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# Factors Determining the Prognosis of Acute Mesenteric Ischemia

## Akut Mezenterik İskemide Prognozu Belirleyen Faktörler

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## Abstract

**Objective:** Acute mesenteric ischemia (AMI) is a fatal vascular pathological condition requiring urgent surgical intervention, where early diagnosis significantly affects the prognosis. The aim of this study was to investigate the preoperative, perioperative and postoperative factors affecting mortality in patients who were operated with the diagnosis of AMI.

**Methods:** Patients who were operated with the diagnosis of AMI between January 2012 and January 2016 were evaluated. The patients were grouped as survivors (group 1) and non-survivors (group 2). Age, gender, concomitant disease history, clinical and laboratory findings, surgical treatment, the remaining bowel amount, short bowel syndrome, ileocecal valve intactness, ostomy opening status, the first 30-day mortality and morbidities were recorded.

**Results:** Among group 1 and group 2, respectively there was no statistically significant difference in terms of age, gender, concomitant disease, remaining bowel amount, short bowel syndrome, providing total parenteral nutrition support, ileocecal valve intactness and opening ostomy ($p>0.05$). Hemodialysis was found to be a risk factor for mortality ($p=0.020$).

**Conclusion:** AMI is a disease with high mortality, and prognostic factors that can predict pre-op and postoperative mortality are still being investigated. While it is observed that ileocecal valve intactness does not affect mortality, the preoperative urea and creatinine elevation and the need for postoperative hemodialysis may be a predictors of mortality.

**Keywords:** Mesenteric ischemia, prognostic factor, ileocecal valve, hemodialysis, mortality

## Öz

**Amaç:** Akut mezenterik iskemi, erken tanının prognozu önemli ölçüde etkilediği, acil cerrahi müdahale gerektiren ölümcül bir vasküler patolojik durumdur. Bu çalışmanın amacı, akut mezenterik iskemi tanısı ile opere edilen hastalarda mortaliteyi etkileyen preoperatif, perioperatif ve postoperatif faktörleri araştırmaktır.

**Yöntem:** Ocak 2012-Ocak 2016 tarihleri arasında akut mezenterik iskemi tanısı ile opere edilen hastalar değerlendirildi. Hastalar sağ kalanlar (grup 1) ve sağ kalmayanlar (grup 2) olarak gruplandırıldı. Yaş, cinsiyet, eşlik eden hastalık öyküsü, klinik ve laboratuvar bulguları, cerrahi tedavi, kalan bağırsak miktarı, kısa bağırsak sendromu, ileoçekal kapak sağlamlığı, ostomi açılma durumu, ilk 30 günlük mortalite ve morbidite kaydedildi.

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## Öz

**Bulgular:** Grup 1 ve grup 2 arasında sırasıyla yaş, cinsiyet, eşlik eden hastalık, kalan bağırsak miktarı, kısa bağırsak sendromu, toplam parenteral beslenme desteği sağlama, ileoçekal valv sağlamlığı ve ostomi açma açısından istatistiksel olarak anlamlı fark yoktu (p>0,05). Hemodiyaliz mortalite için bir risk faktörü olarak bulundu (p=0,020).

**Sonuç:** Akut mezenterik iskemi mortalitesi yüksek bir hastalıktır ve preop ve postoperatif mortaliteyi öngörebilecek prognostik faktörler halen araştırılmaktadır. İleoçekal valv sağlamlığının mortaliteyi etkilemediği görülürken, preoperatif üre ve kreatinin yüksekliği ve postoperatif hemodiyaliz ihtiyacı mortalitenin öngördürücüleri olabilir.


