Kase *et al.*
World Journal of Emergency Surgery (2025) 20:46
https://doi.org/10.1186/s13017-025-00616-4

World Journal of
Emergency Surgery

RESEARCH

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Comparison between endovascular and surgical treatment of acute arterial occlusive mesenteric ischemia

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Abstract

Background The optimal strategy for initial treatment of acute occlusion of superior mesenteric artery (SMA) is debated. The aim of the study was to compare the effectiveness, timelines and outcomes of endovascular versus open surgical treatment in patients with acute SMA occlusion. This was a preplanned substudy of the prospective observational multicenter AMESI (Acute MESenteric Ischaemia) study.

Methods Patients with SMA occlusion were divided into surgical and endovascular treatment groups. The surgical group included patients initially subjected to open surgical treatment with surgical or hybrid revascularization or intestinal resection only. The endovascular group included patients initially revascularized endovascularly and was further divided according to treatment effectiveness. Patients were also categorized according to revascularization or no revascularization, and subanalysis performed for different revascularization methods. Baseline

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and outcome comparisons were made using Fisher and Mann–Whitney U tests. Risk-factors for in-hospital mortality were analysed using a logistic regression model.

Results Of 158 patients 107 had surgical and 51 endovascular treatment. The surgical group had higher baseline illness severity scores, higher C-reactive protein and lactate values. The mortality in the endovascular effective, endovascular insufficient as monotherapy and surgical groups was 2.9%, 41.2% and 45.8%, respectively. In multivariable analysis surgery was not an independent risk factor for in-hospital mortality. The rate of arterial embolism was higher in the endovascular revascularization as monotherapy insufficient treatment group (10/17) compared to the endovascular revascularization as monotherapy effective (5/34) and surgical (27/107) groups. We could not identify useful best thresholds for discriminating between effective and insufficient endovascular treatment. Analysis comparing the effect of any revascularization versus no revascularization on in-hospital mortality did not show a clear benefit of revascularization and the method of revascularization did not independently influence mortality.

Conclusion The beneficial effect of endovascular compared to surgical treatment in unadjusted analyses is largely explained by selection of patients. None of the compared management approaches had an independent effect on mortality. The choice between endovascular and surgical treatment should not be based solely on the time elapsed from symptom onset but rather on the patient's general condition and possibly on the cause of SMA occlusion.

Keywords Acute mesenteric ischemia, Occlusion of superior mesenteric artery, Endovascular revascularization, Surgical revascularization

Background

Acute mesenteric ischemia (AMI) is a life-threatening vascular insult which can frequently be fatal without timely intervention. However, there is an ongoing debate regarding the optimal initial treatment modality for arterial occlusion: endovascular versus surgical.

Recently published guidelines on AMI note a benefit of endovascular therapy compared to open surgery in terms of lower bowel resection rates and lower 30-day mortality rates [1]. Nevertheless, it is important to note that all studies scrutinizing endovascular revascularization have a significant level of population heterogeneity. Thus, the authors recommend endovascular treatment in the early phases of acute mesenteric ischemia (AMI); however, acute peritonitis universally mandates open surgery [1]. Endovascular treatment may in some instances be associated with adverse outcomes. Li et al. suggested that endovascular treatment as a primary approach did not improve outcomes compared to open surgery [2]. These investigators documented that endovascular treatment may raise several concerns that could potentially worsen patient outcomes. Firstly, endovascular treatment cannot preclude assessment of the viability of the gastrointestinal tract and may delay necessary bowel resection. Secondly, endovascular treatment failures may delay open revascularization and worsen outcomes. These concerns were also noted by Murphy et al. and Arthurs et al. [3, 4].

Another novel approach is retrograde open mesenteric stenting (ROMS), combining open and endovascular interventions, thus also allowing inspection of gut viability. Studies comparing it to open surgical revascularization or solely endovascular treatment are still lacking [5].

Due to the absence of randomized controlled studies, any valid comparisons of endovascular and surgical treatment modalities are lacking. Hypothetically, improved outcomes are achieved with endovascular interventions early after onset of symptoms or in "acute-on-chronic" AMI, whereas the opposite may be true for delayed interventions. Evidence-based time-limits for efficient revascularization are followed in stroke [6] and acute coronary syndrome [7] treatment guidelines, but still lacking for AMI. Watada and co-authors observed in their retrospective study on 48 AMI patients that 78% of patients did not suffer transmural necrosis within 3.5 h from onset of symptoms to diagnosis in patients with proximal SMA occlusion [8]. However, the time to admission of about 24 h from onset of symptoms in multiple investigations far exceeds the window of opportunity to intervene without the need for bowel resection [9, 10]. Given the nonspecific symptoms and lack of biomarkers, it seems currently unrealistic to achieve a verified diagnosis followed by endovascular treatment within the very first few hours from the onset of symptoms.

The primary aim of the current study was to compare the effectiveness of treatment modality, timelines and outcomes in patients with acute arterial occlusive mesenteric ischemia subjected to endovascular versus open surgical treatment. Secondary aims were to compare the effect of revascularization and revascularization strategies on in-hospital mortality. The current study was a preplanned substudy of the prospective observational multicenter AMESI (Acute MESenteric Ischaemia) study [9].

We hypothesized that the initial intervention, endovascular or surgical, is not an independent risk-factor for in-hospital mortality and that there is a time threshold within which endovascular treatment as a monotherapy may be curative.

Methods

Approval for the AMESI study was obtained from the Research Ethics Committee of the University of Tartu (number 357 T-8 and 364 M-7-amendment). All participating sites obtained local Ethics Committee approval according to their local regulations.

