

*Current Concepts***MESENTERIC VENOUS THROMBOSIS**

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**M**ESENTERIC venous thrombosis was recognized as a cause of intestinal gangrene more than a century ago by Elliot,<sup>1</sup> but Warren and Eberhard<sup>2</sup> were the first to characterize mesenteric venous thrombosis as a cause of intestinal infarction distinct from mesenteric arterial occlusion. Mesenteric venous thrombosis accounts for 5 to 15 percent of all mesenteric ischemic events<sup>3</sup> and usually involves the superior mesenteric vein; the inferior mesenteric vein is involved only rarely.<sup>4</sup> The diagnosis is often delayed, and most cases are identified either at laparotomy or at autopsy. Improvements in imaging techniques have led to early diagnosis, and a better idea of the cause of mesenteric venous thrombosis has led to changes in treatment.

**NORMAL MESENTERIC CIRCULATION**

The superior mesenteric artery arises from the abdominal aorta just distal to the celiac trunk and has several branches to the pancreas and duodenum, two large branches that supply the proximal two thirds of the colon, and an arcade of arterial branches that supply the jejunum and ileum, terminating as the arteriae rectae of the small bowel. The venous drainage follows a similar pattern, with the venae rectae forming a venous arcade that drains the small bowel and proximal colon through the ileocolic, middle colic, and right colic veins to form the superior mesenteric vein (Fig. 1). The superior mesenteric vein and the splenic vein join and continue to the liver as the portal vein.

**PATHOGENESIS OF MESENTERIC VENOUS THROMBOSIS**

Mesenteric venous thrombosis is classified as either primary or secondary. When an etiologic factor is found, patients are said to have secondary mesenteric venous thrombosis (Table 1). The proportion of pa-

tients with primary, or idiopathic, mesenteric venous thrombosis continues to decline as our ability to diagnose inherited thrombotic disorders<sup>5</sup> and to recognize hypercoagulable states<sup>6</sup> improves. Currently, an etiologic factor can be identified in about three quarters of patients. The most common causes are prothrombotic states due to heritable or acquired disorders of coagulation or to cancer, intraabdominal inflammatory conditions, the postoperative state, and cirrhosis and portal hypertension. Oral-contraceptive use accounts for 9 to 18 percent of the episodes of mesenteric venous thrombosis in young women.<sup>5,7</sup> Although certain hypercoagulable disorders such as resistance to activated protein C and prothrombin mutations can be identified by molecular methods, the use of plasma measurements to diagnose protein C, protein S, and antithrombin III deficiencies can result in errors because plasma levels of these proteins can be falsely low in the presence of acute thrombosis.

