



Research Article

The Sensitivity and the Specificity of the Fecal Immunochemical Testing in Detecting Colonic Cancerous and Precancerous Lesions among the Lebanese Population

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Abstract

Background: Fecal Immunochemical Test (FIT) is a screening tool used for colorectal cancer (CRC). Research has demonstrated that FIT detects the majority of CRC. Thus, the aim of the current study was to determine the specificity and the sensitivity of FIT test in detecting colonic cancerous and precancerous lesions among the Lebanese population.

Subjects and Methods: This was a retrospective study carried out in two Lebanese Hospital, among asymptomatic patients who had underwent both colonoscopy and FIT between January 2016 and December 2021. The following information were collected: age, gender, lifestyle, diet, alcohol and smoking habits, physical activity, clinical symptoms, past medical history, family history of CRC, FIT results, and colonoscopy findings. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for FIT, were calculated. **Results:** A total of 54 patients were included in this study. A portion of 55.6% of patients were males and 44.4% were females. Of all study participants, 20 (37.1%) patients tested positive by FIT and 15 of these patients had positive findings on colonoscopy compared to 5 patients who had no abnormal findings. The sensitivity of FIT in detecting CRC was 38.4% and the specificity was 66.6%. The calculated positive predictive value and negative predictive value were 75.0% and 29.4% respectively. When studying the association of demographic and lifestyle factors among patients with a positive FIT, we failed to find a significant association between all the studied variables and positive results of FIT (gender: p-value = 0.614, family history of CRC: p-value = 1.00, cigarette smoking: p-value = 0.66, healthy diet: p-value = 0.053, and physical activity: p-value = 0.59). **Conclusion:** FIT had acceptable sensitivity and high specificity in detecting CRC among asymptomatic patients. Additional research is still needed to improve the diagnostic performance of FIT in detecting CRC.

Keywords: Colorectal cancer CRC; fecal immunochemical test FIT; specificity; sensitivity

Abbreviations: CTC: Computed Tomographic Colonography; DCBE: Double Contrast Barium Enema; DNA: Deoxyribonucleic Acid. FOBT: Fecal Occult Blood Test

Introduction

Cancer is considered the most common cause of death after cardiovascular disease [1]. Colorectal Cancer (CRC) is ranked in frequency as the 4th malignant tumor in the world and it represents the second cause of death after lung cancer. It is associated with several factors such as alcohol, tobacco, obesity, foods, diseases such as inflammatory bowel diseases and genetic factors [2].

Several types of treatments for CRC are valid such as surgery, radiotherapy, chemotherapy and targeted therapy [3].

The United States Preventive Service Taskforce (USPSTF) recognizes the higher colorectal cancer incidence and mortality and strongly encourages clinicians to ensure that patients receive recommended colorectal cancer screening, follow-up, and treatment [1].

Several screening methods for CRC are valid such as sigmoidoscopy, colonoscopy and the Fecal Occult Blood Test (FOBT). However, these methods have many limitations and are therefore poorly tolerated by some patients. The goal of scientific

research is to find effective methods with a lower limitation profile [4].

Stool-based screening requires individuals to collect samples directly from their feces which may be unpleasant for some. However, the test is quick, noninvasive, can be done at home and no bowel preparation is needed to perform the screening test [5].

Screening by direct visualization tests, such as colonoscopy or sigmoidoscopy, should be performed in a clinical setting rather than at home. When performed solely, direct visualization tests allow for a much longer time between screenings compared with stool-based screening [4].

Direct evidence on the benefits of colorectal cancer screening to decrease colorectal cancer mortality are available from randomized clinical trials (RCTs) on g-FOBT and flexible sigmoidoscopy as well as from cohort studies on Fecal Immunochemical Test (FIT) and colonoscopy [6].

Endoscopy is not widely available for many patients in Lebanon due to the country's many economic challenges, and the FOBT requires particular dietary restrictions and the stopping of certain medications, such as anticoagulants and antiplatelets, prior to performing the test in order to obtain an accurate result. The FIT, on the other hand, does not impose any of these restrictions and could be an essential component of CRC screening programs in Lebanon. As a result, we conducted this study to establish the sensitivity and specificity of the test as a CRC screening test in the Lebanese community. (Figure 1)

