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ORIGINAL ARTICLE

Acute mesenteric ischemia (AMI): absence of renal insufficiency and performance of early bowel resection may indicate improved outcomes

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Abstract

Purpose Acute mesenteric ischemia (AMI) is still associated with very high morbidity and mortality while the rareness and heterogeneity hamper the establishment of evidence-based guidelines. We sought to help standardize contemporary treatment by a cohort study at our tertiary center in the rising endovascular age.

Methods A retrospective cohort study was conducted from 2005 to 2015. Patients with occlusive (OMI), non-occlusive (NOMI), and venous mesenteric ischemia (VMI) were compared with respect to clinical and treatment parameters as well as outcome.

Results The study cohort consisted of 48 patients composed of 27 males and 21 females with an average age of 63 years and an average BMI of 25.1 kg/m^2. In 48% of patients ($N = 23$), an acute arterial OMI had occurred while NOMI was present in 31% ($N = 15$) and VMI in 21% ($N = 10$). Interventional and intraoperative recanalizations were significantly more often required in OMI patients compared with other entities ($p = 0.003$). Patients with venous mesenteric ischemia had a significant better overall survival than patients with OMI or NOMI in the univariate analysis ($p = 0.027$). Patients with renal failure had a 14.7-fold higher relative risk (Cox $p = 0.013$) and patients without bowel resection during primary surgery had a 17.8-fold higher relative risk (Cox $p = 0.047$) to die of AMI in the postoperative course.

Conclusions AMI remains a rare but oftentimes fatal disease. Our study provides evidence that outcome may depend on the AMI subtype, presence of renal insufficiency, and early bowel resection. Further research should help individualize treatment for optimized outcomes.

Keywords Mesenteric ischemia · Acute abdomen · Visceral artery occlusion · Venous thrombosis

Introduction

Acute mesenteric ischemia (AMI) is an abdominal emergency with a declining, though remaining high, mortality of approximately 50% in spite of modern multimodal treatment approaches including endovascular techniques [1–3]. AMI may be caused by inflow obstruction through arterial embolism and/or thrombus formation that can be occlusive (OMI) or non-occlusive in patients with temporarily reduced blood flow (NOMI). Venous mesenteric ischemia (VMI) is caused by outflow obstruction through, for example, mesenteric vein thrombosis. AMI is diagnosed in approximately 1% of all patients suffering from acute abdomen while the incidence drastically increases with age. This is reflected by the fact that in patients older than 70 years with acute abdominal pain this vascular emergency is present in approximately 10% [4]. With respect to the demographic changes in Western countries, a further increase in AMI diagnoses is being expected [5]. Frequently misdiagnosed or detected with significant delay, fatal courses in AMI are oftentimes unavoidable. The survivors may suffer from severe and prognostically relevant comorbidities related to short bowel syndrome, which are also associated with a high financial burden on the healthcare system.

Thus, there is an urgent need to improve strategies in order to enable both early diagnosis and appropriate individual intervention before the onset of intestinal gangrene and subsequent fatal courses. The disease presents fairly heterogeneously; therefore, multidisciplinary evaluation and effective treatment by a team consisting of a visceral and vascular surgeon as well as an

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interventional radiologist are demanded for every single patient. Unfortunately, at present there are virtually no results from prospective randomized studies guiding the therapy in AMI; thus, the evidence level remains poor. The aim of the present study was to evaluate prognostic factors and therapeutic options influencing outcome in AMI at our tertiary referral center for over a decade. Hence, we sought to optimize treatment through our research and to obtain impulses for future clinical research in this fatal entity.

Material and methods

A retrospective query was performed in our prospectively maintained electronic patient chart system using the ICD-10 code K.55 (vascular diseases of bowel). Ethical standards of the University of Bonn were fully acknowledged. Thus, a total of 261 patients were identified in a determined 10-year period spanning from July 1, 2005, to June 30, 2015. Patients with chronic intestinal ischemia, mechanically induced intestinal ischemia (e.g., postoperative obstruction, volvulus, intestinal strangulation, incarcerated hernia) or inflammation-induced intestinal ischemia (e.g., necrotizing pancreatitis, toxic megacolon), patients after abdominal aortic aneurysm repair, patients after viscerovascular interventions, and patients with vasculitis-induced ischemia were excluded. All patients with radiologically, intraoperatively, or histopathologically confirmed acute arterial or venous intestinal ischemia were included. There were a total of 48 patients who met the rigid inclusion criteria and further on represented our AMI study cohort. Data were retrieved from electronic and paper charts as well as through a standardized questionnaire sent to the treating general practitioner and referring specialists. The median follow-up was 24 months with minimal observation of 19 months and a maximum of 68 months.

Statistics

The statistical analyses were performed using the IBM® software SPSS® Version 25 (IBM, Armonk, NY, USA). The following statistical tests were used: Fisher's exact test, Pearson's correlation analysis, Spearman's correlation analysis, univariate ANOVA, LSD post hoc test, Welch's *t* test, Kaplan–Meier survival analysis, log-rank test, and multivariate COX analysis. Differences of $p < 0.05$ were considered statistically significant.

