Acute Mesenteric Ischemia: The What, Why, and When?
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Abstract
Acute mesenteric ischemia (AMI) is a complex clinical problem with a high mortality. The mortality associated with AMI has declined steadily over the last three decades. This is due to higher index of suspicion among clinicians, advances in radiographic diagnostic modalities, aggressive surgical approach, endovascular intervention, nutritional supplementation, and better perioperative care. Early diagnosis and prompt, effective treatment are essential to improve the clinical outcome. This article reviews the etiopathogenesis, clinical features, management, and outcomes of AMI.

Key Words: Acute, diagnosis, ischemia, management, mesenteric, outcome

Introduction
Acute mesenteric ischemia (AMI) has high mortality; it is difficult to handle the clinical scenario. With a reported incidence of 1–2 per 1000 hospital admissions, it is still a relatively uncommon condition.¹ The mortality associated with AMI has declined steadily over the last three decades. This is due to clinicians developing a higher index of suspicion for diagnosis, technological progress in radiological diagnostic modalities, aggressive operative intervention, endovascular management, nutritional supplementation, and better perioperative care.²⁻⁶ We find that diagnosis of AMI is more frequent in our practice with both early and late presentations. Despite these advances, diagnosis, and treatment of AMI is challenging. Prompt diagnosis leading to early effective treatment is essential for a good clinical outcome. There is no comprehensive study that addresses etiology and outcomes of patients diagnosed with AMI. Other than the results reported by Barmase et al.; there are no large series from India.²⁻⁷ There are few studies from Asia with varying mortality rates [Table 1].²⁻¹¹ This article reviews the etiopathogenesis, clinical features, management, and outcomes of AMI.

Classification
AMI can be classified into arterial, venous, occlusive, or nonocclusive etiologies. A wide range of conditions can present with AMI. These can be classified as embolic or thrombotic. The conditions range from hypercoagulability, paraneoplastic syndromes, sepsis, and pancreatitis, embolic occlusion secondary to cardiac or aortic emboli, shock, hypovolemia, vasopressor use, and abdominal compartment syndrome. These are depicted in Figure 1. The most common presentation is occlusive mesenteric arterial ischemia (70–50%) occur acutely due to mesenteric arterial embolism (AMAE). Acute mesenteric arterial thrombosis (AMAT) accounts for about 25%, nonocclusive mesenteric ischemia (NOMI) for 20%, and mesenteric venous thrombosis (MVT) for <10%.¹² Haghighi et al. noted that the incidence of MVT was more common (41.9%) than the arterial counterparts in Iran.¹⁰

Pathophysiology
The splanchnic circulation receives approximately 25% of the resting and 35% of the postprandial cardiac output. Seventy percent of the mesenteric blood flow is directed to the mucosal and submucosal layers of the bowel, with the remainder supplying the muscularis and serosal layers.¹⁰ Arterial insufficiency causes tissue hypoxia and mucosal shedding that may cause bleeding into the gastrointestinal tract. Interruption of vascular supply may cause reversible ischemia or transmural infarction with necrosis and perforation. With persistent ischemia; bacteria, toxins, and vasoactive substances are released into the systemic circulation resulting in septic shock, cardiac failure, or multisystem organ failure. As hypoxic damage worsens, the bowel wall becomes edematous and cyanotic. Dehydration

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and excessive third-space fluid loss lead on to hemodynamic instability. Bowel necrosis can occur within 8–12 h from the onset of symptoms. Perforation and peritonitis follow transmural necrosis and have a worse prognosis.[12]

**Presentation**

The clinical features of AMI are nonspecific. The differential diagnosis includes pancreatitis, perforated peptic ulcer disease, small bowel obstruction, acute diverticulitis, ischemic colitis, and acute cholecystitis. This is a clinical challenge as a high index of suspicion is essential to detect AMI and treat appropriately.

Patients with AMAE and AMAT present with sudden onset of symptoms. This caused due to lack of collateralization of the mesenteric vasculature. This causes a rapid clinical decline, whereas patients with NOMI and MVT have an insidious onset with a sub-acute course.

