



The clinicopathological characteristics of gastric polyps and the relationship between fundic gland polyps, *Helicobacter pylori* infection, and proton pump inhibitors

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Background: To explore the clinical characteristics of different types of gastric polyps and the relationship between fundic gland polyps, *Helicobacter pylori* (HP) infection, and proton pump inhibitor (PPI) use.

Methods: The clinical data of 186 patients diagnosed with gastric polyps under endoscopy were selected for retrospective analysis, and the clinical data, gastroscopy, polyp histopathology, HP infection, and PPI usage of all subjects were analyzed.

Results: Among the 186 patients with gastric polyps, there were significantly more women (131 cases) than men (55 cases), with a ratio of 2.38:1. PPIs were used in 78% of cases for more than 5 years. The pathological types of patients with gastric polyps in this study were fundic gland polyps, hyperplastic polyps, inflammatory fibrous polyps, and adenomatous polyps. Fundic gland polyps were mainly located in the fundus and gastric body, while hyperplastic polyps were mostly located in the gastric body (P<0.05). The positive rate of HP infection in patients with fundic gland polyps was significantly lower than that in patients with other types of polyps (P<0.05). In patients with long-term use of PPIs, the incidence of fundic gland polyps increased significantly (P<0.05).

Conclusions: There were significant differences among the different types of gastric polyps in terms of polyp position, shape, and size. The positive rate of HP infection in patients with fundic gland polyps was low. Long-term use of PPIs (>5 years) increased the incidence of fundic gland polyps to some extent. The mechanisms underlying the relationship between gastric polyps, HP infection, and the use of PPIs remain to be further studied.

Keywords: Gastric polyps; fundic gland polyps; *Helicobacter pylori* (HP); proton pump inhibitor (PPI)

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Introduction

Gastric polyps are benign lesions with a wide base or pedicle that protrude into the gastric cavity. However, according to pathological types, different types of gastric polyps have varying degrees of malignant transformation risk, and with

an overall malignant transformation rate of 0.4–10% (1). Early diagnosis and active intervention are key to reducing the risk of cancer (2). With the changes in people's living habits and diet, the incidence of gastric polyps is increasing year by year, which also increases the risk of polyp

canceration to a certain extent. Studies have shown that from 2000 to 2010, the proportion of hyperplastic polyps has declined, from 48.5% to 20.8%, while the proportion of fundic gland polyps has increased from 8.8% to 66.1% (3). Fundic gland polyps have gradually replaced hyperplastic polyps as the main type of gastric polyps. Proton pump inhibitors (PPIs) play an important role in the prevention of *Helicobacter pylori* (HP) infection (4). However, there are no specific clinical manifestations of gastric polyps because the pathological characteristics vary across different types of gastric polyps. This study conducted a retrospective analysis of the clinicopathological characteristics of different types of gastric polyps. In addition, we examined the relationship between fundic gland polyps, HP infection, and PPI use, in order to provide a theoretical basis for preventive diagnosis and treatment, as well as to reduce the rate of polyp canceration. We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/apm-21-39>).

Methods

Patient baseline information

The clinical data of 186 patients with gastric polyps who met the diagnostic criteria from January 2018 to January 2019 were selected for retrospective analysis. The inclusion criteria were as follows: (I) patients who had not previously undergone endoscopic gastric polypectomy; (II) patients who were pathologically diagnosed with benign gastric polyps after gastric polypectomy; (III) no antibiotics, bismuth, or acid inhibitors were used in the 4 weeks before the HP test, and patients had not undergone any HP eradication treatment. The exclusion criteria were as follows: (I) patients with a history of gastric polypectomy, gastric malignancy, or other gastric surgery; (II) patients with a history of inflammatory bowel disease; (III) patients with gastrointestinal polyp syndrome. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Sixth People's Hospital of Dalian (No. 2019-105-002). Individual consent for this retrospective analysis was waived.

Research methods

Retrospective analyses of clinical data, gastroscopy, polyp histopathology, HP infection, and PPI use were performed

for all research subjects. The ^{13}C urea breath test was used to determine HP infection. Judgment criteria for the use of PPIs were as follows: patients who had used PPIs for less than 1 year or needed to take the drug continuously for more than 1 month; or patients with a total medication time of more than 1 year or needed to exceed 3 months per year. The clinicopathological data of patients were compared among the different types of gastric polyps.

Gastroscopy and histopathological examination

A 260/290 electronic gastroscope (Olympus, Japan) was used for routine gastroscopy and treatment. The excised polyp was diagnosed by a specialized pathologist.