Results

Patients and interdisciplinary treatment

The study cohort consisted of 48 patients composed of included 27 males and 21 females with an average age of 63 ± 15.6 years and an average body mass index (BMI) of 25.1 ± 5.28 kg/m^2 (Table 1). All patients presented acute symptoms mainly comprised by the triad of abdominal pain, gastrointestinal dysfunction, and hemodynamic abnormalities. In 23 patients, an acute arterial OMI had occurred, whereas 15 suffered from NOMI (Fig. 1, panel a). In 21 patients, the superior mesenteric artery (SMA) was occluded, whereas the inferior mesenteric artery (IMA) was obstructed in a minority of 2 patients. The smallest subgroup consisted of 10 patients suffering from VMI. Herein, venous mesenteric thrombosis could be radiologically and/or intraoperatively evidenced in the superior mesenteric vein (SMV; $N = 7$) or in the more peripheral mesenteric vein branches ($N = 3$) (Fig. 1, panel b). More than one vessel was occluded in 10 patients. Comorbidities included atrial fibrillation (while in all patients in the absence of intraatrial thrombi) ($N = 18$), coronary heart disease ($N = 18$), peripheral arterial occlusive disease (PAD) ($N = 9$), status/post myocardial infarction ($N = 10$), diabetes mellitus ($N = 11$), and renal insufficiency ($N = 9$). Eleven patients had a history of abdominal surgery prior to the present admission. The preoperatively measured average serum C-reactive protein (CRP) was 130.5 ± 105.6 ng/ml, while the average white blood cell count (WBC) was 16.8 ± 10.6 Gpt/l and the average serum lactate 3.6 ± 2.6 mg/dl. The average hemoglobin (Hb) was 12.0 ± 2.64 g/dl, while the hematocrit (hct) was 35.49 ± 7.14.

Primary surgery lasted on average approximately 2 h (128.7 ± 88.7 min), including intraoperative recanalization in 15 patients, while interventional thrombectomy was performed in 6 patients. A majority of 31 patients underwent initial bowel resection. In the remaining 17 patients, no bowel was resected due to fulminant necrosis ($N = 5$) or due to sufficiently perfused and clinically intact-appearing intestine ($N = 12$). Resected bowel measured on average 62.8 ± 80 cm. Bowel resection was performed in 11 of 28 patients undergoing second-look laparotomy and bowel specimens resected herein were slightly longer (72.83 ± 80 cm). Mostly, small bowel segments needed to be partly removed in 29 patients, while large bowel resections were necessary in 10 and a combination of both in 6 patients. Almost half of the patients suffered from peritonitis at the time of first laparotomy ($N = 23$). In 17, an enterostomy was needed and 8 patients suffered from short bowel syndrome on the course.

Comparison of demographic and clinical features among different AMI cohorts

When comparing the three groups, significant differences were noted regarding the parameter age ($p = 0.012$) with younger patients observed in the VMI cohort (Table 1). Furthermore, distribution of pre-existing comorbidities differed significantly regarding atrial fibrillation ($p = 0.023$) and PAD ($p = 0.043$) since these were only present in subsets of OMI/NOMI patients

Table 1 Demographic and clinical characteristics of all 48 patients who underwent treatment for AMI further stratified based on the subtypes OMI, NOMI, and VMI

	Total ($n=48$)	OMI ($n=23$)	NOMI ($n=15$)	VMI ($n=10$)	p value
Gender					
Female	$n=27$ (56%)	$n=11$ (48%)	$n=11$ (73.3%)	$n=5$ (50%)	0.272
Male	$n=21$ (44%)	$n=12$ (52%)	$n=4$ (26.7%)	$n=5$ (50%)	
Age (years, average)	63 ± 15.6	66.7 ± 13.6	65.7 ± 16.3	50.40 ± 13.3	**0.012**
Body mass index (average)	25.1 ± 5.28 kg/m^2	24.3 ± 6.8 kg/m^2	24.5 ± 4.0 kg/m^2	27.1 ± 3.1 kg/m^2	0.513
Etiology of acute mesenteric ischemia					
Arterial occlusive	$n=23$ (48%)				
Non-occlusive	$n=15$ (31%)				
Venous thrombosis	$n=10$ (21%)				
Occluded main vessel					
Superior mesenteric artery	$n=21$ (44%)	$n=21$ (91.3%)	N/A	–	
Inferior mesenteric artery	$n=2$ (4%)	$n=2$ (8.7%)		–	
Superior mesenteric vein	$n=7$ (15%)	–		$n=7$ (70%)	
Small mesenteric veins	$n=3$ (6%)	–		$n=3$ (30%)	
Non-occlusive	$n=15$ (31%)	–			
Additionally occluded vessels					
Unique vascular occlusion	$n=23$ (69.7%)	$n=18$	N/A	$n=3$ (30%)	
Celiac trunk	$n=5$ (15.2%)	$n=5$		$n=1$ (10%)	
Portal vein	$n=3$ (9.1%)			–	
Splenic vein	$n=1$ (3.0%)			–	
Portal vein and splenic vein	$n=1$ (3.0%)			$n=1$ (10%)	
Comorbidities					
Atrial fibrillation	$n=18$ (38%)	$n=11$ (48%)	$n=7$ (46.7%)	$n=0$ (0%)	**0.023**
Coronary heart disease	$n=18$ (38%)	$n=11$ (48%)	$n=6$ (40.0%)	$n=1$ (10%)	0.116
PAD	$n=9$ (19%)	$n=7$ (30%)	$n=2$ (13.3%)	$n=0$ (0%)	**0.043**
Previous myocardial infarction	$n=10$ (21%)	$n=2$ (9%)	$n=5$ (33.3%)	$n=1$ (10%)	0.317
Heart failure	$n=6$ (13%)	$n=4$ (17%)	$n=4$ (26.7%)	$n=0$ (0%)	0.106
Diabetes mellitus	$n=11$ (23%)	$n=7$ (30.4%)	$n=3$ (20.0%)	$n=1$ (10%)	0.416
Renal failure	$n=9$ (19%)	$n=1$ (4.3%)	$n=7$ (46.7%)	$n=1$ (10%)	**0.004**
Previous laparotomy for non-vascular reasons	$n=11$ (22.9%)	$n=3$ (3.0%)	$n=7$ (46.7%)	$n=1$ (10%)	**0.030**
Preoperatively measured CrP (standard range < 5 ng/ml)	130.5 ± 105.6 ng/ml (1.10–351.00 ng/ml, $n=35$)	112.5 ± 87.0 ng/ml (7.0–264.0, $n=19$)	151.5 ± 127.0 ng/ml (1.10–351.0 ng/ml, $n=10$)	152.4 ± 129.7 ng/ml (8.7–286.0, $n=6$)	0.562
Preoperative white blood cell count (standard range 3.9–10.5 Gpt/l)	16.77 ± 10.6 Gpt/l (2.35–66.3 Gpt/l, $n=44$)	18.6 ± 12.4 Gpt/l (6.2–66.3, $n=22$)	16.67 ± 9.8 Gpt/l (2.35–38.71 Gpt/l, $n=13$)	12.49 ± 4.7 Gpt/l (3.1–19.3 Gpt/l, $n=9$)	0.354
Preoperative lactate (standard range < 2.2 mmol/l)	3.6 ± 2.6 mmol/l (0.9–13.0 mmol/l, $n=17$)	4.7 ± 4.0 (1.9–13.0, $n=11$)	1.54 ± 0.66 mmol/l (0.9–2.6, $n=5$)	1.6 mmol/l ($n=1$)	0.232
Preoperative hemoglobin	12.0 ± 2.64 (6.1–16.1, $n=43$)	12.4 ± 2.7 g/dl (7.1–16.1 g/dl, $n=22$)	10.2 ± 1.3 g/dl (6.1–14.2 g/dl, $n=12$)	13.5 ± 1.6 g/dl (11.2–16.1 mg/dl, $n=9$)	**0.007**
Preoperative hematocrit	35.49 ± 7.14 (19.0–48.0, $n=43$)	36.2 ± 7.34% (21.0–48.0%, $n=22$)	31.1 ± 4.7% (19–42%, $n=12$)	39.7 ± 3.7% (33.0–46.0%, $n=9$)	**0.016**

