Original article

Helicobacter pylori eradication therapy for the remnant stomach after gastrectomy

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Abstract

Background. The remnant stomach after surgery for gastric cancer is at high risk for the metachronous development of multiple gastric cancers. Here, we report on eradication therapy of *Helicobacter pylori* in the remnant stomach, comparing the eradication rate with that in unoperated stomachs. We examined gross and histological changes after treatment. **Methods.** Forty *H. pylori*-positive patients after distal gastrectomy were treated with proton pump inhibitor (PPI)-based dual and triple therapies. After eradication, histological changes were classified on the basis of the updated Sydney system.

Results. The eradication rate in the remnant stomach was 70% (14 of 20) after dual therapy and 90% (18 of 20) after triple therapy, using per-protocol analysis, and these rates were comparable to the rates of 70% (186 of 264) and 88% (58 of 66), respectively, in nonsurgery patients. After eradication, three sites in the remnant stomach showed similar histological changes: significant decreases in inflammation and activity scores ($P < 0.001$) and no significant changes in glandular atrophy and intestinal metaplasia scores.

Conclusion. PPI-based therapy was as effective for *H. pylori* eradication in the remnant stomach as in the unoperated stomach, and eradication therapy resulted in a significant decrease in inflammatory cell infiltration of the mucosal layer.

Key words *Helicobacter pylori* · Remnant stomach · Eradication · Triple therapy · Sydney system

Introduction

Stump cancer after peptic ulcer surgery has been investigated, and bile (alkaline) reflux has been found to be a main causative factor of such new cancers [1,2]. By contrast, cancer in the remnant stomach after surgery for

early gastric cancer is metachronous multiple cancer, and *H. pylori* infection may be a causative factor [3]. Much human and animal evidence has shown a close association between *H. pylori* infection and gastric cancer [4–6]. Although cancer development is a multifactorial process [7], *H. pylori* infection increases the risk of gastric cancer. “The Maastricht Consensus Report” strongly recommends *H. pylori* eradication therapy following early resection for gastric cancer [8]. There are some data showing that *H. pylori* eradication is associated with a decrease in the recurrence rate in patients with early gastric cancer that is resected endoscopically [9,10]. However, few reports have been published on *H. pylori* eradication therapy in the remnant stomach [11,12]. In this study, we investigated the following factors in the remnant stomach after distal gastrectomy: (1) the eradication rate of *H. pylori* in comparison with that in the unoperated stomach, (2) changes in chronic gastritis scores, according to the updated Sydney system [13], after *H. pylori* eradication therapy, in comparison with scores in the unoperated stomach, and (3) changes in gross endoscopic findings after *H. pylori* eradication.

Patients and methods

Patients

The remnant stomachs in 137 patients after distal gastrectomy were *H. pylori*-positive, and 64 were *H. pylori*-negative; 40 of the *H. pylori*-positive patients were randomly selected for *H. pylori* eradication therapy (Table 1). All 40 patients were tested for *H. pylori* 4–6 weeks after the start of the eradication therapy; 14 of them were followed endoscopically for more than 1 year (average, 21 months) and histological examinations were performed. Among the untreated patients, 22 (15 *H. pylori*-positive and 7 *H. pylori*-negative) were endoscopically followed for more than 1 year (average, 32

Table 1. Characteristics of patients with *Helicobacter pylori* infection and eradication therapy for the gastric remnant

	<i>n</i>	<i>H. pylori</i> -positive	Percentage	<i>P</i>	Eradication therapy
Sex					
Male	136	91	67	0.1	25
Female	65	46	71		15
Age (years)					
<50	21	15	71	0.8	7
50–70	120	83	69		25
>70	60	39	65		8
Primary disease treated surgically					
Gastric cancer	147	105	71	0.2	34
Early	100	72	72		25
Advanced	47	33	70		9
Peptic ulcer	45	26	58		5
Others	9	6	67		1
Interval after operation					
<2 Years	53	38	72	0.6	17
2–5 Years	64	45	70		13
>5 Years	84	54	64		10
Reconstruction method					
Billroth I	126	91	72	0.22	28
Billroth II	51	30	59		6
Others	24	16	67		6
Total	201	137	68		40

months) and histological examinations were performed. To compare *H. pylori* eradication rates, 330 nonsurgical patients with some upper abdominal complaint who had undergone *H. pylori* eradication therapy were also recruited (Table 2). As shown in Table 2, the unoperated *H. pylori*-treated patients were significantly younger ($P < 0.001$) and peptic ulcer was more predominant ($P < 0.001$) in comparison with the surgical patients treated for *H. pylori*. A total of 109 unoperated patients were followed endoscopically for more than 1 year after *H. pylori* eradication (average, 28 months), and histological examinations were performed.

