General Review

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Mesenteric Ischemia: Acute and Chronic

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ACUTE MESENTERIC ISCHEMIA

Acute mesenteric ischemia is a circulation-insufficiency event, occurring either suddenly or rapidly over a few weeks, that deprives one or several abdominal organs of adequate respiration to meet metabolic demands. Although mesenteric ischemia occurs infrequently, the mortality rate is from 60 to 100%, depending on the source of obstruction.[1,2] The risk of atherosclerotic-related mesenteric occlusive disease increases with aging and those who have severe cardiovascular disease are at the highest risk. From 20 to 30% of hospital admissions for acute mesenteric ischemia are from nonocclusive mesenteric ischemia.[3] Nearly 5 to 15% of all acute mesenteric ischemic cases are from a venous thrombosis.[4]

Etiology

The etiology of ischemia of the mesenteric vessels is various. Embolization of the superior mesenteric artery is responsible for nearly half of all acute mesenteric ischemias, and a thrombosis at the origin of the vessel causes another quarter of the cases.[5] The emboli are usually found 3 to 10 cm distal of the origin and just past the origin of the middle colic artery. Thrombi usually develop at critical atherosclerotic stenoses. Other causes of acute mesenteric ischemia are summarized in Table I.[2,6] Acute mesenteric venous thrombosis can also occur spontaneously either as a primary event or as a consequence of hypercoagulability, cancer, cirrhosis, splenomegaly, infection, trauma, pancreatitis, or diverticular disease.[4,7] Nonocclusive mesenteric ischemia is caused by low blood flow from persistent vasoconstriction, vasospasm, intestinal hypoxia caused by myocardial infarction, renal failure or other ailments, ischemia-reperfusion injury, increased intestinal metabolic demand, and infection.

Pathophysiology

The three major arteries that arise from the abdominal aorta are the celiac axis, the superior mesenteric artery, and the inferior mesenteric artery. One or more vessels can be involved in the ischemic process. Fortunately, collateral arteries from the esophagogastric junction and rectum can partially restore the circulation to the organs.[8] Primary and secondary collaterals within the mesenteric circulation also support the mesenteric beds. The pancreaticoduodenal vessels supply the celiac and superior mesenteric arteries. Marginal vessels at the splenic flexure can supply the superior mesenteric and inferior mesenteric arteries. Since collateral circulation is present at several levels, patients may be asymptomatic even with stenoses in several arteries. Adequate intestinal perfusion can usually be maintained at near normotensive blood pressures when only one artery is involved, and under these circumstances mesenteric ischemia rarely occurs. When multiple severe occlusions are present, acute intestinal ischemia occurs from the critical reduction in the blood flow. Severe symptoms and possible infarction of the intestines can occur. The bowel becomes ischemic when the intestinal blood pressure becomes <40 mmHg.[1] The extent of damage is determined by the duration of hypoxia. Once bowel necrosis occurs, perforation, sepsis, multiorgan failure, and death

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Table I. Etiology of acute mesenteric ischemia

Arterial obstruction
1. Dissection or trauma of an artery
2. Compression of the celiac axis or superior mesenteric artery by the median arcuate ligament or strangulation obstruction from adhesive bands
3. Carcinoma of the sigmoid colon, carcinoid tumor, or tumor embolus
4. Neurofibromatosis or retroperitoneal fibrosis
5. Medications: ergot alkaloids, contraceptives, diuretics, cocaine, pitressin, pseudoephedrine
6. Connective tissue diseases: amyloidosis, polycythemia, systemic lupus erythematosus, polyarteritis nodosa, anticardiolipin antibodies, Behçet's syndrome
7. Disseminated intravascular coagulation
8. Diabetes mellitus
9. Thromboangiitis obliterans, Takayasu's disease
10. Crohn's disease
11. Atrial fibrillation, recent myocardial infarction, cardiopulmonary bypass
Venous obstruction
1. Hypercoagulation: carcinoma, polycythemia, dehydration, coagulopathy
2. Portal hypertension, Budd-Chiari syndrome
3. Congestive heart failure, shock

can rapidly ensue. Nonocclusive mesenteric ischemia occurs from severe microvascular vasoconstriction and usually no vascular occlusion can be demonstrated because pulsatile blood flow is present in larger arteries.[9] Patients with severe cardiac failure are at risk for nonocclusive mesenteric ischemia from vasospasm related to elevated sympathetic activity or hypovolemia. Other causes of vasospasm, by interfering with the autoregulation of mesenteric circulation, are catecholamines and medications such as digitalis.

