Helicobacter pylori infection: the reduced need for ulcer surgery

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The success of the eradication treatment for *Helicobacter pylori* in managing ulcer disease has further refined the indications for ulcer surgery. More patients are spared unnecessary surgery and its untoward sequelae. It is intriguing that surgery has been effective, given that *Helicobacter pylori* infection is the underlying culprit. Recent studies show that the prevalence of *Helicobacter pylori* infection remains high after a vagotomy but is more markedly reduced following a partial gastrectomy. Such a reduction may be due to the removal of distal stomach, which is the usual site of infection. In addition, bile appears to be bactericidal to *Helicobacter pylori*. The association between *Helicobacter pylori* infection and perforated duodenal ulcer has not been completely settled. A recent study has demonstrated that male gender and positive *Helicobacter pylori* status are independent factors that are associated with recurrent duodenal ulcer after surgery for perforation. Hence, eradication therapy should be given to any patient who has a *Helicobacter pylori* infection, after surgery has been performed for perforated duodenal ulceration.

Introduction

The discovery of *Helicobacter pylori* has revolutionised the management of peptic ulcer disease. In the past, the majority of patients with ulcer disease were treated with antisecretory drugs, and elective surgery was necessary when medical therapy failed. Surgery is now seldom needed. The success of eradication therapy for *H pylori* in managing ulcer disease, has further refined the indications for elective surgery and has dramatically reduced the need for such operations. Nevertheless, surgery has been effective in managing ulcer disease when traditional antisecretory drugs have failed.[1] It is intriguing that surgery has been effective, given that *H pylori* infection is the actual culprit.

The management of perforated peptic ulceration has been controversial. Simple closure has been associated with high ulcer recurrence rates of 30% to 80%.[2-5] Since acid has been considered the most important cause of ulcer disease and ulcer recurrence, concurrent acid-reduction surgery was advocated for the emergency treatment of fit patients with a perforated duodenal ulcer to reduce the likelihood of recurrent ulceration occurring.[6,7] If *H pylori*, rather than acid, is the cause of ulcer disease, acid-reduction surgery may not be necessary at all.

The development of ulcer surgery

The first successful distal gastrectomy for gastric cancer was performed by Billroth in 1881. This landmark procedure was followed by a successful Billroth-I gastrectomy performed by Rydygier for a benign pyloric ulcer.[8] Rydygier also introduced gastrojejunostomy in the treatment of duodenal ulceration in 1884. After Pavlov's many experiments of vagotomy in animals, Bircher reported the performance of what appeared to be an incomplete vagotomy in 20 patients with various gastric symptoms.[9] Latarjet was also widely acclaimed for his work on the vagal innervation of the stomach. In 1922, he reported the need to add a drainage procedure, namely gastrojejunostomy, after a vagotomy.[10] Unfortunately, Latarjet never formally confirmed that vagotomy was a successful treatment for peptic ulcer disease.

During the 1920s, ulcers were generally thought to be due to gastric stasis, and the good results achieved by Latarjet were attributed to the concomitant gastrojejunostomy. It was not until the 1940s that Dragstedt established that a truncal vagotomy helps heal duodenal

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ulcers because it depresses gastric secretion.[11] Subsequently, the role of the antrum in gastric physiology became better understood, and vagotomy with antrectomy was shown to reduce gastric acid secretion the most.[12] In fact, the ulcer recurrence rate after this procedure has been reported to be as low as 1%.[13]

In the 1960s and 1970s, recognising the side effects of truncal vagotomy, more selective types of vagotomy (selective vagotomy, proximal gastric vagotomy, and posterior truncal vagotomy with lesser curvature seromyotomy) were introduced. The more selective types of vagotomy, however, are reported to be associated with a higher ulcer recurrence rate of up to 15%.[13]

