CURRENT MANAGEMENT OF PEPTIC ULCER PERFORATIONS

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ABSTRACT: Perforation is a life-threatening complication of peptic ulcer disease. Smoking and use of non-steroidal anti-inflammatory drugs are important risk factors for perforation. Diagnosis is made clinically and confirmed by the presence of pneumoperitoneum on radiographs. Nonoperative management is successful in patients identified to have a spontaneously sealed perforation proven by water-soluble contrast gastroduodenogram. Operative management consists of the time-honoured practice of omental patch closure, but now this can be done by laparoscopic methods. The practice of addition of acid-reducing procedures is currently being debated though it continues to be recommended in good-risk patients. Laparoscopic approaches to closure of duodenal perforation are now being applied widely and may become the gold standard in the future especially in patients with <10mm perforation size presenting within the first 24 hours of onset of pain. The role of Helicobacter pylori in duodenal ulcer perforation is controversial and more studies are needed to answer this question though recent indirect evidence suggests that eradicating H pylori may reduce the necessity for adding acid reducing procedures and the associated morbidity.

Perforation is a life-threatening complication of peptic ulcer disease. The management of peptic ulcer disease has evolved over the decades, due to advances in operative techniques, bacteriology and pharmacology. While the recognition of the role of Helicobacter pylori (H. pylori) in peptic ulceration has resulted in a paradigm shift in the management of uncomplicated peptic ulcers, debate continues about the appropriate management of perforated duodenal bulb and prepyloric ulcers. A new dimension has been added to this controversy by the advent of laparoscopic techniques for closing the perforation. A medline search of all articles dealing with the management of peptic ulcer perforation published after 1985 was undertaken. The shortlisted articles were analysed and studies which were well designed and had important inferences were selected. Based on these inferences, the controversies surrounding the management of peptic ulcer perforation have been discussed in this review article.

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The first clinical description of perforated peptic ulcer was made by Crisp in 1843. The features of the disease and of the patients affected have changed, ever since. During the nineteenth century ulcer perforation was a rare disease that occurred mainly in young women with the perforation located near the cardia of the stomach1. During the early twentieth century, ulcer perforation increased in incidence and these were situated in the duodenum in middle-aged men2. The management of peptic ulcer disease has evolved over the
decades, due to advances in operative techniques, bacteriology and pharmacology. While the recognition of the role of *Helicobacter pylori* (*H. pylori*) in peptic ulceration has resulted in a paradigm shift in the management of uncomplicated peptic ulcers, debate continues about the appropriate management of perforated duodenal bulb and prepyloric ulcers.

Mikulicz introduced closure of perforation by suture in 1880 when he closed a gastric ulcer perforation. Nonoperative management for perforated peptic ulcer disease (PUD) was first described in 1935 by Wangensteen and is still applicable in specific conditions. The first two cases of primary gastric resection for ulcer procedure was described in 1919 by von Haberer. In 1937, Roscoe Graham described simple closure of duodenal perforation. Recognition of the high rate of both recurrent symptoms and recurrence of ulcer with simple closure led many authors to recommend a definitive ulcer curative procedure. Introduction of antibotics in the 1950’s reduced the rate of postoperative complications and deaths.

The revolution in ulcer treatment that occurred with the discovery of the role of *H. pylori* has not yet led to any detectable changes in the incidence of ulcer perforation. The potential for prevention thus lies in better understanding of causal factors which have not been known till lately, but apparently differ somewhat from those of uncomplicated ulcer. However, the recent recognition that *H. pylori* eradication after simple closure might prevent ulcer recurrence has challenged the role of definitive surgery and will complicate the debate surrounding the management of this difficult problem.

**INCIDENCE**

About half a million people are diagnosed to have peptic ulcer each year in the United States. Duodenal bulb and prepyloric ulcers are approximately five times as common as gastric ulcers. Ulcer perforation was a rare disease in the nineteenth century; however its incidence increased greatly at the turn of the twentieth century. Since then the world has seen an epidemic of duodenal perforations among young men which now seems to be waning.