This study was approved as ethical by the Nippon Medical School, Tokyo, Japan, and informed consent was obtained for *H. pylori* treatment and histological examinations.

Gross endoscopic findings, histopathological examination, and bacteriological culture

Upper gastrointestinal endoscopy was performed after the patients fasted overnight. Routine endoscopic examination of the esophagus, remnant stomach, and anastomosis region was performed with a gastrointestinal fiberscope (GIF Type Q-240; Olympus, Tokyo, Japan). Macroscopic mucosal changes, i.e., erythema of the mucosa and edema of gastric folds and the presence of bile reflux and food residue were scored in four grades (0, none; 1, mild; 2, moderate; and 3, severe).

Mucosal biopsy specimens for the histological examination of the remnant stomach were collected with sterilized biopsy forceps (Olympus) from: (1) the greater curvature of the stoma, (2) the greater curvature of the upper corpus, and (3) the suture line of the lesser curvature. Biopsy specimens were also taken for culture from: (1) the stoma and (2) the upper corpus. In the unoperated stomach, biopsy specimens were taken from the antrum and the upper corpus for histological examination [13] and culture. The updated Sydney system was used for scoring inflammation (an increase in lymphocyte and plasma cells in the lamina propria); activity (density of neutrophil polymorphs in the lamina propria); and glandular atrophy, intestinal metaplasia, and *H. pylori* infection [14]. Hematoxylin-and-eosin staining, improved toluidine blue staining, and *H. pylori* specific-antibody (Ab) immunostaining (DAKO, Glostrup, Denmark) were used for the histological diagnosis of *H. pylori* infection in selected cases. Parameters of the updated Sydney system were scored in four grades (0, none; 1, mild; 2, moderate; and 3, severe). All biopsy specimens were examined by a pathologist (N.Y.) who was unaware of the results of the bacterial culture and the treatment regimens.

Biopsy specimens used for culture of *H. pylori* were immediately put into a transport tube with culture medium in a microaerophilic atmosphere (Seed tube HP; Eiken, Tokyo, Japan). On the same day, the biopsy specimens were transferred to the culture medium with

Table 2. Characteristics of patients with *H. pylori* eradication therapy for the gastric remnant and the unoperated stomach

	Gastric remnant	Percentage	Unoperated stomach	Percentage	<i>P</i>
Sex					
Male	25	63	224	68	0.49
Female	15	37	106	32	
Age (years)					
<50	7	17	118	36	<0.001
50–70	25	63	179	54	
>70	8	20	33	10	
Smoker	5	13	183	55	<0.001
Alcohol drinker	10	25	200	61	<0.001
Disease					
Gastric cancer	34	85	13	4	<0.001
Peptic ulcer	5	12	237	72	
Chronic gastritis	0	0	65	20	
Others	1	3	15	4	
First-line therapy					
Dual therapy	20		264		0.97
Eradication	14	70	186	70	
Triple therapy	20		66		0.89
Eradication	18	90	58	88	
Second-line therapy	7		73		0.79
Eradication	7	100	65	89	
Total	40		330		

Dual therapy, lansoprazole 30 mg bid + amoxicillin (AMPC) 500 mg tid + ecabet sodium 1.0 g bid $\times$ 14 days; triple therapy, lansoprazole 30 mg bid + AMPC 750 mg bid + clarithromycin (CAM) 400 mg bid $\times$ 7 days; second-line therapy: lansoprazole 30 mg bid + AMPC 500 mg tid + metronidazole 250 mg tid + ecabet sodium 1.0 g bid $\times$ 14 days

Skirrow plates and incubated at 35°C in an atmosphere of 5% O₂, 10% CO₂, and 85% N₂ for 3–7 days. Culture was judged to be positive for *H. pylori* based on colony morphology; the results of Gram staining; and positive oxidase, catalase, and urease activity. All of the bacterial cultures were performed at Mitsubishi Kagaku BCL (Tokyo, Japan).