The advent of laparoscopic surgery in the late 1980s is an important development in the history of surgery. With its advantages of a shorter and less painful post-operative course, shorter recovery times, earlier return to work, reduced scarring, and preservation of abdominal strength, laparoscopic surgery has stimulated interest in transforming previously established open techniques into laparoscopic procedures. Various laparoscopic acid-reduction procedures have been developed.[14] While there was great excitement about the development of various laparoscopic procedures for peptic ulcer disease, the eradication of *H pylori* became an established treatment for peptic ulcer disease in the early 1990s.[15] As a result, the need for elective surgery for peptic ulcer disease has markedly decreased,[13,16] although the exact extent of the reduction has not been documented. At the Department of Surgery of the Queen Mary Hospital, an average of 36 elective operations to treat peptic ulcer disease were being performed annually between 1989 and 1993. From 1994 to 1998, however, an average of only three such operations per year were performed (unpublished data, 1999). Such a marked reduction (92%) has been possible because the majority of patients with ulcer disease were treated successfully with *H pylori* eradication therapy.[17]

Patients in whom gastric outlet obstruction develops as a result of established pyloric stenosis with fibrosis and scarring are unlikely to respond to *H pylori* eradication therapy. Surgery is indicated in these patients if they do not respond to conservative treatment. Since most patients can now be treated with eradication therapy, the incidence of recurrent ulceration and scarring would be reduced in the long term. In future, benign acquired pyloric stenosis may become rare.

Emergency operations are performed to treat ulcer complications such as bleeding or perforation. The advent of therapeutic endoscopy has dramatically diminished the need for emergency surgery to treat bleeding peptic ulcers.[18] Nevertheless, an emergency operation is still indicated when endoscopic therapy fails—nowadays, such patients are usually frail and elderly individuals who have multiple medical problems. While the judicious use of non-steroidal anti-inflammatory drugs (NSAIDs) by elderly patients is important, whether the use of NSAIDs that specifically inhibit cyclo-oxygenase-2 helps reduce the occurrence of gastro-intestinal complications is still unconfirmed.[19,20] In contrast, recent studies of *H pylori*–related ulcer haemorrhage have confirmed the significant value of eradication therapy in reducing ulcer recurrence and rebleeding, as compared with maintenance therapy with an antisecretory drug.[21,22] In addition, in patients with a duodenal ulcer that has not bled before, eradication therapy has been shown to diminish the risk of the future occurrence of ulcer bleeding.[23]

Ulcer surgery and *H pylori* infection

Acid used to be considered the most important cause of duodenal ulcer. In the past, reduction of gastric acid was the primary goal of drug or surgical treatment for peptic ulcer disease. Surgery has been the standard treatment option when medical therapy fails.[1] If *H pylori* infection is the cause of peptic ulcer disease, it would be interesting to study the effect of surgery on the infection. It would be unethical to subject a patient with *H pylori*–related duodenal ulcer to surgery, and most recent studies thus involve patients who had previous surgery for ulcer disease. Published studies reveal that the prevalence of *H pylori* infection remains high—at approximately 80%—after vagotomy, but that the prevalence may be less in patients whose vagotomy is complete.[24-26] Hence, a modest reduction of *H pylori* infection following complete vagotomy could be due to a reduction of gastric secretion. In contrast, the prevalence of *H pylori* infection has been shown to be markedly reduced—to approximately 50%—following partial gastrectomy.[26-29] Such a reduction could be linked to the removal of distal stomach, which is the usual site of infection. In addition, bile reflux, which occurs especially after a Billroth-II reconstruction, seems to have a bactericidal effect on *H pylori*.[27,30]

Of the surgical procedures for duodenal ulceration, vagotomy with antrectomy has been known for years to have one of the lowest ulcer recurrence rates.[13] For decades, therefore, surgeons have been quite unknowingly eradicating *H pylori* by removing its favourite habitat (the antrum), thereby reducing gastric secretion and subjecting the organism to bile.

Perforated duodenal ulceration and *H pylori* infection

In the emergency management of perforated duodenal ulceration, the addition of acid-reduction surgery has been advocated to reduce the risk of recurrent ulceration,[6,7] but closure with an omental patch remains the standard treatment in many hospitals.[31,32] As with elective ulcer surgery, laparoscopic surgery has been introduced for the treatment of perforated duodenal ulceration. Because laparoscopy involves a longer operating time compared with the conventional open procedure, all laparoscopic techniques described have involved simple closure without an additional acid-reduction procedure.[33-36] It is thus important to evaluate whether simple closure is adequate for the treatment of perforated duodenal ulceration.

