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ORIGINAL PAPER

FAR Ratio as Prognostic Biomarker in AMI

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Abstract

Acute mesenteric ischemia (AMI) is a vascular emergency resulting from decreased blood flow caused by the occlusion of the mesenteric vessels, hypoperfusion, or vasospasm. This study aimed to investigate the prognostic value of the fibrinogen-to-albumin (FAR) ratio in patients with acute mesenteric ischemia. A total of 91 patients were enrolled in the study. Patients' demographics such as age and gender, pre- and postoperative hemoglobin, CRP, white blood cell (WBC), neutrophils, preoperative lymphocyte, alanine transaminase (ALT), aspartate transaminase (AST), thrombocytes, and postoperative D-dimer values were recorded. In addition, pre- and postoperative fibrinogen and albumin levels were recorded, and FAR was calculated. Patients were divided into two groups, survivors and non-survivors. The mean pre- and postoperative fibrinogen levels were statistically significantly higher in the non-survivor group than in the survivor group ($p < 0.001$). The mean pre- and postoperative albumin levels were significantly lower in the non-survivors than in the survivors ($p = 0.059$, $p < 0.001$; respectively). The mean pre- and postoperative FAR ratios were considerably higher in the non-survivor than in the survivor groups ($p < 0.001$). The change between pre- and postoperative fibrinogen, albumin, and FAR values was statistically significant between the non-survivors and the survivors (for all, $p < 0.05$). The preoperative and postoperative fibrinogen levels were significantly lower, and albumin levels were significantly higher in the survivor compared to the non-survivor patients with AMI. Furthermore, the preoperative and postoperative FAR ratio was significantly higher in the non-survivors. The FAR ratio may be a valuable prognostic biomarker for patients with AMI.

Keywords Acute mesenteric ischemia · Fibrinogen · Albumin · Fibrinogen-to-albumin ratio · Prognosis

Introduction

Acute mesenteric ischemia (AMI) is a vascular emergency resulting from decreased blood flow caused by the occlusion of the mesenteric vessels, hypoperfusion, or vasospasm. Despite improvements in diagnostic and surgical methods, AMI remains a life-threatening emergency with mortality rates between 50–70% [1, 2]. The high mortality rate associated with AMI is mainly because of the difficulty in early diagnosis and subsequent delays in appropriate management. The time to diagnosis of AMI is the most critical

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prognostic factor; therefore, early diagnosis and intervention are essential to reduce mortality in these patients [3]. AMI only accounts for 1% of all patients with acute abdomen, while its incidence significantly increases in patients >70 years of age [4]. AMI occurs in 1 of every 1000 hospital admissions, while some studies have reported up to 5% hospital mortality [5]. AMI is a potentially lethal vascular emergency associated with mortality over 60% if diagnosis takes more than 12 h and 90% if it takes longer than 24 h [6]. Risk factors for developing AMI include heart failure, peripheral vascular disease, and arterial hypertension [7]. The clinical symptoms often associated with AMI include mild but sudden-onset pain, diarrhea, low gastrointestinal bleeding, abdominal distension, nausea, vomiting, fever, and tachypnea; however, these symptoms are not specific enough to differentiate AMI from other abdominal disorders [8]. Currently, the diagnosis of AMI is mostly achieved by a high degree of clinical suspicion after ruling out the other acute abdominal diseases and a prompt confirmation by an abdominal computed tomography angiography (CTA) [9].

So far, several biomarkers, including L-lactate, creatine kinase, lactate dehydrogenase, D-dimer, leukocyte, nesfatin-1, neutrophil/lymphocyte ratio (NLR), and C-reactive protein (CRP), have been studied to predict the outcome of patients with AMI [10–12]. However, there is no universally accepted biomarker to predict the prognosis of AMI.

High levels of fibrinogen and low level of albumin are associated with the occurrence and severity of systemic disorders. Fibrinogen, an acute-phase protein, is an essential part of the coagulation cascade and an indicator of systemic inflammation [13]. In contrast, albumin is an anti-acute phase protein and an important clinical parameter for liver functioning and nutritional status [14]. Low serum albumin levels at admission are associated with increased mortality in intracranial hemorrhage patients [15]. As an inflammatory serum biomarker, the fibrinogen-to-albumin ratio (FAR) has been identified in several studies as a predictor of poor outcomes and adverse events in patients with cardiovascular diseases, sepsis, stroke, and cancer [16–19]. This study aimed to investigate the prognostic value of FAR in patients with acute mesenteric ischemia.

