THE RELATIONSHIP BETWEEN FUNDIC GLAND POLYP AND COLONIC POLYP OR COLORECTAL CARCINOMA

FUNDİK GLAND POLİPLERİ İLE KOLON POLİBİ VEYA KOLOREKTAL KANSER İLİŞKİSİ

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ABSTRACT

PURPOSE: Conflicting results are present whether colorectal carcinoma and colorectal polyps are more frequently detectable in patients with fundic gland polyp (FGP). The aim of this study was to evaluate the interaction between FGP and colorectal neoplasm in a Turkish population.

MATERIALS AND METHODS: A retrospectively analyzed case-control study was performed. Patients with FGP who also underwent colonoscopy recently were classified as the FGP group, and patients who had no FGP on endoscopy and had a colonoscopy within six months were classified as the control group. The colorectal polyp and colorectal carcinoma prevalence were compared between groups.

RESULTS: Fifty patients were included in the FGP group and 158 patients in the control group. There was no statistically significant difference between two groups according to colorectal polyp detection, but colorectal carcinoma was more frequently seen in patients with FGP. When female patients were included in the analysis, patients with FGP had a higher prevalence for colorectal carcinoma. Similar difference was not detected in men.

CONCLUSION: Colorectal carcinoma is more common in female patients with FGP compared to female patients without FGP.

Key words: *colonic polyps, colonoscopy, colorectal carcinoma, fundic gland polyp, gastric polyps*

ÖZET

AMAÇ: Fundik gland polip (FGP) olan hastalarda kolorektal kanser ve kolorektal polip sıklığının artıp artmadığına dair çelişkili veriler mevcuttur. Bu çalışmanın amacı ülkemizdeki bir hasta grubunda FGP ile kolorektal neoplaziler arasındaki ilişkiyi ortaya koymaktır.

GEREÇ VE YÖNTEM: Bu çalışma retrospektif olarak yapılmış bir vaka-kontrol çalışmasıdır. Endoskopide FGP saptanan ve yakın zamanda kolonoskopi yapılmış olan hastalar FGP grubu olarak alındı. Endoskopide FGP saptanmayan ve endoskopi yapılan tarihe göre 6 ay içinde kolonoskopi yapılmış olan hastalar kontrol grubu olarak çalışmaya dahil edildi.

BULGULAR: FGP grubunda 50 ve kontrol grubunda 158 hasta çalışmaya dahil edildi. İki grup kıyaslandığında kolorektal polip sıklığının benzer olduğu izlendi, ancak FGP grubunda kolorektal kanser daha fazla saptandı. Cinsiyete göre alt grup analizi yapıldığında kadınlarda FGP grubunda kolorektal kanser riskinin artmış olduğu izlendi, ancak benzer bir ilişki erkeklerde saptanmamıştır.

SONUÇ: FGP olan kadın hastalarda kolorektal karsinom sıklığı FGP olmayan kadınlara göre daha fazladır.

Anahtar kelimeler: *Kolon polipleri, kolonoskopi, kolorektal karsinom, fundik gland polip, mide polipleri*

INTRODUCTION

Fundic gland polyps (FGP) are one of the two most common seen histological types of gastric polyps, worldwide. In Western countries where Helicobacter pylori is uncommon, FGP is the mostly seen polyp of the stomach, whereas in regions where Helicobacter pylori is frequently seen, such as Turkey, FGP is seen much rarely and accounts the second mostly seen gastric

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polyp after hyperplastic polyps (1-5). The association between FGP and familial adenomatous polyposis (FAP) has been known for years (6). On this basis, studies were carried out to examine the relationship between FGP and colorectal neoplasia, but conflicting results were achieved whether colorectal carcinoma and colorectal adenomatous polyps were more frequently detectable in patients with FGP (7-11).

To the best of our knowledge, there is no study evaluating the correlation between FGP and colorectal neoplasms in Turkey. The aim of this study was to evaluate the relation between FGP and colorectal neoplasms in a Turkish population.

MATERIALS AND METHODS

The clinical records of patients who had esophagogastroduodenoscopy (EGD) between January 2008 and August 2015 were retrospectively analyzed. Patients who underwent EGD and colonoscopy within six months between the two procedure, and had FGP on EGD were included in the study as the case group. The diagnosis of FGP was confirmed by histological evaluation. The control group consisted of all patients who underwent colonoscopy between September 2015 and December 2015, and had no FGP detected on EGD, which was performed within six months before or after the colonoscopy was performed. Patients with known colorectal adenomatous polyps or colorectal carcinoma history, colonic surgery and inflammatory bowel disease were not included in the control group. Fifty patients in the FGP group and 158 patients in the control group were included in the study. All endoscopic procedures were performed with standard video-endoscopes (GIF type-160 and 180; Olympus).