**Anahtar Kelimeler:** Mezenterik iskemi, prognostik faktör, ileoçekal valv, hemodiyaliz, mortalite

## Introduction

Acute mesenteric ischemia (AMI) is a cause of abdominal pain that requires urgent surgical intervention, due to total or partial occlusion on mesenteric vascular structures secondary to vasospasm, necrosis and perforation[1,2]. According to the pathophysiology of AMI, it can be divided into four different types: embolism and thrombotic occlusion are responsible for approximately 2/3 of AMI cases, representing 1/6 of non-occlusive mesenteric ischemia and mesenteric venous thrombosis cases[3]. Treatment of AMI cases includes early diagnosis, preoperative and postoperative intensive care support, resection of perioperative ischemic areas, anastomosis or ostomy performed and the regulation of the nutrition of the remaining intact small bowel loops[3]. Despite the improvements in diagnosis and treatment, the causes of high mortality among the patients we can list following; the advanced age, additional comorbid diseases, lack of specific physical and laboratory examinations that can enable early diagnosis[2-4]. Controlled randomized trials on AMI are limited due to the low incidence and wide spectrum of the disease. Therefore, most of the studies in the literature have a retrospective design as it is in our study[1,3,5].

## Materials and Methods

Fifty-four patients who were followed up and treated with the diagnosis of AMI between January 1, 2012 and January 1, 2016 at the general surgery clinic of a tertiary hospital were evaluated retrospectively. Fifteen patients had ischemia involving the entire small intestines and the colon, including the duodenum; and these patients were excluded from the study by evaluating them as inoperable. Thirty-nine patients were included in the study and evaluated retrospectively. The patients were grouped as survivors (group 1) and non-survivors (group 2). Evaluation and post-surgical results were recorded according to the age, gender, concomitant disease, clinical and laboratory findings, surgical treatment, remnant intestinal length, short bowel syndrome, ileocecal valve intactness, ostomy status and postoperative complications. Second look laparotomy within postoperatively 12-48 hours was performed in 7 (17%, 9) of the patients who underwent surgery. This decision was determined and the operation was performed by the surgeon who performed the first operation; in cases where recurrent ischemia is suspected in the remaining intestinal segment and the feeding limit was uncertain or when ischemic changes were detected in the stoma tip formed during resection. The information of the patients included in the study was evaluated through the Probel system. Approval from the University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital Research Ethics Board was obtained (decision number: 2020/6-3, date: 13.05.2020).

### Statistical Analysis

Whether the distribution of continuous numerical variables is close to normal or not was investigated with Shapiro-Wilk test and the homogeneity of variances was investigated with Levene test. Descriptive statistics were expressed as mean ± standard deviation or median (minimum-maximum) for continuous numerical variables; whereas categorical variables were expressed as the number of the cases and percentage (%). The significance of the difference in terms of mean values between the groups was examined with the Student's t-test and the significance of the difference in terms of non-dispersible variables was examined with the Mann-Whitney U test. Categorical variables were evaluated with continuity correction chi-square or Fisher's exact probability tests The combined effects of all possible factors thought to be the most determinative in distinguishing group 1 and group 2 cases were investigated by multivariate logistic regression analysis. All variables determined as $p<0.25$ because of univariate statistical analysis were included in the multivariate regression model as patient's risk factors. The Odds ratio, 95% confidence intervals and

wald statistics were calculated for each variable. Data analysis was performed in the package program of IBM Statistical Package for the Social Sciences statistics 17.0 (IBM Corporation, Armonk, NY, USA). Results for p<0.05 considered statistically significant.

## Results

Twenty males and 19 females, with an average age of 68.3±11.6, were diagnosed with AMI. While 20 (51.28%) of the operated patients survived (group 1), 19 (48.71%) were exitus (group 2). The demographic and clinical features of the patients are given in Table 1.

