Chapter

The Surgical Management of Peptic Ulcer Disease

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Abstract

The treatment of peptic ulcer disease has evolved substantially through the decades since the discovery of acid-reducing agents and helicobacter pylori bacteria. With the success of medical treatment, surgical therapy continues to play a less prominent role in the care of this disease. Operative candidates include the naive patient treated with over-the-counter NSAIDs who are often those with undiagnosed Helicobacter pylori, requiring less complicated initial surgery. With more surgeons graduating with less experience operating on PUD with evolving operative techniques, the question arises as to what constitutes the optimal surgical approach, especially in the elective vs. emergent settings. Recent literature discussing GI bleeding associated with COVID-19 also merits discussion of surgical options in this chapter. Future surgical options may include minimally invasive endoscopic surgeries akin to per-oral endoscopic myotomy of the pylorus; however, this has not yet been described in this disease.

Keywords: peptic ulcer disease, Helicobacter pylori, surgical treatment

1. Introduction: The beginnings of peptic ulcer disease surgery and discovery of H. Pylori

Peptic ulcers are not a modern disease. Ulcers have plagued mankind since the age of Hippocrates (born 460 BCE), who had been known to use honey and mastic oil for symptomatic relief. Record of surgery for a gastric ulcer was found written in stone in the temple of Aesculapius at Epidaurus as described by Goldstein in 1943: "A man with an ulcer in his stomach…Asklepios opened his stomach, cut out the ulcer, sewed him up again, and loosed his bonds. He went away whole, but the chamber was covered with his blood" [1], (Goldstein HI. Ulcer and cancer of the stomach in the middle ages. J Internal Coll Surgeons. 1943;**6**:482–489.) Millenia would pass by before Polish surgeon, Dr. Ludwik Rydygier, would begin the era of modern peptic ulcer surgery. In 1881, Rydygier performed the first successful antral resection for a gastric ulcer penetrating to the pancreas. Rydygier would go on to advocate for resection in the treatment of gastric ulcers in cases characterized by perforation or bleeding, and for antral cancer. The gastroenterostomy too was pioneered by Rydygier, performed for the first time by the Polish surgeon on a patient with a duodenal ulcer [2].

Exactly 100 years after Rydygier's groundbreaking surgery, pathologist Dr. Robin Warren met Dr. Barry Marshall at the Royal Perth Hospital, Australia during internal medicine fellowship training. Sharing an interest in the physiology of

gastritis, they spent 2 years studying the stomach and discovered the spiral bacteria *H. pylori*. Marshall and Warren developed the hypothesis that this bacterium played a role of the development of peptic ulcers. The pair went so far as to drink solution containing H. Pylori, predicting eventual ulcer development, and discovering in the following weeks that H. pylori had colonized the stomach and caused gastritis [3]. While initially met with some skepticism, the link between H. pylori and peptic ulcer disease served a pioneering discovery that changed the treatment for PUD and earned Marshall and Warren the Nobel Prize in Medicine in 2005 [4].

In the wake of Marshall and Warren's achievement, new therapies evolved against peptic ulcer disease. Proposed treatments have been published since the 1990s and updated to reflect the advancements in diagnostics, resistance to antibiotics, and geographic prevalence patterns. General regimens include acid-reducing agents and various antimicrobials [1]. Medical therapy has proven to be largely successful in combating H. Pylori, with eradication rates of 70–95% across several trials [5, 6]. The patterns of peptic ulcer disease have therefore shifted from a once-common surgical problem to an entity treated effectively through oral medications.

2. The relevance of invasive intervention for PUD in 2020s

Several studies have shown that hospitalizations for peptic ulcer disease have declined since the 1980s [7–10]. However, despite improvement due much in part to the advancement of medical therapy, PUD persists in the population with a lifetime prevalence in of 5–10% and incidence of 0.1–0.3% yearly. Roughly 10–20% of these patients experience complications, including hemorrhage and less commonly, perforation [11]. The sequelae of PUD complications are often life-threatening and it is in these cases that surgical evaluation must be sought.

