# REVIEW

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# Management of acute mesenteric ischaemia in adult patients: a systematic review and meta-analysis



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# Abstract

**Background** Guidance on managing acute mesenteric ischaemia (AMI) is largely based on expert opinion and retrospective studies pooling different subtypes of AMI. In clinical practice, management strategy is often selected based on the patient's severity of illness, whereas randomized controlled trials or even adjusted analyses comparing different strategies are rarely available. We aimed to perform a systematic review and meta-analysis on the effect of different management options when adjusted for the baseline severity of illness.

**Methods** A literature search was performed in PubMed, the Cochrane Library, Web of Science and Scopus. Studies recruiting patients after the year 2000, assessing at least 10 adult patients with reliably confirmed AMI, and comparing different management approaches were considered for inclusion. Thirteen study questions on different management strategies in different subtypes of AMI were formulated a priori. We included studies reporting results of adjusted analyses or reporting any variables reflecting the severity of illness in both study groups under comparison.

**Results** A total of 3324 publications were identified, 321 were selected for full-text review and 31 included in the review and analysis. Most of the studies comparing different management strategies of AMI did not report the severity of illness in the groups under comparison. Any variable that could be considered to reflect the severity of illness was reported in 26 studies. The available data only allowed one meta-regression analysis comparing initial endovascular revascularization *versus* open surgery in arterial occlusive AMI, including four studies that reported white blood cell count and lactate. The results indicate that the significant advantage of the endovascular approach suggested in the crude analysis may be abolished when adjusting for the severity of the illness. Narrative summaries and raw data are presented for other research questions.

**Conclusions** The severity of illness plays an important role in the selection of management strategy and largely determines the outcome of any treatment, yet is generally not considered in available studies assessing the management of AMI. There is a major gap in the literature precluding appropriate analyses on treatment effects. Future studies should report subtypes of AMI and the severity of illness for each group.

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Keywords Acute mesenteric ischaemia, Endovascular, Open surgery, Management, Treatment

# Background

Acute mesenteric ischaemia (AMI), a sudden onset hypoperfusion of the intestines, may occur via various etiopathogenetic mechanisms. AMI may result from embolic occlusion, most commonly in the superior mesenteric artery (SMA), thrombotic occlusion in the presence of underlying pathology, such as atherosclerosis or dissection, or it may have non-occlusive etiology, such as splanchnic vasoconstriction or spasm, or mesenteric venous thrombotic occlusion [1, 2]. Although AMI is an uncommon clinical condition, accounting for only 0.038% [3] to 0.05% [4] of hospital admissions, it is associated with high mortality, ranging from 48 to 60% [4]. Management of AMI is widely variable, and clear guidance is often unavailable or based on scarce evidence (2, 5-6). Available systematic reviews and meta-analyses concerning the management of AMI have focused mainly on arterial occlusive AMI, comparing endovascular revascularization with any open surgery or specifically with open revascularization [7-11]. Importantly, none of these meta-analyses considered that the selection of management strategy is often based on the individual clinical condition of patients, with an endovascular approach being chosen for less severely ill patients as compared to open surgery [3], and that this may considerably affect the results in observational studies providing unadjusted results. Additionally, while endovascular revascularization techniques are commonly well-reported in studies included in meta-analyses, it is often not clear how many patients in the included studies under "open surgery" were not revascularized (12-13).

There are no randomized controlled trials or systematic reviews that allow evidence-based recommendations regarding optimal management strategies in patients with AMI. Available systematic reviews have not considered potential selection bias for management strategies due to patients with different severity of illness at baseline likely being allocated to a specific treatment [7–13]. Recent data shows large differences in severity of illness in patients with AMI at different hospitals [3]. For these reasons, before planning randomized controlled trials for any management strategy of AMI, an attempt to assess available studies reporting these treatments in comparable patient groups or groups that are adjusted for the severity of illness is needed.

In this systematic review and meta-analysis, we aimed to assess the effect of available management strategies for different subtypes of AMI in adult patients with similar severity of illness or adjusted for severity of illness to allow meaningful comparisons between the study groups.

# Methods

Thirteen study questions on different management strategies in different subtypes of AMI were formulated a priori, while the list was kept open for other comparisons. We included studies assuring the similarity of study groups at baseline, reporting results of adjusted analyses, or reporting any variables reflecting severity of illness in both study groups under comparison.

## **Review questions**

In adult patients with:

A) occlusive arterial AMI (with similar disease severity in both study groups or in analysis adjusted for severity of illness):

- Is endovascular revascularization compared to open surgery (including primary bowel resection alone) as an initial treatment associated with better outcomes?
- 2. Is endovascular compared to open revascularization associated with better outcomes?
- 3. Is revascularization in addition to bowel resection compared to bowel resection alone, associated with better outcomes?

# B) different subtypes of AMI:

- 4. Is therapeutic anticoagulation compared to no or prophylactic anticoagulation associated with better outcomes?
- 5. Is antiplatelet therapy, compared to no antiplatelet therapy, associated with better outcomes?
- 6. Does the use of intestinal endoscopy influence treatment decisions and is it associated with better outcomes?
- 7. Are there any factors associated with extremely high hospital mortality independent of the applied treatment strategy?

#### C) AMI without peritonitis:

8. Is antibacterial treatment, compared to no antibacterial treatment, associated with better outcomes?

## D) Occlusive venous AMI:

9. Is revascularization in addition to conservative treatment compared to conservative treatment only, associated with better outcomes?

E) non-occlusive mesenteric ischaemia (with similar disease severity in both study groups or in analysis adjusted for severity of illness):

- 10.Is intra-arterial vasodilation in addition to conservative treatment compared to conservative treatment only, associated with better outcomes?
- 11.Is withholding/cessation of enteral and oral nutrition (EN) compared to provision of EN, associated with better outcomes?
- F) AMI after achieved reperfusion:
  - 12.Is initiation of EN within the first 48 h compared to no EN, associated with better outcome?
- G) Occlusive arterial AMI:
  - 13. Which criteria should be used for referral to a specialist center for revascularization and does ignoring any of these criteria worsen the outcome?

