Acute Mesenteric Ischemia in the Elderly Patient

18

Luís Filipe Pinheiro, Henrique Alexandrino, and Beatriz Costa

18.1 Introduction

In 1961, Cokkinis stated that "occlusion of the mesenteric vessels is regarded as one of those conditions in which the diagnosis is impossible, the prognosis hopeless, and the treatment almost useless" [1].

These words reflect the sense of helplessness most surgeons feel in the treatment of acute mesenteric ischemia (AMI), a disease with an increasing incidence [2], accounting for 0.1–0.2% of urgent hospital admissions [3] and 18% of emergency laparotomies [4]. In fact, despite all the advances in diagnosis and treatment in recent years, AMI remains a morbid condition with high short-term mortality rate, ranging from 60 to 80%, and represents one of the most frequent etiologies of short bowel syndrome and chronic intestinal failure [2, 5, 6]. Although no large population-based data have been published, a study from a secondary hospital serving a stable population demonstrated that the incidence of AMI increases drastically from the age of 75 and upward, surpassing the incidence of another seemingly more common acute abdominal emergency, acute appendicitis [7].

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L. F. Pinheiro (✉)
Serviço de Cirurgia Geral, Centro Hospitalar Tondela-Viseu, Viseu, Portugal

H. Alexandrino · B. Costa
Faculty of Medicine, University of Coimbra, Coimbra, Portugal

Coimbra University Hospital Center, Coimbra, Portugal

Coimbra Institute for Clinical and Biomedical Research (iCBR) area of Environment Genetics and Oncobiology (CIMAGO), Faculty of Medicine, University of Coimbra, Coimbra, Portugal

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In 1967 in an autopsy series, Ottinger and Austen reported a rate of 8.8 cases of AMI per 10,000 hospital admission [8]. Almost 30 years later, Stoney and Cunningham observed an incidence rate of 1 in 1000 hospital admissions [9]. As the mean age of the population increases and the proportion of older patients in our hospitals grows, AMI will predictably be more common. Unfortunately, as reported in many series, the mortality rate in older patients is significantly greater and carries a relative risk of the mortality rate of 3.0 for those more than the age of 60 years.

Two main determinants of the prognosis of AMI are precocity of diagnosis, before the development of irreversible intestinal damage, and celerity and adequacy of the treatment [2, 10]. These are hampered by the absence of accurate clinical and laboratory diagnostic criteria in the initial phase of evolution and the difficulty of rapid integration and coordination of the distinct therapeutic modalities. Pathogenesis of AMI, affected splanchnic vessel(s), location of the obstruction, degree and the extent of ischemia, and segment of intestine involved are additional prognostic parameters [11].

Clinical presentation of AMI is usually nonspecific at the initial stages and, therefore, early recognition must rely on a high degree of clinical suspicion and an immediate confirmation by an abdominal computed tomography (CT) angiography, to identify signs of splanchno-mesenteric ischemia and intestinal injury [3, 12–14]. Nevertheless, selection of patients requiring CT angiography remains challenging. In fact, although D-lactate, ischemia modified albumin, intestinal fatty acid binding protein (I-FABP), α-glutathione S-transferase, and other biomarkers are considered promising, there is still lack of a specific biomarker to indicate early mesenteric hypoperfusion in the routine clinical practice [15–18].

Duration of evolution, referral patterns, and triage are important prognostic factors. Prolonged symptoms duration (more than 24 h) was an independent predictor of mortality following surgical interventions for AMI [19]. Mortality was reduced if intervention was performed within 12 h of evolution [12]. Presenting first in a non-surgical emergency room was independently associated with a first door to operation time superior to 12 h, while initial evaluation in a surgical emergency service was associated with a lower 90-days mortality rate and length of stay [20]. This emphasizes the critical role of the emergency surgeon in the initial management of the patient with acute abdominal pain.

This chapter reviews the presentation, diagnosis, and treatment of the four most common causes of AMI: arterial embolism (AE), arterial thrombosis (AT), mesenteric venous thrombosis (MVT), and nonocclusive mesenteric ischemia (NOMI). Although mesenteric vascular disease is more common, albeit not exclusive, of old age, in this chapter we will place focus mainly on particular aspects related to the elderly patient.

Diagnosis of AMI can be challenging but must be recognized early and treated aggressively in order to improve patient survival. However, access to the best care, according to the state of the art, is not universal. For this reason, we also propose an algorithm to treat these patients when full resources are not available. This may prove particularly useful for the emergency surgeon working without full access to endovascular therapy or vascular surgery consultation in a reasonable time frame.

18.2 Definitions, Epidemiology, and Risk Factors

Acute mesenteric vascular diseases are usually considered a rare cause of acute abdomen, with an estimated incidence of 4.5–5.4 cases per 100.000 person-years. However, its incidence may be underestimated, with population-based studies reporting that in patients over 75-years old, its incidence is larger than that of acute appendicitis and 1.5 times more frequent than ruptured abdominal aortic aneurysm [1].

AMI can be classified into four etiological classes [2], namely:

1. Acute embolic mesenteric ischemia (AEMI)
2. Acute thrombotic mesenteric ischemia (ATMI)
3. Venous thrombotic mesenteric ischemia (VTMI)
4. Nonocclusive mesenteric ischemia (NOMI)

These vary in incidence, risk factors, and clinical presentation.

AEMI is characterized by a sudden occlusion of a main visceral artery by a clot, usually embolized from a cardiac source. The superior mesenteric artery (SMA) is the most commonly implicated vessel, probably because of its relatively acute take-off angle from the aorta (unlike the celiac artery) and larger ostium, favoring embolic occlusion [3]. This causes immediate ischemia of a large portion of the embryologically derived midgut, i.e., the jejunum, ileum, and right colon up to the mid transverse colon. However, since an embolus may lodge distally, some sparing of the first branches of the SMA may occur, leaving the proximal jejunum and right colon unaffected [4]. Risk factors for AEMI include atrial fibrillation, valvular heart disease, prosthetic valve, and ventricular aneurysm, diseases highly prevalent in elderly patients. In fact, in developed nations the prevalence of atrial fibrillation is estimated to increase from 6% at the ages of 65–74 to 15% in the population over 75-years old [5].

ATMI can occur in cases of previous chronic atherosclerotic occlusion of visceral arteries, again usually the SMA. In such cases, and similarly to other chronic stenosis in other vascular beds such as the myocardium or the lower limbs, anginal crisis may occur with increased oxygen consumption. Plaque rupture would be a precipitating event, causing sudden-onset occlusion of the vessel and end-organ ischemia, similarly to what occurs in acute myocardial infarction or acute thrombotic occlusion in patients with preexisting peripheral vascular disease. However, since atherosclerosis is frequent at the SMA take-off from the aorta, ATMI will likely affect the entire midgut. Risk factors for ATMI include those usually associated with atherosclerosis, namely adiposity, hypertension, dyslipidemia, and diabetes mellitus, again highly prevalent with increasing age [6].

