



# Updates in laparoscopic surgery for perforated peptic ulcer disease: state of the art and future perspectives

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**Abstract:** Peptic ulcer disease (PUD), which affects 4 million people worldwide annually, has a perforation rate of between 2% to 14%. Perforated peptic ulcer (PPU) carries a substantial morbidity and mortality. Surgical repair remains the treatment of choice for a PPU. This literature review includes the latest updates in laparoscopic repair techniques for a PPU and also focuses on its causation, clinical features, diagnostic workup, laparoscopic and open surgical techniques, outcomes, and future perspectives. An extensive review of the literature was performed, and the most recent meta-analyses and reviews concerning the topic were considered. No substantial differences were found in postoperative mortality between the open and laparoscopic approaches for patients with a PPU. Furthermore, a laparoscopic repair lead to statistically significantly less postoperative pain and carried a lower risk of wound infection. Hence, a laparoscopic repair is justified, where situationally appropriate, as the treatment of choice.

**Keywords:** Perforated peptic ulcer (PPU); laparoscopy; outcome; technique.

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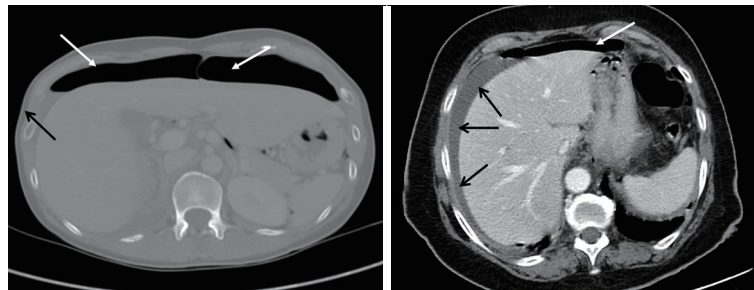
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## Introduction

Every year, peptic ulcer disease (PUD) affects about 4 million people globally (1). According to different series, the prevalence of perforation in patients with PUD ranges between 2–14% (2–4). Perforation is a life-threatening complication of PUD, and patients with a perforated peptic ulcer (PPU) often show up with diffuse peritonitis and generalized sepsis, conditions that carry high risks for morbidity and mortality (5). The prevalence of PUD has decreased in recent decades, but this has not been followed by a similar reduction in the complications from peptic ulcers. The reduction in PUD can be partially attributed

to the onset of *H. Pylori* eradication therapy and the extensive use of proton pump inhibitors (PPIs). Despite the introduction of these therapies, the incidence of PPU has remained constant in many parts of the world (6,7), occurring in about 2–14% of peptic ulcers; it continues to be both the second most frequent cause of hollow viscus perforation requiring urgent surgery and the most frequent indication for gastric emergency surgery (8–10). The reasons for the discrepant incidences of PUD and PPU has yet to be identified. Known risk factors for PPU are nonsteroidal anti-inflammatory drug (NSAID) use, *H. Pylori*, smoking, steroid use, physiological stress (4), fasting, cocaine use, and chemotherapy with bevacizumab (6). The



**Figure 1** CT scans that show free abdominal air (white arrows) and fluid (black arrows).

etiology of PPU is different in developing countries, where patients are typically young, male, and smokers, whereas in developed countries, the etiology is usually linked to NSAID or steroid use in older and more frail patients (4).

The management of PPU is primarily surgical, and several repair techniques have been described.

In 1989, the first laparoscopic repair of a duodenal ulcer was described by Mouret *et al.* (11).

Since then, many papers comparing the laparoscopic and open approaches have been published.

This literature review aims to survey and discuss the most recent and ongoing clinical applications of laparoscopic surgery for PPU, including its indications, different repair techniques, and outcomes.

### **Clinical features**

PPU often presents with non-specific abdominal symptoms which makes early diagnosis somewhat difficult. Typical symptoms include the sudden onset of severe abdominal pain, nausea and vomiting and pyrexia. When a perforation occurs, gastric juice and air enter the peritoneal space and lead to chemical peritonitis, which leads to severe abdominal pain and tachycardia. Sudden-onset abdominal pain, tachycardia, and abdominal rigidity are the typical triad of PPU (4). Fewer than two-thirds of patients present with frank peritonitis, and in some cases this phenomenon may result in a delay in the diagnosis of PPU (12). Early intervention is crucial since each hour from the onset of symptoms reduces the chances of survival by 2.4% (13,14).

