Ensimmäisen päivystyspisteen erikoisala vaikuttaa potilaan hoitotuloksiin akuutissa mesenteriaali-iskemiassa – lähetekäytäntöjen ja triagen tärkeys

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Tiivistelmä – Referat – Abstract

Tutkimuksen tarkoitus: Äkillinen suoliston verenkiertovajaus (akuutti mesenteriaali-iskemia (AMI)) on edelleen, kehittyneistä hoitomuodoista huolimatta, korkean kuolleisuuden tauti. Yksi olennainen hoidon tuloksiin vaikuttava tekijä on viive ensimmäisestä terveydenhuollon pisteestä leikkaukseen (leikkausviive), mutta tämän viiveen syyt ovat huonosti tunnettuja.
Tämän tutkimuksen tarkoitus oli etsiä viiveeseen vaikuttavia tekijöitä, erityisesti hoitoketjun osalta.

Aineisto ja menetelmät: Kyseessä on retrospektiivinen tutkimus, jossa tutkittiin 2006-2015 Meilahden sairaalassa leikattuja AMI-potilaita. Poissuljimme tutkimuksesta potilaat, joilla oli pitkäaikainen, puoliäkillinen, paksusuoleen rajoittunut, laskimoperäinen tai verisuonia tukkimaton mesenteriaali-iskemia. Potilaat jaettiin kahteen alaryhmään sen mukaan, oliko ensimmäinen terveydenhuollon piste, jonka he kohtasivat kirurginen päivystys (KP) vai ei-kirurginen päivystys (ei-KP). Ensisijainen päätemuuttuja oli leikkausviive ja toissijaiset päätemuuttujat olivat sairaalahoidon kesto ja 90-päivän kuolleisuus.

Tulokset: Lopullisessa tutkimuspotilasjoukossa oli 81 potilasta. Ei-KP ensimmäisenä hoitokontaktina oli itsenäisesti yhteydessä yli 12 tunnin leikkausviiveeseen (OR 3.7 (95% luottamusväli 1.3-10.2), mediaani viive 15.2 tuntia (IQR 10.9-21.2) vs. 10.1 tuntia (IQR 6.9-18.5), p = 0.025). Sairaalahoidon kesto oli lyhyempi (mediaani 6.5 päivää (4.0-10.3) vs. 10.8 päivää (7.0-22.3), p = 0.045) ja 90-päivän kuolleisuus matalampi KP-ryhmässä (50.0% vs. 74.5%, p = 0.025).

Johtopäätökset: Ensimmäinen erikoisala johon potilas lähetetään, vaikuttaa oleellisesti AMI-potilaan leikkausviiveeseen ja kuolleisuuteen. Hoitoketjun sujuvoittaminen niin, että potilas pääsee mahdollisimman nopeasti hoitoon vatsaelin- ja verisuonikirurgiseen yksikköön, voi parantaa AMI:n hoidon tuloksia.
(200 sanaa)

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The choice of first emergency room affects the fate of patients with acute mesenteric ischaemia – the importance of referral patterns and triage

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Abstract

Objectives: Despite modern advances in diagnosis and treatment, arterial acute mesenteric ischaemia (AMI) remains a disease of high mortality. One of the key modifiable factors in AMI is the first-door-to-operation delay, but the factors attributing to this delay are largely unknown. The aim of this study was to evaluate the factors affecting delay, with special focus on the pathways to treatment.

Design: This was a single academic centre retrospective study.

Materials and methods: Patients undergoing intervention due to AMI caused by thrombosis or embolism of superior mesenteric artery between 2006 and 2015 were identified from electronic patient records. Patients not eligible for intervention or with chronic, subacute onset, colonic only, venous, or non-occlusive mesenteric ischaemia were excluded. Patients were divided to two groups according to the first speciality examining the patient (surgical emergency room (SER), surgeon examining the patient first or non-surgical emergency room (non-SER), internist examining the patient first). The primary endpoint was first-door-to-operation delay and secondary endpoints were length of stay and 90-day mortality.

Results: Eighty-one patients with AMI were included. Fifty patients (62%) died during the first 30 days and 53 (65%) within 90 days. Presenting first in non-SER (vs. SER) was independently associated with a first-door-to-operation delay of over 12 hours (OR 3.7 (95% confidence interval 1.3-10.2), median delay 15.2 hours (IQR 10.9-21.2) vs. 10.1 hours (IQR 6.9-18.5), respectively, $p = 0.025$). The length of stay was shorter (median 6.5 days (4.0-10.3) vs. 10.8 days (7.0-22.3), $p = 0.045$) and 90-day mortality was lower in the SER group (50.0% vs. 74.5%, $p = 0.025$).

Conclusions: First specialty that the patient encounters seem to be crucial for both delay and early survival of AMI. Developing fast/direct pathways to a gastro-vascular unit offers a possibility to improve outcomes of AMI.

