Relationship between *Helicobacter pylori* and Histological Changes in the Gastric Remnant after Subtotal Gastrectomy

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Objective: The aim of this study was to clarify the influence of histological changes in the gastric remnant on *Helicobacter pylori* (*H. pylori*) infection after distal gastrectomy (DG) and proximal gastrectomy (PG).
Methods: In total, 101 patients who underwent DG (n = 76) or PG (n = 25) for gastric cancer were included in the study. Three biopsy specimens from the remnant stomach were obtained during upper gastrointestinal endoscopy. Each specimen was scored according to the updated Sydney system for classifying gastritis and was examined for *H. pylori* infection.
Results: The *H. pylori* infection rate after DG was 60.5% while that after PG was 20.0% (P < 0.001). The histological score for neutrophils after DG was 60.5% while that after PG was 12.9% (P < 0.001). Intestinal metaplasia after PG was 76.0% while that after DG was 22.4% (P < 0.001). No differences in mononuclear cells or atrophy were observed between the two gastrectomy groups.
Conclusions: *H. pylori* infection occurred more frequently after DG than after PG. Histological inflammation of the gastric remnant after DG was higher than that after PG. Intestinal metaplasia of the gastric remnant after PG was higher than that after DG. The intestinal metaplasia that induced inflammation indicated that *H. pylori* infection after PG was at a low level.

Key words: Remnant stomach, *Helicobacter pylori*, the updated Sydney System, distal gastrectomy, proximal gastrectomy

INTRODUCTION

Warren and Marshall first identified *Helicobacter Pylori* in the stomach in 1984 [1]. *H. pylori* infection plays an important role in many gastrointestinal and other diseases. The International Agency for Research on Cancer has confirmed *H. pylori* infection as a risk factor for gastric cancer [2]. In contrast, studies regarding the remnant stomach mainly concerned that after distal gastrectomy (DG) [3–8]. Total gastrectomy has been considered the standard treatment for proximal gastric cancer. Therefore, proximal gastrectomy (PG) has been performed as a function-preserving surgery for gastric cancer of the upper third of the stomach [9–12]. We performed proximal subtotal gastrectomy for proximal gastric cancer [13–15]. However, few reports have been published on the remnant stomach after proximal gastrectomy. In this study, we investigated the influence of histological changes in the gastric remnant on *H. pylori* infection after DG and PG.

MATERIAL AND METHODS

Patients

One hundred one patients (74 males, 27 females) who underwent gastrectomy for gastric cancer were included in the study. All patients gave informed consent for inclusion. The subjects were divided into two groups based on resection of the stomach: a DG group (n = 76) and a PG group (n = 25). All 101 patients underwent upper gastrointestinal endoscopy between April 2002 and March 2004 at the Department of Surgery, Tokai University Hospital. All endoscopies were performed under postgastrectomy surveillance. No patient received eradication therapy after surgery.

Endoscopic examination

Three biopsy specimens were routinely collected from the greater curvature of the gastric remnant about 5 cm from the anastomosis. A histological microscopic examination and culture of the gastric biopsy specimens was performed in all cases.

Histological examination

The biopsy specimens were fixed in 10% buffered formalin and embedded in paraffin. The sections were stained with Hematoxylin-eosin and Giemsa to detect *H. pylori*. All histological slides were reviewed by an experienced pathologist (K.H.) who was blinded to other details. Each specimen was scored according to the updated Sydney system for classifying gastritis [16]. The presence of *H. pylori* colonization was considered either positive or negative by Giemsa stein. Gastritis grade (infiltration of lymphocytes and plasma cells), gastritis activity (infiltration by neutrophil granulocytes), intestinal metaplasia atrophy, and foveolar epithelium replacement by regenerative epithelium were assessed on a semiquantitative scale (grade 0, normal; grade 1, mild; grade 2, moderate; and grade 3, marked).