## **Diagnosis**

### **Radiology**

An erect chest X-ray is commonly performed in patients with acute upper abdominal pain suspected

of perforation (4). However, a contrast-enhanced computed tomography is the best diagnostic modality with an accuracy of 98% (15). Furthermore, CT scans can rule out other acute abdominal conditions such as acute cholecystitis, acute pancreatitis, acute appendicitis and acute mesenteric ischemia to name but a few. Some of these acute abdominal conditions may not require surgical intervention at least in the initial phase. In resource-poor healthcare facilities, an erect chest X-ray is extremely useful in detecting free air under the diaphragm confirming visceral perforation (4). Peptic ulcer perforation can also generate detectable sonographic signs, such as pneumoperitoneum; free intraperitoneal air tends to accumulate around the liver, duodenum, and stomach, local thickening of the gastroduodenal wall containing an echogenic focus or line, the presence of localized extraluminal gas and fluid. However, sonography does not typically play a role in either first-line investigation or management workup of PPU (16) (*Figure 1*).

### **Laboratory**

Laboratory tests such as full blood count, urea and electrolytes, C reactive protein, serum amylase and lipase and venous or arterial blood gases, are performed in PPU patients in order to rule out other diagnoses, to assess the function of other systems and lastly to gauge the acuteness of surgical condition. For instance, elevated serum amylase and lipase levels are suggestive of acute pancreatitis (17,18). Similarly, white blood cell count and C-reactive protein are usually raised in most acute abdominal conditions due to inflammation or infection and they are non-specific in nature (17). Impaired renal function, increased lactate levels, and metabolic acidosis can be secondary to a number of acute abdominal conditions and reflect hypotension, inadequate perfusion, systemic inflammatory response

**Table 1** Boey score for PPU

Risk score	Mortality (OR)	Morbidity (OR)
0	1%	11%
1	2.4%	2.9%
2	3.5%	4.3%
3	7.7%	4.9%

Boey score factors: (I) concomitant severe medical illness; (II) preoperative shock (persistent hypotension: systolic blood pressure <90 mmHg, mean arterial pressure <60 mmHg, or a reduction in systolic blood pressure >40 mmHg from baseline); (III) duration of perforation >24 hours (duration of the perforation was determined as the time interval between the onset of severe acute abdominal pain, and arrival time at the hospital). Score: 0–3 (each factor scores 1 point if positive). Adapted from Lohsiriwat V, Prapasrivorakul S, Lohsiriwat D. Perforated peptic ulcer: clinical presentation, surgical outcomes, and the accuracy of the Boey scoring system in predicting postoperative morbidity and mortality. *World J Surg* 2009;33:80-5. PPU, perforated peptic ulcer; OR, odds ratio.

syndrome (SIRS) and/or pre-renal injury but are not specific to PPU (7). These signs suggest hypovolemic shock and sepsis.

## Material and methods

An extensive literature search was performed for articles available in the PubMed database. The terms used for the search were “gastric/duodenal/peptic ulcer”, “perforation/perforated”, “laparoscopy/laparoscopic”, and “repair/surgery”. Only articles written in English that used adult patients were considered.

## Laparoscopic approach

For the majority of its treatment history, laparotomy and the direct closure of the perforation with interrupted sutures and an omental pedicle plug (Cellan-Jones) has been the primary approach to PPU (7). However, in the last two and half decades, the minimal access approach has emerged as a viable option. Despite these solutions, not every patient is suitable for laparoscopy and thus patient selection for laparoscopic surgery is crucial (19).

## Patient selection

Guidelines about which patients with PPU are suitable

for the minimally invasive approach have yet to be defined. However, patients with shock at admission, late presentation (24 hours after the onset of symptoms), older than 70 years, American Society of Anesthesiologists (ASA) grade III or IV, and a high Boey score, are considered high-risk patients, and should undergo laparotomy (20). In a multicenter retrospective study, Mirabella *et al.* demonstrated the relationship between a patient’s Boey score and morbidity and mortality (*Table 1*). In their study, patients with Boey scores from 0 to 2 had a morbidity and mortality of 4.7% and 0.8%, respectively, while those with a Boey score of 3 had a morbidity and mortality of 21.4% and 10.7%, respectively (21). These authors therefore selected not to use laparoscopy in high-risk Boey’s score patients. They however suggested that it will be interesting to evaluate the usefulness of a minimally invasive technique in high risk patients in large randomized controlled trials. Teoh *et al.* (22) undertook a retrospective analysis of 373 patients undergoing surgery for PPU with laparoscopic first approach (LFA). Twenty-five point two percent of the patients had a Boey score of  $\geq 2$ . These authors showed that there was a significant increase in the number of operations performed yearly by the LFA. The authors concluded that the adoption of LFA in patients with PPU was associated with acceptable rates of mortality and morbidity. The approach could also be selectively adopted in patients with Boey score  $\geq 2$  provided their ASA grading is low and they are hemodynamically stable (22).

