Portomesenteric Venous Thrombosis
After Laparoscopic Surgery

A Systematic Literature Review

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Background: Portomesenteric venous thrombosis (PVT) is an uncommon but potentially lethal condition reported after several laparoscopic procedures. Its presentation, treatment, and outcomes remain poorly understood, and possible etiologic factors include venous stasis from increased intra-abdominal pressure, intraoperative manipulation, or damage to the splanchnic endothelium and systemic thrombophilic states.

Design: Systematic literature review.

Setting: Academic research.

Subjects: We summarized the clinical presentation and outcomes of PVT after laparoscopic surgery other than splenectomy in 18 subjects and reviewed the treatment strategies.

Main Outcome Measures: Systematic review of the literature on PVT after laparoscopic procedures other than splenectomy.

Results: Eighteen cases of PVT following laparoscopic procedures were identified after Roux-en-Y gastric bypass (n=7), Nissen fundoplication (n=5), partial colectomy (n=3), cholecystectomy (n=2), and appendectomy (n=1). The mean patient age was 42 years (age range, 20-74 years). Systemic predispositions toward venous thrombosis were identified in 11 patients. Clinical symptoms consisted primarily of abdominal pain manifested, on average, 14 days (range, 3-42 days) after surgery. Thrombus location varied, but 8 patients had a combination of portal and superior mesenteric venous thrombosis. Sixteen patients were treated with anticoagulation therapy. Ten patients underwent major interventions, including exploratory laparotomy in 6 patients and thrombolytic therapy in 4 patients. Six patients had complications, and 2 patients died.

Conclusions: Portomesenteric venous thrombosis following laparoscopic surgery usually manifests as nonspecific abdominal pain. Computed tomography can readily provide the diagnosis and demonstrate the extent of the disease. Treatment should be individualized based on the extent of thrombosis and the presence of bowel ischemia but should include anticoagulation therapy. Venous stasis from increased intra-abdominal pressure, intraoperative manipulation of splanchnic vasculature, and systemic thrombophilic states likely converges to produce this potentially lethal condition.

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Portomesenteric venous thrombosis (PVT) is an uncommon, potentially lethal condition accounting for 5% to 15% of all mesenteric ischemic events. Portomesenteric venous thrombosis includes a wide spectrum of clinical presentations ranging from incidental findings in an asymptomatic patient to life-threatening bowel infarction, and most of what is known about acute PVT derives from patients who did not undergo laparoscopic surgery. The etiologic factors of PVT are numerous and can be divided into local and systemic factors. Local predisposing factors to PVT include abdominal malignant neoplasm, trauma to the portal venous system, abdominal inflammatory diseases (eg, pancreatitis, appendicitis, diverticulitis, and inflammatory bowel disease), and factors that decrease portal blood flow such as ascites due to cirrhosis or the pressure created by pneumoperitoneum during laparoscopic procedures. Systemic predisposing factors include inherited thrombophilias (eg, antithrombin III deficiency, protein C and S deficiencies, factor V Leiden deficiency, G20210A prothrombin mutation, and hyperhomocysteinemia) and various acquired prothrombotic states (including sepsis, pregnancy, oral contraceptive use, malignant neoplasm, myeloproliferative disorders, and others). Portomesenteric venous thrombosis has been previously described after procedures that involve ligation of major arteries and veins such as splenectomy, hepatectomy, and gastrectomy.
portal tributaries, such as splenectomy or other surgical procedures involving the portal venous system (including liver transplantation and shunts for portal hypertension, among others)\textsuperscript{21-26} but rarely after surgical procedures without injury to the portal system. Portomesenteric venous thrombosis after various laparoscopic operations without injury to the portal venous system has been described in case reports since 1991.\textsuperscript{27} The dissemination of the use of laparoscopic surgery and the greater availability of modern diagnostic imaging methods likely contribute to the observation of this possible complication. Laparoscopic approaches compare favorably with open surgery for treating most gastrointestinal tract conditions because they provide similar outcomes and offer lower complication rates, less postoperative pain, and faster recovery.\textsuperscript{28,29} However, the greater number of laparoscopic procedures performed has resulted in more complications specific to laparoscopic surgery, including complications associated with trocar insertion or pneumoperitoneum\textsuperscript{30,31} and likely the rare but potentially lethal complication described herein.

