The THAI Journal of SURGERY 2001; 22:115-122.
Official Publication of the Royal College of Surgeons of Thailand

Surgical Management of Peptic Ulcer Complications in the Era of H. pylori Infection

Prakitpunthu Tomtitchong, MD

Division of Surgery, Department of Clinical Sciences, Faculty of Medicine, Thammasat University, Pathumthani 12120 Thailand.

Abstract: **The role of *H. pylori* in surgery is a new topic of therapeutic consideration in peptic ulcer disease. There have been increasing evidences of the research results on this subject published more and more every year. These published data of collective results from researches are forming a new basis toward the line of surgical management in peptic ulcer disease. This new interesting trend envisages for selecting more non-invasive or minimal invasive surgery and to follow with *H. pylori* eradication thereafter. The results of this new trend of surgical approach are expected to be comparable to those achieved by formal conventional definitive procedures.**

It is known that *H. pylori* is definitely related to the pathogenesis of duodenal ulcer (DU), gastric ulcer (GU), and ulcer recurrence. Its role in the case of complicated ulcer, such as bleeding or obstruction, has been focussed on recently. It can be concluded in cases of non-massive bleeding that *H. pylori* eradication can effectively reduce the recurrence of ulcer and re-bleeding. Meanwhile, management of patients with uncontrolled (or massive) bleeding, perforation and obstruction depends mainly on surgery. Since it is expected that such eradication may play role in reducing the complication and recurrence of ulcer, it would be interesting to discuss how treatment of *H. pylori* infection in peptic ulcer might influence the choice and consideration of surgical procedures involved.

At present, a great deal of progress is being made in the area of endoscopic management for bleeding ulcers. Such approach has significantly reduced the number of surgical operation done for peptic ulcer disease. However, patients who need surgery are those with massive bleeding, continuous bleeding, or re-bleeding following endoscopic treatment failure. This group of patients often has adverse effects in the post-operative period.

DU Bleeding

In chronic DU patients with perforation or massive bleeding that necessitate surgical intervention, there are often questions of when a definitive surgery, such as truncal vagotomy and pyloroplasty or antrectomy

and vagotomy, be performed. A simple closure of the perforation or suturing of bleeding point would often result in ulcer or bleeding recurrence due to its chronic nature of the ulcer. However, a definitive surgery done in acute emergency situation might carry the risk of both immediate and long-term postoperative complications. Definitive surgery for peptic ulcer had been a common practice before the *H. pylori* era in the younger age group with good health condition, stable vital sign, and lesser degree of contamination. The following principles are taken into consideration.

1. Vagotomy with or without drainage procedure. Truncal or selective vagotomy done for the purpose of reducing vagal stimulation requires a complementary drainage procedure, such as pyloroplasty or gastroenterostomy to overcome the problem of gastric emptying. A highly selective vagotomy (HSV) as commonly referred to as Proximal Gastric Vagotomy (PGV) is a type of vagotomy whereby the distal vagal fibers, so-called claw web, of the nerve of Latarjet, are preserved to prevent antral stasis. In this case there is no need to have additional drainage procedure.

2. Gastric resection procedures. Some surgeons may prefer to do hemigastrectomy or subtotal gastrectomy. However, this is infrequently performed for this circumstance because of the unnecessary increase in morbidity and mortality. Antral resection, or antrectomy is intended to remove antral G-cells involved in acid production of the antral phase of stomach. Antrectomy is frequently performed with vagotomy for maximal efficiency in acid reduction.

Almost all of the clinical data in the treatment of DU bleeding and recurrence were published before fiberoptic gastroscopy became commonly employed and the use of proton pump inhibitor was just starting. Even when flexible gastroscopy was increasingly performed, a long-term follow-up data of ulcer cases was still limited to the groups of patients with recurrent hematemesis, perforation or persistent symptoms, not an overall study. Therefore, the precise rate of peptic ulcer recurrence before the *H. pylori* era was not clearly known. It was until widespread use of fiberoptic gastroscope in past years, data from several studies about ulcer recurrence and bleeding were reported as shown in Tables 1 and 2.