Statistical analysis

The clinical data were analyzed by SPSS 23.0 statistical software (IBM, New York, USA). The count data was analyzed by a χ^2 test, and the measurement data was analyzed using the *t*-test and analysis of variance. $P < 0.05$ indicated that the difference was statistically significant.

Results

General characteristics of the patients

Among the 186 patients with gastric polyps, there were 55 males and 131 females, with a male to female ratio of 1:2.38. They had an age range of 31–84 years old, with an average age of 55.62 ± 11.9 years. Patients aged between 51–70 years old had a high incidence of gastric polyps. Clinical symptoms such as abdominal pain and reflux were common. PPIs were used for more than 5 years in 78% of cases. The average diameter of polyps was 7.7 ± 5.6 (ranged from 2 to 30 mm), most of which were less than 6 mm (100 cases, accounted for 53.8%). Patients with multiple polyps accounted for 50.5%. Fundic gland polyps were the most common polyp type. The most common locations were the gastric body, antrum, and fundus, with 89 cases (47.8%) located in the gastric body, 49 cases (26.3%) in the antrum, and 36 cases (19.4%) in the fundus of the stomach. The morphology of polyps were mainly broad-based polyps (Table 1).

Analysis of the clinicopathological characteristics of different types of gastric polyps

The pathological types of patients with gastric polyps in

Table 1 Clinical and pathological features of gastric polyps

Clinicopathological feature	N (%)
Gender	
Male	55 (29.57)
Female	131 (70.43)
Age (years)	
Male	52.53±13.7
Female	56.92±10.8
Total	55.62±11.9
Segmented age	
<40	22 (11.8)
41–50	42 (22.5)
51–60	50 (26.9)
61–70	56 (30.1)
Occurrence frequency	
Once	92 (49.5)
Frequently	94 (50.5)
Gastritis type	
Non-atrophy	80 (43.0)
Atrophy	106 (57.0)
Symptom	
None	27 (14.5)
Abdominal pain	63 (33.9)
Nausea	1 (0.5)
Acid heartburn	45 (24.2)
Epigastric discomfort	20 (10.8)
Ventosity	30 (16.1)

Table 1 (continued)**Table 1** (continued)

Clinicopathological feature	N (%)
Polyp size	
Diameter (mm)	7.7±5.6 [2–30]
<6 mm	100 (53.8)
6–10 mm	54 (29.0)
11–20 mm	26 (14.0)
>20 mm	6 (3.2)
Polyp morphology	
Broad-base	142 (76.3)
Flat	7 (3.8)
Protruding	12 (6.5)
Subtropic	25 (13.4)
Polyp type	
Fundic gland	91 (48.9)
Hyperplastic	70 (37.6)
Inflammatory fibrous	22 (11.8)
Adenomatous	3 (1.6)
Polyp sites	
Others	1 (0.5)
Cardia	4 (2.2)
Fundus	36 (19.4)
Gastric body	89 (47.8)
Gastric angle	7 (3.8)
Antrum	49 (26.3)
Length of PPI use	
≤5 years	145 (78.0)
>5 years	41 (22.0)

PPI, proton pump inhibitor.

this study were fundic gland polyps, hyperplastic polyps, inflammatory fibrous polyps, and adenomatous polyps. The analysis of the clinicopathological characteristics of these polyp types are shown in *Table 2*. There were no significant differences in sex ratio and age composition ratio between the 4 types of gastric polyps. Fundic gland polyps were mainly located in the fundus and gastric body, while hyperplastic polyps were mostly located in the gastric body ($\chi^2=77.76$, $P<0.05$). Fundic gland polyps occurred more

frequently, while hyperplastic polyps and inflammatory fibrous polyps mainly occurred once ($\chi^2=8.61$, $P<0.05$). The diameter of fundic gland polyps was predominantly <10 mm, and were most commonly <6 mm ($\chi^2=41.335$, $P<0.05$). In terms of polyp morphology, the fundic gland polyps were mainly broad-based, while the shape of hyperplastic polyps were mainly broad-based or subtropic, and the difference was statistically significant ($\chi^2=41.335$, $P<0.05$). The patients with fundic gland polyps commonly

Table 2 Clinicopathological characteristics of the different types of gastric polyps