VTMI consists of venous thrombosis in the portal venous system extending into the superior mesenteric vein. This will cause venous and capillary congestion of the midgut and subsequent mucosal and transmural necrosis. Risk factors can be divided into local or systemic, which may coexist. Local factors include cirrhosis (with portal hypertension and slowed or even reversed splanchnic venous flow),

pancreatitis, abdominal surgery (including bariatric surgery), or malignancies [7, 8]. Systemic factors mostly relate to hypercoagulability disorders, either congenital (protein C or S deficiency, factor V Leiden mutation) or acquired (neoplasia, cirrhosis, antiphospholipid syndrome) [2]. Since the progression of ischemia is much slower, so is clinical presentation. Of the four classes of AMI, VTMI is the one with clinical presentation at an earlier age and thus might be rarer and clinically less relevant in elderly patients, when compared with the other classes.

NOMI is a particular subset of AMI in which no mechanical obstacle to visceral arterial flow occurs. Instead, an exacerbated response of visceral small arteries and arterioles to vasoconstrictive stimuli occurs, causing small bowel mucosa ischemia. This can be considered the pathological extreme of the physiologic splanchnic vasoconstriction occurring in systemic hypoperfusion (e.g., in hypovolemic, cardiogenic, or distributive shock), in which visceral blood flow is reduced to preserve oxygenation of critical vascular beds. In NOMI, this response is considered pathological and might initiate a self-feeding loop of gut hypoperfusion. Mucosal ischemia and necrosis cause the release of damage-associated molecular patterns (DAMPs) and translocated bacteria into the mesenteric lymph, inducing a knee-jerk immunoinflammatory response and its systemic consequences, namely aggravated circulatory derangement, which in turn further aggravates bowel hypoperfusion. Patients with NOMI are typically admitted to general, cardiovascular, or surgical intensive care units (ICUs), under vasopressor or digitalis treatment [9]. Patients undergoing on-pump cardiac surgery have an incidence of 5%, increasing the risk with advanced age, depressed renal function, longer operative times, and longer cardiopulmonary bypass time [10]. Enteral nutrition is a common precipitating factor, possibly causing a mismatch between oxygen supply and demand of the bowel mucosa [11]. Given the increasing age of patients admitted to ICUs or undergoing cardiovascular surgery, NOMI is a frequent and likely underdiagnosed clinical condition in elderly patients.

18.3 Diagnosis

Early diagnosis of AMI, in any of its different forms, is universally recognized as the critical prognostic factor, being able to dramatically improve outcomes [19, 21]. The main difficulty lies on the lack of specificity of clinical presentation, as well as on the early recognition of patients at risk (Table 18.1). This is particularly relevant in the geriatric patient, as it is known that the incidence of AMI is likely ten-fold higher in 80-year olds than in 60-year olds [24]. Thus, in the lack of specific clinical or laboratory markers, strong clinical suspicion, i.e., an elderly patient with acute abdominal pain, should prompt the performance of computed tomography angiography. However, in clinical practice, delayed presentation of AMI, usually with established bowel necrosis, is commonplace. This requires a thorough discussion of the most relevant aspects in the diagnosis of AMI: clinical findings, laboratory markers and, most importantly, early imaging. In fact, the key issue in early diagnosis is a strong clinical suspicion [8].

Table 18.1 Clinical presentation and risk factors for the four distinct types of acute mesenteric ischemia. Adapted from [19, 22, 23]

Ethiology	Risk factors	Symptoms	Presentation
Embolic (AE)	Myocardial infarction Atrial fibrillation Prior embolism Congestive heart failure Ventricular aneurysm Recent cardiac surgery	Sudden abdominal pain Hematochezia Diarrhea Vomiting	Peritonitis Hypotension Nausea/vomiting Distention Tachycardia
Thrombotic (AT)	Abdominal angina Coronary artery disease Smokers Prolonged hypotension Estrogen hypercoagulability	Progressive abdominal pain Nausea/vomiting	Pain out of proportion Insidious onset Tachycardia Peritonitis Hypotension
Venous (VT)	Recent abdominal surgery Hypercoagulable state estrogens Polycythemia Sickle cell disease malignancy Pancreatitis	Asymptomatic Vague tenderness GI bleeding Nausea/vomiting Fever	Insidious onset GI bleeding Upper—10% Lower—16% Peritonitis Abdominal distension Tenderness
Nonocclusive (NOMI)	Vasopressors Hypotension Low cardiac output Digoxin Hypovolemia Recent cardiac surgery Hemodialysis Diarrhea	Critically ill patient abdominal pain Hypotension Altered mental status Nausea/vomiting	Tenderness Abdominal distension Feeding intolerance

18.4 Clinical Findings

Although in the embolic AMI the onset of abdominal pain is usually sudden, mimicking other causes of acute abdomen (hollow viscus perforation, acute cholecystitis or acute pancreatitis) [25, 26], and might be accompanied by signs of shock, in thrombotic AMI, collateral circulation formed over the time could decrease the severity of presenting symptoms, leading nonetheless to a dismal prognosis [9].

Several other symptoms may also be present, such as nausea, vomiting, hematochezia, melena, hypotension, fever, and abdominal distension. Unfortunately, these signs and symptoms are clearly insufficient to perform a correct diagnosis, let alone distinguish between the different forms of AMI. For instance, only 15% of patients will present with melena or hematochezia [27]. The association of clinical symptoms with the risk factors, obtained from the clinical history, will however aid in raising a strong clinical suspicion, prompting the performance of more sensitive and specific tests.

Clinical signs of peritonitis, such as tenderness and guarding, will only occur at a later stage and are associated with bowel necrosis. Therefore, their absence is unreliable to exclude the diagnosis of AMI.

Nonocclusive mesenteric ischemia (NOMI), because of the scarcity and little specificity of initial symptoms, is only diagnosed several hours after emergency department admission, or much later in sedated patients admitted to medical or surgical intensive care units. According to Mitsuyoshi et al., NOMI should be suspected in the presence of three clinical signs or symptoms in a critical patient: ileus or abdominal pain; need for vasopressors; and elevated aminotransferases [28].

18.5 Biochemical Markers

Unlike acute myocardial infarction, which is readily diagnosed with noninvasive serum markers of myocardial necrosis such as troponin, no such markers are yet disseminated in clinical practice for the diagnosis of ischemic bowel. Some markers (such as L-lactate, C-reactive protein, lactate dehydrogenase, and amylase) are nonspecifically elevated in many acute abdominal emergencies and might have some relevance in the initial clinical suspicion. However, they lack specificity or are only elevated at a late stage, when full-thickness bowel necrosis supervenes [29, 30].

The ideal laboratory marker would be highly specific, present high sensitivity, and be elevated at early stages of the disease, when diagnosis would allow for timely revascularization and potentially decrease, or altogether prevent, the need for bowel resection. Furthermore, it could be readily performed by standard of care laboratory testing in most emergency departments.

Several putative molecules have shown promise, including intestinal fatty acid binding protein (I-FABP) and α-glutathione S-transferase (α-GST). These are two proteins produced by the mature enterocyte that are readily released into the systemic circulation with cell injury. Given that the mucosa is the earliest layer of bowel wall to suffer from ischemia [31], these two molecules are excellent putative markers for early diagnosis of AMI, with reported sensitivity and specificity of 80% and 85%, respectively for serum I-FABP; and pooled sensitivity and specificity of 68% and 85% for α-GST [15] (Table 18.2).