Keywords: embolus, thrombosis, delay, emergency, revascularization

Introduction

Acute mesenteric ischaemia (AMI) is a relatively uncommon abdominal emergency, accounting for about 1:1000 of acute hospital admissions in Europe and the USA, yet incidence increases dramatically with age.[1-4] AMI has historically been a disease in which diagnosis is difficult, if not impossible, treatment nearly futile, and mortality very high.[5-7] Patients present with a wide variety of symptoms and only about 1% of acute abdomen cases are caused by AMI, which makes it difficult to guide all patients immediately to the correct unit.[4] Computed tomography (CT) is today widely available in emergency rooms (ER) facilitating identification of anatomy consistent with a diagnosis of AMI.[8] Treatment of AMI has evolved from mere removal of necrotic material to revascularisation of the remaining bowel.[4,9]2 Mini-invasive revascularisation methods have emerged due to the technological development of endovascular treatment options.[4,10,11]2 Introduction of intestine stroke units with multimodal treatment options have improved both bowel and life outcomes.[12,13] Despite better results in selected revascularisation series, the total AMI mortality has remained very high, usually cited at 42–69 %.[4] In addition to the fact that AMI itself is highly deadly, patients presenting with AMI are usually elderly with several comorbidities.[4]

Much of the effort in the development of treatment strategies for AMI has recently focused on new endovascular treatments. Delays and pathways to treatment have gained much less attention, even though long delays are known to be a major contributing factor for outcome. Patients are often referred to a vascular centre too late, at the time of irreversible ischaemia. Potential reasons for long delays are a low level of suspicion, difficulties in diagnostics and operation room logistics.[14,15] The sensitivity of CT to identify the occlusion of superior mesenteric artery (SMA) in the initial radiologists report varies between 66-86%, and is significantly improved if suspicion of AMI is raised in the referral.[16]

Although delay is a key modifiable factor in the treatment of AMI, few studies have sought addressable targets to reduce it.

The aim of this study was to analyse the delays in the treatment of AMI and to seek out the factors related to this process. Identifying the key steps in the care pathway may lead to shorter delays and ultimately better patient outcomes. Specifically, the role of the first ER where the patient presented was examined.

Materials and methods

This retrospective cohort study was performed in an academic teaching hospital (Helsinki University Hospital) that functions as a tertiary and secondary referral centre covering a population of approximately 1.5 million. Helsinki University Hospital is the only hospital within the area that treats vascular emergencies, and thus all patients with AMI within the catchment area are instructed to be referred there. Open, endovascular, and hybrid revascularisation options are available at all times. Patients who were treated for AMI in Helsinki University Hospital in 2006-2015 were identified from electronic patient records by conducting a search for the International Classification of Diseases 10 (ICD-10) code K55 (Vascular disorders of intestine) or Nomesco Classification of Surgical Procedures (NCSP) codes for procedures on mesenteric vessels (PCE17, PCF16, PCF17, PCHXX, PCJ17, PCN16, PCN17, PCP16, PCP17, PCQ16, PCQ17, PCQ99). Appropriate permits to conduct the study were obtained from the institutional review board.

Definitions

Patients were classified based on the first ER and specialty where they presented. Generally, in Nordic countries, there are two types of ERs – surgical ERs have surgeons (or surgical residents) in the ER seeing the patient first. Non-surgical ERs have internists (or more recently emergency medicine doctors) seeing the patient first but may consult surgeon in deemed necessary.

In this study, surgical emergency room (SER) was defined as any ER (secondary or tertiary) where the patient was seen first by a surgeon (or surgical resident). Non-surgical emergency room (non-SER) was defined as an ER where the patient was first seen by either primary care doctor, internal medicine doctor or an emergency medicine physician. The training and experience of the staff in SER and non-SER is similar (both residents and attendings of respective specialities). SER and non-SER are located in the same premises in some of the hospitals, while in others they are located in different buildings.

In most hospitals, both primary care ER and secondary care ERs (either internal medicine or surgical ER, or both) work at the same premises, and an appointed triage nurse (by consulting an on-call physician if deemed necessary) decides to which specialty and level of care the patient is referred to first. If the patient presented to an ER with both surgical and internal medicine ER, the specialty which patient was referred to first determined whether the patient was classified to SER or non-SER group. The hospital, to which the patient is initially transported to, is decided by the paramedics (by consulting an on-call prehospital emergency physician if deemed necessary). Patients with acute abdomen are instructed to be referred to a SER. Vascular centre refers to Helsinki University Hospital, which is where all the patients were finally referred to.

Timestamps of first ER presentation, CT scan, CT report and arrival to vascular centre were extracted from electronic patient records. Time of diagnosis was the first time hospital notes mentioned AMI as the working diagnosis. Date of death was obtained from electronic patient records, which automatically updates the information from the Population Register Centre thus enabling to record mortality for all patients.