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Table 1 Patient Groups and Characteristics

	DG (n = 76)	PG (n = 25)	Total (n = 101)	P
Age (median)	58.5	59.0	59.0	N.S.
	38 - 87	44 - 82	38 - 87	
Gender (M/F)	57 / 19	17 / 8	74 / 27	N.S.
Months after surgery	36.5	23.0	35.7	N.S.
	6 - 252	6 - 109	6 - 252	
H.pylori infection	46 / 76	5 / 25	51 / 101	P < 0.001
	60.5%	20.0%	50.5%	

DG: distal gastrectomy, PG: proximal gastrectomy

Table 2 Relationship between gastritis of remnant stomach and type of gastrectomy

updated Sydney system	Gastrectomy	Grade 0	Grade 1	Grade 2	Grade 3
Neutrophils	DG (n = 76)	30(38%)	25(33%)	15(20%)	6(8%)
	PG (n = 25)	22(88%)	2(8%)	1(4%)	0(0%)
Mononuclear cell	DG (n = 76)	3(4%)	20(26%)	46(61%)	7(9%)
	PG (n = 25)	0(0%)	17(68%)	8(32%)	0(0%)
Atrophy	DG (n = 76)	9(12%)	38(50%)	28(37%)	1(1%)
	PG (n = 25)	0(0%)	10(40%)	13(52%)	2(8%)
Intastinal metaplasia	DG (n = 76)	59(78%)	9(12%)	7(9%)	1(1%)
	PG (n = 25)	6(24%)	8(32%)	10(40%)	1(4%)

DG: distal gastrectomy, PG: proximal gastrectomy

Grade 0: Normal, Grade 1: Mild, Grade 2: Moderate, Grade 3: Marked (by updated Sydney system)

Statistical methods

Statistical analysis was performed using the $\chi 2$ test, and $P < 0.05$ was considered statistically significant.

RESULTS

Table 1 shows patient characteristics. Median age at endoscopy was 59.0 years (range, 38–87 years), and the follow-up interval after surgery was 35.7 months (range, 6–252 months). Initial surgery for gastric cancer was performed in all patients, and no significant differences were observed for gender and age distributions or months after surgery between the DG and PG groups. The rate of *H. pylori* infection after DG was significantly higher than that after PG ($P < 0.001$) (Fig. 1).

Table 2 shows results of grade of remnant gastritis. We examined grade 1–3 as positive in a mass. Histopathological mucosal changes in the remnant stomach after DG and PG were scored according to the updated Sydney system. The histological score for neutrophils in the gastric remnant of patients who underwent DG was significantly higher than that of patients who underwent PG (60.5 vs. 12.9%, $P < 0.001$). Intestinal metaplasia after PG was significantly higher than that after DG (76.0 vs. 22.4%, $P < 0.001$). However, no differences in the percentage of mononuclear cells (DG: 96.1 vs. PG: 100.0%) or atrophy (DG: 88.2 vs. PG: 100.0%) were observed between the groups (Fig. 2).

Furthermore, the relationship between the histological scores and gastrectomy without *H. pylori* infection, neutrophils after DG was significantly higher than that after PG (50.0 vs. 10.0%, $P < 0.001$) The rate of intestinal metaplasia after PG was significantly higher than that after DG (80.0 vs. 30.0%, $P < 0.001$) (Fig. 3). The relationship between the histological scores and gastrectomy with *H. pylori* infection, neutrophils after DG was significantly higher than that after PG (67.4 vs. 20.0%, $P < 0.001$). The rate of intestinal metaplasia after PG was significantly greater than that after DG (60.0 vs. 17.4%, $P < 0.001$). (Fig. 4).