H. pylori eradication therapy

Patients were deemed *H. pylori*-positive if the organism was identified either in culture or on histological examination, and *H. pylori*-negative if the organism was not detected by either method. Eradication was defined as the absence of *H. pylori* both in culture and on histological examination of biopsy specimens 4–6 weeks after the end of antimicrobial therapy.

Dual therapy was performed from June 1995 to October 2000, and triple therapy was performed from November 2000 to June 2002. In the study design for PPI-based dual therapy, patients with and without surgery received lansoprazole (Takeda Chemical Industries, Osaka, Japan) 30 mg bid, amoxicillin (AMPC) 500 mg tid, plus a mucosal protective agent (ecabet sodium; Tanabe Seiyaku, Osaka, Japan) 1.0 g bid for 2 weeks. For the PPI-based-triple therapy, patients with

and without surgery received lansoprazole 30 mg bid, AMPC 750 mg bid, and clarithromycin (CAM) 400 mg bid for 1 week. The second-line therapy for failure of both dual and triple therapy was lansoprazole 30 mg bid, AMPC 500 mg tid, metronidazole 250 mg tid, plus ecabet sodium 1.0 g bid for 2 weeks.

Serum pepsinogen, gastrin, and H. pylori antibody assay

Fasting blood samples were collected prior to eradication therapy, and the serum was stored at –80°C. Antibody to *H. pylori* was measured by enzyme-linked immunosorbent assay (E-plate; Eiken) in 164 of the 201 patients with distal gastrectomy, and a titer greater than 10 U/ml was considered positive. Pepsinogen I and II were measured with a radioimmunoassay RIA kit (Dainabot, Tokyo, Japan), and serum gastrin was measured with a radioimmunoassay kit (Dainabot). Serum assay was performed by Mitsubishi-Kagaku BCL (Tokyo, Japan).

Statistical analysis

Statistical analyses were performed by Student's *t*-test, Fisher's exact test, and the χ^2 analysis program for PCs

(SPSS, Tokyo, Japan). A *P* value of less than 0.05 was considered significant.

Results

Characteristics of the patients with H. pylori infection and eradication therapy in the gastric remnant

The overall *H. pylori* positive rate in the remnant stomach after distal gastrectomy was 137/201 (68%), and the positive rate did not differ significantly according to sex, age, the primary disease treated surgically, interval after operation, or reconstruction method (Table 1). Forty *H. pylori*-positive patients with a remnant stomach were randomly enrolled for eradication therapy.

The serum pepsinogen I value and the pepsinogen I/II ratio are established markers of glandular atrophy in the nonresected stomach [15], and the *H. pylori*-negative group had a significantly higher pepsinogen I/II ratio (3.16 ± 3.32 ; mean $\pm$ SD) than the positive group (1.86 ± 0.73 ; $P < 0.001$) and a significantly lower serum *H. pylori*-antibody titer (182 ± 236 U/ml) than the positive group (306 ± 243 U/ml; $P < 0.01$) in the remnant stomach. Among those in whom both histological examination and bacterial culture were negative for *H. pylori* in the remnant stomach, only 10/48 (21%) had negative serum anti-*H. pylori* antibody titers. Serum pepsinogen I and gastrin levels were not significantly different in the remnant stomachs that were *H. pylori*-positive (25.5 ± 17.0 ng/ml and 41.2 ± 23 pg/ml, respectively) and those that were negative (36.4 ± 78.9 ng/ml and 38.7 ± 28 pg/ml, respectively).

H. pylori eradication rate in the remnant stomach and the unoperated stomach

Forty *H. pylori*-positive patients after distal gastrectomy were treated with PPI-based dual or triple therapy. A double dose of lansoprazole (60 mg per day) and AMPC 1500 mg per day was used for PPI-based dual therapy. A regular dose (2.0 g per day) of the mucosal protective agent; ecabet sodium, was added to prevent adverse effects and because of its slight inhibitory effect on *H. pylori* growth [16]. Dual therapy was continued for 2 weeks, and the eradication rate in the remnant stomach was 14/20 (70%), using per-protocol analysis. For comparison, the eradication rate of dual therapy with the same regimen in the 264 of 330 patients with an unoperated stomach who received this therapy was 70% (186/264). The characteristics of the patients with unoperated stomachs are shown in Table 2. They were significantly younger, included more smokers and alcohol drinkers, and were peptic ulcer patients ($P < 0.001$) predominantly compared with the remnant stom-

ach group. The protocol of the PPI-based triple therapy was a double dose of lansoprazole (60 mg per day), AMPC 1500 mg per day, and clarithromycin 800 mg per day for 1 week. The eradication rate for the triple therapy in the remnant stomach was 90% (18/20), using per-protocol analysis, and this was comparable to the rate of 88% (58/66) in the unoperated stomach.