Table 18.2 Diagnostic sensitivity and specificity of distinct methods in acute mesenteric ischemia. Adapted and modified from [15, 32, 33]

Laboratory test	Sensitivity (%)	Specificity (%)
WBC	65.4–80	42.1–50
Lactate	86	44
D-Dimer	76.9–96	40–57.9
pH	38–57.7	52.6–84
Amylase	23.1	84.2
I-FABP	80	85
α-GST	68	85

I-FABP intestine-fatty acid binding protein, *WBC* white blood cell count, *α-GST* α-glutathione S-transferase

Other serological markers include D-lactate, ischemia modified albumin, and procalcitonin [15, 34, 35]. However, these are more sensitive for advanced forms of bowel ischemia, with established necrosis, and thus lack in clinical value for early diagnosis [34, 35].

D-dimer biomarker is for ruling out acute intestinal ischemia rather than for making a final diagnosis [36].

In the particular case of NOMI arising in the setting of cardiothoracic surgery, two very promising serum markers are endothelin-1 and presepsin (a cleaved product of the CD-14 monocyte receptor), with both diagnostic and prognostic value [37, 38]. Another addition to the already long list of putative molecules is the enteroendocrine cell product, glucagon-like peptide 1 (GLP-1), which is elevated in bowel ischemia. However, it lacks clinical validation [39].

Still, ongoing research continues for more accurate serum markers of AMI that could enable the early diagnosis and timely initiation of therapy. However, although many promising molecules have emerged, they have yet to enter into clinical practice. The discovery and dissemination of such marker would allow it to be easily included in the diagnostic algorithm of AMI, as much as serum amylase, along with other clinical and radiological markers, is for the diagnosis of acute pancreatitis. In the meantime, in the absence of such molecule, clinicians attending the elderly patient with acute abdominal pain must solely resort to strong clinical suspicion and immediate dedicated imaging.

18.6 Clinical Suspicion and Early Computed Tomography Angiography

Given the prevalence of abdominal complaints in the elderly population, lack of specificity of clinical findings and absence of truly specific laboratory markers, the early and timely diagnosis of AMI relies on the presence of strong clinical suspicion, prompting the immediate performance of triphasic (nonenhanced, arterial phase, and portal phase) multidetector computed tomography angiography (CTA).

This is illustrated in an interesting study by the Helsinki group [20]. In a cohort of 81 patients with AMI, the clinician first observing the patient had a significant impact on early diagnosis and subsequently, prognosis. In fact, when a non-surgeon, usually an internist, was the first clinician assessing the patient there was a median delay of admission to CT of 8.4 h. However, in emergency rooms with the surgeon first seeing the patient, there was a median time of the door to CT of only 2.7 h. This had an impact on prognosis, with a reduction in time to operating room (15–10 h) and decrease in mortality (75–50%).

A major concern of clinicians treating elderly patients is the small but significant risk of contrast-induced nephropathy (CIN), which is a sudden deterioration of renal function caused by the administration of intravascular iodinated contrast, such as that used in diagnostic or therapeutic radiological procedures. The risk factors for CIN are highly prevalent in the patients at risk of AMI, such as advanced age, diabetes, and congestive heart failure. Other cofactors causing renal vasoconstriction,

such as sepsis and dehydration, also coexist in AMI. Thus, some clinicians might choose to delay the performance of CTA until other diagnosis are excluded. Although this attitude may seem reasonable, it is unsupported by the literature. In fact, a meta-analysis of studies of patients undergoing CT for acute abdomen found an incidence of acute kidney injury (AKI) after contrast-enhanced CT ranging from 2.2 to 10.6%. Importantly, patients undergoing unenhanced CT-scan have similar rates of AKI, possibly given the multifactorial causes for deteriorating renal function in the acute abdomen [40]. Therefore, in face of a strong clinical suspicion of AMI, CTA should be performed earlier rather than later, meaning that the diagnosis of AMI should not be one of exclusion, because this might severely delay the time to treatment. Nonetheless, all measures pertaining to the prevention of CNI, namely adequate intravenous hydration should be scrupulously followed in this population.

Moreover, although inevitably many patients with initial clinical suspicion of AMI might not have this condition, CTA will also reveal many other acute conditions potentially requiring surgical treatment. In fact, while as many as 60% of patients might not have AMI, other emergent diagnoses, such as bowel obstruction or hollow viscus perforation may be detected in 10% and 4% of cases, respectively, without unduly delaying surgical therapy [41].

To diagnose acute mesenteric ischemic disease, the radiologist must be acquainted with both the mesenteric arterial and venous anatomies of the bowel and extravascular signs, as well (bowel wall and mesentery). The three major arteries that supply the small and large bowel are the coeliac trunk, superior mesenteric artery (SMA), and inferior mesenteric artery (IMA) (Fig. 18.1) [42]. The venous system returns

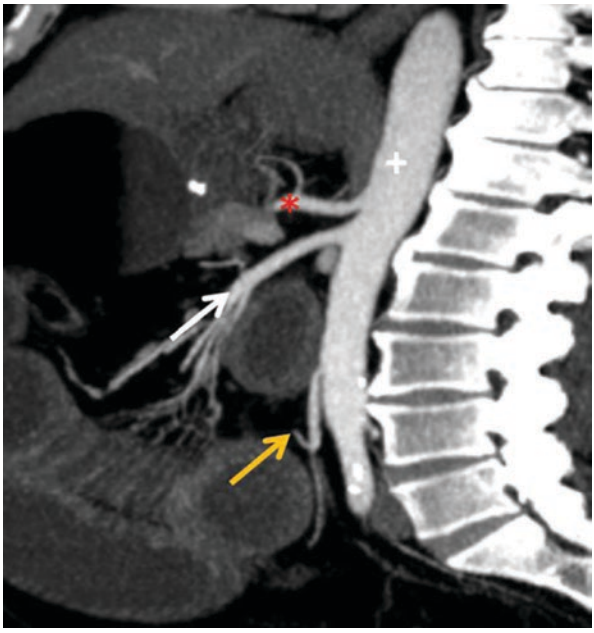

Fig. 18.1 Sagittal view on arterial phase computed tomography angiography (CTA) of the three visceral arteries: celiac trunk (asterix), superior mesenteric artery (white arrow), and inferior mesenteric artery (yellow arrow). (Reprinted with permission from Florim et al. [42])

essentially parallel to the arterial supply. The superior and inferior mesenteric veins run parallel to the arteries and drain the respective part of the bowel. The inferior mesenteric vein (IMV) usually joins the splenic vein, and the splenic vein joins the superior mesenteric vein (SMV) to form the portal vein.

Arterial occlusion most commonly results from thromboembolism, where the embolus originates from the left atrium as a consequence of atrial fibrillation. Emboli from heart origin preferentially affects the SMA because of its small take-off angle, while thrombi and large emboli may occlude the proximal SMA and ostia of major mesenteric vessels, where some images of ostial calcification may be already present, resulting in extensive small bowel and colon ischemia (Fig. 18.2). Smaller emboli may lodge in the distal portions of the vessel and cause smaller regions of segmental ischemia (Fig. 18.3).