## Surgical technique

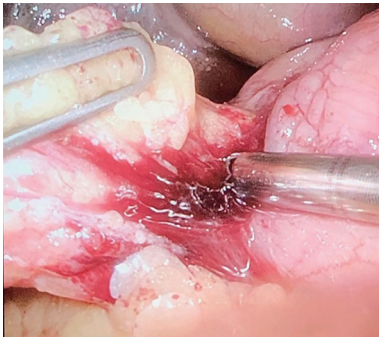
There is no agreement as to how to execute the laparoscopic repair of PPU, as it depends on operator preference. Bertleff *et al.* reviewed 29 studies and reported that 44% of operators chose to stand between the patient’s legs, while 33% preferred to perform the procedure standing on the patient’s left side. Furthermore, the number, placement, and size of trocars varied among surgeons (2). A nasogastric tube was used in 96% of cases, and a drain was left in 79% of cases even though there is no evidence that a drain has any impact on the incidence of post-operative intra-abdominal collections (23).

Also, the ideal surgical technique for laparoscopic repair of perforation remains undefined; laparoscopic repair techniques mirror techniques of open surgery, but it has been reported to require greater operating time. To obviate this problem, some studies of direct suture without omental patching have been published that indicate

a significantly shortened duration of surgery. Avoiding omentoplasty could reduce the duration of surgeries but may be the cause of a higher rate of leakage or duodenal stricture (24,25). A recent study by Wang *et al.* compared the efficacy of a sutureless onlay omental patch with a sutured patch after direct closure of the perforation in 43 patients. The operating time was significantly shorter in the sutureless onlay omental patch group. There was no statistically significant difference in the outcome between sutureless versus sutured omental patch repair. This work indicates that both techniques might be effective and safe for laparoscopic repair of PPU (26). A sutureless technique involving a gelatin sponge plug and fibrin glue sealing has also been described (27). However, it has not been widely adopted due to a high rate of repair site leak (20).

### Peritoneal lavage

Peritoneal lavage is one of the key steps in the surgical treatment of PPU (8), but it can also lengthen the operating time. There is no consensus concerning the amount of fluid



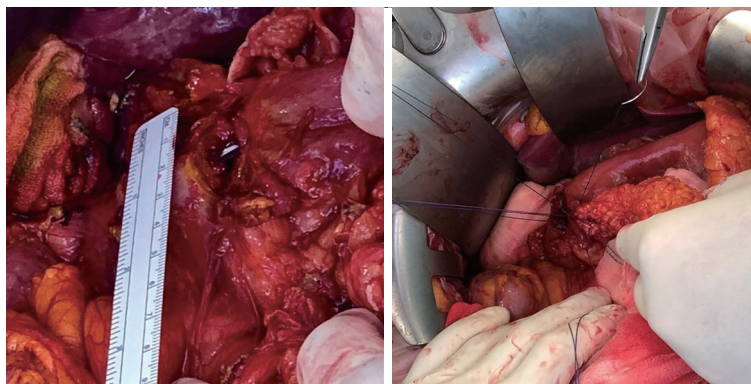
**Figure 2** laparoscopic view of an anterior duodenal perforated ulcer.

to be used for irrigation.

In a review from Bertleff *et al.* that included 29 studies, lavage has been completed with 2 to 6 liters of warm saline solution, but lavage with up to 10 liters have also been reported (2). Siow *et al.* described a focused sequential manner to perform peritoneal lavage that involved quadrant-to-quadrant washing with tilting of the patient and position switching between the surgeon and the camera driver. The fluid was then aspirated until the recesses were clean of debris. In this case series, there were no postoperative intra-abdominal abscesses or collections (28).

### Conversion

The potential reasons for conversion to open surgery include the difficulty in localizing the perforation site for anatomical reasons, i.e., perforation located in a region other than the duodenal anterior wall, large perforations (described by some authors as 6 mm diameter or larger, and by others as over 10 mm) (Figures 2,3), peritoneal adhesions from previous surgeries, and ulcers with fragile edges (20,21,29,30), Mannheim peritonitis index >21, and generalized peritonitis (31). A recent Danish study of 726 patients undergoing surgery for perforated PUD reported a laparoscopy rate of 32.8%, with 24.5% converted from laparoscopic to open (32). However, the UK study has shown a much smaller conversion rate in their cohort of patients; 13.1% of patients underwent surgical repair of their perforated ulcer via a laparoscopic approach, out of which 6.9% were converted to open approach. The authors believed that under reporting may be cause of this low conversion rate (33). A recent systematic review of 32 studies however confirmed a conversion rate of only 4.9% (34) which may suggest that (I) laparoscopic



**Figure 3** large pyloric perforated ulcer (>2 cm) that required conversion to open surgery.

surgical training in the complex gastrointestinal surgery is becoming common place; (II) better surgical equipment and instruments may have a role to play and (III) better senior supervision in these acute surgical cases may have become more routine and lastly (IV) surgeons are gaining more experience in emergency laparoscopic techniques.