Study cohort

The present substudy was based on the AMESI study database. Data were accrued on emergency patients with superior mesenteric artery (SMA) occlusion who received intervention, excluding patients with mesenteric venous thrombosis, non-occlusive mesenteric ischemia (NOMI), other arterial occlusive AMI (e.g. occlusion of inferior mesenteric artery), and patients receiving only conservative treatment or end-of-life-care (EOLC). Patients subjected to exploratory laparotomy with unsalvageable bowel ischemia and patients not subjected to any active interventions were excluded.

Two treatment groups were constructed based on the initially chosen management:

1. the surgical-intervention group included all patients initially subjected to open surgical treatment with surgical revascularization or hybrid therapy (ROMS—considered under surgical-intervention group, because patients received laparotomy) or intestinal resection only;
2. the endovascular-intervention group included patients initially subjected to endovascular therapy and was further divided according to treatment as follows: A. endovascular revascularization (EVR) effective as a monotherapy: no need for open surgical intervention and B. endovascular revascularization as monotherapy insufficient: patients who received initial endovascular treatment but needed subsequent laparotomy (allocated to any surgical revascularization, bowel resection or diagnostic laparotomy) or were induced to EOLC.

Additionally, the following groups were constructed for comparisons: (1) any revascularization versus no revascularization (bowel resection only) and (2) endovascular versus surgical revascularization.

Statistical methods

Pre-treatment data were used to provide baseline descriptive statistics on study groups. Baseline characteristics included age, gender, body-mass-index (BMI), disability, type of AMI, time from beginning of symptoms to treatment, need for mechanical ventilation before diagnosis, need for vasopressors before diagnosis, Acute Physiology and Chronic Health Evaluation (APACHE) II score, sequential organ failure assessment (SOFA) score, white blood cell count (WBC), C-reactive protein (CRP), and lactate value. All group baseline and outcome comparisons were made using Fisher and Mann–Whitney U tests. Outcome variables included progression of bowel necrosis, end-of-life-care (EOLC) introduced after initial active management, intensive care unit admission after treatment, in-hospital mortality, and parenteral nutrition after discharge. Risk-factors for in-hospital mortality were analysed using a logistic regression model. Variables showing significant associations ($p < 0.05$) in univariate analysis were entered into a stepwise logistic regression model (using both directions) and the best predictive model was chosen based on the Akaike information criterion (AIC) [11]. Lactate was introduced in multivariable regression as a continuous variable.The treatment group variable was entered into the best predictive model to estimate the independent association of treatment to in-hospital mortality.

Area Under the Receiver Operating Characteristic curve (AUROC) analysis was performed to identify the cut-off values of biomarkers determining the insufficiency of endovascular treatment as monotherapy. All laboratory values with significant differences in univariate analysis were considered. The best cut-off was chosen based on the Youden index.

Results

A total of 418 cases with acute mesenteric ischemia were obtained from 32 study-sites worldwide, 114 of them were referred to the study site from another hospital. 222 cases were with occlusion of superior mesenteric artery. According to our inclusion and exclusion criteria, a total of 158 cases were analysed (Fig. 1).

Endovascular compared to surgical treatment as initial management strategy

Overall, 107 (67.7%) patients were initially subjected to open surgical treatment and 51 to endovascular treatment. There were 19 patients for whom endovascular approach was not available.

The baseline characteristics between patients who received initially endovascular or surgical treatment are demonstrated in Table 1 (first comparison).

We observed that patients initially subjected to surgical intervention more commonly had more organ failures (need for mechanical ventilation and vasopressors), had higher APACHE II scores and presented with higher C-reactive protein (CRP) and lactate values.

We observed significantly worse outcomes in the surgery-first compared to the endovascular group, with significantly higher rates of: end-of-life care (EOLC) induced after initial management, admission to intensive care unit (ICU) after treatment, and in-hospital mortality (Table 1, first comparison).

Univariate analysis for in-hospital mortality demonstrated that significant variables predicting poor outcomes were: the need for vasopressors and mechanical ventilation before diagnosis, APACHE II and SOFA scores, and lactate values. Multivariable analysis for in-hospital mortality revealed that the need for mechanical ventilation and lactate values before/at diagnosis were independent risk factors for in-hospital mortality. In this adjusted model, surgery as initial intervention was not an independent predictor of mortality, with an odds ratio (OR) of 1.59 (0.57; 4.37) (Table 2).

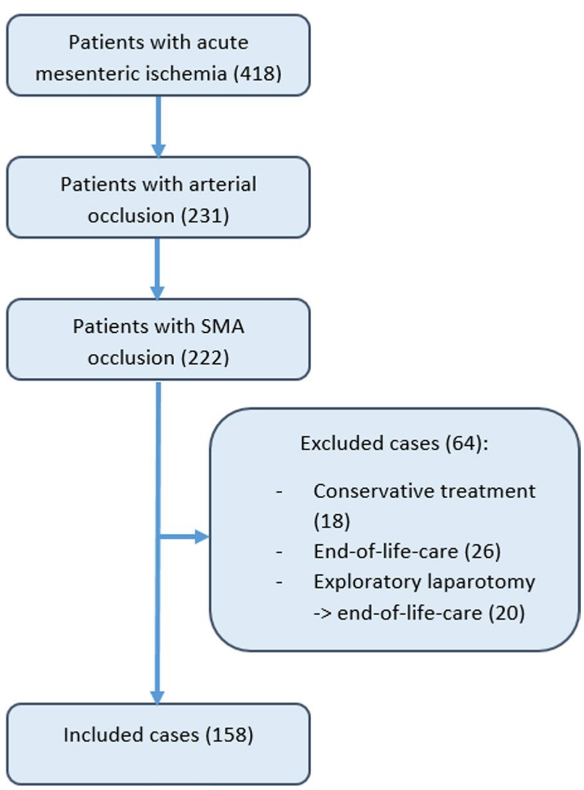

Fig. 1 Study flowchart

Effectiveness of endovascular treatment as monotherapy

Overall, 51 patients were initially subjected to endovascular therapy. 34 (66.6%) patients received endovascular revascularization as monotherapy, whereas 16 (31.4%) patients received open surgical intervention after initial endovascular management and 1 (2%) patient was introduced to EOLC.