Although it is not a specific finding, bowel wall thickness is the most common CT finding in acute bowel ischemia. It is present in 26–96% of reported cases [43].

Bowel wall may be thickened or thinned, depending on the etiological mechanism. In cases of bowel ischemia caused by mesenteric venous thrombosis, bowel wall thickening is more pronounced than in cases caused exclusively by occlusions of mesenteric arteries (Fig. 18.4) and the small bowel may be full of fluid.

Luminal dilatation and air-fluid levels are quite common in acute bowel infarction (56–91% of cases) [44].

Pneumatosis and portomesenteric venous gas have also been reported as one of the more accurate imaging signs of acute bowel ischemia, being present in 6–28% and 3–14% of cases, respectively [45]. Although pneumatosis is not a specific finding of intestinal ischemia when found, bowel ischemia should be considered. Located in the thickness of the bowel wall, it should be differentiated from endoluminal gas. Portomesenteric venous gas may consist only of some small gaseous inclusions within the mesenteric veins or may extend into the intrahepatic branches of the portal vein, where it is typically found in the periphery of the liver (Fig. 18.5).

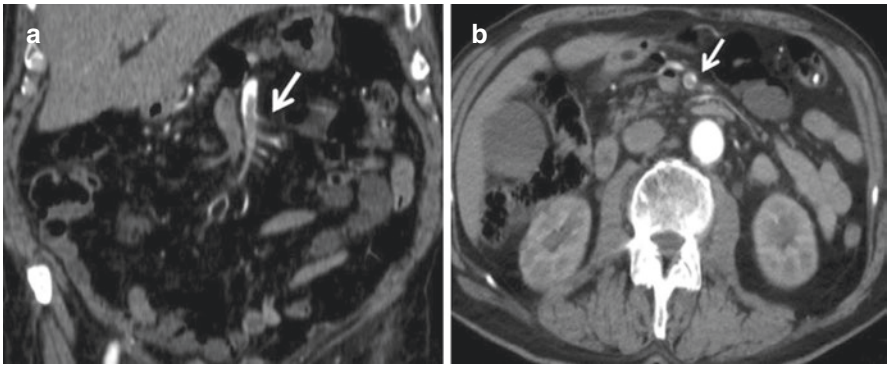

Fig. 18.2 Thrombotic acute mesenteric ischemia. (Reprinted with permission from Florim et al. [42]). (**a**)Coronal view of thrombus in the lumen of the superior mesenteric artery. (**b**)Axial view

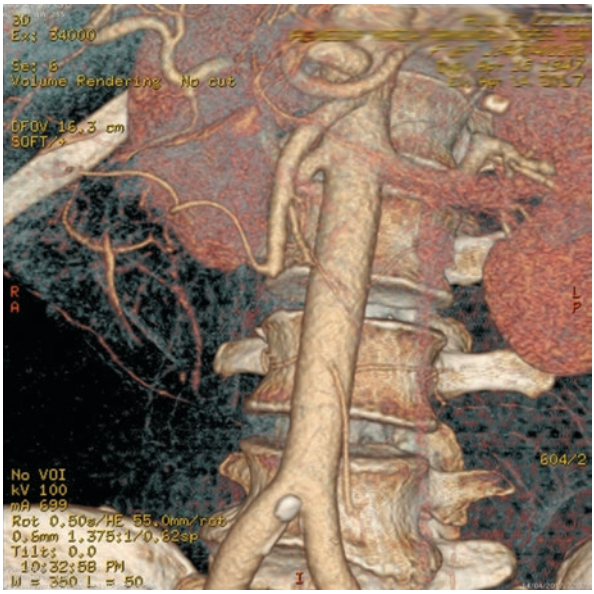

Fig. 18.3 Embolic acute mesenteric ischemia. Sagittal view on computed tomography angiography reconstructed images of embolus in the distal superior mesenteric artery, sparing the first branches. (Image courtesy of Prof. Paulo Donato—Coimbra, Portugal)

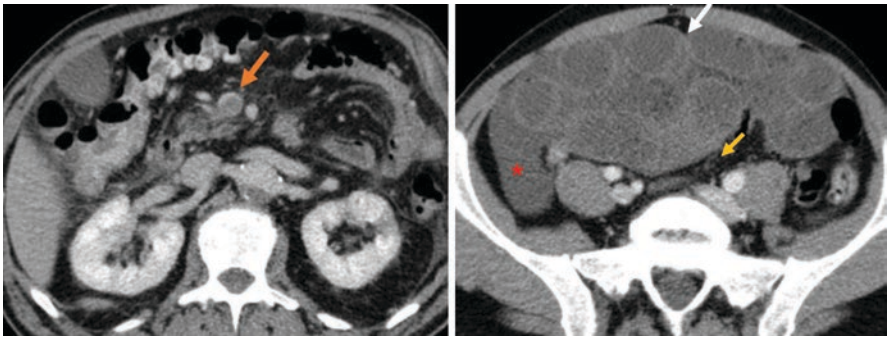

Fig. 18.4 Venous thrombotic mesenteric ischemia. Hypodense thrombus inside the superior mesenteric vein (left) and marked bowel wall thickening (right). (Reprinted with permission from Florim et al. [42])

18.7 Other Imaging Methods

Duplex ultrasound (US) scanning and Doppler flowmetry can be used to evaluate patients with suspected AMI, but these techniques are limited in their clinical use by several factors. First, only the proximal portions of the major splanchnic vessels can be studied reliably, not the peripheral aspect of the vasculature. Secondly, vascular occlusions are not diagnostic of intestinal ischemia, because complete occlusions can be seen in asymptomatic patients. Moreover, blood flow through the SMA is highly variable, which may make interpretation difficult. Finally, NOMI cannot be diagnosed reliably by US studies [46].

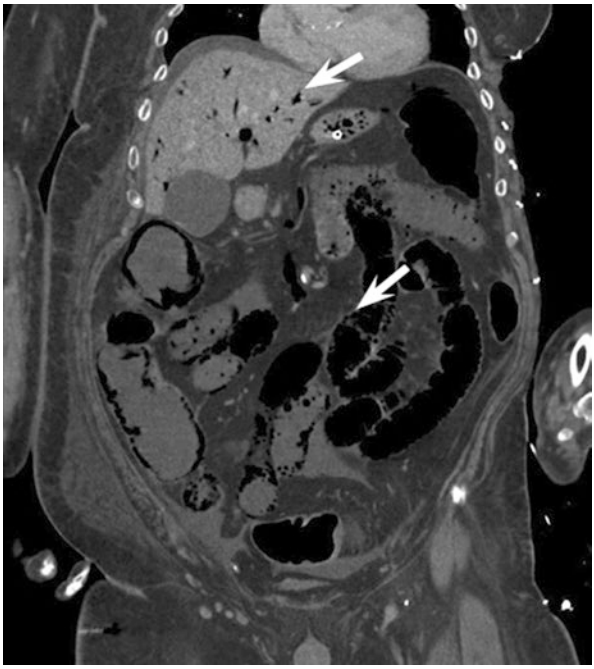

Fig. 18.5 Coronal view in computed tomography angiography of gas in the portal venous system, both at the level of the bowel wall and intrahepatic. (Reprinted with permission from [42])

Plain abdominal radiography has absolutely no role in the early diagnosis of AMI, as it lacks sensitivity and specificity, only demonstrating the signs of advanced bowel necrosis, i.e., pneumoperitoneum and eventually portal venous gas [3, 12].

