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Risk Factors Effecting Mortality in Acute Mesenteric Ischemia and Mortality Rates: A Single Center Experience

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The objective of this study is to discuss the effective factors on morbidity and mortality in patients who were operated on for acute mesenteric ischemia. Between 2006 and 2011, 95 patients, who underwent emergent surgery for acute mesenteric ischemia, were analyzed retrospectively. The study group consisted of 56 men (58.9%) and 39 women (41.1%), with an average age of 68.4 ± 14.4 years. Elapsed time between the onset of the symptoms and the surgical operation was less than 24 hours in 47 (49.5%) cases, and more than 24 hours in 48 cases (50.5%) ($P < 0.001$). Although all of the patients had intestinal necroses, colon involvement was seen in 38 patients, and mortality was higher in this group of patients ($P < 0.001$). Mortality rate was 42.1%. This was higher in older patients, those with increased leukocyte levels, increased elapsed time to laparotomy, and when the colon was involved.

Key words: Acute mesenteric ischemia – Prognostic factors – Mortality

Acute mesenteric ischemia (AMI) is an infrequent but complicated, life-threatening condition. It is mostly seen in elderly patients. Despite the advances in diagnosis of AMI, morbidity and mortality rates remain high.[1,2] Atypical symptoms, presence of predisposing diseases, delayed surgical intervention due to diagnostic difficulties, and in most cases, elderly patients who have cardiac problems, these may be some of the factors for higher mortality rates.[1,2] Intestinal blood flow is impaired as a result of mesenteric vascular insufficiency, which evolves due to underlying causes such as atherosclerosis, mesenteric artery embolism, generalize vasospasm, and mesenteric vein thrombosis.[3,4] Duration of ischemia, grade of mesentery artery occlusion, and proportion of collateral flow are determining factors of intestinal damage, after acute arterial occlusion.[5] Leukocytosis is common in AMI but it is a nonspecific marker for inflammation and infection.[6] Approximately 50% of patients have metabolic

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acidosis, a late finding to show intestinal infarct, and 25% have hyperamylasemia.[7] Prerenal azotemia, lactate level, increased levels of phosphate and alkaline phosphatase may also accompany. The role of radiologic imaging in AMI diagnosis is limited. Findings in direct abdominal radiographs are nonspecific.[8] Abdominal ultrasonography and mesenteric Doppler ultrasonography are the preferred imaging modalities to reach a diagnosis and are dependent on the experience of the radiologist.[9] Computed tomography (CT) angiography has high sensitivity and specificity.[10] Although mesenteric vessels can be visualized with magnetic resonance (MRI) angiography, its evaluation of the mesenteric arteries is primarily limited to the proximal celiac and superior mesenteric artery (SMA).[11] Angiography must be performed at an early stage of mesenteric artery occlusion suspicion. Even angiography at an early stage may be misleading; early diagnosis is one of the important factors in survival. When there is suspicion of AMI, if emergent angiography is not suitable, then emergent laparotomy must be performed. In patients with findings of peritonitis and suspicions of AMI, need of angiography is controversial.[12] In centers without sufficient radiologic imaging techniques, diagnostic peritoneal lavage may be helpful to evaluate the intestinal activity. In the past 30 years, with the use of diagnostic (CT angiography, MRI angiography) and conventional angiography and the progress in intense care units, new approaches such as SMA bypass, SMA embolectomy, and retrograde open mesenteric stent, have been used.[13] Especially when there are signs of peritonitis, an emergent surgical approach is the standard of care in patients with mesenteric arterial embolism. To reestablish sufficient blood flow to the intestine and to reduce the extent of ischemia-reperfusion damage and the risk for definitive bowel infarction, embolectomy should be applied immediately, when it is possible.[14] If there is not sufficient pulse after embolectomy, a translocation of the SMA onto the infrarenal aorta can be performed, or a bypass between the aorta or iliacal vessels and the mesenteric artery can be considered as an alternative.[15]

Materials and Methods

Between January 2006 and December 2011, 95 patients who had emergency surgery for AMI at Dicle University, Medicine Faculty, General Surgery Department, were analyzed retrospectively. Demographic features (age, gender, time elapsed to laparotomy), serum values of leukocytes, amylase, alkaline phosphatase, and urea, liver enzyme levels, radiologic imaging techniques, surgical techniques, complications, mortality, and hospitalization period were evaluated. AMI was diagnosed on clinical examination supported with laboratory and imaging techniques. Elapsed time between the onset of symptoms and the surgery is defined as 24 hours and more than 24 hours. Patients with findings of peritoneal irritation underwent emergent laparotomy. This was determined by prediagnositic contributory techniques. Patients were allocated to three groups according to the place of the necrosis. Segmental intestinal necrosis (SIN), segmental intestinal necrosis + segmental colon necrosis (SIN+SCN), and total intestinal + total colon necrosis. Comparing the factors effecting mortality between groups, the data on the group with total necrosis were disregarded because all patients died (Table 1). After adjustment of the metabolic disturbances and volume deficiency, prophylactic antibiotic treatment was given to these patients and they underwent surgery.

