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ORIGINAL ARTICLE

Retrospective Study

Correlation between *Helicobacter pylori*-associated gastric diseases and colorectal neoplasia

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Abstract

AIM: To explore the correlation between *Helicobacter pylori* (*H. pylori*)-associated gastric diseases and colorectal neoplasia.

METHODS: Patients included in this study underwent a colonoscopy and esophago-gastro-duodenoscopy (EGD) along with histopathological measurement between March 2012 and March 2015 at Qi-Lu Hospital of Shandong University, who also had results of *H. pylori* detection. A total of 233 cases were selected. Demographic data, *H. pylori* infection status (including results of rapid urease tests and gastric mucosa pathological examinations) and histopathological examination results of gastric and colorectal mucosa were gathered and analyzed. The statistical analysis focused on the prevalence of colorectal neoplasms among patients with various histopathological categories of the stomach. ORs and their 95%CI were calculated to describe the strengths of the associations.

RESULTS: The incidence rates of colorectal adenoma without high-grade intraepithelial neoplasia (HGIEN) (OR = 2.400, 95%CI: 0.969-5.941), adenoma with HGIEN (5.333, 1.025-27.758) and adenocarcinoma (1.455, 0.382-5.543) were all higher for patients with *H. pylori*-associated gastritis than for those in the control group. The incidence rate of colorectal adenoma with HGIEN (3.218, 0.767-13.509) was higher in patients with intestinal metaplasia than in the control group, while the incidence rates of adenoma without HGIEN (0.874, 0.414-1.845) and adenocarcinoma (0.376, 0.096-1.470) were lower in the intestinal metaplasia group than in the control group. The incidence rate of colorectal adenoma without HGIEN (3.111, 1.248-7.753) was significantly higher in the gastric intraepithelial neoplasia group than in the control group, while the rates of adenoma with HGIEN (1.481, 0.138-15.941) and adenocarcinoma (2.020, 0.561-7.272) were higher in the gastric intraepithelial neoplasia group. Incidence rates of colorectal adenoma without HGIEN (1.067, 0.264-4.314), adenoma with HGIEN (2.667, 0.231-30.800) and adenocarcinoma (2.182, 0.450-10.585) were all higher in the gastric adenocarcinoma group than in the control group.

CONCLUSION: *H. pylori* infection as well as *H. pylori*-associated gastric diseases are risk factors for colorectal neoplasia.

Key words: *Helicobacter pylori*; *Helicobacter pylori*-associated gastric diseases; Colorectal neoplasia; Endoscopy with pathological biopsy; Chinese population

Core tip: Few studies have investigated the relationship between *Helicobacter pylori* (*H. pylori*)-associated gastric diseases and colorectal neoplasia. In particular, no such research on the Chinese population has been reported so far. To explore this correlation in the Chinese population, demographic data, *H. pylori* infection status and histopathological data of gastric and colorectal mucosa of 233 Chinese patients were gathered and analyzed. The results demonstrated that *H. pylori*-associated gastric diseases might increase the risk of colorectal neoplasia regardless of the number, size and location of the neoplasm. Therefore, we can assume that *H. pylori*-associated gastric diseases are potential risk factors for colorectal neoplasia in the Chinese population.

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INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignancies worldwide. In China, the incidence and mortality rates of CRC have increased in recent years[1]. Due to the lack of specific clinical manifestations, the early diagnosis of CRC is relatively difficult, leading to the poor prognosis. Therefore, it is of great importance to elucidate the pathogenesis and risk factors of CRC, and develop relevant prevention and early detection strategies. During the development of CRC, the mucosa will progress from normal mucosa to adenoma first, and then to adenocarcinoma. This process provides the chance for early detection and intervention of CRC, and colorectal adenoma is considered the most important precancerous lesion for CRC. These two diseases, colorectal adenoma and CRC, are collectively called colorectal neoplasia.