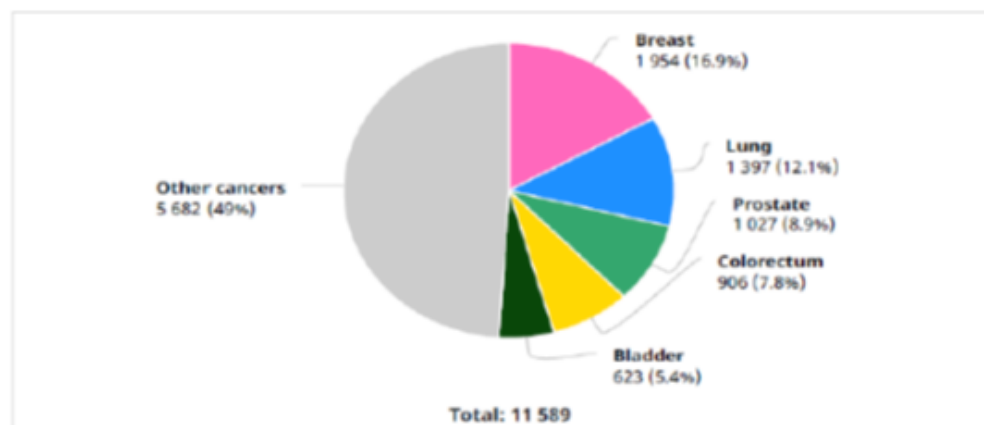
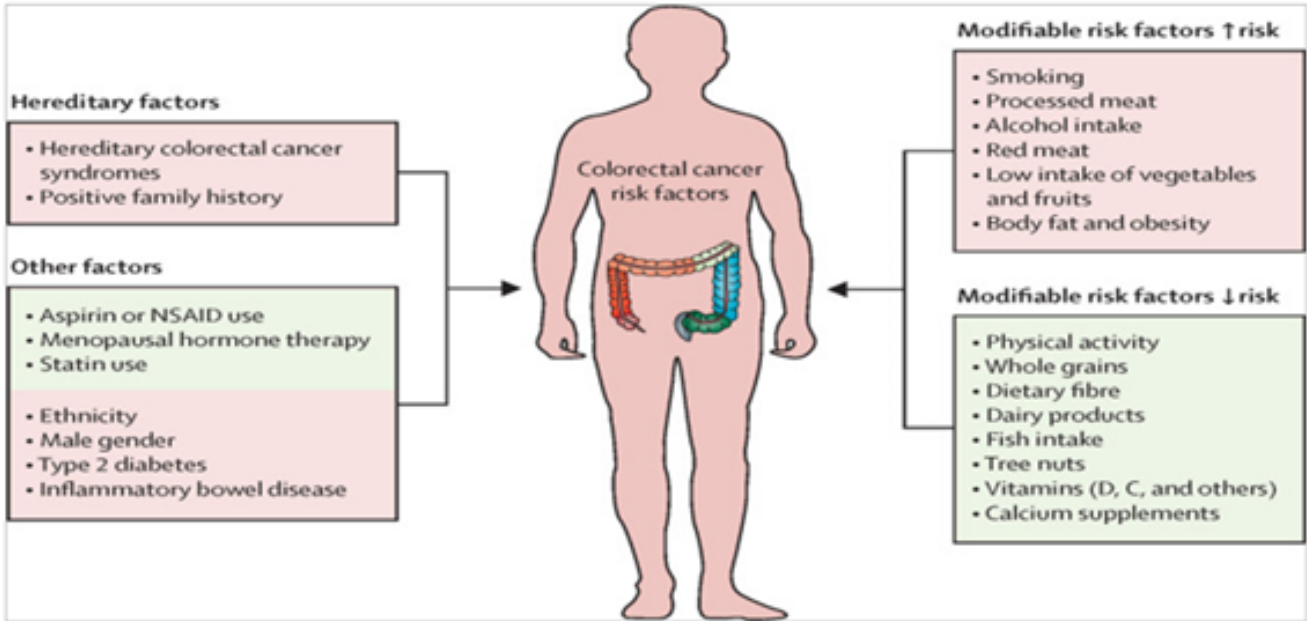


Figure 1. The number of new cancer cases in Lebanon, 2020. The 2020 GLOBOCAN database shows that in Lebanon, 906 new cases of CRC have been diagnosed in 2020 (12).

CRC is more common in economically developed countries. Indeed, several studies have shown that colorectal cancer in descendants born in these countries presents higher risks than descendants born abroad. This difference may be due to the varying lifestyles from one region to another, concerning factors such as diet, physical activity, obesity, tobacco and alcohol consumption [7] (Figure 2).



Several factors such as smoking, alcohol consumption and meat consumption are associated with increased risk of CRC, while physical activity, and healthy diet are protective factors that decrease the risk of the development of CRC (abbreviation: NSAIDs=Non-Steroidal Anti-Inflammatory Drugs) [2]. (Figure 3)

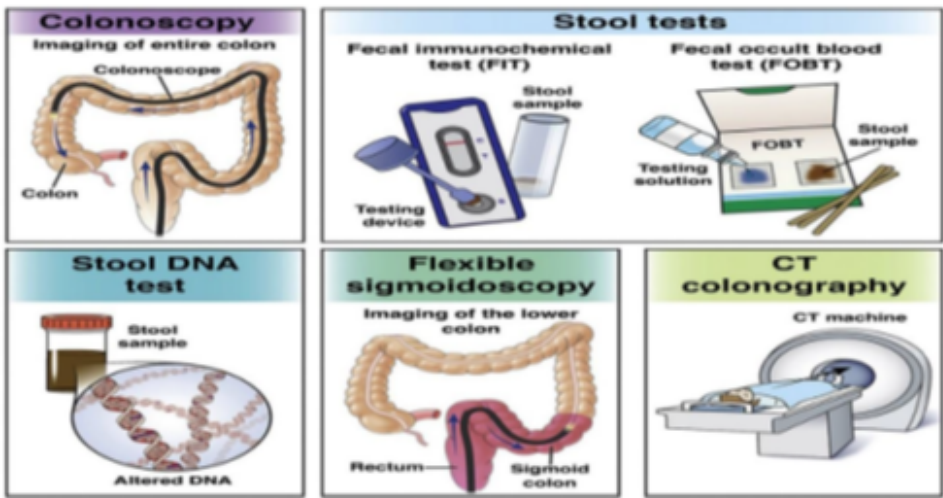


Figure 3. Colorectal cancer screening tests. Several screening methods are currently used for the detection of CRC. Stool based tests, including FIT and FOBT, represent important non-invasive procedures that can be done at home and detect signs of CRC in the stool (17).

FIT is a simple and non-invasive screening tool used for the detection of CRC, especially among patients at average risk for CRC, in a large and increasing number of countries. FIT screening should be done at least once a year [8]. After a positive FIT result; however, patients are then referred to colonoscopy to indicate the source of the bleeding. In cases of negative FIT, the test should be repeated yearly (Figure 4) [9].