#### Searches

A literature search was performed in PubMed, the Cochrane Library, Web of Science, and Scopus.

The search was limited to studies published after 01.01.2001, aiming to identify all studies commencing patient recruitment after the millennium. This time limit was set based on the availability and advances in CT-scan diagnostics [14] and is in line with our previous systematic review on the incidence and outcome of AMI, addressing earlier and later studies with a cut-off in the year 2000 [4]. No language restrictions were applied.

Additional studies were searched by screening the references of relevant articles, including systematic reviews identified through the search.

The final search was performed on the 31st of July 2024, the search strategy is presented in Additional File 1.

#### Inclusion criteria

- Studies assessing the management of acute mesenteric ischaemia.
- Acute mesenteric ischaemia diagnosed at either surgery, Computed Tomography (CT)-angiography, invasive mesenteric angiography, endoscopy, and/or histopathological examination.
- Clinical studies in adult patients including at least 10 adult patients and addressing any type of management of AMI in comparison to two or more groups.
- Studies reporting adjusted results or indicators of severity of illness such as Acute Physiology and Chronic Health Evaluation (APACHE) II score [15],

Sequential Organ Failure Assessment (SOFA) score [16], vasoactive treatment, mechanical ventilation, laboratory markers such as lactate and inflammation markers, and clinical signs of peritonitis.

## Exclusion criteria

- Studies where AMI was not the studied condition or was not confirmed as defined above (e.g. only clinical diagnosis was used).
- Studies did not assure the similarity of study groups regarding the severity of illness at baseline and did not report adjusted results or summaries for both groups in comparison for any of the indicators of severity of illness.
- Publications not presenting original data (e.g. reviews, editorials), case reports, cohort studies with <10 patients, animal studies, studies in neonates and children, and studies published only as abstracts.</li>
- Studies that commenced patient recruitment before the year 2000.

#### **Data extraction**

Titles and abstracts of studies identified in the search were screened independently by two reviewers to identify studies for full-text review. The full texts of these studies were independently assessed by two reviewers. For any disagreements during title/abstract and full-text review, consensus was reached, involving a third reviewer, if necessary.

The following information was extracted from the reviewed full texts: study setting, patient selection, age, gender, indicators of severity of illness, subtype of AMI, progression of AMI and localization of AMI if available, management modality, hospital mortality (or any other short term mortality if hospital mortality is not available), total number of interventions related to management of AMI, length of hospital stay, stoma or diagnosis of short bowel syndrome, and parenteral nutrition at discharge, referral from another hospital.

Regarding treatment outcome, the following information was extracted, where available: mortality (all reported mortality data, e.g. in-hospital or 30-day mortality), reinterventions, hospital length of stay, short bowel syndrome, and home parenteral nutrition.

## Risk of bias (quality) assessment

The Newcastle-Ottawa scale [17] was used to assess the risk of bias in observational cohort studies and the Cochrane Risk of Bias 2.0 tool [18] in randomized controlled trials included in the review by two research team members in parallel assessed the risk of bias for each study included in the analysis. Decisions were made after reaching consensus, or by involving a third reviewer, when necessary.

#### Data synthesis and analysis

Clinical data was extracted as reported in included studies, i.e., as a mean±Standard Deviation (SD) or median [interquartile range, IQR] for continuous variables and as number and percentages for categorical variables.

A random-effects model was used to calculate pooled OR with 95% CI or mean differences (MD), as appropriate.

Calculation of pooled effect size for studies that report effect sizes, adjusted for severity of illness, was planned. If at least three studies reported unadjusted effect sizes, providing details on the severity of illness for the groups under comparison, a multiple meta-regression randomeffects model [19] was used to adjust the result for illness severity. We assessed study heterogeneity by the Chi-squared tests and I-squared measures. Studies with an I-squared value below 25% were considered homogeneous, 26–50% as low, 51–75% as moderate, and over 75% as high heterogeneity, respectively [20].

A p-value of < 0.05 was considered statistically significant.

The results of the meta-regression were presented in a forest plot.

Sensitivity analyses, excluding all the studies with a high risk of bias from the analysis, were planned.

For the management approaches where meta-analysis was impossible, narrative summaries of available studies were provided.

Analysis was conducted in R and metafor package [19, 21].

## Results

The literature search identified 3288 original publications, and 36 additional publications were identified from systematic reviews and reference lists of papers included in the review. Altogether, 321 studies were selected for full-text review (Fig. 1).

For five of the papers, full text was not available, and 285 papers were excluded after full-text review (Fig. 1). Finally, 31 studies were included in the review [3, 22–51].

For none of our research questions, two or more studies with adjusted effect sizes were identified.

