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Yield of Colonoscopy After a Positive Result From a Fecal Immunochemical Test OC-Light

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Abstract

Background & Aims—The fecal immunochemical test (FIT) is widely used in colorectal cancer (CRC) screening. The OC-Light FIT is 1 of 2 FITs recommended for CRC screening by the Preventive Services Task Force guidelines. However, little is known about its ability to detect CRC in large average-risk populations.

Methods—We performed a retrospective cohort study of patients (50–75 years old) in the San Francisco Health Network who were screened for CRC by OC-Light FIT from August 2010 through June 2015. Patients with a positive result were referred for colonoscopy. We used

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electronic health records to identify participants with positive FIT results, and collected results from subsequent colonoscopies and pathology analyses. The FIT positive rate was calculated by dividing the number of positive FIT results by the total number of FIT tests completed. The primary outcome was the positive rate from OC-Light FIT and yield of neoplasms at colonoscopy. Secondary outcomes were findings from first vs subsequent rounds of testing, and how these varied by sex and race.

Results—We collected result from 35,318 FITs, performed on 20,886 patients; 2930 patients (8.3%) had a positive result, and 1558 patients completed the follow-up colonoscopy. A positive result from the FIT identified patients with CRC with a positive predictive value of 3.0%, and patients with advanced adenoma with a positive predictive value of 20.8%. The FIT positive rate was higher during the first round of testing (9.4%) compared to subsequent rounds (7.4%) ($P<.01$). The yield of CRC in patients with a positive result from the first round of the FIT was 3.7%, and decreased to 1.8% for subsequent rounds ($P=.02$).

Conclusion—In a retrospective analysis of patients in a diverse safety-net population who underwent OC-Light FIT for CRC screening, we found that approximately 3% of patients with a positive result from a FIT to have CRC and approximately 21% to have advanced adenoma.

Keywords

early detection; colon cancer; prevention; stool; abnormal

Introduction

Colorectal cancer (CRC) is the second leading cause of cancer-related deaths and the third most common diagnosed cancer in the United States.(1) The incidence and mortality rates of CRC have declined over the last three decades corresponding to multiple factors including increases in CRC screening rates.(2)(3) The U.S. Preventive Services Task Force (USPSTF) recommends CRC screening between ages 50-75 in average-risk adults.(3) However, screening rates remain suboptimal, and it is estimated that further reductions in CRC incidence rates by 22% and mortality rates by 33% are possible if screening rates of 80% in the U.S. were achieved.(4) To capture the patients not up-to-date with CRC screening and to maintain high rates of CRC screening, organized population-based programs that include stool-based testing are needed.(5)(6)

The USPSTF recommends the use of the fecal immunochemical test (FIT) as a stool-based test for CRC screening.(3) The Food and Drug Administration (FDA) has cleared the use of many FIT in the U.S. for use in CRC screening programs and granted the tests a waived status under the Clinical Laboratory Improvement Amendments (CLIA).(7) However, performance characteristics of many FDA-cleared FIT have not been evaluated in large average-risk populations and the quality of their development and interpretation have not been validated. FIT detects the globin moiety of human hemoglobin in the stool.(8) OC-Light FIT is a qualitative test analyzed by immunoassay methods and differ from quantitative FIT.(9) Qualitative FIT can be developed and interpreted at point-of-care (POC), which raises concern for consistency in sample application and visual interpretation. The positivity threshold of qualitative FIT (cutoff concentration for a test to be positive) is set by

the manufacturer and cannot be adjusted by the end user. In contrast, quantitative FIT, which is also FDA-cleared to provide only qualitative results, requires laboratory-based calibration using standard curves. The positivity cutoff can be adjusted, which allows the end user to adjust the sensitivity and specificity of the test.(10) The development and interpretation is automated after calibration and offers high throughput of specimens.