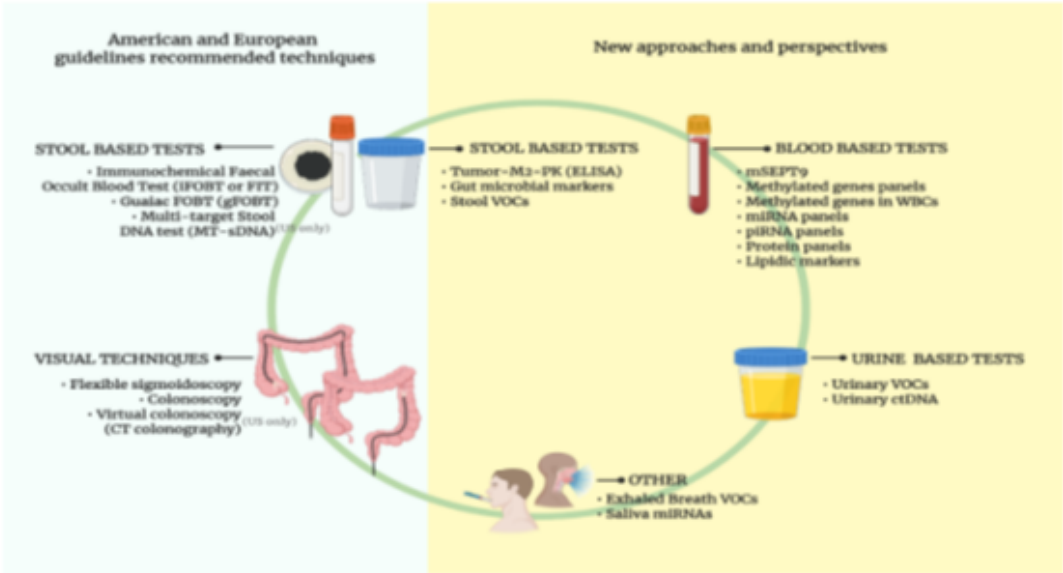
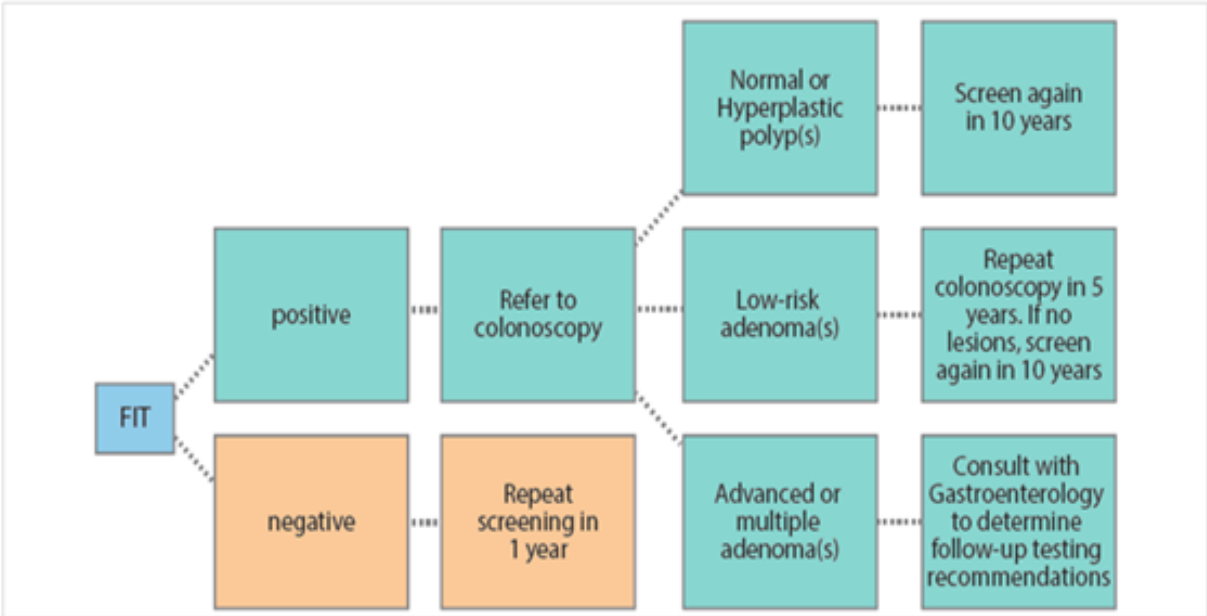


Figure 4. Classification of CRC screening test, and future perspectives. For a complete CRC

Positive FIT is usually followed by a colonoscopy to localize the source of bleeding. In case of normal colonoscopy, it is recommended to repeat the colonoscopy in 10 years [9]. (Figure 5)



FIT testing can be qualitative or quantitative. Quantitative FIT tests detect the amount of occult hemoglobin, whereas qualitative FIT tests only detect the presence of hemoglobin in stool studies [10]. When the quantitative test result surpasses the set standardized threshold, which varies between manufacturing laboratories, the result is considered to be positive [10].

Several studies have demonstrated that the FIT is highly effective in detecting the majority of CRC. For detecting CRC, FIT has a high sensitivity (73% to 88%) and a high specificity (91% to 95%) [8]. Similarly, in a meta-analysis from 2019, the sensitivity of FIT for diagnosing CRC ranged from 71% to 91%, and the specificity ranged from 90% to 95%.

According to several studies, the accuracy of FIT in detecting advanced adenoma is low [11]. For instance, imperial et al, in their meta-analysis of 31 studies, reported a sensitivity of 29% for advanced adenomas [12]. Other studies reported that the sensitivity of FIT decreased with age. According to a study, individuals aged 70 years and older have decreased specificity for colorectal cancer detection when using the FIT [13].

When compared with g-FOBT, FIT is found to be more sensitive and specific for identifying CRC. FIT has the added benefit of not requiring any dietary restrictions and only requiring a single stool sample [8]. The rate of test positivity with FIT was found to be 4.8 percent versus 3.7 percent with G-FOBT. The anticipated positive readings for adenoma using the G-FOBT were 35.9% versus 50.6 percent using the FIT [14].

A FIT-DNA assay combines FIT with biomarker detection for changed DNA. In a prospective analysis of 9,989 people aged 50 to 84 who had a screening colonoscopy, researchers discovered that FIT-DNA was more sensitive (92 percent vs. 74 percent) but less specific (90 percent vs. 96 percent) for detecting CRC than FIT alone [15]. For detecting adenomatous polyps and serrated polyps measuring 1 cm or more, FIT-DNA has a low sensitivity (42 percent). FIT-DNA screening should be done every one to three years, however Medicare only reimburses it every three years [15]. In Lebanon, the Ministry of Public Health (MOPH) recommends the use of the FIT as a screening tool for the early detection of CRC among patients at average risk [9]. However, the screening guidelines for CRC is classified into screening for population at “Average Risk” and screening for population at “Increased Risk”. To mention that FIT is not recommended among patients at increased risk [9]. Table 1 displays the characteristics of the population at average risk for CRC. The primary objective of this study was to determine the specificity and the sensitivity of FIT test in detecting colonic cancerous and precancerous lesions among the Lebanese population.

