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TOPIC HIGHLIGHT

WJG 20th Anniversary Special Issues (6): *Helicobacter pylori*

Management of *Helicobacter pylori* infection after gastric surgery

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Abstract

The Maastricht IV/Florence Consensus Report and the Second Asia-Pacific Consensus Guidelines strongly recommend eradication of *Helicobacter pylori* (*H. pylori*) in patients with previous gastric neoplasia who have undergone gastric surgery. However, the guidelines do not mention optimal timing, eradication regimens, diagnostic tools, and follow-up strategies for patients undergoing gastrectomy and do not indicate if eradication of *H. pylori* reduces the risk of marginal ulcer or stump cancer in the residual stomach after gastrectomy. The purpose of this review is to provide an update which may help physicians to properly manage *H. pylori* infection in patients who have undergone gastric surgery. This review focuses on (1) the microenvironment change in the stomach after gastrectomy; (2) the phenomenon of spontaneous clearance of *H. pylori* after gastrectomy; (3) the effects of *H. pylori* on gastric atrophy and intestinal metaplasia after gastrectomy; (4) incidence and clinical features of ulcers developing after gastrectomy; (5) does eradication of *H. pylori* reduce the risk of gastric stump cancer in the residual stomach? (6) does eradication of *H. pylori* reduce the risk of secondary metachronous gastric cancer in the residual stomach? and (7) optimal timing and regimens for *H. pylori* eradication, diagnostic tools and follow-up strategies for patients undergoing gastrectomy.

Key words: *Helicobacter pylori*; Gastrectomy; Gastric stump; Treatment outcome; Stomach neoplasms; Stomach ulcer; Atrophic gastritis; Metaplasia

Core tip: For patients undergoing gastric surgery due to acute complications of peptic ulcer diseases or gastric cancer, this surgical procedure may increase the occurrence of biliary enterogastric reflux and potentially inhibit the growth of *Helicobacter pylori* (*H. pylori*) in the stomach. Bile reflux and *H. pylori* infection appear to have a synergistic effect on cell proliferation in the gastric remnant and may explain the increased risk of cancer after gastrectomy. First-line triple therapy is effective for the eradication of *H. pylori* in gastrectomized patients. Serology is the only test that is not affected by local changes in the stomach, and could be used to avoid the false-negative results obtained with other tests.

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INTRODUCTION

Helicobacter pylori (*H. pylori*) is a human pathogen that has infected half the global population, and its discovery has revolutionized the concept of gastroduodenal diseases. *H. pylori* infection is an important etiologic factor in gastritis, peptic ulcer, and gastric malignancy. In 2012, the Maastricht IV/Florence Consensus Report reinforced the finding that *H. pylori* infection is the most commonly proven risk factor for gastric cancer in humans[1]. Eradication of *H. pylori* has been shown to prevent gastric cancer in patients with this infection; a pooled analysis of 6 studies with mostly Asian participants followed up for 4-10 years showed that the relative risk of gastric cancer after eradication of *H. pylori* was 0.65 (95%CI: 0.43-0.98), and a significant reduction in cases of gastric cancer was seen in subjects with eradication before the development of atrophic gastritis or intestinal metaplasia[2]. The authors suggest that *H. pylori* eradication treatment reduces the risk of gastric cancer, however, the risk is not abolished.

Currently, eradication of *H. pylori* is strongly recommended in (1) patients with gastroduodenal diseases such as peptic ulcer disease and low-grade gastric mucosa-associated lymphoid tissue lymphoma; (2) patients with atrophic gastritis; (3) first-degree relatives of patients with gastric cancer; (4) patients with unexplained iron deficiency anemia; and (5) patients with chronic idiopathic thrombocytopenic purpura[3]. Prophylactic eradication of *H. pylori* after endoscopic resection of early gastric cancer should be used to prevent the development of metachronous gastric carcinoma[4]. However, the effect of *H. pylori* eradication on the gastric remnant after surgical resection has not been clearly determined[5]. There is some new evidence regarding this, and the Maastricht IV/Florence Consensus Report and the Second Asia-Pacific Consensus Guidelines strongly recommend eradication of *H. pylori* in patients with previous gastric neoplasia who have undergone subtotal gastric resection[1,6]. However, the guidelines do not mention optimal timing, eradication regimens, diagnostic tools, and follow-up strategies for patients undergoing gastrectomy and do not indicate if eradication of *H. pylori* reduces the risk of ulcer or stump cancer in the residual stomach after gastrectomy.