Among baseline data, we noted significantly higher rates of male gender, higher BMI, increased occurrence of SMA embolism—10 (60%) versus 5 (15%), higher rates of organ failures (need for mechanical ventilation and vasopressors), higher APACHE II/SOFA scores and higher lactate values in patients where endovascular revascularization as monotherapy was insufficient.

Comparison of outcomes showed that in the endovascular revascularization effective as monotherapy group there were more admissions to the ICU after treatment, and in-hospital mortality was higher (Table 1, second comparison).

Multivariable analysis demonstrated that insufficient endovascular treatment is the only significant risk factor for in-hospital mortality, but with a wide confidence interval due to a small number of observations (Table 3).

Threshold for lactate level

The only significantly different laboratory marker was lactate. The AUROC analysis on lactate done to determine a "cut-off" value when endovascular revascularization as monotherapy is insufficient showed a threshold of 1.75 mmol/l with a specificity of 0.80 and sensitivity of 0.61.

Threshold for time ("therapeutic window")

We aimed to identify a cut-off for time when endovascular treatment is likely to be effective as monotherapy. However, the time from symptoms to treatment was longer in patients in whom endovascular treatment was effective as monotherapy compared to patients in whom endovascular treatment as monotherapy was insufficient (Table 1).

Endovascular treatment was effective as monotherapy in 8/16 patients with time from symptoms to endovascular treatment below 24 h and in 14/20 with time exceeding 24 h. Accordingly, it was impossible to identify a useful time threshold to predict the effectiveness of endovascular treatment.

Additional *post-hoc* comparison was performed to explore if delayed surgery in patients with initial endovascular approach may result in better outcomes compared to an initial surgical approach. While comparing patients with endovascular revascularization effective as monotherapy and those in whom monotherapy was insufficient subjected to upfront surgical treatment we

Table 1 Baseline characteristics and outcome in comparison of endovascular versus surgical approach as initial management strategy

Comparisons									
Variable	**EVR versus surgery as monotherapy**			**EVR effective as monotherapy versus EVR as monotherapy insufficient**			**EVR as monotherapy insufficient versus surgery as monotherapy**		
	EVR (n = 51)	**Surgery (n = 107)**	**p-value**	**EVR as monotherapy (n = 34)**	**EVR as monotherapy insufficient – EOLC or needed subsequent laparotomy (n = 17)**	**p-value**	**EVR as monotherapy insufficient – EOLC or needed subsequent laparotomy (n = 17)**	**Surgery (n = 107)**	**p-value**
Age (years), median (range)	73 (28–93)	68 (23–79)	0.095	72.5 (28–93)	76 (58–84)	0.873	76 (58–84)	68 (23–79)	0.131
Gender, female, n (%)	23 (45.1)	46 (43.0)	0.864	19 (55.9)	4 (23.5)	**0.039**	4 (23.5)	46 (43.0)	0.184
BMI (kg/m$^{2)}$, median (IQR)	23.8 (20.5–25.9)	25.1 (21.9; 27.8)	0.055	22.7 (20.1–24.4)	25.5 (24–28)	**0.017**	25.5 (24–28)	25.1 (21.9; 27.8)	0.592
Disability, n (%)	8 (15.7)	21 (19.6)	0.660	4 (11.8)	4 (23.5)	0.423	4 (23.5)	21 (19.6)	0.756
AMI type, n (%)									
Arterial embolism	15 (29.4)	27 (25.2)		5 (14.7)	10 (58.8)		10 (58.8)	27 (25.2)	
Arterial thrombosis	20 (39.2)	51 (47.7)		15 (44.1)	5 (29.4)		5 (29.4)	51 (47.7)	
Arterial non-specified	16 (31.4)	29 (27.1)	0.583	14 (41.2)	2 (11.8)	**0.004**	2 (11.8)	29 (27.1)	**0.031**
Time from beginning of symptoms to treatment (hours), median (IQR)	25.5 (14–54)	30.5 (16–59)	0.657	28.5 (14–54)	23 (14–71)	0.673	23 (14–71)	30.5 (16–59)	0.589
Need for mechanical ventilation before diagnosis, n (%)	7 (13.7)	49 (45.8)	**< 0.001**	1 (2.9)	6 (35.3)	**0.004**	6 (35.3)	49 (45.8)	0.446
Need for vasopressors before diagnosis, n (%)	4 (7.8)	25 (23.4)	**0.026**	-	4 (23.5)	**0.010**	4 (23.5)	25 (23.4)	1
APACHE II, median (IQR)	10.5 (7–14)	14 (10–18.5)	**0.049**	8 (6–12)	14 (9–18)	**0.014**	14 (9–18)	14 (10–18.5)	0.914
SOFA, median (IQR)	2 (0–4)	3 (1–7)	0.133	2 (0–4)	4 (2–8)	**0.022**	4 (2–8)	3 (1–7)	0.455
WBC ($\times 10^9$/L), median (IQR)	14 (10–19)	16.8 (12.2; 20.4)	0.093	14 (10–17)	16.6 (8.8–19)	0.502	16.6 (8.8–19)	16.8 (12.2; 20.4)	0.635
CRP (mg/L), median (IQR)	32 (7–115)	107 (21–253)	**0.011**	34.5 (7–134)	27.5 (5–100)	0.562	27.5 (5–100)	107 (21–253)	0.051
Lactate 0-12 h before diagnosis (mmol/L), median (IQR)	1.9 (1.2–3.1)	3.1 (1.7; 6.9)	**0.002**	1.6 (0.9–2.8)	2.9 (1.8–4)	**0.015**	2.9 (1.8–4)	3.1 (1.7; 6.9)	0.542
Outcome comparisons									
Progression of bowel necrosis, n (%)	13 (25.5)	31 (29.0)	0.704	-	13 (76.5)	**< 0.001**	13 (76.5)	31 (29.0)	**< 0.001**
EOLC introduced, n (%)	1 (2.0)	21 (19.6)	**0.002**	-	1 (5.9)	0.333	1 (5.9)	21 (19.6)	0.303