Average Risk
Asymptomatic adults 50 years and older who DO NOT HAVE
A positive family history (excluding known inherited familial syndromes)
A family history of known genetic disorders that predispose them to a high lifetime risk of colorectal cancer, such as <ul style="list-style-type: none">• Lynch syndrome• Familial adenomatous polyposis
A personal history of inflammatory bowel disease
A previous adenomatous polyp, or previous colorectal cancer
Patients with alarming symptoms (such as blood in stool, abdominal pain and bowel habits changes, unexplained weight loss, and others).

Table 1: Characteristics of the population at average risk for CRC [9].

Primary objective

The primary objective of this study was to determine the specificity and the sensitivity of FIT test in detecting colonic cancerous and precancerous lesions among the Lebanese population.

Secondary objectives

The secondary objectives of our study are to:

1. Determine positive likelihood ratio (LR), and negative LR, positive predictive value (PPV), and negative predictive value (NPV) for FIT.
2. Determine the accuracy of FIT test, and the factors associated with positive FIT
3. Evaluate the FIT as a possible screening test for detecting colonic pre-cancerous and cancerous lesions among the Lebanese population.
4. Evaluate the need for further endoscopic investigation for CRC after a negative FIT result.

Subjects and Methods Ethical Information

The study protocol was approved by the thesis committee of the Faculty of Medicine, Lebanese University, then by the Institutional Review Board (IRB) of the ethical committee of both Al Rassoul and Bahman hospital before beginning this research study (Annexure 1). During analysis, patient data were kept confidential using assigned codes.

Study Design

This was a retrospective study conducted to assess the sensitivity and the specificity of FIT in detecting CRC. We retrospectively reviewed the medical records of all patients who had received both FIT and colonoscopy in the colorectal departments of Bahman hospital, and Al Rassoul Hospital in Lebanon over the period spanning 5 years starting from January 2016 till December 2021.

Study Population

Number of patients: This retrospective study overall included a total of 54 asymptomatic patients who presented to Bahman and Al Rassoul hospitals between January 2016 and December 2021 and who underwent both FIT and colonoscopy examination.

Inclusion and exclusion criteria

We included in this study all asymptomatic patients who are 45 years of age and older, who have undergone both an FIT and a colonoscopy after FIT result.

Patients were excluded if they were younger than 45 years of age, and those with alarming symptoms including rectal bleeding, weight loss, severe constipation, and/or obstipation. We also excluded patients with previous colonoscopy findings, and those with a previous positive FIT. Patients with prior colon resection, or other colon/rectal surgery, and those with a history of inflammatory bowel disease were excluded as well.

Procedures of Data Collection and Measurement

Procedures of data collection

We reviewed the computerized medical records of patients to identify the eligible ones using structured case report data sheet (Annexure 2). The following information were extracted: demographic information (age, gender), lifestyle characteristics including diet, alcohol and smoking habits, and physical activity, medical information including clinical symptoms, past medical history, FIT results, and colonoscopy findings.

For the purpose of the study, colonoscopy findings were considered positive only in if polyps with a size > 1 cm or if a tumor was found. Findings with polyp of less than 1 cm and normal findings were considered negative colonoscopy findings.

Study measurement

Sensitivity: Sensitivity is defined as the ability of FIT to correctly diagnose patients with CRC. Sensitivity is calculated as the number of FIT-positive participants with CRC (TP) divided by the total number of participants with CRC (TP+FN).

Specificity: Specificity is defined as the ability of a FIT to correctly classify an individual with no CRC. Specificity is calculated as the number of FIT-negative participants without CRC (TN) divided by the total number of participants without CRC (FP+TN).

Likelihood ratio (LR): Likelihood ratio is defined as how much does the FIT improve the likelihood of making a correct diagnosis. A positive LR (+LR) is the improvement of likelihood of correctly diagnosing the presence of CRC. A negative LR (-LR) is the improvement of likelihood of correctly diagnosing the absence of CRC (to rule out having CRC). It's important to note that a high +LR value and a low -LR provide strong diagnostic evidence to rule in or rule out diagnoses, respectively.

Accuracy

The accuracy is defined as the ability of FIT to differentiate between patients with CRC and healthy cases.

Accuracy = (TP +TN)/(TP +TN + FP+FN).

Positive predictive value (PPV): It is the percentage of patients with a positive FIT who actually have CRC.

PPV = (TP)/ (TP +FP)

Negative predictive value (NPV): It is the percentage of patients with a negative FIT who do not have CRC.

NPV = (TN)/ (FN +TN).

Definitions

- **True positives (TP):** Participants in whom the FIT correctly diagnosed CRC as diagnosed by the gold standard colonoscopy.
- **False positives (FP):** Participants who have positive FIT but do not have CRC according to the colonoscopy. In other words, FIT has wrongly diagnosed CRC.
- **False negatives (FN):** Participants who have CRC on colonoscopy but have negative results in FIT.
- **True negative (TN):** Participants who do not have CRC according to the colonoscopy and have negative results in FIT.

Data Analysis

Data analysis was carried out using the Statistical Package for Social Science (SPSS), version 24. Descriptive analyses including frequencies were used for categorical variables and mean and standard deviation were calculated for continuous variables. To calculate the values of sensitivity, specificity, accuracy, positive Likelihood Ratio (LR), and negative LR, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) for FIT, assuming

the gold standard to be the results of the colonoscopy technique, we constructed a 2 x 2 table using the results of FIT and colonoscopy (Table 2). Finally, Chi-square test was used to identify factors that are associated with a positive result of FIT. A p-value of < 0.05 was considered significant.

