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ORIGINAL ARTICLE

# What predicts the outcome in patients with intestinal ischemia? A single center experience



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## KEYWORDS

Acute abdomen;  
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## Summary

**Background:** Acute mesenteric ischemia (AMI) is associated with a mortality of 60–80%. Early diagnosis and rapid treatment have a decisive influence on therapy. The aim of this study was to evaluate the prognostic value of AMI markers on mortality, in order to better anticipate the clinical course and to initiate therapeutic steps at an early stage.

**Study design:** An analysis from our prospective database of 302 consecutive patients with AMI who were treated surgically in the Department of General Surgery between February 2003 and October 2014 was performed. Uni- and multivariate analysis of risk factors for mortality have been performed in the total cohort and in two subgroups according to their stay in intensive care unit (ICU) at the time of AMI diagnosis.

**Results:** Of the 302 patients with AMI, 115 were in ICU at the time of diagnosis. Totally, 203 patients underwent computed tomography scan (CT-scan) of the abdomen for diagnosis and 68% of them showed specific signs of AMI. A total of 63 (21%) embolectomies were performed during the surgical procedure. The post-operative mortality rate was 68% (204 patients). Among survivors, 85 (87%) patients developed a short bowel syndrome in the post-operative course. Multivariate analysis showed a significant association between mortality and preoperative lactate > 3 mmol/L, C-reactive protein > 100 mg/L and ICU stay at the time of AMI diagnosis.

**Conclusion:** Mortality of patients with AMI remains high. Elevated lactate, elevated C-reactive protein and ICU stay are factors associated with increased mortality. Their presence in a patient with suspicion of AMI should trigger a multidisciplinary management in emergency.

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## Introduction

In acute mesenteric ischemia (AMI), a sudden lack of blood flow to the bowel-supplying blood vessels leads to a relevant

hypoperfusion or a complete circulatory failure. Depending on the extent and duration of ischemia, symptoms may vary from reversible ulceration of the mucosa to complete gangrene of the affected parts of the intestine. With an incidence of 0.09 to 0.2% per year [1,2], AMI accounts for about 1–2% of gastrointestinal diseases [3]. A significant increase in the incidence has been described in recent years and been attributed to an increased awareness of

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gastrointestinal ischemic disease as well as an increase in the population at risk [3,4]. Mortality of AMI remains high around 60–80% [4–6]. Factors associated with mortality are age [7], history of peripheral vascular disease (PVD) [7] and leukocytosis [8–10].

The aim of this study was to evaluate the prognostic value of AMI markers on mortality, in order to better anticipate the clinical course and to initiate therapeutic steps at an early stage.

## Methods

A retrospective analysis from our prospectively maintained database of patients operated on between 2003 and 2014 for AMI in our department of surgery was carried out. Data were collected from patients' digitalized records.

Analysis was performed in the total cohort and in two sub-groups: patients who were in ICU before diagnosis of AMI due to other disease (ICU Group) and patients in the emergency department or in the ward presenting with acute abdomen leading to surgical consultation (Emergency Group). CT-scan was routinely performed with a standard abdominal CT angiography protocol in arterial and portal venous phases. No oral contrast material was administered. If an embolic occlusion of the superior mesenteric artery (SMA) was identified, open embolectomy was performed via arteriotomy of the SMA and balloon embolectomy using the Fogarty catheter. The short bowel syndrome was defined by the need for parenteral therapy [11]. A follow up of the surviving patients was performed and the 1- and 2-year survival rate was evaluated.

## Ethics

The institutional review board of the hospital approved the study.

## Statistical analysis

SPSS was used for Windows version 22.0 (SPSS Inc., Chicago, Illinois, USA). Data are presented as mean  $\pm$  standard deviation (SD). Statistical significance was set at  $P > 0.05$ . Student's *t* test was used to compare continuous variables, and Chi<sup>2</sup> tests or the exact Fisher tests for categorical variables, as appropriate. Multivariate analysis was performed using the multiple logistic regression analysis including parameters that were significant in univariate analysis. Since the decision to create a primary anastomosis was made intraoperatively by the surgeon due to several subjective factors, this has not been included as an independent factor in the multivariate analysis.