DISCUSSION

The results of the present study suggest that the *H. pylori* infection rate after DG for gastric cancer is significantly higher than that after PG. Inflammation by neutrophils after DG was significantly greater than that after PG, and the rate of intestinal metaplasia

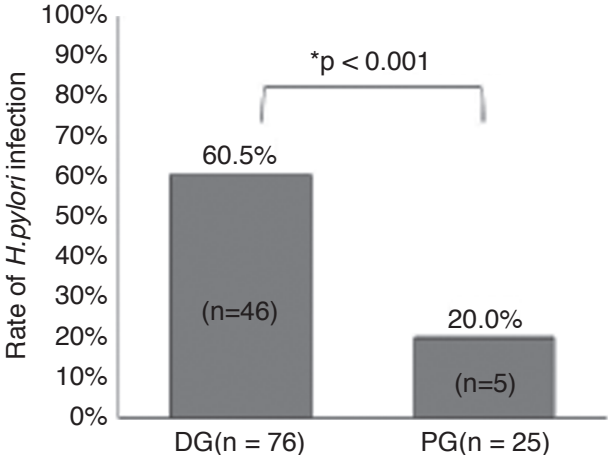

Fig. 1 Correlation between the type of subtotal gastrectomy and *Helicobacter pylori* infection for gastric cancer
DG, distal gastrectomy; PG, proximal gastrectomy; H.P, *Helicobacter pylori*

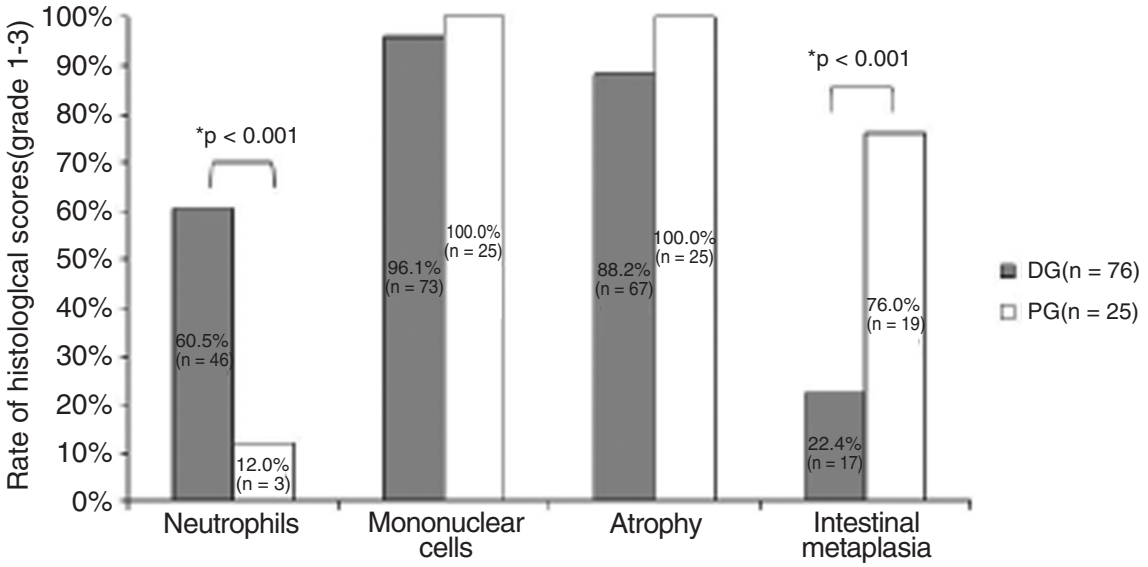

Fig. 2 Relationship between the type of subtotal gastrectomy and histological score
DG, distal gastrectomy (grey bars); PG, proximal gastrectomy (white bars)

after PG was significantly greater than that after DG. Furthermore, no differences were identified between inflammation, intestinal metaplasia, or other histological changes after subtotal gastrectomy between patients with and without *H. pylori* infection.

Several authors have reported that the *H. pylori* infection rate in the remnant stomach after DG is 19–67% and collected plural biopsy specimens [17–20]. In this study, we collected three specimens from greater curvature with the distance of approximately 5 cm from anastomosis. We diagnosed *H. pylori* by Giemsa stein and used culture secondarily. This is because CDC recommends a histologic diagnosis as the gold standard of diagnostic tests [21]. If we collected biopsy specimens from pleural points, precision of *H. pylori* detection might increase. And if we considered *H. pylori* positive in either, *H. pylori* positive rate might increase.

