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ONE MINUTE CONSULT
BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: Fundic gland polyps: Should my patient stop taking PPIs?

A: Fundic gland polyps (FGPs) associated with proton pump inhibitors (PPIs) are generally considered benign, and patients without high-risk features (ie, more than 20 FGPs or polyp size greater than 1 cm) can be advised to continue taking the PPI if there is a clear indication for its use.

It is estimated that 1 in 10 patients in the United States takes a PPI.[1] Long-term PPI use can promote development of FGPs in the stomach because the decrease in stomach acidity leads to increased production of gastrin. Gastrin has trophic effects that lead to parietal cell and enterochromaffin-like cell hyperplasia and the formation of fundic gland cysts and polyps.[2,3] The number and size of FGPs is proportionate to the dose and duration of PPI therapy.[2,4]

SPORADIC AND SYNDROMIC TYPES

There are 2 types of FGPs—sporadic and syndromic—and when encountering FGPs, the most important principle is to distinguish the two (**Table 1**).[5–8] Sporadic FGPs are associated with PPIs. Syndromic FGPs occur with a background of familial adenomatous polyposis (FAP), including classic FAP, attenuated FAP, gastric adenocarcinoma and proximal polyposis of the stomach, and MUTYH-associated polyposis.[9,10]

Sporadic or PPI-associated FGPs exhibit activating beta-catenin gene mutations and rarely show dysplasia.[11,12] In contrast, syndromic or FAP-associated FGPs arise through somatic second-hit mutations of the adenomatous polyposis coli gene. They frequently demonstrate dysplasia, leading to a much higher risk of gastric cancer than PPI-associated FGPs.[6,13] However, these mutations are not routinely checked in histology.

Case reports have described dysplasia in patients with sporadic FGPs who take a PPI, but the true risk of carcinoma in patients with PPI-associated FGPs is unclear.[14] PPI-associated FGPs have not been linked to an increased risk of malignant transformation compared with the risk in the general population.[14,15] While the risk of dysplasia increases with polyp size in FAP-associated FGPs, a study of 132 large (> 1-cm) sporadic FGPs with a median follow-up of 3.2 years reported a rate of dysplasia of 2.6 cases per 1,000-person years of follow-up and no carcinoma.[16] This study may have been limited by its short follow-up period, as reports of cancer with sporadic FGPs do exist.[15]

In the rare cases of sporadic FGPs with carcinomas, most are small polyps with a mean size of 5.4 mm, suggesting that even polyp size may not predict malignancy risk.[14]

CASE 1: FUNDIC GLAND POLYPS, NO DYSPLASIA

A 65-year-old woman underwent esophagogastroduodenoscopy for surveillance of a history of Barrett esophagus without dysplasia. In addition to short-segment Barrett esophagus, 12 sessile polyps 4 to 6 mm in size were found in the body of her stomach. Biopsy results showed fundic gland polyps, negative for dysplasia. The patient has taken omeprazole 20 mg daily for many years. Should she stop using omeprazole?

Benign FGPs are typically small (< 1 cm) sessile polyps with a smooth contour found in the body of the stomach.[7] When upper gastrointestinal endoscopy reveals fewer than 20 gastric polyps with the characteristic appearance of FGPs in the gastric body, biopsy is unnecessary. If the endoscopic appearance has atypical characteristics such as irregular surface, redness, erosion, or depression, the polyp should be resected, as these features have been associated with dysplasia and carcinoma.[14] Polypectomy is also recommended when the size is greater than 1 cm or the

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TABLE 1
Sporadic and syndromic fundic gland polyps compared

Feature	Sporadic fundic gland polyps	Syndromic (FAP-associated) fundic gland polyps
Number	< 20	≥ 20, often hundreds[8]
Location	Body of the stomach	Mostly in the body of the stomach, but can also be seen in the antrum
Presence of dysplasia	Rare	In 25%–40%[5]
Age	Older; average age 40	Under age 40
Sex	More common in females than males	Incidence similar in both sexes[6]
Other EGD findings	None known	Concurrent duodenal adenomas can be seen[7]

EGD = esophagogastroduodenoscopy; FAP = familial adenomatous polyposis

Based on information in references 5–8.

location is antral to assess for other causes such as hyperplastic gastric polyps.[7,17]

The incidence of sporadic FGPs appears to be inversely correlated with *Helicobacter pylori* infection.[3] In the absence of other indications such as dyspepsia and hyperplastic polyps, testing for *H pylori* in the setting of FGPs is unnecessary.