Material and Methods

The study protocol was approved by the local ethics committee of Sakarya University Faculty of Medicine (Decision date: 05/12/2022, No: E-71522473-050.01.04-194706/340). Informed patient consent was waived due to the retrospective design of the study. This study was conducted on the relevant ethical principles of the Declaration of Helsinki, revised in 2013. The study was conducted at Sakarya Training and Research Hospital in Sakarya province and Giresun Training and Research Hospital in Giresun province.

The medical records of the patients treated in our general surgery clinics due to the diagnosis of AMI were analyzed retrospectively. A total of 91 patients were enrolled in the study. Patients with a history of a recent vascular intervention or surgery within two weeks prior to the admission, acute systemic infection within two weeks prior to the admission, known malignancy, history of previous severe hepatic, renal or hematological diseases, and those who were using anticoagulant drugs, oral contraceptives, or steroids during the admission were excluded from the study.

Patients' demographics such as age and gender, pre- and postoperative hemoglobin, CRP, white blood cell (WBC), neutrophils, preoperative lymphocyte, alanine transaminase (ALT), aspartate transaminase (AST), thrombocytes, and postoperative D-dimer values were recorded. The first laboratory parameters of the patients were obtained from the blood samples taken at the time of admission to the emergency department. The laboratory results of the blood taken at the 72nd h after the procedure of the patients hospitalized for the surgical or interventional radiological procedure with the diagnosis of mesenteric ischemia were indicated as postoperative laboratory parameters. In addition, pre- and postoperative fibrinogen and albumin levels were recorded, and FAR was calculated. Patients with missing records were excluded from the analysis. Patients were divided into two groups, survivors and non-survivors, and the results were compared between the two groups. The survivors were followed up for 1 year.

Acute mesenteric ischemia was defined by [1] the presence of new-onset abdominal symptoms (pain, nausea, paralytic ileus) that were confirmed by the general surgeon, [2] the exclusion of the presence of any other pathology with abdominal computed tomography (CT) scan, and [3] imaging of cessation of blood flow on CT-angiography (CTA) or digital subtraction angiography (DSA) or the ischaemic intestinal wall during a surgical procedure.

Statistical Analysis

Data obtained in the study were statistically analyzed using the SPSS version 21.0 (SPSS, Statistical Package for Social Sciences, IBM Inc., IL, Chicago, USA) package program. The kurtosis and skewness coefficients were examined to determine the conformity of the variables to the normal distribution. The kurtosis and skewness values obtained from the variables between +3 and −3 are considered sufficient for the normal distribution [20–23]. Normality was provided for the variables with skewness and kurtosis values between +3 and −3, and parametric tests were used. Therefore, pre- and postoperative change was analyzed with the repeated ANOVA test. Normally distributed variables were

compared between the groups using independent *t*-test, and non-normally distributed variables were compared with the Mann-Whitney U test. The effect of pre- and postoperative FAR variables on the group was analyzed by logistic regression test. Pre-postoperative change for the variables in the survivor group was analyzed with the dependent group's *t*-test, while the variables that were not normally distributed were analyzed with the Wilcoxon test. $p < 0.05$ values were considered statistically significant.

Results

The mean age of the patients was 73.14 ± 10.37 years. Of all patients, 50 were in the survivor and 41 in the non-survivor groups. The distribution of the patients according to the groups is shown in Fig. 1. The mean age was found as 73.94 ± 10.06 in the survivor and 72.17 ± 10.77 in the non-survivor groups ($p = 0.421$). Of all patients, 50 (55%) were male, and 41 (45%) were female, with no significant difference between them ($p > 0.05$).

Of the 91 patients, 61 (67.04%) underwent an operation, 14 (15.38%) underwent angiography, and 16 (17.58%) underwent operation plus angiography. The mean pre- and postoperative fibrinogen levels were statistically significantly higher in the non-survivor group than in the survivor group ($p < 0.001$). The mean pre- and postoperative albumin levels were significantly lower in the non-survivors than in the survivors ($p = 0.059$, $p < 0.001$; respectively). The mean pre- and postoperative FAR ratio was significantly higher in the non-survivor than in the survivor groups (both, $p < 0.001$). Table 1 shows pre- and postoperative values of fibrinogen, albumin levels, and FAR ratio (Table 1).

The change between pre- and postoperative fibrinogen, albumin, and FAR values was statistically significant between the non-survivors and the survivors (for all, $p < 0.05$) (Figs. 2, 3, and 4). Table 2 shows the changes between pre- and postoperative values according to the groups.