Among group 1 and group 2 cases, there was no statistically significant difference in terms of mean age, gender distribution, concomitant disease, remaining bowel length, short bowel syndrome, total parenteral nutrition (TPN) support, ileocecal valve intactness and opening ostomy (p>0.05). The rate of cases who underwent dialysis in group 2 was found to be statistically higher than group 1 (p=0.020). Also, the median length of hospital stay in group 2 was statistically shorter compared to group 1 (p<0.001) (Table 1). There was no statistically significant difference between group 1 and group 2 in terms of laboratory test results (excluding urea and creatinine) (p>0.05). However, the median urea and median creatinine levels were found statistically higher in group 2 compared to group 1 (respectively p=0.050 and p=0.026) (Table 2). The combined effects of all possible risk factors thought to be effective in distinguishing group 1 and group 2 cases were evaluated using multivariate logistic regression analysis. Because of univariate statistical analysis, all variables determined as p<0.25 were included in the multivariate logistic regression model as patient's risk factors (since there was no survival on the hemodialysis cases, the pH and $HCO_3$ variables were excluded from the regression model since the dialysis variable could not be evaluated in sufficient cases). Because of multivariate logistic regression analysis, none of the factors, such as platelet values, cancer history, urea and creatinine values, which were thought to be effective

**Table 1. Demographic and clinical characteristics of surviving (group 1) and non-surviving (group 2)**

| | Group 1 (n=20) | Group 2 (n=19) | p value |
|---|---|---|---|
| **Age (years)** | 67.2±12.0 | 69.4±11.2 | 0.573† |
| **Gender** | | | 0.425‡ |
| Male | 12 (60.0%) | 8 (42.1%) | |
| Female | 8 (40.0%) | 11 (57.9%) | |
| **Concomitant disease history** | | | |
| Diabetes mellitus | 5 (25.0%) | 5 (26.3%) | >0.999ǧ |
| Hypertension | 7 (35.0%) | 6 (31.6%) | >0.999‡ |
| Coronary artery disease | 4 (20.0%) | 4 (21.1%) | >0.999ǧ |
| Atrial fibrillation | 6 (30.0%) | 7 (36.8%) | 0.910‡ |
| Neoplasm | 7 (35.0%) | 2 (10.5%) | 0.127ǧ |
| Congestive heart failure | 2 (10.0%) | 3 (15.8%) | 0.661ǧ |
| Others | 4 (20.0%) | 5 (26.3%) | 0.716ǧ |
| **Mechanical ventilation support** | 19 (95.0%) | 19 (100.0%) | >0.999ǧ |
| **Total parenteral nutrition support** | 20 (100.0%) | 18 (94.7%) | 0.487ǧ |
| **Resection condition** | 20 (100.0%) | 18 (94.7%) | 0.487ǧ |
| **Remaining bowel length (cm)** | 157.5 (45-370) | 135 (30-380) | 0.675$ |
| **Short bowel syndrome** | 13 (65.0%) | 11 (61.1%) | >0.999‡ |
| **Ileoceacal valve intactness** | 15 (75.0%) | 12 (66.7%) | 0.836‡ |
| **Hemodialysis** | 0 (0.0%) | 5 (26.3%) | **0.020ǧ** |
| **Duration of hospitalization** | 18.5 (8-67) | 6 (1-41) | **<0.001$** |
| **Stoma** | 8 (40.0%) | 8 (44.4%) | >0.999‡ |

Student's t-test.
‡Continuity corrected chi-square test, ǧFisher's exact probability test, $Mann-Whitney U

**Table 2. Laboratory findings of the cases in both groups**

| | Group 1 (n=20) | Group 2 (n=19) | p value |
|---|---|---|---|
| **WBC** | 17.6 (11.9-51.5) | 21.6 (2.6-49.2) | 0.351† |
| **Neu** | 16.0 (8.5-46.6) | 20.3 (1.9-47.3) | 0.411† |
| **LYM** | 0.8 (0.3-1.6) | 0.7 (0.2-3.9) | 0.923† |
| **PLT** | 267.4±88.5 | 317.9±144.2 | 0.193‡ |
| **PDW** | 15.2 (12.5-20.7) | 15.1 (13.7-27.8) | 0.857† |
| **MPV** | 8.8±1.3 | 8.8±1.2 | 0.982‡ |
| **Urea** (mg/dL) | 67.5 (23-229) | 87 (37-254) | **0.050**† |
| **Creatinin** (mg/dL) | 1.4 (0.8-5.6) | 2.1 (1.0-6.9) | **0.026**† |
| **AST** | 35 (17-80) | 37 (15-85) | 0.775† |
| **ALT** | 22 (1.9-86) | 18 (7-54) | 0.654† |
| **pH** | 7.4 (7.3-7.5) | 7.3 (6.9-7.5) | 0.128† |
| **Lactate** | 3.4 (1.0-5.9) | 3.3 (0.9-14.1) | 0.757† |
| **$HCO_3$** | 21.1±2.7 | 17.7±7.6 | 0.151‡ |

