# Perforated Peptic Ulcer

# 72

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## 72.1 Introduction

**Learning Goals**

- To educate learners that perforated peptic ulcer (PPU) is a surgical emergency and requires early diagnosis, prompt resuscitation, and expeditious intervention to deliver good clinical outcomes.
- To understand the importance of imaging in PPU diagnosis. This chapter enables learners to understand rationale of patient selection for various treatment options, including non-operative management of PPU.
- The chapter enables learners to realize the role of various scoring systems in PPU, and highlights importance of sepsis bundle in surgical care of PPU.

Peptic ulcer disease (PUD) is an insult to the gastric mucosa resulting from an imbalance between stomach acid-pepsin and mucosal defense barriers [1]. Mucosal insult results in ulceration extending beyond the mucosa and submucosal layers. Peptic ulcers are typically located in the stomach or duodenum but can be found in the esophagus or Meckel's diverticulum [2]. Bleeding and perforation are two common complications of PUD. Perforation is a severe complication that warrants early recognition, prompt resuscitation, and operative repair to ensure sound clinical outcomes [3, 4]. This review provides an update incorporating the evidence-based practice for a perforated peptic ulcer (PPU).

### 72.1.1 Epidemiology

PUD affects 4 million people worldwide annually, with an estimated lifetime prevalence of about 5% [5, 6]. Although complications of PUD have decreased with widespread availability and access to proton pump inhibitors (PPIs), PPU remains one of the most severe surgical emergencies that occur in 2–10% of PUD patients, with 30 and 90-day mortality risk of almost 30% [7]. Recognition of *Helicobacter pylori* (*H. pylori*) as a common microbe causing PUD, and its link with gastric carcinogenesis, has impacted global epidemiologic trends.

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### 72.1.2 Etiology

Etiopathogenesis of PUD is diverse and includes both modifiable and non-modifiable, personal, and population-level risk factors. Seasonal association with PPU risk is reported, but more data is required to prove causation [8, 9]. Young male smokers in developing countries are the typical PPU patient profile. In developed countries, patients tend to be elderly with multiple comorbidities, including the use of nonsteroidal anti-inflammatories (NSAIDs). Other risk factors include *H. pylori* infection, renal dysfunction, and critical illness [10–12]. Despite successful treatment of the ulcer, recurrence is expected in the presence of underlying risk factors. A systemic review of 93 studies has reported ulcer recurrence risk 12.2% (odds ratio [OR]: 95% confidence interval [CI]: 2.4–21.9) [13]. This is important as a minority of gastric ulcers are associated with gastric cancer, and tissue diagnosis is essential to rule out malignancy. Clinicians must be aware that even a malignant ulcer may show signs of healing after a trial of PPI, and thus a high index of suspicion and liberal biopsies of gastric ulcer is essential. In patients where common risk factors cannot be established, a clinician must perform an extended workup to evaluate hypercalcemia (e.g., parathyroid disorders) or hypergastrinemia (e.g., Zollinger Ellison syndrome).

#### 72.1.2.1 *Helicobacter pylori*

*H. pylori* is an aerobic, gram-negative flagellated rod commonly transmitted via the oral-fecal route [14]. This includes consumption of contaminated water and food, sharing of utensils, and improper handwashing techniques. *H. pylori* is prevalent in developing countries (95%) as compared to developed countries (30%) [15, 16]. Locally, our prevalence rate of *H. pylori* is 31% [17]. This is comparable to the prevalence rate of the United States (36%) [18]. *H. pylori* causes chronic gastric inflammation due to urease, toxins, and flagella. Urease breaks down urea into ammonia, and thus *H. pylori* can remain viable in the acidic gastric environment. Toxins such as CagA/VacA can also cause host tissue damage. Flagella helps motility and movement towards the gastric epithelium. *H. pylori* is more associated with duodenal ulcers, but it is also linked with gastric ulceration. Studies have shown that *H. pylori* eradication is crucial to prevent PUD recurrence [19]. If unrecognized or untreated, chronic infection can cause perforation. *H. pylori* is detected in 50–80% of patients with PPU [11, 20]. A randomized controlled trial by El-Nakeeb et al., which included 77 patients with PPU, showed that 84.8% of patients had *H. pylori* [21]. Of those who had *H. pylori* infection, they were further divided into the control group (omeprazole alone) and eradication group (triple therapy with amoxicillin, metronidazole, and omeprazole). After 1 year, ulcer recurrence was 6.1% in the eradication group versus 29.6% in the control group ($p = 0.001$). This emphasizes the importance of *H. pylori* eradication after repairing the perforation, so future re-ulceration risk is reduced. We routinely treat all PPU patients with empiric *H. pylori* therapy upon discharge following uneventful recovery following surgical repair.

#### 72.1.2.2 Nonsteroidal Anti-inflammatory Drugs

NSAIDs are used mainly for their analgesic, anti-inflammatory, and antipyretic effects. Its inhibition of cyclo-oxygenase 1 (COX-1) in the gastrointestinal tract inhibits prostaglandin secretion and reduces cytoprotective effects in the gastric lining, promoting mucosal injury [22]. NSAIDs increase the PPU risk by six to eight times and are responsible for about a quarter of perforation events in PUD patients [23, 24]. Antiplatelet medications are in widespread global use for prophylaxis of cerebrovascular and cardiovascular disease [25–27]. Although prophylaxis is less used in Asia than in Western countries, anti-platelet use continues to increase [28]. Authors have observed a local trend by primary care physicians prescribing PPI alongside antiplatelets, a practice that is primarily based on personal views about PUD risk reduction. In a prospective study including 2416 Danish adults, though Rosenstock et al. did not find a strong association between NSAIDs and PUD, NSAID consumption was associated with bleeding ulcers in elderly patients (OR: 0.4, 95% CI: 0.1–2.3,

$p < 0.001$) [29]. NSAIDs are widely used for post-operative analgesia. In four patients treated by the Caesarean section, Shirazi et al. reported PPU [30]. As gastrointestinal symptoms following orthopedic or gynecological procedures are infrequent, physicians must have a high index of suspicion if a patient develops abdominal symptoms.

