since there is no similar study on this subject, a comparison could not be made.

There were some limitations to our study. The most important of these limitations was that our study was retrospective and some of the data obtained were dependent on physician notes. Our second limitation was that cases of peptic ulcer perforation that used a different diagnosis code were missed, except for the patients obtained by scanning the diagnosis codes. Another limitation is that since the comorbidities (chronic disease history, chronic drug use history and predisposing factors (chronic smoking or alcohol habits) of the cases could not be found for each patient, these parameters could not be used in the study. However, we do not think that the factors that may arise from this situation will create a significant change in the study results.

In our study, we think that SIII can be a significant parameter in both diagnostic evaluation and prediction of complications and mortality in PUP cases. We also found that NLR and LNR showed promising results in the diagnosis of PUP. However, SIII needs to be supported with more patients and multicentre studies before it can be used in PUP cases.

Conflict of Interest: The authors have no conflicts of interest to declare.

Researchers' Contribution Rate Statement: Concept/Design: ÖK, MAT, FDA, ÖZK, MK, AOÇ; Analysis/Interpretation: ÖK, ÖZK; Data Collection: ÖK, FDA; Critical Review: ÖK, MAT; Approver: ÖK, ÖZK, FDA, MAT, AOÇ, MK

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Ethics Committee Approval: The study protocol was approved by the Çanakkale Onsekiz Mart University Clinical Research Ethics Committee (Date: 26.02.2025, Number:2024-155)

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