The patients' demographic features, endoscopic and laboratory findings were investigated and obtained from the recorded computerized database. Subjects who had known gastric malignancies, FAP or inflammatory bowel diseases were excluded from the control group. Informed consent was taken and the local Medical Ethics Committee approved the study design and methods (Approval number: 17.02.2016 / 49).

All statistical analyses were performed with the SPSS 17.0 software (SPSS, Inc; Chicago, IL, USA). Means and standard deviations were calculated and Student t-Test was used to determine the differences between groups. Chi-square test was used to compare categorical variables. Age and sex adjusted odds ratios for colorectal adenomatous polyps and colorectal carcinoma were calculated from multiple logistic regression models. P values less than 0.05 were considered as significant.

RESULTS

Between the time interval the data was evaluated, 30180 patients underwent EGD, and 105 patients had FGP detected on EGD (0.35%). The mean age of all FGP patients was 57.12 years and women constituted the majority (70 women and 35 men). Among these 105 patients, 50 patients underwent colonoscopy within 6 months before or after EGD, and were suitable for inclusion to the study. The control group consisted of 158 patients with no FGP detected on EGD. The mean age of the FGP group and control group were 59.56 ± 14.83 and 56.11 ± 13.07 years, respectively. Patients with colorectal carcinoma were statistically significantly older than the patients with polyps and normal colonoscopy (72.38 ± 9.24, 59.65 ± 10.6 and 54.83 ± 14.2, respectively). The FGP group had a female dominancy and included 37 (74%) women and 13 (26%) men, whereas the control group consisted of 75 (47.5%) men and 83 (52.5%) women (p: 0.015).

Five patients in the FGP group (10%) and 4 patients in the control group (2.5%) had colorectal carcinoma (p: 0.038). An age- and sex- adjusted odds ratio of 3.00 (95% CI of 0.50 - 10.38, p: 0.14) was detected for colorectal carcinoma in patients with FGP. Between the groups colonic polyp detection rate was not statistically significant (13 (26%) and 49 (31%) patients in FGP and control group, respectively). On pathological analysis, adenomatous polyps were detected in 76.92% and 85.7% of patients with polyps, respectively in FGP and control groups. The pathological results of the polyps are shown in **Table 1.** The mean number and size of the polyps in the FGP group were 2.33 and 5.17 mm, and 1.61 and 6.37 mm in the control group (no statistically significant difference was detected).

Table 1. The distribution of the polyps and colorectal cancer in the FGP and control group

	FGP (n:50)	Control (n:158)	p
Colorectal carcinoma	5 (10%)	4 (2.5%)	**0.038**
Polyp	13 (26%)	49 (31%)	0.499
Adenomatous polyp	10 (20%)	42 (26.1%)	0.349
Tubular adenoma	7 (14%)	38 (24.1%)	0.133
Villous and tubulovillous adenoma	3 (6%)	4 (2.5%)	0.362
Hyperplastic polyp	2 (4%)	3 (1.9%)	0.595
Inflammatory polyp	1 (2%)	4 (2.5%)	1

FGP: Fundic gland polyp

The statistical analysis was also performed separately for men and women. Eighty-eight men were included in the study, 13 in the FGP and 75 in the control group. In the men FGP group colorectal carcinoma and colon polyps were detected in one (7.7%) and five (38.5%) patients, respectively. In the men control group 3 (4%) and 28 (37.3%) had colorectal carcinoma and colon polyps (the difference was not statistically significant). Thirty-seven women in the FGP group and 83 in the control group were evaluated. In female patients colorectal carcinoma was present in one patient in the control group (1.2%) and 4 patients in the FGP group (10.8%) (p: 0.013).

Ten patients in the FGP group (20%) had Helicobacter pylori on histopathological examination, whereas in the control group the incidence was 52.8% (p<0.001). Among the 105 patients who had FGP on endoscopy, Helicobacter pylori was detected in 23 patients (21.9%).

Thirty-nine patients in the FGP group were using proton pump inhibitor (PPI) for more than 6 months at the time of EGD (78%). The colorectal carcinoma and polyps in patients who were not taking PPIs were detected in 1 and 3 patients, respectively (9.1% and 27.3%). In patients who were taking PPIs, respectively 3 and 10 patients had colorectal carcinoma and polyps (10.3% and 25.6%). The difference was not statistically significant.