#### 72.1.2.3 Cigarette Smoking

Smoking is a public health nuisance and a population hazard. Smoking is harmful to the upper gastrointestinal tract and negatively impacts global human health and well-being [31]. PUD risk is associated with the quantity and duration of tobacco use, and cigarette smokers are more likely to develop ulcers that are more difficult to heal [32]. Smoking inhibits pancreatic bicarbonate secretion and causes vasoconstriction of the gastric mucosa with resultant ischemia [33, 34]. Thus, the effectiveness of the bicarbonate buffer against acidic gastric juices is reduced, and PUD occurs [35]. In a retrospective study including 168 patients with PPU and 4469 control subjects, Svanes et al. reported that smoking predisposes to perforation and accounts for the majority of perforations in the population aged below 75 years (OR: 9.7, 95% CI: 4.9–15.4, $p < 0.001$) [35]. A study including 110 PPU patients with ulcer size ≥2 cm showed that 35.5% ($n = 39$) of patients smoked [9]. Even in a casual smoker, or second-hand smoker, emergency surgery morbidity risk is high as the active ingredients (nicotine and carbon monoxide) decrease oxygen levels and increase the likelihood of cardiovascular morbidity.

#### 72.1.2.4 Marginal Ulcer

Marginal ulcers can develop at the jejunal side of the gastrojejunal anastomosis, with an incidence rate of 1–16% [36, 37]. Perforation of a marginal ulcer is a rare complication and can be potentially life-threatening [38]. Some risk factors for perforation include local ischemia, anastomotic tension, duodenal reflux, cigarette smoking, NSAIDs, and chronic irritation due to the type of suture material used for anastomosis [39]. With the increasing role of surgery in the management of diabetes and obesity, marginal ulcers are increasingly reported following procedures such as Roux-en-Y reconstruction.

### 72.1.3 Pathogenesis

Peptic ulcer occurs due to an imbalance between the protective and ulcerogenic factors. However, it is still unclear why some perforate and some do not [40]. Prostaglandins are a crucial defense as they inhibit acid secretion and stimulate bicarbonate release [41]. As NSAIDs reduce prostaglandin production, chronic NSAID consumption leads to PUD. Though *H. pylori* infection is associated with PUD, reports mention that half of PPU patients do not have *H. pylori* infection [42, 43]. Multiple other overlapping factors increase the burden of risk for perforation. Once an ulcer occurs, the size and location may predispose to perforation. However, small ulcers may perforate too [44]. Perforations happen in the morning, suggesting the circadian variation in acid secretion [40]. The reportedly increased risk of perforations during Ramadan may be due to prolonged fasting and acid secretion and release [45].

PUD and PPU are also reported in relevance to the ongoing coronavirus disease 2019 (COVID-19) pandemic. The use of corticosteroids and NSAIDs increases this risk [46]. Agnes et al. reported that the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus causes direct epithelial injury and systemic inflammation resultant cytokine storm may predispose to gastrointestinal bleeding or perforation [47]. In addition, interleukin-6 (IL-6) inhibitors may predispose to perforation. However, to accurately determine whether COVID-19 increases the incidence of PPU, more data is necessary.

## 72.2 Diagnosis

### 72.2.1 Clinical Presentation

Symptoms of PUD include abdominal pain, upper abdominal discomfort, bloatedness, and a

feeling of fullness. In 1843 Edward Crisp stated that the symptoms are typical; I hardly believe that anyone can fail to make a diagnosis [1]. As PUD develops, the risk of perforation increases, resulting in extravasation of gastric juices and gas into the peritoneal cavity, causing peritonitis. A patient presenting with a clinical triad of sudden severe epigastric abdominal pain, tachycardia, and abdominal rigidity is the hallmark of PPU [1]. In patients with posterior gastric ulcer perforation, gastric contents leak into the lesser sac and mask peritonitis symptoms [48]. A posterior duodenal ulcer perforation can cause a localized retroperitoneal abscess and occasionally present with right iliac fossa pain (Fig. 72.1). This can masquerade as acute appendicitis and is known as Valentino's syndrome [49]. Therefore, it is essential to have a high clinical suspicion for PPU, especially in patients with risk factors.

PPU can present in three phases [50]. In the first 2 h, epigastric tenderness, tachycardia, and cool and clammy peripheries are characteristic. This phase is then followed by generalized abdominal pain that is exacerbated by movement. Other signs may include involuntary guarding and abdominal rigidity with right iliac fossa tenderness due to fluid accumulating in the right paracolic gutter. Initial local peritonitis becomes generalized, and chemical peritonitis transforms into bacterial peritonitis. In the last phase, abdominal distension, fever, and hemodynamic instability ensue [1]. In rare instances, perforation is sealed off by a tag of omentum or adjacent tissues so that progressive peritonitis does not occur (*forme fruste*), and nonoperative management may be undertaken.

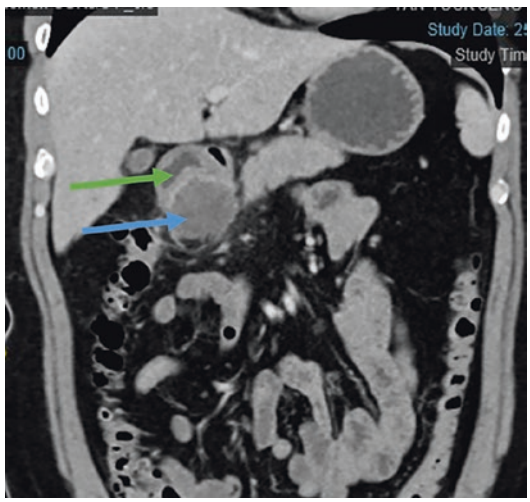


**Fig. 72.1** A computerized tomography scan of an adult patient showing the first part of duodenum (green arrow) and a localized retroperitoneal abscess (blue arrow). Nonoperative management was successful in this patient