Table 1 (continued)

Comparisons									
Variable	**EVR versus surgery as monotherapy**			**EVR effective as monotherapy versus EVR as monotherapy insufficient**			**EVR as monotherapy insufficient versus surgery as monotherapy**		
	EVR (n = 51)	**Surgery (n = 107)**	**p-value**	**EVR as monotherapy (n = 34)**	**EVR as monotherapy insufficient – EOLC or needed subsequent laparotomy (n = 17)**	**p-value**	**EVR as monotherapy insufficient – EOLC or needed subsequent laparotomy (n = 17)**	**Surgery (n = 107)**	**p-value**
Patient admitted to ICU, n (%)	18 (35.3)	85 (79.4)	**< 0.001**	4 (11.8)	14 (82.4)	**< 0.001**	14 (82.4)	85 (79.4)	1
Anticoagulation/antiplatelet therapy, n (%)	49 (96.1)	97 (90.7)	0.340	32 (94.1)	17 (100.0)	0.547	17 (100.0)	97 (90.7)	0.355
In-hospital mortality, n (%)	8 (15.7)	49 (45.8)	**< 0.001**	1 (2.9)	7 (41.2)	**0.001**	7 (41.2)	49 (45.8)	0.797
Parenteral nutrition at discharge, n (%)	5 (9.8)	11 (10.3)	0.413	2 (5.9)	3 (17.6)	0.073	3 (17.6)	11 (10.3)	0.418

EVR—endovascular revascularization, EOLC—end-of-life-care, BMI—body-mass-index, IQR—interquartile, range, AMI—acute mesenteric ischemia, APACHE II—Acute Physiology and Chronic Health Evaluation score, SOFA—Sequential Organ Failure Assessment score, WBC—white blood cell count, CRP—c-reactive protein, ICU—intensive care unit

Table 2 Multivariable analysis evaluating the impact of surgical compared to endovascular treatment on in-hospital mortality

Variable	OR (95% CI)	p-value
Group, surgical	1.59 (0.57; 4.37)	0.367
Need for vasopressors	2.08 (0.65; 6.63)	0.216
Need for mechanical ventilation	3.64 (1.34; 9.84)	**0.011**
Lactate (mmol/L)	1.21 (1.04; 1.40)	**0.009**

OR—odds ratio, CI—confidence interval, Group, surgical = surgical versus endovascular treatment as initial management approach

Table 3 Multivariable analysis evaluating the impact of insufficiency compared to sufficiency of endovascular treatment on in-hospital mortality

Variable	OR (95% CI)	p-value
Group, endovascular revascularization as monotherapy insufficient	22.29 (2.09; 236.89)	**0.010**
Need for vasopressors	1.26 (0.10; 14.42)	0.855
Need for mechanical ventilation	0.78 (0.05; 10.89)	0.856
Lactate (mmol/L)	1.17 (0.68; 2.00)	0.567

OR—odds ratio, CI—confidence interval

observed similar baseline characteristics, with the only statistically important difference being the mechanism of AMI (higher rates of embolism in the endovascular ineffective group, 10 (60%) versus 27 (25%), respectively). From the outcome variables we observed that patients initially proposed for surgical treatment had decreased incidence of progression of bowel necrosis (Table 1, third comparison).

Multivariable analysis for in-hospital mortality showed that surgery itself is not an independent risk factor; however, the need for mechanical ventilation before diagnosis and lactate values were significant predictors of in-hospital mortality (Table 4).

Revascularization compared to no revascularization

When comparing patients who received any type of revascularization (endovascular, hybrid or surgical) to patients who received only bowel resection, we observed that patients who received revascularization were less severely ill (based on APACHE II and SOFA scores), less frequently received mechanical ventilation and vasopressors, and presented with lower lactate and inflammation levels (lower WBC, CRP). Revascularized patients had better outcomes in crude analysis with less EOLC introduced, less need for ICU admission and lower in-hospital mortality (Table 5). Of the patients who received revascularization, CT-scan was performed in 102 patients (98.1%), in 89 cases (85.6%) with arterial phase. Of the 54 patients who did not receive revascularization,

Table 4 Multivariable analysis evaluating the impact of surgery compared to endovascular treatment as monotherapy insufficient on in-hospital mortality

Variable	OR (95% CI)	p-value
Group, initial surgical treatment	0.57 (0.16; 1.96)	0.373
Need for vasopressors	1.84 (0.59; 5.72)	0.293
Need for mechanical ventilation	2.80 (1.02; 7.63)	**0.045**
Lactate (mmol/L)	1.19 (1.03; 1.37)	**0.014**

OR—odds ratio, CI—confidence interval

CT-scan was performed in 47 patients (87%), in 35 patients (64.8%) with arterial phase. None of the non-revascularized patients had angiography performed.

