Overview of complications of peptic ulcer disease

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INTRODUCTION

Complications of peptic ulcer disease (PUD) include bleeding, penetration, perforation, and gastric outlet obstruction. This topic will provide an overview of the complications of PUD and their general management. The specific management of complicated PUD, the endoscopic management of peptic ulcer bleeding, and the surgical approaches to complications of PUD are discussed separately. (See "Peptic ulcer disease: Clinical manifestations and diagnosis" and "Peptic ulcer disease: Treatment and secondary prevention" and "Overview of the treatment of bleeding peptic ulcers" and "Surgical management of peptic ulcer disease".)

EPIDEMIOLOGY

Incidence — The risk of complications in patients with chronic PUD is 2 to 3 percent per year. There has been a consistent decrease in the incidence of bleeding and perforation and hospitalization rates due to complications of PUD, presumably reflecting the fall in *Helicobacter pylori* prevalence [1,2]. As an example, in the United States there has been a 30 to 40 percent fall in hospitalizations for PUD complications between 1993 and 2006 [3]. Similar data have been reported in other countries [4]. (See "Peptic ulcer disease: Epidemiology, etiology, and pathogenesis", section on 'Epidemiology'.)

In the United States, bleeding is the most common complication of PUD (73 percent), followed by perforation (9 percent), and obstruction (3 percent) [3]. A large systematic review estimated

that the annual incidence of peptic ulcer hemorrhage ranges from 19 to 57 cases per 100,000 individuals, and that the annual incidence of ulcer perforation ranges from 4 to 14 cases per 100,000 individuals [5].

Mortality — In patients with bleeding peptic ulcer, the majority of deaths are related to multi-organ failure or cardiopulmonary causes rather than to bleeding itself [6]. Not surprisingly, in patients with gastrointestinal bleeding requiring endoscopic therapy, hypovolemic shock, multiple co-morbidities, and rebleeding in the hospital were predictive of mortality [7].

In patients undergoing surgery for perforated PUD, the long-term mortality is high, with one in three patients dying in the follow-up period. Older age, co-morbid illnesses, and post-operative complications were predictors of mortality [8].

Penetration of an ulcer into adjacent organs is a rare complication of PUD in the era of proton pump inhibitors [9]. Penetration occurs in descending order of frequency into the pancreas, lesser omentum, biliary tract, liver, greater omentum, mesocolon, colon, and vascular structures. Gastric outlet obstruction is the least frequent complication of PUD in developed countries. Most cases are associated with duodenal or pyloric channel ulceration. (See "Gastric outlet obstruction in adults", section on 'Peptic ulcer disease'.)

Risk factors for ulcer complications — Complications can occur in patients with PUD due to any etiology. However, *H. pylori* infection and nonsteroidal anti-inflammatory drugs (NSAIDs), including low-dose aspirin, are the primary causes of ulcer bleeding and perforation [10-13]. (See "Peptic ulcer disease: Epidemiology, etiology, and pathogenesis".)

H. pylori infection — *H. pylori* infection increases the risk of peptic ulcer bleeding in NSAID and aspirin users but not in patients on anticoagulants such as warfarin. *H. pylori* infection also increases the risk of bleeding in patients on non-aspirin antiplatelet therapy and combination antiplatelet therapy with aspirin [14]. *H. pylori* infection has also been associated with perforated peptic ulcer [15].

NSAID use

Drug- and dose-specific risk — The magnitude of the risk of PUD complications associated with NSAIDs vary by the specific drug and are also dose dependent [5]. As an example, in a study of 2777 patients, the overall relative risk (RR) of bleeding associated with NSAID use was 5.3 (95% CI 4.5-6.2). However, the risk varied by drug and was lowest for aceclofenac (RR 3.1, 95% CI 2.3-4.2) and was highest for ketorolac (RR 14.4, 95% CI 5.2-39.9) [16]. The risk was higher in patients taking high-dose NSAIDs compared with those taking medium- or low-dose NSAIDs (RR 6.8, 95% CI 5.3-8.8 versus RR 4.0, 95% CI 3.2-5.0). The risk was highest in

the first 30 days of NSAID use (RR 7.6, 95% CI 6.0-9.5). The risk remained high between days 31 and 90 days (RR 7.3, 95% CI 4.0-13.2), but dropped after 91 days (RR 2.6, 95% CI 1.6-4.1).

