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SMALL INTESTINE (D SACHAR, SECTION EDITOR)

Acute and Chronic Ischemic Disorders of the Small Bowel

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Abstract

Purpose of Review Ischemic disorders of the small bowel represent a rare but highly morbid disease process which is often difficult to diagnose and has a complex management course involving multidisciplinary care. Given recent advances in radiologic modalities and surgical/endovascular techniques, this review seeks to provide a disease overview as well as a summary of emerging management strategies.

Recent Findings In cases of acute mesenteric ischemia without evidence of frank bowel necrosis, an endovascular-first strategy employing thrombolysis, pharmacomechanical thrombectomy, and/or adjunctive angioplasty/stenting has been shown to have positive outcomes. In cases requiring open laparotomy, retrograde open mesenteric stenting may facilitate less dissection and more straightforward revascularization. While endovascular intervention for chronic mesenteric ischemia was historically limited by high rates of restenosis, use of covered stents in these vascular beds has been shown to have excellent patency rates.

Summary Ischemia of the small bowel can be acute or chronic in nature—endovascular treatment modalities have been shown to have excellent results given appropriate patient selection and should be an important tool in the armamentarium of management options for this complex disease process.

Keywords Mesenteric ischemia · Acute mesenteric ischemia · Chronic mesenteric ischemia · Endovascular · Open surgery · Thrombolysis · Angioplasty · Pharmacomechanical thrombectomy · Mesenteric bypass

Introduction and Disease Overview

Ischemic disorders of the small bowel represent a relatively rare, but very morbid disease processes which necessitate accurate diagnosis and appropriate treatment strategy selection by the clinician. The pathway of diagnosis and management often involves multiple specialties: Primary care physicians, internists, emergency physicians, radiologists, gastroenterologists, general surgeons, and vascular surgeons are all frequently involved in the care of these patients, and thus an interdisciplinary approach is paramount.

The small bowel is one of the most critical abdominal organs, responsible for nearly 90% of the body's nutritional absorptive functions. The length of the small bowel is variable, but typically ranges from four to 6 m. The small intestine can be subdivided into three parts (proximal to distal): the duodenum, jejunum, and ileum. The blood supply of the small intestine comes from various mesenteric vessels which branch off of the aorta. Additionally, key collateral networks help maintain consistent perfusion even in situations in which there is compromised flow through one of the mesenteric vessels. The first portions of the duodenum and the stomach both have an embryologic origin in the foregut. As such, the blood flow is derived from the celiac axis, the first major mesenteric branch off of the aorta. The rest of the duodenum along with the jejunum and ileum derive blood supply from the superior mesenteric artery. The superior mesenteric artery (SMA) takes off from the anterior aorta at an acute angle ranging from 25 to 60° [1]. The SMA subsequently gives rise to the following major branches: inferior pancreaticoduodenal, middle colic, right colic, and ileocolic. These branches, along with interconnecting vessels, form a network of arcades which ultimately lead to end arteries, known as the vasa recta, which directly perfuse the small intestine wall [2].

Ischemia of the intestines can be defined as inadequate perfusion through the mesenteric vasculature to meet the demands of downstream organs. The condition, while rare, can result in a very symptomatic and life-threatening clinical

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presentation. Intestinal, or mesenteric, ischemia is generally divided into *acute mesenteric ischemia* and *chronic mesenteric ischemia*. This work aims to review in brief the epidemiology, pathogenesis, clinical manifestations, and diagnostic modalities of mesenteric ischemia, and will provide a special focus on the emerging literature as it pertains to the management of this condition.

Acute Mesenteric Ischemia

Epidemiology and Pathogenesis

There is a lot of variation in the present literature: acute mesenteric ischemia (AMI) is thought to have an incidence ranging from 0.63 per 100,000 person years in a UK population–based study to 12.9 per 100,000 patient years in an autopsy based Swedish population study. AMI accounts for less than 1/1000 hospital admissions, but carries a mortality rate which ranges from 30 to 90% [3•].

