INVITED REVIEW

Ischemic Gut in Critically Ill (Mesenteric Ischemia and Nonocclusive Mesenteric Ischemia)

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Abstract

Ischemic gut or splanchnic hypoperfusion is a life-threatening emergency and it is associated with high mortality. It requires prompt diagnosis and intervention to establish the mesenteric blood flow, hence an attempt to avoid gut necrosis. Despite the understanding of pathogenesis of acute mesenteric ischemia and advanced treatment and revascularization techniques, it still remains a big diagnostic dilemma for the clinicians. Any delay in diagnosis and appropriate treatment affects the overall outcome of the patient. The high incidence of sepsis and multiorgan failure requires high-quality intensive care management.

Keywords: Computed tomographic angiography, Damage control surgery, Mesenteric ischemia.

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Introduction

Mesenteric ischemia (MI) is a life-threatening emergency and it signifies insufficient blood supply to the intestinal architecture to meet their metabolic demands. If not dealt with emergent intervention, the risk to the life of the patient is high. Even with the advancements in the diagnostic and therapeutic intervention modalities for MI, the diagnostic challenge is very high for the clinicians as it is not a very common cause of abdominal pain among patients. Although with the help of such increasing awareness, the mortality has come down to nearly 50% from 90%.[1] The mortality is around 10–20% if treated within first 6 hours, so the importance of early diagnosis becomes more obvious. In this review, we would discuss the types of MI, its clinical presentation, diagnosis, treatment modalities, and prognosis.

Mesenteric Circulation

The abdominal aorta trifurcates into celiac axis (CA), superior mesenteric artery (SMA), and inferior mesenteric artery (IMA) to form the mesenteric arterial circulation.[2] The supply territory of all the three arteries is shown in Box 1. The small intestine is primarily supplied by SMA with collateral supply via the pancreaticoduodenal artery. These collaterals increase as the stenosis in mesenteric vessels increases above 70%.

Types of Mesenteric Ischemia

There are primarily two forms of MI—occlusive and nonocclusive with the primary etiology further categorized as mesenteric arterial embolism (50%), mesenteric arterial thrombosis (15–25%), or mesenteric venous thrombosis (5–15%).[3,4]

Embolic Acute Mesenteric Ischemia

Acute occlusion of SMA by an embolic episode, mostly cardiac in origin, is the most common cause of MI.[5] Patients with arrhythmias, cardiomyopathy, myocardial infarction, or valvular disorders are at high risk of developing a mural thrombus, which can eventually embolize to mesenteric arteries. Around 15% emboli block the origin of SMA, whereas around 50% emboli lodge at the origin of the middle colic artery, which is the first major branch of SMA.[6]

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Thrombotic Acute Mesenteric Ischemia

Thrombotic occlusion of SMA is seen in progressive atherosclerotic disease and is slow in onset. As it develops over time, there is an extensive development of collaterals to maintain blood flow. The symptoms develop generally when there is acute stenosis of CA along with the occlusion by the atherosclerotic plaque of SMA.[6]

Acute Mesenteric Venous Thrombosis

Mesenteric vein thrombosis (MVT) occurs due to thrombosis of the superior mesenteric venous system. Patients with hypercoagulable

Box 1: Supply territories of mesenteric arterial circulation

Artery	*Supply area*
Celiac axis	Stomach
	First and second part of duodenum
	Part of pancreas
	Liver, spleen
Superior mesenteric artery	Remaining duodenum
	Jejunum
	Ileum
	Ascending colon
	Proximal transverse colon
Inferior mesenteric artery	Distal transverse colon
	Descending and sigmoid colon
	Proximal rectum

states like having disorders of factor V Leiden, protein C or S deficiency, or anti-thrombin deficiency, anti-phospholipid syndrome or hematologic disorders, and patients on oral contraceptive pills are at risk of developing MVT.[7]

Nonocclusive Mesenteric Ischemia

A profound drop in systemic blood pressure results in reflex mesenteric artery vasoconstriction in an attempt to divert the splanchnic circulation to brain and heart. This hampers the intestinal perfusion, resulting into intestinal hypoxia and necrosis giving rise to features of nonocclusive mesenteric ischemia (NOMI). As a result of this, certain endogenous vasoconstrictors get released into the systemic circulation giving rise to disseminated intravascular coagulation and reperfusion injury. Shock (septic or cardiogenic or hemorrhagic), acute myocardial infarction, elderly, renal or liver disease, or major abdominal surgery are certain risk factors for NOMI.[8]

Clinical Presentation

A "clinical triad" of acute-onset severe abdominal pain, diarrhea or vomiting, and presence of embolic source like atrial fibrillation is the most common presentation in embolic MI. The pain is generally referred as "out of proportion to the clinical signs" and does not have a localization point. The clinical course is manifested as severe pain in phase 1 suggestive of reversible ischemia, then some relief in phase 2, and followed by second bout of severe pain in phase 3, which refers to irreversible damage due to ischemia and peritonitis.[9]

Thrombotic occlusive disease is more challenging as it has an insidious course and have vague symptoms like abdominal pain and vomiting. The presence of atherosclerotic disease somewhere else and history of weight loss may suggest toward the diagnosis.