	Positive colonoscopy	Negative colonoscopy
Positive FIT	a (TP)	b (FP)
Negative FIT	c (FN)	d (TN)
	Sensitivity = TP/(TP+FN)	Specificity = TN/(TN+FP)
	+LR = sensitivity/(1-specificity)	-LR = (1-sensitivity)/(specificity)
	PPV = TP/(TP+FP)	NPV = TN/(FN+TN)
	Accuracy = TP+TN/(TP+FP+FN+TN)	

TP: True Positive, FP: False Positive, FN: False Negative, TN: True Negative, +LR: Positive Likelihood Ratio, -LR: Negative Likelihood Ratio, PPV: Positive Predictive Value, NPV: Negative Predictive Value.

Table 2: Calculation of sensitivity, specificity, LR, PPV, and NPV, accuracy.

Results

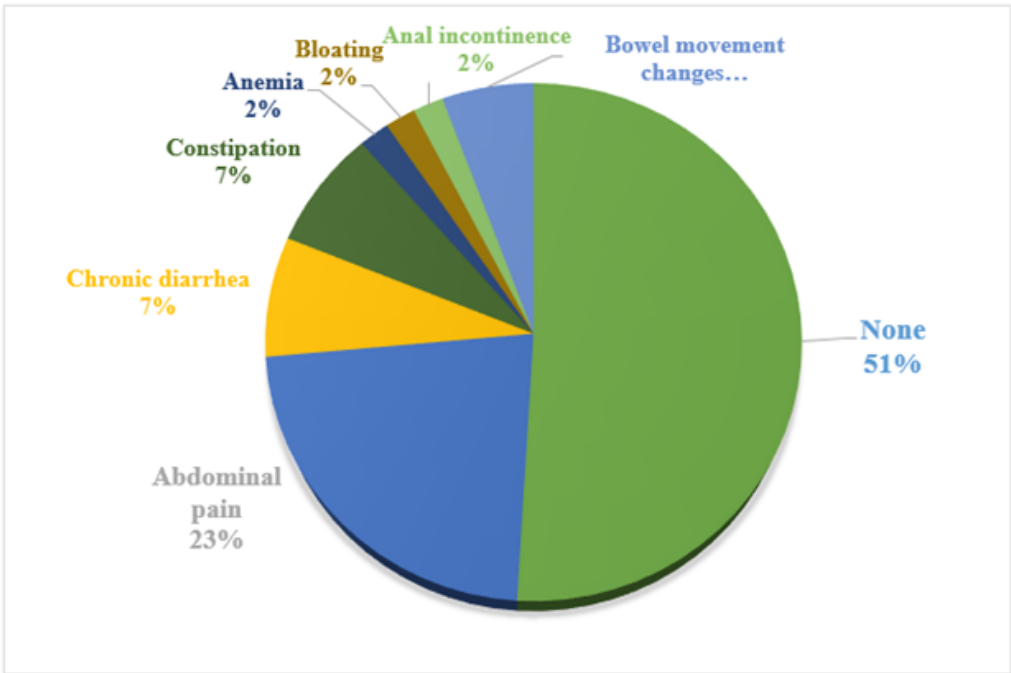
Patients Characteristics

During the study period, from January 2016 to January 2021, a total of 54 patients who underwent FIT followed by colonoscopy in the colorectal departments of Bahman hospital (42 patients, 77.8%) and Al Rassoul Hospital (12 patients, 22.2%) were enrolled in this study. The mean age of patients was 66.89 ± 10.67 years. Fifty-five point six percent of patients were males and 44.4% were females. Description of the study population is shown in table 3.

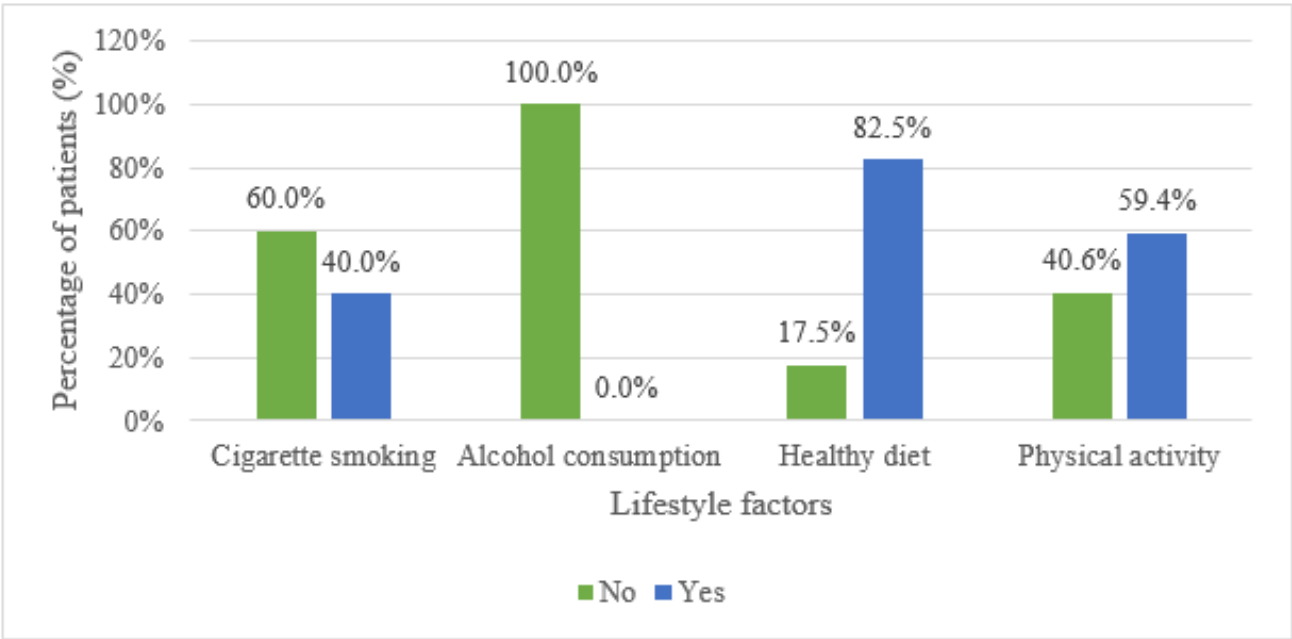
Demographic Characteristics	
Mean Age in years (SD)	66.89 (10.67)
Hospital, N (%)	
Bahman Hospital	42 (77.8)
Al Rassoul Hospital	12 (22.2)
Gender, N (%)	
Male	30 (55.6)
Female	24 (44.4)
SD: Standard Deviation; CRC: Colorectal Cancer	

Table 3: Demographic characteristic of patients.

