

## 한국인에서 위저선용종과 결장암의 상관관계: 16년간 후향적 고찰

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### Gastric Fundic Gland Polyps and Their Relationship to Colorectal Neoplasia in Koreans: A 16-year Retrospective Study

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**Background/Aims:** There is an ongoing debate on the relationship between gastric fundic gland polyps and increased incidence of colorectal neoplasia in Caucasians. However, there was no report on the relationship between gastric fundic gland polyp and colorectal neoplasia in Korea. The aim of this study was to identify the characteristics of gastric fundic gland polyps and whether a relationship exists between fundic gland polyps and colorectal neoplasia in Korean population.

**Methods:** Persons who underwent an esophagogastroduodenoscopy and colonoscopy from 1992 to 2007 at the Health Promotion Center of Incheon St. Mary's Hospital, The Catholic University of Korea were reviewed retrospectively. The relationship between gastric fundic gland polyps and colorectal neoplasia were analyzed.

**Results:** Among 22,451 subjects, fundic gland polyps were found in 328 subjects (1.5%). Fundic gland polyps were more common in women than in men (odds ratio of 6.25; 95% CI of 4.68-8.34). The odds ratios for colorectal neoplasia in all subjects with gastric fundic gland polyps were 0.56 (95% CI of 0.33-0.95) and men who were 50 years of age or older had an odds ratio of 2.81 (95% CI of 1.03-7.66) as compared to the control group. However, age and sex-adjusted odds ratios for all gastric fundic gland polyps were 0.73 (95% CI of 0.42-1.26), for men 1.78 (95% CI of 0.80-3.98), and for women 0.37 (95% CI of 0.16-0.87).

**Conclusions:** Surveillance colonoscopy in patients with fundic gland polyps can be performed in the same manner as general population in Korea. (Korean J Gastroenterol 2011;58:20-24)

**Key Words:** Gastric fundus; Polyps; Colorectal neoplasms

### INTRODUCTION

Gastric fundic gland polyps (FGPs) are considered the most common or second most common histologic type of gastric polyps, and may be observed in 0.8-1.9% of patients undergoing esophagogastroduodenoscopy.<sup>1-3</sup> FGPs are more commonly encountered in middle-aged women and are not usually considered premalignant lesions.<sup>4</sup>

A significant proportion of Caucasians with FGPs develop colorectal neoplasias such as an adenoma and an adenocarcinoma. However, one of the previous studies used radiologic examination of the colon and histologic evaluation of the colonic lesions were limited.<sup>5</sup> Another prospective study showed a high incidence of colonic neoplasia in patients with FGPs, but, only 80 patients were examined in that study.<sup>6</sup> This limited number of patients made it difficult to analyze the data

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according to the age and the sex of the patient. Recently, a large-scale retrospective study on the characteristics of patients with FGP was performed in Caucasians. However, patient age and sex were not fully considered.<sup>7</sup> In Korea, the pattern of colorectal neoplasia is somewhat different from that of Caucasians. A relationship between FGPs and colorectal neoplasia in Koreans has never been reported.

The aims of the present study were to identify the characteristics of FGPs and to investigate the relationship between FGPs and colorectal neoplasia in Korean population.

## SUBJECTS AND METHODS

### 1. Gastric FGP group

Subjects who underwent an esophagogastroduodenoscopy (EGD) and a colonoscopy within six months of each other, from 1992 to 2007, at the Health Promotion Center of Incheon St. Mary's Hospital, The Catholic University of Korea, were reviewed retrospectively. This research has been approved by the Institutional Review Board of The Catholic University of Korea (OC10RISI0005). Subjects who came to the Health Promotion Center underwent a cancer surveillance EGD, and surveillance colonoscopy was performed at their request.