Multivariate analysis for in-hospital mortality revealed the need for mechanical ventilation and lactate level as independent factors influencing mortality (Table 6).

Comparison of revascularization methods

We noted significantly higher BMI and more frequent need for mechanical ventilation on admisson in patients who received surgical revascularization. Comparison of outcomes showed that in the surgical revascularization group there were more admissions to ICU after initial treatment and that in-hospital mortality was higher (Table 7). Multivariable analysis did not identify any independent factors influencing mortality (Table 8).

Discussion

In this substudy of the AMESI study [9] we assessed the different treatment strategies in patients with arterial occlusive AMI. We acknowledge that a patient's clinical condition probably influences selection of treatment strategy, making the groups differ at baseline and show that the effect of applied treatment strategy on mortality was largely absent when adjusted to the severity of illness.

Table 6 Multivariable analysis for in-hospital mortality evaluating the impact of revascularization compared to no revascularization

Variable	OR (95% CI)	p-value
Group, no revascularization performed	1.37 (0.53; 3.54)	0.515
Need for vasopressors	1.98 (0.61; 6.36)	0.251
Need for mechanical ventilation	4.01 (1.52; 10.54)	**0.005**
Lactate (mmol/L)	1.21 (1.04; 1.40)	**0.009**

OR—odds ratio, CI—confidence interval

Table 5 Baseline characteristics and outcome in comparison of revascularization compared to no revascularization

Variable	Any revascularization (n = 104)	No revascularization (n = 54)	p-value
Age (years), median (range)	70.5 (28–93)	69.5 (23–92)	0.503
Gender, female, n (%)	48 (46.2)	21 (38.9)	0.403
BMI (kg/m^{2}), median (IQR)	24.8 (22.1–27.3)	22.8 (21.2–27.7)	0.324
Disability, n (%)	17 (16.3)	12 (22.2)	0.381
AMI type, n (%)			
Arterial embolism	29 (27.9)	13 (24.1)	
Arterial thrombosis	48 (46.2)	23 (42.6)	
Arterial non-specified	27 (26.0)	18 (33.3)	0.635
Time from beginning of symptoms to treatment (hours), median (IQR)	28 (14–54)	34 (20–60)	0.660
Need for mechanical ventilation before diagnosis, n (%)	30 (28.8)	26 (48.1)	**0.022**
Need for vasopressors before diagnosis, n (%)	12 (11.5)	17 (31.5)	**0.004**
APACHE II, median (IQR)	11.5 (8–15)	17 (11–20)	**0.004**
SOFA, median (IQR)	2 (0–5)	3 (2–7)	0.091
WBC ($\times 10^{9}$/L), median (IQR)	15.6 (10–18.3)	17.0 (12.9–23)	**0.034**
CRP (mg/L), median (IQR)	50 (9–146)	163 (22–306)	**0.019**
Lactate 0-12 h before diagnosis (mmol/L), median (IQR)	2 (1.38–3.6)	5.4 (2.5–7.1)	**< 0.001**
Progression of bowel necrosis, n (%)	32 (30.8)	12 (22.2)	0.347
EOLC introduced, n (%)	8 (7.7)	14 (25.9)	**0.003**
Patient admitted to ICU, n (%)	61 (58.7)	42 (77.8)	**0.022**
In-hospital mortality, n (%)	27 (26.0)	30 (55.6)	**< 0.001**
Parenteral nutrition at discharge, n (%)	11 (10.6)	5 (9.3)	0.5233

BMI—body-mass-index, IQR—interquartile range, AMI—acute mesenteric ischemia, APACHE II—Acute Physiology and Chronic Health Evaluation score, SOFA—Sequential Organ Failure Assessment score, WBC—white blood cell count, CRP—c-reactive protein, EOLC—end-of-life-care, ICU—intensive care unit

As all treatment groups differed at baseline and matching was not possible due to the number of cases available, the groups under comparison in this observational multicenter study reflect broad clinical decisions: (1) bringing the patient to the angiography suite versus the operating theatre; (2) to revascularize additionally to bowel resection or not. These decisions are obviously dependent on local resources and expertise as well as on the patient's condition, and are largely taken in a non-standardized fashion. Accordingly, our results need to be interpreted with caution and taken as hypothesis generating. Most importantly, our results provide guidance for reporting in future studies, and the authors cannot provide guidance regarding management decisions in individual patients.

Table 8 Multivariable analysis for in-hospital mortality evaluating the impact of endovascular compared to surgical revascularization

Variable	OR (95% CI)	p-value
Group, open revascularization	1.69 (0.57; 4.92)	0.338
Need for vasopressors	1.56 (0.36; 6.64)	0.546
Need for mechanical ventilation	2.91 (0.90; 9.39)	0.073
Lactate (mmol/L)	1.14 (0.98; 1.32)	0.084

OR—odds ratio, CI—confidence interval

Endovascular compared to surgical treatment as initial management strategy

Scientific debate about the preference of endovascular versus surgical treatment as the first-line strategy in patients suffering from AMI has been ongoing in the literature for some time now. In a transatlantic "pro-con" discussion Orr and Endean emphasized that endovascular treatment was not the best first-line option due to delays in assessment of bowel viability and restoration of mesenteric blood flow in addition to lack of proven survival advantage following endovascular treatment. The authors of the "con" part concluded that the main question is not whether endovascular treatment can be done, but whether it should be done [12]. In contrast, the "pro" part of this debate by Björck underlined results of several investigations showing improved outcomes with an endovascular strategy [12]. Likewise,