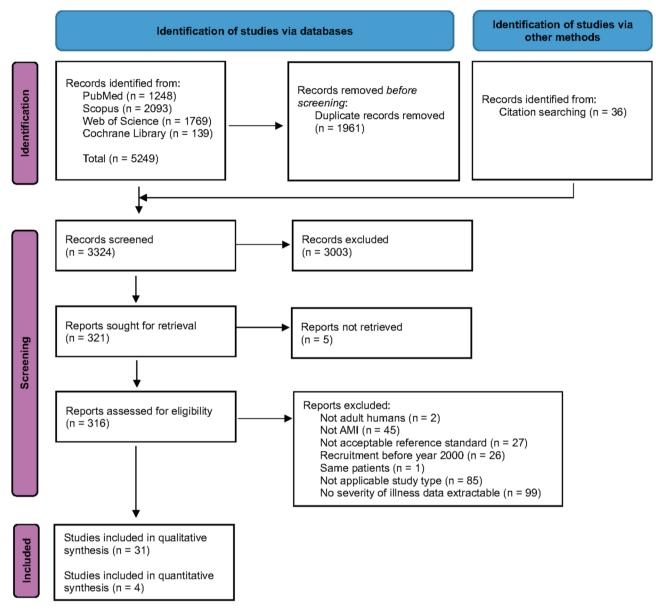
A meta-regression analysis was performed, including four studies [3, 22–24] comparing *endovascular revascularization versus open surgery* as the initial strategy in patients with occlusive arterial AMI (Question #1). We assessed mortality as reported in studies, and adjusted the analysis for white blood cell count and lactate at baseline (Fig. 2). Crude mortality (in-hospital or 30 days) was significantly higher in initial open surgery compared to endovascular revascularization (OR 3.09; 95% CI 1.75–5.46) whereas the adjustment for the abovementioned two laboratory variables moved the results towards a non-significant benefit of endovascular revascularization (Fig. 2). Figure 2 does not include an overall pooled estimate; the meta-regression model assumes that mortality is influenced by white blood cell count and blood lactate in addition to management strategy. Accordingly, the meta-regression model results in adjusted estimates for each study that vary based on the adjusted covariates.

Original data are presented in Supplementary Table **S1** (Additional File 2). Analysis of outcomes other than mortality was not possible.

While trying to answer the other research questions, adjustment for any of the illness severity indicators was not possible, and thus a narrative overview of the information obtained from applicable studies is provided below.

Endovascular versus open revascularization (Question #2, Supplementary Table S2, Additional File 2) was assessed in four studies. One small single-center study reported similar disease severity according to proportions of peritonitis, and WBC, CRP and plasma lactate levels, and no difference in 30-day mortality rates [25]. The second, a large register-based study included a large number of comorbidity data and the American Society of Anesthesiologists (ASA) class in the adjusted analysis, showing lower odds for 30-day mortality after endovascular revascularization (OR 0.4; 95% CI 0.2-0.9) [26]. The third retrospective study showed no difference between endovascular and open revascularization in 30-day mortality. The two groups were similar according to ASA class [27]. The fourth retrospective study compared three groups (endovascular, open and hybrid treatment) and showed no difference in the presence of peritonitis or sepsis on presentation but differences in the white blood counts (WBC) counts and lactate levels between these three groups [28]. The proportions and absolute values for all the abovementioned values were the lowest in the endovascular group. There was a higher 30-day mortality (p = 0.05 between the three groups) after endovascular revascularization compared to open and hybrid approach in univariate analysis. History of diabetes (OR 2.77; 95% CI 1.37-5.61) and sepsis on presentation (OR 2.32; 95% CI 1.18-4.58) were identified as independent risk factors for postoperative major adverse effects, whereas open revascularization was associated with lower odds of bowel resection in the adjusted analysis (OR 0.23, 95% CI 0.13-0.61) [28].

*Revascularization versus no revascularization* (Question #3, Supplementary Table **S3**, Additional File 2) was assessed in two studies. In a multi-center retrospective study, patients who underwent any surgery for AMI were divided into two groups based on timeliness



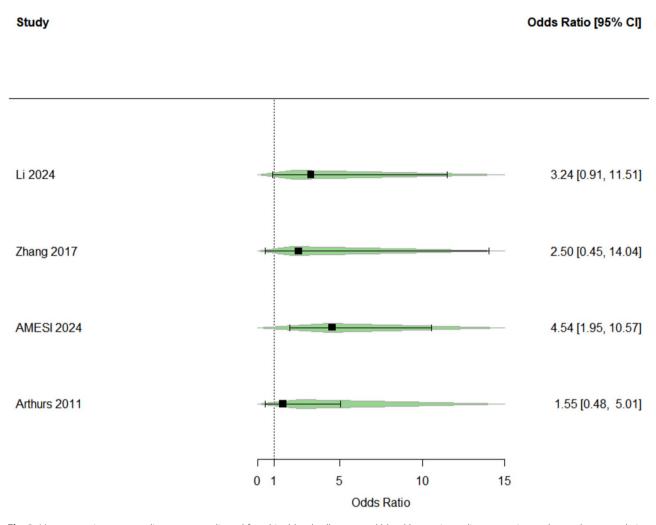


of mesenteric revascularization after presentation [29]. Early revascularization was defined as having both vascular consultation in  $\leq 12$  h of presentation and vascular surgery performed during patient's initial operation. Delayed revascularization was defined as having either delays to vascular consultation or vascular surgery. Patients in the early and delayed revascularization group were mostly comparable in baseline demographic characteristics as well as severity of illness (e.g., proportion of patients with sepsis and peritonitis, WBC count and lactate concentration at presentation). Delayed revascularization was a significant predictor of 30-day (OR 2.09; 95% CI 1.4–4.9) and 2-year mortality (hazard ratio (HR) 1.55, 95% CI 1.0–2.3). Delayed revascularization was also

independently associated with increased bowel resection length (OR 7.47; 95%CI 2.8–19.5; p < 0.01) and postoperative short bowel syndrome (OR 2.4; 95%CI 1.1-5.0; p = 0.03) in multivariate analyses.

In a small single-center retrospective study by Plumereau et al. [30], revascularization by either endovascular or surgical approach was associated with lower mortality compared to no revascularization. However, the sample size was small, and shock was present only in the no-revascularization group (5/13 patients).