Bold values mark significant results ($p < 0.05$)

and entirely absent in all VMI individuals. Similarly, renal failure was significantly more present in patients with artery-related AMI ($p=0.004$). NOMI patients had the highest rate of previous laparotomies ($p=0.03$) and preoperative Hb and preoperative Hct were lowest in these ($p=0.007$ and $p=0.016$, respectively). No differences were noted regarding gender, BMI, presence of coronary artery disease, previous myocardial infarction, heart failure, diabetes mellitus, and preoperatively measured CRP, WBC count, and serum lactate.

Comparison of treatments among different AMI cohorts

Interventional as well as intraoperative recanalization was significantly more often required in OMI compared with VMI patients ($p=0.024$ and $p=0.003$, respectively) (Table 2). No differences could be evidenced for the factors operation time, bowel resection, length and type of resected bowel segment, development of postoperative peritonitis, and short bowel syndrome, as well as the necessity of an enterostomy.

Comparison of survival rates among different AMI cohorts

While 30 days after primary surgery 81% ($N=39/48$) of the entire cohort were still alive, the 1-year survival (1YS) and 5-year survival (5YS) were 68% ($N=33/48$) and 48% ($N=23/48$), respectively (Table 3). A few factors proved to independently correlate with survival (Table 4): Patients with NOMI had the most adverse prognosis with merely 60% survivors

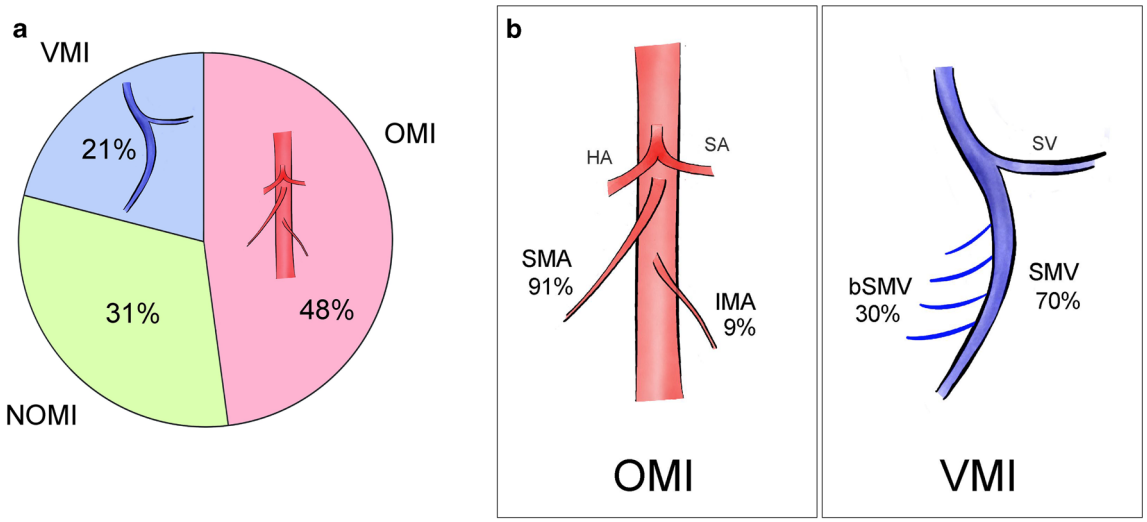

Fig. 1 Panel **a** Relative frequencies of AMI subtype. Panel **b** Relative frequencies of occluded vessels in OMI and VMI. HA, hepatic artery; SA, splenic artery; SMA, superior mesenteric artery; IMA, inferior mesenteric artery; SV, splenic vein; SMV, superior mesenteric vein; bSMV, superior mesenteric vein branches

after 30 days and a 1YS of 45% (7/15) and a 5YS of 34% (5/15). The outcome was significantly better on univariate analysis in the VMI group with 100% survivors after 5 years (log-rank $p = 0.027$; Cox $p = 0.131$) (Fig. 2). Patients suffering from renal failure had significantly inferior survival of merely 55.6% after 30 days (5/9) and a 1YS of 33% (3/9) and a 5YS of 0% (0/9) (log-rank $p = 0.002$; Cox $p = 0.013$) (Fig. 3). Also, patients without bowel resection during primary laparotomy had a significantly worse outcome with a 30-day survival rate of 65.2% (11/17) and also similar trends within 3YS (58.8%; 10/17) and 5YS (41.2%; 7/17) (log-rank $p = 0.033$; Cox $p = 0.047$) (Fig. 4). No independent impact on survival could be measured for the factors gender, age, BMI, atrial fibrillation, coronary heart disease, PAD, previous myocardial infarction, heart failure, and diabetes mellitus, and preoperatively measured Hb, hct, CRP, WBC count, and serum lactate.