There are four distinct pathophysiologic processes which can result in the clinical manifestation of acute mesenteric ischemia: acute embolism, acute arterial thrombosis, mesenteric venous thrombosis, and non-occlusive mesenteric ischemia (NOMI). Acute embolism is the most common cause of AMI, representing 30–50% of cases. This is often seen in the context of atrial fibrillation, structural or ischemic heart disease, and other cardiac impairments. Emboli are most commonly directed into the superior mesenteric artery, given the relatively low aorto-mesenteric take-off angle. The caliber of the superior mesenteric artery narrows significantly after the take-off of the middle colic artery, and thus emboli often lodge at this location, resulting in ischemia of the jejunum, ileum, and proximal colon, while sparing the duodenum and transverse colon. Arterial thrombosis accounts for approximately 15–30% of AMI cases. Non-laminar blood flow around vessel branch points make the ostia of mesenteric vessels a common location for the development of atherosclerotic disease. Acute thrombosis often occurs at this location, resulting in an occlusion of blood flow at a level that is typically more proximal to that seen in embolic AMI. The result is a larger amount of ischemic bowel and consequently a higher mortality rate—up to 90% in a number of studies (Herbert et al). Mesenteric venous thrombosis accounts for 5–15% of all AMI cases, and almost always involves the superior mesenteric vein [4]. This is often associated with portal hypertension, cirrhosis, malignancy, or other hypercoagulable states. Finally, non-occlusive mesenteric ischemia (NOMI) occurs during low-flow states in the absence of acute arterial or venous occlusion. NOMI accounts for 20–30% of all AMI cases and is most commonly seen in elderly patients with diminished cardiac, hepatic, and renal function. Increasingly, it has been documented in end-stage renal disease patients following the hemodynamic shifts of dialysis sessions. A systemic low-flow or hypotensive state results in (a) a reduced peripheral/mesenteric perfusion at baseline and (b) the triggering of sympathetic responses which cause further mesenteric vasoconstriction and vasospasm [5].

Clinical Manifestations and Diagnosis

Patients with AMI often present with severe abdominal pain, in addition to a variety of non-specific abdominal complaints including nausea, vomiting, and diarrhea. Patients may present with septic shock secondary to ischemic or necrotic bowel and may be at imminent risk of hemodynamic compromise. While laboratory tests, such as an elevated serum lactate level or a leukocytosis can increase the clinical suspicion for AMI, imaging is required for a more definitive diagnosis. Abdominal radiographs offer limited information—the findings of pneumatosis intestinalis and pneumobilia are ominous signs indicative of late ischemia [6]. CT angiography has been shown to have a sensitivity of approximately 94% and a specificity of 95% [7]. Biplanar mesenteric angiography is widely accepted as the gold standard for diagnosis of AMI and offers the added benefit of possible therapeutic intervention [8].

Chronic Mesenteric Ischemia

Epidemiology and Pathogenesis

Chronic mesenteric ischemia (CMI) is a disease process that develops over an extended period of time secondary to atherosclerosis. Accurate epidemiological estimates are difficult to obtain since not all patients are accurately diagnosed during their lifetime. It is thought that less than one in every 100,000 admissions is due to CMI. Due to the presence of the aforementioned collateral networks, the clinical manifestations of chronic mesenteric ischemia typically occur when at least two out of the three mesenteric vessels have either an occlusion of a high-grade stenosis [9]. Under normal physiologic conditions, there is a hyperemic response in the immediate postprandial state; the resultant vasodilation allows for the intestinal organs to meet the increased oxygen demands of digestion. In patients with CMI, the hyperemic response is inadequate to meet those needs due to the presence of atherosclerotic stenosis or occlusion [10]. The result is the development of abdominal symptoms as described below as well as an increased risk of progression to bowel gangrene or necrosis if there is an additional acute insult.

Clinical Manifestations and Diagnosis

While most patients with atherosclerotic disease of the mesenteric vessels remain asymptomatic, the classic symptomatic

presentation in CMI is the finding of post-prandial abdominal pain and associated weight loss. Often it is noted to be a dull, cramping epigastric pain approximately 1 h after oral intake. It is thought that this occurs due to transient small bowel hypoperfusion while blood flow is preferentially shunted to the stomach [11]. Patients often lose weight over time as a result of food fear.

Diagnosis is often dependent on high clinical suspicion, and a variety of other abdominal pathologies are often considered and worked-up prior to the consideration of CMI. As with AMI, computed tomography is a very important diagnostic modality which provides information not just about the presence of atherosclerotic disease but also possible extrinsic factors such as compressive tumors which may be contributing to the clinical presentation. Duplex ultrasonography has a sensitivity/specificity of 92%/96% for detecting SMA stenosis > 70% (based on peak systolic velocity cutoff > 275 cm/s); and a sensitivity/specificity of 87%/82% for detecting celiac stenosis > 70%. This is a useful modality in the outpatient setting and is frequently employed in the post interventional surveillance setting [12].