18.8 Treatment

As with other acute conditions, immediate resuscitation, ensuring oxygenation and peripheral perfusion, is mandatory. Supplemental oxygen by face mask, large bore intravenous lines, and a fluid bolus with crystalloid is warranted since most patients are hypovolemic due to vomiting and ileus. Nasogastric tube is desirable and placement of a Foley catheter, for assessment of hourly urinary output, is paramount. Further resuscitation should be guided by the response to fluid challenge, more accurately assessed by physiologic parameters such as base deficit and arterial lactate. Invasive monitoring, such as a central line, may be required in cases of suspected or proved cardiac dysfunction but can be delayed to after admission in intermediate or intensive care unit. Large spectrum antibiotics, covering enterobacteria and anaerobes, should be given, as well as correction of associated metabolic and electrolyte disturbances [3, 12].

Alongside with resuscitation efforts, immediate attention should be given to revascularization and source control if there are signs of bowel necrosis.

Although the trends in treatment are changing, with an increasing emphasis on endovascular techniques in the management of the different forms of AMI, the

reality is that in low- and middle-income countries this approach has not gained popularity. Moreover, even in high-income countries, not all institutions are equipped with all the resources, namely endovascular techniques, and the patients' condition may not allow for safe transfer in a reasonable timeframe. This notorious lack of resources, either in diagnosis or in therapy, still makes the exploratory laparotomy the most used method to confirm the diagnosis and complete the therapy [6].

Usually, the two main factors that prompt the performance of laparotomy are: the presence of peritoneal signs, which are associated with full-thickness bowel necrosis; and the lack of resources, such as CTA and endovascular therapy.

Apart from the peritoneal signs, other factors have also been identified as surrogate markers of bowel necrosis: coexisting organ failure; elevated arterial lactate >2 mmol/L; elevated white blood cell count >10.000/mL; and decreased bowel wall enhancement or dilated loops [47, 48]. When present, these findings will be pivotal in the decision for immediate surgery.

In practical terms, the approach to AMI is totally different if one is working in an environment of full resources (FR) or limited resources (LR).

18.9 Full Resources (FR) Setting

In a center with full resources, all patients with clinical suspicion will undergo CTA for diagnostic confirmation and for assessment of signs of bowel necrosis. If there are no clinical signs of peritonitis, these patients will then undergo endovascular therapy: aspiration of embolus and thrombolysis in embolic AMI (Fig. 18.6); angioplasty (with or without stent placement) in cases of thrombotic AMI (Fig. 18.7); or direct intra-arterial infusion of vasodilator drugs (papaverine, prostaglandin

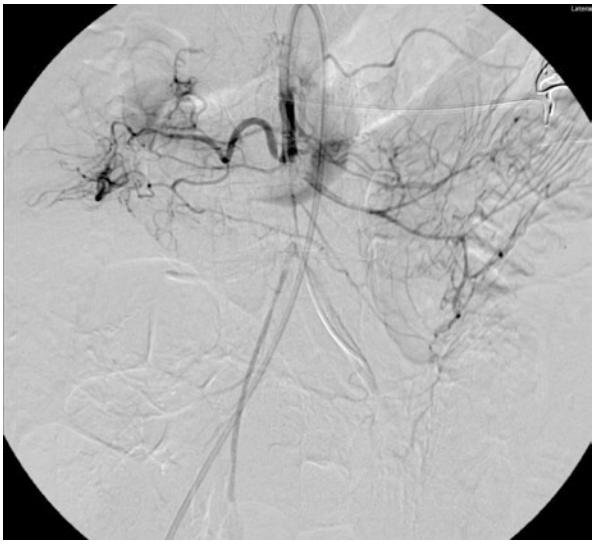

Fig. 18.6 Thrombus aspiration through endovascular approach in acute embolic mesenteric ischemia. (Image courtesy of Prof. Paulo Donato—Coimbra, Portugal)

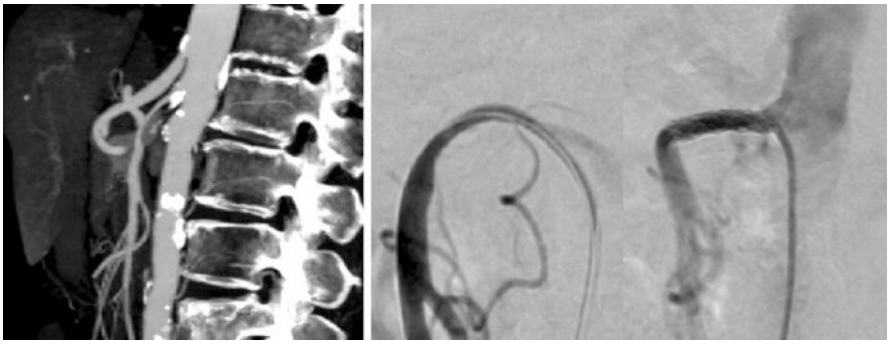

Fig. 18.7 Thrombotic acute mesenteric ischemia managed with angioplasty and stent placement through endovascular approach. (Image courtesy of Prof. Paulo Donato—Coimbra, Portugal)

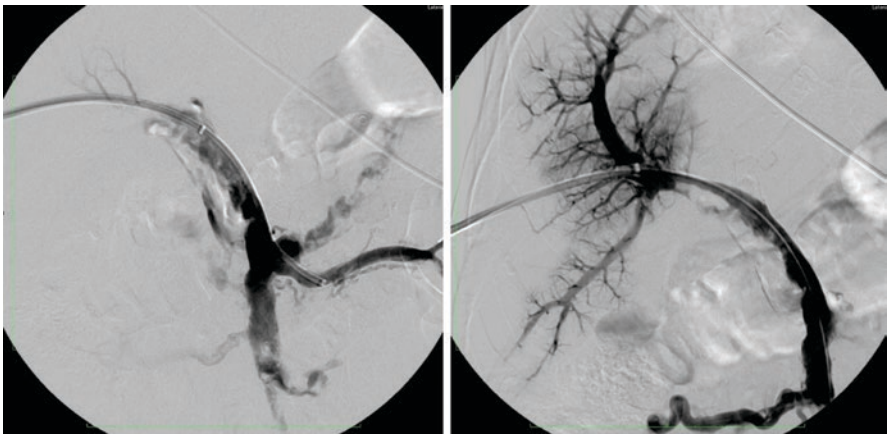

Fig. 18.8 Direct catheter-based percutaneous thrombolysis of extensive mesenterico-portal venous thrombosis. (Image courtesy of Prof. Paulo Donato—Coimbra, Portugal)

E1—PGE1), in cases of NOMI, respectively. In MVTI, continuous infusion of unfractionated heparin is still the first choice [12], with percutaneous transhepatic endovascular therapy as a choice in selected cases (Fig. 18.8).

