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Colorectal cancer screening; colonoscopy and biopsy results in people undergoing colonoscopy due to positive fecal occult blood test

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ABSTRACT

Objective: Screening programs are important for the early detection of colorectal cancer, which is one of the causes of high morbidity and mortality. In this study, we investigated the colonoscopy results, the incidence of adenoma and cancer, and the relationship between test results and cancer in individuals with a positive fecal occult blood test for colorectal cancer screening.

Material and Methods: Within the scope of the colorectal cancer screening program, colonoscopy was requested for individuals aged 50-70 years who applied to our outpatient clinic with a positive fecal occult blood test. The results were collected and analyzed.

Results: The results of the colonoscopy could be obtained in only 237 (56.43%) of the 420 patients who were referred for a colonoscopy because of a positive fecal occult blood test. Colonoscopy results were normal in 15 (6.33%), benign anal disease in 64 (27%), benign colonic disease in 12 (5.06%) and polyp + adenocarcinoma in 146 (61.61%). Pathology results were benign polyp in 37 (15.61%), adenomatous polyp in 86 (36.29%) and adenocarcinoma in 23 (9.71%). Quantitative test results were higher in the adenomatous polyp + adenocarcinoma group and statistically significant (p= 0.03).

Conclusion: Individuals with positive fecal occult blood tests, especially those with high quantitative test results, should be encouraged to have a colonoscopy, and they should be warned about the high probability of adenomatous polyps and colorectal cancer.

Keywords: Colorectal cancer screening, fecal occult blood test, immunochemical test, colonoscopy

INTRODUCTION

Colorectal cancer (CRC) remains a major health problem worldwide due to its high incidence and high mortality rates. According to the Global Cancer Observatory, CRC is the 4th most common and 3rd most fatal cancer worldwide. CRCs develop slowly and are usually advanced when they become symptomatic. If these cancers can be diagnosed at an early stage, the chances of a cure can be high. Early diagnosis is only possible through screening programs. Screening increases the likelihood of detecting early-stage cancer or precancerous lesions. Studies have shown that colorectal cancer-related deaths are significantly reduced with screening programs (1,2).

A fecal occult blood test (FOBT) is one of the methods used for CRC screening. Despite its disadvantages such as being affected by medication and food intake and not being able to show the bleeding focus, it ranks first in screening programs since it is easily applicable and inexpensive. In this study, we aimed to investigate the colonoscopy results, the incidence of adenoma and cancer, and whether there is a correlation between FOBT results and cancer in patients with positive FOBT performed in primary health care centers and admitted to our hospital for colonoscopy.

MATERIAL and METHODS

This prospective study was designed for patients who applied to the General Surgery Outpatient Clinic of Ümraniye Training and Research Hospital, University of Health Sciences for colonoscopy due to positive FOBT performed in a primary health center between July 2019 and January 2023. The ethics committee of our institution approved the study (28.06.2019/12832). In line with the ethics principles of the Declaration of Helsinki, the identity and health information of the patients were protected by observing confidentiality and privacy.

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As part of the national CRC screening program, asymptomatic people aged 50-70 years were asked to undergo FOBT at primary health care centers. Initially, a quantitative test based on immunochemical immunoassay with numerical results was used as a screening test, and a result above 100 ng/ml was considered positive. Later, a qualitative test based on the rapid chromatographic immunoassay method was used, which gives positive/negative results. Patients with positive FOBT were referred to more advanced centers for colonoscopy. Patients who applied to our outpatient clinic, for this reason, were included in the study. Patients who underwent colonoscopy for colorectal or anal complaints, patients with inflammatory bowel disease, and/or gastrointestinal system tumors were excluded.

Colonoscopy was ordered for patients who applied to our outpatient clinic for colonoscopy due to positive FOBT. The results of colonoscopy performed in our institution were checked through the hospital information system and the results of colonoscopy performed in an external center were checked through the national database. Patients were recorded in an excel file.

Colonoscopy results were grouped as normal, benign anal disease (hemorrhoids, anal fissure, etc.), benign colonic disease (diverticulum, angiodysplasia, etc.), and polyp + adenocarcinoma. Pathology results in patients in the polyp and adenocarcinoma group who underwent biopsy were divided into subgroups as a benign polyp (hyperplastic polyp), low-grade tubular adenoma, high-grade tubular adenoma, low-grade tubulovillous adenoma, high-grade tubulovillous adenoma, low-grade villous adenoma, high-grade villous adenoma and adenocarcinoma. In the presence of more than one lesion or pathological result in the same patient, the more malignant one was considered to avoid confusion (Figure 1).