The current role for surgery in peptic ulcer disease is largely in the emergent setting, with bleeding, perforation, and obstruction as the major indications for intervention.

3. Operative approach: perforated peptic ulcers

In patients with perforated peptic ulcer disease with significant pneumoperitoneum, extraluminal contrast extravasation on diagnostic study, or signs of peritonitis, operative treatment is recommended [11]. It is further suggested that the operation is performed promptly (within 24 hours) to decrease morbidity and mortality [12, 13]. Endoscopy currently has no role in the treatment of acutely perforated peptic ulcers. The laparoscopic and open approaches have both been described in the management of perforated peptic ulcers. Selection of surgical approach is based at least partially on surgeon experience and available equipment. In unstable patients, open surgery is favored. Several studies have pointed to comparable outcomes between open and laparoscopic surgery including overall postoperative complication rate, mortality, and reoperation rate. Laparoscopic surgery may have advantages in reducing hospital stay, lowering rate of surgical site infection, and less postoperative pain when compared to open surgery [14–16]. Robotic-assisted laparoscopic surgery has not been widely used for perforated or bleeding peptic ulcers and is not currently recommended in an emergent setting.

Several factors will tailor the ultimate surgical intervention to be performed. These include ulcer location, ulcer size, history of prior surgeries, prior ulcer treatment and patient stability. With gastric ulcers, excision of the ulcer with reconstruction of the resultant defect is the operative goal. For gastric ulcers located

in the greater curvature, antrum, or body of the stomach, a wedge excision of the ulcer usually can be performed easily with linear staplers. Wedge resection results in both closure of the perforation and obtaining a tissue sample for biopsy—a critical consideration give the reported 4–14% rate of malignancy in perforated gastric ulcers [17]. Ulcers along the lesser curvature present a challenge given the proximity to the GE junction and the left gastric arterial flow. In distal lesser curvature ulcer cases, a distal gastrectomy may be considered. The proximal ulcer close to the gastroesophageal junction may require a subtotal gastrectomy with a subsequent Roux-en-Y esophagogastrojejunostomy.

It is important to note that perforations of the pyloric channel and the duodenum are functionally grouped together. Treatment of a small perforated duodenal ulcers (<2 cm) classically involves pedicled omentum placed into the defect as a repair. Primary repair, with or without an omental patch has also been described. Historically, an omental patch has been advocated to buttress a primary repair; however, recent studies point to no meaningful difference in leakage rate or mortality with addition of this step [18]. The operative approach to larger duodenal ulcers requires thorough calculation and a large range of interventions are available based on each patient's individual scenario. An omental patch repair in duodenal ulcer perforations that are greater than 2 cm in size have an increased rate of postoperative leaks (up to 12%) [17]. Partial gastrectomy with subsequent reconstruction via a gastroduodenostomy (Billroth I) or gastrojejunostomy (Billroth II) may be performed to address the ulcer and restore gastrointestinal continuity. Additionally, the jejunum can be used in a pedicled graft or serosal patch approach. The involvement of the duodenum containing the ampulla of Vater is a particularly arduous challenge. When in doubt, the integrity of the ampulla should be investigated with intraoperative cholangiography. Damage-control procedures such as the Roux-en-Y duodenojejunostomy or pyloric exclusion may be warranted in patients with tenuous stability. The duodenostomy tube should be considered as last-resort procedure when the patient's hemodynamic status on the operating table will not allow for a more complex operation. An emergent Whipple comes with a high rate of morbidity and mortality and should generally not be attempted.