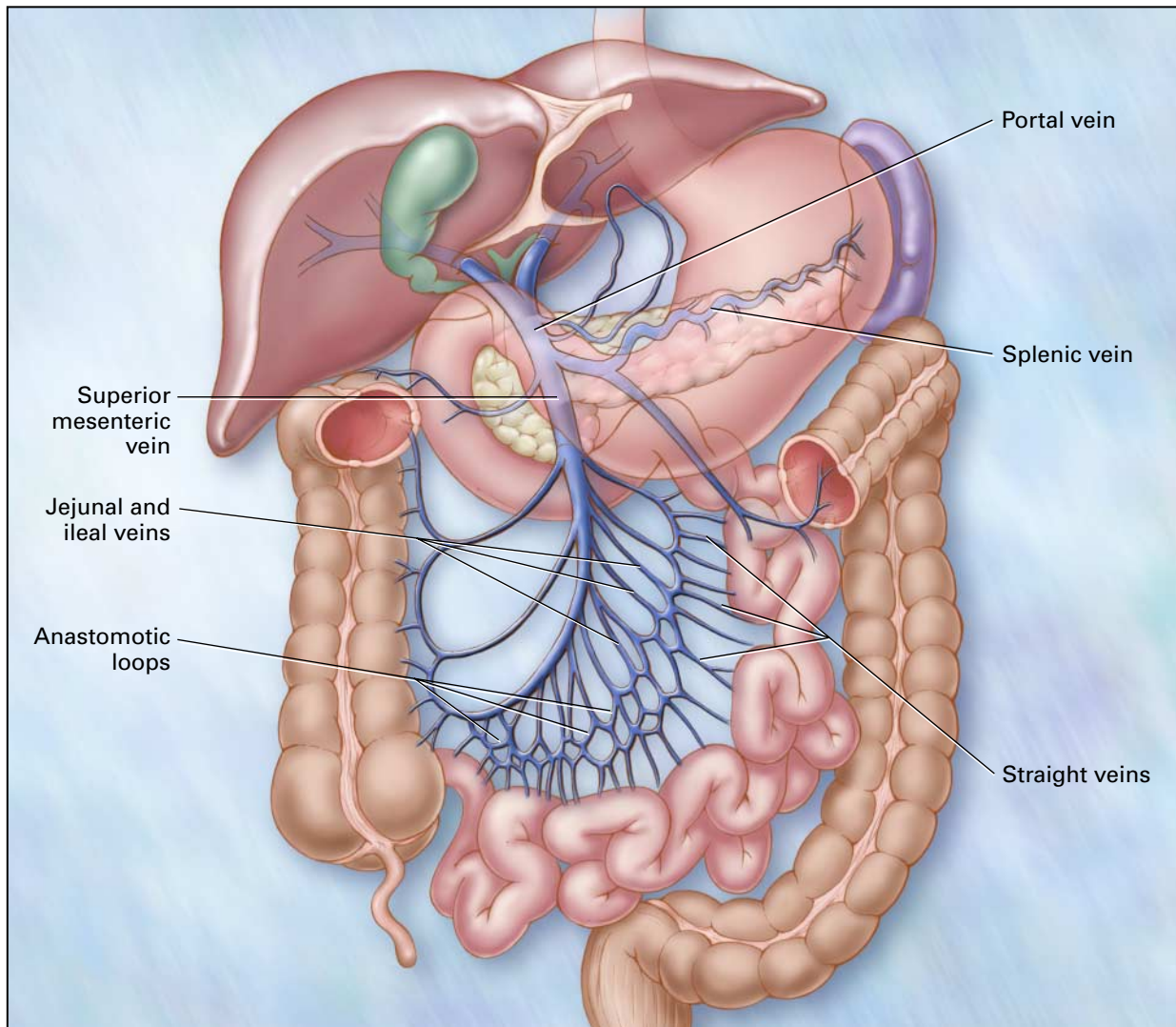
Mesenteric venous thrombosis appears to be a manifestation of a hypercoagulable state resulting from or exacerbated by an event such as pancreatitis or surgery. The clinical manifestations depend largely on the extent of the thrombus, the size of the vessel or vessels involved, and the depth of bowel-wall ischemia. When ischemia is restricted to the mucosa, the manifestations consist of abdominal pain and diarrhea; transmural ischemia leads to necrosis, with gastrointestinal bleeding, perforation, and peritonitis.

The location of the thrombus may be determined on the basis of the underlying cause. Thrombosis due to intraabdominal causes starts in the larger vessels at the site of compression and then progresses peripherally to involve the smaller venous arcades and arcuate channels. In contrast, thrombosis due to underlying prothrombotic states begins in the small vessels and progresses to involve the larger vessels. Occlusion of the venae rectae and the intramural vessels interferes with venous drainage, with subsequent hemorrhagic infarction of the involved bowel segment. The transition from ischemic to normal bowel is usually gradual, unlike that seen with arterial occlusion.

**CLINICAL PRESENTATION**

Mesenteric venous thrombosis can be acute, subacute, or chronic.<sup>8</sup> Acute mesenteric venous thrombosis is diagnosed in patients whose symptoms begin suddenly, the subacute form in those who have abdominal pain for days or weeks without bowel infarction, and the chronic form in those who present with complications of portal-vein or splenic-vein thrombosis such as esophageal variceal hemorrhage. Acute thrombosis is associated with a definite risk of bowel

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**Figure 1.** Normal Mesenteric Venous Circulation.

infarction and peritonitis. In patients with subacute mesenteric venous thrombosis, abdominal pain is prominent, but neither bowel infarction nor variceal hemorrhage is likely. Patients with chronic mesenteric venous thrombosis do not have pain and have extensive venous collateral circulation. Management is therefore geared toward preventing variceal hemorrhage. In rare instances, patients with a long history of abdominal pain may have an intestinal infarction, thus blurring the distinction between acute and subacute presentation. Accordingly, the following discussion focuses on acute and subacute mesenteric venous thrombosis together; the chronic form will be addressed separately.