Use of concomitant medications — Concomitant use of anticoagulants, antiplatelet agents, corticosteroids, and other NSAIDs, including low-dose aspirin, increase the risk of ulcer complications [14].

Concurrent H. pylori infection — *H. pylori* infection is both an independent and synergistic risk factor for bleeding PUD in patients on NSAIDs [17-19]. A meta-analysis of nine case-control studies that assessed the prevalence of *H. pylori* infection and NSAID use in patients with peptic ulcer bleeding suggested that the *H. pylori* infection combined with NSAID use increases the risk of bleeding above that associated with either risk factor alone [20]. The analysis found that individually, the odds ratios for bleeding peptic ulcers associated with *H. pylori* and NSAID use were 1.8 and 4.9, respectively, whereas the odds ratio increased to 6.1 when both *H. pylori* and NSAID were present.

Other risk factors — The most important risk factor for ulcer complications in patients on NSAIDs is a prior history of clinical ulcer disease or ulcer complications. Other risk factors for NSAID-induced peptic ulcer complications include advanced age (>65 years) and chronic debilitating disorders, especially cardiovascular disease [21].

Ulcer characteristics — Refractory ulcers, giant ulcers (>2 cm), and pyloric channel ulcers are associated with higher complications rates. (See "Peptic ulcer disease: Clinical manifestations and diagnosis" and "Approach to refractory peptic ulcer disease", section on 'Refractory peptic ulcer'.)

CLINICAL PRESENTATION

While most patients may have typical ulcer symptoms prior to the development of complications, there is a subset of patients with silent ulcers and are only brought to medical attention due to peptic ulcer complications.

Bleeding — Patients with bleeding from peptic ulcers may present with hematemesis (either red blood or coffee-ground emesis), or melena (black, tarry stool). In rare cases, patients have massive bleeding and present with hematochezia (red or maroon blood in the stool) and orthostatic hypotension. (See "Causes of upper gastrointestinal bleeding in adults", section on 'Peptic ulcer disease'.)

Gastric outlet obstruction — Ulcers located in the pyloric channel or duodenum can cause gastric outlet obstruction. Symptoms include early satiety, bloating, nausea, vomiting, epigastric pain shortly after eating, and weight loss. Prolonged vomiting and poor fluid intake may lead to hypokalemia and hypochloremic metabolic alkalosis. (See "Gastric outlet obstruction in adults", section on 'Clinical manifestations'.)

Penetration — Patients with penetrating ulcers often present with a change in symptoms due to symptomatic involvement of adjacent structures.

- Gastrocolic or duodenocolic fistulas can present with halitosis, feculent vomiting, postprandial diarrhea, dyspepsia, and weight loss.
- Penetration into a surrounding organ can result in a perivisceral abscess.
- Erosion into vascular structures can result in gastrointestinal hemorrhage (eg, aortoenteric fistula or erosion into the cystic artery) [22].
- Erosion into the biliary tree can result in a choledochoduodenal fistula that can cause hemobilia and/or extrahepatic biliary obstruction.
- Fistulization into the pancreatic duct [9].

