ORIGINAL ARTICLE

Predictive and prognostic value of L-lactate, D-dimer, leukocyte, C-reactive protein and neutrophil/lymphocyte ratio in patients with acute mesenteric ischemia

Sabahattin Destek, M.D.,[1] Ayşegül Yabacı, M.D.,[2] Yağmur Nur Abik, M.D.,[1] Vahit Onur Gül, M.D.,[3] Kamuran Cumhur Değer, M.D.[1]

[1]Department of General Surgery, Bezmialem Foundation University Faculty of Medicine, İstanbul-*Turkey*
[2]Department of Statistic, Bezmialem Foundation University Faculty of Medicine, İstanbul-*Turkey*
[3]Department of General Surgery, Gülhane Training and Research Hospital, Ankara-*Turkey*

ABSTRACT

BACKGROUND: Acute mesenteric ischemia (AMI) is a disease that causes an ischemia in the intestines due to the obstruction of the mesenteric vessels feeding the intestines, with a mortality rate reaching up to 80%. The overall incidence of AMI is 0.63 per 100,000 people. Early diagnosis and treatment are very important for survival. There is no ideal biomarker that can reflect different types and stages of AMI. This study investigated the predictive and prognostic value of L-lactate, D-dimer, leukocyte, C reactive protein (CRP) and neutrophil/lymphocyte ratio (NLR) in the preoperative period were investigated in patients operated for AMI.

METHODS: A total of 44 patients operated for AMI between 2015 and 2019 were evaluated in this study. Demographic, clinical, radiological, laboratory and surgical findings of the patients included in this study were recorded. The patients were divided into groups according to the etiological type of AMI. L-lactate, D-dimer, CRP, leukocyte, and NLR levels of these patients were determined. Statistical analysis was performed according to AMI groups.

RESULTS: The mean age of the 44 patients included in this study was 67.7 years and the female to male ratio was 0.76. According to tomography results, 31.8% (n=14) of the patients had mesenteric artery embolism, 29.5% (n=13) had mesenteric artery thrombus, 25% (n=11) had mesenteric vein thrombus and 13.6% (n=6) had non-occlusive mesenteric ischemia. When AMI types were compared, D-dimer and CRP levels were found to be significantly different from other markers. The total length of stay in the hospital was found to be significantly correlated with the L-lactate (p=0.047) and CRP (p=0.045) levels. In the analyses, CRP was determined to be the common biomarker that could be used in the diagnosis of mesenteric ischemia in all AMI types.

CONCLUSION: Particularly, the CRP level can be used effectively in the preoperative period to diagnose AMI and to determine its subtype and clinical course. However, L-lactate, D-dimer, leukocyte and NLR are markers that have no predictive value in the diagnosis of all AMI subtypes.

Keywords: Acute mesenteric ischemia; C-Reactive protein; D-dimer; L-lactate; Leukocyte; neutrophil/lymphocyte ratio.

INTRODUCTION

Acute mesenteric ischemia (AMI) is a rare disease with high mortality rates that result in ischemia/reperfusion injury due to the obstruction, venous congestion, or vasoconstriction of mesenteric vessels feeding the intestines.[1] AMI accounts for 0.09–0.2% of the acute surgical intervention.[2] The incidence increases with the increasing age, reaching 18% in patients older than 65 years of age.[3] The mean age of onset of AMI is 67 years, and its incidence in men and women is the same.[4,5] Typical symptoms include sudden-onset widespread abdominal pain, nausea, vomiting, diarrhea and rectal bleeding.

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Address for correspondence: Vahit Onur Gül, M.D.
Gülhane Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, Ankara, Turkey
Tel: +90 312 - 304 50 16 E-mail: vonurgul@hotmail.com

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[1,5] There are four different etiological types of AMI: arterial embolism (EAMI) (50%), arterial thrombosis (TAMI) (25%), non-occlusive mesenteric ischemia (NOMI) due to vasoconstriction of the mesenteric artery (20%), and venous thrombosis (VAMI) (10%).[1,4,5]

Despite the improvements in diagnosis and treatment methods, mortality rates have been still ranging 60–80%.[5,6] Following the surgical intervention, the mortality rates may increase to 32.1% in VAMI, 54.1% in EAMI, 72.7% in NOMI and 77.4% in TAMI.[4,7] The reasons for the increase in mortality rates include late hospital admission, late diagnosis, and the presence of coexisting comorbidities, such as atrial fibrillation (AF), heart failure, atherosclerosis, thrombophilic conditions, and shock with the increasing age.[4–6] Emergency intervention is of great importance, and the mortality rates can decrease to 10–20% with the interventions made within the first six hours; however, the mortality rates may reach 79–100% after 24 hours.[8]

The key to early diagnosis is increased clinical suspicion and multidetector computed tomography angiography (MDCTA) should be performed as soon as possible.[1,5] For the biochemical diagnosis of AMI, many biomarkers, such as intestinal fatty acid-binding protein (I-FABP), α-glutathione S-transferase (α-GST), citrulline, D-dimer, L and D-lactate, white blood cell (WBC) count, and neutrophil/lymphocyte ratio (NLR) have been evaluated. However, no consensus has been achieved in this regard.[5,8] There have been still studies being carried out to find an ideal biomarker that is able to reflect different types and stages of AMI.[1,5,8] This retrospective study aims to investigate the predictive value of L-lactate, D-dimer, leukocyte, C reactive protein (CRP) and NLR levels in the preoperative period in patients operated for AMI and to find an ideal biomarker.