## Results

### Epidemiology

Overall, 302 patients were operated due to AMI during the study period. During the postoperative course, 204 (68%) patients died. There was no difference regarding mortality according to gender (female 63.8%;  $P = 0.178$ ) and age (survivors  $70.9 \pm 14.3$  years, deceased  $70.6 \pm 13.2$  years,  $P = 0.906$ ).

At the time of diagnosis, 115 patients were in ICU: 72 (63%) patients for cardiac diseases (myocardial infarction,

**Table 1** Pre-existing general condition and medication of all patients.

	Survivor		Dead		P-value
Artrial fibrillation	30	37%	51	63%	0.779
Diabetes	16	36%	29	64%	0.606
Atherosclerosis	53	34%	103	66%	0.498
Heart surgery	36	33%	74	67%	0.356
ASA <sup>a</sup>	35	40%	52	60%	0.562
Heparin	16	37%	27	63%	1.000
Warfarin	18	51%	17	49%	0.085
Clopidogrel	3	18%	14	82%	0.115

<sup>a</sup> Acetylsalicylic acid.

postoperative course of cardiac surgery), 29 (25%) patients for sepsis, and 14 (12%) patients for other reasons. The one- and two-year survival rates were 47% and 38% respectively. Nine patients were lost to follow up.

## Pre-existing general conditions and medication

Overall, no significant impact on mortality was found when comparing patients with no pre-existing illness vs. patients suffering from atrial fibrillation, diabetes, atherosclerosis or status post heart surgery. There was also no significant difference in mortality between patients who received anticoagulant medication like acetylsalicylic acid (ASA), heparin, clopidogrel and those who did not (Table 1).

Patients in the ICU group had a significantly higher mortality compared to patients in the emergency group (86% vs. 56%;  $P = 0.001$ ).

Dose of preoperative catecholamines infusion was higher in patients who died than in those who survived ( $25 \pm 49 \mu\text{g}/\text{min}$  vs.  $9 \pm 33 \mu\text{g}/\text{min}$ ,  $P = 0.001$ ). A preoperative increase in catecholamines infusion by more than  $10 \mu\text{g}/\text{min}$  within 12 hours was associated with a significant increase in mortality (59 of 66 patients;  $P = 0.001$ ) (Table 2).

## Laboratory findings

In the total cohort, lactate, pH, Haemoglobin, platelet count, Creatinin, AST, Creatinin Kinase, PTT, CRP and dose of catecholamin infusion were associated in univariate analysis with mortality (Table 2).

## Radiological findings

Abdominal CT-scan was performed in 203 (67%) patients. Non-specific signs such as intestinal wall thickening or ascites were most frequently observed. Findings that are more likely to indicate ischemia, such as portal gas or intramural gas, have been reported less frequently (Table 3). Overall, specific signs (portal or intramural gas or vascular occlusion) were found in 68% of the patients. No significant association between the finding of free abdominal air, portal gas, intramural gas, ascites, vascular occlusion and mortality was found (Table 3).

## Surgical procedure

A free or covered perforation of the intestine was detected in 44 patients (15%) (Table 4). In 149 patients (49%),

**Table 2** Laboratory findings and catecholamines at the time of AMI diagnosis. Univariate analysis of mortality in the total cohort and the two subgroups.