No studies addressing Question #4 (*therapeutic versus* prophylactic anticoagulation) and Question #5 (antiplatelet therapy) in patients with any subtype of AMI, Question #11 (cessation/withholding of EN in patients



**Fig. 2** Meta-regression on mortality outcome adjusted for white blood cell count and blood lactate in studies comparing endovascular revascularization and open surgery (including revascularization and bowel resection alone) as initial treatment for patients with arterial occlusive AMI. Endovascular revascularization is taken as Reference, OR > 1 indicates higher mortality in the open surgery group. Squares and black lines with numbers indicate crude odds ratios (OR) with 95% confidence interval (CI). Green rhombs indicate adjusted OR and 95% CI. Adjustment was performed using the difference in the median white blood cell count (WBC) and in the median blood lactate between the groups under comparison in each study. AMESI study [3] results for this analysis were obtained from the original database. Heterogeneity, I-squared = 0.00%, Chi-squared test *P*-value = 0.304

with NOMI) and Question #13 (*referral criteria*) were identified.

*Intestinal endoscopy* (Question #6) was assessed in two studies of colon ischaemia [31, 32], *futility of treatment* (Question #7) described in three studies [33–35], *application of antibiotics* (Question #8) in one study [36], and the *effect of enteral nutrition* after revascularization of AMI (Question #12) in one study [42] (Additional File 2, Supplementary Tables S4 and S5).

Only one study [37] was identified on *revascularization in venous AMI* (Question #9, Supplementary Table S6, Additional File 2), where 15 patients received catheterdirected thrombolysis (CDT) of the SMA as a sequential treatment of emergency surgery patients with acute superior mesenteric venous thrombosis and 17 received systemic anticoagulation. The authors demonstrated that the CDT group had better outcomes in terms of thrombolysis success rate (80% CDT *versus* 29% anticoagulation, p = 0.001), second-look laparotomy (20% CDT *versus* 79% anticoagulation, p = 0.002), short bowel syndrome (6.7% CDT *versus* 41.2% anticoagulation, p = 0.001) and one-year survival (93.3% CDT *versus* 52.9% anticoagulation, p = 0.014).

Four studies assessed *intra-arterial vasodilation in NOMI* (Question #10, Supplementary Table S7, Additional File 2). In a small single-center retrospective study, intra-arterial use of PGE1 was investigated in patients with NOMI [38] Thirteen conservatively treated and nine patients with intra-arterial PGE-1 infusion for 5 days had comparable baseline characteristics with a high burden of cardiovascular disease in older patients, whereas shock was present in only one patient in each group. In the PGE1 group in-hospital mortality was numerically lower, compared to patients not receiving intra-arterial vasodilation therapy (22% *versus* 69%).

In a German two-center retrospective study, according to different in-house standard procedures, patients with NOMI were treated conservatively or interventionally by a standardized local infusion of intra-arterial papaverine into the splanchnic arteries [39]. There was a significant difference in 30-day mortality between the conservative (96.8%; 1/31 survived) and the interventional (65.7%; 12/35 survived) group (HR 2.44; p = 0.005, adjusted for the covariate lactate). The mean of the blood lactate in the interventional group was  $8.8 \pm 6.8$  mmol/l and in the conservative group  $12.7 \pm 7.9$  mmol/l; p = 0.025), there were no significant differences in other variables including SOFA score.

Takiguchi et al. [40]. performed a retrospective analysis of the nationwide inpatient database assessing the use of vasodilators (intra-arterial or intravenous papaverine and/or PGE1 within 2 days of admission) in patients with NOMI. In a total of 795 patients (159 patients in vasodilator group versus 636 in control group, following matching with a 1:4 propensity matching score), the authors demonstrated that the risk of hospital mortality and of abdominal surgery (excluding patients needing surgery within two days of admission) was lower in the vasodilator group compared to the conservative group (risk difference – 11.6%, p = 0.005; and risk difference -10.2%, p = 0.002, respectively). However, in this study, intravenous PGE1 was adopted most frequently as vasodilator, and half of the patients who received papaverine were administered the drug intravenously. Of note, patients included in this study were considered mild to moderate in terms of severity, because patients who received abdominal surgery for NOMI within 2 days of admission were excluded from analysis. Consequently, in-hospital mortality in this study was significantly lower than reported in most other studies investigating NOMI. Thereafter, the same group [41] used the same database to assess the use of vasodilators (intravenous or intraarterial papaverine and/or PGE1) as adjuvant therapy in the postoperative period in patients with NOMI undergoing abdominal surgery. The authors identified 745 patients (149 in the vasodilator group and 569 in the control group, following matching with a 1:4 propensity matching score). The overall disease severity in this study [41] was significantly higher (approx. four times more mechanical ventilation and two times more renal replacement therapy) in these patients compared to the previous reported patient collective [40]. There was no significant difference in in-hospital mortality (risk difference 3.4%, p = 0.42) and no significant difference in the prevalences of abdominal surgery, bowel resection  $\geq 3$  days after admission, or short bowel syndrome.

In addition to the initially formulated study questions, we identified three additional research questions during assessment:

- *damage-control strategy* (resection with blind closure, open abdomen) compared to immediate definitive surgery (anastomosis and abdominal closure) [43–49] (Additional File 2, Supplementary Table S8);
- vasopressor use [50] (Additional File 2, Supplementary Table S9);
- a rectus sheath block in addition to standard anesthetic management [51] (Additional File 2, Supplementary Table S10).

Assessment of risk of bias in studies included in this review is presented in Supplementary Table S11 and Table S12 (Additional File 3). Planned sensitivity analyses excluding studies with lower quality, were not performed as only four studies qualified for analysis.

# Discussion

This systematic review aimed to compare different management strategies applied in patients diagnosed with acute mesenteric ischaemia of various subtypes, while considering the severity of illness at baseline. Despite identifying a relatively large number of potentially applicable studies, planned analyses were not possible due to missing data on the severity of illness in most of the studies. Accordingly, the main finding of this systematic review does not come from the results of meta-analyses or qualitative/narrative summaries, but from revealing the fact that reporting in available studies addressing the management of AMI is inappropriate and requires urgent improvement. Currently, disease severity as well as patient selection criteria cannot be properly assessed in most studies.

