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• BRIEF REPORTS •

Helicobacter pylori in gastric corpus of patients 20 years after partial gastric resection

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Abstract

AIM: To determine the long-term prevalence of *Helicobacter pylori* (*H pylori*) gastritis in patients after partial gastric resection due to peptic ulcer, and to compare the severity of *H pylori*-positive gastritis in the corpus mucosa between partial gastrectomy patients and matched controls.

METHODS: Endoscopic biopsies were obtained from 57 patients after partial gastric resection for histological examination using hematoxylin/eosin and Warthin-Starry staining. Gastritis was graded according to the updated Sydney system. Severity of corpus gastritis was compared between *H pylori*-positive partial gastrectomy patients and *H pylori*-positive duodenal ulcer patients matched for age and gender.

RESULTS: In partial gastrectomy patients, surgery was performed 20 years (median) prior to evaluation. In 25 patients (43.8%) *H pylori* was detected histologically in the gastric remnant. Gastric atrophy was more common in *H pylori*-positive compared to *H pylori*-negative partial gastrectomy patients ($P<0.05$). The severity of corpus gastritis was significantly lower in *H pylori*-positive partial gastrectomy patients compared to duodenal ulcer patients ($P<0.01$). There were no significant differences in the activity of gastritis, atrophy and intestinal metaplasia between the two groups.

CONCLUSION: The long-term prevalence of *H pylori* gastritis in the gastric corpus of patients who underwent partial gastric resection due to peptic ulcer disease is comparable to the general population. The expression of *H pylori* gastritis in the gastric remnant does not resemble the gastric cancer phenotype.

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INTRODUCTION

Helicobacter pylori (*H pylori*) is the major etiological factor for peptic ulcer disease and gastric MALT lymphoma, and is strongly linked to the development of gastric carcinoma[1-3]. Recently, a gastric cancer phenotype of *H pylori* gastritis has been proposed, which is characterized by an increased inflammation of the corpus mucosa[4]. This phenotype of *H pylori* gastritis is significantly more common in patients with early gastric cancer, and also in those with advanced stages of gastric cancer[4,5]. An increased severity of corpus inflammation has also been described in particular risk groups for gastric cancer, such as first-degree relatives of gastric cancer patients[6]. In contrast, patients with duodenal ulcer disease are characterized by a severe gastritis in the antrum, but a mild gastritis in the corpus[7]. The risk for gastric cancer in duodenal ulcer patients is low compared to the general population[8].

Patients underwent partial gastric resection for peptic ulcer are at high risk for developing cancer in the gastric remnant[9]. Several mechanisms have been proposed for this phenomenon. It has been suggested that stump cancers uniformly develop upon a background of chronic mucosal changes in the gastric remnant[10-12]. Factors that may contribute to cancer of the gastric remnant include enterogastric pancreaticobiliary reflux, hypochlorhydria, microflora, and N-nitroso compounds[13,14].

The role of *H pylori* gastritis with respect to cancer risk in patients underwent partial gastric resection for benign peptic ulcer disease is not clearly defined. Assuming that the majority of peptic ulcer patients were *H pylori*-infected at the time of surgery, persisting *H pylori* infection and long-term inflammation of the gastric corpus mucosa might contribute to carcinogenesis in these patients.

The aim of our study was therefore to determine the prevalence of *H pylori* gastritis in the gastric remnant of patients who underwent partial gastric resection, and to test the hypothesis that *H pylori*-positive patients with partial gastric resection may have a more severe corpus gastritis resembling the gastric cancer phenotype of *H pylori* gastritis.

MATERIALS AND METHODS

The study included consecutive patients who were admitted to our institution for surveillance endoscopy after partial gastric resection due to peptic ulcer disease. Exclusion criteria included previous surgery for gastric cancer, previous treatment for *H pylori* infection, and a present ulcer or tumor under endoscopy. Further exclusion criteria included pretreatment with antibiotics, proton-pump inhibitors, non-steroidal anti-inflammatory within the 4 wk before study entry.