MATERIALS AND METHODS

Study Population and Design

This study included a total of 51 patients who underwent surgery for AMI between 2015 and 2019. Ethical approval was obtained from the Bezmialem Foundation University Faculty of Medicine Ethics Committee with the decision no. 10/161 dated 07.05.2019 to conduct this study. Four of these patients were operated and sent to an external intensive care unit (ICU), and their treatment was continued in another center and data of three patients could not be obtained in full. Therefore, they were excluded from the study. A total of 44 patients whose data could be accessed from hospital archives and patient files were included in this study.

Age, sex, body mass index (BMI), Charlson Comorbidity Index (CCI), most prevalent cardiovascular disease (CVD) comorbidities, deep vein thrombus, pulmonary embolism, history of embolism and thrombus (e.g. cerebrovascular disease), previous history of abdominal surgery, duration of complaints, days), and the most common complaints were recorded. L-lactate levels were biochemically measured in venous blood gas (0.3–1.3 mmol/L) and D-dimer (0–0.5 μg/mL FEU), amylase (25–125 U/L), lactate dehydrogenase (LDH) (125–220 U/L), CRP (0–5 mg/L), leukocyte (4.6–10.2 10^3/LL), and NLR (10^3/LL) values were measured in blood plasma samples.

Then, the mesenteric vessels involved, for example, superior mesenteric artery (SMA), superior mesenteric vein (SMV), inferior mesenteric artery (IMA) and inferior mesenteric vein (IMV) were examined via CTA. The etiological type of AMI (EAMI, TAMI, VAMI, or NOMI) was identified based on pn clinical and CTA findings of the patients.

The following parameters were examined: type of surgical intervention (e.g. laparotomy/laparoscopy, small or large bowel resection), small and large bowel with ischemia, anastomosis or stoma status, presence of drain, operation time (hours), second look application after 24 hours, postoperative bleeding, complications (e.g. intraabdominal abscess or wound infection), length of stay in ICU (days), total treatment duration (days), healing and death status. Demographic, clinical and laboratory parameters of the patients were evaluated according to the AMI types.

Statistical Analysis

Descriptive statistics for the categorical variables were expressed as frequency and percentage. Descriptive statistics for the numerical variables following normal distribution were expressed as mean ± standard deviation whereas those not following normal distribution were expressed as median (min-max). Shapiro–Wilk test was used to determine whether the data followed a normal distribution. Student's t-test was used to determine whether there was a significant difference between the mean values of independent data following normal distribution in the presence of two groups, whereas a one-way analysis of variance (ANOVA) test was used in the presence of three or more groups. Pearson chi-square, Fisher Exact, and Fisher Freeman Halton tests were used to determine whether there was a correlation between the categorical variables or whether they were independent of each other. For the evaluation of quantitative variables, the Mann-Whitney U test was used to compare the mean values of two independent groups, which did not follow a normal distribution. Kruskal Wallis-H Test was used to evaluate whether the difference between the mean values of three or more groups was significant in non-normally distributed groups. Dunn and Bonferroni tests were used for post hoc analyses. The correlation between the numerical variables was determined using Spearman's Correlation Analysis. The receiver operating characteristic (ROC) curve was used to determine the diagnostic value of biochemical markers (NLR, CRP, L-Lactate, and D-dimer) according to the etiological type of AMI. Youden J index was used to determine cut-off

values in ROC results. All statistical analyses were performed using IBM SPSS Statistics version 22.0 software (IBM Corporation, Armonk, NY, USA). Results were evaluated at a 95% confidence interval and a p-value of <0.05 was considered statistically significant.

RESULTS

The age range of 44 patients included in this study was 24–96 years (mean: 67.7 years), and the female to male ratio was 0.76. The BMI was 20.2–47.2 (mean: 28.8) kg/m^2. The CCI of the patients ranged from 0 to 9, with a maximum index of 5 (n=11, 25%), and the index was 0 in 6.8% (n=3) of the patients. In general, the most prevalent CVD comorbidity was coronary artery disease (n=18, 47.4%), whereas 13.6% (n=6) of the patients had no CVD comorbidity. Of the patients, 22.7% (n=10) had a history of previous thromboembolism and half of these patients had a history of previous cerebrovascular disease. Of the patients, 27.3% (n=12) had a history of previous abdominal surgery. There were generalized abdominal pain, nausea, and vomiting in 97.7% (n=43), 81% (n=36) and 65.9% (n=29) of the patients. When the time between the onset of complaints and the time of hospital admission was examined, 9% (n=4) of the patients were admitted to the hospital within the first 12 hours, whereas 43% (n=19) between 12–24 hours and 47.7% (n=21) later than 24 hours.

The CTA examinations showed that 63.6% (n=28) of the patients had isolated SMA involvement, 13.6% (n=6) had isolated SMV involvement, 9% (n=4) of them had SMV and IMV involvement, and 2.3% (n=1) of them had both SMA and SMV involvement, whereas there was no mesenteric vessel obstruction was observed in 11.4% (n=5) of the patients.