Clinical Presentation and Diagnosis

Most patients complain of severe abdominal pain that is usually much out of proportion to the physical findings, and many will have been vomiting and/or defecating. Leukocytosis is also a frequent finding. Tenderness in the right lower quadrant and hyperactive bowel sounds are usually found. Distention of the abdomen develops later. Necrosis progresses from the intestinal villus tips to the peritoneum. Patients develop oliguria, metabolic acidosis, elevated hepatic enzymes, hyperamylasemia, and shock.

Most patients will rapidly develop symptoms and seek medical care without delay following a severe obstruction of the superior mesenteric artery by an embolus. Patients who have a possible cardiac source of an embolus and have sudden abdominal pain and intestinal emptying should be considered at a high risk of acute ischemia. Symptoms tend to progress more slowly in patients with a thrombosis and are related to the degree of bowel perfusion. These patients with slower-developing acute symptoms will usually delay seeking help and obtaining a diagnosis, and thus have a higher mortality rate.[10] Unfortunately, symptoms of nonocclusive mesenteric ischemia are vague and the diagnosis is difficult. Most patients complain of vague abdominal pain. Other findings may be abdominal distension, abdominal tenderness, hypotension, leukocytosis, fever, diminished bowel sounds, nausea and vomiting, and metabolic acidosis. Some patients with cardiogenic shock can also suddenly develop acute nonocclusive mesenteric ischemia. Acute venous thrombosis can be asymptomatic or patients present with vague, generalized abdominal pain. Typically pain becomes progressively severe, and nausea, vomiting, and bloody diarrhea occur.[8] Severe dehydration may be present.

Diagnostic findings can often be nonspecific, which can delay obtaining a diagnosis. Some surgeons will forego imaging techniques because delays in restoring the circulation are associated with rapid deterioration of some patients, who may expire before surgery can be performed. Thus, the use of imaging techniques for diagnosis remains controversial. It has been suggested that the appropriate treatment can be determined by the appearance of the bowel and the absence of a pulse in the arteries.[11] Before necrosis occurs, the bowel has a dull gray look without the normal sheen. The viability of the bowel must be determined if the vasa recta is pulseless. A thrombosed superior mesenteric artery is frequently associated with an absent pulse.

Patients who are hemodynamically stable without evidence of peritonitis and without significant

Table II. Fullen's anatomical classification of superior mesenteric artery injury

Zone	Injured segment	Grade	Ischemia class	Bowel aected
I	Trunk proximal to first major branch (inferior pancreaticoduodenal segment)	1	Maximal	Jejunum, ileum, right colon
II	Trunk between inferior pancreaticoduodenal and middle colic segments	2	Moderate	Major segment, small bowel, right colon or both
III	Trunk distal to middle colic segment	3	Minimal	Minor segments of small bowel or right colon
IV	Segmental branches, jejunal, ileal, colic	4	None	No ischemic bowel

Table was adapted from Asensio et al.[12]

abdominal pain may avoid a delay in revascularization if a diagnosis can be made with a color duplex scan. Imaging the celiac axis and superior mesenteric artery, however, can be difficult in some patients. Angiography and computed tomography are excellent for imaging the mesenteric vessels and can locate the source of the disease if time permits. Patients who have severe abdominal pain, are hemodynamically stable, and lack leukocytosis and acidosis might benefit from one of these techniques for determining the location and extent of occlusions before the revascularization is planned. When there are signs of peritonitis, deterioration of hemodynamics, or metabolic acidosis, bowel infarction is likely and emergent laparotomy is required.[10] Both early diagnosis and prompt surgical intervention are necessary for survival because the prognosis is related to the duration and extent of bowel infarction. Most patients who have a venous thrombosis will have intermittent generalized abdominal pain of several days or weeks, and have predisposing conditions for mesenteric ischemia.[4] Computed tomography is the most useful diagnostic method for these patients.

Trauma to the superior mesenteric artery results in high mortality from the complications of intestinal infarction or ischemia, failure of the repair, short bowel syndrome, or graft thrombosis. Mortality can be associated with the severity of the ischemia grade of Fullen's anatomic classification of the superior mesenteric artery injury (Table II), the American Association for the Surgery of Trauma–Organ Injury Score (AAST-OIS), high intraoperative transfusions, acidosis, and disrhythmias.[12]