## 72.2.2 Investigations

### 72.2.2.1 Serum Investigations

Blood and biochemical investigations are not diagnostic for PPU but provide information of physiologic insult. Serologic data are nonspecific and have complementary utility in PPU management [51]. Serum amylase is raised less than four times the normal levels and should be done at the emergency department along with an erect chest radiograph [52]. Full blood count for leukocytosis and raised C-reactive protein (CRP) suggest inflammation or infection [52] and is also associated with PPU [53]. A renal panel helps assess if a contrast computerized tomography (CT) scan is safe. PPU can cause organ dysfunction due to systemic inflammatory response syndrome (SIRS) and pre-renal acute kidney injury [54]. Serum albumin levels provide information beyond the nutritional status of the patient. In a single-institution retrospective study comprising of 537 patients, Seow et al. reported that low serum albumin might predict the need for gastric resection (OR: 5.57, 95% CI: 1.56–19.84, $p < 0.001$) [55]. If other etiologies of PPU are suspected, such as Zollinger Ellison syndrome or parathyroid disorders, serum gastrin and calcium levels may be ordered [1]. Inflammatory ratios like platelet to lymphocyte ratio (PLR) are easy to compute and help predict clinical outcomes. In a retrospective study including 152 patients, Omer et al. reported that patients with high PLR had a length of hospital stay of >1 week ($p = 0.005$) [56]. More evidence is required before any recommendations can be made to include PLR or similar ratios in routine clinical practice. In our opinion, serum lactate is an important marker to assess the physiologic insult

from secondary peritonitis, and it not only guides resuscitation but also can predict prognosis. In a single-center retrospective study including 50 PPU patients, serum lactate predicted post-operative morbidity [57].

#### 72.2.2.2 Imaging

In a patient with acute upper abdominal pain, the most essential and initial imaging that should be performed is an urgent erect chest X-ray (CXR) [1]. An erect CXR should be ordered to visualize free air under the diaphragm, pneumoperitoneum (Fig. 72.2) [58]. Erect CXR and lateral decubitus radiographs have similar diagnostic accuracy, and should a patient not tolerate an erect CXR due to severe peritonitis; the latter should be done [59]. The free air under the diaphragm is unfortunately only present in about 30–85% of PPU; a negative CXR does not rule out PPU. Thus, an abdominal CT scan [59] is warranted to establish a definite diagnosis. If an abdominal X-ray (AXR) had been performed instead, it might show distinct outlining of the bowel wall due to the appearance of intra and extraluminal air (Rigler's sign) (Fig. 72.3) or a large volume of free gas resulting in a large black area (Football sign). We do not recommend an AXR to be done in the setting of a negative CXR and suggest a CT scan of the abdomen-pelvis. CT scans have a high diagnostic rate of 98% [60]. CT scans are helpful in PPU diagnosis and in excluding other abdominal pathology (like acute pancreatitis). Some findings on the CT scan to note are fluid and air in the peritoneal cavity, thickening of the bowel wall, mesenteric fat stranding, and extravasation of water-soluble contrast. A non-contrast CT scan can be ordered in patients with renal impairment, and visualization of air within the peritoneal cavity is sufficient to diagnose PPU. In patients with no CT scan features of PPU, administering an oral (or via nasogastric tube (NGT)) water-soluble contrast may increase diagnostic yield. Leakage of contrast confirms the diagnosis of PPU. However, the absence of a leak does not eliminate the diagnosis of PPU as the perforation may be sealed off spontaneously [61]. In patients without free air under the diaphragm on the erect CXR and unavailability of CT scan facilities, NG air insufflation may increase diagnostic yield [62]. Ultrasound may detect intraperitoneal free fluid and intestinal paresis and may be used as an adjunct in selected patients.

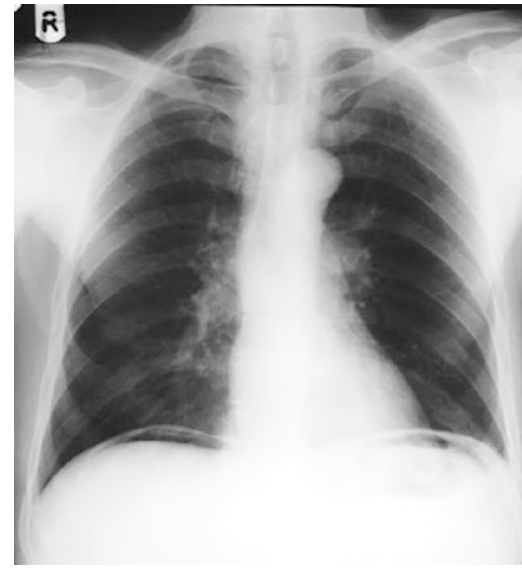


**Fig. 72.2** An erect chest X-ray of an adult patient with sudden onset severe epigastric pain showing free air under the diaphragm, suggestive of perforated peptic ulcer

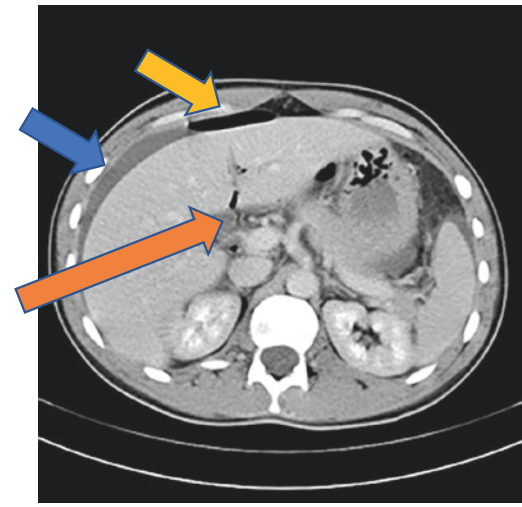

**Fig. 72.3** A computerized tomography scan showing free air along (yellow arrow) with perihepatic free fluid (blue arrow). Air pockets are also seen along the portal triad and first part of duodenum (orange arrow). This is highly suggestive of perforated peptic ulcer

**Differential Diagnosis**

The three categories of differential diagnosis of PPU include: (a) differential diagnosis for epigastric abdominal pain, (b) differential diagnosis of elevated serum amylase, and (c) differential diagnosis of free air under the diaphragm on imaging.