It is believed that the development of colorectal neoplasia is associated with *Helicobacter pylori* (*H. pylori*) infection[2,3], although the pathophysiological mechanism underlying the correlation remains unclear. Most scholars believed that *H. pylori* might induce colorectal neoplasia by regulating the expression of serum gastrin[4,5]. Persistent *H. pylori* infection can lead to various gastric diseases, including gastritis, gastric intestinal metaplasia, gastric intraepithelial neoplasia and gastric adenocarcinoma. Chronic atrophic gastritis (CAG), which may progress to intestinal metaplasia, intraepithelial neoplasia and adenocarcinoma, can lead to decreased gastric acid secretion by extensive glandular atrophy. Serum gastrin level will increase accordingly through the negative feedback regulation, which shall then act as a trophic factor for colorectal mucosa. Therefore, different kinds of *H. pylori*-associated gastric diseases may be correlated with different levels of colorectal neoplasia depending on the serum gastrin level. Although several previous studies concluded that *H. pylori* seropositivity was associated with colorectal neoplasia[4,6-8], few have investigated the relationship between *H. pylori*-associated gastric diseases and colorectal neoplasia. In particular, no such research on the Chinese population has been reported so far.

In this research, we carried out a retrospective analysis of a database of 60501 Chinese patients who underwent esophago-gastro-duodenoscopy (EGD) and/or colonoscopy, trying to explore the possible correlation between *H. pylori*-associated gastric diseases and colorectal neoplasia.

MATERIALS AND METHODS

Patient selection

A total of 60501 Chinese patients underwent EGD and/or colonoscopy between March 2012 and March 2015 at Qi-Lu Hospital of Shandong University. Out

Table 1 Clinical indications for esophago-gastro-duodenoscopy and colonoscopy *n* (%)

Indication for EGD and colonoscopy	EGD	Colonoscopy
Abdominal discomfort	78 (33.5)	65 (27.9)
Diarrhea	26 (11.2)	47 (20.2)
Hematochezia	12 (5.2)	34 (14.6)
Weight loss	10 (4.3)	13 (5.6)
Others	58 (24.9)	39 (16.7)
Dyspepsia	33 (14.2)	
Reflux esophagitis	42 (18.0)	
Emesis	21 (9.0)	
Colorectal cancer screening		25 (10.7)
Polypectomy following-up		24 (10.3)

EGD: Esophago-gastro-duodenoscopy.

of those 60501 patients, those who had both EGD and complete colonoscopy (including the colonoscopy of the entire large intestine) were selected in the study. Histopathological results of gastric mucosa and colorectal mucosa as well as the results of *H. pylori* measurement were taken for all subjects. None of those patients in this study had a previous history of inflammatory bowel diseases (IBS), hereditary non-polyposis colorectal cancer (HNPCC) or familial adenomatous polyposis (FAP). None of them received *H. pylori* eradication therapy, gastrointestinal surgery, radiotherapy, chemotherapy, or other biotherapies targeting the cancer. No patients had a long-term drug use history. Based on the aforementioned criteria, a total of 233 patients were chosen.

Data collection

Demographic data, *H. pylori* infection status and histopathological results of gastric and colorectal mucosa were collected for all subjects. *H. pylori* infection status was determined by rapid urease test (RUT) and histopathological examination of gastric mucosa. *H. pylori* positivity was defined as results from one or both examinations were positive. EGD and colonoscopy were performed with EG-2990i electronic gastroscopes and EC-3890Fi electronic colonoscopes (Pentax, Tokyo, Japan), respectively. The location, number, and size of polyps were recorded during the colonoscopy.

All data were from existing records and personal identities were removed before the data were used in this study. Therefore, there was no need to obtain informed consent from patients.

Diagnostic criteria

Among the 233 patients, 159 (68.2%) had gastric antrum biopsies, 59 (25.3%) had gastric body and fundus biopsies, 29 (12.4%) had cardia biopsies, and 20 (8.6%) had multiple-site biopsies. The diagnostic criteria of the gastric biopsies were set according to the updated Sydney system[9]. Based on the sample size of this study, patients were divided into four groups according to their histopathological results of gastric mucosa: chronic gastritis group (including chronic non-atrophic gastritis and CAG), gastric intestinal metaplasia group, gastric intraepithelial neoplasia group and gastric adenocarcinoma group.

The following four histopathological categories were used for the colorectal mucosa: inflammation or non-adenomatous polyps (including hyperplastic polyps, inflammatory polyps, *etc.*), adenoma (including tubular adenoma, tubulovillous adenoma and villous adenoma) without high-grade intraepithelial neoplasia (HGIEN), adenoma with HGIEN and colorectal adenocarcinoma. Polyps were grouped based on their location such as rectum (including rectosigmoid junction), sigmoid colon, descending colon, transverse colon and ascending colon (including ileocecal junction). Polyps were also grouped based on the number: 1-3, 4-9 and > 10. Adenomas were grouped based on their size: 0-9 mm, 10-19 mm and > 20 mm.

