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The Clinical Significance of Shock Index and GFR in the Differential Diagnosis of Perforated Appendicitis

Şok İndeksi ve GFR'nin Perfore Apandisit Ayırıcı Tanısındaki Klinik Önemi

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Abstract

Aim: The aim of the study is to investigate whether the shock index (SI) and glomerular filtration rate (GFR) have significance in differentiating acute appendicitis from complicated perforated acute appendicitis.

Material and Method: Patients were searched retrospectively on the hospital database. Age, gender, C-reactive protein (CRP), leukocyte (WBC), total bilirubin (T.BIL), urea, creatinine, pulse , and arterial blood pressure (TA) values of the patients were searched retrospectively on the hospital database and a database was created by using these patient variables. GFR and SI were calculated by using these data. The shock index (SI), calculated by dividing heart rate by systolic blood pressure. The surgical notes about patients were reviewed retrospectively, and they were divided into two groups, namely perforated appendicitis and non-perforated appendicitis. The data were analyzed to investigate whether GFR and SI were effective in predicting perforation.

Results: It was observed that Pulse/TA (shock index) (SI) value had more frequent pathological findings in patients with perforated appendicitis (p<0.001). It was found that age (p=0.001), CRP (p<0.001), WBC (p<0.001), T. BIL (p=0.002), Pulse (p=0.017), and SI (p<0.001) values of the patients in the perforated appendicitis group were higher than those of the patients in the normal appendicitis group, while GFR (p<0.001) and TA (p<0.001) values were lower (p<0.05).

Conclusion: It is thought that SI and GFR may be a prognostic parameter for showing both perforation and the associated increased mortality rate.

Keywords: Shock index, perforated appendicitis, abdominal pain

Öz

Amaç: Çalışmanın amacı akut apandisit ile komplike olmuş perfore akut apandisit ayırımında şok indeksinin (SI) ve glomerüler filtrasyon hızı (GFR)'nin öneminin olup olmadığı araştırılmasıdır.

Gereç ve Yöntem: Hastalar hastane veri tabanı kullanılarak retrospektif olarak taranmıştır. Hastaların yaş, cinsiyet, C-reaktif protein (CRP), lökosit (WBC), total bilirubin (T.BİL), üre, kreatinin, nabız (NBZ), arteryal tansiyon (TA) değerleri hastane kayıt sisteminden geriye dönük taranmış ve veri tabanı oluşturulmuştur. Bu veriler kullanılarak GFR ve SI hesaplanmıştır. Şok İndeksi nabız sayısının sistolik kan basıncına bölünmesiyle bulunmuştur. Hastaların ameliyat notları retrospektif olarak incelenmiş ve hastalar perfore apandisit ve perfore olmayan apandisit olarak iki gruba ayrılmıştır. Veriler analiz edilerek GFR ve SI'nin perforasyonu öngörmede etkili olup olmadığı araştırılmıştır.

Bulgular: Perfore apandisit hastalarında NBZ/TA değerinin daha sık patolojik bulguya sahip olduğu gözlenmiştir (p<0,001). Perfore apandisit grubunda yer alan hastaların Yaş (p=0,001), CRP (p<0,001), WBC (p<0,001), T. BİL (p=0,002), NBZ (p=0,017) ve NBZ/TA (p<0,001) değerlerinin normal apandisit grubunda yer alan hastalara göre daha yüksek; GFR (p<0,001) ve TA (p<0,001) değerlerinin ise normal apandisit grubunda yer alan hastalara göre daha düşük olduğu gözlenmiştir (p<0,05).

Sonuç: SI'nin ve GFR'nin hem perforasyonu hem de buna bağlı artan mortalite oranını göstermede prognostik bir parametre olabileceği düşünülmektedir.

Anahtar Kelimeler: Şok indeksi, perfore apandisit, karın ağrısı

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INTRODUCTION

Acute abdominal pain accounts for about 10% of emergency department admissions. Acute appendicitis (AA) is among the most common causes of these admissions.[1] Although it has well-known symptoms such as right lower quadrant pain and loss of appetite, early diagnosis can be difficult in some cases.[2] Although physical examination (PM), ultrasonography (USG), computed tomography (CT), and diagnostic laparoscopy are methods used in diagnosis, they are known to be costly.[3] Scoring systems, such as Alvarado, RIPASA, Fenyo, Tzakis, and Eskelinen, have been developed to assist diagnosis. Although these scoring systems have been developed to aid diagnosis, their sensitivity and specificity are low.[4,5] Failure to detect AA early has been associated with significant morbidity and mortality. While mortality is 0.1% in non-perforated AA cases, it has been reported as 5% in perforated AA.[6] For this reason, various blood tests and their combinations have been used recently to determine the diagnosis and severity of appendicitis. While leukocyte (WBC), C-reactive protein (CRP), and bilirubin are the most commonly used blood tests, CRP was found to be superior to others in predicting perforation.[7] Inflammation markers, such as platelet/lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR), and delta neutrophil index (DNI), have also been introduced recently, and it has been emphasized that they may be important in the diagnosis and prognosis of AA.[8,9] The shock index (SI), calculated by dividing heart rate by systolic blood pressure, is known as an estimator for hemodynamic stability and is widely used to predict mortality and morbidity in various diseases, especially under shock conditions.[10] Low glomerular filtration rate has been associated with increased complication rates in many cases.[11]