In the logistic regression analysis, postoperative FAR value affected survival ($B = 0.043$; $p < 0.05$), while preoperative FAR did not affect ($p > 0.05$) (Table 3).

The mean pre- and postoperative values of the other variables were also analyzed. Accordingly, the preoperative hemoglobin value was significantly higher in the survivor group compared to the non-survivor group ($p < 0.05$). Preoperative WBC and neutrophil count were statistically significantly higher in the non-survivor group ($p < 0.05$). Postoperative CRP and D-dimer values were statistically significantly higher in the non-survivor group ($p < 0.05$) (Table 4). There was no statistically significant difference between the survivor and non-survivor groups regarding the other properties.

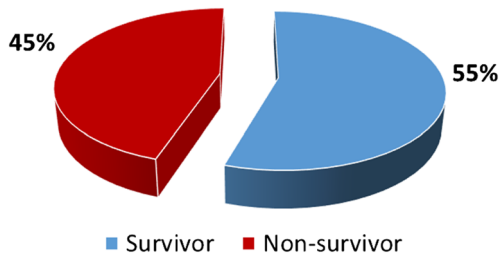

Fig 1 Distribution of the patients according to the groups

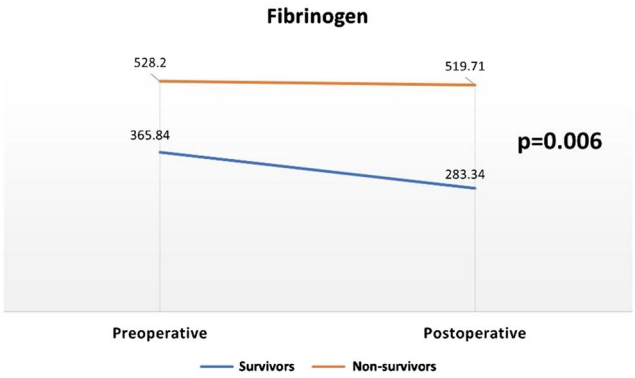

Fig. 2 Pre- and postoperative change in the mean fibrinogen value according to the group

Table 1 Pre- and postoperative fibrinogen, albumin and FAR levels of the groups

	Group				*t*	*p*
	Survivor		Non-survivor			
	Mean	±SD	Mean	±SD		
Preoperative fibrinogen	365.84	135.49	528.20	175.02	−4.988	<0.001*
Postoperative fibrinogen	283.34	104.09	519.71	161.64	−8.089	<0.001*
Preoperative albumin	2.96	.49	2.76	.51	1.911	.059
Postoperative albumin	2.92	.40	2.37	.53	5.442	<0.001*
Preoperative FAR	126.58	58.48	200.17	82.36	−4.812	<0.001*
Postoperative FAR	97.64	36.73	230.98	86.00	−9.260	<0.001*

*$p < 0.05$, *t* test

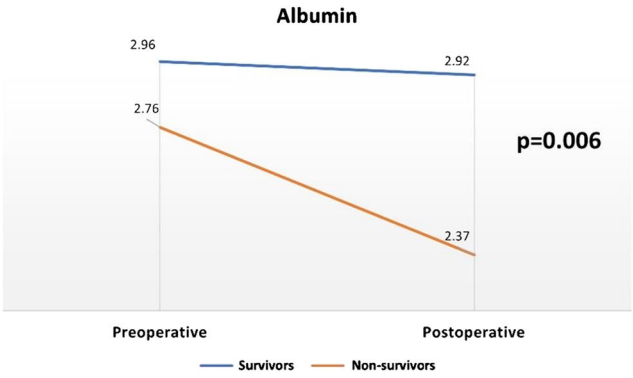

Fig. 3 Pre- and postoperative change in the mean albumin value according to the groups

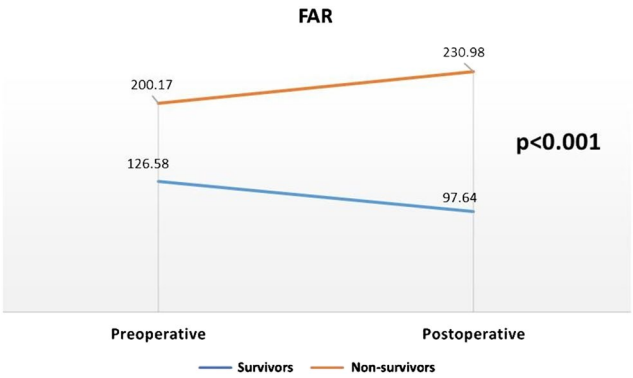

Fig. 4 Pre- and postoperative change in the mean FAR value according to the groups