Gastric polyps	Fundic gland	Hyperplastic	Inflammatory fibrous	Adenomatous	χ^2 value	P value
Gender					6.6	0.86
Male	21	22	10	2		
Female	70	48	12	1		
Age (years)					12.224	0.428
≤ 40	13	9	0	0		
41–50	24	11	7	0		
51–60	24	17	8	1		
61–70	24	25	5	2		
>70	6	8	2	0		
Polyp sites					77.76	0.000 ^a
Others	0	1	0	0		
Cardia	0	3	1	0		
Fundus	27	6	3	0		
Gastric body	61	22	5	1		
Gastric angle	1	6	0	0		
Antrum	2	32	13	2		
Occurrence frequency					8.61	0.035 ^b
Once	36	40	15	1		
Frequently	55	30	7	2		
Polyp diameter					41.335	0.000 ^c
<6 mm	64	25	10	1		
6–10 mm	27	20	6	1		
11–20 mm	0	20	5	1		
>20 mm	0	5	1	0		
Polyp morphology					31.81	0.000 ^d
Broad-base	79	46	16	1		
Flat	4	0	2	1		
Protruding	2	7	3	0		
Subtropic	6	17	1	1		
Gastritis type					8.354	0.039 ^e
Non-atrophy	48	24	8	0		
Atrophy	43	46	14	3		

^a, the distribution of fundic gland polyps was significantly different from that of hyperplastic polyps ($\chi^2=77.76$, $P<0.05$). ^b, fundic gland polyps were significantly more common than hyperplastic polyps and inflammatory fibroid polyps ($\chi^2=8.61$, $P<0.05$). ^c, the diameter of fundic gland polyps was more than 6 mm, which was significantly different from other polyps ($\chi^2=41.335$, $P<0.05$). ^d, fundic gland polyps were mainly broad-based polyps, while hyperplastic polyps were mainly broad-based and subtropic polyps, and the difference was statistically significant ($\chi^2=41.335$, $P<0.05$). ^e, compared with the other 3 types of gastric polyps, there was a significant difference in gastritis types complicated by fundic gland polyps ($\chi^2=8.354$, $P<0.05$).

Table 3 Relationship between the status of *HP* infection and the length of PPI use

	<i>HP</i> infection status		Length of PPI use	
	Positive	Negative	<5 years	>5 years
Fundic gland polyps	17	74	65	26
Other types	42	53	80	15
χ^2	77.814		4.419	
P value	0.000 ^a		0.036 ^b	

^a, the positive rate of *HP* infection in patients with fundic gland polyps was significantly different from that in patients with other types of polyps ($\chi^2=77.814$, $P<0.05$). ^b, the incidence of fundic gland polyps was significantly increased in long-term PPI patients, and the difference was statistically significant compared with other types of polyps ($\chi^2=4.419$, $P<0.05$). *HP*, *Helicobacter pylori*; PPI, proton pump inhibitor.

had combined non-atrophic gastritis, while patients with the other 3 kinds of gastric polyps mainly had atrophic gastritis ($\chi^2=8.354$, $P<0.05$).

The relationship between fundic gland polyps, HP infection status, and the length of PPI use

There were 17 *HP* positive patients with fundic gland polyps, with a positive rate of 18.7%, and 42 *HP* positive patients had other types of polyps, with a positive rate of 44.2%. The results indicated that the positive rate of *HP* infection in patients with fundic gland polyps was significantly lower than in patients with other types of polyps ($\chi^2=77.814$, $P<0.05$).

Among the 41 patients who were treated with PPIs for a long time (>5 years), 26 cases were diagnosed with fundic gland polyps and 15 cases were diagnosed with other types of polyps, suggesting that patients with long-term use of PPIs had a statistically significant increase in the incidence of fundic gland polyps ($\chi^2=4.419$, $P<0.05$, Table 3).

Discussion

Gastric polyps are commonly observed in women aged 40–60 years. The clinical manifestations of gastric polyps are generally atypical, and commonly include abdominal discomfort, dull pain, acid reflux, and heartburn. Some patients have severe reflux symptoms such as bile reflux, acid reflux, and heartburn (5,6). Among the 186 patients in this study, the ratio of males to females was 1:2.38, and patients aged 51–70 years old had the highest incidence of gastric polyps. Clinical symptoms were common, including abdominal pain and reflux. However, in general, age, gender, and clinical symptoms between the different types of gastric polyps (gastric fundus polyp, hyperplastic,

inflammatory fibrous, and adenomatous polyps) were not statistically significant.

The results of this study showed that fundic gland polyps tended to grow on the fundus and gastric body, with a diameter of less than 10 mm. Polyps were mostly broad-based and occurred frequently, while hyperplastic polyps were mostly distributed on the gastric body with broad-based or subtropic morphology. The hyperplastic polyps and inflammatory polyps mostly occurred once, which was generally consistent with previous studies (7). Patients with gastric polyps often have concomitant gastritis. The results of this study suggest that patients with fundic gland polyps mostly have combined non-atrophic gastritis, while patients with the other 3 types of gastric polyps mostly have atrophic gastritis. There are currently no related reports in the domestic or foreign literature, and the underlying mechanisms still require further study. The findings of this study may have significance for the clinical screening and follow-up of patients with fundic gland polyps.