Patients in whom both dual and triple therapy failed, except for 14 dropout patients, were immediately enrolled into a second-line therapy group without testing for antibiotic sensitivity. The protocol of the second-line therapy consisted of a double dose of lansoprazole (60 mg) per day, AMPC 1500 mg per day, metronidazole 750 mg per day, and ecabet sodium 2.0 g per day for 2 weeks. The eradication rate for second-line therapy, using per-protocol analysis, was 7/7 (100%) in the remnant stomach and 65/73 (89%) in the unoperated stomach. There was no significant difference in the eradication rate by second-line therapy between the unoperated patients who had had dual therapy and those who had had triple therapy (57/65 vs 8/8, respectively; $P = 0.65$).

The main side effect of eradication therapy was diarrhea (Table 3). Diarrhea occurred in 4/40 (10%) of the remnant-stomach patients and in 19/330 (5.8%) of the unoperated patients, and it diminished after therapy without any additional medication. No other side effects occurred in the remnant-stomach group, but other side effects occurred in 25 of the 330 (7.6%) unoperated patients. Gastroesophageal reflux disease (GERD) developed after eradication therapy in 2/40 (5%) of the remnant stomach patients and in 9/330 (2.7%) of the unoperated patients. The overall incidence of side effects was 6/40 (15%) in the remnant-stomach group and 53/330 (16%) in the unoperated group, and the difference was not significant ($P = 0.96$). Patients with a past history of penicillin allergy were excluded from first- and second-line therapy. Unexpectedly, 2/40 (5%) of the operated patients experienced an improvement in bowel movements after *H. pylori* eradication therapy (Table 3).

Sequential histopathological changes in the remnant stomachs with and without eradication therapy

Histopathological mucosal changes in the remnant stomachs after successful eradication therapy were scored according to the updated Sydney system. As shown in Fig. 1, the inflammation score was significantly decreased 4–6 weeks after the end of treatment ($P < 0.001$), when eradication was diagnosed, and it decreased even more after 1 year (average, 19 months; $P < 0.001$). The activity score was significantly decreased 4–6 weeks after the end of treatment ($P < 0.001$), and no significant difference was found after 1 year or more.

Table 3. Incidence of side effects of PPI-based dual and triple therapies in patients with a remnant stomach and those with an unoperated stomach

Side effects	Remnant stomach (<i>n</i> = 40)				Unoperated stomach (<i>n</i> = 330)			
	Dual therapy	Triple therapy	Total	Percentage	Dual therapy	Triple therapy	Total	Percentage
Adverse event								
None	17	17	34	85	223	54	277	84
Diarrhea	2	2	4	10	13	6	19	6
Taste disturbance	0	0	0	0	4	3	7	2
Nausea	0	0	0	0	7	0	7	2
Skin rash	0	0	0	0	11	0	11	3
GERD after treatment	1	1	2	5	6	3	9	3
Symptom amelioration								
None	18	18	36	90				
Bowel movement	2	2	4	10				

GERD, gastroesophageal reflux disease; PPI, proton pump inhibitor

Fig. 1. Sequential histological changes in the mucosa in the remnant stomach after successful *Helicobacter pylori* eradication therapy, scored according to the updated Sydney system [14]. The scores for each parameter at three points: (1) stoma, (2) greater curvature of the upper corpus, and (3) the suture line of the lesser curvature, were added. The inflammation score (diagonally striped bars) was significantly decreased when eradication was diagnosed (4–6 weeks after the end of treatment; * $P < 0.001$, and it decreased even more after more than 1 year (** $P < 0.001$). The activity score (vertically striped bars) was significantly decreased after eradication (+ $P < 0.001$) and fell to almost zero after more than 1 year. The atrophy score (dashed-line bars) and intestinal metaplasia score (horizontally striped bars) did not significantly change after treatment

These scores did not differ according to the three biopsy sites, i.e., stoma, upper corpus, and suture line. There was no change in glandular atrophy and intestinal metaplasia scores after treatment.