Discussion

To date, the evidence level for the treatment of AMI is still low and biomarker research for early diagnosis and intervention is

Table 2 Treatment-related information of all 48 patients who underwent therapy for AMI stratified based on the subtypes OMI, NOMI, and VMI

	Total ($n = 48$)	OMI ($n = 23$)	NOMI ($n = 15$)	VMI ($n = 10$)	p value
Duration of primary operation	128.7 ± 88.7 min	141.30 ± 98.8 min	101.3 ± 48.1 min	141.9 ± 109.8 min	0.286
Interventional recanalization	$n = 6$ (13.6%)	$n = 6$ (26.1%)	$n = 0$ (0%)	$n = 0$ (0%)	**0.024**
Intraoperative recanalization	$n = 15$ (31.3%)	$n = 12$ (52.2%)	$n = 0$ (0%)	$n = 3$ (30%)	**0.003**
Primary bowel resection	$n = 31$ (64.6%)	$n = 13$ (56.5%), 7 with recanalization	$n = 10$ (66.6%)	$n = 8$ (80%), 3 with recanalization	0.353
Average length of resected bowel	62.8 ± 80 cm	62.5 ± 10.6 cm	79.2 ± 29.8 cm	41.7 ± 33.1 cm	0.645
Second-look laparotomy	$n = 28$ (58.3%)	$n = 16$ (69.6%)	$n = 6$ (40.0%)	$n = 6$ (60%)	0.194
Bowel resection during second-look laparotomy	$n = 11$ (22.9%)	$n = 5$ (21.7%)	$n = 3$ (20%)	$n = 3$ (30%)	0.829
Cumulated length of resected bowel	72.83 ± 80 cm	73.0 ± 10.3 cm	88.9 ± 45.7 cm	57.2 ± 55.9 cm	0.828
Resected bowel segments					
No resection	$n = 15$ (31.3%)	$n = 10$ (43.5%)	$n = 3$ (20.0%)	$n = 2$ (20%)	0.070
Small bowel	$n = 23$ (47.9%)	$n = 8$ (34.8%)	$n = 8$ (53.3%)	$n = 7$ (70%)	
Large bowel	$n = 4$ (8.3%)	$n = 0$ (0.0%)	$n = 3$ (20.0%)	$n = 1$ (10%)	
Large and small bowel	$n = 6$ (12.5%)	$n = 5$ (21.7%)	$n = 1$ (6.7%)	$n = 0$ (0%)	
Peritonitis	$n = 23$ (47.9%)	$n = 11$ (47.8%)	$n = 8$ (53.3%)	$n = 4$ (40%)	0.808
Postoperative short bowel syndrome	$n = 8$ (16.7%)	$n = 6$ (26.1%)	$n = 2$ (13.3%)	$n = 4$ (40%)	0.166
Enterostomy	$n = 17$ (35.4%)	$n = 6$ (26.1%)	$n = 7$ (46.7%)	$n = 0$ (0%)	0.407

Bold values mark significant results ($p < 0.05$)

Table 3 Survival analysis using patient and treatment related data (univariate analysis)

