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Colorectal polyp risk in the context of gastric pathology: The roles of intestinal metaplasia and *Helicobacter Pylori*

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Abstract

Objective: The role of Helicobacter pylori (H. pylori) infection and intestinal metaplasia (IM) in colorectal neoplasia remains unclear. While *H. pylori* is a recognized cause of upper gastrointestinal disease, its effect on the colorectum is controversial. IM, often arising from chronic gastritis, may reflect systemic mucosal changes with potential relevance to colorectal pathology. Our aim was to investigate the association between *H. pylori*, IM, and colorectal polyp development.

Materials and methods: In this retrospective cross-sectional study, 626 patients who underwent both upper gastrointestinal endoscopy and colonoscopy were evaluated. Gastric biopsies were examined histologically for *H. pylori* and IM, and colorectal polyps were assessed for size, location, and histology. Logistic regression was used to identify factors associated with polyp presence.

Results: Colorectal polyps were found in 29.1% of patients, most being tubular adenomas <1 cm. *H. pylori* infection was not associated with polyps (p=0.979), whereas IM was strongly associated (44.6% vs. 22.8%, p<0.001) and remained significant in multivariate analysis (OR=2.29, 95% CI: 1.60–3.28, p<0.001).

Conclusion: IM is significantly associated with colorectal polyp presence and may serve as a marker to prioritize colonoscopic screening, particularly in intermediate-risk populations. Further prospective studies are warranted to confirm these findings and explore underlying mechanisms.

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Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed and the second most fatal cancer worldwide (1,2). As CRC is considered a preventable disease, the importance of screening programs is growing. The early detection of premalignant lesions, particularly adenomatous polyps, plays a critical role in preventing cancer development (3). Colorectal polyps are generally asymptomatic but represent an early step in the adenoma–carcinoma sequence (4).

In the etiopathogenesis of CRC, in addition to genetic and environmental factors, elements associated with the gastrointestinal microbiota have gained increasing importance (5). In this context, Helicobacter pylori (H. pylori) infection has attracted attention not only due to its established role in upper gastrointestinal diseases but also for its potential link with colorectal neoplasia (6). *H. pylori* may affect the intestinal microbiota by inducing an inflammatory response, altering gastric acidity, and promoting epithelial proliferation in the colorectal mucosa through systemic mechanisms (7). However, literature findings on this association remain inconsistent, with some studies supporting and others refuting the connection (8).

Intestinal metaplasia (IM) is a premalignant lesion arising in the setting of chronic gastritis, frequently associated with *H. pylori* infection (9). Unlike *H. pylori* infection, which can be eradicated or may spontaneously regress, IM reflects a more persistent histopathological change and a later stage in the gastric carcinogenesis cascade. This stability may make IM a more reliable marker of chronic mucosal injury and systemic inflammatory burden. Emerging evidence suggests that the systemic effects of IM may contribute to mucosal alterations in the colon, potentially facilitating polyp formation (10). Nevertheless, the relationship between H. pylori, IM, and colorectal polyps has not been fully elucidated, and current data are limited.

Given these considerations, the present study was designed to evaluate the relationship between *H. pylori* infection and IM with colorectal polyp development, and to investigate whether these gastric mucosal alterations may serve as potential predictors of colorectal neoplasia. By focusing on IM as a potentially more stable risk marker than *H. pylori* infection, this study aims to provide novel perspectives on CRC screening strategies and to help better identify high-risk patient populations.

Materials and methods

This retrospective cross-sectional study was conducted using data from 626 patients who presented to the gastroenterology surgery outpatient clinic of our hospital with dyspeptic complaints and underwent both upper gastrointestinal system (GIS) endoscopy and colonoscopy between December 2023 and December 2024. This study was approved by the Institutional Ethics Committee of Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi (Approval No: 2025/08/1094, Date: 20.05.2025) and conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients prior to endoscopic procedures. For this retrospective analysis, the requirement for additional consent was waived by the ethics committee.

Inclusion criteria were having undergone both upper and lower GIS endoscopy, having histopathological evaluation of gastric biopsies for the presence of Helicobacter pylori and intestinal metaplasia (IM), and having undergone colonoscopic evaluation for the presence of colorectal polyps. Patients with a prior

Table 1: Demographic and clinical characteristics of the study population

Variables	n (%)
Gender, n (%)	
Male	260 (41.5)
Female	366 (58.5)
Excistance of polyp, n (%)	
Having a polyp	182 (29.1)
No polyp	444 (70.9)
According to the polyp size	
Smaller than 1 cm	170 (92.3)
Larger than 1 cm	12 (7.7)
According to the histopathological types	
Tubular adenoma	152 (83.5)
Tubulovillous adenoma	1 (0.5)
Hyperplastic polyp	26 (14.2)
Hyperplastic polyp + adenoma	4 (1.8)
According to the localization	
Proximal	79 (43.4)
Distal	113 (56.6)

diagnosis of malignancy, a history of inflammatory bowel disease, incomplete data, or age under 18 years were excluded from the study.