This study was conducted to investigate the significance of shock index and GFR in differentiating acute appendicitis from complicated perforated acute appendicitis.

MATERIAL AND METHOD

The approval of the Balıkesir University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee was obtained for the study (date: January 26, 2022; decision number: 2022/009). In the study, 158 patients who underwent an operation with the diagnosis of acute appendicitis in the Department of General Surgery, Faculty of Medicine, Balıkesir University between the dates of 2019-2021 were examined retrospectively.

Data Collection and Patient Selection

A total of 158 patients who were admitted to the emergency department with abdominal pain and underwent an operation for acute appendicitis were included in the study. Age, gender, CRP, WBC, total bilirubin (T.BIL), urea, creatinine, pulse , and arterial blood pressure (TA) values of patients were retrospectively searched on the hospital database system and a database was created. GFR and SI were calculated using these data. The surgical notes of patients were reviewed retrospectively, and they were divided into two groups, namely perforated appendicitis and non-perforated appendicitis. The data were analyzed to find out whether GFR and SI were effective in predicting perforation.

Statistical Analysis

The SPSS (Statistical Package for the Social Sciences) 25.0 software package was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean and standard deviation values (median and 95% CI values where appropriate). Shapiro-Wilk test was used to determine whether the parameters in the study showed a normal distribution. Chi-square and Fisher's exact tests were employed to compare categorical expressions. Mann-Whitney U test was used for the parameters that did not show normal distribution. The predictive diagnostic value of the Pulse/TA levels of patients included in the study in terms of normal and perforated appendicitis groups was analyzed by ROC curve analysis. According to the findings, the area under the ROC curve for Pulse/TA was 0.759 (95% confidence interval (CI): 0.685-0.823; p<0.001). The Pulse/TA cut-off (threshold) value of the patients in terms of groups was 0.87 (specificity: 87.23%, 95% CI: 74.3-95.2, sensitivity: 61.26%, 95% CI: 51.5-70.4) (**Table 1**, **Figure 1**). The level of statistical significance was taken as 0.05 in all tests.

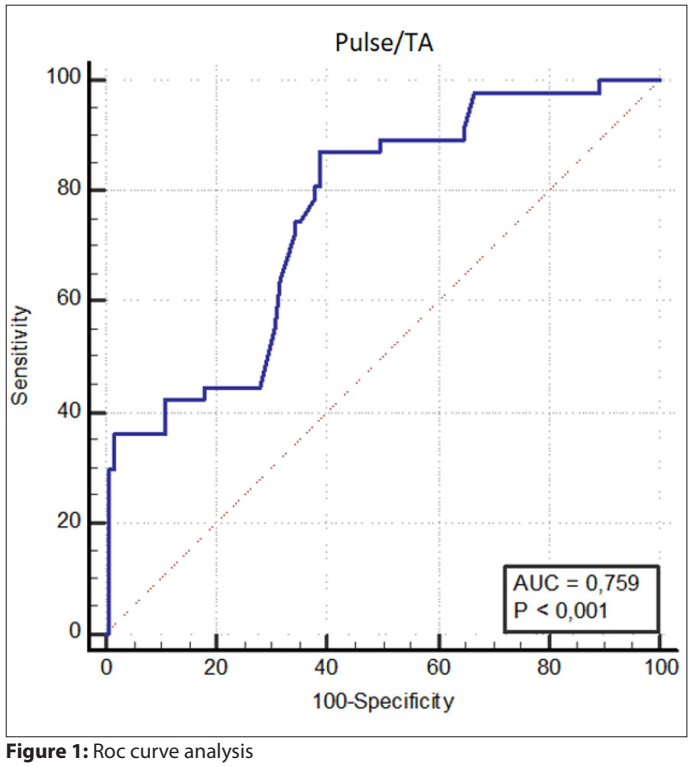

Figure 1: Roc curve analysis

Table 1. Roc curve analysis

	Pulse/TA
AUC (95%-CI (%))	0.759 (0.685-0.823)
Cut-off	>0.87
Sensitivity (%)(95%-CI (%))	87.23 (74.3-95.2)
Specificity (95%-CI (%))	61.26 (51.5-70.4)
PPV (95%-CI (%))	48.8 (42.4-55.2)
NPV (95%-CI (%))	91.9 (84.1-96.0)
P	<0.001