In AMAE, the severity of abdominal pain is disproportionate to the findings on physical examination. Other manifestations such as vomiting not responding to antiemetics, severe abdominal pain, nausea, melena, hematochezia, and diarrhea should raise red flags to suggest AMAE. Patients with fimbriae, myocardial infarction, congestive cardiac failure, and/or postaortic intervention are prone to develop AMI. Patients with AMAT frequently report prodromal symptoms of chronic intestinal insufficiency. These patients reach hospital later than those with AMAE. However, when this ischemia becomes acute on chronic, patients develop sudden worsening and have a clinical presentation similar to those with AMAE.

NOMI can occur in patients with the preexistent atherosclerotic disease who are subject to further acute hemodynamic challenge. Such patients are mostly elderly and critically ill and are often intubated and sedated. Therefore, the intestinal ischemia may not become clinically evident until hours or days after the initial hemodynamic insult. These patients frequently experience an unexplained worsening in their clinical condition or a failure to follow a recovery course. Treatment with alpha-adrenergic agonists predisposes to NOMI.

Patients with MVT typically present days to weeks after the onset of the insult, with abdominal pain that is nonspecific and diffuse. They complain of anorexia, loose stools that may be bloody or dark (hemocult-positive), abdominal distention or fever. Dehydration due to bloody ascites or third space fluid loss causes hypotension. This vicious cycle causes further clot propagation with worsening bowel edema leading to increased arterial ischemia. This finally leads to intestinal infarction. When this occurs, hemodynamic instability and peritonitis become clinically apparent, if untreated this can progress to sepsis or multiorgan dysfunction syndrome.

**Diagnosis**

The cornerstone of diagnosis is a high degree of clinical suspicion in the presence of risk factors, symptoms, and physical examination findings. Once suspected, the clinician should immediately start resuscitative efforts, administer broad spectrum antibiotics, confirm the diagnosis, and alert the general surgeons. Laboratory findings are nonspecific: These include metabolic acidosis with elevated anion gap, increased lactate levels, and elevated leukocyte counts. Plain abdominal X-rays are of limited value but serve to exclude other abdominal pathologies such as perforated viscus or intestinal obstruction. Rarely, pneumatosis intestinalis or portal venous pneumatosis can be appreciated on plain films, but these are extremely advanced signs and indicate a missed diagnosis.

Computerized tomography (CT) with intravenous contrast (CT angiogram-diaphragm to iliacs, plain water as negative bowel contrast) is a fast, effective and noninvasive test to confirm the diagnosis and identify the etiology.[13] It can assess the degree of bowel viability and rule out other causes of acute abdomen. Highly specific CT findings with specificity >95% for AMI include superior mesenteric artery (SMA) or superior mesenteric vein thrombosis, intestinal pneumatosis, portal venous gas, lack of bowel wall enhancement, and ischemia of other organs.[13] Further management depending on the specific etiology of AMI is detailed below. In patients with chronic kidney disease, in whom contrast CT might push them toward end-stage renal disease, laparoscopy may be a useful alternative to the diagnosis of bowel ischemia when the suspicious is high.
Use of newer modalities matrix metalloproteinase, myeloperoxidase, portomesentric venous blood gas, increased neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, procalcitonin, gastric tonometry, visfatin levels, urine fatty acid, and D-dimer has been studied but are not in routine clinical use.\textsuperscript{[14]}

**Management**

Once suspected, time is of the essence to improve the prognosis. Active resuscitation with crystalloids, initiation of broad-spectrum antibiotics, insertion of arterial and central lines, adequate analgesia along with input from critical care physicians, vascular surgeons, and anesthesiologists is paramount. Efforts should be made to avoid vasoconstrictors and digitalis to prevent worsening of the associated arterial spasm. This also deters intravascular coagulation. A summary of the treatment algorithm is depicted in Figures 2 and 3. Patients who are critically ill with signs of peritonitis or CT angiography (CTA) showing acutely ischemic bowel should undergo exploratory laparotomy without delay regardless of underlying etiology to assess intestinal viability. Signs of bowel viability are good (pink) intestinal color, strong peristalsis, and palpable mesenteric arterial pulsation. Other tests such as mesenteric arterial duplex ultrasonography, arterial fluorescein uptake test have a limited role when the diagnosis is in doubt.\textsuperscript{[15,16]} If the bowel viability is unclear, it is prudent to preserve it and reassess on second look laparotomy.\textsuperscript{[17]} Once bowel viability has been addressed then the causative pathology is tackled.

In noncritical patients, i.e., hemodynamically stable and nonperitonitic, the underlying pathology is addressed immediately by revascularization. This can be either via endovascular technique, surgical intervention, or systemic anticoagulation based on the etiology of the mesenteric ischemia.