The sub-etiological type of AMI was identified through the CTA results of the patients who were operated for AMI. Of the patients, 31.8% (n=14) of them had EAMI, 29.5% (n=13) of them had TAMI, 25% (n=11) had VAMI, and 13.6% (n=6) of them had NOMI. According to these sub-types, patients with the highest mean age and BMI were in the EAMI group. The AMI sub-types were generally more common in male patients. The highest CCI level was found to be in patients with NOMI. Considering the CVD comorbidities, the disease was accompanied by AF in 46.1% of patients with EAMI, whereas it was accompanied by CVD in 50% of the patients with TAMI, 55.5% of the patients with VAMI, and 50% of the patients with NOMI. The rate of embolism and thrombus history was higher in the EAMI group; one-third of the patients had this history. However, there was no statistically significant difference between the demographic characteristics and AMI types (p>0.05) (Table 1).

Comparison of AMI types with auxiliary biochemical tests performed to make a diagnosis and to determine the level of inflammation before surgery showed a significant difference between the patients with AMI concerning D-dimer and CRP results. The highest D-dimer level (3.46±1.8 µg/mL FEU)

Table 1. Demographic characteristics of the patients with acute mesenteric ischemia according to ischemia types

Demographic features	Acute mesenteric ischemia types				p
	EAMI	TAMI	VAMI	NOMI	
Sex, n (%)					
Male	7 (50)	8 (61.5)	6 (54.5)	4 (66.7)	0.903$^{\alpha}$
Female	7 (50)	5 (38.5)	5 (45.5)	2 (33.3)	
Age (year), mean±SD	71.4±12.2	68.7±13.8	60.0±21.0	70.6±14.7	0.312$^{\beta}$
Body mass index (kg/m^2), mean±SD	29.7±7.1	27.3±4.1	29.6±5.9	29.3±5.2	0.711$^{\beta}$
Charlson Comorbidity Index, mean±SD	4.2±1.7	4.0±2.1	3.4±2.7	5.6±1.8	0.276$^{\beta}$
Cardiovascular disease, n (%)					
Atrial fibrillation	6 (46.1)	4 (40)	2 (22.2)	1 (16.6)	0.768$^{\alpha}$
Coronary artery disease	5 (38.4)	5 (50)	5 (55.5)	3 (50)	
Embolism/thrombus history, n (%)					
No	9 (64.3)	10 (76.9)	9 (81.8)	6 (100)	0.449$^{\alpha}$
Yes	5 (35.7)	3 (23.1)	2 (18.2)	0 (0)	
Previous abdominal surgery, n (%)					
No	12 (85.7)	9 (69.2)	8 (72.7)	3 (50)	0436$^{\alpha}$
Yes	2 (14.3)	4 (30.8)	3 (27.3)	3 (50)	

$^{\alpha}$Fisher Freeman Halton test; $^{\beta}$One-Way ANOVA test. EAMI: Mesenteric artery embolism; TAMI: Mesenteric artery thrombosis; VAMI: Mesenteric vein thrombosis; NOMI: Non-occlusive mesenteric ischemia; SD: Standard deviation.

was in the EAMI group, whereas the lowest D-dimer level (1.25±0.9 µg/mL FEU) was in the NOMI group. The difference between the groups was statistically significant (p=0.040). The highest CRP level (65.13±103.2 mg/L) was in the EAMI group, whereas the lowest CRP level (17.65±12.9 mg/L) was in the NOMI group. The difference between the groups was statistically significant (p=0.032). However, no statistically significant difference was found between the groups concerning L-lactate, amylase, LDH, Leukocyte and NLR values (p>0.05) (Table 2).

As a surgical treatment, diagnostic laparotomy/laparoscopy (n=12, 27.2%), small bowel resection (n=23, 52.2%), and small bowel and colon resection (n=9, 20.4%) were performed. During the operation, 84% (n=37) of the patients were found to have small intestinal ischemia and 16% (n=7) had colon ischemia as well as small intestinal ischemia. There was a significant difference between the site of involvement in AMI and D-dimer and CRP tests. The D-dimer level was high (2.89±2.10 µg/mL FEU) in small intestinal involvement, but it was low (1.24±0.99 µg/mL FEU) in small and large intestinal involvement. This difference was statistically significant (p=0.029). The CRP level was high (44.46±75.3 mg/L) in small intestinal involvement whereas it was low (10.50±7.8 mg/L) in the small and large intestinal involvement, and the difference was statistically significant (p=0.018). However, no statistically significant difference was found between the groups concerning L-lactate, amylase, LDH, Leukocyte and NLR values (p>0.05) (Table 3).