Epigastric or right upper abdominal pain is a common presenting symptom of acute cholecystitis, acute pyogenic cholangitis, pyogenic liver abscess, acute gastroenteritis, and acute colitis. Appropriate history and physical examination would suggest a clinician of foregut versus midhindgut pathology. Serology and imaging will aid to narrow down the list of differential diagnosis. Elevated serum amylase can be noticed in PPU patients due to peritoneal reabsorption of leaked contents. Acute pancreatitis should be differentiated as PPU warrants an emergency surgery, while management of acute pancreatitis is largely supportive. Free air under the diaphragm can be evident in other abdominal pathologies like perforated small or large bowel. Appropriate clinical history and demographic profile could assist to achieve diagnosis. In selected stable patients, CT scan of the abdomen could be considered even if chest X-ray detects free air under the diaphragm. A prior knowledge about organ of origin of perforation can alert the duty surgeon and he or she is well prepared rather than caught up with a surprise of sigmoid colon cancer perforation as a cause of free air on chest X-ray.

## 72.3 Management

The management of PPU involves integration of principles of critical care, sepsis bundle, and timely surgical intervention for source control. It is essential that surgical team co-ordinates the care and involve necessary stakeholders (e.g., radiologist or anesthetist) for optimal and timely care to ensure good clinical outcomes. Figure 72.4 shows the flowchart of management principles of PPU.

### 72.3.1 Resuscitation

PPU is frequently associated with peritonitis and septic shock and is thus a medical and surgical emergency requiring rapid evaluation and timely intervention [63]. It is of utmost priority to monitor and recognize sepsis complications and adequately define if a patient is hemodynamically stable or unstable as it impacts management [64, 65]. Symptoms such as altered mental status (low Glasgow coma scale (GCS)) suggest that perforation occurred a few hours ago. Signs such as tachycardia, tachypnea, reduced pulse pressure, reduced urinary output, and laboratory findings of metabolic acidosis and raised creatinine must be promptly evaluated. It is also essential to keep in mind that such findings may be confounded by underlying disease or medications, and thus clinical history must be meticulous [66]. Nil by mouth, nasogastric tube insertion, intravenous PPIs, urinary catheterization, analgesia, and broad-spectrum antibiotics are essential to initial measures along with intravenous fluids and oxygenation. In the "Surviving Sepsis Campaign," it is recommended that in sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloids are administered within the first 3 h [65, 67].

Principles of sepsis management include source control and treatment of underlying etiology with antibiotics. Routine microbiologic cultures (two sets of aerobic and anaerobic blood cultures) should be obtained before starting broad-spectrum empirical antibiotics [68]. Antibiotics such as third-generation cephalosporins and metronidazole to cover for gram-negative, gram-positive, and anaerobic species are given pre-operatively to reduce the risk of intraperitoneal bacterial translocation. Antifungals are recommended based on patient factors, such as those who are immunocompromised, of advanced age, with severe co-