Endoscopic biopsies were routinely obtained in 4 quadrants from the anastomosis, or from any suspicious macroscopic lesion. In addition, 2 biopsies were obtained from the middle of the remnant corpus and 2 from the cardia for assessing prevalence, severity of *H pylori* gastritis, and gastric atrophy. All biopsy specimens were fixed in 40 g/L formaldehyde and embedded in paraffin. Sections were stained with hematoxylin and eosin and Warthin-Starry. The presence of *H pylori* colonization as well as intestinal metaplasia and atrophy were judged as positive or negative. The grade of gastritis (infiltration of lymphocytes and plasma cells), the activity of gastritis (infiltration of neutrophil granulocytes), and the replacement of foveolar epithelium by regenerative epithelium were assessed by a semiquantitative

scale (grade 0 = negative, grade 1 = mild, grade 2 = moderate, grade 3 = severe) in accordance with the updated Sydney system[15].

The control group consisted of *H pylori*-positive patients with duodenal ulcer disease who participated in previous clinical trials[7] and who were age- and gender-matched. In these patients, endoscopic biopsies have been obtained from the antrum and the corpus, and were processed as described above. All histological slides were assessed by a single pathologist.

Data analysis was performed using the statistical software package SPSS 10.0 for Windows. The Chi-square test or Fisher exact test was used when appropriate. $P<0.05$ was considered statistically significant.

RESULTS

A total of 57 patients with partial gastric resection were included into the study (19 males and 38 females, median age 64 years, range 26-92 years). The time period between surgery and histology assessment ranged from 8 to 47 years with a median of 20 years. None of the intraepithelial neoplasia was detected at the gastric anastomosis. In 25 patients (43.9%) *H pylori* was detected histologically in the gastric remnant.

Table 1 summarizes the histological features in the corpus and cardia of partial gastrectomy patients. For analysis purposes, patients with grade 0 and 1, and patients with grade 2 and 3 were combined, respectively. There was a higher proportion of patients with moderate or severe activity of gastritis in the corpus ($P<0.0005$) and cardia ($P=0.007$) among *H pylori*-positive patients compared to *H pylori*-negative partial gastrectomy patients. In addition, the proportion of patients with atrophy in the corpus mucosa was significantly higher among *H pylori*-positive compared to *H pylori*-negative patients ($P = 0.047$). No significant differences were found with regard to grade of gastritis, regenerative epithelium and the presence of intestinal metaplasia between *H pylori*-positive and *H pylori*-negative partial gastrectomy patients.

The comparison of corpus gastritis between *H pylori*-positive partial gastrectomy patients and *H pylori*-positive duodenal ulcer patients is summarized in Table 2. The proportion of patients with moderate or severe grade of gastritis in the corpus ($P = 0.001$) and with moderate or severe regenerative epithelium ($P = 0.004$) was significantly lower in *H pylori*-positive partial gastrectomy patients than that in *H pylori*-positive duodenal ulcer patients, respectively. A similar trend was observed for the activity of gastritis in the corpus, however the differences were not statistically significant. The prevalence of intestinal metaplasia in the corpus mucosa was similar in both groups. The prevalence of atrophy in the corpus mucosa was higher in partial gastrectomy patients, however the difference did not reach statistical significance.

Table 2 Severity of corpus gastritis in *H pylori*-positive partial gastrectomy patients and *H pylori*-positive duodenal ulcer patients matched by age and gender

	Partial gastrectomy (n = 25)	Duodenal ulcer (n = 25)	P
Grade of gastritis			
Grade 0 or 1, n (%)	24 (96)	13 (52)	
Grade 2 or 3, n (%)	1 (4)	12 (48)	0.001
Activity of gastritis			
Grade 0 or 1, n (%)	16 (64)	11 (44)	
Grade 2 or 3, n (%)	9 (36)	14 (56)	0.256
Regenerative epithelium			
Grade 0 or 1, n (%)	25 (100)	17 (68)	
Grade 2 or 3, n (%)	0 (0)	8 (32)	0.004
Intestinal metaplasia			
Present, n (%)	5 (20)	5 (20)	1.00
Atrophy			
Present, n (%)	11 (44)	5 (20)	0.128

DISCUSSION

In the present study the prevalence of *H pylori* gastritis in patients underwent partial gastrectomy was 43.9% which is comparable to the average population in Germany and which is within the range of other studies on the *H pylori* prevalence in partial gastrectomy patients[16-20].