DISCUSSION

FGP is a relatively new group of polyps detected in the stomach, which was first described in 1976 (12). Sporadic FGPs are seen in the gastric fundus and body, are generally small and multiple, their surface is smooth, shiny or translucent and the surrounding gastric mucosa is normal (13-15). On histopathologic examination cystically dilated glands lined by mucus and parietal and chief cells are seen (14, 16). Dysplasia is uncommon in patients with FGP, and FGP predicts a low risk of future gastric carcinogenesis (15, 17, 18). FGP is the mostly seen gastric polyp in Western countries and the prevalence of FGP has been reported to be up to 7.7% (2, 10, 19, 20). In our literature review we could find no data about the prevalence of FGP in Turkey. But studies from Turkey showed that polyps are detected in 1-2% of endoscopic examinations and FGPs accounts only around 10% of all gastric polyps (3-5, 21). This shows that the FGP prevalence in Turkey is much lower than the Western countries. There is also evidence that FGP rates are increasing in populations where it was seen more rarely in the past (22).

Conflicting results exists whether colorectal carcinoma and colorectal adenomatous polyps are more frequently detectable in patients with FGP (7-11, 23). Lee et al. found a higher prevalence of colorectal carcinoma in patients with FGP (11). Similarly Jung et al. showed that colorectal neoplasm was detected frequently in patients with FGP, and they found a high prevalence of colorectal carcinoma (12.5%) (23). One study showed that colorectal carcinoma was frequently seen in FGP patients, but adenomatous polyps were not significantly frequent, whereas another study showed increased risk for colorectal adenoma just in women (7,10). Two studies showed no interaction between FGP and colorectal neoplasia (8, 9). Because FGP have different characteristics in Turkey, it is not known whether these results could be generalized to the Turkish population, and to the best of our knowledge there is no study evaluating colorectal neoplasms in patients with FGP in Turkey. Our study revealed that colorectal carcinoma prevalence is increased in patients with FGP. The underlying pathogenetic association between FGP and colorectal carcinoma remains unclear and needs to be investigated.

When male and female patients were evaluated separately only female FGP patients showed an increased prevalence of colorectal carcinoma. Similarly Genta el al. showed increased prevalence of colonic adenomas only in women, but not in men (10). In the light of these findings we can say that colorectal neoplasia is more common in women patients with FGP, but a similar association cannot be stated for men with FGP. The low incidence of FGP in men may be an explanation for these insufficient data, but Genta et al's study included a larger number of men and could not find an interaction between FGP and colorectal neoplasia in men (10). We could not find an explanation why the gender had an effect on these results. This difference may be a coincidence and must be validated with further studies.

We also could not find an explanation why the colorectal carcinoma prevalence was higher, but the adenoma prevalence was similar. A similar result was detected in the study from Lee et al. (11). They found an increase in colorectal carcinoma but not in colorectal adenomatous polyps (11). It has been accepted that most colorectal carcinomas arise from adenomatous polyps, but this is not essential (24). Our study supports that colorectal carcinomas in patients with FGP may not develop with adenoma-carcinoma sequence and may be sporadic, but this hypothesis must be supported with further larger studies.

Long term use of PPIs is an important risk factor for FGP (1, 25). We analyzed patients with and without PPI use separately to evaluate whether the PPI use had an effect on the increased risk of colorectal carcinoma. Similar colorectal carcinoma and polyp detection rates were achieved in patients with and without chronic PPI use. Our findings suggest that the increased risk for colorectal carcinoma is not due to the PPI use, but the study population of patients with FGP who were not taking PPIs was too low to give this advice strongly. Larger studies including larger number of patients with and without PPI use are needed to investigate the effect of PPI on the risk increase of colorectal carcinoma in patients with FGP.

The retrospective design and the low study number are limitations of our study. FGP is an uncommon disorder and the prevalence of FGP in Turkey is much more uncommon. Also in the study only patients with FGP

who had colonoscopy performed was included in the study. Because of these reasons our study population stayed at a low number. Larger multicenter prospectively designed studies may be helpful to give definite results.

CONCLUSION

Colorectal polyps are not more frequently seen in patients with FGP compared to patients without FGP in Turkey. Colorectal carcinoma tends to be more common in female patients with FGP compared to female patients without FGP. Similar findings could not be found in male patients with FGP. The exact conditions of these differences remain unclear and further effort is needed.

The authors declare no conflict of interest.