Mesenteric vein thrombosis is an uncommon condition and is generally associated with strong history of hypercoagulable states. Younger age group patients present with abdominal distension, dull aching abdominal pain, nausea, vomiting, and bloating. These symptoms evolve over few days.

Nonocclusive mesenteric ischemia clinical features are the most challenging as it is seen in very critically ill patients who are often sedated, ventilated, and cannot communicate their symptoms. Patients developing abdominal distension or abdominal pain and rectal bleeding should indicate toward NOMI. Intolerance to oral or enteral feeding should also raise the suspicion of NOMI. Patients receiving vasopressors, calcium channel blockers, or digoxin are at higher risk for NOMI.[10]

As the clinical features are very vague and nondiagnostic; a high index of suspicion is required to diagnose MI.

Diagnosis

Laboratory Parameters

Patients suspected of having MI are dehydrated due to decreased oral intake and abdominal third spacing. Laboratory abnormalities most commonly seen are neutrophilic leukocytosis, hemoconcentration due to reduced intravascular volume, lactic acidosis, and elevated anion gap acidosis. D-dimer has also been used to diagnose MI but it is nonspecific. Some patients may also have altered renal and liver parameters, raised serum amylase and lipase levels, and lactate dehydrogenase (LDH) levels.[11] Hyperphosphatemia and hyperkalemia appear late in the disease and are representative of bowel infarction. But as such, no laboratory studies are specific to MI.

Imaging

Plain Abdominal Radiograph

It is not useful in diagnosing MI as it is nonspecific unless there are features of bowel perforation and presence of free gas under diaphragm. Most of the patients have normal findings on abdominal radiography in initial stages of the disease.

Computed Tomography Scan

As per the American College of Radiology (ACR) Appropriateness Criteria, computed tomographic angiography (CTA) is the gold standard diagnostic modality for MI with sensitivity and specificity around 89 and 99%, respectively.[12] Computed tomographic angiography helps in evaluation of vascular as well as bowel abnormalities and also helps in evaluating alternative diagnosis of abdominal pain.

The biphasic CT protocol[12] is followed where an early arterial phase (over 30 seconds) and a delayed venous phase (over 60–70 seconds) are captured by contrast enhancement. The arterial phase highlights the vascular morphology of the mesenteric arteries as well as the collaterals, if any. The venous phase assesses the bowel wall and perfusion of other abdominal organs.

The CT findings in acute MI are shown in Box 2.

In NOMI, the CT findings are nonspecific but the diagnosis can be supported by the presence of the following features: (a) SMA origin narrowing, (b) irregular contours of the branches of SMA, (c) spasm of vessels, and (d) impaired filling of intramural vessels. Along with this, the history and the clinical situation of the patient guides toward the diagnosis.

Contrast CT in Acute Kidney Injury

When the clinical suspicion of MI is high, the contrast-enhanced CT scan should be performed even in the presence of AKI as the risk of delaying the diagnosis of MI is far more than the risk of worsening renal failure due to contrast-induced nephrotoxicity. Most of these patients are in prerenal AKI due to dehydration and third space losses.

Duplex Ultrasound

This modality can be used to assess for SMA stenosis and is mostly found in patients with chronic MI; however, the accuracy is variable as it is operator dependent and the presence of bowel gas may hamper the clear visualization of the mesenteric vessels and their course. Hence, it is not used nowadays for MI.[12]

Box 2: The CT findings in mesenteric ischemia

Ischemia-specific findings	*Nonspecific findings*
• Nonenhancement of bowel wall (most specific finding)[13]	• Bowel wall thickening
• Embolus seen in SMA (oval-shaped filling defect)	• Mesenteric fat stranding due to edema of mesentery
• Thrombosis of SMA (clot superimposed on a calcified lesion)	• Ascites in small subset of patients
• Mesentery edema due to MVT	• Luminal dilatation of the bowel due to intestinal paralysis
• Intestinal pneumatosis[13]	• Free gas due to bowel perforation
• Portomesenteric venous gas	• Other solid organ infarction (due to embolic shower)

SMA, superior mesenteric artery; MVT, mesenteric vein thrombosis

Endoscopy

It is not a good diagnostic tool as it can detect only the infarcted bowel and not the ischemic bowel. Second, it increases the risk of perforation as gas insufflation will increase the wall tension of the bowel wall and any potential weak spot may rupture.