The hallmark of mesenteric ischemia, whether it

is due to arterial or to venous thrombosis, is abdominal pain that is not explained by the physical findings (Table 2). The abdominal pain of acute or subacute mesenteric venous thrombosis is midabdominal and colicky, suggesting an origin in the small bowel. Although the duration of symptoms varies, 75 percent of patients have had symptoms for more than 48 hours before they seek care.<sup>9</sup> Nausea, anorexia, vomiting, and diarrhea are also common. Hematemesis, hematochezia, or melena occurs in about 15 percent of patients,<sup>8</sup> but occult blood will be detectable in the stool in nearly 50 percent of patients.<sup>7</sup> The nonspecific nature of the abdominal symptoms and the rarity of the condition often delay the diagnosis. About half the patients have a personal or family his-

**TABLE 1. CAUSES OF MESENTERIC VENOUS THROMBOSIS.**

Prothrombotic states
Antithrombin III deficiency
Protein C deficiency
Protein S deficiency
Factor V Leiden
G20210A mutation in prothrombin gene
Antiphospholipid antibodies
Hyperhomocysteinemia
Oral-contraceptive use*
Pregnancy
Neoplasms*
Hematologic disorders
Polycythemia vera*
Essential thrombocythemia*
Paroxysmal nocturnal hemoglobinuria*
Inflammatory diseases
Pancreatitis*
Peritonitis and intraabdominal sepsis*
Inflammatory bowel disease
Diverticulitis
Postoperative state
Abdominal operations*
Splenectomy
Sclerotherapy for esophageal varices
Cirrhosis and portal hypertension
Miscellaneous causes
Blunt abdominal trauma
Decompression sickness

\*This factor is among the more common causes of mesenteric venous thrombosis.

tory of deep venous thrombosis or pulmonary embolism.<sup>4,9</sup> The initial physical findings may be entirely normal. Fever, guarding, and rebound tenderness develop later and indicate progression to bowel infarction; peritonitis develops in one third to two thirds of patients with acute mesenteric venous thrombosis. Hemodynamic instability can result from the collec-

tion of fluid within the bowel lumen or the abdominal cavity, and systolic pressures of less than 90 mm Hg denote a poor prognosis.<sup>8</sup>

Patients who present with postprandial symptoms may be mistakenly thought to have a peptic ulcer, and those with diarrhea may be assumed to have an intestinal infection or Crohn's disease. When severe abdominal pain is the sole symptom, pancreatitis is often suspected. The onset of ascites in a patient with a history or family history of thrombotic disease should heighten the clinical suspicion of mesenteric venous thrombosis.

## DIAGNOSIS

Routine blood tests are not helpful in the diagnosis of mesenteric venous thrombosis. The presence of increased serum lactate levels and metabolic acidosis may serve to identify patients with established bowel infarction, but this is a late finding. Abdominal films are abnormal in 50 to 75 percent of patients<sup>3</sup> but have findings specific for bowel ischemia in only 5 percent. Blunt, semiopaque indentations of the bowel lumen (thumbprinting) are indicative of mucosal edema, whereas gas in the wall of the bowel (pneumatosis intestinalis) or in the portal vein and free peritoneal air are characteristic of bowel infarction as a result of mesenteric venous thrombosis.<sup>10</sup> Barium contrast studies should be avoided in patients suspected of having acute mesenteric venous thrombosis.