Bowel anastomosis was performed in 40.6% (n=13) of the patients undergoing resection and stoma was opened in 59.7% (n=19). The operation time was 39–93 (mean: 66.6) minutes. An intraabdominal silicone drain was placed in 56.8% (n=25) of the patients. The second look was performed in 45.5% (n=20) of the patients. Two patients with early-stage SMA embolism underwent embolectomy. Of the patients, 22.7% (n=10) were taken to the service after the surgery, whereas 77.3% (n=34) of them were taken to the ICU. The patients who were taken

Table 2. Correlation between acute mesenteric ischemia types and biochemical markers

Biomarkers evaluated	Acute mesenteric ischemia types				p¥
	EAMI	TAMI	VAMI	NOMI	
	Med. (Min-Max)	Med. (Min-Max)	Med. (Min-Max)	Med. (Min-Max)	
L-lactate (0.3–1.3 mmol/L)	3.40 (1.6–5.6)	2.70 (0.9–5.5)	2.20 (1.4–4.6)	2.65 (1.1–3.1)	0.107
D-dimer (0–0.5 µg/mL FEU)	2.90 (1.30–7.10)	2.10 (0.40–5.90)	0.80 (0.40–7.80)	1.30 (0.20–2.70)	0.040*
Amylase (25–125 U/L)	72.50 (22–593)	122 (41–902)	48 (19–464)	144.50 (27–381)	0.079
LDH (125–220 U/L)	277.50 (218–832)	267 (175–524)	263 (162–823)	304 (207–545)	0.792
CRP (0–5 mg/L)	30.29 (16–412)	18.53 (1.1–50)	12.20 (3.8–248.2)	14.50 (4.6–34)	0.032**
Leukocyte (4.6–10.2 10^3/µL)	19.10 (6.75–42.10)	18.51 (7.51–50.67)	19.28 (11.48–33.46)	13.40 (4.21–25.66)	0.682
Neutrophil/lymphocyte ratio (10^3/µL)	15.83 (8.75–44.88)	12.19 (4.14–96.20)	14.46 (2.97–23.70)	11.02 (1.49–39.43)	0.142

¥Kruskal Wallis test. *D-dimer post hoc EAMI-NOMI: p=0.005, **CRP post hoc EAMI-TAMI p=0.008, EAMI-VAMI p=0.029. EAMI: Mesenteric artery embolism; TAMI: Mesenteric artery thrombosis; VAMI: Mesenteric vein thrombosis; NOMI: Non-occlusive mesenteric ischemia; Med.: Median; Min: Minimum; Max: Maximum.

Table 3. Correlation between bowel involvement and biochemical markers in acute mesenteric ischemia

Biomarkers evaluated	Site of involvement in acute mesenteric ischemia		p∞
	Small intestine	Small and large intestine	
	Med. (Min-Max)	Med. (Min-Max)	
L-lactate (0.3–1.3 mmol/L)	2.90 (0.9–5.5)	1.50 (1.4–5.6)	0.103
D-dimer (0–0.5 µg/mL FEU)	2.30 (0.30–7.80)	0.70 (0.20–2.80)	0.029
Amylase (25–125 U/L)	96 (19–902)	71 (22–464)	0.615
Lactate dehydrogenase (125–220 U/L)	263 (162–832)	330 (223–400)	0.134
C-reactive protein (0–5 mg/L)	23 (1.9–412)	9 (1.1–22)	0.018
Leukocytes (4.6–10.2 10^3/µL)	18.51 (4.21–50.67)	20 (10.80–42.10)	0.730
Neutrophil/Lymphocyte ratio (10^3/µL)	14 (1.49–96.20)	15.86 (4.14–44.88)	0.312

∞Mann-Whitney Test. Med.: Median; Min: Minimum; Max: Maximum.

to the ICU stayed there for 1–60 (mean: 8.23) days. The total length of hospital stay of all patients was 1–60 (mean 11.5) days. While 59% (n=26) of the patients undergoing surgery died, 41% (n=18) were discharged with healing.

There was a significant correlation between D-dimer and L-lactate (p=0.001). No significant correlation was observed between LDH and amylase (p=0.025). The CRP levels were found to have a significant correlation with L-lactate (p=0.0001) and D-dimer (p=0.0001). There was a significant correlation between NLR and leukocyte (p=0.035). The length of stay in the ICU was found to be correlated with LDH (p=0.0001). The total length of stay in the hospital was found to have a significant correlation with L-lactate (p=0.047), CRP (p=0.045), and length of stay in the ICU (p=0.0001) (Table 4).

In the present study, the comparison was made according to the etiologic AMI groups to determine the diagnostic, predictive cut-off value of the biomarkers studied (CRP, NLR, L-Lactate, and D-dimer) and the results were evaluated statistically. The comparison was made between the patients with EAMI, the most common type of AMI, and those with TAMI, VAMI, and NOMI, respectively.

According to the ROC analysis results, it was concluded that the diagnosis could be made using NLR or CRP biomarkers in EAMI and TAMI (Fig. 1) (p=0.012 and p=0.0013). The NLR of 12.5 10^3/μL and above and a CRP level of greater than 19.4 mg/L indicates the presence of mesenteric ischemia (Table 5).

According to the ROC analysis results, it was concluded that the diagnosis could be made using L-lactate and CRP biomarkers in EAMI and VAMI (Fig. 2) (p=0.0245 and p=0.008). If the L-lactate is greater than 3 mmol/L or CRP is greater than 12.4 mg/L (Table 5), mesenteric ischemia diagnosis is made (Table 5).

