



# Prognostic factors in patients with acute mesenteric ischemia

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## ABSTRACT

**Objective:** Acute mesenteric ischemia, one of the causes of acute abdominal pain due to occlusion of the superior mesenteric artery, has a fatal course as a result of intestinal necrosis. There is no specific laboratory test to diagnose acute mesenteric ischemia. The basis of treatment in cases of acute mesenteric ischemia is composed of early diagnosis, resection of intestinal sections with infarction, regulation of intestinal blood flow, second look laparotomy when required, and intensive care support. The aim of this study is to investigate the factors affecting mortality in patients treated and followed-up with a diagnosis of acute mesenteric ischemia.

**Material and Methods:** Forty-six patients treated and followed-up with a diagnosis of acute mesenteric ischemia between January 1<sup>st</sup>, 2008 and December 31<sup>st</sup>, 2014 at the General Surgery Clinic of our hospital were retrospectively evaluated. The patients were grouped as survivor (Group 1) and dead (Group 2). Age, gender, accompanying disorders, clinical, laboratory and radiologic findings, duration until laparotomy, evaluation according to the Mannheim Peritonitis Index postoperative complications, surgical treatment applied, and type of ischemia and outcome following surgery were recorded.

**Results:** A total of 46 patients composed of 22 males and 24 females with a mean age of  $67.5 \pm 17.9$  and with a diagnosis of mesenteric ischemia were included in the study. Twenty-seven patients died (58.7%) while 19 survived (41.3%). The mean MPI score was  $16.8 \pm 4.7$  and  $25.0 \pm 6$  in Group 1 and Group 2, respectively, and the difference between the two groups was statistically significant ( $p < 0.001$ ). Fourteen of the 16 (51.9%) patients who had a Mannheim Peritonitis Index score of 26 or higher died while two of them survived (10.5%). Thirteen out of the 30 (48.1%) patients with a Mannheim Peritonitis Index score of 25 or lower died while 17 (89.5%) patients survived. The increased MPI score was significantly correlated with mortality ( $p = 0.004$ ).

**Conclusion:** Suspicion of disease and early use of imaging in addition to clinical and laboratory evaluations are essential in order to decrease mortality rates in acute mesenteric ischemia. Prevention of complications with critical intensive care during the postoperative period aids in decreasing the mortality rate. In addition, using the Mannheim Peritonitis Index can be helpful.

**Keywords:** Mannheim, mesenteric ischemia, prognostic factors

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## INTRODUCTION

Acute mesenteric ischemia (AMI), one of the causes of acute abdominal pain due to occlusion of the superior mesenteric artery, has a fatal course as a result of intestinal necrosis (1). AMI comprises 1% of all patients admitted to the hospital with acute abdominal pain, and is the etiology in 0.1% of patients who present to emergency departments (2, 3). The mortality rate in AMI remains high due to challenges in early diagnosis, the lack of specific markers, and irreversible intestinal ischemia secondary to delay in diagnosis. Although significant advances in its diagnosis and treatment have been made over the last decade, mortality rates are still reported to be around 40-70% for acute mesenteric ischemia mainly due to a low index of suspicion. Early diagnosis and commencing appropriate treatment is essential in AMI. A delay of twenty-four hours can decrease survival by 20%. Therefore, the development of new diagnostic methods is extremely important (1-5).

The etiologic cause in 70-80% of cases with AMI is intestinal ischemia that occurs as a result of occlusion of the mesenteric artery due to an embolus or thrombus. Embolic occlusion results in earlier ischemia and transmural necrosis as compared with other causes, due to the absence of a well-developed collateral circulation (6). Strangulated hernia, venous thrombosis, and non-occlusive causes are rare reasons of AMI. Individuals with a prior history of arterial embolus, vasculitis, deep venous thrombosis, and post-prandial pain constitute the high-risk group (7).