Perforation — The incidence of perforation is lower than previously reported, ranging from 3 to 6.5 per 100,000 individuals (image 1) [23,24]. Prepyloric gastric ulcerations account for most perforations followed by duodenal bulb ulcers [25]. Ulcer perforation should be suspected in patients who suddenly develop severe, diffuse abdominal pain. The classic triad of sudden onset of abdominal pain, tachycardia, and abdominal rigidity is the hallmark of peptic ulcer perforation. If the perforation is walled off, if the gastric fluid is confined by fibrosis, or if the perforation is retroperitoneal, symptoms may be much less severe as compared with free intraperitoneal perforations. In such cases, the upper abdominal pain is more insidious, the presentation often delayed, and the abdominal examination is frequently equivocal. (See "Overview of gastrointestinal tract perforation", section on 'Clinical features'.)

DIAGNOSIS

Specific complications of PUD are often suspected based on a change in pattern of existing symptoms or development of new symptoms. As examples, the development of hematemesis, melena, or hematochezia suggest an ulcer bleed; nausea, vomiting, and epigastric pain shortly after eating suggest a gastric outlet obstruction; and sudden onset of abdominal pain,

tachycardia, and abdominal rigidity are suggestive of a perforation. The diagnosis is established by endoscopic evaluation and/or abdominal imaging. (See 'Clinical presentation' above.)

INITIAL MANAGEMENT

General management

Supportive measures — Supportive measures include fluid resuscitation based on the hemodynamic status, correction of associated electrolyte abnormalities, and blood transfusions in selected patients with gastrointestinal bleeding. Patients should be kept fasting in anticipation of endoscopic or surgical intervention. Early surgical consultation allows for preoperative preparation should urgent surgical intervention become necessary. (See "Approach to acute upper gastrointestinal bleeding in adults", section on 'General management' and "Approach to acute upper gastrointestinal bleeding in adults", section on 'Hemodynamically unstable patients'.)

Acid suppressive therapy — Patients with active peptic ulcer bleeding (eg, hematemesis, hemodynamic instability) should receive initial acid suppressive therapy with an intravenous (IV) proton pump inhibitor (PPI; eg, esomeprazole 80 mg bolus). Typically, endoscopy is performed on these patients within 12 hours. However, if endoscopy is delayed, a second dose of an IV PPI should be given 12 hours later (eg, esomeprazole 40 mg). For patients who may have stopped bleeding (eg, patients who are hemodynamically stable with melena), we give an IV PPI every 12 hours (eg, esomeprazole 40 mg). Subsequent dosing will then depend on presence of high-risk stigmata of recent hemorrhage on endoscopic evaluation. (See "Overview of the treatment of bleeding peptic ulcers", section on 'Acid suppression'.)

In patients with other peptic-ulcer-related complications (gastric outlet obstruction, penetration, perforation), high-dose twice-daily PPI treatment is reasonable to enhance healing (eg, oral omeprazole 40 mg twice daily), but dosing should generally be reduced to once daily after four weeks [26-28].

The duration of treatment is based on the ulcer location and underlying etiology. (See "Peptic ulcer disease: Treatment and secondary prevention", section on 'Duration'.)

Discontinue NSAIDs — If aspirin or non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) can be discontinued, even complicated ulcers readily heal and uncommonly recur. If non-aspirin NSAIDs must be continued, the incidence of recurrent PUD can be decreased by switching to a COX-2 inhibitor with concomitant therapy with a PPI or misoprostol (for rare patients who are unable to take PPIs or have contraindications to PPI use). Likewise, when

continued low-dose aspirin is justified, concomitant cotherapy with a PPI is indicated. Strategies for secondary prevention of gastroduodenal toxicity due to NSAIDs are discussed in detail elsewhere. (See "NSAIDs (including aspirin): Secondary prevention of gastroduodenal toxicity".)

Evaluation for H. pylori — Patients should be evaluated for *H. pylori.* Eradication of *H. pylori* dramatically reduces recurrent ulcers and complications. *H. pylori* testing (eg, biopsy urease test, urea breath test) in the setting of ulcer bleeding or PPI use may result in false-negative results, so repeat testing is required for patients whose initial tests are negative [10]. A urea breath test for *H. pylori* performed as soon as the patient has resumed oral feedings is a reasonably sensitive predictor of *H. pylori* infection.