Both bile reflux and *H. pylori* infection are important factors responsible for inflammatory changes in the remnant stomach after gastrectomy [22]; however, only *H. pylori* infection is positively associated with histological findings [23]. Furthermore, Johannesson KA *et al.* reported that *H. pylori* infection has no impact on histological development. Factors other than enteric reflux and *H. pylori* infection may also be important [24]. Lee *et al.* reported that *H. pylori* infection is not related to remnant mucosal erythema, as observed by endoscopy, but that it is closely related to active inflammatory cell infiltration in the gastric remnant [22].

In the intact stomach, atrophic gastritis shifts from the pylorus to the gastric corpus with the progression of inflammation. It is thought that the remnant stomach after PG has lesions in areas that are subject to atrophy.

In this study, the rate of inflammation and intestinal metaplasia in the remnant stomach after PG were significantly lower and higher, respectively, than those after DG. In other words, inflammation occurred because of the environmental change after surgery, regardless of whether the remnant stomach was inflamed after PG. the possibility that a mucosa of rem-

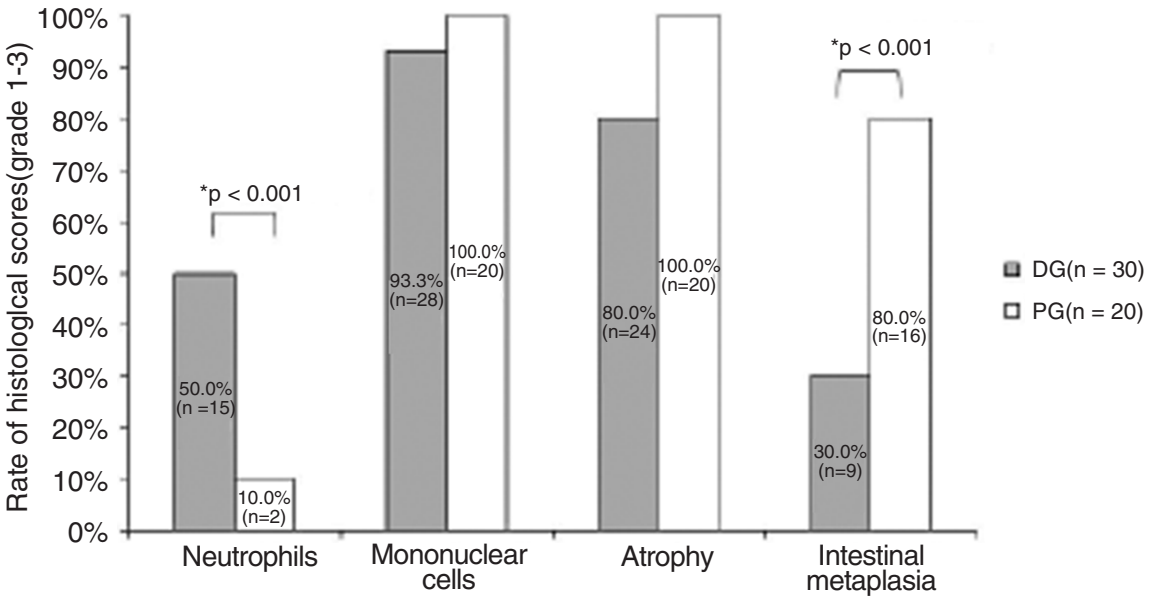

Fig. 3 Relationship between the histological score and type of subtotal gastrectomy in patients without *Helicobacter pylori* infection
DG, distal gastrectomy (grey bars); PG, proximal gastrectomy (white bars)