According to the ROC analysis results, it was concluded that the diagnosis could be made using D-dimer and CRP biomark-

Table 4. Correlation between biochemical markers in acute mesenteric ischemia

Parameters		L-lactate	D-dimer	Amylase	LDH	Leukocytes	CRP	Neutrophil/ lymphocyte ratio	Length of stay in the ICU (days)
D-dimer	r	.706**							
	p	.000							
	n	44							
Amylase	r	–.056	-.009						
	p	.719	.953						
	n	44	44						
LDH	r	.194	.158	.337*					
	p	.207	.307	.025					
	n	44	44	44					
Leukocytes	r	.285	.156	–.119	–.003				
	p	.061	.313	.441	.984				
	n	44	44	44	44				
CRP	r	.691**	.913**	–.053	.097	.117			
	p	.000	.000	.734	.531	.448			
	n	44	44	44	44	44			
Neutrophil/lymphocyte ratio	r	.103	–.029	.010	.108	.319*	.013		
	p	.504	.851	.950	.485	.035	.091		
	n	44	44	44	44	44	44		
Day of stay in the ICU	r	.212	.191	.247	.513**	.250	.266	.047	
	p	.166	.214	.106	.000	.101	.082	.760	
	n	44	44	44	44	44	44	44	
Total length of stay	r	.301*	.226	.066	.150	.002	.304	–.099	.521**
	p	.047	.140	.672	.331	.990	.045	.524	.000
	n	44	44	44	44	44	44	44	44

CRP: C-reactive protein; ICU: Intensive care unit; LDH: Lactate dehydrogenase.

Table 5. The use of biochemical markers in the diagnosis of the acute mesenteric ischemia

Etiological groups	Biomarkers	Cut-off value	Sensitivity	Specificity	AUC	p (area=0.5)	Comparison of the ROC curves (p)
EAMI &	NLR	≥12.5	69.23	85.71	0.753	0.012	0.740
TAMI	CRP	>19.4	92.86	69.23	0.797	0.0013	
EAMI &	L-lactate	>3	90.91	64.29	0.769	0.008	0.554
VAMI	CRP	>12.4	63.64	100.00	0.760	0.0245	
EAMI &	D-dimer	>1.73	83.33	85.71	0.893	<0.001	0.188
NOMI	CRP	>9	50.00	100.00	0.780	0.027	

AUC: Area under the ROC curve; EAMI: Mesenteric artery embolism; TAMI: Mesenteric artery thrombosis; VAMI: Mesenteric vein thrombosis; NOMI: Non-occlusive mesenteric ischemia.

ers in EAMI and NOMI (Fig. 3) (p<0.001 and p=0.027). If the D-dimer is >1.73 µg/mL FEU or CRP is >9 mg/L, mesenteric ischemia diagnosis is made (Table 5).

In the ROC analysis performed according to the etiologic AMI groups, CRP was found to be the common biomarker that can be used in the diagnosis of mesenteric ischemia in all AMI etiology (Table 5).

DISCUSSION

Mesenteric ischemia was first described by Antonio Beniviene in the 15th century in a book titled Vascular Disorders of the Intestines that describes every aspect of mesenteric ischemia in detail, which was published in 1971.[9] However, there are still many aspects of mesenteric ischemia that have not been clarified yet.[1,9]

Ten percent of mesenteric ischemia is a chronic type, whereas 90% is an acute type.[10] While 90% of chronic mesenteric ischemia originates from progressive atherosclerotic disease, 75–80% of AMIs arise from embolism or thrombus.[8,10] The superior mesenteric artery is affected in 75–85% of all mesenteric ischemia cases since the angle at which the SMA comes out from the aorta is narrow and the diameter of the lumen is wide, which plays a major role in the development of AMI.[8,11] Irreversible AMI phase begins in cases where systemic blood pressure is below 40 mmHg and 75% reductions in blood flow for more than 12 hours or 100% occlusion for more than six hours.[4,10,11] Mucosa develops in the first stage of necrosis, submucosa and muscularis propria in the second stage and transmural bowel necrosis develops in the third stage.[10] Development of transmural infarction results in perforation, peritonitis, and death.[1,4]

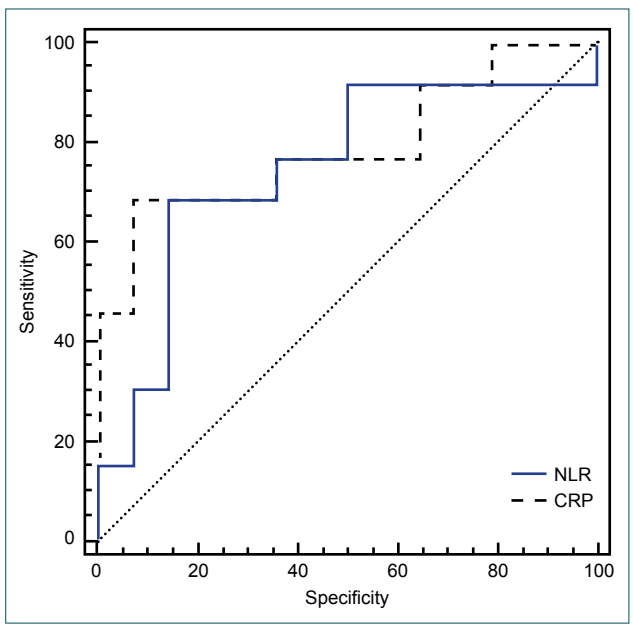

Figure 1. The efficacy of neutrophil/lymphocyte ratio and C-reactive protein in the diagnosis of mesenteric artery embolism and thrombosis.