In the present study, we found that abdominal pain was the main symptom reported by 23% of patients, followed by chronic diarrhea and constipation reported by 7% of patients each. Less common symptoms were anal incontinence (6%), anemia (2%), and bloating (2%). However, 51% of patients reported not having any symptom (figure 6).



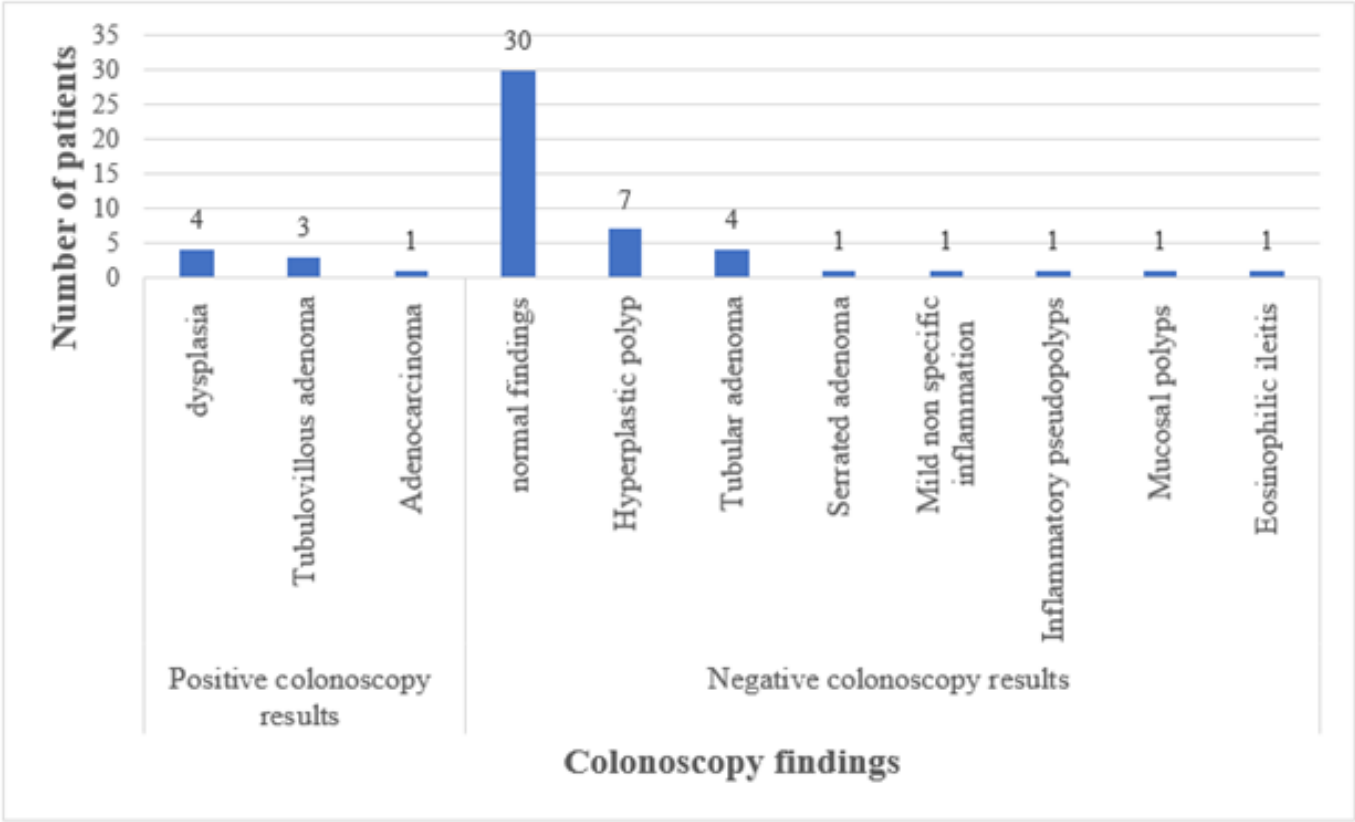
Results of lifestyle characteristics are represented in figure 7. We found that 40.0% of patients were cigarette smokers. As for the alcohol consumption, none of patients reported that they drink alcohol. Finally, the majority of our participants reported that they consumed healthy food (82.5%), and 59.4% of them were physically active.



Colonoscopy Findings

The current study included 8 patients who had positive colonoscopy results which encompassed 4 patients with tubular adenoma measuring more than 1 cm, 3 patients with tubulovillous polyps measuring more than 1 cm, and one patient with adenocarcinoma.

Negative colonoscopy findings included mild non-specific inflammation (1 patient), eosinophilic ileitis (1 patient), and polyps or adenomas measuring less than 1 cm including inflammatory pseudopolyps (1 patient), mucosal polyps (1 patient), hyperplastic adenoma (7 patients), tubular adenoma (4 patients), and serrated adenoma (1 patient), (figure 8). Finally, 30 patients had normal findings.



Colonoscopy and Fit Results

When looking at all 54 study patients, 8 (14.8%) patients had positive colonoscopy results and 46 (85.1%) had negative colonoscopy results. On the other hand, 34 (62.9%) of the 54 patients tested negative by FIT and 20 (37.1%) patients tested positive by FIT.

In regards to the 34 patients with positive FIT, 5 (25%) patients had positive colonoscopy results and 15 (75%) patients had negative colonoscopy results. Of those with negative FIT, 3 of 34 (8.8%) patients had positive colonoscopy results, and 31 (91.2%) patients had negative colonoscopy results (table 4).

	Positive colonoscopy	Negative colonoscopy	Total
Positive FIT	5 (TP)	15 (FP)	20 (37.1%)
Negative FIT	3 (FN)	31 (TN)	34 (62.9%)
Total	8 (14.8%)	46 (85.1%)	54
FIT: Fecal Immunochemical Test; TP: True Positive; FP: False Positive; FN: False Negative; TN: True Negative			

Table 4: Summary of Data that compare the presence of CRC in FIT to the presence of CRC in colonoscopy.