In the remnant stomachs without *H. pylori* treatment, the inflammation and activity scores were significantly higher in *H. pylori*-positive mucosa than in the negative mucosa ($P < 0.001$), and the follow-up study showed a significant increase in inflammation and activity scores

Fig. 2. The inflammation and activity scores in the remnant stomachs without *H. pylori* treatment were significantly higher in *H. pylori*-positive mucosa than in-negative mucosa (* $P < 0.001$), and there were significant increases in the inflammation and activity scores (+ $P < 0.001$) in the *H. pylori*-positive mucosa after an average of 32 months. The scores for each parameter at three points (1, 2, and 3 as in Fig. 1 legend) were added. Bars, as in Fig. 1

($P < 0.001$) in the *H. pylori*-positive mucosa after an average of 32 months (Fig. 2). No changes in these scores were detected in the *H. pylori*-negative mucosa during the same period.

Sequential changes in endoscopic gross findings in the remnant stomach after eradication therapy

The endoscopic gross findings changed after eradication (mean, 15 months after treatment). The scores for erythema of the mucosa (pre, 1.20 vs post, 1.25) and bile reflux (1.12 vs 1.25) in the remnant stomach were increased ($P < 0.05$), but the score for edema of the folds decreased after eradication (1.29 vs 1.20; $P < 0.01$).

Food residue was observed in a few patients (5/40; 13%) in this study, but the scores did not significantly change after eradication therapy (before, 0.29 vs after, 0.1).

Discussion

Recent prospective studies in humans and experiments in Mongolian gerbils have shown a close association between *H. pylori* infection in the stomach and gastric cancer [6,17–19], similar to findings in earlier epidemiological studies [4]. The mucosa of the remnant stomach after surgery for early gastric cancer is at high risk for metachronous multiple gastric cancer. An endoscopic finding of erythema in the remnant stomach is correlated with bile reflux, and histological chronic active gastritis is correlated with *H. pylori* infection [3,20]. Many data have indicated that bile (alkaline) reflux is a causative factor in stump cancer after distal gastrectomy for peptic ulcer [1,2]. However, *H. pylori* infection in the remnant stomach may be a causative factor in remnant gastric cancer after gastrectomy for gastric cancer [11].

H. pylori eradication therapy is strongly recommended after surgery for early gastric cancer [8], based on supportive evidence that it prevents the development of new cancers after endoscopic mucosal resection (EMR) for intramucosal gastric cancer [9,10]. Some reports emphasize the importance of *H. pylori* treatment at a young age [21,22]. However, these studies conclude that *H. pylori* eradication is also useful for the prevention of new cancer development from high-risk mucosa of gastric cancer [23].

The regimen for *H. pylori* eradication therapy has been established, and PPI-based triple therapy is the standard throughout the world [8,24]. The protocol for *H. pylori* eradication in the remnant stomach, however, has not been established, and the extent to which the efficacy of PPI-based dual and triple therapies is related to the topical action of the antimicrobials and how much is attributable to their systemic action is unclear, but both are probably important. Thus, there has been concern that the topical action of the antimicrobials is ineffective in the remnant stomach because of the possible rapid transit of the drugs from the small remnant stomach into the duodenum or small intestine. However, the results of the present study clearly showed the same eradication rates for both PPI-based dual therapy and triple therapy in the unoperated stomach and remnant stomach after surgery.

We used lansoprazole as the PPI because it possesses some antibacterial activity against *H. pylori* [25], and lansoprazole-based triple therapy was approved for treatment for *H. pylori* by the National Health Insurance in Japan on November 1, 2000. A mucosal protec-

tive agent, ecabet sodium, obtained from a derivative of pine resin in Japan, was used for dual therapy, and several mucosal protective effects have been reported [15]. Ecabet sodium attaches to the gastric mucosa and inhibits *H. pylori* urease activity in vitro, and the addition of ecabet sodium has been reported to enhance the eradication rate of dual therapy [26].

Second-line therapy for treatment-failure patients is a great problem, and standard second regimens have been under investigation around the world. We used two antibiotics, AMPC and metronidazole [27]. *H. pylori* resistant to CAM have been found in more than half of the patients in whom first-line triple therapy failed, but hardly any colonies were AMPC-resistant. Metronidazole-resistant *H. pylori* is relatively uncommon in Japan [28], and several reports have indicated substantial eradication of *H. pylori* with metronidazole in patients with metronidazole-resistant colonies [29]. Murakami et al. [29] studied eradication rates with a PPI + AMPC + metronidazole second-line regimen, given for 1 week, according to the metronidazole sensitivity of *H. pylori*, and the results showed a 96.8% eradication rate in patients with metronidazole-sensitive *H. pylori* vs 81.8% in patients with metronidazole-resistant *H. pylori*. We did not check antibiotic sensitivity before second-line therapy, but we obtained similar satisfactory eradication rates in both the unoperated and the remnant stomachs.

