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Repeated Fecal Occult Blood Test Positivity Is Associated with Clinically Significant Colonoscopic Findings

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Abstract:

Objective: Guaiac-based fecal occult blood testing (gFOBT) is widely used in colorectal cancer (CRC) screening programs. To evaluate the association between repeated gFOBT positivity and clinically significant colonoscopic and histopathological findings, particularly colorectal malignancy.

Methods: This retrospective, single-center study included patients with positive gFOBT results who presented to the Gastroenterology Outpatient Clinic of Gazi University Faculty of Medicine between June 2017 and October 2025. Patients were categorized into three groups based on gFOBT results: single positive (Group 1), two consecutive positive tests within one month (Group 2), and an initial positive followed by a negative test (Group 3). Colonoscopic and histopathological findings were compared between groups. Multivariable logistic regression analysis was performed to identify independent predictors of clinically significant malignant pathology.

Results: Among 1,442 patients with positive gFOBT results, 735 (50.9%) underwent diagnostic colonoscopy. Colorectal malignancy was detected in 55 (7.5%) patients among those who underwent colonoscopy. Malignancy rates differed significantly between groups: 5.1% in Group 1, 17.4% in Group 2, and 0% in Group 3 (P<0.001). Repeated gFOBT positivity was independently associated with malignant colonoscopic findings (OR: 3.684; 95% CI: 2.027–6.694). Normal colonoscopy findings were significantly more frequent in patients with a single positive test, whereas malignant findings were markedly higher in patients with repeated positivity.

Conclusion: Repeated gFOBT positivity is strongly associated with clinically significant colonoscopic pathology, particularly colorectal malignancy. Patients with consecutive positive gFOBT results represent a high-risk subgroup and should be prioritized for prompt diagnostic colonoscopy within CRC screening programs.

Keywords: Colorectal Cancer, Repeated Positivity, Screening, Fecal Occult Blood Test, Colonoscopy

Colorectal cancer (CRC) is one of the main causes of cancer-related morbidity and mortality worldwide. According to GLOBOCAN 2022 data, it is the third most common cancer in terms of incidence and the second most common cancer in terms of mortality among all cancers worldwide [1]. For this reason, screening of the healthy population after the age of 45 is recommended for early detection of CRC [2].

Recommended screening tests include the highly

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sensitive guaiac fecal occult blood test (gFOBT), fecal immunochemical test (FIT), fecal DNA-FIT, sigmoidoscopy, computed tomography colonography, and colonoscopy [3]. Fecal immunochemical test and gFOBT are widely used due to their non-invasive nature, low cost, and applicability in large populations. Guaiac-based fecal occult blood tests detect the presence of occult blood in stool through the pseudo-peroxidase activity of the 'heme' molecule in 'heme'. However, this method is prone to false positives due to the presence of heme proteins and peroxidase activity in red meat and certain fruits and vegetables, and to false negatives due to the use of vitamin C; it can also detect bleeding originating in the upper gastrointestinal tract [4]. In contrast, FIT is less sensitive to dietary and drug interactions because it works only with antibodies specific to human globin, and it shows higher specificity for lower gastrointestinal bleeding due to the breakdown of globin in the upper gastrointestinal tract [5].

In daily clinical practice, repeating the test instead of diagnostic colonoscopy after a positive gFOBT is a common approach; however, the value of repeated gFOBT positivity in predicting clinically significant pathological findings on colonoscopy is unclear. The aim of this study was to evaluate the relationship between repeated positivity in patients with guaiac-based test positivity and clinically significant findings detected during colonoscopy, particularly colorectal malignancy.

METHODS

Study Design and Patient Selection

This study was designed as a retrospective, single-center analysis. Patients who presented to the Gastroenterology Outpatient Clinic of Gazi University Faculty of Medicine between June 1, 2017, and October 31, 2025, and who underwent gFOBT for various clinical indications were included in the study.

Ethics Approval

This study was reviewed by the Ethics Committee of Gazi University and approved on January 13, 2026, with decision number 2026-01/103.

Exclusion Criteria

Patients were excluded if they met any of the following criteria: incomplete clinical, endoscopic, or laboratory data (n=32); a diagnosis of inflammatory bowel disease, including ulcerative colitis or Crohn's disease (total n=366); age younger than 18 years; pregnancy; or insufficient or unverifiable medical records.