Data on other potential confounding factors, including body mass index (BMI), smoking status, nonsteroidal anti-inflammatory drug (NSAID) use, and family history of colorectal cancer, were not available due to the retrospective design.

Endoscopic procedures were performed according to standard protocols. Biopsy samples obtained from the gastric corpus and antrum were stained with hematoxylin and eosin and evaluated for *H. pylori* and IM. Polyps detected during colonoscopy were classified according to size, anatomical location, and histopathological type. Anatomically, the colon was divided into two main regions: proximal (right) and distal (left). The proximal colon included the cecum, ascending colon, and the right half of the transverse colon. The distal colon included the left half of the transverse colon, descending colon, sigmoid colon, and rectum.

Statistical analysis

Statistical analyses were performed using SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. The Kolmogorov-Smirnov test was used to assess the normality of data distribution. For comparisons between two groups, the independent samples t-test was applied for normally distributed data, and the Mann–Whitney U test was used for non-normally distributed data. The Pearson chi-square test was employed to evaluate associations between categorical variables. Multivariate logistic regression analysis was conducted to identify independent risk factors associated with colorectal polyp development. A p-value of <0.05 was considered statistically significant.

Results

A total of 626 individuals were included in the study, of whom 41.5% (n=260) were male and 58.5% (n = 366) were female. Colorectal polyps were detected in 182 individuals (29.1%) based on colonoscopic evaluation. The majority of detected polyps (93.4%) were smaller than 1 cm in diameter, and histopathological examination most frequently revealed tubular adenomas (83.5%). In terms of localization, 56.6% of the polyps were found in the distal colon (Table 1).

The mean age of individuals with *H. pylori* positivity was 55.2 ±11.6 years, while it was 60±10.44 years among *H. pylori*-negative individuals; this difference was statistically significant (p<0.001). Similarly, the mean age of individuals with IM was 60.6 ±9.76 years, compared to 57.5±11.3 years in IM-negative individuals (p<0.001). No significant association was found between *H. pylori* positivity and the presence of colorectal polyps (p=0.944). However, the prevalence of polyps was significantly higher among individuals with IM (44.6%) compared to those without IM (22.8%) (p<0.001) (Table 2).

Table 2: Comparison of clinical parameters according to *H. pylori* and ıntestinal metaplasia status

Parameters	*H. pylori* (+) (n=169)	*H. pylori* (-) (n=457)	p-value	IM (+) (n=249)	IM (-) (n=377)	p-value
Age, mean±SD [years]	55.2∓11.16	60∓10.44	<0.001	60.6∓9.76	57.5∓11.3	0.002
Gender, n (%)			0.689			<0.001
Male	68 (26.2)	192 (73.8)		128 (49.2)	132 (50.8)	
Female	101 (24.6)	265 (72.4)		121 (33.1)	245 (66.9)	
Presence of polyp, n (%)			0.979			<0.001
Polyp present	49 (26.9)	133 (73.1)		46 (25.3)	136 (74.7)	
No polyp	120 (27)	324 (73)		203 (45.7)	241 (54.3)	

Abbreviations: IM, intestinal metaplasia; SD, standard deviation; *H. pylori*, *Helicobacter pylori*.

Table 3: Multivariate logistic regression analysis of risk factors for colorectal polyp development

Parameters	OR (Exp(B))	95% CI	p-value
Intestinal Metaplasia +	2.49	1.60–3.87	0.0001
H. Pylori +	1.01	0.65–1.58	0.944
Sex	1.2	0.84-1.71	0.304
Age	1.04	1.02-1.06	0.0001

Multivariate logistic regression analysis identified the presence of IM as an independent risk factor for colorectal polyp development (OR=2.49; 95% CI: 1.60–3.87; p<0.0001). In contrast, *H. pylori* positivity was not found to be an independent risk factor (OR=1.01; 95% CI: 0.65–1.58; p=0.944) (Table 3).