There are no guidelines regarding follow-up of sporadic FGPs. In general, for patients with sporadic FGPs in whom syndromic FGPs are ruled out, PPI therapy can be continued at the lowest effective dose for as long as indicated. However, PPI cessation should be considered if there are more than 20 polyps or polyps larger than 1 cm, especially if there are so many polyps as to give a carpeting appearance.[7,8,14] Polyps should be examined carefully with white light and narrow-band imaging. Those larger than 1 cm or with atypical endoscopic features should be resected completely. Several studies suggest that if dysplasia is found in sporadic FGPs, progression to gastric cancer occurs slowly, if at all, and repeat endoscopy 1 to 3 years after polypectomy is reasonable.[18,19] Evidence demonstrates regression of FGPs if PPIs are stopped, even if they were large in size, and endoscopic follow-up to confirm regression is unnecessary.[7,8]

Resolution of case

The FGPs seen in this 65-year-old patient have typical characteristics of sporadic FGPs (< 20 in number, < 1 cm in size, with sessile appearance and located in the gastric body), without any high-risk features, and thus do not need polypectomy or specific follow-up. The patient can continue PPI therapy and surveillance esophagogastroduodenoscopy as indicated for Barrett esophagus.

CASE 2: YOUNG MAN WITH 'CARPETING' AND UNKNOWN FAMILY HISTORY

A 32-year-old man underwent esophagogastroduodenoscopy for evaluation of iron deficiency anemia. Innumerable polyps were found carpeting the fundus of his stomach. Biopsies showed FGPs with low-grade dysplasia. The patient had recently started taking omeprazole for treatment of gastroesophageal reflux disease. He was adopted and his family history is unknown. Should he stop his PPI?

Any of these risk factors raises suspicion for an underlying FAP syndrome:

- The number of gastric polyps exceeds 20
- The patient is younger than 40
- Polyps are present in the antrum
- Dysplasia is seen on polyp biopsy
- There is concurrent duodenal adenoma.

If possible, a detailed family history of cancer, especially colon or other gastrointestinal tract neoplasm, should be sought. Colonoscopy is indicated to evaluate for colonic polyps or neoplasms. Genetic evaluation should be considered in young patients with carpeting of polyps or if there is a family history of cancer. If the diagnosis of FAP is confirmed, the patient should be managed accordingly as described in guidelines.[5,8]

Resolution of case

This patient has multiple factors (age < 40, large number of polyps with dysplasia) concerning for syndromic FGPs. He should undergo colonoscopy and be referred for genetic evaluation. If an inherited polyposis syndrome is diagnosed, the development of his FGPs is unlikely associated with PPI use, and the patient can continue to use PPIs to manage his reflux disease. In fact, acid suppression may protect against dysplasia in syndromic FGPs.[20] On the other hand, if

TABLE 2
Indications for long-term use of proton pump inhibitors

Definitive (> 8 weeks)	Conditional
Barrett esophagus (unrelated to GERD symptoms or esophagitis)	PPI-responsive, endoscopy-negative reflux disease with recurrence on PPI cessation
Erosive esophagitis Los Angeles classification grade C/D	PPI-responsive functional dyspepsia with recurrence on PPI cessation
Esophageal stricture due to GERD	PPI-responsive upper-airway symptoms with recurrence on PPI cessation
NSAID/antiplatelet users with increased risk of ulcers and bleeding	Refractory steatorrhea in chronic pancreatic insufficiency with enzyme replacement
Eosinophilic esophagitis	Secondary prevention of peptic ulcers without concomitant antiplatelet drugs
Pathological hypersecretory conditions (Zollinger-Ellison syndrome)	
Prevention of progression of idiopathic pulmonary fibrosis	

GERD = gastroesophageal reflux disease; NSAID = nonsteroidal anti-inflammatory drug; PPI = proton pump inhibitors

Based on information in references 21 and 22.

a diagnosis of an inherited polyposis syndrome cannot be made, the patient should be advised to stop PPIs and manage his reflux disease with lifestyle modification or a histamine-2 blocker. Whether or not he has syndromic FGPs, this patient should undergo surveillance esophagogastroduodenoscopy to follow up on the low-grade dysplasia.

BOTTOM LINE: NUMBER AND SIZE OF POLYPS, NEED FOR PPI

If syndromic FGPs are ruled out and the patient is taking a PPI, we recommend considering PPI cessation if there are 20 or more FGPs or polyp size is larger than 1 cm. Polyps that are larger than 1 cm or atypical should be resected to evaluate for dysplasia and rule out other types of gastric polyps, but endoscopic surveillance is not needed if no atypical features are found.

With increasing use of PPIs and increasing incidence of PPI-associated FGPs, updated evidence is needed to elucidate the natural history of these polyps and identify risk factors for malignant transformation. Regardless of the presence of any gastric polyp, a review of the indications for chronic PPI use is warranted for all patients taking a PPI for longer than 8 weeks (**Table 2**).[21,22] Inappropriate PPI use should be discontinued to minimize the adverse effects, including FGPs associated with long-term PPI use. ■

DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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