The purpose of this review is to provide an update which may help physicians to properly manage *H. pylori* infection in patients after gastric surgery. A literature search was conducted mainly in PubMed (1948-), and a supplementary search in Embase (1974-) and Google Scholar. Search keywords used controlled vocabulary (MeSH or Emtree) and text words, including: *Helicobacter pylori*[MeSH], *Helicobacter* infections[MeSH], *Helicobacter*, *Campylobacter*, *H. pylori*, *C. pylori*; gastrectomy[MeSH], gastrectom*, hemigastrectom*, gastric surger*, stomach surger*; gastric stump[MeSH], stump*, residual, remnant*; eradicat*; spontaneous remissions[MeSH], spontaneous clearance, spontaneous regression*, spontaneous eradicat*; atrophic gastritis[MeSH], atrophy[MeSH], atroph*, dysplas*; metaplasia[MeSH], metaplas*; peptic ulcer[MeSH], ulcer*; stomach neoplasms[MeSH], local neoplasm recurrence[MeSH], second primary neoplasms[MeSH], cancer*, maliganc*, carcinoma*, cancerogen*, carcinogen*, neoplasmogen*, oncogen*, tumorigen*. The keywords based on PubMed syntax were adequately revised for the remaining databases. The complex search strategies for the individual sub-topics were properly established, including the combinations of the keywords and the filter of the articles (principally according to the Oxford level of evidence).

MICROENVIRONMENT CHANGE IN THE STOMACH AFTER GASTRECTOMY

Food retention and bile reflux have frequently been observed in patients with gastric cancer following subtotal gastrectomy[7]. After gastric surgery, the biochemical profile, microbiological profile, or pH of the gastric juice is dramatically altered. A previous study assessed the presence of N-nitrosamine compounds and bacteria in the gastric juice after gastric surgery[8] and showed that patients who underwent gastric resection with both Billroth (B)-Ⅱ and B-Ⅰ gastrectomies had higher mean pH, N-nitrosamine concentrations, nitrate reductase-positive bacterial counts, and anaerobic bacterial counts. In a higher pH microenvironment, the stomach will subsequently reduce concentrations of ascorbic acid, which is an antioxidant that scavenges carcinogenic N-nitrosamines and reactive oxygen species. Oxygen radicals induced by inflammation could contribute to the risk of developing gastric cancer, and variation in the biochemical and microbiological microenvironment in the gastric juice may also play a role.

Residual mucosa in the stomach after gastrectomy is considered a risk factor for the development of cancer in the gastric remnant. Chronic inflammation due to biliary enterogastric reflux results in hyperplastic changes in the gastric epithelium of the remnant. Bechi *et al*[9] found that the hyperplastic changes gradually decreased with increasing distance from the anastomosis, which means that the gastric histological findings after partial gastrectomy were affected by reflux.

Fukuhara *et al*[10] evaluated the association between bile reflux and gastritis in 62 patients who underwent curative gastrectomy for gastric cancer. The period of bile reflux into the gastric remnant was measured with the Bilitec 2000, and remnant gastritis was semiquantified using the neutrophil infiltration score based on the updated Sydney System 12 wk after surgery. The results showed that the correlation was independent for *H. pylori* infection, and the investigators concluded that biliary entero-

gastric reflux after distal gastrectomy can cause remnant gastritis.

PHENOMENON OF SPONTANEOUS CLEARANCE OF *H. PYLORI* AFTER GASTRECTOMY

Whether *H. pylori* can survive in the altered environment after gastrectomy remains an interesting issue. Suh *et al*[11] reported an overall spontaneous clearance rate of *H. pylori* infection of 38.6% (27/70 patients) during a mean period (from surgery to follow-up tests) of 1.02 ± 0.5 years. The activity and chronic inflammation scores were significantly decreased in the spontaneous clearance group.