Table 1 Recurrent rates in duodenal ulcer disease prior to *H. pylori* study.

Uncomplicated ulcer (2 yrs. Follow-up)[1]	91.1 %
After antrectomy and vagotomy (A & TV)[7]	1-2 %
After truncal vagotomy and pyloplasty (TV & P)[7]	10 %
After proximal gastric vagotomy (PGV)[7]	15 %

Table 2 Recurrent and rebleeding rates in duodenal ulcer disease prior to *H. pylori* study.

Uncomplicated ulcer (1-2 yrs. F/U, recurrent)[2-6]	29-40 %
After oversewing of bleeding point[8]	9.7 %*
After vagotomy and gastrectomy (at least antrectomy with ulcer exclusion or more)[8,9]	0-0.7 %
After oversewing of bleeding point plus truncal vagotomy and pyloroplasty (TV & P)[8,9]	9.5-32 %
After oversewing of bleeding point plus proximal gastric vagotomy (PGV)[10]	6.3 %

**the re-bleeding rate was not too high because fatal re-bleeding terminated this study*

Role of H. pylori infection

PGV has been found to have high (15%) recurrent rate.[7] The basis of this is that preservation of nerve of Latarjet in the area of pyloric ring and antrum retains an intact antral phase of acid secretion by antral G-cell gastrin. Following PGV, persistent antral gastritis is noted up to more than 90 percent in which more than 94 percent was associated with *H. pylori* infection.[14] This high infection rate probably plays a role in the cause of high recurrent rate (Table 3).

On the contrary, we have found that antrectomy and vagotomy (A&TV) is very effective as a definite surgery for DU (1-2 % recurrence[7]). This procedure eliminates gastric acidity by both vagotomy and removal of gastric antral tissue involved in the acid production. Therefore ulcer recurrent rate is minimal as compared to other types of procedure. But in *H. pylori* study point of view, is it possible that an important portion of stomach that *H. pylori* colonizes (the antrum) is also removed? *H. pylori* infection rate of DU after antrectomy and vagotomy for DU is 50 percent[13] (Table 3). Therefore, recurrence after the surgery is very low partly may be because *H. pylori* is automatically eradication.[15]

For vagotomy and pyloroplasty (TV & P), the rate of ulcer recurrence falls in between those of HSV and A & TV, approximately 10 percent.[7] This procedure lowers the acid secretion only by denervation of vagus

nerves without gastrectomy. The intact antrum can allow *H. pylori* colonization to continue. And if the drainage by pyloroplasty is not effective, antral distension resulted from vagotomy may counteract the effect of vagus denervation in acid secretion. It has been reported that *H. pylori* infection rate was 83 percent[13] after TV & P operation for DU. It had been postulated that the chance of *H. pylori* infection was not as high as in PGV (94 %)[14] because of effect of antral bile reflux after surgery that reduced the growth of *H. pylori* in the antrum[15] (Table 4).

It has been found that *H. pylori* eradication can clearly reduce ulcer recurrence in chronic uncomplicated and non-massive bleeding ulcer patients. Because of the variable results of definitive surgery for complicated ulcer patient, especially in emergency massive bleeding, it becomes an issue for reconsideration whether or not such procedures are indeed indicated.

From current data on treatment of *H. pylori* infection, it is tempting to expect that *H. pylori* eradication could prevent recurrence and re-bleeding that may occur later on, even in the complicated ulcer patients with massive bleeding who require surgical intervention. Is it possible for *H. pylori* positive patients with clear indication for definite operation, be simply operated only with conservative surgery of over-sewing of duodenal ulcer bleeding point then followed with *H. pylori* eradication afterwards?