FIT sensitivity for CRC is estimated to be 75%, but has varied between 25% and 100% across different types of FIT tests, while the specificity has varied between 83% and 99%.(11) There is limited data on the real-life application of many qualitative FIT barnds available in the U.S. or their positivity rates in average-risk population. Specific to OC-Light FIT, heterogeneity has been reported in the real-life application of the test, though USPSTF recommended the use of OC-Light FIT. The yield of colonoscopy for CRC using the OC-Light FIT has varied between 1.7% and 10.8%.(12–16) Therefore, the aim of the study was to evaluate the positive rate of the OC-Light FIT and the yield of colonoscopy after a positive result from a FIT in a diverse average-risk patient population in a safety-net system.

METHODS

Study Design and Population

We conducted a retrospective cohort study of patients ages 50-75 in the San Francisco Health Network (SFHN) who received CRC screening by FIT between August 2010 and June 2015. The study cohort and setting have been previously described.(17) In short, SFHN is an integrated healthcare safety-net system that delivers health services to uninsured, Medicaid, and other vulnerable residents of San Francisco. It is an integrated safety-net system comprised of 12 adult community health centers, a centralized laboratory, and a multi-specialty medical center, the Zuckerberg San Francisco General Hospital and Trauma Center (ZSFG).(17)

Screening with FIT

FIT testing with the OC-Light® FIT tests (Polymedco, Inc., New York) started to be used in 2010 and were fully adopted across the system by 2012 as the primary form of CRC screening for average-risk individuals. The OC-Light test was provided to patients at a point-of-care visit and patients returned the completed test by mail to a central ZSFG clinical laboratory, where it was processed. The OC-Light FIT is a lateral flow chromatographic immunoassay using immobilized antibodies specific to human hemoglobin, which provides qualitative results in the form of a visible reddish/pink line at a cutoff of 10 μg hemoglobin/g stool.(7) This cutoff is lower than that of the OC-Sensor® FIT (Polymedco, Inc., New York) (20ug hemoglobin/g stool), which is the only other FIT in the U.S. recommended by the USPSTF. As a result, the OC-Light FIT is likely to have higher positive rate and sensitivity, and lower specificity compared to the OC-Sensor FIT.

Data Sources and Collection

SFHN is supported by E-Clinical Works (eCW) as its primary outpatient electronic health record platform, which is linked to other data sources such as the clinical laboratory and gastroenterology procedures. Demographic information, clinic details, and laboratory data of

individuals with positive results from FIT were abstracted from patients' medical records. Receipt of colonoscopy was confirmed and findings were abstracted using the endoscopy software ProVation® (ProVation Medical Inc., Minneapolis, MN). Pathology results were abstracted and reviewed using CoPathPlus® platform (Cerner, Canada).

Colonoscopy Data

Colonoscopy quality as measured by bowel preparation and cecal intubation rate was abstracted from procedure reports in ProVation. The quality of colonoscopy preparation was considered adequate if the endoscopist reported the preparation was adequate or at least fair and cecal intubation was achieved.(18) However, failure to reach the cecum in procedures with inadequate preparation were excluded from the calculation.(18) The adequacy of colonoscopy preparation rate was reported based on the first colonoscopy for patients with multiple colonoscopy reports following a positive FIT.

Pathological Findings

Pathology reports were reviewed for the following findings: cancer, advanced adenoma, and advanced neoplasia. Advanced adenoma was defined as an adenoma that was 10 mm or more in diameter or any size with villous features or high-grade dysplasia. Advanced neoplasia was defined as cancer or advanced adenoma. Non-advanced adenomas were not reported because clinically, they rarely if ever bleed.(19) Some patients had repeated colonoscopies for inadequate preparation or incomplete examination. Pathology findings were reported based on the most advanced lesion detected, which included subsequent colonoscopy if the initial colonoscopy was inadequate or incomplete.

Statistical Analysis

Patient demographic information was described as proportions, except age, which was described using medians and interquartile ranges. The FIT positive rate was calculated as the number of positive results from FIT divided by the total number of FIT tests completed. The positive rate of FIT was further stratified into first round and subsequent rounds of testing. The primary outcome of the study was the yield or positive predictive value of colonoscopy for the detection of cancer and advanced adenomas after positive results from OC-Light FIT. Secondary endpoints included pathology findings by race and gender. Differences between groups of patients were assessed using χ^2 and Student's *t*-test, as appropriate. The data was collected in Microsoft Excel then analyzed using STATA/IC (version 14.2; StataCorp LLC, College Station, TX, USA). The study was approved by the institutional review board at University of California San Francisco (IRB #: 13-11900).