* p<0,05, **p<0,001, Roc curve test

RESULTS

The mean age ± standard deviation (mean±sd) of all patients included in the study was 42.5±17.5 and it was 50.1±19.7 in the perforated appendicitis group, and 39.2±15.5 in the normal appendicitis group. Age was significantly higher in the perforated appendicitis group (p=0.001). There were 23 female (48.9%) and 24 male (51.1%) patients in the perforated appendicitis group, and 43 female (38.7%) and 68 male (61.3%) patients in the normal appendicitis group. There was no gender-based differences between the groups (p=0.235). It was found that the incidence of perforation was higher in patients with a high shock index that was calculated by dividing the pulse rate by systolic blood pressure (p<0.001). Similarly, CRP (p<0.001), WBC (p<0.001), T.BIL (p=0.002), and pulse (p=0.017) values were found to be significantly higher in the perforated appendicitis group in the normal appendicitis group. On the contrary, GFR (p<0.001) and TA (p<0.001) values were observed to be lower in the perforated appendicitis group than in the normal appendicitis group (**Table 2**).

When the factors affecting the Pulse/TA (Shock Index) ratio were examined, it was found that it affected the shock index of only patients with perforated appendicitis by 7.97 times (OR: 7.971, 95% CI: 2.536-25.052), and that other parameters had no effect (p<0.001) (**Table 3**).

Table 3. Factors affecting the Shock Index

	p	Effect size (OR)	95% Confidence Interval	
			Lowest	Highest
Age	0.489	0.991	0.965	1.017
Gender (1)	0.702	1.187	0.493	2.860
Normal appendicitis		1.000		
Perforated appendicitis	<0.001	7.971	2.536	25.052
CRP	0.562	0.997	0.987	1.007
WBC	0.344	1.064	0.936	1.208
T.BIL/100	0.688	0.809	0.287	2.282
CREATININE /100	0.501	3.829	0.077	190.246
UREA	0.455	1.019	0.969	1.072
GFR	0.981	1.000	0.969	1.032
Constant	0.691	0.273		

Variable(s) entered on step : Age, Gender, Normal appendicitis, Perforated appendicitis, CRP, WBC, T.BIL/100, CREATININ/100, UREA, GFR
CRP:C reactive protein, WBC:Leukocytes, T.BIL:Total Bilirubin, GFR: Glomerularfiltration rate, TA: Arterial Blood Pressure,

Table 2. Evaluation of clinical and demographic data

	Normal appendicitis (n=111)	Perforated appendicitis (n=47)	Total (n=158)	p
	n(%)	n(%)	n(%)	
Gender				
Male	68 (61.3)	24 (51.1)	92 (58.2)	0.235[c]
Female	43 (38.7)	23 (48.9)	66 (41.8)	
Pulse/TA (Shock Index) (SI)				
<0.87 normal	69 (62.2)	9 (19.1)	78 (49.4)	<0.001**.[c]
≥0.87 pathological	42 (37.8)	38 (80.9)	80 (50.6)	
	Normal appendicitis (n=111)	**Perforated appendicitis (n=47)**	**Total (n=158)**	**p**
	Mean±sd Med (%95 CI)	**Mean±sd Med (%95 CI)**	**Mean±sd Med (%95 CI)**	
Age	39.2±15.5 35.5 (32-41)	50.1±19.7 54 (42-60)	42.5±17.5 40 (35-44.95)	0.001**.[b]
CRP	20.9±23.6 12 (8-14)	88.3±63.4 80 (45-109)	41.1±50.3 18 (12-23)	<0.001**.[b]
WBC	11.3±2.7 11 (11-11.3)	13.8±3.5 13 (12-14.5)	12.1±3.2 0.63 (0.59-0.7)	<0.001**.[b]
T. BIL	0.65±0.33 0.6 (0.54-0.64)	0.84±0.39 0.8 (0.66-0.9)	0.71±0.36 0.86 (0.85-0.88)	0.002**.[b]
CREATININE	0.86±0.13 0.86 (0.85-0.87)	0.93±0.25 0.88 (0.78-1.0)	0.88±0.17 25 (23-26)	0.354[b]
UREA	25.5±6.9 25 (23-26)	31.1±17.2 27 (24-31)	27.2±11.2 102 (99-104)	0.077[b]
GFR	105.7±15.6 105 (102.5-107.5)	87.1±22.1 90 (82-96)	100.2±19.7 102 (99-104)	<0.001**.[b]
TA	106.4±9.6 105 (105-110)	93.8±9.6 94 (90-96)	102.6±11.2 100 (100-105)	<0.001**.[b]
Pulse	88.9±8.4 90 (88-90)	93.0±6.7 90 (90-94)	90.2±8.1 90 (90-90)	0.017*.[b]
Shock Index (SI)	0.84±0.14 0.84 (0.78-0.87)	1.0±0.16 0.93 (0.91-1.06)	0.89±0.16 0.90 (0.87-0.91)	<0.001**.[b]