Diagnostic Performance of Fit

In the present study, the sensitivity, and specificity of FIT in detecting CRC were 62% and 67% respectively, yielding a +LR of 1.87, and -LR of 0.57. The calculated PPV and NPV were 25% and 91%, respectively. The overall accuracy of FIT was 66% (table 5).

	Positive colonoscopy	Negative colonoscopy
Positive FIT	5 (TP)	15 (FP)
Negative FIT	3 (FN)	31 (TN)
	Sensitivity = TP/(TP+FN) Sensitivity = 5/(5+3) Sensitivity = 0.62 or 62%	Specificity = TN/(TN+FP) Specificity = 31/(31+15) Specificity = 0.67 or 67%
	+LR = sensitivity/(1-specificity) +LR = 0.62/(1-0.67) +LR = 1.87	-LR = (1-sensitivity)/(specificity) -LR = (1-0.62)/0.66 -LR = 0.57
	PPV = TP/(TP+FP) PPV = 5/(5+15) PPV = 0.25 or 25%	NPV = TN/(FN+TN) NPV = 31/(3+31) NPV = 0.91 or 91%
	Accuracy = TP+TN/(TP+FP+FN+TN) Accuracy = 5+31/(5+15+3+31) Accuracy = 0.66 or 66%	

FIT: Fecal Immunochemical Test, TP: True Positive, FP: False Positive, FN: False Negative, TN: True Negative, +LR: Positive Likelihood Ratio, -LR: Negative Likelihood Ratio, PPV: Positive Predictive Value, NPV: Negative Predictive Value

Table 5: Specificity, Sensitivity, +LR, -LR, PPV, NPV, and accuracy of FIT in predicting CRC.

Factors Associated with Positive Fit

When studying the association of demographic and lifestyle factors with a positive FIT, we found that 40% of male patients had positive FIT while 33.3% of female patients tested positive by FIT. Positive FIT was higher among patients who smoked (31.3%) compared to non-smokers (25.0%). Regarding eating habits, 63.6% of those who eat healthy food had positive FIT. Finally, of those who were physically active, 31.6% tested positive by FIT.

However, none of these variables (age, gender, cigarette smoking, and physical activity) had a significant association with a positive result of FIT (p-value = 0.614, p-value = 0.66, p-value = 0.053, p-value = 0.59 respectively) (table 6).

	Negative FIT N (%)	Positive FIT N (%)	P-value*
Gender, N (%)			
Male	18 (52.9)	12 (60.0)	0.614
Female	16 (47.1)	8 (40.3)	
Cigarette smoking			
No	18 (75.0)	6 (25.0)	0.66
Yes	11 (68.8)	5 (31.3)	
Healthy diet			
No	3 (10.3)	4 (36.4)	0.053
Yes	26 (89.7)	7 (63.6)	
Physical activity			
No	10 (76.9)	3 (23.1)	0.599
Yes	13 (68.4)	6 (31.6)	

*: p-value was calculated using chi square test. CRC: colorectal cancer.

Table 6: Association between demographic and lifestyle factors and the results of FIT.

Discussion

CRC is the third most common cancer worldwide and the fourth leading cause of cancer mortality with 769,000 deaths in 2020 and is responsible for 8.3% of all cancer deaths [30]. Evidence from several studies has shown that screening for CRC could be effective in reducing the incidence and mortality of CRC [31]. FIT is one of several screening modalities for CRC that have been shown to be effective in detecting CRC among asymptomatic patients [32]. To investigate the accuracy of FIT in detecting CRC, we analyzed data from 54 asymptomatic patients who had underwent both FIT and colonoscopy in Lebanon.

Our study suggests that the sensitivity of FIT in detecting CRC was 62%, which is consistent with the values of 25% - 100% reported in the literature [33]. In the meta- analysis of Lee JK et al. the sensitivity of FIT for CRC detection was 79% [33]. Similarly, In the study by Oono Y et al., the sensitivity of FIT in detecting CRC was 74.7% [34]. Research suggests that the number of FIT samples may affect the diagnostic performance of FIT. For instance, H. Nakama et al. conducted a study to evaluate the effect of FIT sample number on the diagnostic accuracy of FIT among asymptomatic patients and found that the pooled sensitivity of FIT increased from 56% with single FIT samples, to 83% with 2 FIT samples [35]. In our study, we reported the sensitivity of single FIT. This consequently might reduce the sensitivity of FIT in detecting CRC.

The estimated specificity of FIT in detecting CRC reported in the literature, ranged from 85%-96% [26]. In the study of

Lee JK et al., the specificity of FIT for diagnosing CRC was 94% [33]. Another study that evaluated the accuracy of FIT for CRC among symptomatic patients showed a 86.4% specificity [34]. In our study, we found lower FIT's specificity (67%). These findings might be related to the age of the study population. Several studies have demonstrated that older age may contribute to a reduced specificity [36,37]. For instance, a large CRC screening study from Germany, that aimed to assess factors that are associated with false-positive FIT results, found that older age (age \geq 65 years) might be a strong predictor for false-positive FIT [37]. However, our study included older patients with a mean age of 66.89 ± 10.67 years.

The ability of FITs to detect CRC at early stages is of particular interest, because when CRC is found at an early stage, the chances of cure of CRC increase when compared with when diagnosed at later stages [36]. Research suggested that FIT might be performed better in late-stages CRC. In a recent meta-analysis from 2020, that evaluated the stage specific sensitivity of FIT for CRC detection, the FIT sensitivity for stage I cancers was significantly lower, by approximately 10% points than the sensitivity for stages II and IV CRC [36]. Another meta-analysis found that FIT sensitivity for stage I cancers was significantly lower than sensitivity for stages II and III. Similarly, Giaia A et al. conducted a study to investigate the sensitivity of FIT according to tumor stage among patients undergoing colonoscopy and newly diagnosed with CRC. In the aforementioned study, a strong association was found between advanced tumor stages and higher sensitivity [38]. The results of these studies indicate the need for further improvement of FIT in the detection of CRC in its early stages.