Although the association between *H pylori* infection and perforated duodenal ulcer is not totally clear,[37-40] it would be reasonable to suspect such an association in a patient who is not taking NSAIDs. If the ulcer is caused by *H pylori*, it would be adequate to treat the perforation with simple closure, followed by postoperative eradication therapy.

In the past, it was unclear why ulcers recurred in some but not all patients after surgery for ulcer perforation; both acute and chronic duodenal ulcers may recur after perforation.[41] Gastric acid secretion and serum gastrin levels do not predict ulcer recurrence after simple closure.[42] Having a young age, smoking, and having a long interval after surgery, however, are associated with recurrence.[41,43] We recently studied 163 patients with a past history of surgery for perforated duodenal ulcer to investigate whether or not ulcer recurrence is related to *H pylori* infection.[44] Patients who had taken NSAIDs were excluded. There was a male preponderance (male to female ratio, 5.3:1) in the group and the mean age was 55.9 years. An upper gastro-intestinal endoscopic examination was performed at a mean interval of 74.5 months (standard deviation, 7.1 months) from the initial operation. *H pylori* testing was found to be positive in 77 patients (47.2%). Recurrent duodenal ulceration was found in 29 patients (17.8%).[44]

The results of univariate analysis have shown that male gender, a history of recurrent epigastric pain, a longer interval from initial surgery, and positive *H pylori* status are significant factors associated with recurrent duodenal ulceration. Other factors such as age, smoking, additional acid-reduction surgery, and the intake of H_2-receptor antagonists were not found

to be associated with ulcer recurrence.[44] Multivariate analysis revealed male gender and positive *H pylori* status to be independent factors associated with recurrent duodenal ulcer.[44] It is not known why male gender is an independent factor in the recurrence. In addition to *H pylori* infection, male gender has also been found to be an independent risk factor for duodenal ulcer disease or its relapse in Chinese populations.[45,46]

Because of the current findings, we recommend the performance of simple closure for perforated duodenal ulcer. Postoperatively, such patients should be given maintenance therapy with antisecretory drugs such as H_2-receptor antagonists until their *H pylori* status is known. We routinely perform gastroscopic examination 2 months postoperatively to confirm the healing of ulcers as well as to obtain biopsies to determine an individual's *H pylori* status. Eradication therapy is recommended for any patient who is found to be positive for *H pylori*.

Despite the success of *H pylori* eradication therapy in the treatment of peptic ulcer disease, there remain a number of conditions that need surgery. These conditions can be subdivided into elective and emergency indications for surgery (Box).

Conclusion

Subsequent to the identification of *H pylori* infection as a major cause of peptic ulcer disease, the indications for surgery have been further refined. More patients are spared from unnecessary surgery and its unwanted sequelae. On the other hand, the decreased

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Peptic ulcer conditions that require surgery*

Elective indications:
(1) persistent ulceration despite medical treatment in a patient without *H pylori* infection;
(2) persistent ulceration in a patient who has *H pylori* infection resistant to multiple attempts of eradication therapy;
(3) persistent ulceration in a patient who could not tolerate eradication therapy for *H pylori* infection;
(4) persistent ulceration despite successful eradication of *H pylori* infection (ie ulcer may be unrelated to *H pylori* infection);
(5) ulcer scarring leading to gastric outlet obstruction which could not be resolved with conservative management.

Emergency indications:
(1) ulcer haemorrhage that could not be controlled endoscopically;
(2) recurrent ulcer haemorrhage despite initial success with endoscopic haemostasis;
(3) ulcer perforation.

* Excludes patients who are taking NSAIDs

performance of elective ulcer surgery also poses an issue for the new generation of general surgeons who will have less exposure to ulcer surgery. Furthermore, the success of endoscopic therapy for ulcer haemorrhage in the past two decades has also resulted in a significant drop in the number of emergency operations for bleeding ulcers. The most frequent indication for surgery to treat ulcer disease now is perforation. Duodenal ulcer perforation is currently managed with a simple closure, which is usually not technically demanding. Complicated ulcer disease may require the attention of the 'older generation'–general surgeon or specialist care in the future.

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