Charlson comorbidity index (CCI) was used to assess comorbidity of patients[17]. Quick Sepsis Related Organ Failure Assessment (qSOFA) was used to evaluate organ dysfunction at the time of the arrival at the vascular centre[18].

Patients

Patient records were analysed and data regarding patient characteristics, hospital stay, treatment, and outcome were manually extracted. Patients with no AMI (incorrect diagnosis code), no timestamp available, non-occlusive or venous ischaemia, bowel ischaemia caused by strangulation, trauma, or isolated coeliac trunk stenosis as well as ischaemia isolated to colon were excluded. Because the study aim was to analyse delays in the treatment of AMI, patients whose symptoms started in the hospital during treatment of another disease, who were not eligible for interventional treatment because of comorbidity or advanced age, who had a diagnosed chronic mesenteric ischaemia as well as patients with subacute onset of mesenteric ischaemia (defined as delay more than 48 hours from symptom outset to vascular centre) were excluded, in an effort to limit the study group to patients with an acute disease.

Statistics

All statistical analyses were done using IBM SPSS Statistics version 23 (IBM Corp©, Armonk, NY, USA). Mann-Whitney U or Chi-square tests were used in univariate analyses. Multivariate analysis was performed using logistic regression. Variables with $p < 0.2$ in univariate analysis were selected for multivariate analysis, except for variables which could be expected to cause multicollinearity. The primary endpoint was first-door-to-operation time, which was defined as the time from arrival at first ER to the onset of surgery. A two-tailed p-value below 0.05 was considered statistically significant.

Results

Patient characteristics and symptoms

A total of 474 patients were identified based on the initial diagnosis and procedural code search. After applying exclusion criteria, 81 patients remained for final analysis. Basic characteristics of the included patients are shown in Table 1. Briefly, the patients were elderly (median age 78 years) with an equal sex distribution. The majority (n=71, (88%) had some form of cardiovascular disease and roughly every third patient (n=29, 36%) had diabetes. More than half of the patients (n=46, 57%) had atrial fibrillation. Two thirds were independent, and 13 (16%) were institutionalised. Abdominal pain was the most common symptom (n=79, 98%), followed by vomiting/nausea (n=48, 59%) (Table 2). CT was performed on 18 (22%) patients in the first ER, and 14 (17%) of the CTs were performed with intravenous contrast. CT was performed on 53 (65%) patients at the tertiary vascular centre, and overall 69 (85%) patients underwent CT before intervention. The most common first working diagnosis was unspecified acute abdomen (n=28, 35%) (Table 2). At the presentation at vascular centre, abdominal guarding was present in 35 (43%) patients (Table 2). Diagnosis of AMI was made during laparotomy in 10 (12%) patients (Table 2).

Factors related to the delay

Factors associated with the delay were analysed in univariate analysis (Supplementary Table 1). The first-door-to-operation time was significantly shorter if the first medical centre was a surgical ER (10.1 hours versus 15.2 hours, p = 0.025), if AMI was correctly diagnosed in the first medical centre (median 9.3 hours versus 13.9 hours, p = 0.006), or if SMA occlusion was correctly identified in the CT (11.7 hours versus 18.0 hours, p = 0.005) (Supplementary Table 1).

In multivariate analysis, first medical centre being SER was independently associated with a shorter first-door-to-operation delay (Table 3).

Pathway to treatment

As the first ER was the strongest predictor of delay, pathways to treatment were examined in more detail. Of 81 patients, 51 presented first to non-SER, 14 to SER without vascular on-call and 16 to SER with vascular on-call (vascular centre). Of the 51 patients presenting first to non-SER, 8 (16%) were referred to SER without vascular on-call, while 43 (84%) patients were referred to SER with vascular on-call. Basic patient characteristics were similar regardless of whether patient presented to SER or non-SER initially (Table 1). There were no differences regarding aetiology (embolism vs. thrombosis), specific symptoms, or duration of symptoms between patients arriving first at SER or non-SER (Table 2). CT was more often obtained in the first ER if patient presented first to SER and the first working diagnosis was more often mesenteric ischaemia in SER (Table 2). The most common incorrect diagnoses in the SER group were ruptured abdominal aneurysm (n=6, 20%) and unspecified acute abdomen (n=3, 10%). In the non-SER group, the most common incorrect diagnoses were non-specific acute abdomen (n=25, 49%) and gastroenteritis (n=4, 8%) (Table 2). In patients with known atheroschlerosis (n=27), AMI was correctly suspected in nine (33%) patients. In patients with known atrial fibrillation (n=46), AMI was correctly suspected in 13 (28%) patients. (Table 2).

Upon arrival at the vascular centre, guarding and qSOFA-scores were similar regardless whether patients first presented to SER or non-SER (Table 2).