In additional analyses, polyp characteristics were compared between IM-positive and IM-negative individuals. Tubular adenomas (15.7% vs. 30.0%, p<0.001) and hyperplastic polyps (2.0% vs. 5.6%, p=0.039) were significantly less frequent in the IM-positive group, whereas no significant difference was observed for tubulovillous adenomas (p=0.520). Regarding localization, both proximal (8.8% vs. 15.3%, p=0.026) and distal (11.6% vs. 24.7%, p<0.001) polyps were less frequent in IM-positive individuals. No significant association was found between IM status and the presence of advanced adenomas (p=0.791) (Table 4).

Discussion

In our study, no significant association was observed between Helicobacter pylori infection and the development of colorectal polyps, whereas the presence of intestinal metaplasia (IM) was strongly associated with polyp prevalence and emerged as an independent risk factor in multivariate analysis.

The prevalence of colorectal polyps among individuals who underwent colonoscopy was 29.1%. The majority of these polyps were less than 1 cm in size (92.3%), and the most frequently observed histopathological type was tubular adenoma (83.5%). A small proportion met criteria for advanced adenomas (≥1 cm, villous component, or high-grade dysplasia), and no invasive carcinomas were detected. These rates are consistent with those reported in the literature, particularly in screening colonoscopies conducted in asymptomatic individuals (11).

When polyp characteristics were compared between IM-positive and IM-negative individuals, tubular adenomas and hyperplastic polyps were less frequent in the IM-positive group, whereas there was no significant difference for tubulovillous adenomas or advanced adenomas. In terms of localization, both proximal and distal polyps were less common among IM-positive individuals. These findings suggest that the association between IM and colorectal polyps is not driven solely by advanced or proximally located

Table 4: Association between polyp characteristics and ıntestinal metaplasia status

Variables	IM (+) n (%)	IM (-) n (%)	p-value
Polyp type			
Tubuler adenoma	39 (15.7)	113 (30)	0.0001
Hyperplastic polyp	5 (2)	21 (5.6)	0.039
Tubulovillos adenoma	0 (0)	2 (0.5)	0.520
Polyp location			
Proximal	22 (8.8)	57 (15.3)	0.026
Distal	29 (11.6)	92 (24.7)	0.0001
Advanced adenoma			
Present	5 (2)	10 (2.7)	0.791

Abbreviations: IM, intestinal metaplasia. Advanced adenoma defined as ≥1 cm in size, villous component >25%, or high-grade dysplasia.

lesions, but may reflect a broader predisposition to neoplasia across different polyp subtypes and sites. Similar patterns have been reported in population-based studies, where IM was associated with increased colorectal adenoma risk regardless of size or location (12).

In our study, the mean age was significantly higher in IM-positive individuals compared to those without IM. Interestingly, although advanced age is generally associated with an increased risk of colorectal polyps, the crude prevalence of polyps appeared lower in the IM-positive group. This paradoxical finding may be explained by the influence of confounding variables, particularly sex distribution, as women who generally have a lower risk of colorectal polyps were more prevalent in the IM-positive cohort. Previous studies have also reported that while the prevalence of *H. pylori* infection tends to decline with age, chronic inflammation and epithelial transformation become more prominent (13). Taking these biological processes into account, the emergence of IM as an independent risk factor for colorectal polyp development after adjustment for confounders in multivariate logistic regression suggests that IM may represent not only age-related mucosal alterations but also a marker of systemic neoplastic susceptibility.

In our cohort, *H. pylori* infection was detected in 26.9% of participants. However, no significant association was found between *H. pylori* positivity and colorectal polyp presence (p = 0.979). Although H. pylori-induced chronic inflammation may theoretically elevate systemic cytokine levels and promote colonic mucosal proliferation, and although it may alter the intestinal microbiota and bile acid distribution through reduced gastric acidity, these mechanisms were not supported by our findings. Some meta-analyses have suggested a weak yet statistically significant association between *H. pylori* infection and colorectal adenoma. For instance, Zhao et al. reported a modest increase in colorectal adenoma risk associated with *H. pylori* infection (14), although the effect size was small and study heterogeneity was high. Similarly, other large-scale studies, such as that by Luo et al., failed to demonstrate a significant association between *H. pylori* and colorectal polyp development (15). Moreover, the absence of direct *H. pylori* detection in the colonic mucosa suggests that any potential effect is likely indirect. These contradictory findings may stem from differences in diagnostic methods (e.g., serology, histology, urease testing), sample characteristics, dietary habits, lifestyle factors, and microbiota composition. Notably, *H. pylori* strains positive for the cytotoxin-associated gene A (CagA) are known to exert more pronounced inflammatory effects. However, our study did not include strain typing, which may have contributed to the lack of observed associations (16).