In the present study, subjects with histologically confirmed sporadic FGPs were included. Histologically, gastric FGPs are defined by cystically dilated and irregularly budded fundic glands that are lined by flattened parietal cells, chief cells, and

variable numbers of mucous neck cells.<sup>4</sup> A representative case of FGP on EGD and on histopathology was presented in Fig. 1. Pathology slides were reviewed by one gastrointestinal pathologist. Exclusion criteria were as follows; 1) Subjects with other co-existing pathologic types of polyps such as an adenomatous polyp, a hyperplastic polyp, or an inflammatory fibroid polyp in the stomach. 2) Subjects with gastric malignancies such as adenocarcinoma, carcinoid tumor, malignant lymphoma or MALToma. 3) Subjects with any kind of polyposis syndrome and subjects with 10 or more FGPs. These groups have a possibility of sporadic fundic gland polyposis.<sup>3</sup> 4) Subjects with inflammatory bowel disease (IBD). This group itself is a risk factor for colorectal neoplasia.

### 2. Control group

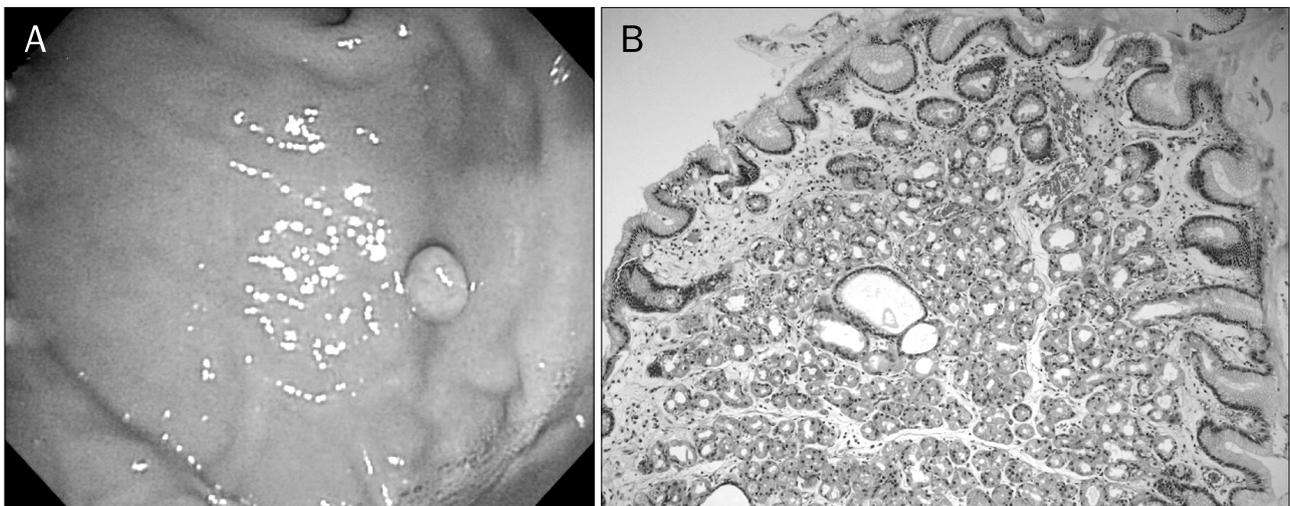
Subjects in the control group underwent an EGD and a colonoscopy within six months at the same center and during the same period as the FGP group, and did not show any FGP. Subjects who underwent previous colonoscopic polypectomy and subjects with IBD were excluded from the control group.

### 3. Colorectal neoplasia

Adenoma and adenocarcinoma of the colorectum were confirmed histologically. Pathology slides were reviewed by one gastrointestinal pathologist.

### 4. Statistical analysis

All statistical analyses were performed using SAS System



**Fig. 1.** A representative case of fundic gland polyp. (A) On esophagogastroduodenoscopy, a polypoid lesion was found on the fundus dome of the stomach. (B) On histopathology, cystically dilated and irregularly budded fundic glands were found (H&E stain,  $\times 40$ ).

for Windows Version 9.1 (SAS Institute Inc., Cary, NC, USA). Distributions of categorical variables were compared with uncorrected  $\chi^2$  tests and multiple correlations were calculated by logistic regression. Simple odds ratio and age- and sex-adjusted odds ratios were obtained with 95% confidence interval.