However, high re-bleeding and high death rates had been reported in over-sewing of the bleeding point with postoperative anti-peptic medication to reduce the acid after surgery.[8] Therefore, it may not be appropriate at present to suggest this approach as standard management in complicated DU patients except in patients whom definitive operation is not indicated. More study data are necessary before a definite conclusion can be made to answer the above question.

Based on current clinical evidences, a practical guideline for management of DU bleeding should include an initial endoscopic intervention option. Endoscopic approach for control of bleeding becomes an important option before making decision for surgery. All available endoscopic treatment techniques such as injection therapy with epinephrine, ethanol or other sclerosing agents; coagulation by bipolar electrocauterization, argon plasma coagulation (APC), or heater probe should be initially attempted. With continuing progress and advancement in endoscopic technique and experience, some cases of massive bleeding or end on arterial bleeding can also be brought under control without surgery. Prevention of re-bleeding requires medical treatment with proton pump inhibitor (PPI) medication and *Hp* eradication to start immediately after hemostasis has been achieved. Endoscopic control of bleeding peptic ulcer combined with minimal invasive surgery for selective vagotomy by laparoscopic approach has been advocated but has not gained widespread popularity.

In those patients who are in need of operation

Table 3 Recurrent and rebleeding rates in duodenal ulcer disease related to *H. pylori* infection.

Uncomplicated DU[11], recurrent	95-100 %
Uncomplicated DU after H. pylori eradication (2 yrs F/U, recurrent)[12]	3 %
Hp infection in Bleeding DU (controlled group = 93 %)[6]	71 %
Re-bleeding DU after Hp eradication[2-6]	0-3 %
Hp infection after antrectomy and vagotomy[13]	50 %
Hp infection after truncal vagotomy and pyloplasty[13]	83 %
Hp infection after proximal gastric vagotomy (PGV)[14]	94 %

Hp = H. pylori

Table 4 Recurrent ulcer and *H. pylori* infection after definitive surgery for peptic ulcer (DU, GU).

Type of Operation	Surgical Basis	Recurrence	Hp infection rate
PGV	Nerve transection (Partial)	15 %[7]	94 %[14]
TV or SV & P	Nerve transection (Total)	10 %[7]	83 %[13]
A & TV	Nerve transection and G-cells removal	1-2 %[7]	50 %[13]
PG	G-cells removal	5 %[7]	43 %[13]

Hp = H. pylori, PGV = Proximal gastric vagotomy, TV = Truncal vagotomy, SV = Selective vagotomy, P = Pyloroplasty, A=Antrectomy PG = Partial gastrectomy

because of active and massive bleeding, there is a question that should a definitive surgical procedure be done after complete control of bleeding. With surgical control of bleeding peptic ulcer by suture ligation followed by immediate medical treatment and eradication of *H. pylori*, a good long-term result may be achieved without emergency definite operation. This issue has now become a subject of controversy with a trend toward less definitive surgery.

GU Bleeding

Gastric ulcer is not caused by excess acid condition as in duodenal ulcer, but it is due to damage or loss of mucous barrier and effect of mucosal ischemia from various etiologic factors. Therefore, when encountered with major bleeding, at least the offending ulcer should be resected and submitted to pathological examination to rule out malignant condition. Definitive surgical treatment of gastric ulcer would depend upon the nature of ulcer etiology. Partial gastrectomy (PG) including ulcer resection is a procedure most performed for chronic benign GU in good risk patients. Data and factors of concern for surgery of chronic benign gastric ulcers are presented in Tables 5 and 6.

Table 5 Recurrent and re-bleeding rates in chronic benign gastric ulcer disease.

Uncomplicated GU, recurrent	47 %[16]
Re-bleeding GU	25-48 %[17]
Re-bleeding GU after oversewing of bleeding point	5 %[18]
Recurrent GU after oversewing of bleeding point (at 1 year follow-up, with history of re-use of NSAIDs or alcohol)	20 %[18]
Recurrent GU after partial gastrectomy	5 %[7]

Table 6 Recurrent and re-bleeding rates in chronic benign gastric ulcer disease related to *H. pylori* infection.