Colonoscopy and Pathological Evaluation

A total of 1,840 patients were identified with a positive gFOBT result. Thirty-two patients were excluded due to incomplete or insufficient medical records, and 366 patients with ulcerative colitis or Crohn's disease were also excluded. After the exclusion criteria were applied, 1,442 patients constituted the final study cohort. Among them, 735 patients consented to undergo diagnostic colonoscopy and were included in the colonoscopic and histopathological analyses. Colonoscopy reports and corresponding histopathological findings, when available, were retrospectively reviewed through patient medical records and the hospital information management system. Colonoscopic findings and pathological diagnoses were systematically recorded and analyzed.

Grouping Based on gFOBT Results

Patients were categorized into three groups based on their gFOBT results. Group 1 consisted of patients with a single positive gFOBT result. Group 2 included patients who underwent repeat gFOBT testing within one month following an initial positive result and had persistent positivity on the second test. Group 3 comprised patients who underwent repeat gFOBT testing within one month after an initial positive result and had a negative result on the second test. Colonoscopic and histopathological findings were compared across these three groups.

Histopathological Classification

Patients were classified into four groups according to their colonoscopic and histopathological findings. In cases where multiple lesions or diagnoses were identified in the same patient, classification was based on the most advanced pathological finding.

The malignant group included invasive carcinomas, intramucosal carcinoma foci, and adenomas with high-grade or low-grade dysplasia.

The premalignant group included tubular, tubulovillous, and villous adenomas, as well as sessile serrated polyps. The benign group included non-neoplastic polyps, perianal diseases, angiodysplasias, diverticulosis, colitis, ileitis, and benign ulcers. Patients with normal colonoscopic findings and no histopathological abnormalities were classified as the normal group.

Statistical Analysis

Statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) software. Continuous variables were expressed as mean±standard deviation or median (minimum–maximum), as appropriate, while categorical variables were presented as numbers and percentages (%). Appropriate parametric or non-parametric tests were used for comparisons between groups. Categorical variables were compared using the chi-square test; Fisher's exact test was applied when the expected cell count was less than five. A multivariable logistic regression analysis was performed to identify independent factors associated with clinically significant colonoscopic pathological findings (adenoma, advanced adenoma, and colorectal malignancy). Given the limited number of variables, age, hemoglobin level, ferritin level, and gFOBT positivity groups were simultaneously included in the multivariable model. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). A P-value <0.05 was considered statistically significant for all analyses.

RESULTS

A total of 735 patients who underwent colonoscopy following a positive gFOBT result were included in the colonoscopic and histopathological analyses. Among the study population, colonoscopy was not performed in 590 patients with a single positive gFOBT result, 98 patients with an initial positive gFOBT followed by a negative result, and 19 patients with two consecutive positive gFOBT results. A statistically significant age difference was observed between patients who underwent colonoscopy and those who did not (P<0.001), while no significant difference was found regarding sex distribution (P=0.135). Pre-procedural hemoglobin levels were comparable between the two groups (P=0.051); however, pre-procedural ferritin levels were significantly lower in patients who underwent colonoscopy (P<0.001).

Of the 735 patients who underwent colonoscopy, 408 (55.5%) were female, and the mean age of all patients was 55.7 years. The mean interval between a positive gFOBT result and colonoscopy was 2.3 months (69 days). The mean pre-procedure hemoglobin level was 13.26±2.14 g/dL, and the median ferritin level was 29 ng/mL. Macroscopic colonoscopy findings are summarized in Table 1.

Patients were categorized into three groups based on their repeat gFOBT results. Group 1 included patients who underwent colonoscopy after a single positive gFOBT result. Group 2 consisted of patients who underwent colonoscopy after two consecutive positive gFOBT results within one month. Group 3 comprised patients who underwent colonoscopy after an initial positive gFOBT result followed by a negative result within one month.

Patients were categorized into four histopathological groups (normal, benign, premalignant, and malignant) according to the most advanced pathological finding identified during colonoscopy. A statistically significant difference in colonoscopic pathological findings was observed among the three gFOBT groups (P<0.001). Overall, colorectal malignancy was detected in 55 (7.5%) of 735 patients who underwent colonoscopy. Group-based analysis demonstrated a markedly higher malignancy rate in Group 2 (26/149, 17.4%) compared with Group 1 (29/565, 5.1%), while no colorectal malignancies were identified in Group 3 (0/21).