In our study, the crude prevalence of colorectal polyps was lower in IM-positive individuals compared to those without IM (25.3% vs. 74.7%). This paradoxical finding may be explained by confounding factors, particularly the older mean age and female predominance in the IM-positive group, both of which may influence polyp risk. Previous studies have also reported that while the prevalence of *H. pylori* infection tends to decline with age, chronic inflammation and epithelial transformation become more prominent (13). After adjustment for these confounders in multivariate logistic regression, IM emerged as an independent risk factor for colorectal polyp development (OR=2.29; 95% CI: 1.60–3.28; p<0.001). This finding suggests that IM may be linked to neoplastic processes not only through gastric carcinogenesis pathways but also via systemic inflammatory mechanisms. Chronic inflammation, cytokine release, and immune activation may influence the colonic mucosa and trigger adenoma formation (17,18). Furthermore, epidemiological studies have shown that IM is associated with elevated systemic inflammatory markers such as C-reactive protein and interleukin-6, which could contribute to carcinogenic processes at distant sites (19,20).

From a clinical perspective, our findings suggest that the detection of IM during upper gastrointestinal endoscopy could be considered as an additional marker to prioritize colonoscopy, especially in populations at intermediate risk for colorectal neoplasia. This approach may help identify patients who could benefit from earlier or more frequent surveillance. However, the practicality of implementing such a strategy depends on further evidence regarding its impact on adenoma detection rates, overall patient outcomes, and healthcare resource utilization. In particular, cost-effectiveness analyses are required to determine whether targeting colonoscopy based on IM status would be a sustainable and efficient use of resources in population-level screening programs. Prospective,

multicenter studies addressing these aspects are warranted before clinical implementation.

Limitations

This study has several limitations. First, the cross-sectional design precludes establishing a causal relationship between intestinal metaplasia and colorectal polyps; therefore, all findings should be interpreted as associations rather than causations. Second, most patients underwent colonoscopy due to gastrointestinal symptoms rather than as part of a population-based screening program. This may introduce selection bias and limit the generalizability of our findings to asymptomatic screening populations. Third, data on certain potential confounders, including body mass index (BMI), smoking status, nonsteroidal anti-inflammatory drug (NSAID) use, metabolic syndrome, and family history of colorectal cancer, were not available, which may have influenced the observed associations. Fourth, although we adjusted for age in the multivariate analysis, we did not perform a stratified or sensitivity analysis by age groups, which might have further strengthened the robustness of our findings. Fifth, while polyp size and histology were recorded, we did not perform subgroup analyses by polyp location or histological subtype in relation to IM; future studies should address these questions. Finally, *H. pylori* strain typing (e.g., CagA/VacA status) was not performed. Since different bacterial genotypes may have distinct pathogenic potentials, future studies incorporating strain-specific analysis are warranted.

Conclusions

This study suggests that IM may serve as an independent risk factor for the development of colorectal polyps and highlights the potential benefit of prioritizing colonoscopic screening in individuals with IM. In contrast, no association was found between Helicobacter pylori infection and colorectal polyp formation. To validate these findings and assess their applicability in clinical practice, further prospective studies with larger sample sizes and molecular-level evaluations are warranted.

Conflict of interest: The authors declare that they have no conflict of interest.

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Ethical approval: This study was approved by the Institutional Ethics Committee of Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi (Approval No: 2025/08/1094, Date: 20.05.2025) and conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients prior to endoscopic procedures.

Informed consent: For this retrospective analysis, the requirement for additional consent was waived by the ethics committee.

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Contributions

Research concept and design: VA,

Data analysis and interpretation: MD, OO, AOS, OU

Collection and/or assembly of data: VA, OO, AOS, ASS, SG, OU

Writing the article: VA, OU

Critical revision of the article: MDu, EP, OU

Final approval of the article: VA, OO, AOS, ASS, SG, MD, MDu, OU, EP

All authors read and approved the final version of the manuscript.

References

1. Abedizadeh R, Majidi F, Khorasani HR, Abedi H, Sabour D. Colorectal cancer: a comprehensive review of carcinogenesis, diagnosis, and novel strategies

for classified treatments. Cancer Metastasis Rev. 2024;43(2):729-53.