	Total	30-day survival	1-year survival	5-year survival	Average survival ± SD in months (95% confidence interval)	*p* value (univariate)
Total group						
All	*n* = 48	39/48 (81.2%)	33/48 (68.7%)	23/48 (48.0%)	40.6 ± 5.0 (30.8–50.3)	
Gender						
Female	*n* = 27 (56%)	20/27 (73.7%)	18/27 (65.3%)	12/27 (45.6%)	38.6 ± 6.4 (29.2–51.1)	0.494
Male	*n* = 21 (44%)	19/21 (90.5%)	15/21 (71.2%)	12/21 (59.3%)	29.6 ± 4.6 (20.6–38.7)	
Age						
≥ 60 years	*n* = 27 (56%)	21/27 (77.4%)	16/27 (58.4%)	12/27 (43.8%)	34.4 ± 6.9 (20.8–48.0)	0.219
< 60 years	*n* = 21 (44%)	18/21 (79.8%)	18/21 (79.8%)	11/21 (53.2%)	47.6 ± 6.6 (34.6–60.5)	
Body mass index						
≤ 24.99 kg/m^2	*n* = 16 (59.3%)	13/16 (80.8%)	12/16 (71.8%)	12/16 (71.8%)	49.6 ± 8.1 (33.7–65.5)	0.625
≥ 25.00 kg/m^2	*n* = 11 (40.7%)	10/11 (90.9%)	9/11 (81.8%)	5/11 (49.1%)	39.8 ± 8.5 (23.1–56.5)	
Etiology of mesenteric ischemia						
Arterial occlusive	***n* = 23 (48%)**	**20/23 (86.5%)**	**16/23 (70.0%)**	**10/23 (43.7%)**	**35.7 ± 6.8 (22.3–49.0)**	**0.027**
Non-occlusive	***n* = 15 (31%)**	**9/15 (60.0%)**	**7/15 (45.0%)**	**5/15 (33.8%)**	**29.4 ± 8.5 (12.8–46.1)**	
Venous thrombosis	***n* = 10 (21%)**	**10/10 (100.0%)**	**10/10 (100.0%)**	**10/10 (100.0%)**	**Not calculated (10 censored cases)**	
Comorbidities						
Atrial fibrillation	***n* = 18 (38%) vs. 30 (62%)**	**13/18 (71.4%) vs. 26/30 (86.5%)**	**9/18 (51.1%) vs. 23/30 (78.3%)**	**4/18 (24.4%) vs. 21/30 (70.5%)**	**27.6 ± 7.4 vs. 49.8 ± 5.8**	**0.037**
Coronary heart disease	*n* = 18 (38%) vs. 30 (62%)	16/18 (88.5%) vs. 18/30 (76.0%)	14/18 (75.4%) vs. 19/30 (63.7%)	9/18 (50.2%) vs. 14/30 (46.3%)	39.4 ± 7.7 vs. 39.7 ± 6.2	0.698
PAD	***n* = 9 (19%) vs. 39 (81%)**	**6/9 (66.6%) vs. 33/39 (84.2%)**	**4/9 (48.6%) vs. 28/39 (72.1%)**	**1/9 (11.1%) vs. 22/39 (57.4%)**	**15.9 ± 5.7 vs. 45.8 ± 5.3**	**0.034**
Previous myocardial infarction	*n* = 10 (21%) vs. 38 (79%)	8/10 (80.0%) vs. 31/38 (81.3%)	8/10 (80.0%) vs. 25/38 (65.4%)	6/10 (60.0%) vs. 16/38 (44.3%)	42.8 ± 9.9 vs. 39.2 ± 5.6	0.568
Heart failure	*n* = 6 (13%) vs. 42 (87%)	4/6 (66.6%) vs. 35/42 (83.0%)	3/6 (50.0%) vs. 30/42 (71.1%)	3/6 (50.0%) vs. 20/42 (48.8%)	27.8 ± 8.5 vs. 41.8 ± 5.3	0.405
Diabetes mellitus	*n* = 11 (23%) vs. 37 (77%)	8/11 (72.7%) vs. 31/37 (83.4%)	8/11 (72.7%) vs. 25/37 (67.3%)	4/11 (36.4%) vs. 20/37 (53.2%)	25.7 ± 5.6 vs. 42.8 ± 5.6	0.416
Renal failure	***n* = 9 (19%) vs. 39 (81%)**	**5/9 (55.6%) vs. 34/39 (86.6%)**	**3/9 (33.3%) vs. 30/39 (77.1%)**	**0/9 (0.0%) vs. 24/39 (62.7%)**	**18.1 ± 8.6 vs. 47.0 ± 5.3**	**0.002**
Preoperatively measured CrP (standard range < 5 ng/ml)						
CRP ≥ 100 mg/l	*n* = 19	17/19 (89.2%)	13/19 (68.3%)	11/19 (59.8%)	43.6 ± 8.1 (27.8–59.4)	0.874
CRP < 100 mg/l	*n* = 16	13/16 (80.4%)	12/16 (73.7%)	8/16 (52.6%)	41.4 ± 8.1 (25.6–57.1)	
Preoperative leukocytes (standard range 3.9–11.5 Gpt/l)						
Leukocytes ≤ 11.5 Gpt/l	*n* = 16	14/16 (87.5%)	13/16 (78.8%)	10/16 (63.0%)	47.0 ± 8.6 (30.1–63.9)	0.392
Leukocytes > 11.5 Gpt/l	*n* = 28	21/28 (75.0%)	17/28 (62.1%)	14/28 (49.7%)	37.6 ± 6.6 (24.8–50.5)	
Preoperative measured lactate (standard range < 2.2 mmol/l)						
Lactate ≤ 2.2 mmol/l	*n* = 7	5/7 (71.4%)	4/7 (53.6%)	4/7 (53.6%)	36.5 ± 13.4 (10.3–62.7)	0.512
Lactate > 2.2 mmol/l	*n* = 10	7/10 (70.0%)	7/10 (70.0%)	7/10 (70.0%)	45.2 ± 9.3 (27.0–63.4)	
Preoperatively measured hemoglobin						
Hb ≤ 10.0 g/dl	***n* = 14**	**9/14 (63.5%)**	**8/14 (54.4%)**	**8/14 (54.4%)**	**25.3 ± 6.4 (17.7–32.8)**	**0.048**
Hb > 10.0 g/dl	***n* = 29**	**26/29 (89.4%)**	**22/29 (76.5%)**	**18/29 (65.4%)**	**44.0 ± 9.0 (33.5–56.4)**	
Preoperatively measured hematocrit						
Hct < 40.0	*n* = 28	22/28 (78.1%)	18/28 (64.7%)	16/28 (58.2%)	41.6 ± 6.7 (28.6–54.7)	0.277
Hct ≥ 40.0	*n* = 15	14/15 (93.3%)	12/15 (78.0%)	9/15 (62.4%)	40.5 ± 8.9 (23.2–57.9)	
Primary bowel resection						
No	***n* = 17**	**11/17 (65.2%)**	**10/17 (58.8%)**	**7/17 (41.2%)**	**31.1 ± 8.8 (13.9–42.5)**	**0.033**
Yes	***n* = 31**	**27/31 (87.6%)**	**22/31 (70.9%)**	**17/31 (54.9%)**	**53.8 ± 5.8 (48.4–65.3)**	
Interventional recanalization						
No	*n* = 42	35/42 (83.1%)	29/42 (69.2%)	20/42 (48.2%)	41.0 ± 5.2 (30.9–51.2)	0.691
Yes	*n* = 6	4/6 (66.7%)	4/6 (66.7%)	4/6 (66.7%)	27.3 ± 9.2 (9.2–45.3)	
Intraoperative recanalization						
No	*n* = 33	26/33 (78.8%)	21/33 (63.6%)	15/33 (45.5%)	38.4 ± 6.2 (26.2–50.5)	0.422
Yes	*n* = 15	12/15 (80.0%)	12/15 (80.0%)	9/15 (60.0%)	44.1 ± 7.3 (29.9–58.4)	

Bold values mark significant results ($p < 0.05$)

in its infancy [6, 7], though various efforts recently addressed this important and increasingly prevalent disease: for example, in 2013 an expert consortium of the European Society for Trauma and Emergency Surgery (ESTES) established guidelines for an optimized management of AMI. Following a comprehensive review of literature, the steering committee formed