Among patients with repeated gFOBT positivity (Group 2), the frequency of malignant pathology was significantly higher than expected based on adjusted residual analysis (adjusted residual = 5.2), whereas the occurrence of normal colonoscopic findings was significantly lower than expected (adjusted residual = −5.1). In contrast, patients in Group 1 exhibited a significantly higher-than-expected rate of normal colonoscopic findings (adjusted residual = 4.2) (see Table 2).

Multivariable logistic regression analysis was conducted to identify independent predictors of

TABLE 1. Macroscopic and Histopathological Results of Colonoscopic Evaluation

	Number	%
Macroscopic results		
Normal colonoscopy findings	222	30.2%
Polyp(s)	214	29.1%
Hemorrhoidal disease	178	24.2%
Malign results	55	7.5%
Diverticulosis	79	10.7%
Colitis	22	3%
Terminal ileal pathologies	15	2%
Colonic Angiodysplasias	12	1.6%
Anal Fissure	10	1.3%
Previously operated colon	9	1.2%
Soliter rectal ulcer	9	1.2%
Ischemic colitis	4	0.5%
Anastomotic line ulcer	2	0.3%
Radiation proctitis	2	0.3%
Histopathological results		
Normal colonoscopy findings	**220**	**30%**
Malign results	**55**	**7.5%**
Adenocarcinomas	39	5.3%
Signet ring cell carcinoma	3	0.4%
Medullary carcinoma	1	0.1%
Adenomas with intramucosal carcinoma foci	4	0.5%
Adenomas with high-grade dysplasia (HGD)	4	0.5%
Adenomas with low-grade dysplasia (LGD)	4	0.5%
Pre-malign (neoplastic) polyps	**175**	**23.8%**
Tubular adenoma	118	16%
Tubulovillous adenoma	39	5.3%
Villous adenoma	13	1.7%
Sessile serrated adenoma	5	0.6%
Non malign (non-neoplastic) polyps	**77**	**10.5%**
Hyperplastic polyps	69	9.3%
Inflammatory polyp	8	1%
Other pathological findings	**54**	**7.3%**
Nonspecific ileitis	13	1.7%
Nonspecific colitis	12	1.6%
Benign ulcer	11	1.5%
Infectious colitis	8	1.0%
Ischemic colitis	4	0.5%
Microscopic colitis	2	0.3%
Eosinophilic colitis	2	0.3%
Eosinophilic ileitis	1	0.1%
Drug-induced ileitis	1	0.1%

TABLE 2. Distribution of Colonoscopic Pathology According to Fecal Occult Blood Test Groups

			gFOBT result groups			Total
			Grup 1 (+)	Grup 2 (+/+)	Grup 3 (+/-)	
Histopathological results	**Normal**	Count	191	19	10	220
		Adjusted residual	4.2	-5.1	1.8	
	Bening	Count	220	76	9	305
		Adjusted residual	-2.6	2.6	0.1	
	Premalign	Count	125	28	2*	155
		Adjusted residual	1.3	-0.8	-1.3	
	Malign	Count	29	26	0	55
		Adjusted residual	-4.4	5.2	-1.3	
Total		Count	565	149	21	735

gFOBT, guaiac fecal occult blood test.

*Among patients in Group 3, premalignant pathology was identified in two cases, both of which were tubular adenomas.

clinically significant malignant colonoscopic pathology. Age, pre-procedural hemoglobin level, pre-procedural ferritin level, and gFOBT groups were included in the model. In the adjusted analysis, gFOBT group status remained an independent predictor of clinically significant malignant pathology. Patients with repeated gFOBT positivity had a significantly increased risk of malignant pathology, with an odds ratio (OR) of 3.684 (95% CI: 2.027–6.694) (Table 3).