	All patients					Emergency department					ICU				
	Survivor		Dead		P-value	Survivor		Dead		P-value	Survivor		Dead		P-value
	98	33%	204	68%		16	13.9%	99	86.1%		82	43.8%	105	56.4%	
Lactate (mmol/L)	3.1	±2.3	6.5	±5.2	0.001	3.1	±2.3	4.5	±3.6	0.001	3.2	±1.9	8.6	±5.8	0.001
pH	7.4	±0.1	7.3	±0.1	0.001	7.4	±0.1	7.3	±0.1	0.008	7.4	±0.1	7.2	±0.2	0.003
Hb <sup>a</sup> (g/dL)	11.7	±2.5	10.7	±2.6	0.001	12.1	±2.5	11.5	±2.6	0.146	10.1	±1.7	9.9	±2.3	0.714
Leukocytes (×10 <sup>9</sup> /L)	16.7	±10.1	16.9	±10.5	0.893	16.2	±7.1	16.4	±8.0	0.84	19.5	±19.5	17.33	±12.7	0.683
Thrombocytes (×10 <sup>9</sup> /L)	240.6	±166.5	183.7	±136.5	0.004	251.8	±169.5	221.6	±124.0	0.178	183.4	±141.2	143.5	±138.3	0.305
Bilirubin (mg/dL)	1.4	±2.7	1.8	±2.7	0.275	1.2	±1.9	1.4	±1.5	0.42	2.7	±4.9	2.2	±3.4	0.702
Creatinine (mg/dL)	1.8	±1.3	2.3	±1.7	0.003	1.8	±1.3	2.2	±1.6	0.043	1.8	±0.9	2.4	±2.1	0.037
AST <sup>b</sup> (U/L)	119.9	±510.1	1106.4	±3116.5	0.001	124.5	±557.3	418	±1812.4	0.12	96.4	±70.5	1836.6	±3948.0	0.001
CK <sup>c</sup> (U/L)	179.6	±388.4	1398.3	±4499.8	0.001	124.5	±166.2	1182.5	±5378.6	0.047	461.8	±851.5	1627.1	±3337.5	0.004
CRP <sup>d</sup> (mg/L)	150	±126.9	183.5	±123.9	0.032	139.6	±129.6	201	±135.3	0.002	203.63	±98.7	164.9	±108.2	0.165
PCT <sup>e</sup> (U/L)	12.7	±18.2	21.7	±39.6	0.228	15.5	±23.1	30	±44.4	0.328	9	±9.6	18.4	±37.7	0.227
INR <sup>f</sup>	1.3	±0.7	1.5	±0.7	0.06	1.3	±0.7	1.5	±0.7	0.176	1.2	±0.2	1.5	±0.7	0.008
PTT <sup>g</sup> (s)	46.6	±26.7	57.2	±29.8	0.002	45.9	±28.3	50.7	±27.6	0.244	49.8	±17.3	64.1	±30.7	0.011
pH < 7.2	7	13%	49	88%	0.001	5	29%	12	71%	0.306	2	5%	37	95%	0.085
Lactate > 3 mmol/L	29	17.4%	138	83%	0.001	24	30%	55	70%	0.002	5	6%	83	94%	0.001
Lactate increase > 2 mmol/l/12 h	3	6%	46	94%	0.001	2	22%	7	78%	0.303	1	3%	39	98%	0.010
Leukocytes > 12 × 10 <sup>9</sup> /L	68	34%	134	66%	0.602	60	46%	72	55%	0.521	8	11%	62	89%	0.411
CRP > 100 mg/L	45	44%	57	56%	0.003	43	62%	26	38%	0.001	2	6%	31	94%	0.148
Catecholamines μg/min.	8.6	±33.2	25.2	±48.6	0.001	3.5	±22.8	9.7	±37.4	0.169	34.3	±59.1	41.6	±53.7	0.647
Increase of catecholamines > 10 μg/min./12 h	7	11%	59	89%	0.001	3	17%	15	83%	0.022	4	8%	44	92%	0.178

<sup>a</sup> Hemoglobin.<sup>b</sup> Aspartate transaminase.<sup>c</sup> Creatine kinase.<sup>d</sup> C-reactive protein.<sup>e</sup> Procalcitonin.<sup>f</sup> International Normalized Ratio.<sup>g</sup> Partial thromboplastin time.

**Table 3** Imaging findings at the time of AMI diagnosis. Univariate analysis of mortality in the total cohort and the two subgroups.

	All patients					Emergency department					CU				
	Survivor		Dead		<i>P</i> -value	Survivor		Dead		<i>P</i> -value	Survivor		Dead		<i>P</i> -value
	n	%	n	%		n	%	n	%		n	%	n	%	
	98	33%	204	68%		16	13.9%	99	86.1%		82	43.8%	105	56.4%	
CT <sup>a</sup> : free abdominal air	5	22%	18	78%	0.245	4	31%	9	69%	0.246	1	10%	9	90%	1.000
CT: ileus	25	33%	51	67%	0.879	19	49%	20	51%	1.000	6	16%	31	84%	0.501
CT: portal gas	9	23%	31	78%	0.096	8	42%	11	58%	0.625	1	5%	20	95%	0.278
CT: intestinal pneumatosis	21	31%	47	69%	0.534	17	49%	18	51%	1.000	4	12%	29	88%	1.000
CT: mesenteric edema	59	38%	98	62%	0.052	50	53%	44	47%	0.055	9	14%	54	86%	0.68
CT: ascites	29	30%	67	70%	0.302	25	51%	24	49%	0.713	4	9%	43	92%	0.304
CT: vascular occlusion	21	36%	37	64%	0.743	20	50%	20	50%	0.848	1	6%	17	94%	0.442

<sup>a</sup> Computer tomography.