Treatment

The aim of surgical intervention is to achieve a pulsatile blood flow in the mesenteric arteries and resect any nonviable bowel. If there is time prior to the operation, hemoconcentration, blood pressure, and acidosis should be corrected, and anticoagulation therapy needs to be started. Since bowel necrosis occurs within hours after an occlusion, there should be no delay in revascularization. The location of ischemic bowel and the presence or absence of pulse in the arcade vessels are determined. The intestinal circulation should be restored as soon as possible and then the extent of the resection determined. If there is an embolus at or distal to the origin of the middle colic artery, the proximal jejunum is usually spared. Circulation can usually be restored by an embolectomy and resection of the necrotic bowel.[2] Achieving adequate thrombectomies in the splanchnic arteries can be difficult. Infarctions usually extend further with acute arterial thrombi than with emboli, and can extend from the duodenum to the transverse colon. Most vascular surgeons prefer antegrade or retrograde bypass grafts over thrombectomy. Vein grafts are preferred, but synthetic grafts can prevent kinking.[2] In one study, the 3-year patency rates were 93% for antegrade grafts, 95% for retrograde grafts, 95% for saphenous vein grafts, and 89% for synthetic grafts.[13] Another study determined the 5-year patency rate at 57% and the 10-year rate at 46% of all grafts.[14] When the superior mesenteric artery is adequate to receive a graft to restore blood flow to the ischemic bowel, revascularization of other splanchnic vessels is probably not required.[15] High-risk patients have been successfully treated with percutaneous transluminal angioplasty of the superior mesenteric artery, celiac trunk, or inferior mesenteric artery or by stent placement.[16-18] Intraarterial fibrinolysis with urokinase or tissue plasminogen activator may be a therapeutic option for some high-risk patients.[19] Patients must be assessed to determine whether there is sufficient time for diagnostic angiography or that an emergent laparotomy is required.

Bowel ischemia has been reversed by angiography and papaverine infusion and the resection of necrotic bowel. Patients with severe cardiac failure can develop nonocclusive mesenteric ischemia from vasospasm that can occur in response to the elevated sympathetic activity of cardiogenic shock or hypovolemia as the body attempts to maintain adequate cardiac and cerebral perfusion. These individuals should undergo intestinal angiography for a diagnosis. Digitalis preparations can also cause vasoconstriction. When the blood pressure in the bowel falls below a critical pressure of 40 mmHg, ischemia develops and the bowel becomes necrotic within hours. After ischemic damage, restoration of oxygenated blood to the hypoxic bowel may cause further injury by oxygen free radical. Elderly patients who have either acute myocardial infarction, congestive heart failure, dysrhythmia, sepsis, or hypovolemia or use splanchnic vasoconstrictors should be considered at a higher risk for induced vasospasm.

Since tissue injury can occur within 3 h of ischemia and can lead to multiple-organ dysfunction and death, restoration of adequate tissue perfusion is necessary. However, hypoxia disrupts bowel metabolism and causes cellular damage,[2] and leads to vasoconstriction that can complicate recovery after treatment. It has been suggested that vasodilators and superoxide–free radical scavengers should be given to improve flow and prevent reperfusion injury after revascularization.[20] The benefit of superoxide–free radical scavengers, however, still needs to be elucidated.

When bowel infraction is associated with acute venous mesenteric ischemia, resection of nonviable bowel and revascularization is required.[1,21] Thrombectomy and embolectomy can be difficult in these patients and are not recommended. The source of the thrombosis should be determined, and those patients with prothrombotic disease may require long-term anticoagulation. Since recurrence rates are high after thrombectomy, ischemic bowel should be resected and anticoagulation therapy given.

A ligation is done in most patients who have trauma to the superior mesenteric artery because these injuries are highly lethal and are related to the location of the injury according to Fullen's anatomic classification for ischemia categories.[12] The outcome is similar with penetrating and blunt trauma.

After arterial reconstruction, bowel perfusion should be improved but visual observation is unreliable. The viability of the bowel can be ascertained by continuous-wave Doppler evaluation, pulse oximetry, or intravenous fluorescein. Postoperative reassessment, however, is necessary to ensure restoration of the circulation. If patients are symptomatic, the possibility of nonviable bowel should be considered. A second-look laparotomy after 24 to 48 h can confirm that the bowel is healthy.[8] While some surgeons advocate that all patients receive a second look, others selectively use an exploratory laparotomy only for patients who do not improve. In either case it is important to evaluate the progress of the patient for at least 48 h postoperatively.