Uncomplicated GU, *Hp* injection	60-80 %[11]
Bleeding GU, *Hp* injection (control = 75 %)	61 %[6]
Re-bleeding GU after *Hp* eradication	0-3 %[1-7]
Recurrent GU after *Hp* eradication	7 %[16]
Hp infection rate of GU after partial gastrectomy for DU	43 %[13]

Hp = H. pylori

At present, endoscopic control of bleeding GU has been as effective as in the cases with DU and open surgery is required only in those patients with massive bleeding. Partial gastrectomy (PG) as a definitive operation had been commonly performed since conservative procedure such as ulcerectomy and oversewing of bleeding point were found in the past to be associated with high ulcer recurrence. However, with more and more effective postoperative anti-ulcer drug regimen, the conservative approach has been increasingly performed at present for its lower mortality and morbidity. Vagotomy has not been routinely added in ulcerectomy and oversewing of bleeding GU owing to the fact that most GU are not related to gastric hyperacidity. For definitive surgical treatment, such as PG for massive GU bleeding which had been suggested in the past, has now been discouraged due to the high mortality rate especially in elderly patients who are the majority of patients with GU.

Role of H. pylori infection

After PG, *H. pylori* infection rate is obviously reduced, only 43 percent of *H. pylori* infection had been reported.[13] Thus, surgical resection of distal stomach where *H. pylori* commonly colonized may be a factor contributing to the reduced recurrent rate of GU as well. Nevertheless *H. pylori* eradication after conservative operation has not been shown to be clearly beneficial in promoting healing process of GU. So far, there has been no study to confirm this effect.

Peptic Ulcer Perforation

Elective operation for intractable pain in peptic ulcer disease has drastically declined after the discovery and clinical use of H_2 blocker and proton pump inhibitor for treatment of peptic ulcer disease. However, the number of patients with perforated peptic ulcer undergoing emergency operation has remained not much changed. Patients who were admitted in good condition shortly after the episode of perforation with minimal intraoperative contamination, vagotomy and antrectomy as definitive surgery for peptic ulcer were recommended. Nevertheless, for most patients who did not come to the hospital within this golden period, simple closure with omental graft was usually performed. Prior to the period of *H. pylori* eradication in peptic ulcer disease, the recurrence rate of DU after

simple closure and omental patch had been reported in the range of 41-42 percent.[19,20] At present, *H. pylori* status has significantly influenced the role of definitive surgery in peptic ulcer perforation as in the case with bleeding.

Role of H. pylori infection

The questions on whether or not *H. pylori* increases chance of perforation in peptic ulcer patients were widely studied by many researchers. Early data reflecting relation between *H. pylori* and peptic ulcer perforation came from the studies by Debongnie and Legros[21] in 1990. Their data clearly showed that prevalence of infection in peptic ulcer perforation patients was lower than in chronic recurrent DU patients. This was confirmed by Reinbach et al[22] from Glasgow, reporting 80 patients in 1993 which concluded that *H. pylori* infection rate did not increase in patients with acute DU perforation when compared with people population of the same age by testing serum IgG antibody (47 % VS 50 % respectively) together with Urea Breath Test during 4-10 weeks after surgery (49% VS 50% respectively). Matsukura et al.[23] in 1997 reported a study from Japan by comparing patients having DU perforation with control group based on serum IgG antibody (95% VS 93% respectively) and gastric juice PCR obtained via gastroscopy during the 2nd week after surgery (74% VS 71% respectively) showing similar results with the earlier studies. They concluded that *H. pylori* did not increase the risk of perforation both in acute and chronic cases. Host factors were assumed more likely to be the main cause of perforation. The limitation of this study was the high IgG sensitivity but low specificity in endemic area of Japan, which raised questions about its interpretation. Although the test for *H. pylori* DNA in gastric juice has considerable accuracy without medications that possibly interfere with the results of the test, it was determined late at 2 weeks after surgery.