Follow-up studies with large sample sizes in recent years have shown that fundic gland polyps have replaced hyperplastic polyps as the predominant polyp type, however, the reason is not yet clear (8). *HP* has different infection rates among patients with different types of gastric polyps, and it has been confirmed that *HP* infection is related to the occurrence of hyperplastic polyps and inflammatory polyps. In contrast, the relationship between *HP* infection and the occurrence of fundic gland polyps has not yet been elucidated. Studies have shown that *HP* infection is negatively correlated with the incidence of fundic gland polyps (9), and the *HP* infection rate in patients with fundic gland polyps is significantly lower than that in patients with hyperplastic polyps (10). However, some studies have mentioned that although *HP* infection has been confirmed to be related to the occurrence of hyperplastic polyps and

inflammatory fibrous polyps, there is no clear relationship between fundic gland polyps and *HP* infection (11,12). Rubio *et al.* suggested that patients with fundic gland polyps may have a natural lysozyme in gastric juice, which is not enough to eradicate *HP*, but can inhibit the growth of *HP* to a certain extent (13). Watanabe *et al.* also suggested that *HP* infection may be a risk factor for hyperplastic gastric polyps and may be a protective factor for fundic gland polyps (14). In this study, the positive rate of *HP* infection in patients with fundic gland polyps was 18.7%, and the positive rate of *HP* infection in patients with other types of polyps was 44.2%. This indicated that the positive rate of *HP* infection for patients with fundic gland polyps was significantly lower than that of other types of polyps, and the occurrence of *HP* infection might be negatively correlated with the incidence of fundic gland polyps. In addition, the canceration rate of fundic gland polyps was low, suggesting that actively eradicating *HP* infection might play a role in preventing polyps from becoming cancerous.

PPIs can act on the H^+K^+ -ATPase, and show a strong and long-lasting acid suppression effect, which can also reduce the secretion of pepsin and protect the gastric mucosa. In recent years, PPIs have become the most widely used acid inhibitors in clinical practice. Since 1992, when JR Graham first proposed that taking PPIs could cause fundic gland polyps (15), researchers began to focus on the relationship between the use of PPIs and the occurrence of fundic gland polyps. Studies at home and abroad have shown that the long-term and extensive use of PPIs may be related to the increasing incidence of fundic gland polyps (16). Studies have reported that while PPIs inhibit gastric acid secretion, they can cause compensatory hypergastrinemia, which increases the incidence of fundic gland polyps (17). A meta-analysis by Tran-Duy *et al.* demonstrated that the risk of fundic gland polyps in patients using PPIs was significantly higher than that of the control group (18). In a study by Carmack *et al.* in 2009, it was also suggested that the increase in the incidence of fundic gland polyps might be related to the use of PPIs (7). However, the relationship between the length of PPI use and the occurrence of fundic gland polyps is not clear. A study by Vieth *et al.* on 2,251 patients who took PPIs for more than 4 weeks found that there was no clear association between the use of PPIs and the occurrence of fundus polyps (19). A study by Martin *et al.* found that the risk of fundic gland polyps in patients taking PPIs continuously for 1 year was 4–5 times that of non-users (20). Our results showed that among the 41 patients who had been using PPIs for a long time

(>5 years), 26 cases were diagnosed with fundic gland polyps, and 15 cases were diagnosed with other types of polyps, indicating a significant increase in the incidence of fundic gland polyps. This shows that the long-term and large-scale use of PPIs can, to some extent, increase the occurrence of fundic gland polyps. Although the canceration rate of fundic gland polyps is low, due to the wide range of indications for PPIs and the gradual increase in patients taking PPIs, the incidence of fundic gland polyps has increased accordingly, therefore the potential risk of canceration has become of increasing concern. Consequently, it is crucial to pay strict attention to the indications of PPIs and effectively follow-up patients who use PPIs over the long term.

In summary, this study showed that different types of gastric polyps were significantly different in terms of polyp position, shape, and size. At the same time, in patients with fundic gland polyps, the positive rate of *HP* infection was significantly lower than in patients with other types of polyps. Furthermore, the long-term use of PPIs (>5 years) increased the incidence of fundic gland polyps. This may be because lysozymes in the gastric juices of patients with fundic gland polyps inhibit the growth of *HP*, or it may be that PPIs have dual effects in reducing the rate of *HP* infection and increasing the incidence of fundic gland polyps. However, the mechanisms underlying the relationship between gastric polyps, *HP* infection, and the use of PPIs remain to be further studied.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related

to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Sixth People's Hospital of Dalian (No. 2019-105-002). Individual consent for this retrospective analysis was waived.

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