Statistical analysis

The degree of correlations between *H. pylori*-associated gastric diseases and colorectal neoplasia was measured by ORs and their 95%CIs. χ^2 test was applied to calculate *P*-values. When the expected frequency was less than 5, Fisher's exact test was used to calculate *P*-values. *P*-values less than 0.05 were considered statistically significant. All statistical analyses were performed using Excel 2013 (Microsoft, Redmond, WA, United States) and SPSS 20.0 (SPSS, Chicago, IL, United States). The statistical methods of this study were reviewed by Dr. Jing Liu from Department of Epidemiology and Biostatistics, School of Public Health, Shandong University.

RESULTS

General characteristics of the study population

All 233 Chinese patients were between 16 and 89 years old, with the mean age at 56.85 ± 12.38 years. Of the 233 patients, 70.4% were males (164 patients), aged between 16 and 83 years with the mean at 56.69 ± 12.06 years, and 29.6% were females (69 patients), aged between 16 and 89 years with the mean at 57.22 ± 13.19 years. The clinical indications for EGD and colonoscopy are listed in Table 1.

Correlation between H. pylori-associated gastritis and colorectal neoplasia

H. pylori-associated gastritis is a gastric disease while the histopathological type was chronic gastritis (including chronic non-atrophic gastritis and CAG) with *H. pylori* infection (the infection status was determined by RUT and histopathological examination). Because no patient included in this research had completely normal histopathological results of gastric mucosa, patients with chronic gastritis and negative *H. pylori* were used as control group 1 in this research. For the

Table 2 Correlation between *Helicobacter pylori*-associated gastritis and colorectal neoplasia *n* (%)

Parameter	Total number of patients (*n* = 233)	*H. pylori*-associated gastritis	Control group 1	OR	95%CI	*P* value
Age	56.85	52.72 ± 11.37	56.42 ± 14.90	-	-	-
Male	164	27 (16.5)	48 (29.3)	1.000	-	-
Female	69	9 (13.0)	36 (52.2)	0.444	0.186-1.060	0.064
Control group 2	95	10 (10.5)	40 (42.1)	1.000	-	-
Adenoma without HGIEN	92	18 (19.6)	30 (32.6)	2.400	0.969-5.941	0.055
Adenoma with HGIEN	16	4 (25.0)	3 (18.8)	5.333	1.025-27.758	0.054
Adenocarcinoma	27	4 (14.8)	11 (40.7)	1.455	0.382-5.543	0.721
Polyp number						
1-3	106	16 (15.1)	36 (34.0)	1.778	0.716-4.414	0.212
4-9	46	10 (21.7)	14 (30.4)	2.857	0.983-8.306	0.049
10+	20	3 (15.0)	9 (45.0)	1.333	0.304-5.852	0.703
Adenoma size (mm)						
0-9	82	15 (18.3)	25 (30.5)	2.400	0.934-6.165	0.066
10-19	30	5 (16.7)	9 (30.0)	2.222	0.609-8.108	0.286
20+	16	4 (25.0)	7 (43.8)	2.286	0.558-9.366	0.256
Polyp location						
Rectum	79	14 (17.7)	33 (41.8)	1.697	0.667-4.315	0.264
Sigmoid colon	77	12 (15.6)	22 (28.6)	2.182	0.813-5.856	0.118
Descending colon	64	13 (20.3)	19 (29.7)	2.737	1.018-7.357	0.043
Transverse colon	55	11 (20.0)	17 (30.9)	2.588	0.927-7.230	0.065
Ascending colon	57	11 (19.3)	18 (31.6)	2.444	0.880-6.787	0.082

HGIEN: High-grade intraepithelial neoplasia; *H. pylori*: *Helicobacter pylori*.

same reason, patients with colorectal inflammation or non-adenomatous polyps were used as control group 2.

As shown in Table 2, compared to the patients in the control group 1, patients with *H. pylori*-associated gastritis were younger and had a higher rate of males. The incidence rates of colorectal adenoma without HGIEN, colorectal adenoma with HGIEN or colorectal adenocarcinoma were higher in the *H. pylori*-associated gastritis group than in the control group 1. The incidence rate of *H. pylori*-associated gastritis was much lower for patients in the control group 2 than for those in the other three groups (the colorectal adenoma group without HGIEN, the colorectal adenoma group with HGIEN and the colorectal adenocarcinoma group). The correlation between *H. pylori*-associated gastritis and colorectal neoplasms was the highest when the number of polyps was between 4 and 9 (OR = 2.857, 95%CI: 0.983-8.306, $P = 0.049$). In addition, the association of *H. pylori*-associated gastritis with colorectal neoplasms was independent of colorectal neoplasms size, with OR values greater than 1. The association was highest when the polyps were located at the descending colon (OR = 2.737, 95%CI: 1.018-7.357, $P = 0.043$).