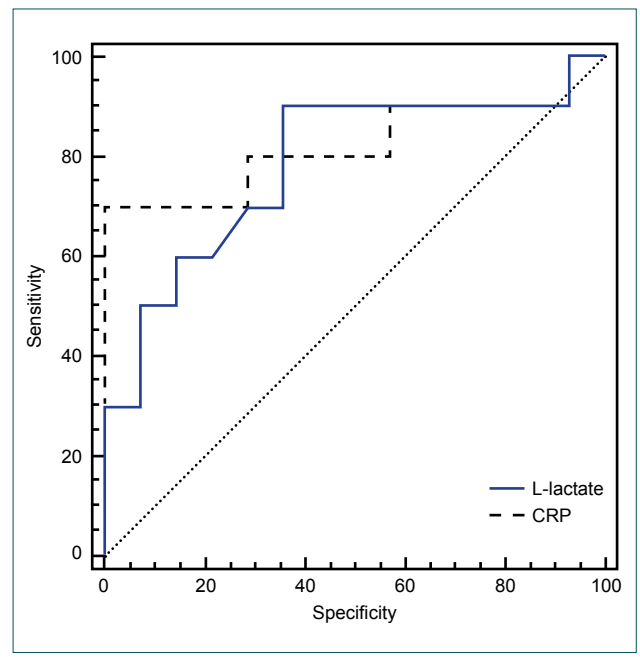

Figure 2. Efficacy of L-lactate and C-reactive protein in the diagnosis of mesenteric artery embolism and mesenteric vein thrombosis.

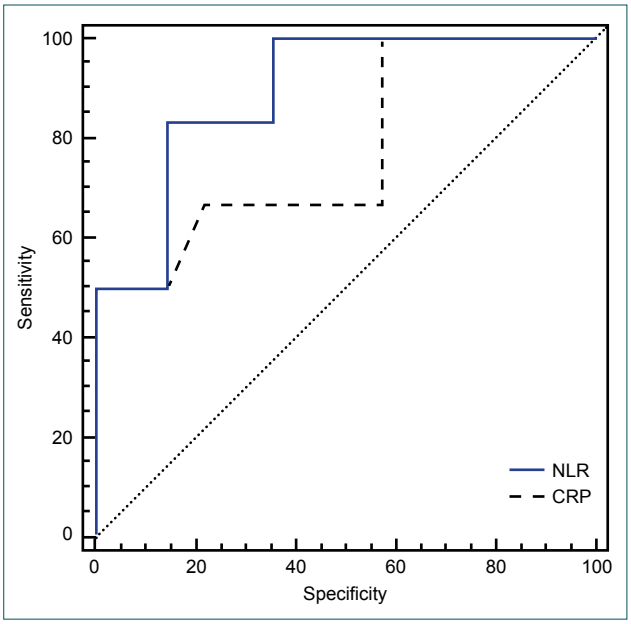

Figure 3. Efficacy of D-dimer and C-reactive protein in the diagnosis of mesenteric artery embolism and non-occlusive mesenteric ischemia.

In Europe and the USA, AMI constitutes 1:1000 of the patients hospitalized with acute abdomen diagnosis in one year.[6,11] The overall incidence of AMI in Europe is 0.63 per 100,000 people.[11] It is seen equally in females and males.[1] However, 70% of the patients have been reported to be females in several studies.[4,6] It is more common in the age of 70.[1,4,11] The disease is accompanied by cardiovascular comorbidities, such as AF, coronary artery disease, and ischemic heart disease, in 80% of the patients.[4,11,12] One-third of the patients have a history of previous embolism/thrombosis.[1,11] The mean age of the patients was 67.7 years in the present study. The rate of male patients was 56.8% and the female to male ratio was 0.76. The mean BMI of the patients included in the present study was 28.8 kg/m^2. Cardiovascular comorbidity was present in 86.4% of the patients, whereas 47.4% had coronary artery disease. The rate of patients with a history of thromboembolism was 22.7%. These data were compatible with the relevant literature. We believe that the high incidence rate in male patients in the present study is due to region and the incidence of AMI has been reported to be higher in studies carried out in Turkey.[13,14]

The most common etiologic form of AMI (45–50%) is EAMI with SMA embolism.[6,11] The main risk factors are AF, cardiac arrhythmias, rheumatic valve disease, coronary artery disease, and myocardial infarction.[1,10,11] In EAMI, 33% of patients have a history of embolism.[11] Sudden and severe non-localized abdominal pain, vomiting, diarrhea are seen in the beginning. However, there might be generalized abdominal pain, fever, bloody diarrhea and shock if transmural infarction develops.[1,11] Heart diseases, such as AF, gastric-emptying disorder and Bergan Triad presenting with incompatible symptoms, may not always occur.[15] Embolism is usually located 6 to 8 cm distal to the origin of the SMA, beyond the middle colic artery outlet and thus, the proximal jejunum and colon are protected.[1,15] If the diagnosis and treatment can be performed within the first 24 hours, the survival rate is 89.4%; however, if the diagnosis is delayed, this rate decreases to 27.1%.[15] Diagnosis is made using CTA.[16] Laboratory findings are insufficient for diagnosis.[15,16] Open embolectomy and laparotomy are performed in its treatment.[15,17] In the present study, 31.8% of the patients had EAMI, the ratio of male patients to female patients was equal and the age at which the disease is seen most was 71.4 years. According to other types, patients with the highest mean age and BMI were in the EAMI group. In EAMI, the disease was accompanied by AF in 46.1% of the patients, whereas 35.7% had a history of embolism/thrombus.