A recent systematic review by Shi et al., comparing endovascular and open surgical revascularization for occlusive arterial AMI, found no difference in shortterm mortality and suggested the need for future multicenter randomized controlled trials [52]. In this study the authors also used meta-regression, attempting to identify factors impacting mortality related to the management while considering the thrombotic etiology and year of publication [52]. A recent large retrospective study, published thereafter, where comorbidities and need for bowel resection (considered accounting for disease severity) were adjusted for, reported better outcomes with endovascular compared to open revascularization [53]. Another recent study in patients with mesenteric artery embolism used adjustment for baseline clinical data and reported no difference in 30-day mortality between endovascular treatment and laparotomy as primary treatment [54]. However, in this study D-dimers > 4 mg/L and procalcitonin > 0.5 ng/mL were identified as independent predictors of 30-day mortality in patients with mesenteric artery embolism [54].

The only meta-regression analysis that could be performed in the current study also compared endovascular revascularization and surgery as the initial management approach in arterial occlusive AMI. This comparison can be questioned, as open surgery may include bowel resection alone as well as revascularization, whereas endovascularly revascularized patients may need bowel resection later. However, in our opinion, presenting such an approach is needed to illustrate the relevance of this concept for future research. Moreover, it needs to be underlined that reporting in studies has been often unclear and potentially confusing regarding details in the open surgery group. For example, the study by Arthurs et al. [24]. has been included in all meta-analyses comparing endovascular and open revascularization, although based on data reported in the original paper, only 72% of patients in the open surgery group were revascularized.

In our analysis, a clear signal for the advantage of the endovascular approach seems to be abolished by adjusting for just two laboratory variables at baseline, available in all four applicable studies [3, 22–24]. Such an analysis, including only four studies, is of low precision, and the two laboratory variables probably do not adequately represent disease severity. Nevertheless, our results support the hypothesis that in these studies, mortality is driven by patients' severity of illness rather than the management strategy and highlight that the current level of detail when reporting the results is insufficient.

In our review, it was decided not to adjust for age and comorbidities of AMI patients. These characteristics are commonly reported in studies, but while they may be important prognostic factors for mortality and may, in some cases, also influence the selection of the treatment strategy (e.g., initiation of end-of-life care, or decision not to operate if endovascular approach fails), they do not reflect AMI-related severity of illness.

In clinical practice, patients presenting with peritonitis due to any subtype of AMI are commonly allocated to initial surgical treatment, whereas patients with mild symptoms and occlusive arterial AMI undergo endovascular revascularization, when available. Thus, patients allocated to these two treatments differ in their severity of illness at baseline, and it is not surprising that crude analysis comparing endovascular revascularization and open surgery as initial treatment approaches shows higher mortality in the open surgery group. Additionally, patient selection through referral may also play a role, as most severely ill patients will unlikely be transferred to a center with competence in endovascular approach. In the recent AMESI study, mortality in a specialized intestinal stroke unit with 99% of patients being referred for mainly endovascular treatment, was six times lower than in other sites, whereas clinical indices (need for vasopressors and mechanical ventilation, illness severity and organ dysfunction scores, and laboratory variables reflecting inflammation, disordered metabolism and coagulation) suggested significantly less severe illness at admission. These findings suggested that direct unadjusted comparisons of treatment strategies in observational studies are not appropriate, giving rationale to the current systematic review. In line with our findings, a retrospective study in patients with AMI has demonstrated that anatomical factors alone, measured using the American association for the surgery of trauma grading system for acute mesenteric ischemia, are not sufficient in predicting outcomes and can only be improved by further adjusting for disease severity reflected as vasopressor use, creatinine, and lactate [55].

Available studies show different directions of the treatment effect in adjusted analyses, e.g. for endovascular versus open revascularization [26, 56] or damage-control versus immediate definitive treatment [44, 45, 47]. These results may indicate difficulties to properly adjust the analyses and may also arise from different patient cohorts being studied. Treatment strategies may appear to be beneficial in certain populations, whereas any treatment itself is unlikely causing mortality. To address these questions, meticulous standardized reporting in future studies without subjective interpretation of results is required.

Many observational studies only summarize descriptive data without reporting the severity of illness or any adjusted comparisons. In our opinion, adding more such studies will unlikely bring any new information nor lead to progress in identifying optimal AMI management strategies based on evidence, as the patient selection process cannot be assessed. Moreover, presenting descriptive results and unadjusted analyses may even be misleading. For example, it is possible that revascularization/reperfusion of a bowel segment with already transmural damage may impair outcome, but to our knowledge, this has not been studied specifically. Accordingly, advocating the endovascular approach for the majority of patients based on results of crude analyses in studies where the groups differed at baseline may not be appropriate. The expected clear advantages of a less invasive (endovascular) over a more invasive (open surgery) approach could be lost due to patient selection. Therefore, it is of great interest to identify patient groups in whom endovascular treatment alone could be successful.

While observational studies with different baseline characteristics are problematic, planning randomized controlled trials in this area is difficult and necessitates defining a patient group where both tested treatment strategies are considered appropriate. Randomizing a patient without transmural ischaemia to surgery and a patient with peritonitis to endovascular management would not be appropriate. Any evidence-based guidance can probably not be achieved without an appropriate description of groups under comparison in future studies.

It needs to be underlined that there is no consensus on which markers should be used to describe the severity of illness. Moreover, the severity of illness can only be considered as a surrogate marker of the progression/ magnitude of intestinal ischaemia. In case of NOMI, the severity of illness may reflect the primary pathology (e.g., septic or cardiogenic shock) rather than bowel damage. Accordingly, markers (e.g., laboratory, radiological) reflecting the magnitude of intestinal damage are still most warranted and this research area should be prioritized. These markers could provide cut-offs for patient allocation to various treatment strategies. As a good start, a recent retrospective study assessed patients with considered low probability of bowel necrosis and undergoing first-line endovascular revascularization and identified persistent bowel wall enhancement in CT scan and C-reactive protein level < 100 mg/L as factors associated with intestinal resection-free survival in patients undergoing endovascular revascularization [57].