Correlation between gastric intestinal metaplasia and colorectal neoplasia

There were more old people and males in the gastric intestinal metaplasia group than in the control group 1 (Table 3). The incidence rate of colorectal adenoma with HGIEN was higher in the gastric intestinal metaplasia group than in the control group 1, while the incidence rates of colorectal adenoma without HGIEN and colorectal adenocarcinoma were lower in the gastric intestinal metaplasia group. The inconsistency may be due to the small sample size, as there were only three patients with both gastric intestinal metaplasia and colorectal adenocarcinoma. Therefore, each individual case had a big impact on the OR value, leading to poor reliability of the final conclusion.

The association of gastric intestinal metaplasia with the number of colorectal neoplasms was also impacted by the small sample size, as the OR values varied considerably. The OR value was greater than 1 when the number of polyps was between 1 and 3 or between 4 and 9, while the OR value was smaller than 1 when the number of polyps was greater than 10. There were only five patients with both gastric intestinal metaplasia and more than 10 colorectal polyps. Also affected by the small sample size, the association of gastric intestinal metaplasia with the size of colorectal neoplasms was inconsistent. Since there was only one patient with both gastric intestinal metaplasia and colorectal adenoma larger than 20 mm, the analysis result could hardly be representative. This was also the case for the association of gastric intestinal metaplasia with the location of colorectal neoplasms.

Correlation between gastric intraepithelial neoplasia and colorectal neoplasia

Compared to patients in the control group 1, patients in the gastric intraepithelial neoplasia group were slightly older and had a significantly higher proportion of males ($P = 0.002$, Table 4). The incidence rate of colorectal adenoma without HGIEN was significantly higher in the gastric intraepithelial neoplasia group than in the control group 1 ($P = 0.013$). Similarly, the incidence rates of colorectal adenoma with HGIEN

Table 3 Correlation between gastric intestinal metaplasia and colorectal neoplasia *n* (%)

Parameter	Total number of patients (*n* = 233)	Gastric intestinal metaplasia	Control group 1	OR	95%CI	*P* value
Age	56.85	58.39 ± 7.34	56.42 ± 14.90	-	-	-
Male	164	44 (26.8)	48 (29.3)	1.000	-	-
Female	69	15 (21.7)	36 (52.2)	0.455	0.219-0.941	0.032
Control group 2	95	29 (30.5)	40 (42.1)	1.000	-	-
Adenoma without HGIEN	92	19 (20.7)	30 (32.6)	0.874	0.414-1.845	0.723
Adenoma with HGIEN	16	7 (43.8)	3 (18.8)	3.218	0.767-13.509	0.172
Adenocarcinoma	27	3 (11.1)	11 (40.7)	0.376	0.096-1.470	0.149
Polyp number						
1-3	106	30 (28.3)	36 (34.0)	1.149	0.582-2.270	0.688
4-9	46	12 (26.1)	14 (30.4)	1.182	0.477-2.929	0.717
10+	20	5 (25.0)	9 (45.0)	0.766	0.232-2.527	0.661
Adenoma size (mm)						
0-9	82	23 (28.0)	25 (30.5)	1.269	0.605-2.663	0.528
10-19	30	10 (33.3)	9 (30.0)	1.533	0.553-4.248	0.410
20+	16	1 (6.3)	7 (43.8)	0.197	0.023-1.690	0.140
Polyp location						
Rectum	79	19 (24.1)	33 (41.8)	0.794	0.379-1.664	0.541
Sigmoid colon	77	24 (31.2)	22 (28.6)	1.505	0.710-3.187	0.285
Descending colon	64	17 (26.6)	19 (29.7)	1.234	0.549-2.775	0.611
Transverse colon	55	14 (25.5)	17 (30.9)	1.136	0.484-2.668	0.770
Ascending colon	57	12 (21.1)	18 (31.6)	0.920	0.384-2.201	0.851

HGIEN: High-grade intraepithelial neoplasia.