Demographic characteristics of the patients, colonoscopy results, pathology results in those who underwent biopsy due to polyps or masses, and whether there was a correlation between the results of FOBT and pathology results were investigated, and the data were analyzed.

Statistical Analysis

Statistical analyses were performed online using the GraphPad QuickCalcs program. Continuous variables were expressed as mean ± standard deviation (SD), and categorical data were expressed as count and percentage. The Fisher's exact, Chi-square, and student's t-test were used to analyze group comparisons. The difference was considered statistically significant if $p< 0.05$.

RESULTS

During the study period, colonoscopy was requested for 420 patients. However, the results were available in 237 (56.43%) patients, and these patients were included in the study. Of these 237 patients, 112 (47.26%) were females and 125 (52.74%) were males with a mean age of 59.69 years.

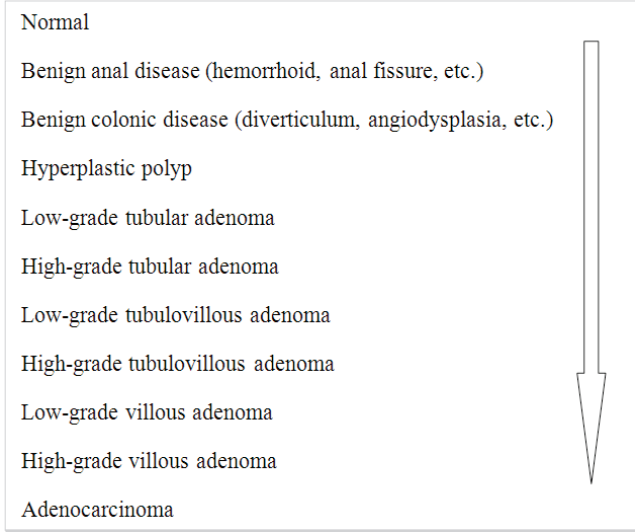

Figure 1. Ranking of lesions detected in colonoscopy and pathology from benign to more malignant.

Of the 237 patients with available colonoscopy, colonoscopy results were reported as normal in 15 (6.33%), benign anal disease in 64 (27%), benign colonic disease in 12 (5.06%) and polyp + adenocarcinoma in 146 (61.61%) (Table 1).

The pathology results of the biopsied polyp and adenocarcinoma group were as follows: 37 (25.34%) benign polyp, 64 (43.84%) low-grade tubular adenoma, 6 (4.11%) high-grade tubular adenoma, 3 (2.06%) low-grade tubulovillous adenoma, 13 (8.90%) high-grade tubulovillous adenoma and 23 (15.75%) adenocarcinoma (Table 1). The rates of these lesions in the total study population were 15.61%, 27%, 2.53%, 1.27%, 5.49%, and 9.71%, respectively.

There were 73 patients who underwent quantitative immunochemical testing and colonoscopy. In the subgroup analysis of this group of patients, there was no statistically significant difference in terms of gender ($p= 0.64$). There was no statistically significant difference between polyp + adenocarcinoma and normal + benign anal and colonic disease ($p= 0.13$). There was no statistically significant difference between hyperplastic polyp and adenomatous polyp + adenocarcinoma ($p= 0.22$). There was no statistically significant difference between adenomatous polyp and adenocarcinoma ($p= 0.38$). The FOBT result was higher in patients with adenocarcinoma, and the difference was statistically significant ($p= 0.04$). In the adenomatous polyp+adenocarcinoma group, the FOBT results were higher and the difference was statistically significant ($p= 0.03$) compared to the other benign disease group, including hyperplastic polyp (Table 2).

Table 1. Demographic characteristics, colonoscopy, and pathology results of the study population

	Total (n= 237)		Quantitative (n= 73)		Qualitative (n= 164)	
	n	%	n	%	n	%
Sex						
Female	112	47.26	22	30.14	90	54.88
Male	125	52.74	51	69.86	74	45.12
Colonoscopy Result						
Normal	15	6.33	2	2.74	13	7.93
Benign anal disease	64	27	22	30.14	42	25.61
Benign colonic disease	12	5.06	4	5.48	8	4.88
Polyp + Adenocarcinoma	146	61.61	45	61.64	101	61.58
Pathology Result						
Hyperplastic polyp	37	25.34	10	22.22	27	26.73
Low-grade tubular adenoma	64	43.84	17	37.78	47	46.54
High-grade tubular adenoma	6	4.11	1	2.22	5	4.95
Low-grade tubulovillous adenoma	3	2.06	1	2.22	2	1.98
High-grade tubulovillous adenoma	13	8.90	5	11.11	8	7.92
Low-grade villous adenoma	-	-	-	-	-	-
High-grade villous adenoma	-	-	-	-	-	-
Adenocarcinoma	23	15.75	11	24.45	12	11.88