CHRONIC MESENTERIC ISCHEMIA

Chronic mesenteric ischemia is a gradually developing circulation-insufficiency event that occurs over a few months. It occurs more frequently in older females.[22]

Etiology

The etiology of chronic ischemia is also various and many of the causes are similar to those listed for acute ischemia, but rarely from emboli. The most common cause of chronic intestinal ischemia is atherosclerotic occlusion or severe stenosis of the mesenteric arteries. A stenosis of >50% is present in 18% of patients older than 65 years,[23,24] but very few patients have symptoms. Slow-growing obstructions are usually the source of this disease.

Pathophysiology

Symptoms are caused by the gradual reduction in blood flow to the intestine. Since blood flow to the intestine can vary from 20% when fasting to 35% after eating, symptoms occur with the demand for blood flow. Most patients develop adequate collateral circulation to the intestine which usually provides sufficient flow to prevent ischemic symptoms. When the superior mesenteric artery is occluded, the pancreaticoduodenal arteries supply blood via the hepatic and gastroduodenal arteries to the bowel, and when the celiac artery is also occluded, the inferior mesenteric artery supplies blood to the small bowel via the left colic branch. Frequently angiography will demonstrate a large meandering mesenteric artery, which is an important vessel in the collateral circulation from the inferior mesenteric artery. Symptoms occur if two or more vessels are occluded.

Clinical Presentation and Diagnosis

Chronic mesenteric arterial ischemia typically causes postprandial abdominal pain and weight

loss. As the obstructive process progresses, chronic dull pain ensues. Patients will seek medical care when they become concerned about their problem. Chronic venous occlusions cause vague abdominal pain or distention and usually do not infarct the bowel. Frequently, it is found incidentally on abdominal imaging.

Color duplex scanning should be done in patients with suspected chronic mesenteric ischemia because blood flow can be measured in the visceral arteries using this noninvasive technique, which is relatively inexpensive compared to other diagnostic methods. The Doppler-derived peak systolic blood flow velocities are measured from several sites along the course of the vessels. The celiac artery may not be adequately visualized in 20% of the patients.[25] Quantifying the inferior mesenteric blood flow has been difficult and it is usually not measured. However, angiography remains the most essential technique for the establishment of the diagnosis and is important for the determination of any occlusion and collateral circulation, which must be known to plan the optimal revascularization. Since malabsorption and maldigestion do not usually occur, studies of intestinal absorption are not useful.

Angiography can usually be performed in patients who present with the classical symptoms of chronic mesenteric ischemia. When mesenteric venous thrombosis is suspected, the duplex scan that has a high sensitivity for a diagnosis should be used initially. If there is doubt, computed tomography is used because it has the highest sensitivity for a diagnosis. Angiography and abdominal radiography provide little value for a reliable diagnosis.

Treatment

Single-vessel bypass to the superior mesenteric artery has been very successful, even in patients with multiple-vessel occlusions. In one study, the procedure had a perioperative mortality rate of 3%, a 5-year survival rate of 61%, and a 9-year assisted primary graft patency of 79%.[26] Bypass grafts have been antegrade from the abdominal aorta, and retrograde from the aorta, the common iliac artery, or previous grafts. Those who advocate multiple-vessel revascularization suggest that there is a higher incidence of graft failure and recurrence of symptoms after single-vessel revascularization.[27,28] At the Mayo Clinic, the 5-year graft patency rates have been 90%, 54%, and 0% with three-vessel, two-vessel, and one-vessel bypasses respectively.[27] Palmaz stents in the proximal celiac artery have completely resolved, abdominal angina.[29,30] When the results of open surgery are compared to those of percutaneous angioplasty and stenting, there is a higher incidence of recurrent symptoms after percutaneous angioplasty.[31] Antegrade aortoceliac bypass and transaortic endarterectomy have been successful for poor-risk patients, and are usually adequate for multiple outflows. Antegrade mesenteric bypass grafts from the distal thoracic aorta have also been associated with low mortality and morbidity rates.[32] Antegrade bypass to the supraceliac aorta can reduce kinking, compression, turbulence, and thrombosis, but has been associated with renal ischemia and can be technically challenging. Retrograde bypass from the infrarenal aorta or iliac artery is easier technically and avoids renal ischemia, but has been related to a lower inflow and kinking. Revascularization of the superior mesenteric artery and celiac axis has been used to minimize the recurrence of symptoms and organ infarction if one graft fails.[33] Graft failure has been reported to be higher in males.[34] While most patients with chronic venous mesenteric ischemia can be treated with anticoagulation therapy, the source of the thrombus must be determined and treated.

CONCLUSION

Survival after mesenteric ischemia is dependent upon the timely restoration of circulation and resection of the nonviable bowel. The mortality rate still remains high for acute intestinal ischemia, in spite of emergent revascularization.

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