Discussion

Acute mesenteric ischemia (AMI) is a vascular emergency caused by an interruption in blood flow to the small intestine, leading to cellular damage, intestinal necrosis, and death if untreated [24]. The most common etiologies of AMI include in situ thrombosis, which has been reported in approximately 60 %, embolism from atrial fibrillation in 30 %, and non-occlusive mesenteric ischemia in 10 % of patients [25]. The overall incidence is low, accounting from 0.09 to 0.2% of all acute admission to emergency departments and representing an uncommon cause of abdominal pain [26, 27]. Prompt diagnosis and intervention are essential to reduce mortality. However, despite constant improvements in diagnostic, interventional and surgical techniques and advances in radiologic modalities, AMI remains a life-threatening emergency with high mortality rates reported between 50 and 70% [28–30]. In our study, the mortality rate was found as 55%, consistent with the literature. The incidence of AMI significantly increases with age. In a study by Yilmaz et al., the mean age of the patients with AMI was found as 67.62 years [31]. In a study by Yildirim et al., the mean age of the patients was found as 67.5 [32]. In another study by Otto et al., investigating prognostic factors for mortality in patients with AMI, the median age of the patients was found as 71 years [33]. In our study, the mean age of all patients was found as 73.14 ± 10.37 years. Our finding was similar to the ages reported in previous studies.

The diagnosis of acute mesenteric ischemia can be established upon clinical suspicion, CT, and CT angiography examinations in addition to laboratory investigations. This has prompted researchers to seek novel diagnostic and prognostic biomarkers for the management of AMI. In the present study, we compared pre- and postoperative fibrinogen, albumin, FAR ratio, hemoglobin, CRP, WBC, neutrophil, preoperative lymphocyte, ALT, AST and PLT, and postoperative D-dimer values between the survivor and non-survivor patients with AMI.

Fibrinogen is an acute phase soluble plasma glycoprotein, synthesized primarily in the liver and converted by thrombin into fibrin during blood coagulation. It has been studied in several diseases, including chronic obstructive pulmonary disease (COPD) [34], periprosthetic joint infection [35], the severity of COVID-19 [36], non-cystic fibrosis

Table 2 Changes between pre- and postoperative values according to the groups

	Preoperative		Postoperative		t	p
	Mean	±SD	Mean	±SD		
Fibrinogen						
Survivor	365.84	135.49	283.34	104.09	5.327	.023*
Non-survivor	528.20	175.02	519.71	161.64		
Albumin						
Survivor	2.96	.49	2.92	.40	7.922	.006*
Non-survivor	2.76	.51	2.37	.53		
FAR						
Survivor	126.58	58.48	97.64	36.73	17.045	.000*
Non-survivor	200.17	82.36	230.98	86.00		

*$p < 0.05$, repeated ANOVA test

Table 3 Logistic regression analysis of FAR in terms of survival

Dependent variable	Independent variable	*B*	S.E.	Wald	*p*	*OR*	95% C.I. for EXP(B)	
							Min	Max
Group	Preoperative FAR	−.002	.005	.181	.671	.998	.987	1.008
	Postoperative FAR	.043	.010	18.894	<0.001*	1.044	1.024	1.065

*$p < 0.05$, logistic regression analysis

Table 4 Comparison of pre- and postoperative parameters between the survivor and non-survivor groups

	Group				Statistic	*p*
	Survivor		Non-survivor			
	Mean	±SD	Mean	±SD		
PreHGB	13.21	1.82	11.71	2.15	3.609	<0.001*
PostopHGB	11.10	1.97	10.38	2.19	1.643	.104
PreCRP	151.29	107.24	180.46	122.94	−1.209	.230
PostopCRP	163.82	89.11	214.68	106.35	−2.482	.015*
PreWBC	15.72	8.21	17.92	6.40	−2.370	.018*
PostopWBC	13.42	8.27	14.16	7.24	−1.037	.300
PreNeutrophil	14.72	8.33	18.96	9.07	−2.322	.023*
PostopNeutrophil	11.56	5.63	11.10	5.36	.391	.697
PreLymphocyte	1.05	.89	.89	.38	−.004	.997
PreALT	29.92	19.05	62.93	98.91	−1.848	.065
PreAST	34.46	18.75	78.60	138.98	−1.609	.108
PrePLT	228.63	63.24	228.24	83.41	.024	.981
PostopDdimer	1,151.98	574.23	2,262.51	1,361.52	−6.030	<0.001*