RESULTS

FIT positivity rate and colonoscopy completion

A total of 35,318 FIT tests were completed in 20,886 patients during the period of August 2010 to June 2015. The total number of patients with positive results from FIT was 2,930 with an overall positive rate of 8.3%. The FIT positive rate was higher in the first round compared to subsequent rounds (9.4% vs. 7.4%, $P<.01$). Men had higher positive rate compared to women (10% vs. 6.9%, $P<.01$). The rate of positive results from FIT was lowest

among Asians (7.0%), followed by Hispanics (8.2%), then African Americans (11.7%) and non-Hispanic Whites (11.9%) (P<0.01). FIT positive rates stratified by gender and race are summarized in Table 1.

Of patients with positive results from FIT, 1,558 patients (53.2%) completed the follow up colonoscopy procedure. Reasons for incomplete colonoscopy in this study population have been previously reported.(10) The median age of patients who had colonoscopy was 59.7. Among the patients completing the colonoscopy, 44.5% were Asian, 19.1% were non-Hispanic White, 16.2% were Hispanic, and 14.9% were African American (Table 1). Patients who completed their colonoscopy had the following insurance coverage: Medicaid 34.3%, Medicare 33.6%, Healthy Worker 22.2%, and Healthy San Francisco 5.8%.

Yield of Colonoscopy following positive results from FIT

CRC was diagnosed in 3.0% of patients who underwent colonoscopy, advanced adenoma in 20.8%, and advanced neoplasia in 23.8% (Table 2). The yield of CRC in patients who had positive results from FIT during the first round of testing was 3.7%. During the subsequent rounds, the yield of CRC declined to 1.8% (3.7% vs. 1.8%, *P*=.02). Among the patients who completed their colonoscopy, the bowel preparation during the first colonoscopic examination was adequate in 91.5%.

Overall, neoplasia was more frequent in men than women. Men were nominally more likely than women to be diagnosed with CRC following positive results from FIT, but this did not reach statistical significance (3.7% vs. 2.4%, *P*=.16). Similarly, men were more likely to have advanced adenoma (26.7% vs. 15.5%, *P*<.01), and advanced neoplasia (30.4% vs. 17.9%, *P*<.01) (Table 3).

Nominally, the rate of CRC was highest in Asians (3.8%), followed by non-Hispanic White (3.4%), Hispanic (2.0%), and African American patients (1.3%), although the absolute cases of CRC were small among African Americans (n=3) and Hispanics (n=5). Other pathologic findings were stratified by race and available in Supplementary Table 1.

Discussion

This is the largest study of the OC-Light FIT evaluating its performance for CRC screening in a diverse average-risk safety net population. The results showed a positive rate of approximately 8% and a positive predictive value (PPV) for CRC of 3%. These estimates vary by first round versus subsequent rounds of FIT testing. In this integrated safety-net system, OC-Light FIT effectively risk stratified patients for colonoscopy.

To our knowledge, our study is the largest to focus specifically on the OC-Light FIT; moreover, the population was diverse. Unlike most other screening programs, the OC-Light tests were developed and interpreted in a certified clinical laboratory. For these reasons, our results may be more reliable and reproducible than those reported from study settings or clinical practices where the tests were developed and interpreted in doctor’s offices or non-certified laboratories. Prior to this study, the yield of colonoscopy for CRC ranged between 1.7% and 10.8%. Our study suggests that the yield of colonoscopy for CRC after a positive

results from a FIT is 3.0%, which falls within the range reported in the literature (Supplementary Table 2).(12–16) Given the size of our study, this is likely a valid estimate. As such, OC-Light FIT screening program can effectively allocate colonoscopy procedures by identifying one CRC case in 33 colonoscopy procedures instead of identifying one CRC case in 200 procedures.