Statistical analysis

To analyze the study results statistically, SPSS (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA) Windows 11.5 program was used. The quantitative data are indicated as mean ± SD. Kolmogorov-Smirnov test was used for the compatibility of normal distribution of the data. In comparison of the groups, Mann-Whitney *U* test was used in analyzing nonparametric data, and the χ^2 test was used for categorical data. P values < 0.05 are accepted to be significant for all variables.

Results

The study group consisted of 56 men (58.9%) and 39 women (41.1%). Average age was 68.4 ± 14.4 years (range, 27–92 years) and 63 patients (66.3%) were more than 65 years old. At the time of admission to the emergency service, the main symptoms and findings were abdominal pain and peritoneal irritation in all cases. Demographic features, coexisting diseases, clinical findings, and laboratory test results are shown in Table 2.

All of the patients underwent surgical operation after preoperative arrangements. Elapsed time between the onset of the symptoms to operation was less than 24 hours in 47 patients (49.5%), and more than 24 hours in 48 patients (50.5%) of them, with an average of 29.4 ± 18.3 hours (range, 8–72 hours). During surgery, segmental intestinal ischemia/

Table 1 Factors effecting mortality

	Alive n (%)	Deaths n (%)	*P* value
Age (y)			0.001
<65	25 (78.1)	7 (21.9)	
≥65	30 (47.6)	33 (52.4)	
Gender			0.276
Female	20 (51.3)	19 (48.7)	
Male	35 (53)	21 (47)	
Comorbidity			0.82
Absent	40 (67.8)	19 (32.2)	
Present	15 (41.7)	21 (58.3)	
Leukocyte	17.3 ± 7.6 (4.5–37.4)	22.4 ± 10.2 (5.6–47.9)	0.007
Urea			0.807
Normal	33 (58.9)	23 (41.1)	
Elevated	22 (56.4)	17 (43.6)	
AST			0.697
Normal	8 (53.3)	7 (46.7)	
Elevated	47 (58.7)	33 (41.3)	
ALT			0.155
Normal	12 (46.2)	14 (53.8)	
Elevated	43 (62.3)	26 (37.7)	
ALP			0.669
Normal	42 (59.2)	29 (40.8)	
Elevated	13 (54.2)	11 (45.8)	
Amylase			0.502
Normal	38 (60.3)	25 (39.7)	
Elevated	17 (53.1)	15 (46.9)	
Lactate			0.171
Normal	13 (72.2)	5 (27.8)	
Elevated	42 (54.5)	35 (45.5)	
Elapsed time to surgery			< 0.001
<24 hours	42 (89.4)	5 (10.6)	
>24 hours	13 (27.1)	35 (72.9)	
Colon involvement			< 0.001
Absent	43 (74.4)	14 (25.6)	
Present	12 (31.6)	26 (68.4)	
Second look			0.967
Performed	4 (57.1)	3 (42.9)	
Not performed	51 (58)	37 (42)	
Complication			0.601
Absent	40 (54.8)	33 (45.2)	
Present	15 (68.2)	7 (31.8)	

SCN, segmental colon necrosis; SIN, segmental intestinal necrosis.