Different subtypes of AMI obviously need different approaches, but in all cases exact reporting of the subtypes and the severity of illness is crucial. Accurate data on arterial occlusive AMI, the most common subtype of AMI [3], should contribute to the progress in the management of less common subtypes of AMI. Radiological and biomarker data differentiating between nontransmural and transmural ischaemia together with the known time point of reperfusion are useful for other subtypes (e.g., venous AMI, NOMI) where the decision on the presence/absence of AMI and detection of reperfusion is less straight-forward.

Patients with NOMI, usually identified in the ICU, receive sedation, analgesia and mechanical ventilation, making interpretation of the clinical abdominal status much more difficult. Hence, the presence of peritonitis from a clinical point of view in NOMI patients is challenging and cannot be obtained from reports. Our study suggests that at least to some extent, routine biomarkers (e.g., WBC, lactate, C-reactive protein) may reflect the severity of illness, that influences the outcome, and should thus be reported in all studies assessing any type of AMI and any management strategy of it. However, a much broader selection of characteristics is needed to identify the best set of markers reflecting the severity of illness in patients with AMI, considering that severity of illness is used as a surrogate for bowel damage in these patients.

The strengths of our study are the novel approach, uncovering the existing problems, allowing suggestions for future research, and the rigorous methodology. The limitations are related to the quality of the available studies, the interpretation of our meta-regression analysis, and the descriptive nature of the narrative summaries that were used to answer most of our research questions. The research questions may not have covered all the available AMI management strategies, some comparisons (e.g., endovascular revascularization *versus* open surgery) may not capture all specific management aspects, and outcomes beyond mortality were not possible to assess.

# Conclusions

Patients' severity of illness is generally not reported in available studies assessing the management of AMI, precluding a fair comparison of different treatment strategies. Since there are no direct markers adequately reflecting the magnitude of intestinal damage, the severity of illness as its surrogate plays an important role in the selection of the management strategy and the evaluation of its effectiveness. Future studies on AMI management should always report the subtypes of AMI and the patients' severity of illness for each study group.

# Abbreviations

Abbreviations		
AMI	Acute mesenteric ischaemia	
APACHE	Acute physiology and chronic health evaluation	
CDT	Catheter-directed thrombolysis	
CI	Confidence interval	
CT	Computed tomography	
EN	Enteral nutrition	
HR	Hazard ratio	
ICG	Indocyanine green	
ICU	Intensive care unit	
IQR	Interquartile range	
MD	Mean difference	
NOMI	Non-occlusive mesentheric ischaemia	
OR	Odds ratio	
PGE1	Prostaglandin E1	
POSSUM	Physiologic and operative severity score for the study of mortality	
	and morbidity	
SD	Standard deviation	
SMA	Superior mesenteric artery	
SMVT	Superior mesenteric venous thrombosis	
SOFA	Sequential organ failure assessment	
WBC	White blood cell count	

#### Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s13017-025-00614-6.

Supplementary Material 1	
Supplementary Material 2	
Supplementary Material 3	

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None.

#### Author contributions

ARB, MK, KFB, PDG, EK, KTL, SP, KS, KT and SA participated in the study conception, wrote the study protocol, reviewed the extracted abstracts and full papers, and read and approved the final version of the manuscript. ARB drafted the manuscript. EK performed literature searches. MK performed the statistical analysis.

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#### Data availability

No datasets were generated or analysed during the current study.

#### Declarations

Ethics approval and consent to participate Not applicable

#### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

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#### References

- Yang B, Norton EL, Rosati CM, Wu X, Kim KM, Khaja MS, et al. Managing patients with acute type A aortic dissection and mesenteric malperfusion syndrome: A 20-year experience. J Thorac Cardiovasc Surg. 2019;158(3):675– 687 e4.
- Park WM, Gloviczki P, Cherry KJJ, Hallett JWJ, Bower TC, Panneton JM et al. Contemporary management of acute mesenteric ischemia: factors associated with survival. J Vasc Surg. 2002;35(3):445–52.
- Reintam Blaser A, Mandul M, Bjorck M, Acosta S, Bala M, Bodnar Z et al. Incidence, diagnosis, management and outcome of acute mesenteric ischaemia: a prospective, multicentre observational study (AMESI Study). Crit Care. 2024;28(1):32–4.
- Tamme K, Reintam Blaser A, Laisaar K, Mandul M, Kals J, Forbes A et al. Incidence and outcomes of acute mesenteric ischaemia: a systematic review and meta-analysis. BMJ Open. 2022;12(10):e062846.
- Bala M, Catena F, Kashuk J, De Simone B, Gomes CA, Weber D et al. Acute mesenteric ischemia: updated guidelines of the world society of emergency surgery. World J Emerg Surg. 2022;17(1):54.
- Ersryd S, Djavani-Gidlund K, Wanhainen A, Björck M. Editor's Choice– abdominal compartment syndrome after surgery for abdominal aortic aneurysm: A nationwide population based study. Eur J Vasc Endovasc Surg. 2016;52(2):158–65.