**Table 4** Surgical procedure and intraoperative findings. Univariate analysis of mortality in the total cohort and the two subgroups.

	All patients			Emergency department			ICU								
	Survivor	Dead	<i>P</i> -value	Survivor	Dead	<i>P</i> -value	Survivor	Dead	<i>P</i> -value						
Embolectomy	5	28%	13	72%	0.798	5	36%	9	64%	0.587	0	0%	4	100%	1.000
Bowel discontinuity	42	28%	107	72%	0.140	33	36%	59	64%	0.039	9	16%	48	84%	0.601
Stoma	33	42%	46	58%	0.050	25	52%	23	48%	0.237	8	26%	23	74%	0.035
Primary anastomosis	44	68%	21	32%	0.001	40	82%	9	18%	0.001	4	25%	12	75%	0.234
Second look operation	44	31%	96	69%	0.539	33	36%	59	64%	0.026	11	23%	37	77%	0.054
Peritonitis	51	34%	100	66%	1.000	42	44%	54	56%	1.000	9	16%	46	84%	1.000
Perforation	13	30%	31	71%	0.600	10	40%	15	60%	0.666	3	16%	16	84%	1.000

**Table 5** Multivariate analysis of risk factors for mortality in the total cohort.

	P-value	OR	95% CI
Male	0.763	0.918	0.526–1.603
Age > 70	0.919	0.972	0.559–1.688
pH < 7.2	0.432	0.758	0.412–2.015
Lactat > 3 mmol/L	<0.001	2.717	1.561–4.729
CRP > 100 mg/L	0.041	1.758	1.012–3.054
Increase of lactate > 10/12 h	0.349	1.936	0.486–7.711
Increase of catecholamines > 10/12 h	0.738	1.131	0.395–2.782
ICU stay pre-AMI	0.003	2.847	1.440–5.629

intestinal ends were blindly closed, in 79 patients (26%) a stoma was placed while a primary anastomosis was performed in 65 patients (21%). In 9 patients, no resection was performed due to total infarction of the intestine.

Totally, 63 (21%) embolectomies were performed during the surgical procedure. Only 18 (29%) embolectomies resulted in arterial flow recovery that prevented intestinal resection. In the remaining cases a bowel resection was required despite embolectomy.

Performance of intestinal anastomosis during the first surgical procedure was strongly associated with lower mortality in the total cohort (32% mortality with primary anastomosis vs. 77% mortality without anastomosis (Table 4)) and in the emergency group (18% mortality with primary anastomosis vs. 70% mortality without anastomosis ( $P=0.001$ )).

Totally, 140 patients (47%) underwent a second look operation. The decision for a second look operation was based on intraoperative findings. All patients with blind closure of the intestine and patients for whom a progress of ischemia appeared possible due to the macroscopic findings were scheduled for a second look operation.

Patients with localized mesenteric infarction who underwent primary anastomosis or diverting stoma, without signs of severe peritonitis, and with stable clinical conditions were not scheduled for second look. The need for a second look surgery was associated with increased mortality in the emergency group (64% mortality with 2nd look surgery vs. 47% mortality without 2nd look ( $P=0.026$ )).

## Postoperative course

The average length of hospital stay (preoperative and postoperative) was  $17 \pm 24$  days for the patients who survived. Among them survivors, 85 patients (87%) developed a short bowel syndrome.

## Multivariate analysis of factors associated with mortality

In multivariate analysis in the total cohort, lactate > 3 mmol/L, CRP > 100 mg/L and ICU at the time of AMI diagnosis were associated with mortality (Table 5).

## Discussion

In the present study, age [12,13], atrial fibrillation [13,14] and diabetes [13–16] were not associated with increased mortality, which is consistent with previously published series.

There was a significant increase in mortality for patients who were already hospitalized in ICU before AMI diagnosis.