OC-Light FIT has a 10 μg hemoglobin/g stool cut-off. Correspondingly, the FIT positive rate in this study is higher than studies utilizing other brands of FIT. Indeed, when the cutoff is less than 20 μg hemoglobin/g stool, the FIT positive rate has ranged between 5.3% and 14.2%, while those that used a cutoff of 20 to 50 μg hemoglobin/g stool, the range was between 1.4% and 7.5%.(12) Lower cutoff results in higher positive rates, which in turn results in lower PPV for CRC. Given the 10 μg hemoglobin/g stool cutoff for OC-Light FIT, our results fall within the ranges reported in the literature.(12–16)

It is notable that the positive rate of FIT and yield of CRC vary by gender and race.(2)(20) Gender has been strongly associated with differences in CRC incidence and mortality rates, where men have higher rates compared to women by 30% and 40%, respectively.(20)(21) Across race, our study showed that cancer detection rate was the highest among Asian population, while their positive rate was the lowest. African Americans have historically had the highest CRC incidence and cancer related mortality.(20) In our study, although we reported relatively higher FIT positive rates among African-Americans, this did not result in downstream higher rates of CRC as reported in the literature. This limitation may be due to differences in our sample size compared to population health studies.(20) The advanced neoplasia rate is fairly consistent across race, so the low CRC in African Americans may be reflecting the small sample size.

There are several limitations to this study. Because we sought to determine the real-life performance of OC-Light FIT, we were not able to calculate the sensitivity and specificity of the test as colonoscopy was not performed in all patients. Specifically, we did not have reliable long term follow-up for each patient, which precluded our ability to examine whether negative results from FIT may have missed interval CRC. Moreover, the lack of follow up colonoscopy for all individuals with positive FIT may have confounded the colonoscopy findings if differential follow-up occurs for those with and without colonic pathology. In particular, the colonic pathology may have been overestimated assuming that patients with CRC are more likely to complete their colonoscopy. However, given that FIT is used to screen average-risk asymptomatic individuals, the majority of patients should be asymptomatic and therefore, differential follow-up should be limited. Any symptom would have prompted a direct referral for colonoscopy, which is readily accessible in this health system.

In conclusion, this study is a large real-life summary of the performance of OC-Light FIT in a diverse safety-net population. OC-Light appears to effectively identify high-risk individuals, resulting in high-yield colonoscopy procedures. It provides health systems with perspective on the colonoscopy demand and performance characteristics of OC-Light as a screening tool in diverse patient groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

FIT positive rates by race and gender

	Positive rate % (95% Confidence Interval)
Gender	
Female	6.9 (6.6 – 7.3)
Male	10.0 (9.6 – 10.5)
Race	
Asian	7.0 (6.7 – 7.4)
Non – Hispanic White	11.9 (11.1 – 12.7)
Hispanic	8.2 (7.6 – 8.8)
African American	11.7 (10.8 – 12.6)
Overall	8.3 (8.0 – 8.6)
First round	9.4 (9.0 – 9.8)
Subsequent Rounds	7.4 (7.0 – 7.9)

Table 2

Summary of colonoscopy findings among patients with positive results from FIT

	Percentage (n)	95% Confidence Interval
Colonoscopy follow-up	1,558	
Gender		
Female	52.6 (820)	50.1 – 55.1
Male	47.4 (738)	44.9 – 49.9
Race		
Asian	44.5 (693)	42.0 – 47.0
Non-Hispanic White	19.1 (298)	17.2 – 21.2
Hispanic	16.2 (252)	14.4 – 18.1
African American	14.9 (232)	13.2 – 16.7
Pathology findings*		
Cancer	3.0 (47)	2.3 – 4.0
Advanced adenoma	20.8 (324)	18.9 – 22.9
Advanced neoplasia	23.8 (371)	21.8 – 26.0

*Pathology findings were reported based on the most advanced lesion detected. The bowel preparation was adequate in 91.5% of patients during the first round of colonoscopy.

Table 3

Pathology findings by gender in patients with positive results from FIT

	Male N = 738 (%)	**Female N = 820 (%)**	***P*-value**
Cancer	27 (3.7)	20 (2.4)	.16
Advanced adenoma	197 (26.7)	127 (15.5)	< .01
Advanced neoplasia	224 (30.4)	147 (17.9)	<.01