necrosis was established in 57 patients (60%). Segmental ischemia/necrosis areas in both intestine and colon were determined in 26 patients (27.4%), whereas 12 patients (12.6%) had total necrosis in all segments of the intestine and colon (inoperable AMI). Statistically significant differences ($P < 0.05$) have been found between patients with only SIN and patients with SIN+SCN when comparing age, comorbid diseases, lactate levels, and elapsed time to surgery. As a result, mortality levels were found to be higher in the patients with SIN+SCN ($P = 0.013$) (Table 1). Intestinal resection + anastomosis was performed on 12 patients (12.6%) who had only intestinal involvement. A total of 42 patients (44.2%) had resection + ostomy and 3 patients underwent embolectomy. Twenty-six of the patients (27.4%), who also had colon involvement, underwent segmental intestinal and colon resection + ostomy. Second look was applied to 7 of these patients (7.4%) and 5 of them had re-resection during the second operation. In 22 patients (23.2%) one or more postoperative complications (associated with lungs and heart, anastomosis leakage, evisceration, and sepsis) were observed. Average hospitalization was 12.2 ± 11.1 days (range, 1–50 days). Fifty-five patients (57.9%) were discharged from the hospital in good health, and 40 patients (42.1%) died. Factors effecting mortality are shown in Table 3. Twenty-one of patients who died were men and 19 were women ($P = 0.276$). Average age of patients who died was 74.1 ± 10.3 years (range, 42–91 years), whereas in the surviving patients it was 64.2 ± 15.5 years (range, 27–92 years). This difference was statistically significant ($P = 0.001$). Only 5 of 47 patients who were admitted to the hospital and underwent operation within the first 24 hours died, whereas 35 of 48 patients who underwent surgery after 24 hours died ($P < 0.001$). Average leukocyte count at the time of admission to emergency service was 22.4 ± 10.2 /mm^3 (range, 5.6–47.9 /mm^3) in patients who died, and it was 17.3 ± 7.6 /mm^3 (range, 4.5–37.4 /mm^3) in the surviving patients ($P = 0.007$). Serum urea, aspartate aminotransferase, alanine aminotransferase, amylase, alkaline phosphatase, and lactate levels of dead and surviving patients were not significantly different. Of 55 surviving patients, 15 (27.2%) had one or more coexisting diseases, whereas 21 of 40 dead patients (52.5%) had coexisting diseases, but the difference was not statistically significant. Fourteen patients (24.6%) of 57 with only intestinal involvement died, and 16 patients (42.1%) of 38 patients who also had colon involvement died ($P < 0.001$).

Discussion

The incidence of AMI is 1 in 1000 hospital admissions. Because it is relatively infrequent, most

Table 2 Comparison between groups according to the location of ischemia

	SIN (n = 57)	SIN + SCN (n = 26)	*P* value
Age (y)	64.7 ± 14.7	72.5 ± 13.6	0.017
Gender			0.810
Female	22	9	
Male	35	17	
Comorbidity			0.006
Absent	43	11	
Present	14	15	
Leukocyte	20.1 ± 9.5 (4.5–47.9)	17.5 ± 7.5 (5.7–34)	0.456
Lactate			0.038
Normal	16	2	
Elevated	41	24	
Elapsed time up to surgery			0.037
<24 hours	36	10	
>24 hours	21	16	
Complication			0.291
Absent	44	17	
Present	13	9	
Mortality			0.013
Alive	43	12	
Deaths	14	14	

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; COPD, chronic obstructive pulmonary disease; CT, computed tomography; DPL, diagnostic peritoneal lavage; USG, ultrasonography.

data come from retrospective studies with a limited number of patients.[16,17] Similarly, risk factors effecting mortality have not been studied much and published studies are not in harmony.[18,19] Mortality rates of AMI are reported as 30% to 100% in the scientific literature[5,8] and in our study it is 42.1%. AMI is a fast progressing disease, therefore early admission and early diagnosis are of critical importance. One of the leading reasons of high mortality rate is difficulty and delay in the diagnosis before necrosis. The most important factor determining survival rate is the ability to diagnose before necrosis and peritonitis development in intestines. Kassahun *et al*[20] reported that 50% of patients diagnosed within the first 24 hours, beginning from initial symptoms, survived. Survival rate is lower than 30% for patients diagnosed after 24 hours. In our study, 47 patients (49.5%) underwent surgery in the first 24 hours from the emergence of symptoms. In this group, 5 patients (10.6%) died. Forty-eight patients (50.5%) were diagnosed and operated on after 24 hours; 35 patients (72.9%) in that group died. The difference between the two groups was statistically significant ($P < 0.001$) and it was observed that a late diagnosis is a negative prognostic factor. Some complications of AMI, like ileus, peritonitis, pancreatitis, and gastrointestinal hemorrhage, may mask the AMI and delay diagnosis.[21] Usually imaging techniques, except angiography, are not sufficient to diagnose AMI and are only helpful in differential diagnosis.[8,22] Although angiography is the gold standard in the diagnosis of AMI, its usage is limited in practice. There are two major reasons for this limitation. First, it is not possible to do selective mesenteric angiography in most centers and second, most often the patient is not suitable for the procedure. Bradbury *et al*[23] have suggested that these patients must be operated directly. In our study, 39 patients (41.1%) were taken into surgery after physical examination and peritoneal lavage. For 56 patients (58.9%), radiologic imaging is used (ultrasonography, CT), especially for differential diagnosis. Mamode *et al*[19] reported that angiography can be applied to only 5.3% of AMI cases and according to Acosta-Merida *et al*,[24] it is 13.6%. Park *et al*[16] reported that early revascularization decreases mortality rates nearly by half, whereas Christensen *et al*[25] reported that mortality rates are high (44%–90%) even in revascularized cases. For mesenteric arterial embolism, laparotomy and embolectomy are still the best treatment options. However, in patients who are not suitable for immediate surgery, angiographic revascularization techniques may be used as an alternative, especially when the AMI is diagnosed quickly. Some studies also reported that using thrombolytic agents, papaverin or anticoagulants, was a successful pharmacologic treatment of patients with minor emboli. Thus, after surgery, patients must be evaluated whether they need further pharmacologic treatment (e.g., anticoagulative drugs) to prevent recurrent embolic events.[26] When there is a suspicion of AMI, if not supported by imaging techniques, peritoneal irritation findings are sufficient to show intestinal ischemia or necrosis, and emergent laparotomy is indicated. During laparotomy, if intestinal necrosis is widespread, intestinal resection is necessary. There is an increased risk of short intestine syndrome in the postoperative period. Therefore, the resection of only the necessary intestinal segments may reduce the risk of short intestine syndrome.[21,22] In our patients, we made our decision based on the color of the intestines, arterial pulsation, and peristalsis. We performed intestinal resection and anastomosis in 12 patients (12.6%), resection and ostomy in 42 patients (44.2%)