Management

Basic Intensive Care Management

Fluid Resuscitation and Electrolyte Balance

All patients suspected of having MI should be managed in ICU. The initial management of patients with MI revolves around optimization of hemodynamic status. These patients should undergo fluid resuscitation with crystalloids and blood products as they have large volumes of third spacing due to ischemic bowel segments.[1]

These patients should have an invasive central venous catheter in place along with other vital monitoring including continuous urine output monitoring. Fluid resuscitation should be targeted and not overzealous as the risk of abdominal compartment syndrome is high in such patients. Intravesical pressure monitoring should be done intermittently to keep a check on intra-abdominal pressure (IAP). If IAP rises, then measures to tackle it should be undertaken.

Acid-base status monitoring should be performed as these patients are very prone to have metabolic acidosis and hyperkalemia due to infarction. As the acidosis worsens, it causes a rapid deterioration in hemodynamics and leads to systemic inflammatory response syndrome with ensuing risk of sepsis. Acidosis also causes myocardial depression and may lead to further hemodynamic compromise.

Vasopressors

Vasopressors should be avoided as far as possible in patients with ischemia as they will further reduce the mesenteric circulation. This is more problematic in sicker population as it may increase the risk of NOMI. If still required, drugs like dobutamine, milrinone, or low-dose dopamine[4] can still be considered as they cause minimal impairment of splanchnic blood flow. But even after this if the patient remains hemodynamically unstable, then administration of vasopressors like noradrenaline or adrenaline should be done.

Antibiotics

To counteract the massive gut bacterial translocation, patients with MI should be started on broad-spectrum antibiotics like the third-generation cephalosporin and metronidazole for anaerobic cover.[14] These antibiotics should be started even when there is no clinical evidence of sepsis. The risk of antibiotic resistance does not outweigh the risk of infection in these patients.

Nil Per Os

These patients should undergo nasogastric tube insertion and it should be kept on continuous drainage. They should be kept nil per mouth as it reduces the postprandial intestinal hyperemia and also keep these patients prepared for any emergency surgery.

Anticoagulant Therapy

If there are no contraindications to systemic anticoagulation, then intravenous unfractionated heparin infusion should be initiated to prevent the further progression of thrombotic process.[8] Unfractionated heparin is the drug of choice due to short half-life and an available antidote. There are many regimens of heparin administration but the most commonly preferred dose is 80 IU/kg as bolus followed by 18 IU/kg/hour infusion with the target of maintaining activated partial thromboplastin time (APTT) around 1.5–2 times the normal range (between 50 and 70 seconds).

Definitive Treatment

Endovascular Repair

If the expertise for endovascular repair is available, then all attempts should be made to establish mesenteric artery revascularization before subjecting any patient to surgical intervention unless there are clear signs of peritonitis and bowel perforation. The advantage of endovascular treatment is less morbidity as most of these patients belong to the geriatric age group and are critically sick. Moreover, open repair is associated with a surge of cytokine and endotoxin shock, which may be difficult to manage in such patients. Branco et al.[15] showed a mortality reduction to 23–26% in the endovascular group as compared to 36–56% in the open surgical group.

The target vessel (generally the SMA) can be approached by femoral or brachial access. Selective thrombectomy with or without administration of thrombolytic agent like alteplase or urokinase can be achieved. Prostaglandin E_1 is also administered to decrease the thrombus load.[16] Thrombus fragmentation should not be attempted as it increases the risk of peripheral embolization. Repeat angiography should be performed to assess the success of pharmacotherapy.

Stent placement can be performed if an underlying stenosis is documented. Balloon-expandable or self-expandable stents are placed depending on the location of the stenosis. Patients with NOMI should be given vasodilators like Alprostadil (PGE_1) for selective vasodilatation.