The type of mesenteric infarction (commonly the nonocclusive mesenteric ischemia, favored by high doses of catecholamines) and the clinical course seem to differ from patients presenting with acute abdominal pain in the emergency department, where the occlusive form is commonly found. Indeed, catecholamines may decrease bowel perfusion through adrenergic receptors in patients with severe vascular sclerosis and hence trigger an AMI [17,18].

Biphasic contrast-enhanced computed tomography is the gold standard in acute abdomen [2,19,20,9]. In the present study, only 68% of the CT-scans in patients with AMI revealed at least one sign of AMI. Therefore, AMI cannot be excluded by a normal abdominal CT-scan. None of the imaging findings was significantly associated with increased mortality, as demonstrated by Koungias et al. [15].

pH was significantly lower in patients who died of AMI than in those who survived. Metabolic acidosis is known to have prognostic significance for critically ill patients, although sensitivity and specificity are low [14,15,21].

The diagnostic and prognostic impact of lactate in patients with AMI has been well studied. Sensitivity ranges from 33 to 100% and specificity from 53 to 74% [22] for diagnosis of mesenteric ischemia. In this study, lactate > 3 mmol/L was associated with mortality in the total cohort and in Emergency and ICU groups. In the largest published multicenter study with 780 patients, Leone et al. described an average lactate level of  $4.0 \pm 3.3$  mmol/L in the patients who survived and  $6.6 \pm 5.1$  mmol/L in those who died ( $P=0.01$ ) [23]. In the study from Nuzzo et al. serum lactate levels > 2 mmol/L were associated with irreversible transmural intestinal necrosis in a multivariate analysis [24].

Regarding renal failure and creatinin levels, there was a strong association with mortality in the total cohort, and in both emergency and ICU groups. Although many studies found an increased incidence of renal failure in patients with AMI, most of them showed no positive correlation with mortality [13,15,16]. However, Acosta-Merida revealed an increase in creatinin as an independent prognostic factor for mortality [14].

In the total cohort and especially in ICU, patients who died had significantly higher level of AST. There is only little published data on this observation. In a study of 26 patients, Delaney et al. described elevation of AST in several patients as a secondary finding without predictive value [25]. Increased AST levels may reflect the poor hemodynamic state of the supramesocolic territory, since liver enzymes are well-known sensitive parameters of liver injury. This may be due to a critical hypodynamic circulatory situation in sepsis; but also occlusion of the celiac trunk should be considered, especially in patients with vasosclerosis.

As a result of rapid ischemic tissue damage usually a nonspecific inflammatory response accompanied by leukocytosis and an increase of CRP and PCT occurs. Here, CRP was

found to be an important prognostic marker with a 100 mg/L threshold. In the literature, the authors report an increase in CRP in most patients with AMI [4,13], but its impact on mortality has not been studied so far.

A prolonged PTT and low platelet counts were associated with increased mortality, most probably as part of septic disseminated intravascular coagulation.

The goal of the surgical treatment is to preserve as much of the intestine as possible. If computed tomography revealed a central occlusion of AMS, catheter thrombectomy was first performed and only intestinal segments that did not recover were resected. In 18 cases out of 63 embolectomies, an improvement of initially underperfused intestinal sections occurred and allowed a smaller intestinal resection and thus could prevent short bowel syndrome with the associated complications due to the malabsorption of vitamins and minerals.

Overall, the mortality of patients was 68%. The mortality rate was significantly lower in emergency department patients compared to ICU patients with a mortality rate of 86%. Most publications indicate a mortality between 60–70% [4,8,12,14,26–29]. Since mesenteric ischemia requires multidisciplinary therapy and the coordination of the participating clinics is often challenging, there are some recent reports of “intestinal stroke center” coordinating the multidisciplinary approach. Initial results indicate that this concept could lead to a reduction in mortality [30].

## Conclusion

Mortality of patients with AMI remains high. Abdominal CT-scan is an important diagnostic tool for AMI, but the absence of specific signs of intestinal infarction shall not exclude the diagnosis. Elevated lactate and C-reactive protein level and ICU stay are factors associated with increased mortality. Their presence in a patient with suspicion of AMI should trigger a multidisciplinary management in emergency.

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## Disclosure of interest

The authors declare that they have no competing interest.

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