Table 3 Demographic characteristics of the patients

Characteristic			
Age (y)	n (%)	Clinical findings	n (%) or mean ± SD
≥65	63 (66.3)	Pain	95 (100)
<65	32 (33.7)	Tenderness	95 (100)
		Fever	32 (33.7)
Gender			
Male	56 (58.9)	Laboratory findings	
Female	39 (41.1)		
		Leukocyte (× 1000)	19.4 ± 9.1 (4.5–47.9)
		Urea (mg/dL)	45.4 ± 14.7 (21–86)
		AST	50.7 ± 11.8 (24–76)
		ALT	41.6 ± 9.3 (25–64)
		ALP	112.9 ± 52.4 (35–219)
		Amylase	127.9 ± 55.5 (56–235)
		Lactate	414.8 ± 168.7 (145–715)
Coronary artery disease			
Present	20 (21.1)		
Absent	75 (78.9)		
Diabetes mellitus			
Present	25 (26.3)		
Absent	70 (73.7)		
COPD		Method of diagnosis	
Present	10 (10.6)	Physical examination	26 (27.4)
Absent	85 (89.4)	USG	46 (48.4)
		CT	5 (5.3)
		Doppler USG	5 (5.3)
		DPL	13 (13.7)
Hypertension			
Present	34 (35.8)		
Absent	61 (64.2)		
Atrial fibrillation			
Present	14 (14.7)		
Absent	81 (85.3)		

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

with segmental intestinal necrosis. On all patients with colon involvement, resection + ostomy were performed. In 7 patients in whom we could not distinguish necrosis borders, a second look was applied and 5 of these patients had re-resection during the second operation. Twelve patients (12.6%) had nearly total necrosis in all segments of intestine and colon and we did not perform resection. We observed anastomosis leakage in 1 patient and evisceration in 2 patients in the postoperative period. Being older is reported as a negative prognostic factor.[16,27] We also found that mortality in patients older than 65 years was higher ($P = 0.001$). Acosta-Merida *et al*[24] reported that colon involvement added to intestinal involvement is a negative prognostic factor. Our findings were compatible. Patients who had colon involvement in addition to intestinal involvement had higher mortality rates ($P < 0.001$). One of the reasons for higher mortality rates in these patients may be that wider resection is necessary, including the colon. Another reason may be due to the intense microbiologic flora in colon, bacterial translocation, and its systemic effects.[28] The literature[24] reports coexisting systemic diseases as a risk factor for mortality, but in our study its effect was not found to be significant ($P = 0.82$). Different results have been reported in the relation between serum leukocyte, liver enzymes, urea/creatinine, amylase, lactate, bilirubin levels, and mortality.[1,2] We found that increased levels of leukocyte have a significant effect on mortality ($P = 0.007$). Although it is established that there are some increases in the levels of serum urea, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, amylase, and lactate, there was not a statistically significant effect on mortality ($P > 0.05$).

In conclusion, AMI is a disease that is mostly seen in elderly and morbidity and mortality rates remain high despite the advances in diagnosis and treatment. We observed that advanced age, high leukocyte levels, elapsed time between onset of symptoms and the operation when it is more than 24 hours, and colon involvement have an increasing effect on mortality rate. Based on these findings we recommend that these parameters be considered as negative prognostic factors and emphasize the importance of early surgical treatment.

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