The major side effect of the dual and triple therapies was diarrhea, which occurred in about 6%–10% of patients, and there was no significant difference between the incidence in patients with unoperated and those with remnant stomachs. Gastroesophageal reflux disease (GERD) after *H. pylori* therapy has attracted attention [30]. Exacerbation of GERD was found in 5% of remnant-stomach patients after *H. pylori* eradication, although no long-term effect was clear from this study. Some postoperative complaints, such as a feeling of fullness, were unchanged after the eradication therapy, but a few patients (10%) in the remnant-stomach group experienced improvement in bowel movements after treatment.

H. pylori-positivity in the remnant stomach did not differ according to any of the clinical characteristics in this study. A previous study showed that age, reconstruction (anastomosis) method [31], and postoperative follow-up period [20] affected *H. pylori*-positivity, because bile reflux interferes with *H. pylori* survival [32]. Serum was positive for anti-*H. pylori*-antibody in 80% of the *H. pylori*-negative patients based on both the histological examinations and bacterial culture. We previously reported that, even after total gastrectomy, more than 1 year was necessary for negative seroconversion to anti-*H. pylori* antibody [33]. Thus, the *H. pylori* colonizing the middle to lower stomach before

the operation were removed by distal gastrectomy, but in many patients serum antibody against *H. pylori* persisted for more than 1 year after the operation. Serum pepsinogen I and II assays are not only useful for detecting chronic atrophic gastritis without X-ray or endoscopic examinations but they have also been useful in mass screening Japanese for gastric cancer [15]. A low pepsinogen I/II ratio (<3.0) is an especially good marker for indicating a high risk of gastric cancer [15], and *H. pylori* infection has been correlated with a lower pepsinogen I/II ratio [34]. After distal gastrectomy in the present study as well, the *H. pylori*-positive remnant stomachs also had a significantly lower pepsinogen I/II ratio than the *H. pylori*-negative remnant stomachs.

Lymphocyte and leukocyte infiltration of the lamina propria was detected to almost the same extent in the stoma, upper corpus, and suture line of the *H. pylori*-positive remnant stomachs. In the *H. pylori*-positive remnant stomachs, infiltration by these inflammatory cells increased after an average of 32 months of follow-up, whereas minimal inflammatory cell infiltration was found in the *H. pylori*-negative remnant stomachs. After eradication, the inflammatory cell infiltration quickly decreased during the 4–6 weeks after treatment, when chronic inactive gastritis was observed, as scored by the updated Sydney system [14]. Chronic inactive gastritis persisted for more than 1 year, but the scores for glandular atrophy and intestinal metaplasia, possible precursory lesions of gastric cancer [7], were unchanged. The changes in scores after the eradication therapy were exactly the same as the changes in scores for the upper corpus of the unoperated stomach (data not shown).

The endoscopic findings in the remnant stomach were also influenced by *H. pylori* eradication therapy. Gross features of erythema were observed in the remnant stomach. Our data showed a positive correlation ($r = 0.92$; $P < 0.001$) between the grade of erythema in the remnant stomach and the degree of 24-h bile reflux, determined with Bilitec 2000 (Synectics Medical, Stockholm, Sweden; data not shown). Erythema and bile reflux were slightly increased 15 months after the eradication therapy, but edema of the folds had decreased significantly. Inflammatory cell infiltration of the lamina propria in *H. pylori* infection causes edema of gastric tissue, and, thus, it is not surprising that the endoscopic gross findings showed a decrease in edema after eradication.

In conclusion, (1) the same regimens of *H. pylori* eradication therapy were as applicable to the remnant stomach after distal gastrectomy as to the unoperated stomach, (2) clinical symptoms in operated patients were not changed significantly after the eradication therapy, and (3) chronic active gastritis immediately converted to inactive gastritis after the eradication

therapy, but the glandular atrophy and intestinal metaplasia in the remnant stomach were unchanged after a middle-term observation period.

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