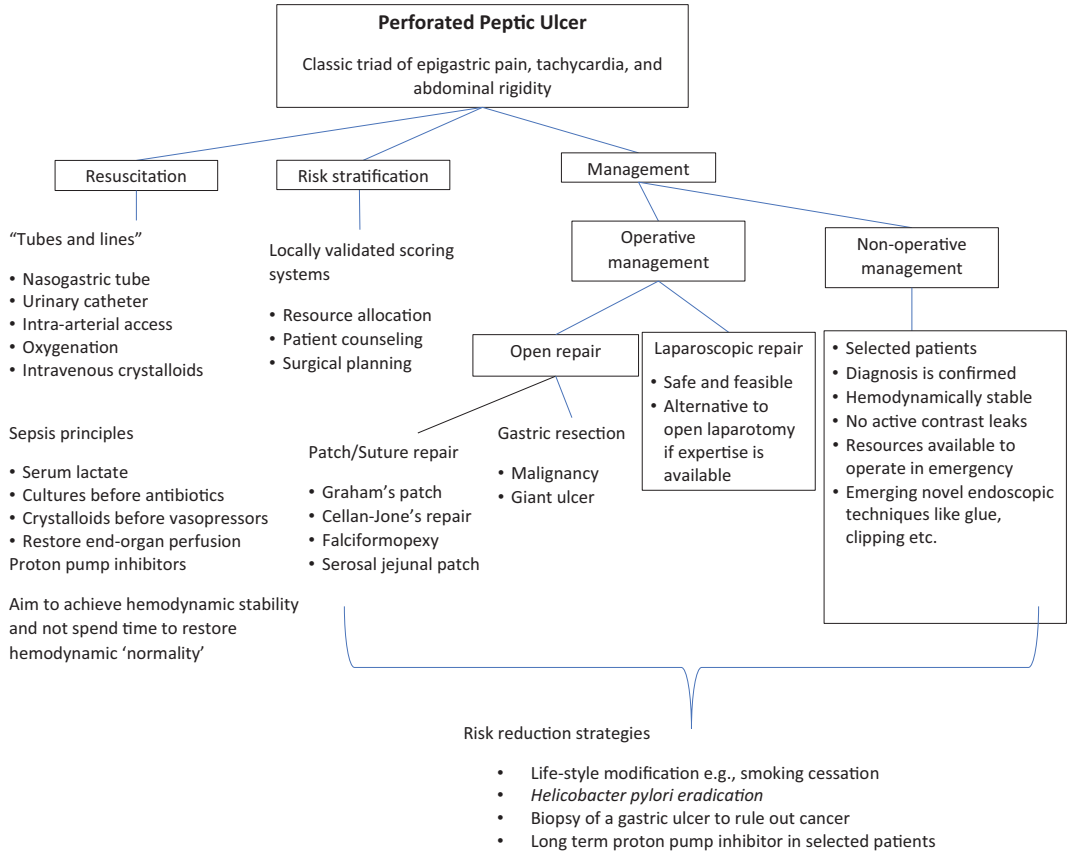


**Fig. 72.4** Flowchart of management principles of perforated peptic ulcer

morbidities, and prolonged ICU-stay or persistent intra-abdominal infections [59, 69]. In a single-center retrospective study including 673 adult patients with perforated gastric and duodenal ulcers over 10 years (January 2004–2014), Kwan et al. reported that on multi-variate analysis, fungal isolates in peritoneal fluid cultures are more likely to occur in older patients who have PPU (OR: 1.031, 95% CI: 1.01–1.047, $p < 0.001$). However, the presence of fungal isolates does not impact perioperative outcomes [70]. Intra-abdominal sepsis management requires a multidisciplinary team approach involving the general surgeon, radiologist, critical care physician, nurses, microbiologist, and allied health personnel. Continuous assessment of the patient's heart rate, blood pressure, arterial oxygen saturation, respiratory rate, temperature, and urine output are essential. Serum lactate helps to serve as a surrogate marker for tissue perfusion and, monitoring of lactate can help identify improvement or deterioration in septic patients. The possible endpoints of resuscitation include mean arterial pressure (MAP) ≥65 mmHg, urine output ≥0.5 mL/kg/h, and lactate normalization. In practice, source control by prompt surgical intervention is a "part of resuscitation." Thus, the resuscitation goal is not to achieve hemodynamic "normality" but hemodynamic "stability."

### 72.3.2 Scoring Systems in PPU

Scoring systems assist with the prediction of severity or morbidity/mortality outcomes. Knowledge of predicted outcomes can assist in allocating resources, patient and family counseling, and timely evidence-based care. The main

scoring systems for PPU are the Boey score, the American Society of Anesthesiologists (ASA) score, the Sepsis score, the Charlson Comorbidity Index, the Mannheim Peritonitis Index (MPI), the Acute Physiology and Chronic Health Evaluation II (APACHE II), the Simplified Acute Physiology Score II (SAPS II), The Physiology and Operative Severity Score for the Enumeration of Mortality and Morbidity Physical Sub-score (POSSUM-phys score), the Mortality Probability Models II (MPM II), Peptic Ulcer Perforation (PULP) score, the Hacettepe score and the Jabalpur score [71]. The most widely used and validated scoring systems are the Boey and ASA scores [54, 72–75]. The other scores are not commonly used due to the lack of validation data or cumbersome to compute. This review focuses on Boey's score, PULP score, and MPI.

Boey's score includes three variables: comorbidity, pre-operative shock (defined as systolic blood pressure <90 mmHg), and time from onset of abdominal pain (≤24 or >24 h). The minimum possible score is zero, and the maximum possible score is three. Boey et al. demonstrated 0%, 10%, 45.5% and 100% mortality for a score of 0, 1, 2 and 3 respectively [4]. Boey score is simple to compute and is still widely utilized [76]. However, as the understanding of comorbidity is varied, and the time from onset of abdominal pain is sometimes not exact, the score is not consistent in the predictive ability for mortality outcomes [73, 77, 78]. The PULP score includes seven clinical and biochemical variables: age, active comorbidities, liver cirrhosis, steroid use, shock on admission, time from perforation to admission, serum creatinine, and ASA score [79]. The minimum possible score is zero, and the maximum possible score is 18. PULP score is regarded as complex and impractical, and more validation studies are required. We could not validate the PULP score due to very few patients with liver cirrhosis and steroid therapy in our cohort. The ASA score is a subjective assessment of a patient's fitness for operation based on five classes (I–V). A patient with a higher ASA score has a higher mortality rate [80, 81]. The MPI score includes eight variables: age >50 years, female sex, presence of organ failure, presence of malignancy, the evolution of peritonitis for >24 h, non-colonic origin, generalized peritonitis, and fecal peritonitis [82]. The maximum possible score is 47 points, and patients are categorized into three risk profiles in increasing order of severity of peritonitis: <21, 21–29, and >29 points. The score is only possible to compute after completion of surgery. In a study involving 332 patients who underwent emergency surgery for PPU, Anbalakan et al. found that all four systems have moderate accuracy of predicting mortality rates, with an area under the receiver operator curve of 72–77.2% [83]. Upon diagnosis, resuscitation, and risk stratification by scoring systems, definite treatment must be done. In general, definitive treatment can be divided into surgical treatment, endoscopic interventions, and nonoperative management. Other novel techniques such as endoscopic clipping, gelatin sponge, and glue sealing will also be discussed.

### 72.3.3 Surgical Treatment

Figure 72.5 shows the perforated duodenal ulcer. Johan Mikuliczradecki stated that every doctor faced with a PPU must consider opening the abdomen, sewing up the hole, and averting a possible inflammation by a careful cleansing of the abdominal cavity [1]. Historically, selective vagotomy was done to prevent gastric acid production from the parietal cells to reduce gastric

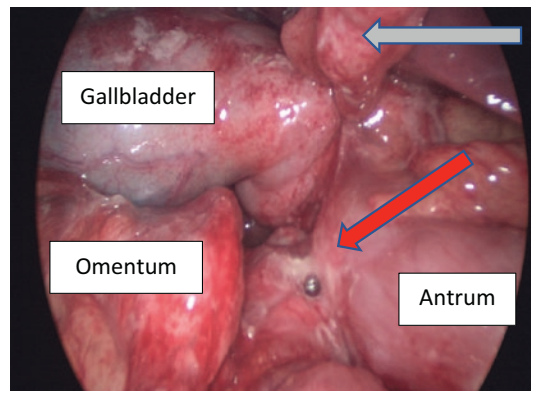


**Fig. 72.5** A laparoscopic view of a patient with perforated duodenal ulcer (red arrow). Grey arrow shows falciform ligament