REFERENCES

1.)Jalving M, Koornstra JJ, Wesseling J, Boezen HM, DE Jong S, Kleibeuker JH. Increased risk of fundic gland polyps during long-term proton pump inhibitor therapy. Aliment Pharmacol Ther. 2006; 24(9): 1341-8.
2.)Sonnenberg A, Genta RM. Prevalence of benign gastric polyps in a large pathology database. Dig Liver Dis. 2015; 47(2): 164-9.
3.)Atalay R, Solakoğlu T, Ozer Sarı S, et al. Evaluation of gastric polyps detected by endoscopy: a single-center study of a four-year experience in Turkey. Turk J Gastroenterol. 2014; 25(4): 370-3.
4.)Vatansever S, Akpınar Z, Alper E, et al. Gastric polyps and polypoid lesions: Retrospective analysis of 36650 endoscopic procedures in 29940 patients. Turk J Gastroenterol. 2015; 26(2): 117-22
5.)Gencosmanoglu R, Sen-Oran E, Kurtkaya-Yapicier O, Avsar E, Sav A, Tozun N. Gastric polypoid lesions: analysis of 150 endoscopic polypectomy specimens from 91 patients. World J Gastroenterol. 2003; 9(10): 2236-9.
6.)Bertoni G, Sassatelli R, Nigrisoli E, et al. Dysplastic changes in gastric fundic gland polyps of patients with familial adenomatous polyposis. Ital J Gastroenterol Hepatol. 1999; 31(3): 192-7.
7.)Teichmann J, Weickert U, Riemann JF. Gastric fundic gland polyps and colonic polyps - is there a link, really? Eur J Med Res. 2008; 13(5): 192-5.
8.)Hwang SM, Kim BW, Chae HS, et al. Gastric Fundic Gland Polyps and Their Relationship to Colorectal Neoplasia in Koreans:A 16-year Retrospective Study. Korean J Gastroenterol. 2011; 58(1): 20-4.
9.)Cimmino DG, Mella JM, Luna P, et al. Risk of colorectal polyps in patients with sporadic gastric polyps: A case-control study. World J Gastrointest Endosc. 2013; 5(5): 240-5.
10.)Genta RM, Schuler CM, Robiou CI, Lash RH. No Association Between Gastric Fundic Gland Polyps and Gastrointestinal Neoplasia in a Study of Over 100,000 Patients. Clin Gastroenterol Hepatol. 2009; 7(8): 849-54.
11.)Lee LS, Choi Y, Jung JY, et al. Do we need colonoscopy verification in patients with fundic gland polyp? Intest Res. 2016; 14(2): 172-7.
12.)Elster K. Histologic classification of gastric polyps. Curr Top Pathol. 1976; 65: 77-93.
13.)Stolte M, Sticht T, Ebert D, Ebert D, Finkenzeller G. Frequency, location, age and sex distribution of various types of gastric polyp. Endoscopy. 1994; 26(8): 659-65.
14.)Weston BR, Helper DJ, Rex DK. Positive predictive value of endoscopic features deemed typical of gastric fundic gland polyps. J Clin Gastroenterol. 2003; 36(5): 399-402.
15.)Goddard AF, Badreldin R, Pritchard DM, Walker MM, Warren B; British Society of Gastroenterology. The management of gastric polyps. Gut. 2010; 59(9): 1270-6.
16.)Randall GL, Randall WB. The histopathology of fundic gland polyps of the stomach. Am J Clin Pathol. 1986; 86(4): 498-503.
17.)Stolte M, Vieth M, Ebert MP. High-grade dysplasia in sporadic fundic gland polyps: clinically relevant or not. Eur J Gastroenterol Hepatol. 2003; 15(11): 1153-6.
18.)Kishikawa H, Kaida S, Takarabe S, et al. Fundic gland polyps accurately predict a low risk of future gastric carcinogenesis. Clin Res Hepatol Gastroenterol. 2014; 38(4): 505-12.
19.)Declich P, Isimbaldi G, Sironi M, et al. Sporadic fundic gland polyps: an immunohistochemical study of their antigenic profile. Pathol Res Pract. 1996; 192(8): 808-15.
20.)Dickey W, Kenny BD, McConnell JB. Prevalence of fundic gland polyps in a western European population. J Clin Gastroenterol. 1996; 23(1): 73–5.
21.)Kekilli M, Beyazit Y, Karaman K, et al. Endoscopic and pathological aspects of gastric polyps: a Turkish referral center study. Hepatogastroenterology. 2012; 59(116): 1147-9.
22.)Cao H, Wang B, Zhang Z, Zhang H, Qu R. Distribution trends of gastric polyps: an endoscopy database analysis of 24 121 northern Chinese patients. J Gastroenterol Hepatol. 2012; 27(7): 1175-80.
23.)Jung A, Vieth M, Maier O, Stolte M. Fundic gland polyps (Elster's cysts) of the gastric mucosa. A marker for colorectal epithelial neoplasia? Pathol Res Pract. 2002; 198(11): 731-4.
24.)Leslie A, Carey FA, Pratt NR, Steele RJ. The colorectal adenoma-carcinoma sequence. Br J Surg. 2002; 89(7): 845-60.
25.)Ally MR, Veerappan GR, Maydonovitch CL, et al. Chronic proton pump inhibitor therapy associated with increased development of fundic gland polyps. Dig Dis Sci. 2009; 54(12): 2617-22.