4. Operative approach: bleeding peptic ulcers

The evolution of endoscopic skills and technology in the last several decades has brought this technique to the forefront of bleeding ulcers and often obviates the need for surgical intervention. Early endoscopy (within 24 hours) is first-line therapy with the employment of therapeutic endoscopic interventions as needed, along with the initiation of parenteral proton pump inhibitors [11]. Roughly 10–20% of patients will have recurrent bleeding despite endoscopic therapy, at which time repeat endoscopy should be considered [19]. Patients who remain hemodynamically stable thereafter without high-risk ulcer features may then be safely discharged with continued oral PPI management. Surgery becomes warranted in cases of bleeding peptic ulcers when endoscopy fails or when the patient is deemed high-risk of a rebleeding event. Large ulcers (>2 cm) and hypotension at rebleeding are reported independent factors of predicting failure in further endoscopic treatment. Other features reported to prompt surgical consultation for further management include pulsatile bleeding, visible blood vessels in posterior duodenal ulcers, and transfusion requirement greater than 6 units of blood in the first 24 hours [20].

The surgical procedures currently used in bleeding gastroduodenal ulcers are on a spectrum of minimal to definitive interventions. The principal objective in life-saving surgery is hemorrhage control, which may be achieved through simple

intraluminal oversewing or ligature, plication, or excision of the ulcer and repair of the defect [20]. The initial procedure may also include control of the arteries of the stomach or duodenum through direct ligation.

5. The role of acid-reducing procedures

The management of emergent PUD has largely left out procedures that were designed to address the underlying problem--a once common consideration in all patients with PUD up until the 20th century. Acid-reducing procedures historically included division of the vagus nerve at various points in order to decrease the acetylcholine-mediated secretion of acid from parietal cells [21].

The truncal vagotomy is the division of the anterior and posterior trunks of the vagus nerves roughly 4 cm proximal to the gastro-esophageal junction. Stimulation of parietal cells is interrupted through this procedure; however, the lack of sympathetic input to the stomach results in a lack of relaxation, thereby decreasing the propulsion of solids from the stomach into the small intestine. Therefore, a concomitant drainage procedure, consisting of a pyloroplasty or antral resection would be performed. A selective vagotomy is similar but involves division of the vagus nerves at the more distal anterior and posterior branches after the level of the celiac and hepatobiliary branching. The highly selective vagotomy (HSV) was tailored to avoid the need for a drainage procedure. The HSV involves division of the nerve fibers supplying the parietal cells of the fundus and body of stomach, sparing the "crows's foot" fibers innervating the antrum and pylorus. Given the rise of medical management, the role of the vagotomy with or without drainage procedures in peptic ulcer disease is limited to very few cases [22].

The main indication for consideration of an acid-reducing procedure are patients whose disease is refractory to medical management or those who cannot reliably participate or tolerate proton-pump inhibitors. Specifically, it is cases of duodenal ulcers (Type II and III) in which a vagotomy may be considered--gastric ulcers (TYpe I, IV) are not related to acid hypersecretion and therefore resection alone is indicated. In emergent situations, including bleeding duodenal ulcers and perforated duodenal ulcers, the use of a vagotomy is debated and is often surgeon-dependent. In general, the presence of peritonitis, shock, abdominal abscess, delay in treatment over 24 hours, or severe concurrent medical illness are contraindications to lengthening the surgery by adding a vagotomy to the rest of the surgical management plan [22, 23].

6. Future surgical considerations

In the era of rapidly advancing surgical instruments and techniques, innovations in peptic ulcer disease surgery are rising in efforts to improve patient outcomes. The robotic platform is emerging as a feasible alternative to surgical treatment in the elective settings for many diseases. There have a been case reports of gastric resections performed safely with the assistance of the surgical robot, and whether the robot has a wider role for peptic ulcer disease merits exploration [24, 25]. Most prior reports of robotic assisted laparoscopic surgery for the stomach are those done for malignancy.