The influence of different procedures and duration after surgery on spontaneous clearance of *H. pylori* has been addressed. Generally, with B-Ⅰ anastomosis, the gastrointestinal tract has normal continuity and the remaining duodenum offers more resistance to recurrent ulceration than the jejunum. The prevalence of *H. pylori* infection was significantly higher in patients who had a partial wedge resection compared with subtotal gastrectomy, because wedge resection results in less biliary enterogastric reflux due to preservation of the pylorus[12]. The lower rate of *H. pylori* infection found in patients who underwent B-Ⅱ may reflect the role of bile reflux, which may interfere with colonization of *H. pylori*[13].

There was a trend toward a decreasing prevalence of *H. pylori* colonization as the length of time after surgery increased. In our previous study, the prevalence of *H. pylori* 1 to 15 years after surgery was 29.5%, after 16 to 30 years it was 13.6%, and after more than 30 years it was 10%[13]. The overall spontaneous clearance rate of *H. pylori* after partial gastrectomy was 43%. We also confirmed that B-Ⅱ was associated with a higher rate of bile reflux and lower prevalence of *H. pylori* infection than the B-Ⅰ procedure.

It was assumed that the microenvironment for *H. pylori* colonization after surgical interventions changes dramatically and thus influences their survival. First, the hypochlorhydric environment due to antrectomy is an unfavorable factor for the growth of *H. pylori*[14]. Second, biliary enterogastric reflux emerges due to loss of the pyloric ring, which may inhibit *H. pylori* growth. Third, the substitution of intestinal-type epithelium for gastric parietal cells makes the mucosa more resistant to *H. pylori* infection[15]. Finally, loss of the usual site of infection plays a major role because the prevalence of *H. pylori* remains high after vagotomy, which carries only the hypochlorhydric environment[16]. All of these factors may make the microenvironment unfavorable for *H. pylori*.

EFFECTS OF *H. PYLORI* ON GASTRIC ATROPHY AND INTESTINAL METAPLASIA AFTER GASTRECTOMY

After gastrectomy, a potential cause of remnant gastritis is *H. pylori* infection accompanied by biliary enterogastric reflux[17]. If eradication of *H. pylori* in patients after gastrectomy is beneficial, what would be the effect of *H. pylori* eradication on gastric atrophy and intestinal metaplasia at the gastric remnant? Fukuhara *et al*[18] investigated concentrations of interleukin (IL)-8, a sensitive marker of inflammation in the gastric mucosa, 3 mo after surgery. In the absence of *H. pylori* infection, IL-8 concentrations were 13, 56, and 87 pg/mg in groups A (Roux-en-Y), B (B-Ⅰ), and C (B-Ⅱ), respectively ($P < 0.05$). In the presence of *H. pylori* infection, IL-8 concentrations were 61, 161, and 234 pg/mg protein in groups A, B, and C, respectively ($P < 0.01$)[18]. Both bile reflux and *H. pylori* infection are independent risk factors for the development of gastritis and intestinal metaplasia in the remnant stomach after distal gastrectomy. Cho *et al*[19] found that in the absence of *H. pylori*, regardless of eradication, treatment or spontaneous clearance may lead to regression of gastric atrophy and intestinal metaplasia in the remnant stomach with time. It is difficult to separate causally relevant factors of bile reflux and *H. pylori* infection from co-incidences or collateral changes. Abe *et al*[20] examined the severity of remnant gastritis in 184 patients who had undergone distal gastrectomy performed using the B-Ⅰ ($n = 106$), B-Ⅱ ($n = 36$) and jejunal interposition ($n = 42$). *H. pylori* infection was confirmed in 55.6% of the B-I patients and in 76.1% of the jejunal interposition patients. The rate of *H. pylori* infection was higher for jejunal interposition patients than for B-Ⅰ ($P < 0.05$)[20]. The severity of chronic and active inflammatory cellular infiltration tended to have an inverse proportional relation to the endoscopic severity of the remnant gastritis. We still do not know if bile reflux with its subsequently decreased *H. pylori* incidence may neutralize the effect on cancer development.