* p<0,05, **p<0,001, [b]: Mann-Whitney-U test, [c]: chi-square and Fisher Exact test, sd: standard deviation, Med: median, %95 CI: %95 confidence interval. CRP: C reactive protein, WBC: Leukocyte, T.BIL: Total Bilirubin, GFR: Glomerularfiltration rate, TA: Arterial Blood Pressure,

DISCUSSION

Early detection of acute appendicitis can prevent negative consequences such as perforation, which can be associated with significant morbidity and even mortality. Studies on biomarkers used in addition to clinical findings and imaging methods are used to help diagnose patients with suspected appendicitis, especially in children, women with pregnancy, and elderly patients.[12,13] Recently, there has been an increasing trend in non-surgical treatment methods in patients whose AA cannot be diagnosed clearly or in selected patient groups.[14] Antibiotic treatment or endoscopic retrograde appendicitis therapy (ERAT) are some of these treatments.[15] Non-surgical treatment modalities are considered especially in uncomplicated AA cases. Therefore, it has become important to distinguish perforated appendicitis cases from normal appendicitis cases. It is known that WBC values mostly increase in cases of acute appendicitis, but it has been emphasized that they do not have a predictive significance in differentiating normal appendicitis from complicated appendicitis. Similarly, the serum bilirubin value has also been shown to be a potential biomarker for perforated appendicitis, but it has been stated that it does not have enough sensitivity and specificity. CRP, on the other hand, was found to be superior to bilirubin.[7,16,17] In our study, WBC, CRP and blood bilirubin levels were found to be significantly higher in perforated appendicitis, which is consistent with previous studies. The SI calculated by dividing heart rate by systolic blood pressure has been used to predict adverse outcomes in hemorrhagic shock and cardiovascular, pulmonary, and neurological diseases.[10,18] In the pulmonary embolism study, in which the cut-off value was taken as 1.0 for SI, a SI value of greater than 1.0 was associated with an increase in mortality.[19] In a study conducted by Chung et al. in geriatric patients with influenza, a SI value that was greater than the determined cut-off value was found to be associated with high mortality. Of these patients, those who had a high shock index were shown to have a seven times higher risk of mortality than those who did not. In addition, it was stated that SI had a high specificity and negative predictive value for showing 30-day mortality.[20] In their study on patients with septic shock, Jouffroy et al. determined the SI cut-off value as 0.9 and found that there was an increase in mortality in patients above this value.[21] Similarly, in patients with COVID-19, the rate of mortality was found to be 21% in those with an SI below the determined value, while it was found to be 70% in patients above the determined value.[22] In our study, the SI cut-off value was determined as 0.87 (specificity: 87.23%, 95% CI: 74.3-95.2, sensitivity: 61.26%, 95% CI: 51.5-70.4) (**Table 1**, **Figure 1**). The high rate of perforated appendicitis in patients with a high SI was found to be statistically significant.

GFR is a parameter that has been used for a long time and is accepted as the gold standard in the evaluation of kidney function.[23] Yoshioka et al. stated that low GFR after gastric endoscopic submucosal dissection (ESD) in patients diagnosed with chronic kidney disease (CKD) was directly related to postoperative bleeding.[24] In a case-control study conducted on patients with appendicitis, GFR was found to be low in the perforated appendicitis group.[25] In our study, GFR rates were found to be low in the perforated appendicitis group, which was consistent with the literature.

CONCLUSION

It is known that perforation increases mortality. In addition to previous studies to predict mortality, SI and GFR are thought to be prognostic parameters for showing both perforation and the associated increased mortality rate. The limitation of the study is that it is retrospective, but it is thought to be significant since it is the first study in which SI and GFR were evaluated together to predict the diagnosis of perforated appendicitis.

ETHICAL DECLARATIONS

Ethics Committee Approval: The approval of the Balıkesir University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee was obtained for the study (date: January 26, 2022; decision number: 2022/009).

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.

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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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