- Murphy B, Dejong CHC, Winter DC. Open and endovascular management of acute mesenteric ischaemia: A systematic review. World J Surg. 2019;43(12):3224–31.
- El Farargy M, Abdel Hadi A, Abou Eisha M, Bashaeb K, Antoniou GA. Systematic review and meta-analysis of endovascular treatment for acute mesenteric ischaemia. Vascular. 2017;25(4):430–8.
- Zhao Y, Yin H, Yao C, Deng J, Wang M, Li Z et al. Management of acute mesenteric ischemia: A critical review and treatment algorithm. Vasc Endovascular Surg. 2016;50(3):183–92.
- Hou L, Wang T, Wang J, Zhao J, Yuan D. Outcomes of different acute mesenteric ischemia therapies in the last 20 years: A meta-analysis and systematic review. Vascular. 2022;30(4):669–680.
- Salsano G, Salsano A, Sportelli E, Petrocelli F, Dahmane M, Spinella G et al. What is the best revascularization strategy for acute occlusive arterial mesenteric ischemia: systematic review and Meta-analysis. Cardiovasc Intervent Radiol. 2018;41(1):27–36.
- Wang L, Wang E, Liu F, Zhang W, Shu X, Guo D et al. A systematic review and meta-analysis on endovascular treatment as an attractive alternative for acute superior mesenteric venous thrombosis. Vascular. 2022;30(2):331–40.
- Stahl K, Rittgerodt N, Busch M, Maschke SK, Schneider A, Manns MP et al. Nonocclusive mesenteric ischemia and interventional local vasodilatory therapy: A Meta-Analysis and systematic review of the literature. J Intensive Care Med. 2020;35(2):128–39.
- Furukawa A, Kanasaki S, Kono N, Wakamiya M, Tanaka T, Takahashi M et al. CT diagnosis of acute mesenteric ischemia from various causes. AJR Am J Roentgenol. 2009;192(2):408–16.
- Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818–29.
- Vincent JL, Moreno R, Willatts S, De Mendonca A, Bruining H, Reinhart CK et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med. 1996;22(7):707–710.
- Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analysis. https://www.ohri.ca/programs/clinical\_epidemiolog y/oxford.asp
- Higgins JPT, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.
- Wolfgang Viechtbauer. Conducting Meta-Analyses InRwith themetaforpackage. J Stat Softw. 2010;36(3):1.
- Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557–60.
- 21. R. A Language and Environment for Statistical Computing. Available at: https: //cran.r-project.org/doc/manuals/r-release/fullrefman.pdf
- 22. Li W, Liu M, Jin L, Feng H, Chen X, Zhang Z. Treatment outcomes in patients with acute thromboembolic occlusion of the superior mesenteric artery. J Cardiothorac Surg. 2024;19(1).
- Zhang Z, Wang D, Li G, Wang X, Wang Y, Li G, et al. Endovascular treatment for acute thromboembolic occlusion of the superior mesenteric artery and the outcome comparison between endovascular and open surgical treatments: A retrospective study. Biomed Res Int. 2017;2017:1–10.
- Arthurs ZM, Titus J, Bannazadeh M, Eagleton MJ, Srivastava S, Sarac TP, et al. A comparison of endovascular revascularization with traditional therapy for the treatment of acute mesenteric ischemia. J Vasc Surg. 2011;53(3):698–705.
- Acosta S, Block T, Bjornsson S, Resch T, Bjorck M, Nilsson T. Diagnostic pitfalls at admission in patients with acute superior mesenteric artery occlusion. J Emerg Med. 2012;42(6):635–41.
- Branco BC, Montero-Baker MF, Aziz H, Taylor Z, Mills JL. Endovascular therapy for acute mesenteric ischemia: an NSQIP analysis. Am Surg. 2015;81(11):1170–6.
- Arya S, Kingman S, Knepper JP, Eliason JL, Henke PK, Rectenwald JE. Open mesenteric interventions are equally safe as endovascular interventions and offer better midterm patency for chronic mesenteric ischemia. Ann Vasc Surg. 2016;30:219–26.
- Andraska EA, Tran LM, Haga LM, Mak AK, Madigan MC, Makaroun MS, et al. Contemporary management of acute and chronic mesenteric ischemia: 10-year experience from a multihospital healthcare system. J Vasc Surg. 2022;75(5):1624–1633 e8.
- 29. Tran LM, Andraska E, Haga L, Sridharan N, Chaer RA, Eslami MH. Hospitalbased delays to revascularization increase risk of postoperative mortality

and short bowel syndrome in acute mesenteric ischemia. J Vasc Surg. 2022;75(4):1323–e13333.

- Plumereau F, Mucci S, Le Naoures P, Finel JB, Hamy A. Acute mesenteric ischemia of arterial origin: importance of early revascularization. J Visc Surg. 2015;152(1):17–22.
- Lorenzo D, Barthet M, Serrero M, Beyer L, Berdah S, Birnbaum D, et al. Severe acute ischemic colitis: what is the place of endoscopy in the management strategy? Endosc Int Open. 2021;09(11):E1770–7.
- 32. Champagne BJ, Lee EC, Valerian B, Mulhotra N, Mehta M. Incidence of colonic ischemia after repair of ruptured abdominal aortic aneurysm with endograft. J Am Coll Surg. 2007;204(4):597–602.
- Murata T, Kawachi J, Igarashi Y, Suno Y, Nishida T, Miyake K et al. Monitoring the sequential organ failure assessment score in nonocclusive mesenteric ischemia increases the survival rate: A single-center observational study. Medicine. 2021;100(48):e28056.
- Yukaya T, Saeki H, Taketani K, Ando K, Ida S, Kimura Y, et al. Clinical outcomes and prognostic factors after surgery for Non-Occlusive mesenteric ischemia: a multicenter study. J Gastrointest Surg. 2014;18(9):1642–7.
- 35. Zargar I, Robanni I, Shah O, Gojwari T, Rasool R, Choh N et al. Imaging evaluation of mesenteric ischemia: is there a golden period for this entity? Galician Med J. 2022;29(1):E202212.
- Feuerstadt P, Gnanapandithan K, Aroniadis O, Mansoor S, Bhutta A, Silverman M et al. S0142 Antibiotics do not improve outcomes in colon ischemia (CI)