Diagnosis of AMI is based on clinical suspicion and clinical findings. In AMI, severe abdominal pain is present disproportionate with the findings of a physical examination. Intestinal ischemia progresses transmurally, and in most cases peritonitis and sepsis has already ensued by the time of diagnosis, and

the role of imaging modalities is limited (8). Direct radiography and abdominal ultrasonography are non-diagnostic and abdominal computed tomography has a low sensitivity and specificity (9, 10). Although mesenteric vessels are visualized with an abdominal MRI, studies on the reliability of the results are limited. The American Society of Gastroenterology practice guidelines (2000) defined angiography as the gold standard for mesenteric ischemia (11). However, catheter angiography is invasive and time consuming. Furthermore, it is unavailable in many hospitals. Over the last decade, computed tomography-angiography (CTA) has replaced angiography as the gold standard in the diagnosis of mesenteric ischemia with a sensitivity and specificity of 0.86% and 0.94%, respectively, since it is less invasive and can be performed in a shorter time (12, 13). There is no specific laboratory test for acute mesenteric ischemia.

The basis of treatment in cases of acute mesenteric ischemia is composed of early diagnosis, resection of the intestinal sections with infarction, regulation of intestinal blood flow, second look laparotomy when required, and intensive care support (1).

The aim of this study is to investigate the factors affecting mortality in patients treated and followed-up with a diagnosis of AMI.

#### MATERIAL AND METHODS

Forty-six patients treated and followed-up with a diagnosis of AMI between January 1<sup>st</sup>, 2014 and December 31<sup>st</sup>, 2014 at the General Surgery Clinics of our hospital were retrospectively evaluated. The patients were grouped as survivors (Group 1) and dead (Group 2). Age, gender, accompanying disorders, clinical, laboratory and radiologic findings, duration until laparotomy, evaluation according to the Mannheim Peritonitis Index (MPI), postoperative complications, surgical treatment applied, type of ischemia, and outcome following surgery were recorded. In the patients who underwent operations, a second look laparotomy was performed within 12-48 hours. This decision was made by the surgeon who had performed the first operation and for the following reasons: in cases of suspicion of recurrent ischemia in the remaining intestinal segments after resection, if the line of demarcation was unclear or if ischemic changes were detected at the tip of the stoma created at the time of resection.

An ethics committee approval was obtained along with written informed consent from patients who participated in this study.

#### Statistical Analysis

All statistical analyses were performed using Statistical Package for the Social Sciences 17.0 (SPSS Inc.; Chicago, IL, USA). Descriptive statistics were expressed as number and percentage for categorical variables and mean and standard deviation for numerical variables. Comparisons of independent two groups were made by using the Student-t Test where numerical variables were normally distributed and using the Mann Whitney U test when they were not normally distributed. More than two-group comparisons of independent numerical variables were performed by using the One Way Anova test when variables were normally distributed and the Kruskal Wallis test

when they were not normally distributed. Subgroup parametric analyses were made with the Tukey test and nonparametric tests were made with the Mann Whitney U test and interpreted with the Bonferroni correction. Categorical variables were tested using the Chi-Square test. The statistical alpha level of significance was accepted as  $p < 0.05$ .

#### RESULTS

A total of 46 patients, composed of 22 males and 24 females with a mean age of  $67.5 \pm 17.9$ , with a diagnosis of mesenteric ischemia were included in the study. Twenty-seven patients died (58.7%) while 19 survived (41.3%). The mean age of the patients who died and survived was  $71.3 \pm 12.2$  years and  $61.7 \pm 23.2$  years, respectively. There was no statistically significant difference in terms of gender between the groups ( $p = 0.161$  and  $p = 0.329$  respectively).

There was no statistically significant difference in the interval between the onset of complaints and presentation to the hospital between the two groups ( $30.9 \pm 23.8$  hours in Group 1 and  $27.7 \pm 20.7$  hours in Group 2 ( $p = 0.675$ ).