### Perioperative morbidity and mortality

A PPU is related to significant postoperative morbidity and mortality regardless of whether the surgery is laparoscopic or open (35). The estimated post-operative mortality ranges from 1.3% to 20%, with the 30-day mortality rate reaching 20% and the 90-day mortality rate reaching up to 30% (13,18,36-40). Risk factors for mortality are no different for either an open or laparoscopic approach and include shock at admission, co-morbidities, resection surgery, female, elderly patients, a delay presentation of more than 24 hours, metabolic acidosis, acute renal failure, hypoalbuminemia, being underweight and smokers.

The reported surgical complications after laparoscopic repair of PPU include surgical site infection (SSI), intra-abdominal collection/abscess, wound dehiscence, enterocutaneous fistulas, peritonitis, ileus, pneumonia and incisional hernias (4,21,41). A meta-analysis by Tan *et al.* stated that laparoscopic repair had a lower overall complication rate than an open repair for PPU, but this difference did not achieve statistical significance ( $P>0.05$ ) (41). When subgroup analysis of complications was performed, the laparoscopic approach had a similar incidence of repair site leakage, intra-abdominal collections, postoperative ileus, urinary tract infection, and pneumonia. However, the SSI rate was lower in the laparoscopy group ( $P<0.005$ ) (41).

The latest meta-analysis assessing eight randomized controlled trials comparing the laparoscopic to open approach in patients with PPU has shown slightly lower mortality in the laparoscopy group (1.6%) compared to an open repair (4.2%). Reoperations rates were higher in the laparoscopy group: 4.2% compared to 1.8% in the open group; rates of repair site leaks were 3.7% in the laparoscopy group versus 1.7% in the open group; the intra-abdominal abscess rate was 4.4% in the laparoscopy group versus 3.3% in the open group; and reoperation rates for intra-abdominal collections were 1.2% in both the laparoscopy and open groups. Statistically significant differences in the study included reduced early (first 24 hours) postoperative abdominal pain and fewer wound

infections in laparoscopic repair (42). The main reasons for reoperation after the laparoscopic repair were suture site leak or reperforation. Previous studies have shown a suture leak rate of 7% with laparoscopic repair; however, more recent studies have demonstrated that this can be substantially reduced to around 2.18%, however it is still three times higher than an open repair according to a recent systematic review (30,34,43). Surgeons' inexperience and the steep learning curve involved may be possible explanations; indeed, more recent investigations have shown that progress in a surgeon's surgical technique and experience could improve this outcome (29,44).

### Conclusions

Perforation occurs in 2–14% of peptic ulcer patients, and it remains the second most common cause of visceral perforation that requires urgent surgery. The diagnosis should be based on high index of suspicion which requires good clinical history and examination complimented by blood tests and radiological studies, of which contrast-enhanced abdominal CT scan represents the most reliable diagnostic tool in hemodynamically stable patients. Early intervention (<24 hours from symptom onset) is crucial for a good outcome. A literature review of recent meta-analyses suggests the slight advantage of the laparoscopic approach over open surgery in terms of postoperative pain and length of hospital stay, but these results are biased towards the selection of younger patients, ASA risk scores I–II, small perforations (<10 mm), and access to the Emergency Department within 24 hours from the onset of symptoms. No studies have evaluated laparoscopic repair in high-risk patients, such as those with a Boey score of 3, duration of symptoms >24 hours, patient  $\geq 70$  years, and ASA 3. High-risk patients should indeed be treated with open surgery, especially those who are hemodynamically unstable (20). An LFA could also be selectively adopted for patients with a Boey score  $\geq 2$ , provided that the ASA score was <3, and the patient was hemodynamically stable (22). A sutureless omental patch can reduce operative time but may increase the risk of leak rate and reoperation. The best current and most up-to-date evidence suggests that there is no difference in postoperative mortality when comparing the open to the laparoscopic approach in patients with PPU. The advantages of laparoscopy in terms of postoperative pain and wound infection rate may support a minimally invasive approach as the treatment of choice where it is situationally appropriate. Outcomes in subpopulations

including elderly, frail, and high-risk patients need further investigation and multicenter randomized controlled trials.

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