Details of the delays

The delays were compared in more detail between patients presenting first at SER versus non-SER. Door-to-CT, door-to-diagnosis, and door-to-operation times were all shorter in the SER group compared to the non-SER group (Table 2).

Primary operative treatment

Of the 81 patients, 4 (5%) underwent endovascular therapy only. Of those undergoing laparotomy (n = 77), extensive and unsalvageable bowel necrosis was found in 14 (18%) patients and due to poor prognosis, these patients underwent explorative laparotomy only. Of the rest of patients, 20 (26%) underwent bowel resection only, 15 (19%) underwent revascularisation without bowel resection and 28 (36%) underwent revascularisation followed by bowel resection (Table 4). The abdominal cavity was left open in 9 (12%) patients who were planned to undergo a second look laparotomy. Consultation of vascular surgeon was mentioned in thirteen patients' (65%) records of the twenty patients who underwent bowel resection only.

There were no significant differences in the choice of operative treatment between the SER and non-SER groups, including the number of futile explorative laparotomies (Table 4).

Outcomes

Median follow-up time was 1.3 weeks (IQR 0.2-59.4), much due to the high mortality. Fifty patients (62%) died during the first 30 days and 53 (65%) during the first 90 days. While there were no significant differences in rate of intensive care unit (ICU) admission or ICU stay, shorter hospital stay (median 6.5 days (4.0-10.3) vs. 10.8 days (7.0-22.3), p = 0.045), as well as lower 90-day mortality (50% vs. 75%) were noted in the SER group compared to the non-SER group (Table 4). Factors associated with 90-day mortality in univariate analyses and multivariate analysis were non-SER as the first ER (OR 3.2), no antithrombotic medication at presentation (OR 4.8), patients' dependency (OR 6.9), and qSOFA > 0 on arrival to the vascular centre (OR 4.7) (Supplemenatry Table 2, Table 3).

Discussion

In this study, the most important prognostic factor of the patients with AMI was the type of ER the patients were examined first. Patients examined first in a surgical ER had shorter first-door-to-operation times (10 versus 15 hours), shorter hospital stays (7 versus 11 days) and lower 90-day mortality rate (50% versus 75%) compared to being examined first in a non-surgical ER. Although selected in retrospect the two groups were similar in regards to medical history, clinical presentation, final diagnosis (embolic vs thrombotic) and selected treatment, suggesting that there is an element of chance that has an effect on the choice of the initial ER and outcome. We should therefore target an educational effort to triage-nurses and paramedics in order to minimise the false referrals.

Various studies have stressed the need for more efficient diagnostics and shorter delays in the treatment of AMI.[3,14,19] Previous studies have shown that clinical suspicion and CT imagining are crucial components of delay.[14-16] The study of Lehtimäki et al. also found that radiological detection of AMI in CT is improved if the clinician suspects the diagnosis.[16] In our study, we found both clinical suspicion and CT imagining to be related to the status of the first medical centre. It is widely recommended that patients with a suspicion of AMI should be imaged with adequately timed CT angiography.[3,4,20] Our material was too small to detect a difference between contrast enhanced and native CT.

Our mortality rates (51% in SER group and 72% in non-SER group) did not differ significantly from previously published mortality figures of 42-69%.[11,21-24] Lower rates of mortality for AMI have been presented[25] but the mortality figures are significantly influenced by a selection bias, when only revascularized patients are reported. In order to focus specifically on AMI and avoid cases with subacute onset, we excluded the patients with a prolonged referral (more than 48h) and in-hospital initiated symptoms, a decision that led to a smaller, but more homogenous patient group with acute and severe AMI. Also our material includes specifically only arterial AMI, whereas patients with venous mesenteric ischaemia were excluded as they have more favourable prognosis and different delay pattern.[26-29]

Some studies have shown mortality to increase with the lengthening of first-door-to-operation time.[15,30,31] We did not detect this in our material (Supplementary Table 2), which we believe to be due to the inevitable remainder of heterogeneity of our patient sample despite efforts to homogenize the cohort. Another reason might be the fact that patients with more serious symptoms travel through the system faster. These patients are usually the ones with a more severe disease and hence have a higher mortality. The patients with less severe disease often have less serious symptoms thus it may take more time to proceed to operation. These patients might be able to tolerate longer delays, possibly due to the extent and anatomy of the obstruction (partial vs total, proximal vs more distal), among other things. We believe this disparity of patients to be a possible explanation to the lack of correlation between delay and outcome. As a matter of fact, another report from Sweden did not find correlation between survival and delay from onset of symptoms to operation.[11] We made an effort to further subgroup the occlusions in regards to number of side branches prior to the occlusion, length of occlusion etc, but the number of contrast enhanced CT:s remained too small to make any conclusions. In order to be able to achieve fast track diagnosis and revascularisation, these patients need to be identified from a large cohort with more or less unspecific symptoms. A high level of suspicion and a low threshold for contrast enhanced CT imaging should be practiced.[20] The fear of acute kidney injury should not prevent proper diagnostics for this deadly disease, especially as the nephrotoxicity of contrast media has been questioned.[32] Once the diagnosis is suspected and confirmed, immediate treatment should be undertaken. The vascular surgeons choose the method of revascularisation and should be capable of performing all forms of interventions either by themselves or together with endovascular operators. There is suggestive information in the literature that endovascular treatment should be favoured, but all comparative studies suffer from selection bias.[4,33] Therefore, the level of evidence is low, and the choice of treatment must ultimately be made on an individual basis.