Transabdominal color Doppler ultrasonography<sup>11</sup> may demonstrate thrombus in the mesenteric veins, but computed tomography (CT) is the test of choice for suspected cases of mesenteric venous thrombosis. Although CT will establish the diagnosis in 90 percent of patients,<sup>7,9,12</sup> it is less accurate in those with early thromboses of small mesenteric vessels. An acute

**TABLE 2. COMPARISON OF ACUTE MESENTERIC VENOUS THROMBOSIS AND ACUTE MESENTERIC ARTERIAL THROMBOEMBOLISM.**

VARIABLE	VENOUS THROMBOSIS	ARTERIAL THROMBOEMBOLISM
Risk factors	Prothrombotic states Inflammatory bowel disease Abdominal cancer	Atherosclerotic vascular disease Valvular heart disease Arrhythmias
Abdominal pain	Insidious onset	Sudden onset with embolic disease
Tests		
Plain films	Usually nonspecific	Usually nonspecific
Computed tomography	Sensitivity of more than 90%	Sensitivity of approximately 60%
Mesenteric angiography	Not usually required for diagnosis	Often helpful
Involvement of inferior mesenteric vessels	Uncommon	Common
Operative findings		
Mesenteric arterial pulsations	Preserved except late in disease	Absent
Type of transition from ischemic to normal bowel	Gradual	Abrupt
Therapy		
Thrombolysis	Rarely useful	Often useful
Long-term anticoagulation	Indicated	Indicated
Sequelae	Short bowel, varices	Short bowel

thrombus is evident as a central lucency in the mesenteric vein (Fig. 2). Other CT findings are enlargement of the superior mesenteric vein and a sharply defined vein wall with a rim of increased density. Persistent enhancement of the bowel wall, pneumatosis intestinalis, and portal-vein gas are late findings.<sup>8</sup> The finding of a well-developed collateral circulation in the mesentery and retroperitoneum indicates mesenteric venous thrombosis of more than a few weeks' duration.

Selective mesenteric angiography will demonstrate thrombus in the larger veins, or there may be late visualization of the superior mesenteric vein. Other findings include impaired filling of mesenteric veins, arterial spasm, and prolonged opacification of the arterial arcades.<sup>13</sup> Magnetic resonance imaging has excellent sensitivity and specificity for the diagnosis of mesenteric venous thrombosis,<sup>14</sup> but its use is cumbersome and the equipment is not universally available. Further advances in the technique may eventually establish a place for magnetic resonance imaging in the diagnosis of mesenteric venous thrombosis.

Abdominal paracentesis is sometimes helpful, because patients with acute mesenteric venous thrombosis may have serosanguineous ascites.<sup>3,15</sup> Laparoscopy is best avoided, because the increased abdominal pressure associated with the procedure decreases mesenteric blood flow. Gastroduodenoscopy and colonoscopy are of limited value, given the rarity of colonic

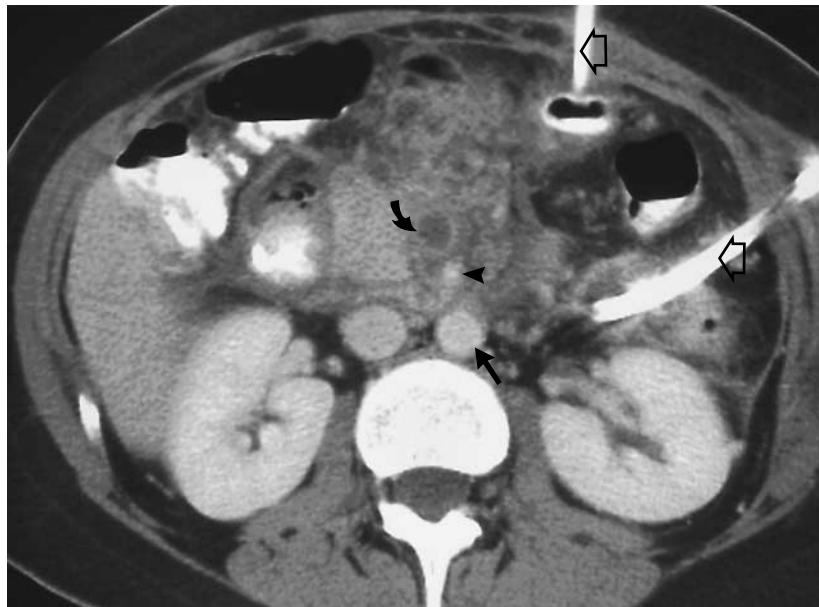
and duodenal involvement. Endoscopy with duplex Doppler ultrasonography may detect thrombosis of mesenteric vessels,<sup>16</sup> but given the bowel distention associated with this procedure, it is best restricted to patients who do not have acute symptoms.