DISCUSSION

The principal finding of this study is that repeated gFOBT positivity was strongly and independently associated with colorectal malignancy and clinically significant colonoscopic findings. Analysis according to gFOBT groups demonstrated that normal colonoscopy findings were significantly more frequent in patients with a single positive test, whereas malignant pathologies were markedly more common among patients with repeated positivity, with a malignancy rate reaching 17.4% in Group 2. These findings suggest that recurrent gFOBT positivity may serve as a valuable risk stratification marker for colorectal neoplasia, helping to identify high-risk individuals who should be prioritized for diagnostic colonoscopy. Our results add to the growing body of evidence that the pattern of fecal occult blood test positivity, rather than a single positive result alone, may provide clinically meaningful information for

TABLE 3. Multivariable Logistic Regression Analysis of Factors Associated with Clinically Significant Malignant Colonoscopic Findings

	OR	95% CI	P-value
Age	1.029	1.004 – 1.054	0.062
Pre-procedural ferritin level	1.000	0.993 – 1.007	0.908
Pre-procedural hemoglobin level	0.911	0.795 – 1.044	0.181
gFOBT group	3.684	2.027 – 6.694	**<0.001**

gFOBT, guaiac fecal occult blood test; OR, odds ratio; CI; confidence interval.

Statistically significant P-value is shown in bold.

colorectal cancer screening and patient management.

Failure to complete or delays in diagnostic colonoscopy following a positive gFOBT result represent a major limitation to the effectiveness of colorectal cancer screening programs. A recent systematic review evaluating repeat fecal occult blood testing in colorectal cancer screening reported that repeat testing to confirm an initial positive result is a common practice, despite limited evidence supporting its clinical benefit [6]. The same review highlighted the lack of data evaluating the relationship between repeated positive fecal occult blood tests and colonoscopic findings, revealing a significant gap in the literature. Accordingly, this study aimed to evaluate the relationship between repeated gFOBT positivity and clinically significant colonoscopic findings. Colorectal cancer screening methods differ in terms of effectiveness, sensitivity and specificity, safety, ease of use, screening intervals, availability, and cost [7]. The guaiac-based fecal occult blood test remains one of the most widely used screening tools in clinical practice due to its non-invasive nature, repeatability, and relatively low cost. For this reason, gFOBT continues to be used in national colorectal cancer screening programs in our country [8].

Guaiac-based fecal occult blood testing requires specific pre-test preparations, including dietary restrictions [9] and medication adjustments [10], which may adversely affect patient compliance and reduce test completion rates [9]. In our study, approximately half of the patients with a positive screening test (50.9%) agreed to undergo diagnostic colonoscopy. A systematic review conducted in Türkiye reported that participation rates in colorectal cancer screening programs ranged between 4.5% and 33.8% [11]. The relatively low rates of colonoscopy uptake may be attributed, at least in part, to sociocultural factors.

In our study, 222 of the 735 colonoscopies performed showed no macroscopic pathological findings. Biopsy results from 2 patients, obtained due to clinical suspicion, were reported as ‘microscopic colitis’. Therefore, the colonoscopy results for 220 (30%) patients were recorded as ‘normal colonoscopy’. In a study conducted in the United Kingdom, completely normal colonoscopy findings were reported in 39.9% of patients following a positive fecal occult blood test result [12]. In a similar study conducted in Türkiye, the proportion of colonoscopies reported as normal following a positive gFOBT result was 38% [13].

The adenoma detection rate (ADR) is one of the most important quality indicators of colonoscopy. The American College of Gastroenterology guidelines recommend an ADR of ≥35%(14). In a large meta-analysis published in 2025, including more than three million patients, the ADR was reported to be 26.2% [15]. In our study, polyps of various sizes and numbers were detected in 214 (29.1%) of 735 patients. Previous studies from Türkiye have reported ADR ranging between 26.2% [13] and 33.8% [16]. The ADR observed in our study is consistent with both the published literature and current guideline recommendations.

In our study, colorectal malignancy was detected in 55 (3.8%) of all 1,442 patients who were gFOBT positive. When the analysis was restricted to patients who underwent diagnostic colonoscopy, the malignancy rate increased to 7.5% (55/735). Group-based analysis demonstrated colorectal malignancy in 5.1% of patients in Group 1 (29/565) and in 17.4% of patients in Group 2 (26/149), whereas no malignancies were detected in Group 3 (0/21). These findings indicate a markedly higher malignancy detection rate among patients with repeated gFOBT positivity. In two national Bowel Cancer Screening Programs conducted in the United Kingdom, colorectal malignancy was detected in 8.36% [17] and 7.4% [18] of gFOBT-positive participants undergoing colonoscopy. Similarly, an Italy-based screening study reported a malignancy detection rate of 6.9% [19], while a prospective study from Brazil reported a higher rate of 11.1% [20]. Consistent with international data, several studies from Türkiye have evaluated colonoscopic findings following positive fecal occult blood tests. In one such study, including 237 patients who underwent colonoscopy after a positive gFOBT result, adenocarcinoma was detected in 9.71% of cases [21]. In the literature, colorectal cancer detection rates following positive gFOBT results are generally reported to range between 6% and 11%. In comparison with these series, the overall malignancy detection rate observed in our colonoscopy cohort (7.5%) is consistent with international data.