Table 7 Comparison between endovascular and surgical revascularization

Variable	EVR versus surgical revascularization with or without bowel resection		
…	EVR (n = 51)	Revascularization with or without bowel resection (n = 53)	p-value
Age (years), median (range)	73 (28–93)	67 (31–87)	0.118
Gender, female, n (%)	23 (45.1)	25 (47.2)	0.847
BMI (kg/m^{2}), median (IQR)	23.8 (20.5–25.9)	25.8 (23.8–28.0)	**0.006**
Disability, n (%)	8 (15.7)	9 (17.0)	1
AMI type, n (%)			
Arterial embolism	15 (29.4)	14 (26.4)	0.315
Arterial thrombosis	20 (39.2)	28 (52.8)	
Arterial non-specified	16 (31.4)	11 (20.8)	
Time from beginning of symptoms to treatment (hours), median (IQR)	25.5 (14–54)	30 (16–56)	0.774
Need for mechanical ventilation before diagnosis, n (%)	7 (13.7)	23 (43.4)	**0.001**
Need for vasopressors before diagnosis, n (%)	4 (7.8)	8 (15.1)	0.359
APACHE II, median (IQR)	10.5 (7–14)	11.5 (8–15)	0.478
SOFA, median (IQR)	2 (0–4)	3 (1–6)	0.477
WBC ($\times 10^9$/L), median (IQR)	14 (10–19)	16.7 (11–18.3)	0.424
CRP (mg/L), median (IQR)	32 (7–115)	106 (12–180)	0.096
Lactate 0-12 h before diagnosis (mmol/L), median (IQR)	1.9 (1.2–3.1)	2 (1.5–4.2)	0.165
Progression of bowel necrosis, n (%)	13 (25.5)	19 (35.8)	0.286
EOLC introduced, n (%)	1 (2.0)	7 (13.2)	0.060
Patient admitted to ICU, n (%)	18 (35.3)	43 (81.1)	**< 0.001**
In-hospital mortality, n (%)	8 (15.7)	19 (35.8)	**0.025**
Parenteral nutrition at discharge, n (%)	5 (9.8)	6 (11.3)	0.523

EVR—endovascular revascularization, BMI—body-mass-index, IQR—interquartile range, AMI—acute mesenteric ischemia, APACHE II—Acute Physiology and Chronic Health Evaluation score, SOFA—Sequential Organ Failure Assessment score, WBC—white blood cell count, CRP—c-reactive protein, EOLC—end-of-life-care, ICU—intensive care unit

Kärkkäinen et al. reported an overall mortality of 32% with an endovascular-first strategy, and endovascular treatment was then successful in 88% of patients [13]. Also Beaulieu et al. concluded that endovascular treatment was associated with lower mortality and shorter hospital length of stay [14]. Similar conclusions have been reached also by Naazar et al. [15]. It should be noted nevertheless that the aforementioned studies were all retrospective in nature and patients subjected to endovascular treatment pathways were commonly younger [15] and less severely ill [14]. Also, the timing of the onset of ischemia has been poorly documented in previous studies [16]. Based on available evidence [17], the World Society of Emergency Surgery (WSES) guideline summarizes that 40% of patients require open surgical therapy [1]. Our current investigation suggests that initial endovascular treatment may not be beneficial in the majority of cases of occlusive arterial AMI. Despite the pointers that still indicate possible benefit from endovascular initial approach, an independent effect on in-hospital mortality was not confirmed. Future studies providing more granular information on severity of illness and subtype of arterial occlusive AMI should allow the identification of patients in whom an initial endovascular approach (effective as monotherapy or followed by surgery) is beneficial and those in whom it may be harmful, and possibly a group in between, where both approaches have similar effect on outcomes (not limited to mortality). Also, the novel approach of laparoscopy to evaluate viability of bowel needs to be studied more as it has had promising results [18]. Our study does not allow us to answer these questions due to the small number of patients.

Effectiveness of endovascular treatment as monotherapy

Our results demonstrate that the initial treatment modality (endovascular versus surgical) should not be chosen solely based on the duration of symptoms. Likewise, other authors have previously concluded that it is not entirely clear when exactly the tissue necrosis becomes irreversible, and it may anyway be alleviated by collateral flow due to underlying chronic ischemia [19]. Some authors suggest that necrosis commences as early as 6 h following the vascular event, others estimate after 12 h [20, 21]. We were unable to observe a time window during which patients could safely be managed with endovascular treatment as monotherapy, but we had only 36 cases for that observation. Also, the precise time of the onset of symptoms is difficult to estimate due to the often vague and non-specific clinical presentation, particularly in non-embolic AMI events. Larger cohorts are necessary to analyse the timing for successful intervention. However, as shown in the AMESI study, selection of patients has a major role in the success of treatment. Selected patients in specialist referral centers had the longest time from symptoms to treatment, related to transfer from another hospital, yet experienced improved outcomes compared to sites admitting patients directly via the emergency department [9]. Accordingly, the mechanism of functioning collaterals (either open due to underlying chronic asymptomatic ischemia or opening during the acute event), seems to be a factor that precludes assessment of time as a solitary predictive factor. Our findings support this hypothesis, suggesting that arterial embolism compared to thrombosis may be associated with less chances for endovascular treatment effective as monotherapy. Our results (33% effective as monotherapy) are similar to earlier studies, describing endovascular treatment effective as monotherapy in 13–21% of patients with SMA embolism, [2, 16, 22]. WSES guidelines recommend endovascular revascularization as primary treatment option in arterial occlusive AMI, while mentioning high heterogeneity in the available studies and the absence of data supporting superiority of an endovascular approach in embolic SMA occlusion [1]. European Society of Vascular Surgery (ESVS) guidelines reached the conclusion that open and endovascular revascularization were equally effective on embolic occlusion of the SMA, but that endovascular revascularization was more effective when there was a thrombotic occlusion [23]. It is possible that the time window for endovascular revascularization to be effective as monotherapy will be different according to the type of AMI (arterial thrombosis versus embolism) because patients with atherosclerosis in SMA develop rather “acute on chronic” AMI and are more pre-adapted to ischemia with enhanced collateral perfusion, thus the gut may tolerate ischemia longer than in patients with embolism. The relationship between the time to intervention and type of AMI should be included in reporting and analysis in future studies. However, distinguishing embolism from thrombosis appears to be challenging, as in almost one third of patients with SMA occlusion investigators were not able to clearly categorize the mechanism.