**BORHYTHMS OF ULCER PERFORATION**

Owing to the typical and dramatic onset of ulcer perforation, the hour of the day when the ulcer perforation occurred can be assessed. A pronounced circadian variation with a greater incidence during the day and lower incidence during late night was described as early as 1903. The circadian pattern seemed to differ between gastric and duodenal perforation with duodenal perforation showing peak incidence during afternoon and evening, and gastric perforation showing a primary peak around midday and secondary peak around midnight.

**AETIOLOGY**

Smoking is a risk factor of major importance for ulcer perforation. A study from Norway showed a strong association between ulcer perforation and smoking with a relative risk factor of ten. It was estimated that smoking might account for 77% of all ulcer perforations in the age group younger than 75 years. A major role for smoking in the aetiology of ulcer perforation is also supported by studies reporting smoking prevalence of 84% and 86% among ulcer perforation patients. Smokers with ulcer perforation have a higher mortality risk as compared to nonsmokers. Use of NSAIDS is another important risk factor for ulcer perforation with a relative risk of 5 to 8. One can estimate that NSAIDS may contribute to one fifth to one third of ulcer perforations.

**DIAGNOSIS**

Perforated PUD typically causes severe epigastric abdominal pain that may progress to involve the entire abdomen. The degree of peritoneal findings is, however influenced by a number of factors, including the size of perforation, the amount of bacterial and gastric...
contents contaminating the abdominal cavity, the time between the perforation and presentation and spontaneous sealing of the perforation. These patients also demonstrate the signs and symptoms of early shock, such as tachycardia, hypotension and anuria. Abdominal and thoracic plain film radiographs are sensitive in the demonstration of pneumoperitoneum (60% to 75% of patients) 13.

Even though this finding is not specific for perforated peptic ulcer, free air is usually in much smaller amounts in perforations of the other abdominal visceras. An upper gastrointestinal study with water-soluble contrast can demonstrate extravasation if the ulcer has not spontaneously sealed.

Currently, upper endoscopy is not recommended if perforation is present or strongly suspected because it may disrupt the spontaneous sealing. 92% of perforated duodenal ulcers do so through the anterior duodenal wall. 10% of these are also associated with a concurrent bleeding ulcer along the posterior wall, the so-called “kissing ulcer”13.

NONOPERATIVE MANAGEMENT

Traditionally, perforated peptic ulcers have been treated by urgent surgical repair, with or without ulcer curative procedure. However, several studies have indicated that many patients can be managed without an operation. Wangensteen first advocated nonoperative treatment in 1935 for patients with perforation but no pneumoperitoneum on the premise that the perforation would probably have been sealed4. More recently, Berne and Donovan emphasized the use of water-soluble upper gastrointestinal study to demonstrate spontaneous sealing of perforation. They noted that 40% of perforated peptic ulcers have sealed on upper gastrointestinal study performed shortly after the patient presents28, 29.

Nonoperative management for perforated duodenal ulcers consists of resuscitation with intravenous fluids, intravenous antibiotics, nasogastric suction and acid reducing drugs. For the last purpose, intravenous H2 blockers have been in use for a long time, although an intravenous form of proton pump inhibitor (pantoprazole) is now available. Treatment for H. pylori should begin when the patient is able to take orally. The patient should undergo serial abdominal examinations with operative therapy reserved for either progression or failure of improvement of peritonitis.

Taylor30 advanced arguments favouring a nonsurgical approach, nearly 50 years ago, at a time when the mortality rates for surgical treatments were close to 20%. In the study by Berne and Donovan, the mortality rate for patients treated operatively was 6.2%, compared to a mortality of 3% in those treated nonoperatively. In addition, the authors noted a very low incidence of intraabdominal abscess or reperforation in the patients managed conservatively28. In another study by Crofts et al31 over a 13-month period, patients with a clinical suspicion of perforated peptic ulcer were randomly allocated to conservative treatment (n=40) or to emergency surgery (n=43). In the surgically managed group, 40 had duodenal ulcer, two had gastric ulcers and one had a perforated gastric carcinoma. Eleven patients (27.5%) including, three with an erroneous diagnosis (two perforated gastric carcinomas and one perforated sigmoid carcinoma), who had no improvement within 12 hours of conservative treatment underwent operation. Extravasation of contrast, on upper gastrointestinal study was not an indication for operation. Morbidity was similar in the nonsurgical and surgical groups (20 vs 17 patients); intraabdominal abscesses developed in six and two patients, respectively. Two deaths occurred in each treatment group with an overall mortality of 4.8%. The duration of the hospital stay was significantly longer (p<0.001) in the nonsurgical group (12.0 days) than in the surgically treated group (7.8 days) Failure of nonoperative policy were significantly (p<0.05) more frequent in patients over 70 years of age (6/9, 67%) than in younger patients (5/31, 16%).