Antithrombotic medication at presentation and patients with a good functional status had a better outcome, while qSOFA > 0 was associated with a higher mortality (Table 4). Because this is a retrospective analysis we are not able to show a clear causation, but we hypothesise that antithrombotic medication might inhibit progression of the thrombotic cascade and thus limit the severity of the event.

A good functional status predicted a better outcome, which might be due to less comorbidity and hence lower risks of organ failure. It might also be that more aggressive treatment was pursued in this patient group.

qSOFA is used as a bedside estimate to identify patients with suspected infection that would benefit from ICU treatment. It consists of an evaluation of Glascow Coma Scale, respiratory rate and systolic blood pressure. Deterioration of these values can, in addition to infection, be a sign of more extensive disturbance of vital functions and bowel ischaemia, which would explain why a higher qSOFA was associated with a higher mortality.

This study has several limitations. As a retrospective study there is an inherent risk of information bias and misclassifications. By identifying and excluding clearly different patient groups we made an effort to make the material more homogenous and focus on acute and severe AMI. Despite this, the pattern of the disease remains variable and limits the conclusions that can be drawn from the material. Focusing on arterial AMI made the study groups smaller and poses challenges on the statistical analysis. On the other hand, the strength of this paper is the population-based study design that diminishes selection bias.

In order to improve the outcomes of AMI, the first-door-to-operation times need to be shortened. One of our main findings was that these patients fare better if they present directly to units with surgical expertise. The awareness of paramedical units and ER personnel performing triage should be improved. The referral patterns need to be improved and all suspected AMI patients should find their way without delay to a unit performing revascularisations, either dedicated intestine stroke centres or as in our situation centralised on-call units with possibilities for multidisciplinary treatment at all times.[12,13] Our results highlight the fact that these units should also take a role in the education and design of the whole treatment chain starting from first responders. Future studies should try to identify simple clinical combinations of symptoms that could guide the triage and improve outcome of AMI patients.

Acknowledgments

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Table 1. Basic demographics based on first emergency room (surgical or non-surgical).

	All n=81 n (%)	Surgical ER n = 30 n (%)	Non-surgical ER n = 51 n (%)	p
Age, years, median (IQR)	78.0 (69.0-85.0)	81.0 (65.3-84.0)	77.0 (70.0-85.0)	0.512
Sex, female	39 (48.1%)	15 (50.0%)	24 (47.1%)	0.798
Comorbidities				
Hypertension	50 (61.7%)	16 (53.5%)	34 (66.7%)	0.233
Atrial fibrillation	46 (56.8%)	16 (53.5%)	30 (58.8%)	0.630
Atherosclerosis	27 (33.3%)	9 (30.0%)	18 (35.3%)	0.625
Coronary artery disease	33 (40.7%)	12 (40.0%)	21 (41.2%)	0.917
Cerebrovascular disease (stroke / TIA)	15 (18.5%)	4 (13.3%)	11 (21.5%)	0.631
History of thromboembolism	5 (6.2%)	2 (6.7%)	3 (5.9%)	0.887
Diabetes				0.858
with complications	4 (4.9%)	1 (3.3%)	3 (5.9%)	
without complications	25 (30.9%)	9 (30.0%)	16 (31.4%)	
No cardiovascular diseases	10 (12.3%)	2 (6.7%)	8 (15.7%)	0.233
Charlson comorbidity index				0.996
0	1 (1.2%)	0 (0%)	1 (2.0%)	
1-2	19 (23.5%)	7 (23.4%)	12 (23.6%)	
3-4	25 (30.8%)	10 (33.4%)	15 (29.4%)	
> 4	36 (44.4%)	13 (43.3%)	23 (45.1%)	
ASA				0.601
1-2	1 (1.2%)	0 (0%)	1 (2.0%)	
3-4	49 (60.5%)	17 (56.7%)	32 (62.8%)	
5	27 (33.3%)	11 (36.7%)	16 (31.4%)	
Medication				
Anticoagulation*	20 (24.7%)	5 (16.7%)	15 (29.4%)	0.145
Antithrombotic#	43 (53.1%)	18 (60.0%)	25 (49.0%)	0.431
Statin	33 (40.7%)	11 (36.7%)	22 (43.1%)	0.602
Functional status				0.633
Independent	57 (70.4%)	21 (70.0%)	36 (70.6%)	
Partially dependent	11 (13.6%)	3 (10.0%)	8 (15.7%)	
Institutionalized	13 (16.0%)	6 (20.0%)	7 (13.7%)	

Abbreviations: ER – emergency room, IQR – interquartile range, TIA – transient ischemic attack, ASA – American Society of Anaesthesiologists physical status classification. *warfarin, direct oral anticoagulant, low molecular weight heparin; #acetylsalicylic acid, dipyridamol, or clopidogrel

Table 2. Symptoms, imaging, clinical presentation and delays based on first emergency room (surgical or non-surgical).