Our identified cut-off for lactate of 1.75 mmol/l distinguishing between endovascular revascularization effective as monotherapy and endovascular revascularization as monotherapy being insufficient, is not helpful because a lactate value under 2 mmol/l is generally considered normal. Moreover, a low lactate level should never be the sole marker to exclude transmural AMI [24–26]. At the same time, a moderately increased lactate could prompt investigations for AMI in patients where AMI fits with the patient’s clinical history and symptoms [27].

Our comparison of endovascular revascularization effective as monotherapy versus monotherapy being insufficient is hypothesis-generating. Future studies should identify the group of patients who should not undergo endovascular intervention before surgery.

Revascularization compared to no revascularization

Our analysis comparing the effect of any revascularization versus no revascularization on in-hospital mortality did not show a clear benefit of revascularization, whereas revascularization was not performed in the most severely ill patients. Also here, although less expectedly, the treatment strategy was obviously selected based on the severity of illness at baseline, we could speculate that revascularization is not undertaken in patients with distal occlusion when only a small area of bowel is affected and bowel resection alone could be considered sufficient. However, these patients would probably not present with severe illness.

Endovascular compared to surgical revascularization

Comparison of endovascular versus surgical revascularization in our study once more underlined the importance of severity of illness, while the method of revascularization did not independently influence mortality. Similar results were reported by Goto et al., Shi et al. and Qiu et al. [28–30].

Some studies assessed the severity of illness in patients with AMI mainly to predict mortality rather than to compare the groups receiving different forms of management. A recent disease-specific AMI grading scale based on anatomical findings, proposed by the American Association for the Surgery of Trauma, did not correlate well with outcomes, whereas factors reflecting organ dysfunction (vasopressors, creatinine and lactate) were significant predictors of mortality [31]. From the conventional severity of illness scoring systems, the Simplified Acute Physiology Score (SAPS) II performed better than the Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scores for prediction of mortality in patients with AMI. While actual mortality rates were commonly lower than predicted, the APACHE II scoring system underestimated mortality among AMI patients with predicted mortality rates of > 50% [32]. A three-component Clichy score (organ failure, serum lactate levels > 2 mmol/l and bowel loop dilatation on computerized tomography scan) was suggested by Nuzzo et al. to predict bowel necrosis but a recent multivariable analysis performed by Garzelli et al. did not confirm its association with 30-day mortality [33, 34]. A modified Clichy score (absence of bowel enhancement, bowel thinning, plasma bicarbonate concentration ≤ 15 mmol/L, and prothrombin rate < 40%) has been proposed by Calame et al. [35].

The severity of illness is seldomly reported and rarely used for adjustment in outcome analysis. More commonly used adjustments like age and comorbidities are probably insufficient, as they are unable to reflect the magnitude of bowel injury, which is the main prognostic factor in AMI. Therefore, studies with detailed reporting of severity of illness including acute organ dysfunctions, but also duration of symptoms and subtypes of AMI with applied management, are warranted.

Our study has several limitations: Firstly, a small number of patients was included, despite being the largest multinational and multicenter prospective observational AMI study to date. Wide heterogeneity related to many different sites provides a real-world view of the problem, but also makes generalised applicability challenging. Secondly, the groups generated for analysis may be criticized as primarily not comparable. However, the groups will remain different in observational studies, whereas we think that our investigation is a necessary step to improve reporting in future studies. From the sole description of different groups in retrospective single center studies we need to move to analyses that are helpful for evidence-based management guidelines. Thirdly, organ failure/illness severity scores such as SOFA and APACHE II were not documented in all patients in the AMESI study, precluding their use in multivariable models.

Conclusion

Based on our findings, the beneficial effect of endovascular compared to surgical treatment in unadjusted analyses is largely explained by selection of patients. More severely ill patients are more often treated surgically and less often revascularized. None of the compared management approaches has demonstrated an independent effect on mortality in the overall cohort. We conclude that the choice between endovascular and surgical treatment cannot be made solely based on the time elapsed from onset of symptoms but rather according to the patient's general condition and possibly on the cause of SMA occlusion. Future studies with detailed reporting of severity of illness and type of AMI are warranted.