D-dimer, WBC and pH values in Group 1 and Group 2 were  $20220 \pm 9706$  and  $16002 \pm 6176$ ,  $4757 \pm 4603$  and  $5389 \pm 2246$ , and  $7.4 \pm 0.0$  and  $7.3 \pm 0.2$ , respectively, and there was no statistically significant difference in laboratory parameters between the two groups (Table 1). Abdominal pain, nausea and vomiting, diarrhea, hematemesis and melena was found to be present in 44 (95.7%), 32 (69.6%), four (8.7%), three (6.5%) and two (4.3%) patients, respectively. No statistically significant differences were present between the two groups in terms of symptoms, accompanying diseases, and CT findings (Table 2).

Arterial and venous occlusion was detected in 34 (73.9%) and eight (17.8%) patients, respectively, and four patients (8.9%) had non-occlusive disease. Thirty-eight patients (82.6%) underwent surgery. Thirty-two patients underwent resection, while six patients (13%) did not receive an intestinal resection. One patient underwent revascularization. No statistically significant difference was found in the type of ischemia between the groups ( $p = 0.690$ ).

Postoperative complications, in order of frequency, were ostomy creation in 23 patients (60.5%), short bowel syndrome in 16 patients (42.1%), wound site infection in ten patients (26.3%), sepsis in nine patients (23.7%), intra-abdominal abscess in six patients (15.8%), entero-cutaneous fistula in two patients (5.3%), and open abdomen in two patients (5.3%). Duration of intensive care stay was  $5.9 \pm 9.8$  days (median 3 days).

The percentage of patients who underwent an operation was 77.8% ( $n = 14$ ) and 88.9% ( $n = 24$ ) in patients who survived and who died, respectively. There was no statistically significant difference in the rate of operation between the two groups ( $p = 0.694$ ). The type of operations in the two groups were similar ( $p = 0.111$ ). The rates of wound site infection and sepsis were statistically significantly higher in the patients who died as compared with the patients who survived ( $p = 0.034$   $p = 0.007$ ) (Table 3).

Second look operations were performed on eight patients. Second look operations did not correlate with mortality

	Survived	Died	p
Laboratory value			
AST	64.6±134.7	90.9±264.7	0.214
ALT	31.3±20.7	45.1±95.9	0.311
Total Bilirubin	1.3±1.2	1.5±0.8	0.097
Calcium	9.3±0.8	9.0±0.9	0.163
Sodium	137.9±5.4	137.5±4.9	0.795
Potassium	4.4±0.6	4.2±0.9	0.329
Amylase	85.9±60.2	141.5±140.5	0.511
Wbc	20220.0±9706.8	16002.3±6176.6	0.101
Neutrophil	82.3±10.6	77.3±14.7	0.398
Lymphocyte	10.5±9.2	12.2±10.5	0.823
Neutrophil/ Lymphocyte	18.1±27.7	14.4±14.7	0.709
Hg	13.5±2.4	13.3±2.5	0.822
Htc	41.6±6.2	40.4±7.1	0.582
Platelet	303647.1±184947.6	251276.9±105269.9	0.691
MPV	9.4±1.4	18.0±44.9	0.728
RDW	15.4±2.0	14.9±2.0	0.434
CK	649.9±1308.9	248.6±329.5	0.833
CKMB	79.5±217.1	9.6±13.0	0.973
Troponin	1.6±4.2	0.4±1.0	0.471
LDH	521.0±363.7	428.3±242.5	0.334
Lactate	5.6±4.8	7.6±3.7	0.430
D-dimer	4757.7±4603.7	5389.5±2246.7	0.817
HDL	34.9±19.2	30.6±16.9	0.531
LDL	92.9±56.7	83.5±47.8	0.636
Triglyceride	108.6±48.3	176.0±102.7	0.106
VLDL	20.7±9.6	33.4±19.7	0.108
Total cholesterol	150.0±74.2	149.2±57.9	0.975
pH	7.4±0.0	7.3±0.2	0.156

AST: aspartate aminotransferase; ALT: alanine aminotransferase; WBC: white blood cell; Hg: hemoglobine; Htc: hematocrit; MPV: mean platelet volume; RDW: red cell distribution width; CK: creatine kinase; CK-MB: creatine kinase-MB; LDH: low density lipoprotein; HDL: high density lipoprotein; VLDL: very low density lipoprotein

(p=0.141). Anastomosis following resection was performed in ten patients. Statistically, the mortality rate in patients who had undergone anastomosis was significantly lower (p<0.001).