	All **n = 81** **n (%)**	**Surgical ER** n=30 n (%)	**Non-surgical ER** n=51 n (%)	*p*
Symptoms				
Abdominal pain	79 (97.5%)	30 (100.0%)	49 (96.1%)	0.272
Diarrhoea	36 (44.4%)	13 (43.4%)	23 (45.1%)	0.877
Haematochezia	15 (18.5%)	5 (16.7%)	10 (19.6%)	0.742
Vomiting / nausea	48 (59.3%)	16 (53.3%)	32 (62.7%)	0.405
Duration > 24h	19 (23.5%)	9 (30.0%)	10 (19.6%)	0.441
Imaging (in first ER)				
No imaging	37 (45.7%)	3 (10.0%)	34 (66.7%)	<0.001
Abdominal plain x-ray	14 (17.3%)	3 (10.0%)	11 (21.6%)	0.184
Computed tomography (any)	18 (22.2%)	13 (43.3%)	5 (9.8%)	0.001
with contrast	14 (17.3%)	10 (33.3%)	4 (7.8%)	0.003
without contrast	4 (4.9%)	3 (10.0%)	1 (2.0%)	0.107
First working diagnosis				<0.001
AMI	23 (28.4%)	15 (50.0%)	8 (15.7%)	
Acute abdomen, not specified	28 (34.6%)	3 (10.0%)	25 (49.0%)	
Intra-abdominal infection	5 (6.2%)	2 (6.7%)	3 (5.9%)	
Ileus	4 (4.9%)	1 (3.3%)	3 (5.9%)	
Gastrointestinal bleeding	3 (3.7%)	0 (0%)	3 (5.9%)	
Gastroenteritis / colitis	5 (6.2%)	1 (3.3%)	4 (7.9%)	
Ruptured aortic aneurysm	6 (7.4%)	6 (20.0%)	0 (0%)	
Acute coronary syndrome	2 (2.5%)	1 (3.3%)	1 (2.0%)	
Decreased general condition	2 (2.5%)	0 (0%)	2 (3.9%)	
Other*	3 (3.7%)	1 (3.3%)	2 (3.9%)	
Correct working diagnosis in patients with atherosclerosis, n=27	9 (33.3%)	6 (66.7%), n=9	3 (16.7%), n=18	0.051
Correct working diagnosis in patients with atrial fibrillation, n=46	13 (28.3%)	7 (43.8%), n=16	6 (20.0%), n=30	0.171
Clinical presentation at vascular centre				
Guarding	35 (43.2%)	9 (30.0%)	26 (51.0%)	0.066
qSOFA				0.494
0	28 (34.6%)	12 (40.0%)	16 (31.4%)	
1	37 (45.7%)	14 (46.7%)	23 (45.1%)	
2	13 (16.0%)	4 (13.3%)	9 (17.6%)	
3	3 (3.7%)	0 (0%)	3 (5.9%)	
CRP, mg/L (median, IQR)	73 (18-193)	93 (11-195)	71 (18-163)	0.825
Creatinine, mol/L (median, IQR)	103 (65-137)	95 (66-153)	105 (64-135)	1.000

Lactate, mmol/L (median, IQR)	2.9 (1.9-5.2)	2.5 (1.8-4.5)	3.1 (1.9-7.5)	0.219
Imaging at vascular centre				
Computed tomography (any)	53 (65.4%)	17 (56.7%)	36 (70.6%)	0.203
with contrast	32 (39.5%)	5 (16.7%)	20 (39.2%)	0.944
without contrast	21 (25.9%)	12 (14.8%)	16 (31.4%)	0.145
Mesenteric ischaemia diagnosis made in laparotomy	10 (12.3%)	3 (10.0%)	7 (13.7%)	0.623
Aetiology				0.195
Embolism	41 (50.6%)	18 (60.0%)	23 (45.1%)	
Thrombosis	40 (49.4%)	12 (40.0%)	28 (54.9%)	
Delay, hours, median (IQR)				
Door-to-CT (n=79)	5.5 (2.7-10.6)	2.7 (1.8-4.9)	8.4 (4.3-12.1)	<0.001
Door-to-surgical ER (n=51)	**n/a**	**n/a**	3.5 (2.4-7.1)	**n/a**
Door-to-diagnosis (n=77)	6.5 (2.8-12.9)	3.1 (0.8-6.8)	10.0 (5.1-15.9)	<0.001
CT-to-operation (n=79)	5.5 (3.4-9.0)	6.0 (3.6-16.5)	5.3 (3.4-8.8)	0.275
Door-to-operation (n=81)	12.6 (9.2-19.7)	10.1 (6.9-18.5)	15.2 (10.9-21.2)	0.025