2. Gül MC, Emin D. Impact of Caudate Lobe Resection on Overall Survival and Liver Disease-Free Survival in Colorectal Liver Metastases: A Pilot Study. Turk J Gastroenterol. 2025;36(7):459-66.
3. Jacobsson M, Wagner V, Kanneganti S. Screening for Colorectal Cancer. Surg Clin North Am. 2024;104(3):595-607.
4. Pettis J, Paruch J. Endoscopic Assessment of Colorectal Polyps. Clin Colon Rectal Surg. 2023;37(5):271-6.
5. Sun Y, Zhang X, Hang D, Lau HC, Du J, Liu C, et al. Integrative plasma and fecal metabolomics identify functional metabolites in adenoma-colorectal cancer progression and as early diagnostic biomarkers. Cancer Cell. 2024;42(8):1386-1400.e8.
6. Chen L, Cao R, Han J, Yu H, Li Y, Wang X, et al. Association of Helicobacter pylori infection with colorectal polyps/adenomas: A single-center cross-sectional study. Cancer Epidemiol. 2024;92:102626.
7. Liu Q, Sadr-Azodi O, Engstrand L, Fall K, Brusselaers N. Helicobacter pylori Eradication Therapy and the Risk of Colorectal Cancer: A Population-Based Nationwide Cohort Study in Sweden. Helicobacter. 2024;29(6):e70001.
8. Teimoorian F, Ranaei M, Hajian Tilaki K, Shokri Shirvani J, Vosough Z. Association of Helicobacter pylori Infection With Colon Cancer and Adenomatous Polyps. Iran J Pathol. 2018;13(3):325-32.
9. Drnovsek J, Homan M, Zidar N, Smid LM. Pathogenesis and potential reversibility of intestinal metaplasia - a milestone in gastric carcinogenesis. Radiol Oncol. 2024;58(2):186-95.
10. Wei H, Li W, Zeng L, Ding N, Li K, Yu H, et al. OLFM4 promotes the progression of intestinal metaplasia through activation of the MYH9/GSK3β/β-catenin pathway. Mol Cancer. 2024;23(1):124.
11. Pan J, Cen L, Xu L, Miao M, Li Y, Yu C, et al. Prevalence and risk factors for colorectal polyps in a Chinese population: a retrospective study. Sci Rep. 2020;10(1):6974.
12. Ünler GK, Teke Özgür G, Göktürk HS, Korkmaz H, Erinanç ÖH. Is there any association between colonic polyps and gastric intestinal metaplasia? Turk J Gastroenterol. 2016;27(3):221-6.
13. Iwata E, Sugimoto M, Asaoka D, Hojo M, Ito M, Kitazawa N, et al. Characteristics of Helicobacter pylori Eradication Therapy in Patients 80 Years or Older Living in a Metropolitan Area: A Multicenter Retrospective Study. Helicobacter. 2024;29(4):e13125.
14. Zhao XX, Liu MH, Wang RL, Tian T. Effect of Gender and Age on the Correlation between Helicobacter pylori and Colorectal Adenomatous Polyps in a Chinese Urban Population: A Single Center Study. Gastroenterol Res Pract. 2020;2020:8596038.
15. Luo F, Zhou P, Ran X, Gu M, Zhou S. No evident causal association between Helicobacter pylori infection and colorectal cancer: a bidirectional mendelian randomization study. Sci Rep. 2023;13(1):18544.
16. Shmuely H, Passaro D, Figer A, Niv Y, Pitlik S, Samra Z, et al. Relationship between Helicobacter pylori CagA status and colorectal cancer. Am J Gastroenterol. 2001;96(12):3406-10.
17. Emir S, Aydin M, Can G, Bali I, Yildirim O, Öznur M, et al. Comparison of colorectal neoplastic polyps and adenocarcinoma with regard to NLR and PLR. Eur Rev Med Pharmacol Sci. 2015;19(19):3613-8.
18. Sonnenberg A, Turner KO, Genta RM. Associations between gastric histopathology and the occurrence of colonic polyps. Colorectal Dis. 2020;22(7):814-7.
19. Feng L, Zhao K, Wang G, Dong R, Zhang M, Xia S, et al. Relationship between endoscopic gastric abnormalities and colorectal polyps: a cross-sectional study based on 33439 Chinese patients. Int J Med Sci. 2023;20(2):219-24.
20. Thomsen M, Kersten C, Sorbye H, Skovlund E, Glimelius B, Pfeiffer P, et al. Interleukin-6 and C-reactive protein as prognostic biomarkers in metastatic colorectal cancer. Oncotarget. 2016;7(46):75013-22.