Large-scale data from gFOBT-based screening

programs indicate that colorectal malignancy risk may vary not only according to test positivity, but also according to the pattern of positivity. Systematic reviews evaluating repeat screening strategies have shown that gFOBT is frequently repeated in clinical practice and that this approach has become an integral component of screening programs [22]. For example, data from the UK National Bowel Cancer Screening Programme has demonstrated a significant increase in colorectal cancer detection rates on colonoscopy with rising spot positivity percentage (SP%) in gFOBT screening. While colorectal cancer was detected in approximately 4% of individuals with low SP%, detection rates increased markedly and reached up to ~25% in those with higher SP% levels. These findings further suggest that the pattern of gFOBT positivity is a valuable predictor of malignancy risk. Moreover, in three-sample gFOBT testing, individuals with a higher number of positive samples have a substantially greater likelihood of colorectal cancer detection compared with those showing weak positivity or a single positive test [18].

Strengths and Limitations

This study has several notable strengths. First, it addresses a clinically relevant but relatively underexplored question regarding the significance of repeated gFOBT positivity. Second, all major outcomes were confirmed by colonoscopic and histopathological evaluation, providing robust diagnostic accuracy. Finally, the inclusion of a large real-world cohort enhances the applicability of our findings to routine clinical practice and colorectal cancer screening programs.

This study has several limitations. First, its retrospective design may have introduced selection and information bias, and some potentially relevant clinical variables could not be evaluated because of incomplete documentation. Second, only approximately half of the patients with a positive gFOBT result underwent colonoscopy, raising the possibility of selection bias and limiting the generalizability of the findings. Third, colonoscopic examinations were performed by different endoscopists, and variations in adenoma detection rates or missed lesions cannot be completely excluded. Fourth, this was a single-center study with a relatively limited sample size, which may restrict the external validity of the results.

CONCLUSION

In this study, colonoscopic and histopathological findings were evaluated in patients with guaiac-based fecal occult blood test (gFOBT) positivity, and it was demonstrated that recurrent gFOBT positivity is strongly associated with clinically significant colonic pathologies, particularly colorectal malignancy. The main finding of our study is that the rate of malignancy detection (17.4%) was significantly higher in patients with recurrent gFOBT positivity within one month compared to those with a single positive test. In contrast, no malignancies were detected in patients whose repeat test became negative, suggesting that recurrent positivity may serve as a clinically meaningful indicator for identifying high-risk patient subgroups. In conclusion, recurrent gFOBT positivity should be considered a practical and strong risk marker for identifying patients who should be prioritized for diagnostic colonoscopy in CRC screening. These findings indicate that a single repeat test following a positive gFOBT may not be sufficient, and recurrent positivity should be integrated into clinical decision-making processes.

Ethics Approval and Consent to Participate

This study was approved by the Gazi University Ethics Committee. (Decision No: 2026-01/103; date: 03.01.2026). All procedures were conducted in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments. Informed consent was waived because of the retrospective nature of the study and the analysis used anonymous clinical data.

Data Availability

All relevant data supporting the findings of this study have been included in the article. Data with identifying information removed may be obtained from the corresponding author upon reasonable request, subject to the approval of the ethics committee and, where necessary, institutional permissions.

Authors' Contribution

Study Conception: HK; Study Design: HK, GK; Supervision: GK, MC, TK, ÇK, MK, AK; Funding: N/A; Materials: HK, AK, GK; Data Collection and/or Processing: HK, BD, EC, DK; Statistical Analysis and/or Data Interpretation: HK; Literature Review: HK, BD, EC, DK; Manuscript Preparation: HK; and Critical Review: HK, GK, AK.

Conflict of Interest

The author(s) disclosed no conflict of interest during the preparation or publication of this manuscript.

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Grammarly was used in parts of the manuscript for English language editing. No AI-assisted tools were used for data collection, statistical analysis, result generation, or the creation of tables and figures. All scientific content and conclusions are the responsibility of the authors.

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