Abbreviations: AMI – acute mesenteric ischaemia, CRP – C-reactive protein, IQR – interquartile range, qSOFA – quick sepsis related organ failure assessment. *(intra-abdominal infection, perforation)

Table 3. Multivariate analysis on parameters affecting first-door-to-operation delay and 90-day mortality.

	First-door-to-operation delay > 12h OR (95% confidence interval)	90-day mortality OR (95% confidence interval)
First ER Surgical Non-surgical	 reference 3.7 (1.3-10.2)	 reference 3.2 (1.03 - 9.6)
No antithrombotic medication at presentation		4.8 (1.45 – 15.9)
Dependent		6.9 (1.63 – 29.1)
qSOFA > 0 on arrival to vascular centre		4.7 (1.5 - 14.3)

Abbreviations: ER – emergency room, OR – odds ratio, qSOFA – quick sepsis related organ failure assessment.
Parameters in Suppmentary Table 1 with p < 0.2 were selected for multivariate logistic regression for door-to-operation delay > 12h, except for variable "mesenteric ischaemia suspected before CT" to avoid collinearity.

Parameters in Supplementary Table 2 with p < 0.2 were selected for multivariate logistic regression for 90-day mortality, except for variable "mesenteric ischaemia suspected before CT" to avoid collinearity.

Table 4. Primary intervention and outcomes, based on whether first ER was surgical or not.

	All **n=81** **n (%)**	**Surgical ER** **n = 30** **n (%)**	**Non-surgical ER** **n = 51** **n (%)**	***p***
Primary intervention				
Endovascular treatment only	4 (4.9%)	2 (6.7%)	2 (3.9%)	0.582
Laparotomy, only exploration	14 (17.3%)	3 (10.0%)	11 (21.6%)	0.184
Laparotomy, only bowel resection	20 (24.7%)	4 (13.3%)	16 (31.4%)	0.069
Laparotomy, only vascular procedure	15 (18.5%)	7 (23.3%)	8 (15.7%)	0.392
Embolectomy	13 (16.0%)	5 (16.7%)	8 (15.7%)	
Bypass	2 (2.5%)	2 (6.7%)	0 (0%)	
Endarterectomy	0 (0%)	0 (0%)	0 (0%)	
Endovascular therapy	0 (0%)	0 (0%)	0 (0%)	
Laparotomy, bowel resection and vascular procedure	28 (34.6%)	14 (46.7%)	14 (27.5%)	0.079
Embolectomy	14 (17.3%)	6 (20.0%)	8 (15.7%)	
Bypass	10 (12.3%)	4 (13.3%)	6 (11.8%)	
Endarterectomy	1 (1.2%)	1 (3.3%)	0 (0%)	
Endovascular therapy#	3 (3.7%)	3 (10.0%)	0 (0%)	
Irreversible bowel ischaemia	62 (76.5%)	21 (70.0%)	41 (80.4%)	0.286
Open abdomen	9 (11.1%)	6 (20.0%)	3 (5.9%)	0.149
ICU admission	29 (35.8%)	10 (33.3%)	19 (37.3%)	0.722
ICU-free days*, median (IQR)	5 (1-24)	12 (1-26)	4 (0-24)	0.189
Length of ICU admission within 28 days, days, median (IQR)	5.0 (2.8-7.3)	5.0 (3.8-6.3)	4.0 (2.0-8.0)	0.363
Length of hospital stay, days, median (IQR)	8.8 (5.9-15.5)	6.5 (4.0-10.3)	10.8 (7.0-22.3)	0.045
30-day mortality	50 (61.7%)	15 (50.0%)	35 (68.6%)	0.096
90-day mortality	53 (65.4%)	15 (50.0%)	38 (74.5%)	0.025

Abbreviations: ASA – American Society of Anaesthesiologists physical status classification, ICU – intensive care unit, IQR – interquartile range. *Days in which patient was not in ICU and alive within 28 days from intervention #endovascular therapy was performed via groin puncture prior laparotomy

Supplementary Table 1. Univarite analysis on parameters affecting door-to-operation delay.