†Mann-Whitney U test, ‡Student's t-test. WBC: White blood cell, LYM: Lymphocyte, Neu: Neutrophil, PLT: Platelet, PDW: Platelet distribution width, MPV: Mean platelet volume, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

**Table 3. Investigation of the effects of all possible risk factors thought to be effective in distinguishing group 1 and group 2 together with multivariate logistic regression analysis**

| | Odds ratio | %95 confidence interval | | Wald | p value |
|---|---|---|---|---|---|
| | | Lower limit | Upper limit | | |
| Platelet number | 1.007 | 0.999 | 1.014 | 3.159 | 0.076 |
| Neoplasm history | 0.111 | 0.012 | 1.014 | 3.794 | 0.051 |
| Urea (mg/dL) | 0.999 | 0.974 | 1.025 | 0.004 | 0.948 |
| Creatinin (mg/dL) | 2.410 | 0.800 | 7.258 | 2.443 | 0.118 |

in differentiating survivors, were found to be statistically unsignificant (p>0.05) (Table 3).

## Discussion

AMI is still a clinical condition with ahigh mortality, despite increased imaging methods, laboratory investigations and advanced postoperative intensive care follow-up[1]. 0.1-1% of patients admitted to the hospital due to abdominal pain are diagnosed with mesenteric ischemia[1,2,6]. The '3R' rule is important in the diagnosis and treatment management of AMI patients: resuscitation, rapid diagnosis and revascularization[7]. Many laboratory tests such as blood lactate level, pH, D-dimer, neutrophil/lymphocyte, platelet/lymphocyte ratio used to predict the diagnosis of AMI in patients presenting to the emergency department with the complaint of abdominal pain[1,4,5]. Due to its simple, accessible and easy application, lactate level in peripheral blood is one of the frequently used samples. In AMI patients, patients can get suspected of early AMI with preoperative increased serum lactate level and are used very frequently in routine practice as a possible predictor of early AMI[5]. In our study, although the lactate levels in patients with AMI seemed to increase in both groups, there was no significant difference in predicting postoperative mortality with the blood lactate levels pre-operatively examined.

In our study, statistically significant results from preoperative tests, which were evaluated as the determinants of mortality, were found to be only high in urea and creatinine levels in group 2. In the studies conducted by Acosta-Merida et al.[8] and Akyıldız et al.[9], the average creatinine value was found to be higher in those declared exits. Considering these data, we suggest that renal dysfunction is a mortality determining risk factor and that normal kidney functions should be preserved. For this reason, we should not focus only on early surgical intervention in the AMI treatment processes and we recommend applying the '3R' rule[7]. Fluid resuscitation is critical for treating

patients with suspected AMI. Severe metabolic acidosis and hyperkalemia are seen in these patients due to intestinal ischemia and reperfusion injury. This situation may cause cardiovascular collapse in anesthesia induction in patients[10]. Preoperative appropriate intravenous fluid replacement should focus on protecting kidney function by avoiding contrast agent nephrotoxicity that may develop secondary to abdominal angio computed tomography and contrast agents used for diagnostic purposes. Low blood volume, metabolic acidosis secondary to incomplete fluid resuscitation and consequent development of kidney failure is an inevitable outcome. Furthermore, developing kidney failure also plays an important role in mortality[7-9]. In addition to urea and creatinine values, in the study by Acosta-Merida et al.[8], pH, and bicarbonate levels were determined among the factors affecting prognosis; but in our study, pH and bicarbonate levels did not have a significant effect on prognosis. Although the detection of metabolic acidosis in blood gas has been associated with perioperative mortality in different studies, it was not found significant in our study[8,9]. Likewise, many studies have evaluated as an important prognostic factor in age and having advanced age increases the mortality[6,9,11]. In their studies of Akyıldız et al.[9] and Gupta et al.[11], the age of 70 and over, and in the study of Çolak et al.[6], the age of 60 and over were found to be effective factors in mortality; but in our study, age did not affect mortality.