Ando *et al*[5] found that chronic inflammation and atrophy scores were improved after eradication and no secondary stomach cancers were found on endoscopy. In a study by Kato *et al*[21], the pH of gastric juice was measured in 112 *H. pylori*-positive patients who underwent distal gastrectomy and *H. pylori* eradication therapy. The pH of the gastric juice showed an inverse correlation with the serum pepsinogen Ⅰ / Ⅱ ratio, which could be a suitable surrogate marker of gastric mucosal atrophy. The investigators concluded that eradication therapy for the remnant stomach contributes to the possible improvement of stomach conditions by normalizing the pH of gastric juice.

INCIDENCE AND CLINICAL FEATURES OF ULCERS DEVELOPING AFTER GASTRECTOMY

The need to perform gastrectomy on patients with peptic ulcer disease has decreased since the discovery of *H. pylori* and the development of proton pump inhibitors. The sequelae of gastrectomy are recurrent ulcers, especially marginal ulcers, or cancer of the gastric remnant.

It has been reported that the incidence of marginal ulcers varies from 0.6% to 16%[22,23]. Development of a marginal ulcer after gastrectomy for a bleeding ulcer is a serious threat to the patient. *H. pylori* infection is the primary risk factor for gastric ulcers. However, its role in marginal ulcers after surgery is unclear. A study by Chung *et al*[24], which included a consecutive series of 78 patients with endoscopic ulcers and 759 patients without ulcers after gastrectomy, showed that the incidence of ulcers after gastrectomy was 9.3% and the majority (92%) were marginal ulcers. Ulcers were more common in patients with B-Ⅱ anastomosis and pre-existing peptic ulcer disease. Infection rates of *H. pylori* did not differ significantly between the 2 groups and suggested that *H. pylori* is not an important factor in ulcerogenesis after gastrectomy.

In a study by Leivonen *et al*[25], 41 of 155 patients had an ulcer at the site of anastomosis or in the gastric stump after a median interval between surgeries of 4 years. The recurrence rate was higher after B-Ⅱ (34%) than after Roux-en-Y (14%) or B-Ⅰ reconstruction (24%). Interestingly, recurrent ulcer was less often found in those with *H. pylori*-positive gastritis (18%) than *H. pylori*-negative gastritis (26%). It seems that *H. pylori* infection plays a minor role in the pathogenesis of ulcer recurrence after partial gastrectomy. Eradication of *H. pylori* of the remnant stomach is therefore presumably not effective in preventing ulcer recurrence. A randomized controlled study on a larger scale to assess the clinical relevance is therefore still necessary.

DOES ERADICATION OF *H. PYLORI* REDUCE THE RISK OF GASTRIC STUMP CANCER IN THE RESIDUAL STOMACH?

Gastric stump cancer (GSC) is defined as a carcinoma developing in the gastric remnant more than 5 years after surgery for benign disease[26]. It is recommended that patients with previous gastric neoplasia already treated by subtotal gastric resection undergo eradication therapy[1,6], however, the recommendations do not mention the need for eradication of *H. pylori* to prevent GSC in patients who have undergone gastrectomy for benign lesions such as ulcer with bleeding, perforation, or obstruction.

In a study by Chung, GSC was found in 6 (0.7%) of 837 patients who underwent gastrectomy[24]. The overall risk increased over time, and the median interval between the initial gastrectomy and diagnosis of GSC was 25 years[24]. The occurrence of GSC is higher in patients with an initial diagnosis of gastric rather than duodenal ulcer and after B-Ⅱ reconstruction[27], and GSC is predominantly found in men[24]. A meta-analysis of 22 studies showed that the overall relative risk for GSC was 1.66 (95%CI: 1.54-1.79)[27]. Patients who underwent surgery 15 or more years previously had a weighted mean relative risk of 1.48 (95%CI: 1.31-1.67). Spontaneous clearance of *H. pylori* after partial gastrectomy was noted with time after surgery[13,19] and had an inverse association with the occurrence of GSC. Biliary enterogastric reflux may impair the growth of *H. pylori*.