An association between *H pylori* infection and an increased acute and chronic inflammatory response and a higher prevalence of chronic atrophic gastritis and intestinal metaplasia in the gastric remnant mucosa has been described[16,18] while others were non-confirmatory[20]. Our study suggests that *H pylori* leads to a higher proportion of atrophy in the corpus of the gastric remnant compared to *H pylori*-negative partial gastrectomy patients.

Several studies have shown that a severe although non-atrophic gastritis in the corpus mucosa is a particular risk factor for gastric cancer among those individuals infected with *H pylori*[4-7]. These findings were recently confirmed by a prospective observational study from Japan where gastric cancer developed only in those patients infected with *H pylori*[21] and where a

Table 1 Histology in the corpus and cardia of partial gastrectomy patients

	Corpus			Cardia		
	HP + n = 25	HP − n = 32	P	HP + n = 25	HP − n = 32	P
Grade of gastritis						
Grade 0 or 1, n (%)	24 (96)	32 (100)	-	24 (96)	32 (100)	-
Grade 2 or 3, n (%)	1 (4)	0	0.439	1 (4)	0	0.439
Activity of gastritis						
Grade 0 or 1, n (%)	16 (64)	32 (100)	-	16 (64)	32 (100)	-
Grade 2 or 3, n (%)	9 (36)	0	<0.0005	9 (36)	0	0.007
Regenerative epithelium						
Grade 0 or 1, n (%)	25 (100)	32 (100)	-	24 (96)	32 (100)	-
Grade 2 or 3, n (%)	0	0	-	1 (4)	0	0.439
Intestinal metaplasia						
Present, n (%)	5 (20)	7 (22)	1.00	4 (16)	4 (12.5)	0.720
Atrophy						
Present, n (%)	11 (44)	6 (19)	0.047	0	3 (9.5)	0.248

No partial gastrectomy patient had a grade 2 or 3 regenerative type of epithelium in the corpus. Based upon this result a statistical analysis with regard to regenerative type of epithelium in the corpus was not appropriate.

corpus-dominant gastritis or pangastritis was associated with an 34-fold increased risk for gastric cancer. Based upon the increased risk for gastric cancer in the presence of severe corpus gastritis we hypothesized that patients with partial gastrectomy due to ulcer disease may develop a corpus-dominant phenotype of *H pylori* gastritis, which may contribute as a risk factor for cancer in these patients. Surprisingly, we found a significant lower grade of gastritis in the corpus of *H pylori*-positive partial gastrectomy patients compared to the control group consisting of *H pylori*-positive duodenal ulcer patients. Possible explanation for this finding might include that in some patients the infection may have disappeared spontaneously due to an altered gastric milieu, or that some of the patients may have been operated due to *H pylori*-negative ulcer caused by nonsteroidal anti-inflammatory drugs. Other patients may have received antibiotic therapy for other indications that *H pylori* infection potentially leads to coincident eradication of the bacteria. Nevertheless, we conclude that partial gastrectomy patients should be tested for *H pylori* infection, and, if diagnosed positive, eradication therapy should be initiated to reduce the risk of ulcer relapse[22].

Other factors than *H pylori* have been implicated in the pathogenesis of the mucosa alterations in partial gastrectomy patients, including enterogastric reflux, achlorhydria and increased mucosal proliferation, effects of vagotomy and dietary factors[23-26]. Bile reflux may play a promotional role by increasing permeability to initiating carcinogens. This enterogastric reflux has been reported to be more pronounced after a gastrojejunostomy than after a gastroduodenostomy, which may explain the higher stomach cancer risk after a Billroth II operation[27-29].

In conclusion, our study suggests that the *H pylori* prevalence in partial gastrectomy patients (former peptic ulcer patients) is comparable to the general population. *H pylori*-positive partial gastrectomy patients appear not to develop a corpus-dominant gastritis resembling the gastric cancer phenotype of *H pylori* gastritis.

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