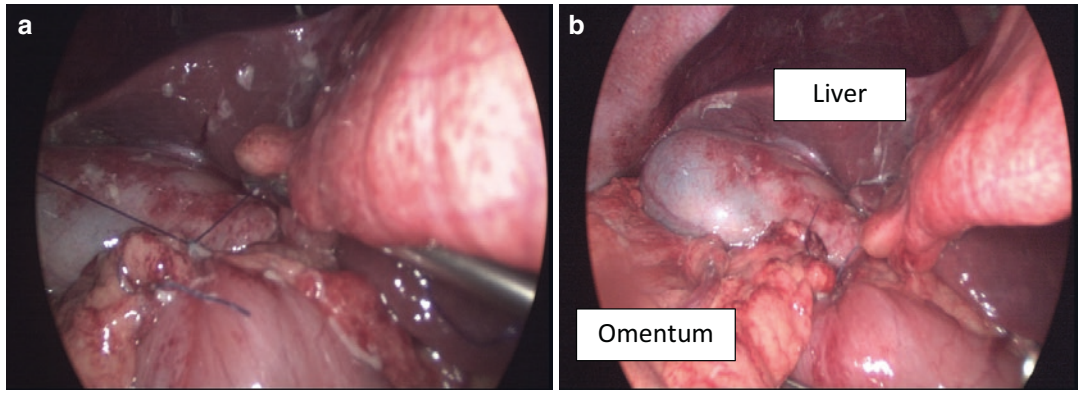


**Fig. 72.6** Laparoscopic omental patch suture repair. (**a**) Shows intracorporeal suturing and (**b**) shows a completed omental patch repair

acid secretion and reduce recurrence rates of PUD [47]. However, with the emergence of histamine receptor antagonists and PPI, vagotomy is obsolete [1]. In surgical treatment, the approaches are broadly divided into open or minimally invasive surgery approaches (MIS), that is, laparoscopic surgery. Figure 72.6a, b shows laparoscopic omental patch repair of perforated duodenal ulcer.

#### 72.3.3.1 Open Surgery

The most common techniques for repairing PPU include primary closure by interrupted sutures—Cellan-Jones repair and Graham patch repair. Graham patch involves placement of sutures at a right angle to the long axis of stomach or duodenum, placing a tail of omentum without tension over the ulcer, and tying the sutures snug over to close the ulcer without causing ischemia to omental tissue. Cellan-Jones repair involves tying sutures before placing the omental patch. In addition, some authors have reported using falciform ligament to patch the ulcer. Falciform ligament patch may be helpful in patients with previous omentectomy or omental adhesions following previous abdomino-pelvic surgery. In general, omentopexy and falciformopexy are considered comparable. However, in a retrospective study involving 303 patients, Ölmez et al. reported higher failure rates for falcioformopexy (2.6% and 8.7%, $p = 0.04$) [84]. In a recent report, Tran et al. has reported that falciformopexy was safe and feasible with comparable outcomes to omental patch [85]. However, the authors reported high 30-day mortality (17.5%). Overall, there are less than 100 reported cases of falciformopexy, and more evidence is warranted to establish if falciformopexy has comparable clinical outcomes [85]. Sometimes, it is difficult to identify a healthy omentum or falciform ligament to perform a patch closure. In such instances, a serosal jejunal patch is an option. This can avoid the need for gastrectomy. When deciding between gastrectomy and patch repair, the decision lies in whether there is a suspicion for gastric malignancy, and if so, whether the patient is hemodynamically stable enough to undergo an emergent gastrectomy. Kuwabara et al. compared two techniques and found no significant differences in patient outcomes [86]. However, gastrectomy was associated with higher risks of duodenal stump blowout and anastomotic leak, longer intraoperative time, higher intraoperative blood loss, and longer length of hospital stay [7, 72, 87]. In a study including 601 patients, of which 62 patients had undergone gastrectomy, those who had undergone a gastrectomy had a higher mortality risk of 24.2% than those who did not have a gastrectomy [55]. Thus, one must follow Theodore Kocher's maxim: To do everything necessary and to do nothing unnecessary. The traditional omental patch repair is still considered the gold standard today, as it has lower morbidity and peri/post-operative transfusion rates than

gastrectomy [86]. International guidelines and local hospital algorithms advocate gastrectomy beyond a specific ulcer size with variable cut-offs [36]. However, the exact cut-off beyond which omental patch repair is associated with a higher leak rate remains to be determined, and a multicenter prospective randomized study is warranted.

Open surgery can be performed by a smaller wound—minilaparotomy. A minilaparotomy is defined as an abdominal skin incision with a maximum length of 7 cm. In a retrospective review of 87 patients treated for PPU, Ishida et al. reported that patients treated by minilaparotomy ($n = 37$) had 18.4 min shorter mean operative time ($p < 0.01$), lower analgesic requirements ($p = 0.03$), earlier first pass of flatus ($p > 0.01$), and shorter hospital length of stay ($p = 0.04$) [88]. These results need to be validated. In our opinion, an emergency laparotomy is not a "cosmetic procedure," and surgical conduct should never be compromised for the sake of a smaller incision.

#### 72.3.3.2 Laparoscopic Surgery

Adoption of minimally invasive surgery to acute care has been slower compared to elective surgery. However, with increasing experience, laparoscopic repair of PPU is widely reported to be safe and feasible, with potentially lower perioperative morbidity [89]. A meta-analysis of seven randomised controlled trials (RCTs) reported that laparoscopic PPU surgery has lower overall postoperative morbidity (OR: 0.54, 95% CI: 0.37–0.79, $p < 0.01$), wound infections (OR: 0.3, 95% CI: 0.16–0.5, $p < 0.01$), as well as shorter duration of hospital stay (6.6 vs. 8.2 days, $p = 0.01$). Although a one-to-one propensity score-matched analysis demonstrated that there is no difference between the 90-day mortality between those who had undergone laparoscopic versus open surgery (7.2% vs. 8.5%, OR: 0.80, 95% CI: 0.56–1.15, $p = 0.23$), Coe et al. demonstrated that over the 4-year study period involving 5253 patients, usage of laparoscopic surgery has increased from 20% to 26% and conversion rates have decreased from 40% to 31% [90]. In addition to comparable or even more superior operative outcomes to open techniques, the laparoscopic repair was reported to be more cost-effective with a decreased length of hospitalization (7.0 vs. 8.0 days, $p < 0.001$) and lower mean hospital bill ($44,095 vs. $52,055, $p = 0.019$). Laparoscopic repair avoids a larger midline laparotomy with potential benefits of reduced pulmonary and wound-related complications, especially in the elderly. This is established by a retrospective analysis carried out using data of the Frailty and Emergency Surgery in Elderly (FRAILESEL) study [91]. The authors reported that out of the 67 patients who fulfilled the inclusion criteria, 47.8% underwent laparoscopic repair. Patients managed by laparoscopic repair had less blood loss and shorter length of hospital stay, but results were not significant likely due to the small sample size. In a propensity score-matched study including 576 patients from the ACS-NSQIP database, Jayaraman et al. has reported that about 10% of patients are treated by laparoscopy, and laparoscopic repair is associated with longer operating time (92 vs. 79 min, $p = 0.003$) and shorter hospital length of stay (8.2 vs. 9.4 days, $p = 0.044$) [92]. Authors also reported that open laparotomy group patients had higher risk of bleeding (14.6% vs. 8%, $p = 0.012$) and pneumonia (8.7% vs. 4.5%, $p = 0.044$).