Table 4 Correlation between gastric intraepithelial neoplasia and colorectal neoplasia *n* (%)

Parameter	Total number of patients (*n* = 233)	Gastric intraepithelial neoplasia	Control group 1	OR	95%CI	*P* value
Age	56.85	57.68 ± 11.24	56.42 ± 14.90	-	-	-
Male	164	32 (19.5)	48 (29.3)	1.000	-	-
Female	69	5 (7.2)	36 (52.2)	0.208	0.074-0.588	0.002
Control group 2	95	9 (9.5)	40 (42.1)	1.000	-	-
Adenoma without HGIEN	92	21 (22.8)	30 (32.6)	3.111	1.248-7.753	0.013
Adenoma with HGIEN	16	1 (6.3)	3 (18.8)	1.481	0.138-15.941	1.000
Adenocarcinoma	27	5 (18.5)	11 (40.7)	2.020	0.561-7.272	0.306
Polyp number						
1-3	106	17 (16.0)	36 (34.0)	2.099	0.832-5.293	0.112
4-9	46	10 (21.7)	14 (30.4)	3.175	1.071-9.413	0.033
10+	20	3 (15.0)	9 (45.0)	1.481	0.333-6.596	0.689
Adenoma size (mm)						
0-9	82	16 (19.5)	25 (30.5)	2.844	1.092-7.410	0.029
10-19	30	4 (13.3)	9 (30.0)	1.975	0.496-7.868	0.444
20+	16	3 (18.8)	7 (43.8)	1.905	0.411-8.829	0.409
Polyp location						
Rectum	79	12 (15.2)	33 (41.8)	1.616	0.607-4.304	0.335
Sigmoid colon	77	16 (20.8)	22 (28.6)	3.232	1.227-8.512	0.015
Descending colon	64	14 (21.9)	19 (29.7)	3.275	1.205-8.899	0.017
Transverse colon	55	13 (23.6)	17 (30.9)	3.399	1.223-9.443	0.016
Ascending colon	57	13 (22.8)	18 (31.6)	3.210	1.162-8.864	0.021

HGIEN: High-grade intraepithelial neoplasia.

and colorectal adenocarcinoma were also higher in the gastric intraepithelial neoplasia group. Gastric intraepithelial neoplasia was found more frequently in all other three groups (the colorectal adenoma group without HGIEN, the colorectal adenoma group with HGIEN and the colorectal adenocarcinoma group) than in the control group 2.

The association of gastric intraepithelial neoplasia with the number of colorectal neoplasia was similar to that of *H. pylori*-associated gastritis, as the OR values were all greater than 1. The association was the highest when the number of polyps was between 4 and 9 (OR = 3.175, 95%CI: 1.071-9.413, $P = 0.033$). The associations of gastric intraepithelial neoplasia with the size of colorectal neoplasia were also similar, with the association being strongest when the size of adenoma was 0-9 mm (OR = 2.844, 95%CI: 1.092-7.410, $P = 0.029$). Compared to that of *H.*

Table 5 Correlation between gastric adenocarcinoma and colorectal neoplasia *n* (%)

Parameter	Total number of patients (*n* = 233)	Gastric adenocarcinoma	Control group 1	OR	95%CI	*P* value
Age	56.85	62.36 ± 16.31	56.42 ± 14.90	-	-	-
Male	164	10 (6.1)	48 (29.3)	1.000	-	-
Female	69	4 (5.8)	36 (52.2)	0.533	0.155-1.838	0.314
Control group 2	95	5 (5.3)	40 (42.1)	1.000	-	-
Adenoma without HGIEN	92	4 (4.3)	30 (32.6)	1.067	0.264-4.314	1.000
Adenoma with HGIEN	16	1 (6.3)	3 (18.8)	2.667	0.231-30.800	0.418
Adenocarcinoma	27	3 (11.1)	11 (40.7)	2.182	0.450-10.585	0.379
Polyp number						
1-3	106	5 (4.7)	36 (34.0)	1.111	0.297-4.155	1.000
4-9	46	1 (2.2)	14 (30.4)	0.571	0.061-5.323	1.000
10+	20	0 (0.0)	9 (45.0)	-	-	-
Adenoma size (mm)						
0-9	82	3 (3.7)	25 (30.5)	0.960	0.211-4.372	1.000
10-19	30	2 (6.7)	9 (30.0)	1.778	0.296-10.671	0.614
20+	16	1 (6.3)	7 (43.8)	1.143	0.115-11.311	1.000
Polyp location						
Rectum	79	2 (2.5)	33 (41.8)	0.485	0.088-2.663	0.459
Sigmoid colon	77	3 (3.9)	22 (28.6)	1.091	0.238-5.003	1.000
Descending colon	64	1 (1.6)	19 (29.7)	0.421	0.046-3.859	0.657
Transverse colon	55	1 (1.8)	17 (30.9)	0.471	0.051-4.336	0.664
Ascending colon	57	3 (5.3)	18 (31.6)	1.333	0.287-6.192	0.702