This article reviews the available literature about PVT after laparoscopic surgery. A summary of reported cases of PVT after laparoscopic surgery is presented, with discussion of possible causative factors.

### METHODS

We used PubMed to search MEDLINE for articles published between January 1, 1990, and December 31, 2007, using the search terms portal vein thrombosis, mesenteric venous thrombosis, pyelonephritis, laparoscopic surgery, and laparoscopy. Additional articles culled from references were obtained. The inclusion criterion was documented PVT by imaging studies (angiography, ultrasonography, computed tomography [CT], or magnetic resonance imaging) or surgery following a laparoscopic procedure other than splenectomy. We also included 2 cases at our institution, one in which the index operation was performed at the University of California, San Francisco, and another that was referred to our institution after PVT was diagnosed following a laparoscopic procedure. Age and sex of the patients, type of surgery, method of PVT detection, location and extent of thrombosis, timing of symptom onset, type of symptoms, physical findings at presentation, and abnormal laboratory test results, treatment, and outcomes were recorded.

We excluded cases of laparoscopic splenectomy because they have been thoroughly reported elsewhere in the literature and because postsplenectomy PVT is likely a distinct entity related to ligation of the splenic vessels and associated hemolytic diseases.\textsuperscript{32-37} Other exclusion criteria included documented PVT predating surgery or documented mechanical injury to the portal vein or its major branches.

### RESULTS

Eighteen cases of PVT following laparoscopic surgery were reviewed (Table). Portomesenteric venous thrombosis was found after diverse laparoscopic procedures, including appendectomy (n = 1), cholecystectomy (n = 2), colostomy (n = 3), Nissen fundoplication (n = 5), and Roux-en-Y gastric bypass (n = 7). The mean patient age was 42 years (age range, 20-74 years); 7 patients were female. Perioperative pharmacologic anticoagulation therapy with low-molecular-weight heparin was reported in 7 patients. Pneumoperitoneum was established at standard pressures in all patients, the mean operative time was 100 minutes (range, 40-150 minutes), and blood loss was consistently minimal.

Local or systemic predispositions to PVT were commonly identified. Abdominal inflammatory processes were present in 4 patients and included appendicitis,\textsuperscript{38} cholecystitis,\textsuperscript{39,40} or...
and diverticulitis. At least 1 systemic predisposition toward venous thrombosis was present in 11 patients. These include prothrombogenic factors such as morbid obesity (n=7), oral contraceptive use (n=2), and a history of venous thrombosis (n=2), all of which were identified before surgery. Other systemic predisposing factors were discovered in the postoperative period, including protein S deficiency (n=2) and anticardiolipin antibody (n=1).

On average, symptoms of PVT manifested clinically 14 days (median, 12 days; range, 3-42 days) after surgery. The most common symptoms included abdominal pain (16 patients) with variable distribution and severity, nausea (5 patients), vomiting (3 patients), diarrhea (4 patients), and fever (3 patients). Common findings on physical examination included abdominal tenderness (8 patients), distension (3 patients), and elevated temperature (2 patients). Most important, the initial physical examination findings were normal in 7 patients. Routine laboratory test results were abnormal in only 9 patients. The most commonly found abnormalities were leukocytosis and mildly elevated liver function test results.