The pedicled omental plug for a large duodenal ulcer is a described twist on the classic omental patch closure. In this procedure, a nasogastric tube is inserted through the oropharynx and down through the perforation. A tongue of omentum is then secured to the tube via sutures and withdrawn into the stomach, where it is

sutured to the ulcer edges. This omental plug shows promise, as was associated with a lower recurrent leak and duodenal stenosis rate in a randomized trial comparison against the standard omental patch [26]. Falciform flaps may be a feasible option in patients who do not have a viable omentum [27].

7. PUD and the advent of COVID-19

With the introduction of SARS-CoV-2 to the world's collective biome we have observed unprecedented patterns of illness, with both the aversion of presenting to an affected hospital and the virus itself affecting disease across multiple organ systems. We here present a look at the relationship, if any, between COVID-19 and peptic ulcer disease.

It is well-known that COVID-19 presents with respiratory symptoms; however, several other manifestations are being seen. In one study comprised of over 20,000 patients, up to 29% had enteric symptoms including abdominal pain, nausea, vomiting, and diarrhea [28]. The pathophysiology of gastrointestinal tract manifestations of COVID-19 is thought to stem from several biochemical mechanisms including infection of the GI tract/liver leading to cellular inflammation and damage, dysbiosis enhancing the inflammatory response and cytokine storm, and affliction of the neuroenteric system [29].

GI bleeding is a reported, though less common manifestation associated with COVID-19. A rather high prevalence of PUD complicated by bleeding was noticed in one cohort of patients with moderate-to-severe ARDs caused by COVID-19 [29]. In another study performed on COVID-positive hospitalized patients undergoing endoscopy (n = 106), one-fourth of the studied population had peptic ulcers while an additional 16% had erosive/ulcerative gastro-duodenopathy [30]. The mainstay of treatment in peptic ulcer disease is proton-pump inhibitors; however, at least one study has demonstrated that PPI treatment is associated with worse outcomes in those infected by SARS-CoV-2 and development of COVID-19 when compared to individuals who are not taking a PPI [28]. The mechanism responsible for this finding remains unclear.

Another factor to consider in patients afflicted with peptic ulcer disease is the pattern of behavior in seeking medical evaluation during a pandemic. As the admissions for COVID-19 related respiratory illnesses increased dramatically, several hospitals reported decreased admissions and emergency medicine visits for non-COVID related diseases [31–33]. Theories concerning this trends in admissions during the pandemic include failure to present to a hospital secondary to fear of contracting COVID-19, which may have made some cases of illness more profound up to the point of death in the community [33]. The first United States Coronavirus epicenter in New York performed a multicenter study looking specifically at emergent general surgery admissions. Comparison to prior years indicated that there was an overall decrease in admissions with an overall increase in mortality. Peptic ulcer disease was one of the seven diagnoses that was observed [34]. A delay of 12 hours was found in 10 cases of complicated peptic ulcer disease in one institution during a two-month period [35]. The question arises if the increase in mortality is at least in part attributable to delayed presentation.

The full clinical spectrum of COVID-19 has not yet fully been elucidated. There is surprisingly limited data on the relationship between COVID-19 and peptic ulcer disease. The pathogenesis of ulcers in the setting of SARS-CoV-2 affliction may be related to direct gastric epithelial damage, stress resulting from the acute disease, or active mucosal inflammation sustained by cytokine storming [36]. Development of treatment guidelines in COVID-19 positive patients who sustain gastrointestinal manifestations of disease warrants further investigation.

8. Final reflections

Peptic ulcer disease remains a healthcare issue across the world and requires an interdisciplinary approach. In linking H. Pylori and NSAID use to peptic ulcers, pioneering efforts in controlling PUD have largely been seen in the primary care setting. However, complications from PUD persist in the population, and surgical intervention will continue to play a role in the very worst of the disease burden. It is therefore the responsibility of the surgical community to advance care through innovation of technique to provide optimal outcomes. This is especially true in the era of a pandemic where healthcare dynamics are adversely affected.

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