Table 2. Association of colonoscopy and pathology results with quantitative test results

	Quantitative ICT (Mean ± SD)	p
Sex		
Female	3849.73 ± 8896.23	0.64
Male	2817.27 ± 8538.13	
Normal + Benign anal and colonic disease	1207.21 ± 3225.85	0.13
Polyp + Adenocarcinoma	4323.84 ± 10525.67	
HP	684.40 ± 1223.18	0.22
AP + Adenocarcinoma	5363.69 ± 11746.06	
AP	4158.58 ± 11893.64	0.38
Adenocarcinoma	7993.00 ± 11517.50	
Normal + Benign anal and colonic disease + HP	1069.63 ± 2830.55	0.03
AP + Adenocarcinoma	5363.69 ± 11746.06	
Normal + Benign anal and colonic disease + HP +AP	2265.35 ± 7778.01	0.04
Adenocarcinoma	7993.00 ± 11517.50	

ICT: Immunochemical test, SD: Standart deviation, HP: Hyperplastic polyp, AP: Adenomatous polyp.

DISCUSSION

Colorectal cancers are common cancers worldwide and cause increased morbidity and mortality in the late stage. They grow slowly and are often advanced when they become symptomatic. They usually occur in old age and the majority develop from an adenoma. It takes approximately 8-10 years to develop cancer from an adenoma. Therefore, if it is detected in the pre-malignant stage and diagnosed early, it is a treatable disease. Early diagnosis will reduce morbidity and mortality as well as treatment costs (3-5).

Screening programs are important to detect early-stage colorectal cancer in the asymptomatic period. Different methods such as fecal occult blood test, fecal DNA test,

sigmoidoscopy, colonoscopy, double contrast barium enema, CT colonography, and capsule endoscopy are used for screening. Countries that screen for colorectal cancer use one of these methods as the primary screening test to the extent of their means. In our country, as in most countries, individuals between the ages of 50 and 70 are screened by performing a colonoscopy every 10 years and a FOBT every two years. Although colonoscopy is superior to other tests because it allows direct detection of the lesion and biopsy, it is an invasive method. Despite its disadvantages such as not being able to distinguish between upper and lower gastrointestinal bleeding and being affected by many factors in the diet, FOBT is used in the first place in screening programs in many countries because it is easily applicable and cost-effective (1,6-8).

Guaiac and immunochemical methods are used for the detection of fecal occult blood. Since the guaiac method is a test based on determining the peroxidase-like activity of the heme group, it is affected by all molecules and foods with peroxidase activity. Therefore, foods with peroxidase activity such as turnips, radishes, cabbage, cauliflower, broccoli, apples, bananas, red meat, and iron therapy should be stopped a few days before the test is performed. The immunochemical test is more specific than the guaiac test since it screens only human hemoglobin (9-13). Although it is more expensive, it reduces the need for unnecessary colonoscopies because it has a lower false positive rate and is therefore cost-effective. These tests are divided into two as quantitative and qualitative. The quantitative immunochemical test measures the hemoglobin concentration in the stool sample with an automatic device and gives a numerical value. In qualitative immunochemical testing, the results are based on visual inspection. If hemoglobin is present in the stool, a colored band appears on the test strip. The positivity rate of the qualitative immunochemical test is higher, but the quantitative immunochemical test is superior in detecting cancer (14-16). Although there was no statistically significant difference in this study, adenocarcinoma was detected in 15.07% of patients with positive quantitative test results and in 7.32% of patients with positive qualitative test results (p= 0.09).

In studies, different cut-off values ranging from 25-200 have been used for quantitative immunochemical testing, and sensitivity and specificity have been found to be 25%-100% and 20%-97%, respectively (17-19). In a meta-analysis by Meklin et al. pooled sensitivity and specificity have been calculated as 86% and 85%, respectively (6). When the cut-off value is low, the rate of unnecessary colonoscopy increases, whereas when it is high, the risk of failing to detect malignancy arises. While the high cut-off values are used in populations with limited opportunities to perform a colonoscopy, the lower cut-off values are used in populations with adequate opportunities. In our study, we accepted the cut-off value for FOBT positivity as 100 ng/mL and requested colonoscopy in the next step for individuals with a result above this. The quantitative test result was statistically significantly higher in patients with adenomatous polyps and adenocarcinoma compared to the others (p= 0.03).