HGIEN: High-grade intraepithelial neoplasia.

pylori-associated gastritis, the association of gastric intraepithelial neoplasia with the location of colorectal neoplasms was even stronger. The association was statistically significant when the polyps were located at the sigmoid colon, descending colon, transverse colon and ascending colon.

Correlation between gastric adenocarcinoma and colorectal neoplasia

Fourteen gastric adenocarcinoma patients were enrolled in the study (Table 5). Their average age (62.36 ± 16.31 years) was significantly higher than that of the control group 1 (56.42 ± 14.90 years). There was also a higher percentage of males in the gastric adenocarcinoma group than in the control group 1. The incidence rates of colorectal adenoma without HGIEN, colorectal adenoma with HGIEN and colorectal adenocarcinoma were higher in the gastric adenocarcinoma group than in the control group 1. However, the results were not statistically significant due to the small sample size. The incidence rate of gastric adenocarcinoma was higher in all three case groups than in the control group 2.

The relationship of gastric adenocarcinoma with the number of colorectal neoplasia varied widely because of the small sample size. There was no patient with both gastric adenocarcinoma and more than 10 colorectal polyps in this study. Also because of the small sample size, the association of gastric adenocarcinoma with the size of colorectal neoplasms was inconsistent, leading to low reliability. It was the same situation for the association of gastric adenocarcinoma with the location of colorectal neoplasia.

DISCUSSION

The first report that *H. pylori* infection might be associated with colorectal neoplasia (particularly colorectal adenomas) could be traced back to 1997[10]. Several previous studies have shown a positive correlation between *H. pylori* infection and colorectal neoplasia in different populations, such as African American[11], German[6,8], and Israelite[12]. However, other studies did not support the idea that *H. pylori* infection was associated with the development of colorectal neoplasia. For example, Strofilas *et al*[4] found that there was no significant difference of anti-*H. pylori* IgG antibodies between the colorectal cancer group and the control group in Greeks. A recent meta-analysis also failed to find a statistical association between *H. pylori* infection and colorectal neoplasia among the East Asian population[13]. In addition, such lack of association between *H. pylori* and colorectal adenomas was also reported in the United States Hispanic population[14]. Therefore, it was speculated that the relationship between *H. pylori* infection and colorectal neoplasia was race dependent[15], making it important to analyze data based on race.

Most previous studies used positive serology as the indicator of *H. pylori* infection[16-19], while others used the presence of *H. pylori*-associated gastritis as the indicator[20-22]. Yet very few studies used other *H. pylori*-associated gastric diseases as indicators during the investigation of the association of colorectal neoplasia with *H. pylori*-associated gastric diseases as well as their severity. In particular, to our knowledge, no such study has been performed on the Chinese population. Since Chinese represent more than one fifth of the

world total population, it is of great significance to investigate the relationship between *H. pylori*-associated gastric diseases and colorectal neoplasia in the Chinese population.

Our study demonstrated that *H. pylori*-associated gastric diseases might increase the risk of colorectal neoplasia regardless of the number, size and location of the neoplasm, although some results were not statistically significant as the sample size was too small. Generally we can assume that *H. pylori* infection as well as *H. pylori*-associated gastric diseases are potential risk factors for colorectal neoplasia.

Chinese population has a high prevalence of *H. pylori* infection and *H. pylori*-associated gastric diseases[23]. The incidence rate of colorectal adenocarcinoma is also high in China[24]. Early diagnosis of colorectal adenocarcinoma is relatively low even though early diagnosis is very important to lower the mortality[25]. Our research showed that people who had *H. pylori*-associated gastric diseases did have high risk of colorectal neoplasia. It is important to encourage patients with *H. pylori*-associated gastric diseases to undergo colonoscopy earlier and more frequently, to improve the early diagnostic rate of colorectal adenocarcinoma. In addition, people in the high-risk group should receive some interventions, such as lifestyle changes, which may lower the risk of developing cancer.