The cause of cancer in the gastric stump is multifactorial, and the increased mucosal cell proliferation caused by bile reflux has been claimed to increase the risk of GSC[28]. Leivonen conducted a retrospective study of 130 patients who underwent partial gastrectomy for peptic ulcer. Cell proliferation was determined using immunohistochemical staining of Ki-67 antibodies from gastric remnants, and there was no clear association between proliferation and *H. pylori*. However, a significant difference was seen between reconstruction types, which is known to be associated with bile reflux[29]. One large population-based study from Sweden revealed an increased risk of cancer in the gastric remnant only 30 years or more after gastric resection for benign disease, whereas other factors did not influence this risk[30]. Roux-en-Y reconstruction has been shown to eliminate the symptoms of bile reflux gastritis. Twenty-nine patients partially gastrectomized for peptic ulcer were reoperated 4-13 years later with a Roux-en-Y reconstruction due to reflux gastritis in 12 patients and severe gastric dysplasia/early gastric cancer in 17 patients[31]. The prevalence of *H. pylori* infection was not statistically different between the patients with reflux gastritis (6/12) and those with severe dysplasia or gastric neoplasms (12/17). This meant that *H. pylori* plays less of a role in GSC after gastric surgery for peptic ulcer. The subsequent biopsies from the new anastomotic region were taken 5-17 years after Roux-en-Y reconstruction and were evaluated for active chronic gastritis, atrophy, intestinal metaplasia and dysplasia. The progression of active chronic gastritis, atrophy, intestinal metaplasia and dysplasia was seen even when an attempt to divert reflux after Roux-en-Y reconstruction was made, but was independent of *H. pylori* infection.

In the intact stomach, *H. pylori*-associated gastritis is considered a major risk factor for cancer and as for other cancers; removing one factor does not prevent all gastric cancers. Based on these clinical observations, it is difficult to determine the role of *H. pylori* eradication in the prevention of GSC[32]. A cohort study to assess the clinical relevance of *H. pylori* eradication under these circumstances is therefore necessary.

Table 1 Effect of *Helicobacter pylori* eradication in preventing metachronous gastric cancer after endoscopic surgery in prospective randomized controlled trials

Ref.	Year	Treatment method	Case number	Metachronous cancer	Metachronous cancer	Definition of new cancers	*P* value	Follow-up, yr
				Eradication	No eradication			
Choi *et al*[35]	2013 RCT	Endoscopic submucosal dissection	901	10/444	17/457	New carcinoma in areas other than the site of primary gastric cancer	0.150	3
Maehata *et al*[34]	2012 Restropective	Endoscopic submucosal dissection	268	15/177	13/91	New carcinoma in areas other than the site of primary gastric cancer; at least 1 yr after endoscopic resection	0.262 0.007	3 5
Fukase *et al*[33]	2008 RCT	Endoscopic submucosal dissection	544	9/272	24/272	New carcinoma in areas other than the site of primary gastric cancer	0.009	3

RCT: Randomized controlled trial.

DOES ERADICATION OF *H. PYLORI* REDUCE THE RISK OF SECONDARY METACHRONOUS GASTRIC CANCER IN THE RESIDUAL STOMACH?

In patients with endoscopic resection of early gastric cancer

EGC is thought to develop from precursor lesions such as chronic atrophic gastritis, intestinal metaplasia, and dysplasia. Uemura *et al*[4] provided the first evidence that eradication of *H. pylori* had a direct effect on decreasing the occurrence of secondary metachronous gastric cancer in patients undergoing endoscopic resection. However, the results were limited by a non-randomized study design.

The effect of *H. pylori* eradication in the prevention of metachronous gastric cancer remains a controversial issue. We reviewed recent randomized controlled trials to highlight the controversy (Table 1). Fukase *et al*[33] confirmed that eradication of *H. pylori* after endoscopic resection of EGC was beneficial after 3 years of follow-up in a randomized controlled trial. However, the results were limited by the open-label study and by non-blinded follow-up endoscopy. Many synchronous cancers, which were detected within 1 year were included in the study. A recent retrospective study conducted by Maehata *et al*[34] in patients with metachronous gastric cancer after endoscopic resection of EGC showed that the rates of metachronous cancer were 14.3% in the persistent infection group and 8.5% in the eradicated group ($P = 0.262$). Because the median follow-up period in the retrospective study was 3.0 years, there was uncertainty based on the small sample size and short-term follow-up. When the follow-up period was 5 years, the incidence rate in the eradicated group was lower than that observed in the persistent infection group ($P = 0.007$).