Many different laparoscopic techniques, including omentopexy alone, suture repair with omentopexy, or falciformopexy, are described [91, 93]. Such techniques require experience and proficiency in intracorporeal suturing skills. With increasing experience of elective laparoscopic procedures, incorporating laparoscopic skills in the residency training curriculum, and widespread availability and accessibility to minimal access surgery, more emergency abdominal procedures are managed by laparoscopy. Patient selection is integral to good outcomes. Patients with severe cardiopulmonary instability should not undergo laparoscopic surgery, as insufflation of the abdomen increases intra-abdominal pressure and worsens hypercarbia [59]. In the learning curve period, surgeons should select their patients to reduce open conversion and leak risk. We suggest that patients with a Boey score of 3, age more than 70 years, and who have been symptomatic for more than 24 h should undergo

an open omental patch repair instead as they are at risk of high morbidity and mortality [1]. PPU >9 mm, and duration of pain ≥12.5 h are reported as risk factors for open conversion [94]. Shelat et al. have shown that with the adoption of strict selection criteria during the learning curve of laparoscopic omental patch repair, conversion can be kept low and good outcomes can be achieved [95]. Authors recommended that patients without suspicion of malignancy and with Boey score of 0 or 1, ulcer size of less than 10 mm, ulcer location in the pyloro-duodenal area, hemodynamic stability, no previous abdominal surgeries, ASA score of 2 and below are ideal candidates during the learning curve.

In a retrospective study involving 103 patients, Lau et al. concluded that sutureless repair techniques are faster and have comparable clinical outcomes as suture techniques [96]. In another study involving 43 patients, Wang et al. compared the effectiveness of a sutureless onlay omental patch with sutured omental patch method and reported nil post-operative leaks in both groups. In addition, operating time and length of hospital stay were shorter in the sutureless onlay omental patch group [97].

#### 72.3.3.3 Endoscopic Interventions

Novel techniques such as gelatin sponge plug, fibrin glue sealing, polyglycolic acid sheet placement, and endoscopic clipping are reported to be safe and feasible in selected patients with PPU [96]. Endoscopic interventions can be combined with surgical treatment, that is, the laparo-endoscopic hybrid approach. Some authors report that sutureless techniques require strict patient selection and should not be routinely recommended in all PPU patients due to higher post-operative morbidity and mortality [98–100]. In the World Society of Emergency Surgery (WSES) guidelines, endoscopic therapy with clipping, fibrin glue sealing, and stenting is not recommended due to the ineffectiveness of such modalities in fibrotic tissues [59].

Self-expendable metal stents (SEMS) may also be used to treat PPU [101]. SEMS can also be used as a salvage procedure to manage post-operative leaks. In the case series, including eight patients with PPU treated with SEMS, two patients underwent a stent procedure due to post-operative leakage after initial surgical closure. In comparison, the other six patients were treated with SEMS due to extensive co-morbidities. Seven out of eight patients fully recovered without any complications [101]. This was also supported by a RCT including 28 patients with a confirmed perforated duodenal ulcer (stenting, $n = 13$ vs. open repair, $n = 15$). Patients treated by stent had a shorter operating time (68 vs. 92 min, $p = 0.001$). Stents were removed after a median of 3 weeks without complications. These studies show that patients with PPU can be treated with primary stenting if expertise is available. Although endoscopic techniques are not ideal for irrigating the peritoneal cavity and do not permit post-procedure drainage tube placement, the RCT by Vázquez et al. reported that there is no significant difference in mortality and morbidity rates between stent and surgical treatment for PPU [79]. They emphasize that endoscopic intervention for PPU, such as the utilization of SEMS and hybrid laparoscopic lavage plus drainage, is an effective and safe alternative to traditional surgical repair. Most surgeons prefer peritoneal washout with warm saline, although no reports support that irrigation can lower the risk of post-operative sepsis [102, 103]. In our institution, drainage is at the discretion of the primary surgeon as some surgeons believe it prevents intra-abdominal fluid collection, and others believe that it increases skin and soft tissue infections at the drain site and poses a risk of intestinal obstruction [104]. There is a paucity of reports about the success of nonsurgical interventions in special situations like marginal ulcers.

### 72.3.4 Nonoperative Management

Some reports have shown that about 40–80% of PPU are self-resolving and tend to seal off with nonsurgical management spontaneously, and overall outcomes are comparable with surgical repair [61, 105–107]. The protocol for nonsurgical management includes a nasogastric tube, intravenous fluids, antibiotics, PPIs, and

repeated clinical assessment [1]. However, before nonsurgical management is decided, patients must undergo a contrast study with gastrografin dye to confirm the absence of free intraperitoneal leakage of dye/gastric contents [1, 59]. Should patients remain clinically stable with progressive signs of improvement, surgery may be avoided. However, surgery must be performed immediately if patients show clinical signs of deterioration. Many authors exclude old patients from nonsurgical management. In a nationwide inpatient database study involving 14,918 patients with PPU, Konishi et al. reported 14,918 patients who underwent nonoperative treatment than prior studies, which only included a total of 107 patients [106–110]. Unlike previous studies, this study included more patients >65 years of age and divided their patients into three distinct groups—young (ages 18–64 years old), old (ages 65–74 years old), and old-old (ages ≥75 years old). Authors reported higher morbidity (15% and 17% vs. 6.6%, $p < 0.001$) and morality (8.3% and 18% vs. 1.4%, $p < 0.001$) in patients >65 years compared to younger age (young group) patients. Nonsurgical treatment is resource-intensive and requires active monitoring of the patient's clinical status, and a surgeon must be available on-demand if the patient deteriorates. Lastly, before nonsurgical management, absolute diagnostic certainty must be ensured as the wrong diagnosis could increase mortality risk [59, 106, 111]. We have summarized the principles of nonoperative management as six R's: radiologically undetected leak; repeated clinical examination; repeated blood investigations; respiratory and renal support; resources for monitoring; and readiness to operate [1].