Table 4 Multivariate analysis of univariately significant risk factors (Cox analysis)

	p	RR	95% CI
Etiology of mesenteric ischemia	0.131	–	–
NOMI vs. VMT	0.150	–	–
NOMI vs. AMI	0.179		
AMI vs. VMT	0.212		
Preoperatively measured hemoglobin	0.396	–	–
Atrial fibrillation	0.103	–	–
PAD	0.273	–	–
Primary bowel resection (none vs. primary resection)	*0.047*	*17.8*	*1.04–223.5*
Renal failure (yes vs. none)	*0.013*	*14.7*	*1.75–123.2*

an expert consensus aiming at improved patient outcomes in this fatal disease [8]. Furthermore, Zhao et al. published a systematic review in 2016 wherein the authors scrutinized available literature on AMI and eventually analyzed 28 articles including a total of 1110 treated patients. As one important finding, the authors concluded, for example, that endovascular procedures may be appropriate even as a first-line treatment while open surgery should be reserved for patients in whom thorough exploration of the abdominal cavity is demanded due to, for example, suspected intestinal necrosis [9]. This was supported by the recent guidelines by the American College of Cardiology and American Heart Association (aka ACC/AHA guidelines) on the management of peripheral arterial occlusive disease that attempted to define current therapy in AMI. It was stated that the principle treatment of acute obstructive intestinal ischemia includes revascularization, potentially resection of necrotic bowel, and, if indicated, a second-look laparotomy 24–48 h after revascularization (evidence level B). Also, modern percutaneous endovascular interventions such as balloon angioplasty and stent placement are recommended with an evidence level C. In spite of accumulating experience and various contemporary consensus guidelines, there is a common sense within the expert community that further research is urgently needed to eventually allow more evidence-based and individualized management in AMI giving fuel to our present study [10].

What are the main factors hampering standardization of treatment? First, patients with AMI are relatively rare as we evidenced in our retrospective 10-year spanning cohort study at our tertiary referral center. Second, AMI is caused by various vascular and extravascular disorders in a heterogeneous group of individuals. Thus, while courses of disease might resemble one another, the three AMI entities (OMI, NOMI, and VMI) need to be regarded individually. The largest fraction of approximately 50% experience acute mesenteric embolism, while arterial thrombosis is observed in another 25% and occurs mainly in

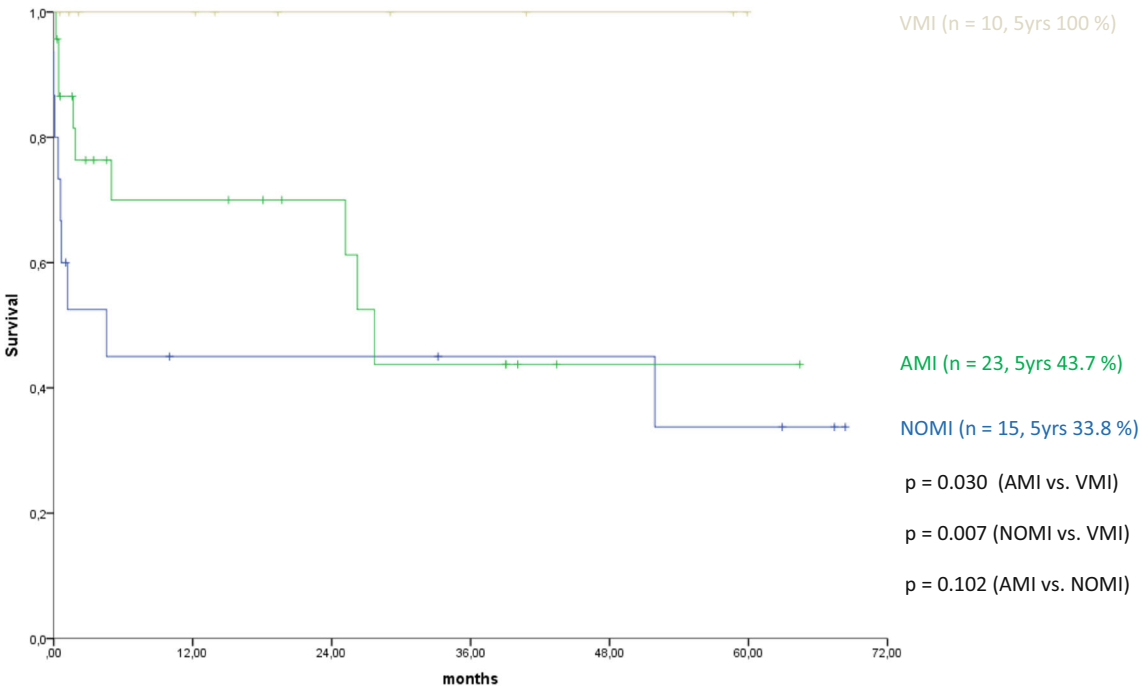

Fig. 2 Kaplan–Meier survival analysis comparing patients with different types of acute mesenteric ischemia (AMI). The median survival for patients with OMI ($N=23$) was 35.7 months (30-day survival, 86.5%; 1-year survival, 70%; 5-year survival, 43.7%), whereas in NOMI ($N=15$) it was 29.5 months (30-day survival, 60%; 1-year survival, 45%; 5-year survival, 33.3%). There were no deaths among the patients with venous mesenteric ischemia (VMI). There was a significant difference on patients' survival on univariate analysis according to presence or absence of (log-rank $p=0.027$)