## RESULTS

### 1. Characteristics of subjects in the gastric FGP group compared to the control group

From 1992 to 2007, a total of 22,451 subjects underwent an EGD and 3,357 subjects underwent a colonoscopy at the Health Promotion Center of Incheon St. Mary's Hospital, The Catholic University of Korea. The number of subjects who underwent both an EGD and a colonoscopy within six months was 2,684. FGPs were found in 328 subjects (1.5%) among 22,451 subjects who underwent an EGD, and consecutive colonoscopic evaluation was performed in 158 of those subjects. These 158 subjects were enrolled as the FGP group. A total of 2,356 subjects did not have FGPs and underwent a colonoscopy; these subjects were enrolled in the control

group. Comparison of age did not show any difference between the FGP group and the control group. However, the sex ratio differed between these two groups (Table 1).

FGPs were found in 81.1% (266/328) of women and 18.9% (54/328) of men (odds ratio of 6.25; 95% CI of 4.68-8.34). Of the 328 subjects with FGPs, 310 had only one FGP, while 18 had two or more FGPs. No subject in this study had 10 or more FGPs. Histologically, FGP dysplasia was not found in any of the subjects. Table 1 describes the demographic features of the FGP and control groups.

### 2. FGPs and colorectal neoplasia

Colorectal neoplasia was detected in 16 (1 adenocarcinoma, 15 adenoma) of the 158 subjects (10.1%) enrolled in the FGP group and in 394 (13 adenocarcinoma, 381 adenoma) of the 2,356 subjects (16.7%) in the control group (Table 2). The odds ratio was 0.56 (95% CI of 0.33-0.95). The odds ratio for men diagnosed with colorectal neoplasia was 2.07 (95% CI of 0.95-4.50) and the odds ratio for women was 0.37 (95% CI of 0.16-0.87). The odds ratio for men younger than 50 years of age was 0.54 (95% CI of 0.07-4.23) while the odds ratio for men 50 years of age or older was 2.81 (95% CI of 1.03-7.66) as compared to the control group. The odds ratio for women younger than 50 years of age was 0.33 (95% CI of 0.08-1.38) while the odds ratio for women 50 years of age or older was 0.40 (95% CI of 0.14-1.14; Table 2) as compared to the control group.

Age- and sex-adjusted odds ratios for total FGPs were 0.73 (95% CI of 0.42-1.26), for men 1.78 (95% CI of 0.80-3.98), and for women 0.37 (95% CI of 0.16-0.87; Table 3).

**Table 1.** Demographic Data of Subjects in the Gastric Fundic Gland Polyp Group and the Control Group

	Gastric FGP group	Control group
Total number of patients	158	2,356
Mean age, yr ( $\pm$ SD) <sup>a</sup>	48.5 ( $\pm$ 13.1)	47.8 ( $\pm$ 10.4)
No. of males:No. of females <sup>b</sup>	29:1,209	1,397:959
Number of patients with colorectal neoplasia	16 (10.1%)	394 (16.7%)

FGP, fundic gland polyp.

<sup>a</sup>p=0.50.

<sup>b</sup>p<0.001.

## DISCUSSION

Aging is a critical factor in the development of colorectal

**Table 2.** Odds Ratio of Colorectal Neoplasia in the Fundic Gland Polyp Group and the Control Group

	Gastric FGP group (%)	Control group (%)	Odds ratio (95% CI)	p-value
Total	16/158 (10.1)	394/2356 (16.7)	0.56 (0.33-0.95)	0.03
Male	10/29 (34.5)	283/1397 (20.3)	2.07 (0.95-4.50)	0.06
< 50	1/13 (7.7)	113/859 (13.2)	0.54 (0.07-4.23)	0.31
$\geq$ 50	9/16 (56.3)	170/538 (31.6)	2.81 (1.03-7.66)	0.04
Female	6/129 (4.7)	111/959 (11.6)	0.37 (0.16-0.87)	0.02
< 50	2/73 (2.7)	41/531 (7.7)	0.33 (0.08-1.38)	0.11
$\geq$ 50	4/56 (7.1)	70/428 (16.4)	0.40 (0.14-1.14)	0.08

FGP, fundic gland polyp.