We typically defer treatment of *H. pylori* with oral antibiotics until patients are tolerating oral feedings. Interrupted treatment may encourage resistance and should be avoided. (See "Indications and diagnostic tests for Helicobacter pylori infection in adults", section on 'Diagnostic tests'.)

Management of specific complications

- **Bleeding** – Upper endoscopy is the best initial diagnostic and therapeutic procedure in the management of bleeding peptic ulcers. Surgery and transcatheter arteriography/intervention are generally reserved for patients with failed therapeutic endoscopy. The management of patients with bleeding peptic ulcers is discussed in detail separately. (See "Overview of the treatment of bleeding peptic ulcers" and "Approach to acute upper gastrointestinal bleeding in adults".)

- **Penetrating ulcers** – Management of penetrating ulcers should follow the intensive measures outlined for refractory ulcers. (See "Approach to refractory peptic ulcer disease".)

- **Perforation** – Many ulcer-related perforations of the stomach and duodenum require surgical repair (open or laparoscopic). However, nonoperative management may be used is selective patients. The management of gastric and duodenal perforations and surgical repair of PUD are discussed in detail separately. (See "Overview of gastrointestinal tract perforation", section on 'Initial management' and "Surgical management of peptic ulcer disease", section on 'Perforated gastric ulcer'.)

- **Gastric outlet obstruction** – Initial management consists of acid suppression with a parenteral PPI, avoidance of NSAIDs and, if present, eradication of *H. pylori* infection. In patients who fail to respond to a brief (three to seven day) trial of conservative management, endoscopic dilation is indicated. Surgery is reserved for patients with a complete pyloric obstruction that cannot be safely dilated, or if the obstruction persists or

recurs despite endoscopic management. (See "Gastric outlet obstruction in adults", section on 'Management'.)

SUBSEQUENT MANAGEMENT

Upper endoscopy — Upper endoscopy is indicated for most patients with PUD who present with a PUD complication in order to exclude neoplasia, unless there is confidence that the ulcer site was adequately evaluated and biopsied endoscopically or surgically at the time of presentation. To allow ulcers to heal, upper endoscopy is performed after 8 to 12 weeks. (See "Peptic ulcer disease: Treatment and secondary prevention", section on 'Repeat upper endoscopy in selected patients' and "Gastric outlet obstruction in adults", section on 'Management'.)

Prevention of recurrence — The natural history of complicated PUD is for the recurrence of complications unless the underlying cause can be treated. Strategies to reduce the risk of recurrence include NSAID avoidance and eradication of *H. pylori*. The decision to continue maintenance antisecretory therapy varies based on the patient and ulcer characteristics and risk factors for recurrent PUD. Strategies to decrease the risk of recurrent PUD are discussed in detail separately. (See "Peptic ulcer disease: Treatment and secondary prevention", section on 'Prevention of recurrence'.)

SUMMARY AND RECOMMENDATIONS

- The major complications of peptic ulcer disease (PUD) include perforation, gastric outlet obstruction, penetration, and bleeding. The risk of complications in patients with chronic PUD has been decreasing due to *Helicobacter pylori* eradication and widespread use of proton pump inhibitors (PPIs). There has been a decrease in the incidence of bleeding and perforation and hospitalization rates due to complications of PUD, presumably reflecting the fall in *H. pylori* prevalence. (See 'Epidemiology' above.)

- *H. pylori* and nonsteroidal anti-inflammatory drugs (NSAIDs), including low-dose aspirin, are the primary causes of ulcer bleeding and perforation. Other risk factors for ulcer complications include refractory, giant (>2 cm), and pyloric channel ulcers. (See 'Risk factors for ulcer complications' above.)

- While most patients may have typical ulcer symptoms prior to the development of complications, a subset of patients have silent ulcers and are brought to medical attention due to peptic ulcer complications. (See 'Clinical presentation' above.)