One advantage of this study was that RUT and histopathological results were used to determine the *H. pylori* infection status. As the gold standard for *H. pylori* infection diagnosis[26], histopathological examination can diagnose the *H. pylori* infection and pathologic changes of the stomach at the same time. Compared to serological tests that cannot differentiate existing infections from historical ones, RUT and histopathological tests diagnose only existing *H. pylori* infection. Such a distinction is vital since only existing *H. pylori* infection stimulates immune responses that can induce or perpetuate chronic inflammation in the gastrointestinal tract, and many malignancies are associated with epigenetic alterations induced by chronic inflammation[27,28].

How *H. pylori* infection increases the risk of colorectal neoplasia has not yet been elucidated. One common hypothesis is that hypergastrinemia induced by *H. pylori* infection contributes to the colorectal carcinogenesis, as high levels of gastrin can promote colorectal cell growth *in vitro* and increase colorectal cancer rates in animal models[29-31]. Since serum gastrin levels increase significantly as the healthy stomach progresses to malignancy[32], it could be inferred that the correlation between *H. pylori*-associated gastric diseases and colorectal neoplasia should be higher as the severity of the gastric lesions increases. However, our study showed that there was little association of the type of *H. pylori*-associated gastric diseases with colorectal neoplasia. This negative result might be due to the small sample size. As no gastrin level data was included in the study, it might also be because the gastrin levels were similar in different *H. pylori*-associated gastric diseases, as gastrin levels could be influenced by many factors. Yet other studies did show that gastrin levels were not related to colorectal neoplasia[6]. That being said, more studies are needed to clarify this issue. The relatively small sample size of our study also made it impossible to perform multivariate logistic analysis to eliminate possible confounding factors, restricting the research conclusion. Another limitation is that since all data were collected from the same center, some bias such as environmental factor might impact the results.

In conclusion, our study revealed that *H. pylori* infection and *H. pylori*-associated gastric diseases are potential risk factors of colorectal neoplasia. Early colonoscopy and interventions should be taken to reduce the risk of colorectal neoplasia for people with *H. pylori*-associated gastric diseases. Studies with larger sample size and multi-center data collection for Chinese population are needed to further clarify this association and to understand the underlying pathophysiological mechanism.

COMMENTS

Background

Colorectal cancer (CRC) is one of the most common malignancies worldwide. Colorectal adenoma is considered the most important precancerous lesion for CRC, and these two diseases are collectively called colorectal neoplasia. Accumulating evidence indicates that in addition to being a major risk factor of gastric cancer, *Helicobacter pylori* (*H. pylori*) infection is also associated with colorectal neoplasia. Although several previous studies concluded that *H. pylori* seropositivity was associated with colorectal neoplasia, few have investigated the relationship between *H. pylori*-associated gastric diseases and colorectal neoplasia. In particular, no such research on the Chinese population has been reported so far. In this study, we carried out a retrospective analysis of a database of 60501 Chinese patients who underwent esophago-gastro-duodenoscopy and/or colonoscopy, trying to explore the possible correlation between *H. pylori*-associated gastric diseases and colorectal neoplasia.

Research frontiers

Early diagnosis of colorectal cancer is very important to lower the mortality. Based on these results, it is critical for patients with *H. pylori*-associated gastric diseases to receive colonoscopy and interventions earlier to improve prognosis.

Innovations and breakthroughs

In this study, the authors investigated the possible correlation between *H. pylori*-associated gastric diseases and colorectal neoplasia in the Chinese population for the first time. Since the relationship between *H. pylori* infection and colorectal neoplasia was considered race dependent, these results supplemented the hypothesis that *H. pylori*-associated gastric diseases are potential risk factors of colorectal neoplasia with evidence from the Chinese population.

Applications

These results suggest that *H. pylori* infection and *H. pylori*-associated gastric diseases are potential risk factors of colorectal neoplasia, encouraging people in the high-risk group to receive colonoscopy and some interventions earlier and more frequently, thus improve the early diagnostic rate of colorectal adenocarcinoma.

Peer-review

It is an interesting study, but includes too few subjects to have such a conclusion. It is in the text that *H. pylori* infection may affect colorectal neoplasm formation differently in different races. And this study reported for the first time how *H. pylori*-associated gastric diseases are correlated with colorectal neoplasm in the Chinese people, representing its innovation.

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