In 1973, Boley et al. proposed an aggressive plan of management employing early angiography and the intra-arterial infusion of the vasodilator papaverine to interrupt splanchnic vasoconstriction [49]. This approach resulted in the salvage of compromised bowel and improved survival. The authors present a protocol for the use of papaverine through percutaneous selective catheterization of the superior mesenteric artery, adapted from Kozuch et al. [50] (Table 18.3).

When AMI is suspected, treatment includes resuscitation of the patient and correction, as far as possible, of predisposing or precipitating causes. These patients should be admitted to high dependency units (intensive or intermediate care), for close surveillance of signs of organ dysfunction. Should clinical deterioration

Table 18.3 Protocol for the use of papaverine through percutaneous selective catheterization of the superior mesenteric artery, adapted from Kozuch et al. [50]

Papaverine infusion protocol
Use concentration of 1 mg/mL
Infuse bolus of 60 mg papaverine into the SMA through an angiogram catheter
Left the catheter in situ and follow with infusion at 30–60 mg/h
Adjust dose for clinical response for at least 24 h, continued until 12–24 h
Flush catheter with normal saline for 30 min after the initial treatment cycle
Repeat the angiogram
Repeat the entire cycle every 24 h for maximum of 5 days if vasospasm persists

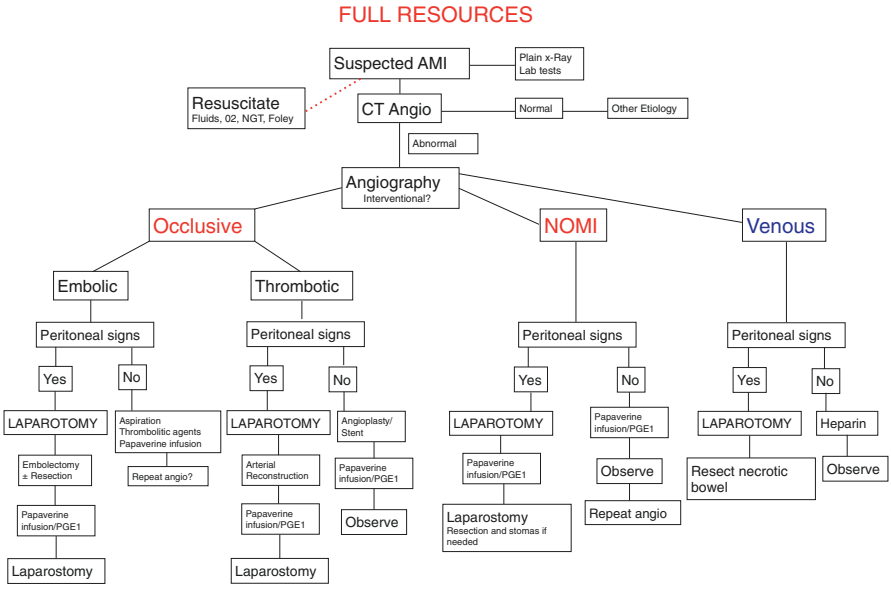

Fig. 18.9 Algorithm for management of acute mesenteric ischemia in a full resources setting

develop, or peritoneal or imagiological signs occur suggesting bowel necrosis, prompt laparotomy should be performed [2].

In this circumstance, the aim of laparotomy is to resect irreversibly affected bowel, along with, if needed, revascularization of the remaining splanchnic territory (embolectomy, thrombectomy, aorto- or ilio-mesenteric bypass, or spleno-mesenteric bypass) [51]. At this stage, it is the authors recommendation that no anastomosis or stoma be performed. The bowel ends should be stapled closed and the abdomen left open, in a damage-control context [52], easily allowing second-look procedures.

The authors propose an algorithm for the management of AMI in a full resources setting (Fig. 18.9).

18.10 Limited Resources (LR) Setting

Unfortunately, not all centers have the full resources to offer the best available treatment to all patients, particularly endovascular therapy. Although interventional cardiologists may be involved in emergent mesenteric revascularization procedures, this approach should be considered the exception rather than the rule [53]. As such, these patients require a distinct approach, based on locally available resources (Fig. 18.10). Given the emergent and life-threatening context of AMI, most patients undergo emergent laparotomy. These patients will present an acute abdomen with peritoneal signs, with or without the preoperative clinical suspicion of AMI, possibly with CT confirmation.

After adequate initial resuscitation, the conduction of the laparotomy should suit the intraoperative findings, especially the presence of bowel necrosis. Should this be present, affected bowel must be resected. However, this resection should be conservative, as the full extension of the affected bowel can only be ascertained after revascularization, which requires direct approach of the SMA.

There are two transperitoneal methods for the exposure of the SMA. In the lateral approach, the transverse colon is reflected superiorly, and the small bowel is retracted to the right upper quadrant. The ligament of Treitz is divided to mobilize the fourth portion of the duodenum. The SMA is palpated at the root of the mesentery over the junction of the third and fourth portions of the duodenum. Its identification can be very difficult due to the absence of pulse. In the anterior approach,

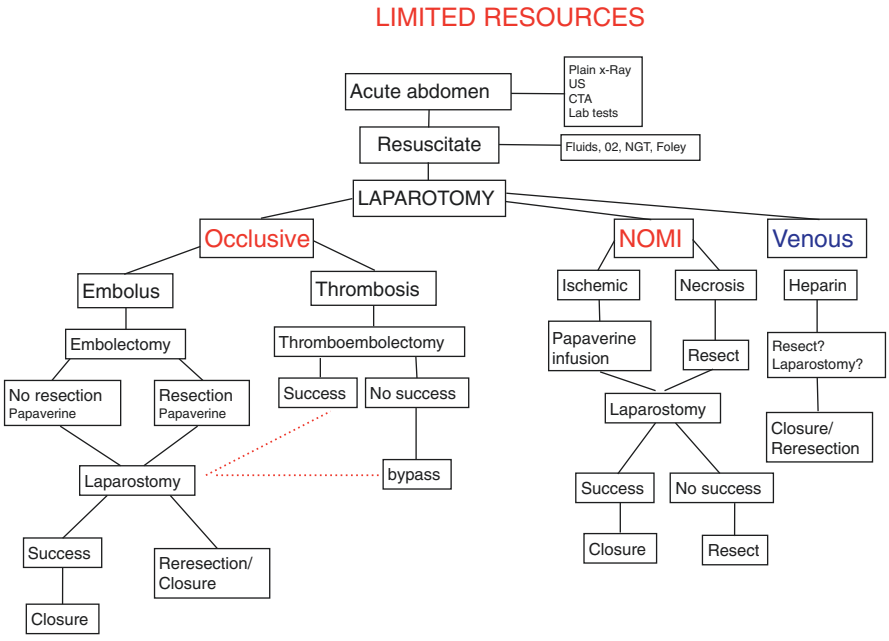

Fig. 18.10 Algorithm for management of acute mesenteric ischemia in a limited resources setting

after superior retraction of the transverse colon, the small bowel is retracted to the right. The middle colic artery is traced proximally, and a horizontal incision at the root of the mesentery is made. The SMA is identified medial to the SMV after careful dissection of surrounding lymphatic and autonomic nerve fibers with proximal and distal vascular control. If a thrombotic etiology is suspected, longitudinal arteriotomy, rather than transverse arteriotomy, is made, and an embolectomy balloon catheter is passed proximally and distally to ensure complete removal of the embolus if possible. When proximal inflow and distal backflow are adequate, an autogenous vein patch is used for closure of the arteriotomy.