In a later study by Donovan et al29, the authors proposed stratifying the patients based
on their *H. pylori* status. They noted a high incidence of *H. pylori* in patients with perforated duodenal ulcer and demonstrated that long-term eradication of *H. pylori* could be achieved with appropriate medical therapy. In patients, known to be either *H. pylori* negative or with perforations despite previous treatment for *H. pylori* infection, definitive surgery was recommended in suitable candidates. *Helicobacter pylori* negative patients without prior treatment usually have another cause for ulceration, such as NSAID use, severe acute stress, or Zollinger-Ellison syndrome.

**OPERATIVE MANAGEMENT**

Despite evidence that nonoperative management may be appropriate for many patients with perforated peptic ulcer; many surgeons still practise universal operative intervention in these patients. The type and timing of operative intervention has been a matter of debate for decades. The first issue is the performance of simple closure versus closure with ulcer curative procedure. Secondly, doubt exists about both the type of ulcer curative procedure that should be performed and whether this should be performed concurrently with simple closure or as a staged procedure.

Although the method of closure described by Graham continues to be effective at providing adequate closure of the perforation, many authors have noted a high recurrence of both ulcer symptomatology and reulceration. In fact 37% to 58% of patients treated with simple closure were found to have recurrence of an ulcer, whereas 48% to 85% were found to have recurrent symptoms of PUD. However, some authors argue that definitive surgery prolongs what is already an emergency procedure and that recurrences can usually be managed with medical therapy. Moreover, several of the definitive ulcer operations have been associated with significant side effects, including diarrhea, dumping, vomiting, and weight loss. It is because of these untoward sequelae, as well as the emergent nature of the situation, that some surgeons have argued against routine performance of a definitive procedure at the time of simple closure.

Simple closure of a perforated duodenal ulcer was compared to definitive surgery in three randomized trials. Patients with risk factors were not included in two of these studies. Only one postoperative death was reported among the 328 patients included in the three randomized trials. Postoperative morbidity was not significantly increased by definitive surgery, except for wound sepsis in one trial. With a mean follow up of 20 months, ulcer recurrence was reported on 61% (38/62) and 6% (6/92) of cases following simple closure and definitive treatment, respectively. Boey et al identified certain risk factors that increased operative mortality in patients with perforated PUD. Specifically, significant comorbidity, preoperative shock and perforation of >48 hours increased mortality. Interestingly, age over 70 years and gross peritoneal soiling did not. They concluded that simple closure alone is indicated when any of these aforementioned risk factors is present.

When selecting a patient for a definitive ulcer operation, one must decide which procedure offers an acceptably low rate of recurrence while minimizing attendant side effects. Traditionally, the most effective forms of definitive surgery have been hemigastrectomy and vagotomy and antrectomy (V&A). However, most surgeons currently confine definitive therapeutic options to vagotomy and antrectomy, vagotomy and drainage or highly selective vagotomy (HSV).

Vagotomy with antrectomy has an ulcer recurrence rate of 1% at 5 to 10 years. However, the procedure carries a mortality rate of 1% to 2% and is associated with side effects, such as anastomotic leak, gastric stasis, dumping, diarrhoea, and bilious vomiting. Drainage procedure usually performed in association with truncal vagotomy is pyloroplasty, although a gastrojejunostomy may be performed when local anatomy prevents the former. The operation carries a mortality of 0.7% with a 3% to 30% risk of ulcer recurrence. Avoiding both denervation of the viscera and attendant
drainage procedure with the associated long-term sequelae are the goals of highly selective vagotomy. This has an excellent mortality rate (0% to 0.31%) with a risk of recurrent ulcerations approaching 3% to 12%, five to fifteen years after operation34, 38.