Furthermore, in the same report, strain diversity (cagA, vacA) was also studied. It revealed no effect on the risk of perforation. However, other researchers suggested that cagA positive strain may have effects on ulcer relapse after treatment by surgery.[24]

On the contrary, some researcher believes that *H. pylori* could be the main cause leading to peptic ulcer perforation. Sebastian et al[25] from United Arab Emirates in 1995, reported the findings in 29 Arabian and Indian patients with peptic ulcer perforation, 24 patients (82.8%) were infected. Based on Urea Breath Test on the 8th day of surgery in conjunction with gastroscopy and biopsy urease test at 6th week after surgery, they found high prevalence of infection in this group of patients. The average age of their patients was lower than in others studies that were mentioned. Furthermore, they did not find any difference between NSAID users in this group of patient when compared to general population. They concluded that *H. pylori* might be the major cause of peptic ulcer perforation. However, there are issues of concern in this study. Commonly, surgeons take biopsies from the edge of the ulcer before its closure. These biopsies are taken primarily for ruling out gastric malignancies. The specimens obtained intraoperatively from the edge of the ulcer may also contain considerable amount of necrotic tissues that could make it difficult or inappropriate for *H. pylori* study. This study was also not a controlled study and therefore its data might not clearly depict the true infection rate in an endemic area.

Ng et al.[26] in 1996 from Hong Kong, considered an endemic area, employed intra-operative gastroscopy and gastric biopsy for CLO test, culture, and histologic studies. They found that prevalence of *H. pylori* infection was 70 percent but was not statistically significant when compared with 55 per cent infection in local population. The infection rate in non-NSAIDs user was 80 per cent while that of NSAIDs users was only 23.1 per cent. They concluded that the high prevalence of *Helicobacter pylori* in duodenal ulcer perforations was not caused by non-steriodal anti-inflammatory drugs.

Despite the overwhelming evidences pointing *H. pyroli* infection causes gastric and duodenal ulcers, it remains controversy of whether or not the same infection leads to higher incidence of peptic perforation. As mentioned earlier in peptic ulcer bleeding, postoperative eradication of the *H. pyroli* should similarly lower the chance of recurrent ulcer[23,25,26] without the need of definitive surgery. Thus, it is currently recommended that simple closure is the procedure of choice for peptic ulcer perforation patients, both in acute and chronic cases.[23]

Recent data from Ng et al.[27] reported in 2000 showed *Hp* infection in 99 cases of a total of 129 cases of perforated peptic ulcer. Following simple closure

with omental graft, patients were randomized into two groups. The first group consisted of 51 patients who received *H. pyroli* eradication and a short course of proton pump inhibitor medication. Meanwhile, another 48 patients as the controlled group were treated with proton pump inhibitor for maintenance therapy of one year. Ulcer healing and symptoms were followed-up at two months and one year. They found that in the first group with successful *H. pylori* eradication had statistical significant improvement of symptoms (p = 0.02) and better ulcer healing and prevention of recurrence ($p<0.001$) than the controlled group. They concluded that, "simple repair, open or laparoscopic, for duodenal perforation, especially in the younger patients, *H. pylori* status should be determined and treated in those who were infected". This report may stimulate many surgeons to study to confirm such conclusion that *H. pylori* eradication could replace the need for definite surgical treatment.[28] However, such recommendation for Hp eradication after simple closure of peptic perforation with a tendency towards avoidance of definite surgery has been increasingly supported. Further more, in *H. pylori* negative NSAIDs user patient in good condition who has chronic ulcer and high risk of recurrence, definitive operation may still be indicated.