### 72.3.5 Prognosis

PPU is associated with significant post-operative morbidity and mortality regardless of minimally invasive or open surgery [112]. Common post-operative morbidity includes surgical site infection, intra-abdominal fluid collection/abscess, enterocutaneous fistula, incisional hernia, pneumonia, and ileus. Age >60 years, delayed treatment >24 h, shock (systolic blood pressure <100 mmHg) at presentation with, and co-morbidities predispose to morbidity [105, 113]. Elderly patients experience higher mortality risk (by 3–5 times) due to an atypical presentation or delay diagnosis [114]. To prevent the recurrence, eradication of *H. pylori* infection is important. An upper gastrointestinal endoscopy may be warranted to rule out gastric malignancy. Holistic patient care is essential to optimize the medical comorbidity that is contributory to PUD.

**Dos and Don'ts**

- Do suspect PPU in patients with sudden severe epigastric pain, tachycardia, and abdominal rigidity.
- Do obtain a good quality erect chest X-ray and interpret it promptly.
- Don't delay intervention in pursuit of stabilizing patient's hemodynamics. Resuscitation and intervention for source control must happen concurrent and not sequential.
- Don't embark on laparoscopic PPU repair without proper training and mentoring. In early experience, select your cases well so patient safety is not compromised.
- Don't resort to a routine policy of gastric resections in large or giant gastric ulcers, as outcomes of patients with gastric resections are worse!
- Don't routinely treat all patients with antifungals, as fungus is a commensal, and it is expected in peritoneal fluid samples.
- Don't resort to non-operative management unless your facility has resources and experience to do so.
- Do pay attention towards smoking cessation and *Helicobacter pylori* eradication after patient has recovered from acute illness.

**Take-Home Messages**

- PUD is highly prevalent, and acute care surgical teams must be familiar with the management of PPU.
- The classic triad of sudden onset of epigastric abdominal pain, tachycardia, and abdominal rigidity is the hallmark of PPU.
- Early diagnosis, prompt resuscitation, and surgical repair are the cornerstone to ensure good clinical outcomes.
- Erect chest film may not detect free air, and a computerized tomography scan is warranted if a clinician has a high index of suspicion.
- Laparoscopic omental patch repair is increasingly reported to have lower morbidity compared to open laparotomy.
- Endoscopic interventions have an emerging role, not only for index perforations but also as salvage treatment after surgical complications.
- Selection of patients for non-operative management must be made carefully based on local resources and expertise.

**Multiple Choice Questions**

1. Which of the following is not included in the classic triad of clinical presentation of perforated peptic ulcer?
   A. Abdominal rigidity
   B. **Hypotension**
   C. Sudden severe abdominal pain
   D. Tachycardia
2. The following is not a typical feature of gastric ulcer, in comparison with duodenal ulcer.
   A. Associated with malignancy
   B. **Association with *Helicobacter pylori***
   C. Association with smoking
   D. Epigastric pain is a presenting symptom
3. The primary diagnostic modality for diagnosis of perforated peptic ulcer is?
   A. Computerized tomography scan of abdomen
   B. **Erect chest X-ray**
   C. Gastrografin dye study
   D. Ultrasonography of abdomen
4. Which of the following patient is an ideal patient for a novice (beginner) to embark on laparoscopic omental patch repair?
   A. 75-year-old gentleman, ASA score 3, about 2 cm anterior gastric ulcer
   B. 30-year-old female, ASA score 2, about 3 cm anterior duodenal ulcer
   C. 40-year-old gentleman, ASA score 3, a pinpoint gastric ulcer
   D. **50-year-old gentleman, ASA score 1, 5 mm duodenal ulcer**
5. Which of the following body tissues can be used to patch the perforated ulcer?
   A. Falciform ligament
   B. Omentum
   C. Jejunum
   D. **All of the above**
6. Which of the following drug is ulcer protective?
   A. Famotidine
   B. Prostaglandin
   C. Rabeprazole
   D. **Sucralfate**
7. Which of the following is true for *Helicobacter pylori*?
   A. Are absent in healthy population
   B. Floats in gastric contents and thus can reach all parts of stomach
   C. **Routine eradication helps reduce ulcer relapse**
   D. Serology tests are most accurate in detection of active infection
8. A 50-year-old gentleman wakes up past midnight with severe upper abdominal pain. He is a chronic smoker. He visits emergency department and has tachycardia and abdomi-

nal rigidity. You suspect he has a perforated peptic ulcer. The chest X-ray is normal. What is your next best course of action?

A. Manage as per acute pancreatitis
B. Repeat a chest X-ray after 4 h
C. Insert a wide bore NG tube, insufflate air, and do an ultrasound abdomen
D. **Request an urgent computerized tomography scan of abdomen**

9. A 70-year-old female is admitted with a suspected diagnosis of perforated peptic ulcer. She has diabetes, chronic renal impairment, congestive cardiac failure, and previous history of stroke. You calculate Boey's score of 2 and ASA score of 3. A computerized tomography scan shows generalized free fluid and a small pocket of air near duodenum. Your next best course of action is?
   A. Diagnostic laparoscopy and omental patch repair
   B. Endoscopic clipping of the ulcer
   C. **Laparotomy**
   D. Non-operative management
10. With widespread use of proton pump inhibitors, some complications are infrequently encountered in clinical practice. Which of the following complication of peptic ulcer disease is still commonly seen in modern clinical practice?
   A. Gastric outlet obstruction
   B. Hour-glass stomach
   C. **Perforation**
   D. Tea-pot stomach

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