Most of the recurrent ulcerations after this procedure are caused by incomplete denervation of the parietal cell mass. Thus, the outcome of this operation appears to be operator dependent with the incidence of postoperative sequelae being extremely low38. Consequently, many surgeons have adopted HSV as a compromise between simple closure with its high rate of recurrence and either V&D or V&A and their associated postoperative side effects38, 39.

With the advent of laparoscopic surgery another dimension has been added to the controversy. Lau et al randomized 103 patients with a clinical diagnosis of perforated peptic ulcer to laparoscopic or open repair and inside each group, between suture and suture less repair (plug of gelatin sponge and fibrin glue). Four patients in the laparoscopic group and six in the open group were excluded after randomization either because the ulcer closed spontaneously (n=5). Of 48 patients in the laparoscopic group, 11(23%) were converted to open surgery. Laparoscopic repair of perforated peptic ulcer took significantly (p<0.001) longer than open repair (94 vs 54 min respectively). Patients who had laparoscopic repair required fewer analgesic doses postoperatively than those who had open surgery (p<0.03). No statistically significant differences were noted between the laparoscopic and open groups with regard to duration of nasogastric aspiration, intravenous drips, hospital stay, time to resume normal diet and Visual Analog Scale pain scores for the first 24 hours after surgery. There was no significant difference in morbidity, reoperation rate, or mortality between patients who underwent laparoscopic and open repair10. This study demonstrated the advantages of decreased analgesic requirement by laparoscopic closure without any increase in mortality or morbidity. However, this advantage was offset by the increased operative time.

Increasing familiarity with laparoscopic techniques and innovative ways of repairing the perforation like sutureless closure, single suture closure and use of fibrin glue have all enabled surgeons to decrease operative time.

Siu et al41 in a recent trial have tried to establish the laparoscopic approach as the gold standard for the management of a perforated peptic ulcer. By using a modified technique involving a single suture closure of the perforation they demonstrated a clear advantage to the laparoscopic approach in terms of decreased operating time, less postoperative pain, earlier ambulation, significantly lower incidence of RTI, lower median length of stay and earlier return to normal activity. They also defined the patient population who will stand to gain the above benefits by excluding those patients with a nonpyloric gastric ulcer perforation, an ulcer perforation >10mm in diameter and technical difficulties. Since only one out of a total of 63 patients in this study had a presentation after 24 hours, and only 2 of the 63 patients presented with systolic blood pressure <90 mmHg, patients presenting thus may not sustain the advantages defined by this group.

**H.PYLORI AND PERFORATED DUODENAL ULCER**

Controversy exists regarding the relationship between *H. pylori* and perforated DU. Although the relationship between uncomplicated peptic ulcer disease and *H. pylori* is widely supported, the association with perforation is not accepted fully16,42. However, a recent randomized study sought to determine if eradication of *H. pylori* in patients undergoing simple closure of a perforated duodenal ulcer was effective in preventing ulcer recurrence43. The authors noted that fewer surgeons are acquiring enough experience and expertise in performing definitive procedures such as highly selective vagotony and argued that combining medical therapy for *H. pylori* with simple closure would be more desirable than undergoing definitive operation, given at least a similar rate of recurrence.
This argument does assume an association between \textit{H. pylori} and ulcer perforation, but the study showed that 95\% of \textit{H. pylori} positive patients undergoing simple repair of the perforated duodenal ulcer followed by combined medical therapy and eradication were ulcer-free at one year. If the initial findings of this study continue unchanged, they have great potential to change the traditional management of perforated peptic ulcer disease and, therefore, more evaluation is needed.

**CONCLUSIONS**

The management of perforated peptic ulcer disease has been debated for the last several decades. Opinions between authors differ greatly, with some advocating an algorithm consisting of nonsurgical and surgical approaches depending on the characteristics of the patient presentation and others routinely advocating surgery, whether it be conservative or aggressive. Conservative management can be successfully adopted in patients diagnosed to have sealed duodenal perforations. Though laparoscopic approach does offer definite advantages over the open approach, until further randomized prospective studies clearly determine its safety and advantages only experienced surgeons should attempt this procedure. Although the association between \textit{H. pylori} and perforated peptic ulcer disease continues to be controversial, it has the potential to significantly decrease the number of patients undergoing definitive ulcer surgery. Presently, patients should be managed based on their physical and radiographic findings, risk factors and \textit{H. pylori} status.

**REFERENCES**