Ischemia was detected in only the small intestine in 24 patients, while both the small intestine and colon were ischemic in 12 patients. The presence of colonic ischemia did not effect mortality (p=0.325).

The mean MPI score was 16.8±4.7 and 25.0±6 in Group 1 and Group 2, respectively, and the difference between the two groups was statistically significant (p<0.001). Fourteen of the 16 (51.9%) patients who had a MPI score of 26 or

		Survived		Died		p
		n	%	n	%	
Symptoms	Tenderness	17	94.4	23	85.2	0.634
	Guarding	10	55.6	17	63.0	0.619
	Rebound tenderness	4	22.2	13	48.1	0.079
	Gastric pain	18	100.0	25	92.6	0.509
	Hypoactive bowel sounds	8	44.4	15	55.6	0.465
	Nausea	13	72.2	19	70.4	0.893
	Constipation	4	22.2	7	25.9	1.000
	Anorexia	13	72.2	22	81.5	0.489
	Diarrhea	1	5.6	3	11.1	0.640
	Hematochezia	2	11.1	1	3.7	0.555
Melena	0	0.0	2	7.4	0.509	
Accompanying diseases	Hypertension	11	61.1	20	74.1	0.357
	Diabetes	2	11.1	9	33.3	0.156
	COPD	6	33.3	11	40.7	0.616
	Cerebrovascular events	6	33.3	5	18.5	0.304
	Atrial fibrillation	8	44.4	15	55.6	0.465
	CAD	9	50.0	17	63.0	0.388
CT	Normal	3	27.3	3	20.0	1.000
	Free fluid	4	36.4	9	60.0	0.234
	Thickened bowel wall	7	63.6	10	66.7	1.000
	Thickened bowel wall+ Free fluid	3	27.3	7	46.7	0.428
	Free air	11	0.0	15	0.0	-
	Air fluid level	4	36.4	9	60.0	0.234

COPD: chronic obstructive pulmonary disease; CAD: coronary artery disease; CT: computed tomography

higher died while two of them survived (10.5%). Thirteen of 30 (48.1%) patients who had a MPI score of 25 or lower died while 17 (89.5%) patients survived. The increased MPI score significantly effected mortality (p=0.004).

## DISCUSSION

Controlled randomized studies in the literature on acute mesenteric ischemia (AMI) are limited n number due to the low incidence and wide spectrum of the disease. A large majority of these studies, like ours, have a retrospective design (14,15). The absence of a specific method for the diagnosis of AMI generally results in delayed diagnosis. Mortality rates have been reported in different studies between 30% and 100%, and in this study the rate was found to be 60% (16-19).

An arterial embolus or thrombus in the superior mesenteric artery is the cause of intestinal ischemia in 70-80% of cases.

Table 3. Type of ischemia, operation and postoperative complications

		Survived		Died		p
		n	%	n	%	
Types of ischemia	Arterial occlusion	12	66.7	22	81.5	
	Venous occlusion	4	22.2	4	14.8	0.690
	Non-occlusive mesenteric ischemia	2	11.1	2	7.4	
Operation		14	77.8	24	88.9	0.694
	No resection	0	0.0	6	22.2	0.111
	Resection	14	77.8	17	63.0	
	Revascularization	0	0.0	1	3.7	1.000
Postoperative	Short bowel syndrome	6	33.3	10	37.0	0.799
	Wound site infection	1	5.6	9	33.3	0.034*
	Intra-abdominal abscess	0	0.0	6	22.2	0.067
	Ostomy	8	44.4	15	55.6	0.465
	Sepsis	0	0.0	9	33.3	0.007*
	Entero-cutaneous fistula	0	0.0	2	7.4	0.509
	Open abdomen	0	0.0	2	7.4	0.509