There are controversial results to show that there were no significant differences in the development of metachronous cancers in a prospective, randomized, open-label trial conducted by Choi *et al*[35]. In this study, the incidence of metachronous carcinoma between the 2 groups did not differ significantly at 1, 2, 3, and 4 years after *H. pylori* eradication. To determine the long-term effect of *H. pylori* eradication on the development of gastric cancer, long-term follow-up is necessary. During a mean follow-up period of 5 years, metachronous gastric carcinoma developed in 22 patients in the eradication group and 43 in the control group (HR = 0.497; $P = 0.008$), these results were presented at DDW2012 by Kato *et al*[36]. These findings suggested that *H. pylori* eradication prevented the development of metachronous gastric cancers during the long-term follow-up period.

In patients with subtotal gastrectomy

A well-designed prospective study revealed that *H. pylori*-positive patients undergoing gastrectomy for cancer had a higher risk of precursor malignant lesions compared with *H. pylori*-negative patients in the cancer group (OR = 4.20; 95%CI: 1.10-15.96), and the odds ratio was less significant when compared with that of *H. pylori*-positive and *H. pylori*-negative patients undergoing gastrectomy for duodenal ulcer (OR = 1.59; 95%CI: 0.44-5.73)[37]. This may be indirect evidence that *H. pylori* eradication therapy prevents the development of metachronous gastric cancer after previous gastrectomy[37].

In contrast, a recent randomized clinical trial from Korea showed that 4 of 190 patients had metachronous gastric cancer in the remnant stomach after gastrectomy during a median follow-up of 5 years[19]. There was no difference in the development of metachronous gastric cancer according to eradication of *H. pylori* (3 patients) or not (1 patient). A possible limitation of this study was the small number of target patients, short observation period, and the baseline mucosal conditions differed in many aspects. A meta-analysis showed a favorable overall survival in gastric cancer patients with *H. pylori* infection (HR = 0.71; $P = 0.001$)[38]. *H. pylori* might contribute to an improved anti-tumor immune response and microsatellite instability[38]. However, the study was limited by heterogeneity and it included non-randomized and retrospective data. In addition, patients with advanced gastric cancer and *H. pylori* negative status had a poor prognosis which may have been related to post-operative bile reflux

which eradicated *H. pylori* and destroyed parietal cells.

Taken together, these results indicate that the incidence of metachronous gastric cancer after endoscopic resection does not decrease unless there is early eradication before the progression of gastric mucosal atrophy[35]. To determine the long-term effect of *H. pylori* eradication on the development of metachronous gastric cancer after endoscopic resection of EGC, long-term follow-up seems to be necessary. This approach also prevented the development of metachronous gastric cancer in the remnant stomach after subtotal gastrectomy[39,40]. The Maastricht IV/Florence Consensus Report recommended eradication of *H. pylori* in patients with previous gastric neoplasia treated with endoscopic or subtotal gastric resection, which seems to broaden the indication to include adenoma or dysplasia under the terminology of neoplasia[1]. The risk of gastric cancer may be more effective if eradication occurs before the development of preneoplastic conditions[1,41]. Recent studies showed that eradication of *H. pylori* in the remnant stomach significantly decreased inflammation and activity scores[42,43]. IL-1β was confirmed to be a potent inhibitor of gastric juice secretion, and Kato *et al*[44] proved that IL-1β messenger RNA levels, which lead to gastric dysplasia, correlated with the pH in the remnant stomach after eradication of *H. pylori*. However, a meta-analysis of the role of IL-1β and IL-1 receptor antagonist gene polymorphisms on the risk of gastric cancer showed only an association in white patients, but not in Asian patients[45]. The effects of *H. pylori* eradication in preventing metachronous gastric cancer should be carefully and continually evaluated in well-designed, long-term follow-up studies.