The diagnosis of PVT was made using CT in 14 patients, while ultrasonography, magnetic resonance imaging, and invasive angiography were used to complement CT. The Table gives the location and extent of venous thrombosis. The location of thrombosis among patients was heterogeneous. Eight patients had thrombosis of both the portal and superior mesenteric veins, while 4 patients had a clot detected more extensively throughout the portal venous system. The Figure shows contrast-medium–enhanced CT images of the abdomen in a patient with PVT after laparoscopic gastric bypass and in a healthy subject for comparison. In 4 patients, the radiographic imaging suggested intestinal ischemia (including ascites, fat stranding, bowel wall thickening, and small-intestine dilatation). The investigation, testing, and diagnosis of PVT were delayed in 7 patients (median delay in diagnosis, 7.5 days; range, 2-30 days).

Sixteen patients received anticoagulation therapy on diagnosis of PVT. Of 2 patients who did not receive anticoagulation therapy, one died after an exploratory laparotomy when extensive bowel ischemia was found, and the other was treated only with hydration and bowel rest. Thirteen patients were treated with an oral vitamin K antagonist for a minimum of 6 months. More aggressive therapy was used less frequently, including interven-
Portomesenteric venous thrombosis after laparoscopic surgery is an infrequently observed yet potentially life-threatening condition. Following laparoscopic surgery, PVT usually manifests as nonspecific abdominal pain similar to acute PVT in other clinical settings. However, the clinical presentation varies widely, and the diagnosis is often delayed. The wide spectrum of clinical presentations ranges from incidental findings in an asymptomatic patient to life-threatening bowel infarction. Patients may be initially seen with nonspecific abdominal pain (90% of patients), nausea (54%), vomiting (77%), or diarrhea (36%); other findings may include anorexia, colicky pain, or gastrointestinal tract bleeding. Most patients have had symptoms for more than 2 days before seeking medical care.

Physical findings may be absent or may include low-grade fever (an early indicator), peritoneal signs, splenomegaly due to chronic venous congestion, or hypotension (in case of septic shock due to bowel ischemia). Pain out of proportion to physical findings should raise the clinical suggestion of PVT.

Routine blood tests are typically not helpful in the diagnosis of acute PVT. Leukocytosis and mild elevations in liver function tests may be present, whereas metabolic acidosis is a typical late finding suggestive of bowel infarction. Computed tomography with intravenous contrast medium is most commonly used to diagnose PVT, is up to 90% sensitive, and can readily evaluate the extent of the disease. Signs on CT include a central lucrecy in the lumen of a dilated vein, venous collateral circulation, and signs of intestinal congestion or edema. Several studies have documented a high level of agreement between findings on CT and results of other noninvasive imaging modalities, including ultrasonography and magnetic resonance imaging. Although ultrasonography is readily available and is expedient, it has the lowest specificity for PVT of available imaging techniques and is best used to document restoration of venous flow in a patient with known PVT. Magnetic resonance imaging is highly sensitive and specific for PVT but is not widely available. Invasive angiographic studies remain the standard criterion for the diagnosis.

The development of venous thrombi in general is considered a multifactorial process and a combination of locoregional and systemic prothrombotic factors may be causative in PVT. The increasingly described clinical scenario of PVT after laparoscopy highlights the multifactorial nature of this condition.

Locoregional factors particular to laparoscopic procedures may contribute to the development of PVT. In animal and human studies, insufflation of the abdomen and increased intra-abdominal pressure led to decreased mesenteric and portal venous flow via direct pressure-induced compression. Estimates of this decrease in venous flow vary from 35% to 84%. However, most studies find a dose-dependent relationship between insufflation pressures and venous stasis. Insufflation with carbon dioxide has been shown to cause a more substantial decrease in venous flow than insufflation with other inert gases. Tranperitoneal diffusion of carbon dioxide into the circulation can cause hypercapnia, which in turn has been implicated in decreasing splanchic blood flow related to mesenteric vasoconstriction. Another possible explanation is that a prolonged reverse Trendelenburg position (such as may be necessary for various laparoscopic procedures) may exacerbate laparoscopy-associated portal venous stasis, as observed in experimental models. In addition, intraoperative surgical manipulation may damage the splanchic endothelium and lead to local thrombus formation that may then propagate throughout the portal venous system. This may be particularly true for laparoscopic splenectomy, in which ligation of the splenic vein causes endothelial damage in proximity to the portal vein, but many other procedures also lead to some manipulation of the splanchic vasculature.