While the majority of colon cancers start as polyps, only 5-10% of all polyps will become cancerous. The size of a polyp typically does make a difference. The larger the polyp becomes, the bigger the risk of it developing into colon cancer. That risk increases significantly if the polyp is greater than 10 mm (1 cm) [39]. Research has shown the larger a colon polyp becomes, the more rapidly it grows [39, 40]. In our study, Patients with polyps > 1 cm represented 14.8% (8 patients) of the total population of whom 4 patients had dysplasia, 3 patients had tubulovillous adenoma, and 1 patient had adenocarcinoma, and this proportion was slightly lower than that reported in the study of Lieberman et al. [40] conducted among 13,992 asymptomatic patients who had screening with colonoscopy (7.3%). In this study, 7.4% of patients with polyp > 1 cm had either cancer or adenoma with high-grade dysplasia. 23.2% had adenoma with villous histology or serrated adenoma and 51.4% had tubular adenomas [40].

Several studies have tried to evaluate which characteristics of adenomas are associated with a positive FIT result [39, 41, 42]. Number and size of adenomas, location, and pedunculated mor-

phology seem to be related to a positive result [39, 41, 42]. It has been shown that the sensitivity of fecal occult is significantly higher for adenomas with advanced histology, larger size, and pedunculated shape [43]. A systematic literature review has tried to determine the sensitivity of FIT for proximal neoplasia on the basis of previously published articles [42]. Most of the studies showed a higher sensitivity of fecal occult blood test for advanced neoplasia in the left colon versus right colon [42]. [42] Cubeilla et al., [43] conducted a study to determine the individual characteristics of adenomas independently associated with a positive test, and found a difference in FIT sensitivity for right-sided versus left-sided advanced adenomas, with lower sensitivity for right sided adenoma. According to the author, lower sensitivity for right sided adenomas could be related to a longer bowel passage and to a different stool consistency [43].

Various studies comparing FIT to other screening methods used to detect the presence of CRC have shown it to be superior to the other screening modalities. In our study, the overall accuracy of FIT for detection of CRC was 66% and this results was lower than that reported in a recent systematic review and meta-analysis including 19 studies and showed an overall accuracy of FIT of 95% [34]. Additionally, clinical trials have shown that FIT is more sensitive at detecting both CRC and adenomas than FOBTs [44]. A Canadian study organized among average-risk individuals found that the rate of positivity with FIT was 4.8%, compared to 3.7% with g-FOBT. Moreover, the protective effect of FIT had been demonstrated in several screening programs. For instance, an organized single FIT screening program in Florence where 6961 participants were screened with an average follow-up period of 11 years have shown a 22% decrease in the incidence of CRC [45]. However, several studies have demonstrated that the sensitivity of FIT for detecting colon poly is low [46].

A false negative was defined as an individual with a negative FIT result in whom CRC were detected during colonoscopy. Whereas, a false positive test was defined as an individual with a positive FIT result and no CRC detected during colonoscopy [47]. In our study, we found a false positive rate of 9% which is consistent with the false-positive FIT rates of 4.3%–15.7% reported in the prior studies [37]. However, our study reported a high rate of false-negative results (44.4%). Recent studies suggested that some subgroups had higher risk of inaccurate FIT results [37, 48]. For example, it was found that the possibility of having false positive results is higher among male patients, while smokers and patients with advanced age had higher rates for false negative results [37, 48, 49]. As mentioned previously, this study included older patients, with 40% of the study group being smokers. This might explain the high rates of false-negative results reported in our study.

Finally, few previous studies have assessed the effect of socio-demographic and lifestyle characteristics in the diagnostic

performance of FIT. For instance, in a large cohort screening study conducted to assess the variation of diagnostic accuracy of FIT by gender and age among 3,211 patients aged between 50 and 79 years in Germany, the diagnostic performance of FIT was similar for both sexes and age groups [50]. Similarly, in our present study, we did not find a significant variation in the ability of FIT to detect CRC by gender or lifestyle characteristics.

Study Limitations and Strengths

This study, to the best of our knowledge, is the first to report accuracy of FIT in detecting CRC among Lebanese asymptomatic patients. It is important because starting with such a small sample size could anticipate the results that will be obtained from future studies that could be conducted over larger sample sizes to finally give a definitive proof of FIT effectiveness.

In terms of limitations, first, this study was retrospective, and accordingly some patients' data were missing or incomplete. Second, because the locations of the polyps were not specified in the medical record, we were unable to determine on which side of the colon the polyps developed. Third, the study included a small number of patients, and accordingly, these numbers limit the possibility to detect risk factors associated with positive FIT. Finally, lifestyle habits were based on patients' self-reports which might add data collection bias.

Study Perspectives

Considering the limited research on the accuracy of FIT in evaluating patients with CRC, further prospective studies should be conducted over a larger group of patients to evaluate the effectiveness of this screening modality and to explore the predictive factors of positive diagnosis with FIT in asymptomatic patients. We also recommend further research to evaluate the stage-specific sensitivity of FIT for CRC detection. Finally, we recommend future research to investigate risk factors associated with having false-negative and false positive FIT.

Conclusion

FIT has become an important screening tool for the detection of CRC. Its use is increasing all over the world and several studies have demonstrated its ability to detect the majority of CRCs [36]. In Lebanon, The Lebanese Ministry of Health adopted FIT as a screening test for early detection of CRC among average risk groups [23]. Accordingly, and to investigate the accuracy of FIT in detecting CRC, we conducted this retrospective study that aimed to determine the values of specificity and sensitivity of FIT among asymptomatic patients who had received both FIT and colonoscopy in Lebanon.

In summary, we found that the FIT test is 66% accurate at predicting if a patient had CRC. It had a moderately high sensitiv-

ity (62%) and specificity (67%) in detecting CRC among asymptomatic patients.

To conclude, screening plays an increasing role in the early diagnosis of patients at average risk for CRC, and therefore in reducing CRC mortality [31]. However, future research should focus on including diagnostic markers, that can be combined with FIT in order to improve the ability of FIT to early detect CRC.

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