Treatment Options for Acute and Chronic Mesenteric Ischemia

The interventional and operative management of mesenteric ischemia is an actively evolving field. Here, we review both the longstanding standard of care as well as emerging data on novel therapeutic approaches. Selecting the appropriate management strategy is dependent on both the etiology and the acuity of the mesenteric ischemia. Generally, if there is a high suspicion for dead bowel based on clinical examination or imaging, a laparotomy is warranted to assess the viability of the bowel. In these scenarios, a mesenteric angiogram is not performed as it would waste valuable time.

Historically, in the case of AMI secondary to an embolic etiology, a laparotomy with open SMA embolectomy is performed in addition to possible bowel resection in the case of necrotic bowel. A second look laparotomy is often warranted 24–48 h after the index case to reassess bowel viability. In the case of AMI secondary to thrombosis, there is almost always underlying atherosclerotic disease at the location of occlusion. The operative standard of care is to perform a vascular reconstructive procedure in order to bypass the site of thrombosis. Autologous vein graft is used to reduce the risk of infection, given the high likelihood of bacterial translocation in the setting of ischemic bowel. Mesenteric bypass can be performed using either the supraceliac aorta or the iliac artery as the inflow vessel. In recent years, endovascular intervention for AMI has become increasingly ubiquitous. A number of studies have demonstrated improved mortality and lower complication rates with endovascular therapy for AMI in comparison to open surgery [13]. It is important to keep in mind that there may be a strong selection bias whereby sicker patients with clinical signs of peritonitis are managed with open laparotomy in order to assess bowel viability, and likewise it may be possible that only patients with anatomically favorable characteristics on imaging (i.e., limited tortuosity and adequate landing zones) are chosen for endovascular intervention. That being said, for the appropriately selected patient, there is increasing evidence that an endovascular approach may offer a quicker, effective, and less morbid alternative to open surgery. In a large retrospective analysis of 70 consecutive patients with AMI, Arthurs and colleagues reported that an endovascular approach was used in 81% of cases, with 69% of these patients subsequently requiring laparotomy. An 87% technical success rate for endovascular intervention was reported with a statistically significant reduction in mortality among successful endovascular interventions when compared with primary laparotomy (36 vs 50%) [14•].

Endovascular interventions for AMI can be broadly divided into the following categories: thrombolysis, pharmacomechanical thrombo-embolectomy, and balloon angioplasty/stenting. In the aforementioned retrospective analysis, these methods were employed in 48%, 12%, and 33% of endovascular cases respectively [14•]. Often two or more of these methods are often used in an adjunctive manner.

Thrombolysis for Acute Mesenteric Ischemia

Intra-arterial thrombolysis involves the placement of a lysis catheter at the level of arterial occlusion, with a lytic agent such as tPA being run as a continuous drip for a period of time ranging up to 48 h. This technique has been used with success in early AMI without signs of peritonitis. It can be performed as a stand-alone treatment or alongside adjunctive additional endovascular therapy. A retrospective review of thrombolysis performed for AMI in Sweden over a 20-year period found that successful thrombolysis was indeed associated with a reduction in mortality. Eighty-eight percent of patients undergoing a thrombolysis procedure had either a partial or complete lysis response, with 47% of all patients undergoing an adjunctive endovascular procedure and 38% of patients subsequently undergoing a laparotomy. Twenty-four percent of patients ultimately went on to have a bowel resection. The majority of patients had acute occlusion of an embolic etiology, and the authors concluded that embolic AMI may be better suited for thrombolysis than thrombotic AMI since there is less surrounding atherosclerotic disease, thus potentially allowing a lysis infusion catheter to be more effective [15].