We recommend abdominal CT in patients who are suspected of having mesenteric venous thrombosis. CT shows the mesenteric vessels and may define the extent of affected bowel, while it rules out other conditions that can cause abdominal pain. Mesenteric angiography should be reserved for patients with a history of thrombophilia in whom small-vessel mesenteric venous thrombosis is suspected.

Once mesenteric venous thrombosis has been confirmed, patients should be screened for hereditary or acquired thrombophilia with tests for protein C and protein S deficiencies, factor V Leiden and other mutations, hyperhomocysteinemia, and paroxysmal nocturnal hemoglobinuria. A bone marrow examination will be useful if a myeloproliferative disorder is suspected. In selected patients, once the acute symptoms have subsided, endoscopy and barium studies may be helpful to rule out the possibility of inflammatory bowel disease.

#### TREATMENT

The treatment of mesenteric venous thrombosis involves anticoagulation alone or in combination with surgery. In patients with acute or subacute mesenter-



**Figure 2.** Computed Tomographic Scan of the Abdomen in a Patient with Acute Thrombosis of the Superior Mesenteric Vein Complicating Acute Pancreatitis.

The superior mesenteric vein is enlarged as a result of the thrombosis (curved arrow) and has a sharply defined wall with a rim of increased density. The vein is anterior and to the right of the superior mesenteric artery (arrowhead), which is immediately anterior to the aorta (arrow). Two drains have been placed (open arrows) as a result of pancreatic necrosis from an infection.

ic venous thrombosis, treatment with heparin should be started immediately.

### Surgical Treatment

Contrary to previous thinking, surgical exploration is not necessary in all patients with mesenteric venous thrombosis. Patients with peritonitis clearly require emergency surgery. As soon as the diagnosis of mesenteric venous thrombosis is made or confirmed intraoperatively, treatment with anticoagulants should be initiated. Subsequent management is dictated by the surgical findings, which range from a segmental infarction of small bowel to necrosis of the entire bowel, with or without perforation. The aim of resection is to conserve as much bowel as possible. Follow-up ("second-look") laparotomy, 24 hours later, is often proposed as a way of avoiding the resection of bowel that may be viable.<sup>17,18</sup> A second-look procedure is especially useful in patients who have extensive bowel involvement but some venous flow. On rare occasions, thrombectomy can be accomplished successfully when the thrombus is recent and is restricted to the superior mesenteric vein.<sup>19</sup> The more diffuse venous thrombosis seen in the acute form of the condition precludes thrombectomy. Arterial spasm is a common finding, and the use of the combination of intraarterial papaverine, anticoagulation, and second-look laparotomy may avert resection of reversibly ischemic bowel.<sup>8</sup>

### Medical Management

Mesenteric venous thrombosis can safely be managed without surgery if there is no evidence of bowel infarction. Unfortunately, there are no precise markers that identify patients who are at risk for bowel infarction. The need for intravenous antibiotics has not been established in the absence of bowel perforation or peritonitis. However, immediate anticoagulation with heparin early in the course of the disease, even intraoperatively, clearly increases survival and significantly decreases the risk of recurrence.<sup>5</sup> Systemic heparin therapy is initiated with a bolus injection of 5000 U, followed by a continuous infusion in which the dose is adjusted so that the activated partial-thromboplastin time remains more than twice the normal level. Anticoagulation may be started even in the presence of gastrointestinal bleeding, if the risk of bleeding is outweighed by the benefit of preventing bowel infarction.

Supportive measures include nasogastric suction, fluid resuscitation, and bowel rest (with no food by mouth). Oral anticoagulation with warfarin should be started once there is evidence of the absence of ongoing ischemia. Although varices and consequent bleeding may eventually develop, the benefits of long-term anticoagulation outweigh the risks of bleeding.<sup>20</sup> In the absence of an ongoing thrombotic disorder, the duration of anticoagulation may be limited to six months to one year.