If an embolic cause is suspected, then a transverse arteriotomy can be done, followed by a complete embolectomy and transverse closure of the artery. If embolectomy is unsuccessful in reestablishing blood flow, then the arteriotomy can be used for distal anastomoses of the bypass graft or anastomotic site with proximal splenic artery [51].

If this approach is successful, all necrosed segments should be resected and the laparotomy abbreviated as a damage-control procedure, meaning that the bowel stumps should neither be anastomosed nor exteriorized as stomas. A second-look procedure at least after 24 h is mandatory, and the patient should be admitted to an intensive care unit. Vasopressors should be avoided, or at least used in the smallest dosage possible, in order to maximize bowel perfusion.

Prognosis is obviously dependent upon the extent of resection, as well as on the systemic repercussions. Several predictive factors for early (<72 h) have been identified [54]: preoperative heart failure, lactate level over 5 mmol/L, aspartate aminotransferase over 200 IU/L, and total cholesterol level below 80 mg/dL, or procalcitonin level over 40 ng/L. From these results, a mortality prognostic score was derived. Probability of mortality within 72 h was estimated to be 5% for patients with none of these factors and 97% for those with all four.

Regarding NOMI, and since there is no actual arterial obstruction rather a low-flow state with splanchnic vasoconstriction, there is no place for performing SMA arteriotomy. In this instance, the authors recommend papaverine infusion through retrograde approach of the SMA by placing a catheter in the stump of the middle colic artery in patients undergoing colectomy (unpublished data) (Fig. 18.11). The catheter is placed in situ, with an infusion rate of 30 mg/h continued in the ICU and until the second look is performed. In the authors' opinion, this method is particularly useful for three main reasons: it avoids the somewhat difficult direct approach to the SMA; it allows the delivery of the drug in the vascular territories where it is most needed, obviating the systemic effects; and it does not require any particular care in the removal of the catheter, as the artery is anyway ligated at the end of the infusion at the second stage procedure (Fig. 18.11).

In all cases requiring laparotomy, the authors strongly recommend a second-look procedure for the assessment of adequate bowel perfusion. Confection of anastomosis or stomas should be delayed until the patient is fully resuscitated and without any vasopressors [55]. Regardless of the setting (full resources or limited resources), the management as an open abdomen after the first operation has numerous advantages: decreases the risk of intra-abdominal hypertension; improves the perfusion of

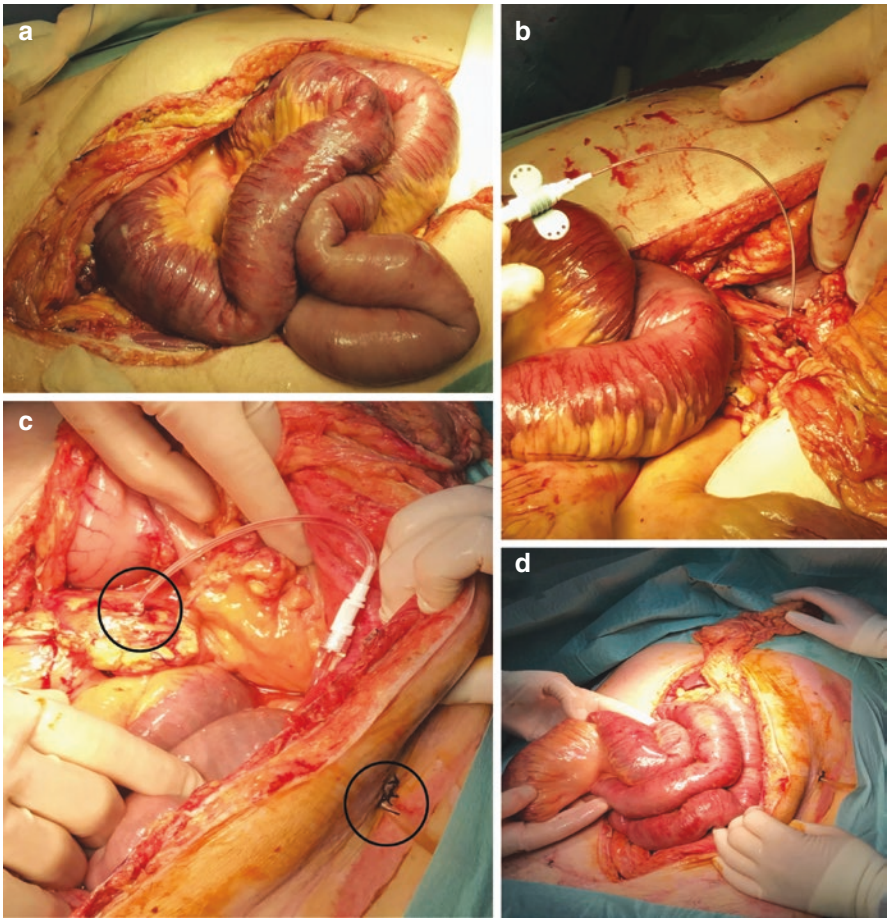

Fig. 18.11 Clinical case of management of nonocclusive mesenteric ischemia (NOMI) in a limited resources setting with damage-control techniques and intraoperative placement of a catheter in the superior mesenteric artery (SMA) through the stump of the middle colic artery for continuous postoperative perfusion of papaverine. (**a**) Intraoperative image of NOMI. Note the dusky bowel and fully viable bowel without a clear demarcation line. (**b**) Placement of catheter in the lumen of the SMA through the stump of the middle colic artery for intraoperative and postoperative perfusion of papaverine (according to the protocol in Table 18.3). Note some clearly ischemic bowel loops, without full-blown necrosis. (**c**) The catheter (black circle) was exteriorized through the abdominal wall and the abdomen temporarily closed. (**d**) Well perfused small bowel at the second-look procedure, 24 h after the index operation. The catheter was removed at this stage, the abdomen definitively closed and the patient ultimately discharged home after 4 days in ICU

bowel; and preserves the fascia for definitive closure after the second-look procedure. Although there are several techniques available, the use of negative pressure wound therapy with mesh-mediated fascial traction seems to present the best outcomes [56].

18.11 Intestinal Stroke Centers and the Multimodal Approach of Acute Mesenteric Ischemia

Despite recent progresses, revascularization rates in AMI remain low. According to the Nationwide Inpatient Sample (NIS) registry, in the United States in 2014, the overall revascularization rate did not exceed 7.9%; only 8.6% and 6.5% of patients received an attempt endovascular or open revascularization, respectively, while most were treated with bowel resection alone or received no intervention whatsoever [57].

Implementation of a systematic, multidisciplinary, and multimodal management of AMI, in a differentiated intestinal stroke center, focused on preserving life and intestinal viability, according to current scientific evidences, seems to improve the vital and functional prognosis of patients [2, 58–60], increasing survival rates and preventing intestinal failure development. In cases of chronic intestinal failure, specialized resources for long-term parenteral nutritional support and dietary, pharmacological, and surgical intestinal rehabilitation programs may be available. Furthermore, a differentiated multidisciplinary approach may also allow accurate detection and proper elective treatment of chronic mesenteric ischemia [61], which has also an increasing incidence, improving the quality of life of affected patients and preventing the occurrence of bowel infarction.