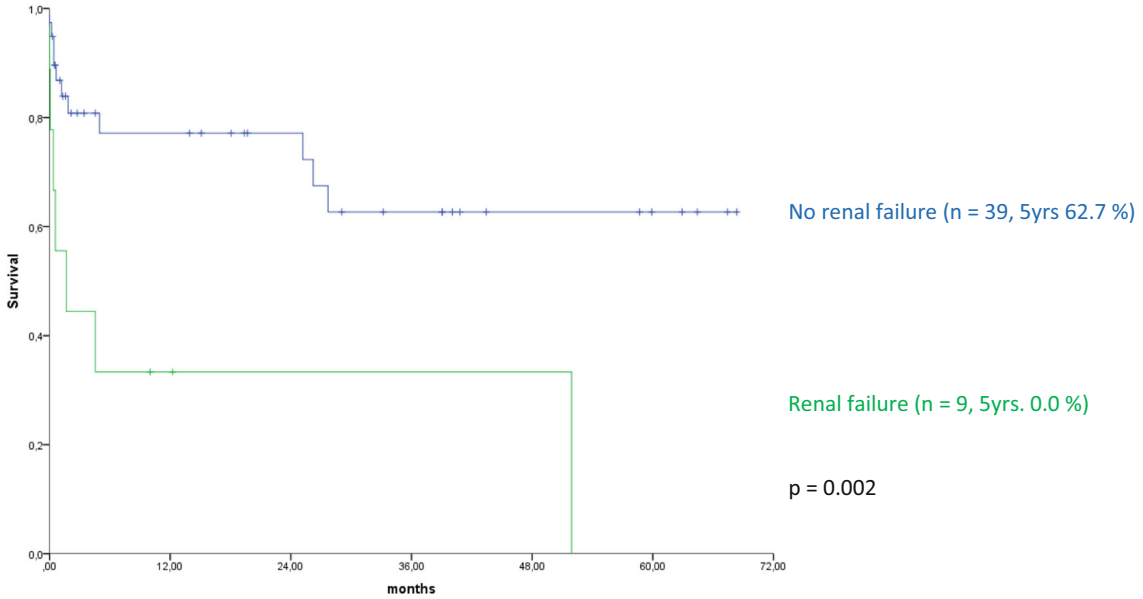

Fig. 3 Kaplan–Meier survival analysis comparing patients with or without renal failure. The median survival for patients with renal failure ($N = 9$) was 14.7 months (30-day survival, 55.6%; 1-year survival, 33.3%; 5-year survival, 0%), whereas in patients without renal insufficiency ($N = 39$) it was 41.2 months (30-day survival, 86.6%; 1-year survival, 77.1%; 5-year survival, 62.7%). There was a significant difference on patients' survival according to presence or absence of renal insufficiency (log-rank $p = 0.002$; Cox $p = 0.027$)

association with PAD [11, 12]. In spite of the characteristic triphasic clinical course with an initial phase of strong abdominal pain followed by a symptom-free interval, and a final phase with fatal peritonitis and sepsis, AMI can present fairly heterogeneously. In part depending on etiology, the clinical status of the patient and the comorbidities, symptoms, and courses of disease may vary significantly among individuals. For example, patients with NOMI may suffer for days from moderate abdominal pain, discomfort, and emesis and also VMI may cause rather subacute symptoms. In fact, patients with NOMI or VMI typically present with a slower clinical course. However, also in arterial thrombosis, the interval from primary symptoms to bowel infarction may

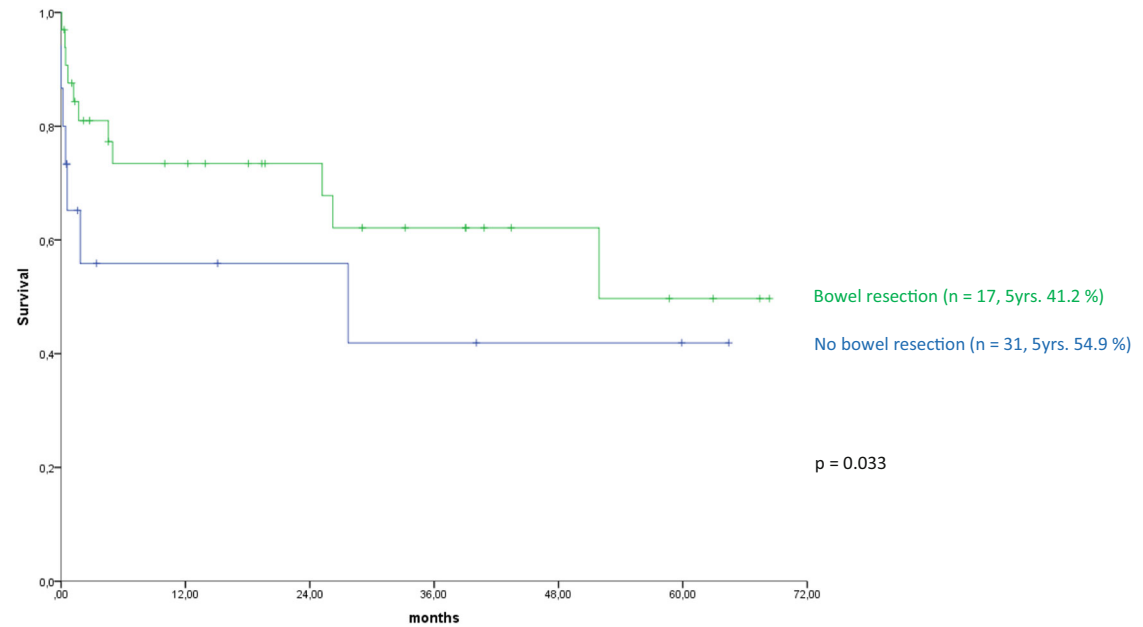

Fig. 4 Kaplan–Meier survival analysis comparing patients with or without early bowel resection. The median survival for patients with bowel resection ($N = 31$) was 61.2 months (30-day survival, 87.6%; 1-year survival, 70.9%; 5-year survival, 41.2%), whereas in patients without bowel resection ($N = 17$) it was 23.5 months (30-day survival, 65.2%; 1-year survival, 58.8%; 5-year survival, 41.2%). There was a significant difference on patients' survival according to presence or absence of bowel resection (log-rank 0.033; Cox $p = 0.047$)

be as long as 12–24 h [13]. Demographically, most patients with AMI are elderly and, as stated above, incidence has been shown to increase with age. With an average age of 50 years, our study evidenced, however, that VMI patients are considerably younger compared with individuals suffering from OMI and NOMI. In addition, predominant comorbidities were distinct. For example, patients suffering from arterial-related AMI (i.e., OMI and NOMI) had significantly more often a history of atrial fibrillation as well as PAD compared with VMI individuals, paralleling their natural cause of thromboembolic disease [14]. Also, renal insufficiency was more prevalent in OMI/NOMI, potentially as a sign or cause of their chronic visceral PAD. Interestingly, prior abdominal surgery was characteristic of VMI in our cohort. A subgroup analysis, however, failed to relate VMI to any specific type of abdominal operation (data not shown); the reason of this coherence remains thus far elusive. In summary, these characteristic clinical features of each AMI subgroup need to be acknowledged by physicians and treatment needs to be individualized accordingly (i.e., interventional recanalization was performed in every fourth of OMI patients and never applied in VMI).