The surgical treatment principle of AMI is damage control surgery. Resection of the necrosis bowel segment developed secondary to ischemia is the main principle of surgical treatment. During laparotomy, thrombectomy, anastomosis, and stoma is among the surgical options that can be performed, and the need for a second look may occur most of the time to re-evaluate intestinal viability after 24-48 hours[6,12]. Total of 16 of 39 patients included in our study were opened an ostomy; 8 in group 1 and 8 in group 2. In their study, Çolak et al.[6] reported a 95% mortality rate in patients with stoma due to AMI and found a significant difference between stoma opening and mortality. However, in our study, no significant difference was found between the groups regarding opening stoma. Among the underlying reasons for this result, we consider that as our hospital's transplantation unit is experienced in small bowel transplantation; this expertise may have a positive effect on postoperative treatment and management of patients developing this type of short bowel. The ileocecal valve is one of the important structures in the gastrointestinal tract, which acts as a barrier by preventing reflux from the cecum to the small intestine, prolonging the transit time of the small intestine content to the colon and increasing absorption[12]. Therefore, the preservation of the ileocecal valve is the most important part of treatment in some patients in cases where extended small bowel resection is required, such as AMI; because ileocecal valve resection may have negative effects on motility in the gastrointestinal tract and especially on absorption of B12 with bile salts[13]. Çolak et al.[6] in their study, 31% of 54 patients whose ileocecal valve was protected was reported to be exitus and it was reported that the protection of the ileocecal valve in the surgical treatment of AMI decreased morbidity and mortality[6]. In our study, it was found that preserving the ileocecal valve did not have a significant effect on mortality.

Short bowel syndrome can develop secondary to large resections, particularly in patients operated on for AMI. Increased intestinal permeability, malabsorption, fluid-electrolyte imbalances, bacterial translocation, septicemia secondary to low intestinal reserve and TPN and catheter-related complications secondary to long-term TPN feeding can be frequently seen[12]. For this reason, it is important to plan and manage the appropriate treatments according to the postoperative intestinal reserve of patients operated on for AMI. Although Aouini et al.[12] and Çolak et al.[6] showed that the AMI prognosis was associated with intestinal infarct width and short bowel syndrome; there was no significant relationship between the remaining intestinal reserve and mortality in our study.

### Study Limitations

The study was single-centred, designed retrospectively, and the number of patients was relatively low. However, our findings show that: unlike the literature, in patients underwent surgery, there was no significant difference in terms of ileocecal valve intactness, remaining intestinal reserve and ostomy opening.

## Conclusion

The rate of mortality in patients who were operated due to mesenteric ischemia and underwent hemodialysis due to acute renal failure postoperatively was found to be higher than in those without the need of hemodialysis. In these patients, the need for hemodialysis in the early postoperative period may be a determinant of mortality. Therefore, we suggest that attention should be paid to protecting kidney function in AMI.

## Ethics

**Ethics Committee Approval:** Approval from the University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital research ethics board was obtained (decision number: 2020/6-3, date: 13.05.2020).

**Informed Consent:** Retrospective study.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Concept: S.D.A., D.K., Design: T.K., D.K., S.D.A., Data Collection or Processing: S.D.A., D.K., Analysis or Interpretation: T.K., D.K., İ.S., K.T., Literature Search: D.K., S.D.A., İ.S., K.T., Writing: S.D.A., T.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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