Although hereditary thrombophilia has been reported in conjunction with PVT, its reported incidence varies widely, likely because of small sample sizes and differences in baseline populations, genetic assays, and inclusion criteria. The factor V Leiden mutation has been observed in 3% to 30% of patients, prothrombin G20210A mutation in 3% to 40%, antithrombin III deficiency in 1% to 29%, and protein C and S deficiencies in 7% to 27% and 2% to 43%, respectively. Deficiencies in proteins C and S and antithrombin III appear in greater frequency in patients with PVT than in patients with lower extremity deep venous thrombosis. Our review identified 2 patients with protein S deficiency.

Finally, the underlying disease process or condition leading to laparoscopic surgery may predispose to PVT. This may be true in laparoscopic splenectomy for myeloproliferative disorders, laparoscopic tumor resections for malignant neoplasm, laparoscopic gastric bypass for morbid obesity, and surgery for abdominal inflammatory conditions.

In our review, PVT occurred in 7 patients despite perioperative thromboprophylaxis with low-molecular-
weight splenectomy. Previous findings after laparoscopic splenectomy have suggested that more aggressive perioperative anticoagulation therapy may be used for prevention of PVT.30 For other general laparoscopic surgical procedures, it is likely impracticable to develop specific guidelines to attempt prevention of PVT, as it is a rare event.

Prompt initiation of anticoagulation therapy is the current standard of care for the treatment of acute PVT. The suggested duration of anticoagulation treatment is 6 to 12 months. In a retrospective study77 of nonsurgical patients who developed acute PVT, anticoagulant therapy decreased the rate of recurrence or extension of PVT by two-thirds without increasing the rate of gastrointestinal tract bleeding. Results of another study78 showed that anticoagulation therapy with heparin or low-molecular-weight heparin led to complete or partial recanalization in 90% of patients. However, the natural history of untreated PVT is not well understood, and no randomized trials have demonstrated the best management for this rare condition, to our knowledge. Supportive measures to complement anticoagulation therapy include bowel rest, fluid resuscitation, and nasogastric suction.79 Endovascular thrombolysis has been shown to be effective in case reports and in small series,79-81 but large studies are lacking. In a retrospective review, Hollingshead et al82 showed that thrombolytic therapy led to complete or partial thrombus resolution in 75% of patients with PVT that was recalcitrant to anticoagulant therapy. Therefore, in the absence of clinical improvement with anticoagulation treatment, thrombolytic therapy should be considered.

The treatment of PVT after laparoscopic surgery is also not fully delineated. Anticoagulation therapy alone has been shown to be of therapeutic benefit in acute PVT,77,84,85 Anticoagulation therapy speeds recanalization of the portal venous system27 and decreases the risk of further thrombotic events.77 Therefore, anticoagulation therapy is recommended for 6 to 12 months.76 Our review found 1 case of spontaneous resolution of portal and superior mesenteric venous thrombosis without anticoagulation therapy.44 More tenuous are the indications for chemical and mechanical thrombolysis. Although thrombolytic therapy has been shown to be effective in resolving thrombus and in avoiding bowel resection, it is associated with a high complication rate.83 Therefore, thrombolysis should be reserved for patients with extensive thrombosis of the portal venous system and for patients whose clinical condition warrants aggressive thrombolytic treatment.

This review indicates that preoperative strategies to identify populations that may be at particularly high risk for PVT have not been well elucidated, although certain hereditary thrombophilias may disproportionately increase the risk for the condition. Signs and symptoms of PVT vary widely, and the diagnosis is often delayed. Treatment should include anticoagulation therapy; additional measures should be individualized based on the extent of the thrombosis and the presence of bowel ischemia. Venous stasis from increased intra-abdominal pressure, intraoperative manipulation, or damage to the splanchnic endothelium and systemic thromophilic states may contribute to the development of this potentially lethal condition.

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