OPTIMAL TIMING AND REGIMENS FOR *H. PYLORI* ERADICATION, DIAGNOSTIC TOOLS AND FOLLOW-UP STRATEGIES FOR PATIENTS UNDERGOING GASTRECTOMY

The optimal timing for eradication of *H. pylori* in gastrectomized patients is not clear. The efficacy of *H. pylori* eradication therapy depends on the gastric pH, bacterial loads, the level of drug in the gastric mucosa, and acquired resistance. Liou *et al*[46] showed that antibiotic resistance, rather than host CYP2C19 polymorphisms or bacterial virulence, was the most important factor for successful eradication of *H. pylori*. Bacteria may produce β-lactamase in the gastric juice of patients with a remnant stomach, leading to the transfer of drug resistance genes and interference with the efficacy of eradication[47].

The eradication rate in the remnant stomach was 90% after first-line triple therapy, which was comparable to the rates of 85%-88% in nonsurgical patients[42,48]. After gastrectomy, alkaline duodenopancreatic juice neutralized gastric acid which inhibited the growth of *H. pylori*. The bacterial load of *H. pylori* would be considered small in patients with gastrectomy, thus a short triple therapy regimen might be effective. In addition, there was no difference in the eradiation rates between the 3-day and 7-day treatment groups (90.9% *vs* 93.8%)[49]. Temporary minor side effects were noted in 3 of 20 cases[42,48]. The effect of *H. pylori* eradication was similar whether it occurred postoperatively or preoperatively[50].

For a good diagnostic tool with a sensitivity of more than 80%, a histological test is better than either the urea breath test (UBT) or rapid urease test (RUT) after gastrectomy[51]. The reduced stomach size and bile reflux decrease the chance of *H. pylori* survival after gastrectomy. In addition, because the test urea passes through the residual stomach faster, UBT is not recommended in patients who have undergone gastrectomy[52]. A modified UBT with a change in body position and using a film-coated ^{13}C-urea table[53] or endoscopic sprayed UBT[54] has been suggested, but these procedures are complicated. Although the RUT is superior to UBT, the pooled sensitivity was 79%, which is still less than 80%[51]. When RUT is considered, the preferred site for biopsy is the fundus[55,56] or corpus[57]. Bile reflux disturbs the environment for *H. pylori* colonization in the distal gastric remnant and leads to a lower density of *H. pylori*. It is also recommended that more than one diagnostic method be used to decrease the false-negative rate in such circumstances.

According to the present Maastricht IV/Florence Consensus Report, serology is the only test that is not affected by local changes in the stomach, which may avoid false-negative results[1]. This is attributable to the fact that antibodies against *H. pylori* and especially against its most specific antigen, CagA, remain elevated despite transient decreases in the bacterial load and for long periods (months, even years) after the disappearance of *H. pylori* from the stomach[58]. By selecting a suitable cutoff value of 0.14, the *H. pylori* stool antigen test is also a reliable noninvasive diagnostic tool with a sensitivity of 93% and specificity of 100%[49].

CONCLUSION

It has been suggested that the biochemical and microbiological profiles of the gastric juice dramatically change after gastric surgery. We believe that this surgical procedure might increase the occurrence of biliary enterogastric reflux and potentially inhibit the growth of *H. pylori* in the stomach. Compared to the B-Ⅰ procedure, the B-Ⅱ procedure had a higher bile reflux rate and was associated with a lower prevalence of *H. pylori* infection. There was a trend toward a decrease in the prevalence of *H. pylori* colonization with time after operation. Bile reflux and *H. pylori* infection appear to have a synergistic effect on cell proliferation in the gastric remnant and may explain the increased risk of cancer after gastrectomy. *H. pylori* is not an important factor in ulcerogenesis after gastrectomy. Eradication of *H. pylori* in the remnant stomach is presumably not effective in preventing ulcer recurrence. *H. pylori* does not appear to be an important risk factor

for GSC; therefore, a cohort study to assess the clinical relevance of *H. pylori* eradication is necessary. The Maastricht IV/Florence Consensus Report recommends eradication of *H. pylori* in patients with previous gastric neoplasia already treated with endoscopic or subtotal gastric resection, which seems to broaden the indication to include adenoma or dysplasia. First-line triple therapy is effective in the eradication of *H. pylori* in gastrectomized patients. Serology is the only test that is not affected by local changes in the stomach, a combination of serology with a histological test or *H. pylori* stool antigen test could be used to avoid false-negative results.

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