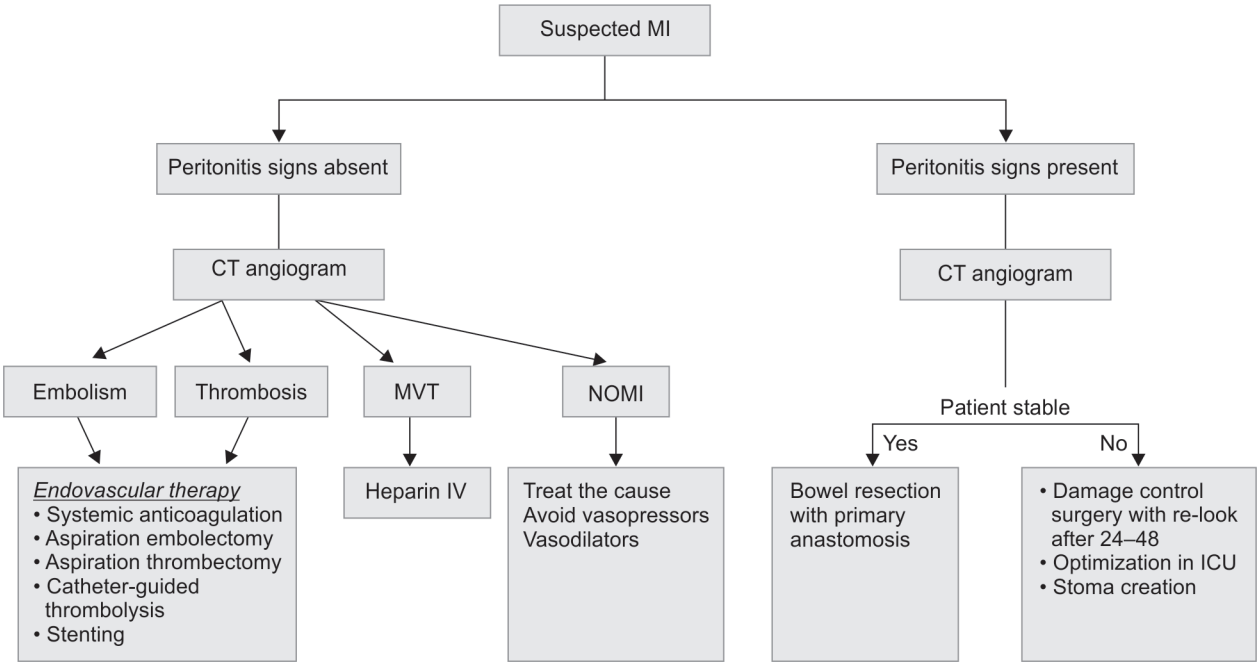
Surgical Repair

Surgical exploration should be considered when there are obvious signs of bowel perforation, peritonitis, or after failed endovascular therapy. The open laparotomy allows direct visualization of the infarcted bowel, resection of nonviable tissue, and helps in reestablishment of perfusion to the remaining bowel.[1] The decision of primary anastomosis should be taken very carefully on the basis of the intra-abdominal condition and sepsis. The risk of anastomotic dehiscence resulting in fulminant sepsis sometimes compels the surgeons to prefer creating a stoma of the healthy bowel and let the distal end heal.[17]

For the unstable patient, the most preferred technique is the "damage control surgery"[18] approach wherein the initial management revolves around resection of infarcted bowel, clearing of pus and fecal matter, and then just closing the skin for relook after 24–48 hours for the definitive procedure. During this time, the physiological restoration is attempted by careful fluid resuscitation in an attempt to avoid abdominal compartment syndrome, monitoring of lactate clearance, and transfusion of blood products to tackle coagulopathy. If the critical length of bowel cannot be saved, then patients have short bowel syndrome, which requires long-term parenteral nutrition and may even become a candidate of bowel transplant.

Certain patients with extensive bowel infarction may be deemed inoperable and probably palliative care is the best approach for such patients.

Flowchart 1: Clinical management plan for a patient with suspected mesenteric ischemia (MI). Fluid resuscitation, systemic anticoagulation, prophylactic antibiotics, and ICU care should be given to all category of patients



Patients with Nonocclusive Mesenteric Ischemia

Removal of the cause is probably the best treatment for NOMI, although it is not always possible due to critical underlying condition of the patient. Therapies like anticoagulation, vasodilators, and regional blockade to relive vasospasm and increase the blood flow have been tried. As the treatment options are limited for NOMI, the mortality is almost similar to patients with MI.

The clinical management plan for a patient with suspected MI is shown in Flowchart 1.

Postoperative Management

Infarcted bowel resection is associated with a surge of cytokines and other inflammatory mediators. These patients postoperatively may go into severe sepsis and multiorgan dysfunction. They would require high-quality intensive care hemodynamic monitoring with aggressive fluid resuscitation and vasopressor administration to optimize the hemodynamics. This is of more significance in patients who undergo a damage control surgery and will return to operation theater for a definitive procedure. Certain subset of patients may require renal replacement therapy for renal failure and metabolic lactic acidosis. The risk of secondary acute respiratory distress syndrome (ARDS) is high in these patients and may require prolonged ventilation.

Prognosis

Patients with advanced age, delayed diagnosis, lactic acidosis at presentation, NOMI, global small bowel ischemia, and arterial occlusion have poor 1-month outcome and is associated with high mortality. Similarly, patients undergoing damage-control surgery have a poor outcome due to high incidence of sepsis and multiorgan failure.

Conclusion

Mesenteric ischemia is a vascular emergency and prognosis of the patient depends on early diagnosis and timely revascularization of the occluded vessels either by the endovascular technique or by open repair. High-quality intensive care is a very important part in the management of acute MI.

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