   Results from a large retrospective multi-center study. Am J Gastroenterol. 2020;115:S68.
- Yang S, Zhang L, Liu K, Fan X, Ding W, He C et al. Postoperative Catheter-Directed thrombolysis versus systemic anticoagulation for acute superior mesenteric venous thrombosis. Ann Vasc Surg. 2016;35:88–97.
- Mitsuyoshi A, Obama K, Shinkura N, Ito T, Zaima M. Survival in nonocclusive mesenteric ischemia: early diagnosis by multidetector row computed tomography and early treatment with continuous intravenous High-dose prostaglandin E1. Ann Surg. 2007;246(2):229–35.
- Winzer R, Fedders D, Backes M, Ittermann T, Gründling M, Mensel B, et al. Local Intra-arterial vasodilator infusion in Non-Occlusive mesenteric ischemia significantly increases survival rate. Cardiovasc Intervent Radiol. 2020;43(8):1148–55.
- Takiguchi T, Nakajima M, Ohbe H, Sasabuchi Y, Matsui H, Fushimi K et al. Vasodilator therapy and mortality in nonocclusive mesenteric ischemia: A nationwide observational study. Crit Care Med. 2020;48(5):e356–61.
- Takiguchi T, Nakajima M, Ohbe H, Sasabuchi Y, Tagami T, Kaszynski RH, et al. Association between postoperative adjuvant vasodilator therapy and In-Hospital mortality for Non-Occlusive mesenteric ischemia: A nationwide observational study. J Nippon Med Sch. 2024;91(3):316–21.
- Yang S, Guo J, Ni Q, Chen J, Guo X, Xue G, et al. Enteral nutrition improves clinical outcome and reduces costs of acute mesenteric ischaemia after recanalisation in the intensive care unit. Clin Nutr. 2019;38(1):398–406.
- Martini V, Lederer A, Fink J, Chikhladze S, Utzolino S, Fichtner-Feigl S, et al. Clinical characteristics and outcome of patients with acute mesenteric ischemia: a retrospective cohort analysis. Langenbecks Arch Surg. 2022;407(3):1225–32.
- Hatchimonji JS, Bakillah E, Kaufman EJ, Dowzicky PM, Braslow BM, Kalapatapu VR, et al. The open abdomen in mesenteric ischemia: A tool for patients undergoing revascularization. World J Surg. 2024;48(2):331–40.

- Elhady MAAA, Mohamed MK, Hafez M, Mahmoud MM. One-stage versus two-stage procedure for the surgical management of patients with acute mesenteric ischemia. Egypt J Surg. 2024;43(2):555–63.
- Awad S, Tarabay A, Negm A, Althobaiti W, Alorabi F, Dawoud I et al. Primary anastomosis versus diverting stoma as a management of intestinal vascular gangrene: a randomized controlled study. Egypt J Surg. 2021;40(1):73–82.
- Endo A, Saida F, Mochida Y, Kim S, Otomo Y, Nemoto D et al. Planned versus On-Demand relaparotomy strategy in initial surgery for Non-occlusive mesenteric ischemia. J Gastrointest Surg. 2021;25(7):1837–46.
- Brillantino A, Lanza M, Antropoli M, Amendola A, Squillante S, Bottino V et al. Usefulness of damage control approach in patients with limited acute mesenteric ischemia: a prospective study of 85 patients. Updates Surg. 2022;74(1):337–42.
- Ding W, Wang K, Liu B, Fan X, Wang S, Cao J et al. Open abdomen improves survival in patients with peritonitis secondary to acute superior mesenteric artery occlusion. J Clin Gastroenterol. 2017;51(9):e77–82.
- Bomberg H, Groesdonk HV, Raffel M, Minko P, Schmied W, Klingele M, et al. Vasopressin as therapy during nonocclusive mesenteric ischemia. Ann Thorac Surg. 2016;102(3):813–9.
- Elbahrawy K, El-Deeb A. Rectus sheath block for postoperative analgesia in patients with mesenteric vascular occlusion undergoing laparotomy: A randomized single-blinded study. Anesth Essays Res. 2016;10(3).
- Shi Y, Zhao B, Zhou Y, Chen L, Su H, Gu J. Endovascular revascularization vs open surgical revascularization as the first strategy for arterial acute mesenteric ischemia: A systematic review and meta-analysis. J Vasc Surg. 2024;80(6):1883–1893 e2.
- Warren AS, Murphy B, Saldana-Ruiz N, Dansey K, Zettervall SL. Open revascularization for acute mesenteric ischemia is associated with increased morbidity and mortality when compared to endovascular intervention. Ann Vasc Surg. 2025;111:386–92.
- 54. Qiu Y, Zhang Y, Wu Z, Yang Z, Zhu G, Miao S et al. Outcomes after open and endovascular treatment for mesenteric artery embolism patients: a retrospective inverse probability of treatment-weighted analysis. Eur J Trauma Emerg Surg. 2024;50(6):2883–93.
- Sindall ME, Davenport DL, Wallace P, Bernard AC. Validation of the American association for the surgery of trauma grading system for acute mesenteric ischemia-More than anatomic severity is needed to determine risk of mortality. J Trauma Acute Care Surg. 2020;88(5):671–6.
- Andraska E, Haga L, Li X, Avgerinos E, Singh M, Chaer R, et al. Retrograde open mesenteric stenting should be considered as the initial approach to acute mesenteric ischemia. J Vasc Surg. 2020;72(4):1260–8.
- Garzelli L, Dufay R, Tual A, Corcos O, Cazals-Hatem D, Vilgrain V et al. Predictors of survival without intestinal resection after First-Line endovascular revascularization in patients with acute arterial mesenteric ischemia. Radiology. 2024;311(3):e230830.

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