Recently published studies suggest that management of AMI in a specialized center can reduce mortality and intestinal resection rates to less than 20 and 30%, respectively [47].

Intestinal stroke centers should have medical and technical expertise for a timely approach of AMI, including endovascular and open revascularization skills, logistical resources and good accessibility, and be available 24 h a day, 7 days a week, ensuring a proper treatment of this potentially fatal condition. Algorithms for an appropriate and expeditious therapeutic decision, based on the international recommendations [3, 12, 62, 63] and integration in a multi-institutional network with clearly defined referral protocols must be also ensured. Early definition of the objectives of treatment and establishment of criteria for the definition of futile care or non-resuscitation are also necessary.

The multimodal integrated management strategy should involve a quick-response team of digestive and vascular surgeons, diagnostic and interventional radiologists, and intensive care specialists, in close cooperation. A hybrid operation room with interventional radiology facilities, as well as, a surgical intensive care unit equipped with advanced multi-organ function support and surveillance devices should be available.

A standardized “3Rs” treatment strategy is designed to reduce mortality rates and to avoid extended intestinal resections, based on Resuscitation, Rapid diagnosis, and early Revascularization. The coordinated multimodal program, targeting life and intestinal viability preservation, combines three therapeutic objectives: excision of nonviable bowel; reperfusion to limit the extent of reversible ischemia; and prevention of multi-organ failure and ischemia-reperfusion syndrome with a

pathophysiological-based medical treatment. An early diagnosis should be achieved and revascularization performed within 12 h from the onset of symptoms. Resection of nonviable bowel should be accomplished promptly [2, 3, 12, 59]. For acute mesenteric arterial occlusive disease, both endovascular and open revascularization techniques are viable options [64]. However, endovascular revascularization confers improved outcomes compared to conventional surgery, as indicated by reduced mortality, risk of bowel resection, and acute renal failure [65]. According to Erben et al. [57], patients treated endovascularly demonstrated one-third the rate of in-hospital mortality, an increased hazard ratio for discharge alive, and a cost saving of $9196 (97.5% CI, $3797–$14,595) per hospitalization. New approaches for intraoperative for evaluation of intestinal viability, implementation of principles of damage control, and liberal use of second-look approach should be included in the treatment [3, 12] (Fig. 18.8).

Extensive resection, with a remaining small bowel length inferior to 200 cm, may lead to a short bowel syndrome (SBS) and intestinal failure, that is, parenteral support dependency. SBS is a complex clinical entity, with variable severity, characterized by dehydration, electrolytic and acid-base imbalance, malnutrition, diarrhea, dysbiosis, and hepatobiliary, renal, and bone complications [1, 2]. Mesenteric ischemia is the second most common underlying disease of SBS in adult patients (after Crohn's disease) and SBS is the most frequent pathophysiological mechanism of chronic intestinal failure [1, 2]. In fact, SBS-associated intestinal failure has been reported in 13–31% of acute mesenteric ischemia survivors [3]. Prognosis of SBS is determined by the anatomy, integrity, and function of in-continuity gastrointestinal tract, including length of remnant small bowel, presence of distal ileum, ileocecal valve and colon, comorbidities, time of evolution and age of patient, among others. Reversibility of intestinal failure and weaning of parenteral support is possible with spontaneous physiological intestinal adaptation, which occurs predominantly during the first 2 or 3 years after resection. Nevertheless, definitive parenteral support dependency is likely in cases of small bowel remnant length inferior to 115 cm, 60 cm, and 35 cm in end-jejunostomy (type I), jejunocolic anastomosis (type II), and jejuno-ileal (type III) SBS, respectively. In this context, long-term parenteral nutrition is a life-saving but also potentially problem-prone therapy. Although considered safe in experienced centers, home parenteral nutrition is associated with non-neglectable risk of morbidity and mortality, including catheter-related complications, intestinal failure-associated liver disease, and metabolic bone disease, significant impact on quality of life and high social and economic costs. Intestinal transplantation may be indicated in cases of life-threatening home parenteral nutrition-related or primary disease-related complications but is not option in elderly patients. SBS-associated chronic intestinal failure requires a multimodal treatment, with highly differentiated multidisciplinary teams, in specialized centers. Pharmacological, surgical, and dietetic rehabilitation strategies may allow the reduction of parenteral support dependency and improvement of the prognosis [1, 2]. In consequence, a massive small bowel resection must be carefully considered, particularly in elderly and frail patients.

In conclusion, prompt diagnosis and intervention included in a multimodal stepwise management, in intestinal stroke centers, may improve the vital and functional prognosis of patients with AMI.

18.12 Other Adjuvant Therapies

18.12.1 Gut Decontamination

Oral antibiotics should be considered an important adjunct to surgical treatment. Decreased bacteria in the bowel lumen may decrease the immunoinflammatory storm that follows gut hypoperfusion and which is, at least in part, responsible for the deranged physiologic status that these patients present. Experimental studies have demonstrated that depletion of gut bacteria decreases intestinal ischemic injury [66] and a prospective cohort study showed that oral antibiotics (gentamicin and metronidazole) could decrease irreversible bowel ischemia and improve survival [67]. However, this was not a randomized control trial and further evidence is needed. Nonetheless, given the simplicity and low risk of this therapy, the authors believe it can be an interesting adjunct to the surgical management of AMI patients.

18.12.2 Direct Peritoneal Resuscitation

Direct Peritoneal Resuscitation (DPR) is a promising therapy in the surgical management of patients with AMI, particularly NOMI. This technique consists of a continuous postoperative infusion of hypertonic dialysis fluid in the abdominal cavity, causing an increase in gut perfusion by a vasoactive effect in small bowel arterioles [68]. When used in the setting of nontraumatic abdominal catastrophes, DPR is associated with improved organ disfunction, decrease length of stay, decreased days in ICU, and reduced time to definitive abdominal closure [69]. However, only 11 and 10 patients in the treatment and control arm, respectively, presented mesenteric ischemia. Although no specific evidence supports its use in AMI, hypothetically DPR could reverse the physiologic derangements associated with bowel ischemia and particularly reverse the self-feeding loop of gut hypoperfusion, release of damage-associated molecular patterns (DAMPs) and bacteria into the mesenteric lymph with its systemic consequences, further circulatory derangement and aggravated bowel hypoperfusion. Further randomized controlled trials are warranted to investigate the full potential of this promising therapy in AMI.

18.13 Concluding Remarks

In spite of the continued improvement in both diagnostic and treatment methods, mortality of AMI is expected to remain high, particularly because the optimal care is yet unavailable in most acute care hospitals managing these patients. Given the

expected aging of the world population, not only in developed but also in underdeveloped countries, the number of AMI cases is likely to increase, prompting the creation of dedicated reference centers. In the meantime, vascular skills and a damage-control frame of mind should be a part of the armamentarium of emergency surgeons, especially when the patient transfer is not feasible in a reasonable timeframe.

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