TAMI, which is the thrombosis of SMA, accounts for approximately 25% of the AMI cases.[1,4,11] The main risk factors are known to be arteriosclerosis, hypertension, diabetes, hyperlipidemia, and antiphospholipid syndrome.[11] It should be suspected, particularly in patients with atherosclerotic disease, who have a recent history of postprandial pain and weight loss.[1,11] Thrombotic obstructions are located more proximal to embolic obstructions and may lead to jejunum, ileum and colon infarction.[2] In TAMI, the mean age is 70 and the female to male ratio is equal.[12,15] There might be thrombosis in the celiac trunk in 33% of the patients with thrombosis in SMA.[12] If possible, endovascular treatment should be the first choice for the treatment of TAMI.[11] In the present study, 61.5% of the patients with TAMI were male and the mean age was 68.7 years. There was a history of coronary artery disease in 50% of the patients, whereas 23.1% had a history of thrombus.

Non-occlusive mesenteric ischemia accounts for 20% of the AMIs.[4] The main risk factors include ischemic heart failure, low flow states (shock, hypovolemia, hypotension), drugs (digitalis, diuretics, beta-blockers, alpha-adrenergic drugs), major abdominal surgery and enteral nutrition. Low cardiac output reduces splanchnic blood flow, causing vasoconstriction of SMA. It occurs when the blood flow decreases below 50% for more than 30 minutes.[1,18] The mean age of patients with NOMI is 76.4 years and 53.8% of the patients are female.[18] Acute and insidious abdominal pain, abdominal distention and blood in the stool can be seen.[11] Progression of the disease to intestinal necrosis leads to an elevation in inflammation markers, such as leukocytes and lactate.[19] Emergency laparotomy should be performed to determine portal venous gas or pneumatosis intestinalis, which are specific radiological symptoms.[19] Although there are no radiological findings, endoscopy and/or laparotomy should be performed if there is high clinical suspicion.[19] Mortality rates reach up to 80% due to advanced age and difficulties in the early diagnosis.[7,19] In the present study, 20% of the patients had EAMI, the ratio of male patients was 66.7% and the age at which the disease is seen most was 70.6 years.

Mesenteric vein thrombosis accounts for 10% of AMIs. The mean age of patients at presentation is 45–60 years with a slight male to female predominance.[10,20] Although approximately 21–49% of the patients are idiopathic, the main risk factors are hereditary thrombophilic diseases (e.g. Factor V Leiden, prothrombin mutation, protein S deficiency, and protein C deficiency), malignancies, cirrhosis, acute pancreatitis, and oral contraceptives.[10,11,20] Previous deep venous thrombosis or pulmonary embolism is reported in 50% of the patients.[11] In general, severe bowel ischemia does not occur due to the large collateral network. However, severe hemorrhagic infarction may occur in the intestinal wall.[10] Laboratory tests are not helpful in diagnosis.[20] Diagnosis is made using CTA.[11,20] In VAMI, subacute abdominal pain, bloating, abdominal distention, fever, and occult blood in the stool, which may be lasting for up to two weeks, may occur.[10,11] The first treatment approach for VAMI is anticoagulation and no surgery is required in general.[11,20] In the present study, 54.5% of the patients with VAMI were male and the mean age was 60 years. There was a history of coronary artery disease in 55.5% of the patients, whereas 18.2% of the patients had a history of thrombus.

At present, there is no specific laboratory test that can be routinely used for early detection of AMI.[11,21] Computed tomography angiography is used for the definitive diagnosis of AMI.[1,10,11] However, CTA has less specificity in NOMI. Furthermore, CTA is contraindicated in patients with renal dysfunction or contrast allergy.[21] Thus, there is a need for an ideal biomarker that can be used in the diagnosis of AMI.[5,21] The most useful biomarker for early diagnosis should be specific to intestinal ischemia and should be very sensitive to show mucosal ischemia.[11] On the other hand, these biomarkers should be able to indicate the success of the intervention and prognosis.[21]

The most common laboratory abnormalities in AMI are hemoconcentration, leukocytosis, high anion gap, high lactate-induced metabolic acidosis, high serum amylase, aspartate aminotransferase, LDH, and creatine phosphokinase levels. None of these are sensitive or specific enough to diagnose AMI.[1,5,11] The large meta-analysis studies on biomarkers studied to date have shown that leukocyte count, L-lactate, LDH, excess base, D-lactate and amylase values cannot distinguish intestinal ischemia. Therefore, they have not been accepted as the ideal biomarkers.[1,5,22] However, it has been shown that plasma I-FABP and α-GST secreted from enterocytes increase in the early stage and might be, therefore, considered as a good biomarker.[5,11,21,22] On the other hand, D-dimer values have been reported to be correlated well with the sequela of intestinal ischemia but have low specificity.[5,21] There are studies in the literature reporting that procalcitonin, ischemia-modified albumin (ET-1), endothelin-1, citrulline, smooth muscle-specific protein (SM-22), cobalt-albumin binding assay (CABA), microRNA-21 (miR-21) and NLR markers can be used in the diagnosis of AMI.[5,14,21,22] D-dimer, α-GST, and I-FABP are potential plasma biomarkers showing intestinal ischemia and they reflect the activation of intravascular coagulation and intestinal mucosal damage, respectively.[22]