Abbrevations

NR	Natural rubber
AMI	Acute mesenteric ischemia
ROMS	Retrograde open mesenteric stenting
AMESI	Acute MESenteric Ischaemia
SMA	Superior mesenteric artery
NOMI	Non-occlusive mesenteric ischemia
EOLC	End-of-life-care
EVR	Endovascular revascularization
BMI	Body-mass-index
APACHE	Acute physiology and chronic health evaluation
SOFA	Sequential organ failure assessment score
WBC	White blood cell count
CRP	C-reactive protein
AIC	Akaike information criterion

AUROC	Area under the receiver operating characteristic curve
ICU	Intensive care unit
OR	Odds ratio
IQR	Interquartile range
CI	Confidence interval
WSES	World society of emergency surgery
SAPS	Simplified acute physiology score
ESVS	European society of vascular surgery

Acknowledgements
Sites and Collaborators (AMESI Investigators): Intestinal Stroke Center, Department of Gastroenterology, IBD and Intestinal Failure, AP-HP. Nord, Beaujon Hospital, Paris Cité University, Paris, France: Olivier Corcos, Yves Castier, Maxime Ronot. Division of General Surgery, University Hospital of Trieste ASUGI, Trieste, Italy: Alan Biloslavo, Lucia Paiano. Universitätsklinikum Schleswig-Holstein, Campus Kiel, Kiel, Germany: Gunnar Elke, Denise Nagel, David I. Radke. Hospital General San Martin de La Plata, Buenos Aires, Argentina. Dr Jacqueline Vilca Becerra, Dr María Elina Abeleyra. Lucerne Cantonal Hospital, Lucerne, Switzerland. Benjamin Hess, Northern State Medical University and City Hospital #1, Arkhangelsk, Russia: Mikhail Kirov, Tatjana Semenkova, Anton Nikonov, Alexey Smetkin. University Hospital North Norway, Tromsø, Norway: Geir Ivar Nedredal, Øivind Irtun. Hadassah Medical Center and Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel: Oded Cohen-Arazi, Asaf Keda. „Nicolae Testemitanu " State University of Medicine and Pharmacy of the Republic of Moldova, Chisinau, Moldova: Gheorghe Rojnoveanu, Tatiana Malcova. Virgen del Rocío University Hospital, Sevilla, Spain: Felipe Pareja Ciuró, Anabel García-Leon, Carlos Javier García-Sánchez. Sarawak General Hospital, Kuching, Malaysia: Lim Jia Hui, Loy Yuan Ling. Rabin Medical Center, University of Tel Aviv, Petah Tikva, Israel: Ilya Kagan, Pierre Singer. North Estonia Medical Centre, Tallinn, Estonia. Edgar Lipping. N. Kipshidze Central University Hospital, Tbilisi, Georgia: Ana Tvaladze. Royal Infirmary of Edinburgh, Edinburgh, United Kingdom: Damian Mole, Darja Clinch. Hospital Melaka, Malacca, Malaysia: Too Xiao Qing. Stavanger University Hospital, Stavanger, Norway: Hanne Fuglseth. Azienda Ospedaliera Universitaria Careggi, Firenze, Italy: Jacopo Martellucci, Giulia Cerino. Fujian Provincial Hospital, Fuzhou, China: Donghuang Hong, Jinsheng Liu. Hospital Bintulu, Bintulu, Malaysia. Ernest Ong. Erciyes University Hospital, Kayseri, Turkey: Kursat Kundogan, Tutkun Talih. Maulana Azad Medical College and Lok Nayak Hospital, New Delhi, India: Lovenish Bains. AOU Cittá della Salute e della Scienza, Turin, Italy: Diego Visconti, Lorenzo Gibello. Hospital Ampang, Ampang, Malaysia. Ruhi Fadzlyana Jailani, Muhammad Amirul Ashra. School of Medical Sciences & Hospital Universiti Sains Malaysia, Kota Bharu, Malaysia: Andee Dzulkarnaen Zakaria. Ahmad Faiz Najmuddin Mohd Ghazi. Hospital Pengajar Universiti Putra, Serdang, Malaysia: Nur Suriyana Abd Ghani. Hospital Sultanah Nur Zahirah, Kuala Terengganu, Malaysia: Mohd Fadliyazid Ab Rahim. University Hospital Centre Zagreb, Zagreb, Croatia: Goran Augustin, Damir Halužan. Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India: Mohan Gurjar, Rahul Rahul. Queen Elisabeth Hospital, Kota Kinabalu, Malaysia: Firdaus Hayati, Jin-Jiun Mah.

Author contributions
K.K., A.R.B., M.M., K.T., P.T. were major contributors in writing the manuscript. M.K. performed the statistical analyses. All authors read and approved the manuscript.

Funding
Estonian Research Council, Grant PRG1255.

Availability of data and materials
Reintam Blaser A, Mändul M, Björck M, et al. Incidence, diagnosis, management and outcome of acute mesenteric ischaemia: a prospective, multicentre observational study (AMESI Study). Crit Care 2024;28:32.

Declarations

Ethics approval and consent to participate
Approval for the AMESI study was obtained from the Research Ethics Committee of the University of Tartu (number 357 T-8 and 364 M-7-amendment). All participating sites obtained local Ethics Committee approval according to their local regulations.

Consent for publication
Not applicable.

Competing interests
A.R.B. received consultancy fee from VIPUN medical and is holding a grant from the Estonian Research Council (PRG1255). A.F. has received speaker fees from B Braun and Fresenius Kabi. A.N. has received speaker or consultancy fees from Abbvie and Janssen, research funding from MSD-Avenir, and PhD grants from Fondation de l'Avenir and SNFGE. K.K., M.K., P.T., K.T., S.A., M.Bj., M.Ba., Z.B., M.C., D.C., Z.D., M.D.O., V.D.M.C., M.V., M.H.I., K.L., M.L., C.I.L., D.D., S.S., M.S., J.S., A.L.V., K.V., M.A.Y., M.M. declare no conficts of interest. All authors completed the ICMJE uniform conflict of interest disclosure form.

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Received: 28 February 2025 Accepted: 27 April 2025
Published online: 02 June 2025

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