Gastric Outlet Obstruction

Gastric outlet obstruction is still being encountered although with reduced frequency. This condition can be due to benign (peptic ulcer) and malignant (gastric cancer) causes. Guideline for treatment of malignant obstruction emphasizes on 'gastric resection' in order to extirpate the tumor mass as well as making relief of the obstuction. Only when gastric resection is technically not possible then palliative bypass procedure such as gastrojejunostomy becomes an alternative. For patients with high risk for major surgery, possibly only feeding jejunostomy can be done, resulting in poor quality of life. One of the newly adopted palliation is through-the-scope-balloon dilatation, in which the patient is left with a stent in order to prevent recurrent obstruction. Most recently, Feretis et al[29] reported the use of balloon dilatation with self expanding metal stent in gastric outlet area without surgery, rendering better quality of life that patient could possibly eat by mouth.

Benign gastric outlet obstruction from peptic ulcer occurs mostly in the prepyloric region. Such ulcer is mainly related to gastric hyperacidity. The acute type of obstruction should be treated conservatively with nasogastric decompression and anti-secretory drugs. Most of the cases will have good response to treatment. In chronic case, the treatment may be less responsive and definitive surgery therefore is needed.

Vagotomy and antrectomy is a highly effective definite surgical procedure that has very low recurrent rate. However, a difficult duodenal stump problem could lead to major complication in this type of definitive surgical procedure. Vagotomy and drainage is a much safer procedure that devoid of difficult duodenal stump problem. Gastrojejunostomy is considered more effective than pyloroplasty.

Although current treatment of chronic benign gastric outlet obstruction depends mainly on surgery, there have been many reports on highly selective vagotomy performed in conjunction with various dilatation methods of the obstruction. At first, digital dilatation[30] or Hegar dilator[31] have been successfully employed. Subsequently with the use of flexible endoscopy, balloon dilatation has been effectively attempted.[32,33] This approach is a less invasive type of treatment and offers no risk of post-vagotomy and post-gastrectomy syndrome. However, the recurrent rate is high in long term follow-up, and therefore has not been popularized. Lau et al[34] reported in a study involving 54 patients receiving balloon dilatation that initially 83.3 per cent was successful, 9.3 per cent failed, and 7.4 per cent having complication due to perforation. But on the long-term 7 years follow-up, half of the patient successfully dilated had developed symptoms of obstruction and needed surgery subsequently. Accordingly, they recommended such attempt in patient with high surgical risk. Kozarek[35] commented in the same journal that although dilatation practice might be useful but selection of suitable patient was necessary. More importantly, medical treatment must be adequate after the dilatation for prevention of ulcer recurrence.

Role of H. pylori infection

The concept of *H. pylori* eradication and adequate ulcer treatment regimen may heal peptic ulcer with obstruction without the need for surgery has been the subject of interest and being investigated by some

authors. Annibale et al[36] in their report from Italy stated that *H. pylori* eradication may help correct peptic ulcer stenosis. De Boer et al[37] reported on patients who failed balloon dilatation but stenosis disappeared only in those with successful *H. pylori* eradication. Tursi et al[38] reported on 2 patients whose gastric outlet obstruction were corrected by *H. pylori* eradication without balloon dilatation. They observed that improvement of obstruction was achieved in the case of obstruction resulted from edema rather than fibrosis. Thus, it would be more suitable for acute obstruction than the chronic ones. Lam et al.[39] reported six *Hp* positive patients treated with balloon dilatation and *H. pylori* eradication found that within 16.5 months of follow-up, there was no return of the symptom. On the contrary, patients with gastric outlet obstruction with *H. pylori* negative and treated with dilatation alone failed to improve.

It is therefore suggested that balloon dilatation and *H. pylori* eradication may be the alternative treatment for patients with benign gastric outlet obstruction who do not want or not ready for surgery. In acute case, patients may suffer the obstruction from tissue edema and *H. pylori* eradication may be sufficient to reduce tissue swelling and obstruction. But in chronic case with fibrosis, *H. pylori* eradication alone is inadequate and must be supplemented by balloon dilatation in the treatment.