*$p < 0.05$, *t* test, Mann-Whitney test

HGB, hemoglobin; *CRP*, C-reactive protein; *WBC*, white blood cells; *ALT*, alanine transaminase; *AST*, aspartate transaminase; *PLT*, thrombocyte

bronchiectasis [37], and lung cancer [38]. In a case series by Al Mahruqi et al., fibrinogen was reported to be elevated in COVID-19 patients complicated with AMI [39]. In a study by Cakmak et al., high levels of fibrinogen were reported to predict mortality in AMI [40]. In our study, fibrinogen values decreased in patients who benefited from the treatment, which was attributed to fibrinogen's acute phase reactant effect. Both pre- and postoperative fibrinogen levels were statistically significantly higher in the non-survivor compared to the survivor patients with AMI ($p < 0.001$).

Historically, albumin has been widely used by physicians as a biomarker [41]. Serum levels of albumin are significantly depressed as a result of inflammation through decreased synthesis and increased catabolism [42]. In a study by Ozdemir et al., investigating mortality in AMI, neutrophil, RDW, lactate, D-dimer, Fibrinogen, and CK-MB levels, furthermore, albumin levels were defined as significantly elevated in the survivor group [40]. Similarly, in our study, both pre- and postoperative albumin levels were significantly higher in the survivor group compared to the non-survivor group ($p = 0.059$, $p < 0.001$; respectively).

The fibrinogen-to-albumin ratio (FAR) is increasingly considered a potential biomarker for predicting prognosis in various diseases [43]. In a study by Cicekli et al., it was reported that FAR levels might be useful in predicting mortality risk in COVID-19 patients [44]. In a study by Afsin et al., the FAR ratio at admission was associated with mortality in patients infected with SARS-CoV-2 in the ICU [45]. In the present study, both pre- and postoperative FAR ratios were statistically significantly higher in the non-survivors compared to the survivors (both, $p < 0.001$). In addition, changes in the FAR ratio between pre- and postoperative periods were again significantly higher in the non-survivor group ($p < 0.001$). While postoperative FAR decreased in the survivor group, this rate increased postoperatively in the non-survivor group. In the logistic regression analysis, postoperative FAR value affected survival ($B = 0.043$; $p < 0.001$), while preoperative FAR did not affect ($p = 0.671$). These results suggested that the FAR ratio may have a prognostic value in predicting the prognosis of AMI. There was no study in the literature to compare FAR values in patients with AMI.

Several promising biomarkers have been reported for predicting the prognosis of AMI, including intestinal fatty acid binding protein (I-FABP), a-glutathione S-transferase (a-GST), D-dimer, L- and D-lactate, citrulline, ischemia modified albumin, and procalcitonin (PCT) [9]. In a study by Destek et al., it was reported that the CRP level could 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 neutrophil-to-lymphocyte (NLR) are markers that have no predictive value in the diagnosis of all AMI subtypes [10]. In another study by Otto et al., it was reported that serum lactate appears to be of primary clinical importance as the risk of fatal outcome increases significantly with higher lactate values in AMI [33].

In our study, preoperative hemoglobin value was significantly higher in the survivor group, while postoperative CRP and D-dimer and preoperative WBC and neutrophil count were significantly higher in the non-survivor group.

Study Limitations

The major limitation of this study is the relatively small number of patients. In addition, a cut-off value, sensitivity, and specificity of FAR in predicting mortality in AMI patients could be studied. Furthermore, we could not compare our findings exactly as there is no similar study in the literature. Being conducted in two separate centers is a strength of this study.

Conclusion

The preoperative and postoperative fibrinogen levels were significantly higher, and albumin levels were significantly lower in the survivor compared to the non-survivor patients with AMI. Furthermore, the preoperative and postoperative FAR ratio was significantly higher in the non-survivors. The FAR ratio may be a valuable prognostic biomarker for patients with AMI. However, further, more comprehensive studies are warranted to support these findings.

Data availability Data used in this study can be provided on reasonable request.

Code Availability Not applicable

Author Contributions Conceptualization: Recayi Çapoğlu
Methodology: Zülfü Bayhan
Formal analysis: Furkan Ali Uygur
Investigation: Ahmet Tarık Harmantepe
Writing—orginal draft: Ali Muhtaroğlu
Writing—review and editing: Emre Gönüllü
Supervision: Ali Muhtaroğlu

Declarations

Ethics Approval Ethical approval from the Ethics Committee of Sakarya University was obtained before the initiation of the study.

Consent to participate Not applicable

Consent for Publication Written consent to publish was obtained from the patient/participant of the study.

Conflict of Interest The authors declare no competing interests.

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