**Table 3.** Age and Sex-adjusted Odds Ratio of Colorectal Neoplasia in the Fundic Gland Polyp group and the Control Group

	Odds ratio	95% CI	p-value
Total	0.73	0.42-1.26	0.25
Male	1.78	0.80-3.98	0.16
Female	0.37	0.16-0.87	0.02

neoplasia.<sup>8</sup> The American College of Gastroenterology guidelines suggests that individuals receive a surveillance colonoscopy starting at the age of 50 when there is no history of colorectal neoplasia before the age of 60 in first relatives of the individual, and when the individual does not have a polyposis syndrome.<sup>9</sup> Based on our findings, the risk of colorectal neoplasia in men 50 years of age or older with FGPs is significantly high enough to recommend surveillance colonoscopy in univariate analysis. However, screening colonoscopies at this age are recommended anyway and patients with FGPs do not need a special surveillance program for colorectal neoplasia in Korea.

Risk factors for colorectal neoplasia include high fat and low fiber diet, low dietary calcium, and specific diseases such as IBD.<sup>10</sup> Other factors such as the use of non-steroidal anti-inflammatory drugs (NSAIDs) is known to be associated with low risk of colorectal neoplasia.<sup>11</sup> In this study, 16-year accumulated data from the Health Promotion Center were analyzed but risk factors or risk-lowering factors for colorectal neoplasia could not be fully covered due to lack of the proper records except IBD. However, most of the subjects were residents in a specific area (Pupyong-gu, Incheon) and their life style might not be so different.

In one German study in which patients were age- and sex-matched, colorectal cancer was more frequently found in FGP patients as compared to control patients.<sup>11</sup> However, in our study, colorectal cancer was found in only one subject with FGPs, and data analysis could not be performed. Though the incidence of colorectal neoplasia is now increasing in Korea, the relatively low incidence of colorectal neoplasia in Koreans as compared to Caucasians is one potential explanation for the low incidence of colorectal neoplasia in both groups.<sup>12,13</sup>

In the present study, FGPs were more frequently found in women, similar to data from studies of Caucasians.<sup>7,14</sup> A pos-

sible influence of hormones such as estrogen on the development of gastric FGPs should be considered. Due to relatively low incidence of FGPs in men, FGPs were found in only 29 men in this study. This might be a limitation of this study and further studies including more male patients with FGPs are anticipated.

Little is known about the role of *Helicobacter pylori* (*H. pylori*) infection in the pathogenesis of FGP. *H. pylori* infection may partially protect patients from the development of FGPs. However, some patients with FGPs were infected with *H. pylori* in their stomach. *H. pylori* status was not included in this study because it was examined only from the available tissues, including routine biopsy and/or FGPs and this limitation might confuse the results.

Several years after the introduction of proton pump inhibitor (PPI) therapy into clinical use, the development of FGPs has been reported in patients receiving such therapy.<sup>15</sup> The development of FGPs seems to be linked to the suppression of gastric acid secretion and not to the use of PPI *per se*. The development of FGPs has also been reported in patients using H2-blockers.<sup>16</sup> In Korea, PPIs were introduced clinically in the middle of the 1990s. The use of PPIs became more widespread in the early 2000s. However, the rate of FGP detection has not changed from the 1990s to the early 2000s in this study (not shown in the results). A prospective randomized control study is necessary to verify whether long-term use of PPI is related to FGPs and colorectal neoplasia.

There are some limitations of this study; this is a retrospective study in one health promotion center, which means that most of the subjects enrolled in this study are interested their health problem and usually did not include people with low socioeconomic class. Other gastrointestinal diseases such as reflux esophagitis and *H. pylori* status were not fully evaluated and drug histories including PPIs were not fully assessed due to limited data.

In conclusion, the statement that "every sporadic FGP patient should undergo colonic surveillance" is not applicable in Korea. Colonoscopic surveillances are not routinely recommended for patients with FGPs in Korea.<sup>17</sup> They can follow the same colonoscopic surveillance schedule as in general population.

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