References

1. Labenz J, Borsch G. Highly significant change of the clinical course of relapsing and complicated peptic ulcer disease after cure of *Helicobacter pylori* infection. Am J Gastroenterol 1994; 89: 1785-8.
2. Labenz J, Gyenes E, Ruhl GH, Borsch G. Role of *Helicobacter pylori* eradication in patients with peptic ulcer bleeding. Gastroenterology 1993; 104: A126
3. Graham DY, Hepp KS, Ramirez FC, et al . Treatment of *Helicobacter pylori* reduces the rate of rebleeding in peptic ulcer disease. Scand J Gastroenterol 1993; 28: 939-42
4. Jaspersen D, Koerner T, Schorr W, et al. *Helicobacter pylori* eradication reduces the rate of rebleeding in ulcer hemorrhage. Gastrointest Endosc 1995; 41: 5-7
5. Rokkas T, Karameris A, Mavrogeorgis A, et al. Eradication *Helicobacter pylori* reduces the possibility of rebleeding on peptic ulcer disease. Gastrointest Endosc 1995; 41: 1-4
6. Hosking SW, Yung MY, Chung SC, Li AKC. Differing prevalence of *Helicobacter pylori* in bleeding and non-bleeding ulcers. Gastroenterology 1992; 102: A85
7. Moody FG, Miller TA. Stomach. On: Schwartz SI, Shire GT, Spencer FC, Husser W, editors. Principles of Surgery. 6th ed. New York: McGraw- Hill; 1994. P. 1123-52
8. Poxon VA, Keighley MRB, Dykes PW, et al. Comparison of minimal and conventional surgery in patients with bleeding peptic ulcer: a multicentre trial. Br J Surg 1991; 78: 1344-5
9. Millat B, Hay JM, Valleur P, et al. Emergency surgical treatment for bleeding duodenal ulcer: oversewing plus vagotomy versus gastric resection, a controlled randomized trial. French Association for Surgical Research. World J Surg 1993; 17: 568-74
10. Brancatisano R, Falk GL, Hollinshead JW, et al. Bleeding duodenal ulceration: the results of emergency treatment with highly selective vagotomy. Aust N Z J Surg 1992; 62: 725-8
11. Graham DY. *Helicobacter pylori*: Its epidemiology and its role in duodenal ulcer disease. J Gastroenterol Hepatol 1991; 6: 105-13
12. Labenz J, Borsch G. Highly significant change of the clinical course of relapsing and complicated peptic ulcer disease after cure of *Helicobacter pylori* infection. Am J Gastroenterol 1994; 89: 1785-8
13. Danesh J, Appleby P, Peto R. How often does surgery for peptic ulceration eradicate *Helicobacter pylori*? Systematic review of 36 studies. Br med J 1998; 316: 746-7
14. Jonsson KA, Strom M, Bodemar G, et al. Histologic changes in the gastroduodenal mucosa after long-term medical treatment with cimetidine or parietal cell vagotomy in patient with juxtapyloric ulcer disease. Scand J Gastroenterol 1988; 23: 433-41
15. Kozol RA. Surgery of peptic ulcer in the *Helicobacter pylori* era. Arch Surg 1995; 130: 1040.
16. Seppala K, Pikkarainen P, Sipponen P, et al. Cure of peptic gastric ulcer associated with eradication of *Helicobacter pylori*. Gut 1995; 36: 834-7
17. Peterson WL. Gastrointestinal bleeding. In: Sleisenger MH, Fordtran JS, eds. Gastrointesitinal diseases. Pathophysiology, diagnosis, management. 3rd ed. Philadelphia: Saunders; 1983. p. 177-207
18. Rogers PN, Murray WR, Shaw R, Brar S. Surgical management of bleeding gastric ulceration. Br J Surg 1988; 75: 16-7
19. Raimes SA, Devlin HB. Perforated duodenal ulcer. Br J Surg 1987; 74: 81-2
20. Bornman PC, Theodorou NA, Jeffery PC, et al. Simple closure of perforated duodenal ulcer: a prospective evaluation of a conservative management policy. Br J Surg 1990; 77: 73-5
21. Debongnie JC, Legros G. Gastric perforation: an acute disease unrelated to *H. pylori*? Rev Esp Enferm Dig 1990; 78(Suppl. 1): 71-2
22. Reinbach DH, Cruickshank G, McColl KEL. Acute perforated duodenal ulcer is not asscociated with *Helicobacter pylori* infection. Gut 1993; 34: 1344-7