Thromboembolectomy with patch or direct closure, mesenteric bypass (antergrade or retrograde; polyester or vein patch), endarterectomy, SMA-reimplantation, balloon angioplasty, thrombolysis, vasodilator infusion, bowel resection at a primary or second look surgery are the surgical procedures performed for AMI. There is no data on individual success/failure rates due to the heterogeneity of the patient population.\textsuperscript{[18-21]} Early complications arise from sepsis and multiorgan failure, recurrent mesenteric thrombosis, myocardial infarction, respiratory complications, and renal failure. Mortality rates are high with older age and necessity of massive bowel resection being poor prognostic factors. Late mortality occurs from cardiac causes, short bowel syndrome, recurrent mesenteric ischemia, cancer, pulmonary embolism, and total parenteral nutrition (TPN)-induced line sepsis.\textsuperscript{[18-21]} Use of prolonged TPN in the angiotensin-converting enzyme of short bowel syndrome is an option, but the cost and complications usually preclude long-term use. Small bowel transplantation has also been reported, but a significant proportion of elderly otherwise unfit patients may not be suitable candidates.

**Detailed management based on the etiology**

Arterial embolism usually originates in the heart in a patient with myocardial infarction, congestive cardiac failure, atrial fibrillation, left ventricular aneurysm, or valvular heart disease. The embolus lodges in the SMA a few centimeters distal to the orifice near the ostium of the middle colic artery. On diagnosis of embolism via CTA, exploratory laparotomy is performed, and the bowel is assessed for viability. The SMA is exposed in the root of the small bowel mesentery, and a transverse arteriotomy is made in the SMA, and the embolus is retrieved with Fogarty catheters [Figure 4]. After reconstitution of flow, the bowel is definitively addressed.

AMAT occurs in those who have preexisting mesenteric arterial stenoses. Symptoms of chronic mesenteric ischemia may be present in these patients.\textsuperscript{[21]} The nature of the thrombosis and presentation depends on the
extent of preexisting arterial insufficiency and extent of collateralization. Severely symptomatic patients with an acute abdomen should be taken up for emergency laparotomy proceed after diagnostic CTA, which usually reveals ostial SMA occlusion in a calcified artery. Options for surgical revascularization include an antegrade or retrograde bypass to the SMA from the supraceliac/infrarenal aorta or iliac arteries respectively depending on the status of these inflow vessels. Dacron can be used as the conduit if the bowel is not necrotic; saphenous vein is preferable if concomitant bowel resection is necessary. In patients with less acute symptoms presumably because of well-developed collaterals mesenteric arteriography with stenting of the SMA is a viable option with potentially lower morbidity and mortality. Postprocedure, the patient, is observed or taken to laparoscopy/laparotomy to evaluate the bowel based on the clinical status. Intraoperative retrograde stenting of the SMA during laparotomy is a superior option in patients presenting with peritoneal signs, especially when bowel resection is necessary.

NOMI is associated with the highest mortality rates due to associated co-morbidities and delay in diagnosis. A high index of suspicion is paramount for improving outcomes as no diagnostic evaluation, including CTA is confirmatory for the diagnosis except to rule out proximal SMA occlusion and other abdominal pathology. When a low flow state is suspected the patient should be taken to angiography. Selective SMA arteriography reveals spasm and low flow with a “chain of sausages” appearance. Treatment is with intra-arterial papavarine until relief of symptoms or confirmation of relief of spasm on repeat arteriography, in conjunction with avoidance of vasopressors and aggressive management of the underlying pathology.

MVT still carries a significant mortality and should be suspected in the setting of hypercoagulable states, dehydration, abdominal trauma, surgery, or inflammation as well as pancreatic/colon cancer. Systemic anticoagulation is the treatment of choice with improvement in the most patients. Surgical or endovenous thrombectomy/thrombolysis have not proved to be advantageous when attempted. Laparotomy is performed in cases with suspected bowel infarction. Bowel loss may be more extensive in these patients when compared to patients with arterial occlusion.

**Conclusion**

AMI is a relatively rare though challenging condition with delayed diagnosis associated with a dismal prognosis. With advances in diagnostic modalities and intervention, patients have a better outcome provided there is a high index of suspicion followed by prompt resuscitation and intervention.

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**Conflicts of interest**

There are no conflicts of interest.

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