Altogether, steadily improving survival can be noticed in AMI as shown in a meta-analysis by Schoots et al. [15] over a time of four decades (1960–2000). Accordingly, we observed a comparably low in-house mortality of 25% which may be related to improved surgical and perioperative management by an experienced team. It seems obvious that patients with relevant comorbidity such as ICU patients suffering from sepsis and demanding intravenous vasopressor treatment share a particularly dismal outcome. This coherence was observed in our cohort study, too. While pre-existing atrial fibrillation as well as PAD was significantly associated with worse prognosis on univariate analysis, only renal insufficiency proved to be an independent prognostic factor. From what is known and according to our analysis, BMI does not significantly influence survival in AMI [16]. The subtype of AMI, however, seems to play an important role on outcome since, for example, patients with NOMI had the highest in-hospital mortality of 47%, while on contrast 5-year survival in VMI was as high as 100%, paralleling findings from previous larger cohorts [17]. Blood parameters have been heavily investigated for their predictive use in AMI. Thus far, no biomarkers have been established indicating the presence and type of AMI [18]. Interestingly, when stratifying our patients into two groups according to a Hb cutoff of 10 g/dl, a significantly lowered cumulative survival was observed for patients when Hb was < 10 g/dl, while this coherence could not be proved on multivariate analysis. As a possible explanation for anemia in NOMI, Constant-Neto et al. [19] evidenced in a mouse model that hemolysis and subsequently lowered serum Hb levels were triggered by mesenteric ischemia. Thus, a low Hb may in turn contribute to a particularly adverse outcome in these patients [20]. Whether or not the threshold for preoperative blood transfusions should be lowered in certain AMI subgroups in contrast to contemporary patient blood management (PBM) recommendations should be discussed in an interdisciplinary fashion [21]. NOMI is usually a consequence of vasoconstriction and low perfusion of the splanchnic arteries. This type is, therefore, typically diagnosed with some delay in patients on intensive care units with cardiac disease, particularly in severe congestive heart failure, sepsis, previous cardiovascular or abdominal surgery, hypovolemia, and associated high-dose systemic vasoconstrictors explaining their comparably dismal outcome [11]. Sedation hides clinical symptoms; thus, NOMI remains undiagnosed in approximately one-fourth of patients stressing the need for reliable AMI biomarkers [22, 23]. Interestingly, a large fraction of more than 20% of our patients suffered from VMI. As a tertiary referral center for hepatopancreatobiliary diseases and also for hemostatic disorders, there might be an accumulation of such cases, although our study is too small to draw reliable conclusions on this possible coherence. The association between bowel resection and survival has been investigated in previous studies [24–26]. Paralleling these findings in our study, a significant impact of early bowel resection on survival could be demonstrated.

On the contrary, early bowel resection may lead to short bowel syndrome that may be associated with higher morbidity and long-term mortality. Merely eight out of all 48 patients in our study developed a short bowel syndrome as a result of bowel resection, and outcome was not significantly impaired in those. We emphasize the importance of an outpatient service for short bowel syndrome patients since their complex clinical management including nutritional advice and infusion therapy must not be transferred to general practitioners.

The present study has some limitations. Besides the retrospective design, our study included a highly heterogeneous cohort treated over a comparably long period of time. The marked differences regarding survival between ours and published studies found in literature can be related to aforementioned relatively heterogeneous study populations of AMI patients. Another possible explanation is a selection bias possibly present in our cohort from a tertiary reference center. In order to focus on AMI as main diagnosis, we excluded, for example, patients who suffered from AMI as a side effect from other diseases (VMI due to sigmoid diverticulitis, malignancy, trauma, abdominal surgery, pancreatitis, liver failure, oral contraception, etc.), while studies found in literature usually did not set such a rigid focus. Multicentric, at least registry, and, if possible, prospective studies should hopefully lead to a more evidence-based treatment of the disease. However, due to the emergency setting in which most AMI patients are seen with individually tailored multidisciplinary approaches, prospectively randomized trials will be conceptionally and ethically difficult. Hopefully, the rising digitalization in medicine may help accelerate the progress toward evidence-based, personalized treatment of AMI.

Conclusions

The present study could demonstrate that the three major entities of AMI differ regarding clinical presentation, results of therapy, and prognosis. Herein, NOMI and renal failure patients have the most dismal outcome. Since prior surgery and ICU predispose patients to the development of NOMI, abdominal symptoms in those patients require particular diagnostic dedication and potentially early appropriate therapy. Furthermore, a Hb lower than 10 g/dl in AMI might indicate a progressed disease and this marker should be further evaluated for a possible clinical implication. An interdisciplinary collaboration of visceral and vascular surgeons as well as interventional radiologists is imperative because revascularization may prevent major bowel resection inevitably leading to short bowel syndrome and the associated adverse side effects. In case bowel resection is required, this should be timely performed since early surgery seems to positively impact prognosis. A more radical resectional approach might be justified under certain clinical conditions (i.e., after complex and long revascularizations), while further research is needed on this topic.

Author Contributions All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Hanno Matthaei, Arne Koscielny, and Alina Klein. The first draft of the manuscript was written by Hanno Matthaei and Arne Koscielny. Vittorio Branchi contributed to drafting of figures. All authors commented on previous versions of the manuscript. Jörg C. Kalff co-supervised the study together with Arne Koscielny. All authors read and approved the final manuscript.

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