Pharmacomechanical Thrombo-Embolectomy for Acute Mesenteric Ischemia

There are a number of devices and techniques which have been employed for the percutaneous removal of embolic or

thrombotic occlusions via pharmacomechanical methods. This offers a faster alternative to thrombolysis which often requires many hours to take effect. Aspiration thrombectomy involves the use of direct suction to remove clot burden (Ierardi 2017) [16•]. Multiple authors have reported the use of the Rotarex device; a device which rotates around a wire at 40,000 rpm, a process which fragments the thrombus and creates sufficient vacuum to allow for aspiration [17, 18]. The Indigo System (Penumbra, Inc.) is a device which uses a combination of mechanical clot breakdown via passing of a wire repeatedly through the clot in combination with suction aspiration (Ierardi 2017). The AngioJet mechanical thrombectomy device injects high-pressure saline in a pulsed manner in order break up thrombus and is coupled with subsequent suction aspiration. The EKOS catheter on the other hand uses ultrasonic vibration to break up clot [19]. All of the aforementioned devices have been used with technical success in AMI cases and notably offer the possibility of reperfusion much faster than a thrombolysis infusion.

Angioplasty/Stenting for Acute Mesenteric Ischemia

The use of balloon angioplasty with or without stenting is another endovascular approach to the management of AMI. Whereas this technique had been used in the past in patients with CMI, VanDenise and colleagues reported the first successful use of percutaneous transluminal balloon angioplasty in a patient with AMI in 1986 [20]. In this case report, the authors described using gradient pressure measurements to identify a critical stenosis with the subsequent inflation of a 7-mm balloon in the superior mesenteric artery. The patient had presented with peritoneal signs, however, had a complete symptomatic resolution within 24 h of intervention thus averting a laparotomy. A number of other authors have also reported success with the use of balloon angioplasty as well as the adjunctive deployment of stents, and have begun to adopt an endovascular-first approach to revascularization followed by laparotomy only as necessitated by the subsequent clinical response. Karkkainen and colleagues described an 88% technical success rate of initial endovascular intervention in 50 patients. Of these 29 patients underwent primary angioplasty/stenting whereas 17 patients underwent mechanical thrombectomy [21]. A retrospective analysis of prospectively collected data of over 10,000 patients with intervention for AMI over a 10-year period demonstrated that patients with endovascular intervention, defined as angioplasty or stenting in this study, had lower in-hospital mortality and an approximate cost savings of over $9000 per hospitalization [22•].

Hybrid Endovascular-Open Procedures in Acute Mesenteric Ischemia

Despite the advances in endovascular therapy, an immediate laparotomy may still be warranted when the clinical presentation or imaging findings are strongly concerning bowel ischemia. In the case of thrombotic AMI, revascularization was traditionally performed via an open antegrade (originating from the supraceliac aorta) or retrograde (originating from the iliac artery) bypass or endarterectomy. Retrograde open mesenteric stenting, or ROMS is a hybrid approach to management in patients who are already undergoing laparotomy. Rather than performing extensive surgical dissection and conduit vein harvest, the vessel of interest (typically the superior mesenteric artery) is exposed and controlled. The vessel is then directly punctured and retrograde wire access is obtained, facilitating the treatment of the proximal thrombotic occlusion via endovascular methods after an initial open dissection. ROMS is also a viable alternative in patients whose anatomy is not conducive to a percutaneous antegrade endovascular approach—usually due to extensive aortic wall and mesenteric ostial atherosclerosis [23]. ROMS is a procedure typically performed in patients who are very ill on presentation, and thus despite a high technical success rate as high as 98%, mortality remains very high (upwards of 39%) [22•].

Management of Chronic Mesenteric Ischemia

In contrast to AMI, the management of CMI is typically undertaken in an elective manner. Ostial atherosclerotic lesions can be treated via a transaortic endarterectomy, whereas more distal occlusive lesions can be treated via a mesenteric bypass procedure. Mesenteric bypass can be performed in either an antegrade or retrograde manner. In an antegrade bypass, the supraceliac aorta is used as the arterial inflow, whereas a retrograde bypass utilizes the infrarenal aorta or iliac artery flow. The antegrade approach allows the bypass to sit in an anatomically more favorable position which is less susceptible to kinks. The retrograde approach allows for aortic cross-clamping to be avoided—this is particularly advantageous in patients with poor cardiac function or circumferential plaque in the supraceliac aorta [24]. In recent years, there has been a shift towards a primary endovascular approach for a majority of CMI patients, especially those presenting with anatomically favorable lesions, or lesions with recurrent stenosis following open intervention. Schermerhorn and colleagues performed an analysis using all patients undergoing mesenteric revascularization in the Nationwide Inpatient Sample between 1988 and 2006. They found that beginning in 2002, the volume of endovascular interventions for CMI surpassed the volume of all open surgical procedures performed. Notably, mortality was significantly lower with angioplasty/stenting for both CMI (3.7 vs 13%) as well as AMI (16 vs 28%) when compared to open surgery [25]. While historically primary mesenteric balloon angioplasty was performed with stenting employed for select lesions with high-risk features, there has been a shift towards primary stenting given high recoil and restenosis rates with angioplasty [26]. Unfortunately, endovascular interventions for mesenteric ischemia have been met with rates of high rates of restenosis, with patency rates at 2 years being as low as 60% [27]. In