Less frequently, ischemia is due to a venous thrombus or non-thrombotic mechanical causes (5). In this present study, arterial occlusion was present in 73.3%, venous occlusion in 17.8%, and non-occlusive mesenteric ischemia (NOMI) in 8.9% of cases. There was no statistically significant difference between the group of patients who died and who survived in terms of types of ischemia ( $p=0.690$ ).

Although clinically not significant, the classical triad of abdominal pain, fever and blood in the stool is present in one third of cases (20). In this present series, abdominal pain, nausea and vomiting, diarrhea, hematemesis and melena were present in 44 (95.7%), 32 (69.6%), four (8.7%), three (6.5%) and two (4.3%) patients, respectively.

Peritonitis and septicemia, when developed, progresses transmurally. Various scoring systems have been used to evaluate the prognosis of peritonitis. In some studies, The Mannheim Peritonitis Index (table 4) has been reported as a reliable risk stratification system. The cut-off value for MPI was reported as 26, and mortality has been reported to significantly increase with higher scores (21-24). In this present study, we evaluated the predictive role of MPI scoring system. The mean MPI score was found to be significantly higher in Group 2 as compared to Group 1. In addition, an MPI score of 26 or higher significantly correlated with mortality.

In many studies, early diagnosis and treatment has been demonstrated to be the most effective criterion effecting

Table 4. Mannheim Peritonitis Index

Risk Factor	Weighting if present
Age >50 years	5
Female sex	5
Organ failure	7
Malignancy	4
Preoperative duration of peritonitis >24 h	4
Origin of sepsis not colonic	4
Diffuse generalized peritonitis	6
Exudate	
Clear	0
Cloudy, Purulent	6
Fecal	12
Definitions of organ failure	
Kidney	Creatine level >177 $\mu\text{mol/L}$ Urea level >167 $\text{mmol/L}$ Oliguria <20 $\text{ml/h}$
Lung	$\text{PO}_2 < 50 \text{ mmHg}$ $\text{PCO}_2 > 50 \text{ mmHg}$
Shock	Hypodynamic or hyperdynamic
Intestinal obstruction	Paralysis >24 h or complete mechanical obstruction
PO <sub>2</sub> : partial pressure of oxygen; PCO <sub>2</sub> : partial pressure of carbon dioxide	

mortality. Kassahun et al. (4) reported in their study that the survival rate was 30% lower in patients who were diagnosed 24 hours after the start of the symptoms. Among our patients, 24 were diagnosed during the 24 hour-period following the onset of symptoms, and treatment was started. Of these patients, 13 (54.2%) died and 11 survived (45.8%). Among the remaining 22 patients who were diagnosed and treated 24 hours later than the start of symptoms, 14 (63.6%) died and eight (36.4%) survived. Even though there are many studies reporting that early diagnosis and commencement of treatment in the first 24 hours decreases mortality, in this present study no statistical difference was detected (25-27).

Although AMI is generally seen in the elderly population, old age has been reported to be a negative prognostic criterion in some studies (28, 29). However, in this present study, no statistically significant difference was detected in the mean age between the two groups ( $p=0.161$ ).

In some studies in the literature, it has been reported that accompanying disease is one of the risk factors for mortality (28, 30, 31). In a study by Alhan et al. (14), the accompanying disorders were reported to be atrial fibrillation in 78.5% of the patients, hypertension in 76.6%, congestive heart disease in 70%, and coronary artery disease in 40.2% of the cases, while in our study atrial fibrillation, hypertension, coronary artery disease and COPD was present in 23 (50%), 31 (67.4%), 26 (56.5%) and 17 (37%) patients, respectively. Presence of comorbidities did not significantly affect mortality in the present or the aforementioned study.