	Door-to-operation delay (h), median (IQR)	Door-to-operation delay (h), median (IQR)	*P value*
Sex (female/male)	16.2 (10.2-21.2) n=39	11.4 (8.7-17.6) n=42	0.255
Age (<65/>65)	9.9 (6.8-15.9) n=15	13.6 (9.5-21.0) n=66	0.102
Cardiovascular disease (yes/no)	12.0 (9.1-19.4) n=71	16.6 (10.9-24.0) n=10	0.389
Diabetes (yes/no)	12.8 (9.2-19.7) n=29	12.6 (8.1-20.7) n=52	0.972
Atrial fibrillation (yes/no)	11.6 (7.2-19.7) n=46	15.2 (10.2-20.0) n=35	0.275
Previous thromboembolism (yes/no)	12.6 (8.5-25.3) n=5	12.7 (9.2-19.9) n=76	0.992
Independent (yes/no)	13.9 (8.4-24.7) n=57	11.8 (9.9-17.1) n=24	0.203
qSOFA (0/other)	11.2 (7.3-20.6) n=28	13.9 (9.6-19.6) n=53	0.427
Defance (yes/no)	12.0 (9.3-20.0) n=35	13.0 (7.6-19.8) n=46	0.901
CRP (>100/<100)	12.6 (9.2-22.2) n=32	13.6 (9.6-19.2) n=46	0.835
First ER (SER/non-SER)	10.1 (6.9-18.5) n=30	15.2 (10.9-21.2) n=51	0.025
First working diagnosis mesenteric ischaemia (yes/no)	9.3 (6.2-18.2) n=23	13.9 (10.5-21.5) n=58	0.006
Mesenteric ischaemia suspected before CT (yes/no)	10.4 (6.2-19.4) n=19	14.5 (10.0-21.1) n=56	0.055
CT (yes/no)	12.7 (9.5-20.3) n=74	9.1 (5.8-19.2) n=7	0.282
CT with contrast (yes/no)	12.8 (7.6-20.0) n=47	12.4 (9.6-19.7) n=34	0.920
CT in first ER (yes/no)	10.5 (7.2-18.3) n=24	14.0 (9.6-21.1) n=57	0.104
Mesenteric ischaemia identified on CT (yes/no)	11.7 (7.5-18.5) n=54	18.0 (11.9-27.6) n=21	0.005

Distance to vascular centre (under 10km/over 10km)	12.6 (7.4-18.9) n=45	12.6 (9.6-20.8) n=36	0.652
Aetiology (thrombosis/embolism)	12.8 (10.1-19.2) n=40	11.6 (7.0-21.9) n=41	0.427

Supplementary Table 2. Univariate analysis on parameters affecting 90-day mortality.

	90-day mortality, n(%)	90-day mortality, n(%)	*Univariate p-value*
Sex (female/male)	29 (74.4%), n=39	24 (57.1%), n=42	0.104
Age (<65/>65)	7 (46.7%), n=15	46 (69.7%), n=66	0.090
Atherosclerosis (yes/no)	18 (66.7%), n=27	35 (64.8%), n=54	0.869
Diabetes (yes/no)	19 (65.5%), n=29	34 (65.4%), n=52	0.990
Atrial fibrillation (yes/no)	32 (69.6%), n=46	21 (60.0%), n=35	0.370
Previous thromboembolism (yes/no)	2 (40.0%), n=5	51 (67.1%), n=76	0.217
Anticoagulation (yes/no)	14 (66.7%), n=21	39 (65.0%), n=60	0.890
Antithrombotic medication (yes/no)	24 (54.5%), n=44	29 (78.4%), n=37	0.025
Independency (independent/no)	33 (57.9%), n=57	20 (83.3%), n=24	0.028
qSOFA (0/other)	12 (42.9%), n=28	41 (77.4%), n=53	0.002
Defance (yes/no)	22 (62.9%), n=35	31 (67.4%), n=46	0.671
First ER (SER/non-SER)	15 (50.0%), n=30	38 (74.5%), n=51	0.025
First working diagnosis mesenteric ischaemia (yes/no)	15 (65.2%), n=23	38 (65.5%), n=58	0.980
Mesenteric ischaemia suspected before CT (yes/no)	14 (73.7%), n=19	35 (62.5%), n=56	0.376
CT in first ER (yes/no)	15 (62.5%), n=24	38 (66.7%), n=57	0.719
CT (yes/no)	48 (64.9%), n=74	5 (71.4%), n=7	0.727
CT with contrast (yes/no)	28 (59.6%),	25 (73.5%),	0.192

	n=47	n=34	
Mesenteric ischaemia identified on CT (yes/no)	33 (61.1%), n=54	16 (76.2%), n=21	0.218
Distance to vascular centre (under 10km/over 10km)	29 (64.4%) n=45	24 (66.7%) n=36	0.834
Aetiology (thrombosis/embolism)	26 (65.0%), n=40	27 (65.9%), n=41	0.936
Delay (under 12h/over 12h)	24 (64.9%), n=37	29 (65.9%), n=44	0.922

Abbreviations: CT – computed tomography, OR – odds ratio, SER – surgical emergency room, non-SER – non-surgical emergency room.