23. Matsukura N, Onda M, Tokunaga A, et al. Role of *Helicobacter pylori* infection in perforation of peptic ulcer: An age and gender matched case-control study. J Clin Gastroenterol 1997; 25(Suppl.1): S235-9
24. Ng EKW, Leung WK, Sung JY, et al. Anti-CagA serology and ulcer recurrence in patients with duodenal ulcer perforation associated with *Helicobacter pylori*. Gastroenterology 1998; 114: A242
25. Sebastian M, Prem Chandran VP, Elashaal YIM, Sim AJW. *Helicobacter pylori* infection in perforated peptic ulcer disease. Br J Surg 1995; 82: 360-2
26. Ng EKW, Chung SCS, Sung JJY, et al. High prevalence of *Helicobacter pylori* in duodenal ulcer perforations not caused by non-steriodal anti-inflammatory drugs. Br J Surg 1996; 83: 1779-81
27. Ng EK, Lam YH, Sung JJ, Yung MY, To KF, Chan AC, et al. Eradication of *Helicobacter pylori* prevents recurrence of ulcer after simple closure of duodenal ulcer perforation: randomized controlled trial. Ann Surg 2000; 231: 153-8
28. Stabile BE. Redefining the role of surgery for perforated duodenal ulcer in the *Helicobacter pylori* era. Ann Surg 2000; 231: 159-60
29. Feretis C, Benakis P, Dimopoulos C, et al. Palliation of malignant gastric outlet obstruction with self-expanding metal stents. Endoscopy 1996; 28: 225-8
30. McMahon MJ, Greenall MJ, Johnston D, Goligher JC. Highly selective vagotomy plus dilatation of the stenosis compared with truncal vagotomy and drainage in the treatment of pyloric stenosis secondary to duodenal ulceration. Gut 1976; 17: 471-6
31. Hooks VH, Bowden TA, Mansberger AR, Sisley JF. Highly selective vagotomy with dilatation or duodenoplasty. A surgical alternative for obstructing duodenal ulcer. Ann Surg 1986; 203: 545-50
32. Pollard SG, Friend PJ, Dunn DC, Hunter DO. Highly selective vagotomy with duodenal dilatation in pateints with duodenal ulceration and gastric outlet obstruction. Br J Surg 1990; 77: 1365-6
33. Mentes AS. Parietal cell vagotomy and dilatation for peptic duodenal stricture. Ann Surg 1990; 212: 597-601
34. Lau JYW, Chung SCS, Sung JYJ, et al. Through-the-scope balloon dilatation for pyloric stenosis: long-term results. Gastrointest Endosc 1996; 43: 98-101
35. Kozarek RA. Endotherapy for gastric outlet obstruction. Gastrointest Endosc 1996; 43: 173-4
36. Annibale B, Marignani M, Luzzi I, Delle Fave GF. Peptic ulcer and duodenal stenosis: role of *Helicobacter pylori*. Ital J Gastroenterol 1995; 27: 26-8
37. de Boer WA, Driessen WMM. Resolution of gastric outlet obstruction after eradication of *Helicobacter pylori*. J Clin Gastroenterol 1995; 21: 329-30
38. Tursi A, Cammarota G, Papa A, et al. *Helicobacter pylori* eradication helps resolve pyloric and duodenal stenosis. J Clin Gastroenterol 1996; 23: 157-8
39. Lam YH, Lau JYW, Law KB, et al. Endoscopic balloon dilation and *Helicobacter pylori* eradication in the treatment of gastric outlet obstruction. Gastrointest Endosc 1997; 46: 379-80