We and others have had occasional success using transhepatic portography to instill urokinase or tissue plasminogen activator directly into the thrombus in selected patients.<sup>21,22</sup> The use of thrombolytic agents is limited by the risk of hemorrhage and the low rate of success in cases in which the diagnosis has been delayed. Thrombolytic therapy should be considered in patients with thrombosis of large mesenteric veins when the perceived benefit outweighs the risks of the procedure.

### OUTCOME

The mortality rate among patients with acute mesenteric venous thrombosis ranges from 20 to 50 percent.<sup>5,9</sup> Survival depends on multiple factors, including age, the presence or absence of coexisting conditions, and the timing of the diagnosis and surgical intervention. Patients who require surgery are sicker and have longer hospital stays and a more complicated course than those who do not require surgery. Postoperative complications include sepsis, wound infection, and the short-bowel syndrome in patients who require extensive resection of the small bowel. Long-term survival depends primarily on the cause of the thrombosis. If cancer is the underlying cause, survival is short and is determined by the nature of the cancer.

Mesenteric venous thrombosis has a high rate of recurrence, and recurrences are most common within 30 days after presentation.<sup>23</sup> The recurrence rate may be lower in patients who receive a combination of surgery and anticoagulation than in those who are treated with anticoagulation alone.<sup>9</sup> The observation that up to 60 percent of recurrences are at the site of the anastomosis<sup>4</sup> may reflect inadequate bowel resection or propagation of the residual thrombus.

### CHRONIC MESENTERIC VENOUS THROMBOSIS

The presentation of chronic mesenteric venous thrombosis is very different from that of the acute and subacute forms. The diagnosis is suggested by the presence of luminal thrombus and extensive venous collaterals or the inability to visualize the superior mesenteric vein on duplex ultrasonography or CT. Angiography can confirm the diagnosis but is rarely required. Though many patients present with non-specific symptoms of several months' duration, an increasing number of patients are identified through imaging studies obtained for unrelated reasons. These patients may have had no symptoms at the time of the thrombotic event; hence, the date of the event is usually unclear.

Patients with thrombosis involving the portal or splenic veins may have portal hypertension with esophagogastric varices, splenomegaly, and hypersplenism. Chronic mesenteric venous thrombosis should be differentiated from isolated splenic-vein thrombosis that is due to pancreatic neoplasm or pancreatitis; throm-

bosis in these conditions is related to a local effect on the splenic vein and not to any disorder of the thrombotic pathway. Patients with chronic mesenteric venous thrombosis often remain asymptomatic because there is extensive collateral venous drainage, but they may have gastrointestinal bleeding from gastroesophageal varices or varices at ectopic sites.

The treatment of chronic mesenteric venous thrombosis is symptomatic, with the aim of controlling variceal bleeding or preventing recurrent bleeding with the use of pharmacologic agents such as propranolol. Long-term anticoagulation is recommended in patients with underlying prothrombotic states. Endoscopic therapy is used both to control active bleeding and to prevent recurrent bleeding.<sup>24</sup> The use of surgical portosystemic shunts is restricted to patients whose bleeding cannot be controlled by conservative measures and who have a suitable vein for anastomosis. When thrombosis is extensive and no suitable large vein is available, gastroesophageal devascularization or nonconventional shunts involving the anastomosis of a large venous collateral vein with a systemic vein may be considered.<sup>25</sup>

### CONCLUSIONS

Mesenteric venous thrombosis, though less common than arterial thrombosis, remains an important cause of mesenteric ischemia. Advances in imaging techniques have permitted the diagnosis of mesenteric venous thrombosis to be made before laparotomy is performed, but there is often a considerable delay in the diagnosis because of a low degree of suspicion on the part of clinicians and the nonspecific clinical presentation. Early diagnosis and the immediate use of anticoagulation can improve the outcome. Surgery should be limited to patients with peritonitis or perforation. The objective of surgical management should be to conserve as much bowel as possible. In patients with inherited thrombotic disorders and those in whom a cause cannot be identified, lifelong anticoagulation is warranted. For patients with reversible predisposing causes, at least six months to one year of anticoagulation is recommended. The long-term prognosis of patients without cancer or other life-threatening disorders is generally good.

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