### Laboratory values

Increases in the leukocyte count, urea, creatinine and amylase levels, and acidosis have been considered as predictors of mortality in different studies (19, 31-35). Although statistically not significant, in some studies mortality was found to increase in cases with leukopenia and this was explained as the result of a decreased or removed preventive effect of the immune system (36). D-dimer, a fibrin product occurring due to an enzymatic breakdown during intravascular coagulation and lactate levels, can also be increased in cases of AMI and in some other diseases (37). In this present study, levels of lactate and D-Dimer were found to have increased in patients with AMI, although their prognostic effect could not be demonstrated. Furthermore, in this present study, no significant differences were found in the laboratory parameters between the patients who died and who survived.

### Imaging

Additional imaging methods may be used in the diagnosis of AMI, since it lacks specific clinical or laboratory findings. Angiography is the gold standard in the diagnosis of AMI (10). However, since it is unavailable in every center and is time consuming, its essentiality has become debatable. Preoperative angiography was not used for any of the patients in this present series, as it is not available in this center.

With a sensitivity and specificity rate of 0.96 and 0.94, respectively, CT angiography is a less invasive method that takes less time and currently it has also become the gold standard in the diagnosis of mesenteric ischemia. In this present study, CT angiography was used as an additional imaging method in 26 of the patients (50%) (11, 12).

### Treatment

The importance of early diagnosis in the treatment of AMI has been repeatedly emphasized in many studies. Fluid resuscitation, invasive hemodynamic monitoring, prophylactic antibiotic therapy, systemic anticoagulation, resection of ischemic and necrotic intestinal loops, restoration of blood supply, consideration of short bowel syndrome in terms of remaining intestine length, and critical intensive care are all essential components of treatment (14). The operative technique performed is directly related to the affected intestinal loop, and the extent of involvement has been reported to effect mortality. Extensive resections, the intense microbiological flora of the colon, bacterial translocation and its systemic effects have all been identified as causes of high mortality (19, 38).

The choice of the operative technique to be performed in our study was left to the surgeon, who decided on the operation according to the viability of the intestines. Viability of the intestine was defined according to the color of the intestinal segment, arterial pulsation and peristalsis. Six patients (13%) who had not undergone resection due to an extensive area of necrosis in both the small and large bowel died during the postoperative period. Seventeen patients (36.9%) in whom only small bowel ischemia was detected underwent resection and anastomosis, and 23 patients (50%) underwent resection and stoma creation. Second look operations were performed in 12 (26%) patients in the first 12-48 hours following the operation and re-resections were performed in four patients (8.6%). One patient (2.1%) underwent revascularization. One patient

died in the early postoperative period. Mortality statistics for patients who had anastomosis following resection were found to be significantly low. We consider that this present study was accomplished with such a result due to the creation of a stoma was selected for patients who were in a worse general condition with a dirty intraabdominal cavity and a large ischemic area, and since the clinical course of such patients was more life-threatening.

In the literature, it is reported that mortality rates are higher in cases with colonic ischemia along with that of the small bowel. However, the presence of colonic involvement in addition to the small bowel had no statistically significant effect on mortality in this present study (26, 30).

### Postoperative Period

The duration of postoperative intensive care and hospital stay did not significantly effect mortality ( $p=0.069$  and  $p=0.146$ , respectively). Statistically, the rate of mortality was found to be significantly higher in patients who developed a wound site infection and sepsis ( $p=0.034$  and  $p=0.007$ , respectively).

### CONCLUSION

Suspicion of disease and early use of imaging (CT angiography) in addition to clinical and laboratory evaluations are essential in order to decrease mortality rates in AMI. Prevention of complications with critical intensive care during the postoperative period aids in decreasing the mortality rate. In addition, using the Mannheim Peritonitis Index can be helpful.

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**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Haseki Training and Research Hospital.

**Informed Consent:** Written informed consent was obtained from patient who participated in this study.

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

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