In the present study, a statistically significant difference was found in CRP and D-dimer tests concerning AMI type. The CRP and D-dimer levels were highest in the EAMI group and lowest in the NOMI group. This difference was more significant in CRP. However, L-lactate, amylase, LDH, leukocyte, and NLR values have been found to have no diagnostic value. There was a statistically significant correlation between CRP and L-lactate values and length of stay, which was more significant in CRP. In the ROC analysis, CRP was found to be the common biomarker that could be used for diagnosis in all etiological types of AMI. In this study, it has been concluded that L-lactate, D-dimer, leukocyte, and NLR values could not be used for diagnostic purposes in the etiological types of AMI.

Conclusion

Despite the improvement in the resolution of CT images, as well as vascular and endovascular intestinal revascularization, the mortality rates in AMI have not changed in the last decade and have remained between 60–80%. Existing clinical, radiological and laboratory tests are not sufficient for the diagnosis of early and reversible mesenteric ischemia. There is a need for easy-to-apply, inexpensive and practical biomarkers that can be measured everywhere. As shown in the present study, CRP is an easily accessible, inexpensive, effective and valuable biomarker that can be used in the diagnosis of various subtypes of AMI. However, further studies are needed to determine threshold values, accuracy standards, and specific biomarkers for different etiologic forms of AMI.

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ORİJİNAL ÇALIŞMA - *ÖZET*

Akut mezenterik iskemi hastalarında L-laktat, D-dimer, lökosit, CRP ve nötrofil/lenfosit oranının prediktif ve prognostik değeri

Dr. Sabahattin Destek,[1] Dr. Aysegül Yabacı,[2] Dr. Yağmur Nur Abik,[1] Dr. Vahit Onur Gül,[3] Dr. Kamuran Cumhur Değer[1]

[1]Bezmialem Vakıf Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, İstanbul
[2]Bezmialem Vakıf Üniversitesi Tıp Fakültesi, İstatistik Anabilim Dalı, İstanbul
[3]Gülhane Eğitim Araştırma Hastanesi, Genel Cerrahi Kliniği, Ankara

AMAÇ: Akut mezenterik iskemi (AMİ) bağırsakları besleyen mezenterik damarların obstrüksiyonuyla bağırsaklarda iskemiye neden olan, mortalite oranı %80'i bulan hastalık grubudur. İnsidansı 100.000'de kişi başına 0.63'tür. Sağkalım için erken tanı ve tedavi çok önemlidir. AMİ'nin farklı tip ve aşamalarını yansıtabilen ideal bir biobelirteç yoktur. Çalışmamızda AMİ tanısıyla ameliyat edilen hastalarda ameliyat öncesi aşamada L-laktat, D-dimer, lökosit, C-reaktif protein (CRP) ve nötrofil/lenfosit oranının (NLO) prediktif ve prognostik önemi araştırıldı.

GEREÇ VE YÖNTEM: Bu çalışmada 2015–2019 tarihleri arasında AMİ tanısı ile ameliyat edilen 44 hasta incelendi. Çalışmaya alınan hastaların demografik, klinik, radyolojik, laboratuvar, cerrahi bulguları dahil edildi. Hastalar etiyolojik olarak AMİ grubuna göre gruplandırıldı. Bu hastaların L-laktat, D-dimer, CRP, lökosit, NLO seviyeleri belirlendi. AMİ gruplarına göre istatiksel analiz yapıldı.

BULGULAR: Çalışmaya alınan 44 hastanın yaş ortalaması 67.7 yıl, kadın erkek oranı 0.76 idi. Tomografi bulgularına göre hastaların %31.8'inde (n=14) mezenter arter embolisi, %29.5'inde (n=13) mezenter arter trombüsü, %25 (n=11) hastada mezenter ven trombüsü, %13.6'sında (n=6) non-oklüsiv mezenter iskemi saptandı. AMİ tipleriyle karşılaştırıldığında D-dimer ve CRP testleri diğer markırlara göre anlamlı şekilde farklı bulundu. Toplam yatış süresi ile L-laktat (p=0.047) ve CRP (p=0.045) ile anlamlı bir korelasyon saptandı. Yapılan analizlerde tüm AMİ tiplerinde mezenter iskemi tanısında kullanılabilecek ortak biyobelirteç CRP olmuştur.

TARTIŞMA: Ameliyat öncesi özellikle CRP düzeyinin AMİ tanısında, alt tipini belirlemede ve klinik seyrini belirlemede etkin şekilde kullanılabilir. Ancak L-laktat, D-dimer, lökosit ve nötrofil/lenfosit oranlarının tüm AMİ alt tiplerinin tanısını koymada etkinliği yoktur.

Anahtar sözcükler: Akut mezenter iskemi; CRP; D-dimer; L-laktat; lökosit; nötrofil/lenfosit oranı.

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