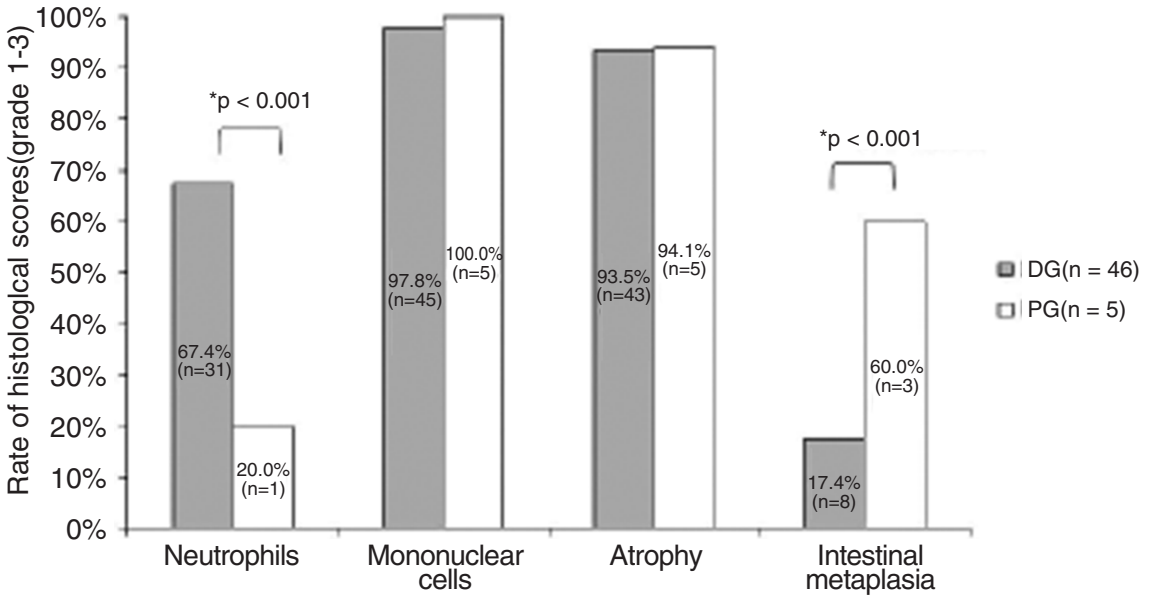

Fig. 4 Relationship between the histological score and type of subtotal gastrectomy in patients with *Helicobacter pylori* infection
DG, distal gastrectomy (grey bars); PG, proximal gastrectomy (white bars)

nant stomach was substituted for intestinal metaplasia was suggested. We showed that the rate of *H. pylori* infection after DG was significantly higher than that after PG. It was believed that the remnant stomach, where intestinal metaplasia progressed, was a difficult environment for *H. pylori*.

Our proximal subtotal gastrectomy removes two-thirds of the stomach, leaving the lower third [13–15]. This may be one of the reasons why the area of the remnant stomach is small.

Inflammation, intestinal metaplasia, and other histological changes after subtotal gastrectomy were not different between patients with and without *H. pylori* infection. This result suggests that the histological changes in the remnant stomach did not depend on *H. pylori*. Tomtitchong *et al.* reported that bile reflux interferes with *H. pylori* colonization [24]. Abe *et al.* reported that the reflux of bile and duodenal juice eliminates *H. pylori*, thus lowering the rate of *H. pylori* infection in patients with endoscopically severe remnant gastritis [25]. The relationship between *H. pylori* and bile reflux in the remnant stomach is complicated

and controversial.

Our results suggest differences between the remnant stomach after DG and that after PG. The remnant gastric mucosa after PG was severely inflamed by intestinal metaplasia, suggesting that the remnant stomach mucosa after PG was in a state of intestinal metaplasia and that inflammation progressed.

This is the first study to investigate the relationships between the remnant stomach and *H. pylori* infection among patients who underwent PG.

CONCLUSION

The rate of *H. pylori* infection after DG was significantly higher than that after PG. Histological inflammation was higher after DG than after PG, but intestinal metaplasia after PG was higher than that after DG. No relationship was identified between *H. pylori* activity and intestinal metaplasia of the remnant stomach after DG or PG. It was believed that the rate of *H. pylori* infection after PG was low because of the intestinal metaplasia, which induced inflammation.

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