light of increasing evidence that covered stents offer improved patency rates compared to bare metal stents in other vascular beds, there has been an increasing trend towards the use of covered stents for mesenteric applications as well. In a retrospective analysis of 225 patients across two institutions, Oderich and colleagues reported a 92% primary patency rate and a 100% secondary patency rate at 3 years when compared with a 52% primary patency rate and a secondary patency rate above 90% with bare metal stenting [28]. Two randomized controlled trials, one in the Netherlands and one in France, are currently underway to directly compare the use of bare metal and covered stents for chronic mesenteric ischemia.

Emerging Concepts in Management of Acute and Chronic Mesenteric Ischemia

Embolic Protection Devices

Embolic protection devices (EPD) are commonly used in both coronary and carotid endovascular procedures in order to prevent the risk of clinically significant distal embolization which may result as the result of the intraluminal manipulation inherent to the procedure itself. In recent years, it has been demonstrated that angioplasty and stenting of the mesenteric vessels may similarly pose a risk of distal embolization [29]. Recently, some vascular surgeons have begun employing EPDs in select endovascular interventions for mesenteric ischemia. In 2018, Mendes and colleagues reported a retrospective analysis of 179 consecutive patients who underwent SMA stenting for both AMI and CMI; EPDs were used in 36% of these cases. The authors reported technical feasibility of using EPDs in the mesenteric vasculature, and found that 66% of patients with EPD placement had macroscopic debris material identified. Major debris was more common in patients presenting with AMI when compared with CMI, in patients with total occlusions, and in patients with concomitant calcification, thrombus, and occlusion. It is important to note that this work by Mendes and colleagues does not offer a head to head comparison of outcomes between patients who underwent intervention with EPDs versus those who underwent intervention without EPDs. The authors offer the following general indications for EPD use: chronic occlusions, lesions longer than 3 cm with greater than 66% luminal or circumferential calcification, and acute/subacute symptom presentation. However, these indications were not absolute and surgeons additionally used EPDs at their discretion [30]. The use of EPDs in mesenteric vascular intervention is an evolving topic with a paucity of literature at the present. The work by Mendes and colleagues is one of the only studies reporting outcomes with EPD use—while it offers proof of technical success and recommendations for use, further investigation is necessary to establish guidelines for practice with regard to embolic protection.

Conclusion/Discussion

Acute and chronic ischemic disorders of the small bowel remain rare but clinically significant entities owing to the high associated morbidity and mortality. While imaging modalities, namely CT angiography, have become the gold standard for diagnosis, there is often a dearth of clinical suspicion which leads to delays in diagnosis. Historically, management for mesenteric ischemia has revolved around open surgery: in the case of acute thrombotic mesenteric ischemia and chronic mesenteric ischemia, this usually involves a bypass procedure, while in the case of acute embolic mesenteric ischemia, a surgical embolectomy is performed. There has been a gradual shift towards endovascular management of chronic mesenteric ischemia over the past two decades. At present, most institutions favor primary balloon angioplasty and stenting in patients with favorable anatomy. The need to assess the bowel for viability has made endovascular management of acute mesenteric ischemia more difficult. In recent years, a number of practitioners have begun to use a primary endovascular approach in cases of acute mesenteric ischemia in patients without obvious signs of peritonitis. In this review, we outline a number of different emerging approaches to endovascular management of acute mesenteric ischemia including catheter-directed thrombolysis, pharmacomechanical thrombectomy using a number of currently available devices, and balloon angioplasty/stenting. In appropriately selected patients, an endovascular-first approach can reduce the need for laparotomy by over 30%, and successful endovascular intervention has a lower mortality rate when compared with open surgery. The adoption of new devices, including embolic protection devices, continues to make endovascular management an increasingly preferrable strategy.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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