- Specific complications of PUD are often suspected based on a change in pattern of existing symptoms or development of new symptoms. As examples, the development of hematemesis, melena, or hematochezia suggest an ulcer bleed; nausea, vomiting, and epigastric pain shortly after eating suggest a gastric outlet obstruction; sudden onset of abdominal pain, tachycardia, and abdominal rigidity are suggestive of a perforation. Endoscopic evaluation and/or abdominal imaging are needed to establish the diagnosis. (See 'Diagnosis' above.)

- General measures for all patients with peptic ulcer-related complications include fluid resuscitation based on the hemodynamic status, correction of associated electrolyte abnormalities, and high-dose intravenous PPI therapy. Blood transfusions may be required in selected patients with gastrointestinal bleeding. Additional measures are specific to the type of complication. (See 'Management of specific complications' above.)

- Upper endoscopy is indicated in most patients with PUD who present with a complication, except those with perforation, in order to exclude neoplasia. To allow for ulcer healing, upper endoscopy is typically repeated after 8 to 12 weeks. (See 'Upper endoscopy' above.)

- The natural history of complicated PUD is for the recurrence of complications unless the underlying cause can be treated. Strategies to reduce the risk of recurrence include NSAID avoidance and eradication of *H. pylori.* The decision to continue maintenance antisecretory therapy varies based on the patient and ulcer characteristics and risk factors for recurrent PUD. (See "Peptic ulcer disease: Treatment and secondary prevention", section on 'Prevention of recurrence'.)

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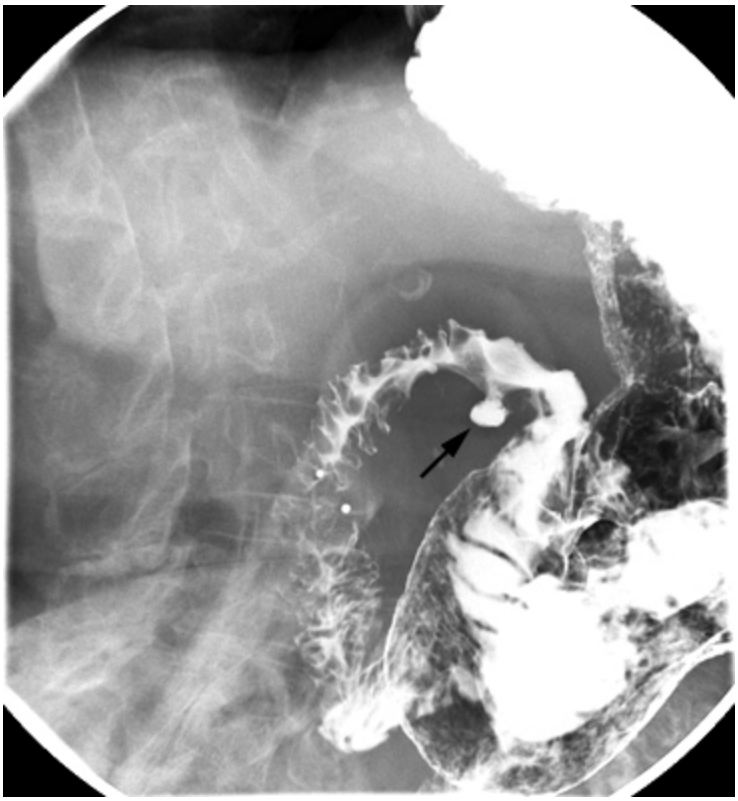
GRAPHICS

Penetrating duodenal ulcer on fluoroscopy



Air contrast upper gastrointestinal series demonstrating an ulcer involving the duodenal bulb. The ulcer was found to penetrate into the pancreas (black arrow).

Courtesy of J Pierre Sasson, MD.

Graphic 81661 Version 8.0

Contributor Disclosures

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