It is observed that the rate of colonoscopy is low in patients who were asked to undergo colonoscopy due to positive FOBT (19-21). In a study conducted by Mayir et al. 42.3% of patients who were requested a colonoscopy because of positive FOBT had a colonoscopy and a malignant polyp was found in one patient (0.8%) (22). In a screening study conducted by Nakazato et al. which included FOBT and colonoscopy, the rate of colonoscopy was 20.36% and cancer was found in 15 (1.79%) of 840 patients with positive FOBT (7). In our study, the rate of colonoscopy was 56.3%, adenomatous polyps were found in 36.29% of them, and adenocarcinoma in 9.71%.

Limitations of the Manuscript

The number of individuals screened for colorectal cancer with FOBT and therefore, the positive rate of the test is unknown. The study was not comprehensive and included only individuals who applied to our outpatient clinic for colonoscopy. Therefore, the number of patients included in the study was low. The immunochemical tests used in the study were not the same in all patients, some were quantitative and some were qualitative. Since colonoscopy was performed in different centers rather than in a single center, it may have caused different evaluations due to the person performing it.

CONCLUSION

Early diagnosis and treatment of colorectal cancer, one of the major causes of morbidity and mortality, is an important issue. Early diagnosis is only possible with screening programs. Although colonoscopy is the gold standard today, it is not always possible to perform it widely. FOBT is one of the leading screening programs and reduces the need for colonoscopy because it is easy to perform and inexpensive. However, it is observed that the rate of colonoscopy in patients with positive FOBT is low. Here, primary healthcare providers and physicians who order colonoscopies have an important responsibility. Individuals with positive FOBT, especially those with high quantitative test results, should be encouraged to undergo a colonoscopy and should be warned about the high probability of colorectal cancer.

Ethics Committee Approval: This study was approved by Ümraniye Training and Research Hospital Clinical Research Ethics Committee (Date: 28.06.2019, Decision no: 12832).

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ORİJİNAL ÇALIŞMA-ÖZET
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Kolorektal kanser taraması; gaitada pozitif gizli kan testi nedeniyle kolonoskopi yapılan kişilerde kolonoskopi ve biyopsi sonuçları

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ÖZET

Giriş ve Amaç: Yüksek morbidite ve mortalite nedenlerinden biri olan kolorektal kanserlerin erken dönemde tespit edilebilmesi için tarama programları önemlidir. Bu çalışmada, kolorektal kanser taraması için yapılan gaitada gizli kan testi pozitif olan bireylerin kolonoskopi sonuçları, adenom ve kanser ensidansı, test sonuçları ile kanser arasındaki ilişki araştırıldı.

Gereç ve Yöntem: Kolorektal kanser tarama programı kapsamında dışkıda gizli kan testi pozitif çıkan ve polikliniğimize başvuran 50-70 yaş arası bireylere kolonoskopi yapılması istendi. Sonuçlar toplandı ve analiz edildi.

Bulgular: Gaitada gizli kan testi pozitifliği nedeniyle kolonoskopi için yönlendirilen 420 hastanın sadece 237'sinde (%56,43) kolonoskopi sonucu elde edilebildi. Kolonoskopi sonucu 15 (%6,33) hastada normal, 64 (%27) hastada benign anal hastalık, 12 (%5,06) hastada benign kolonik hastalık ve 146 (%61,61) hastada polip + adenokarsinom şeklindeydi. Patoloji sonuçları 37'sinde (%15,61) benign polip, 86'sında (%36,29) adenomatöz polip ve 23'ünde (%9,71) adenokarsinom şeklindeydi. Kantitatif test sonuçları adenomatöz polip + adenokarsinom grubunda daha yüksekti ve istatistiksel olarak anlamlıydı (p= 0.03).

Sonuç: Gaitada gizli kan testi pozitif olan bireyler, özellikle de kantitatif test sonuçları yüksek olanlar, kolonoskopi yaptırmaya teşvik edilmeli ve adenomatöz polip ve kolorektal kanser olasılığının yüksek olduğu konusunda uyarılmalıdır.

Anahtar Kelimeler: Kolorektal kanser taraması, gaitada gizli kan testi, immünokimyasal test, kolonoskopi

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