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Adenoma Detection Rate after Positive Stool-Based Screening in a U.S. Population

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Abstract

Introduction and Objectives Over the past two decades, advancements in screening programs have led to a decrease in the incidence and mortality rates of colorectal cancer. The recommended benchmark for primary screening colonoscopy adenoma detection rate (ADR) is 25%. However, recent research supports higher ADR benchmarks following positive stool testing. Findings from a Dutch screening program have suggested higher ADRs in fecal immunochemical test positive patients with an inverse relationship with interval cancer development. Our study aims to assess ADRs in a U.S. patient population with positive stool screenings and investigate any correlation to occurrences of interval cancers.

Materials and Methods Data from all positive stool-based screening participants who subsequently underwent colonoscopy at a tertiary care center between 2017 and 2021 were collected. A retrospective chart review was performed to determine the ADR and interval colon cancers.

Results From a total of 120 patients (32 fecal occult blood test [FOBT] positive patients, 43 fecal immunochemical test [FIT] positive patients, 45 FIT-DNA-positive patients), the average ADR was 35%. Nonadvanced polyps were the most identified adenomas at 78.6%. No interval colorectal cancer cases were identified. There was a clear difference in ADR between stool-testing methods, with FIT-DNA showing higher ADRs than FIT and FOBT.

Conclusion Endoscopists should recognize the importance of higher ADR targets in colonoscopies conducted after positive stool-based screening as a means to maintain high-quality colonoscopy standards.

Keywords
- adenoma detection rate
- colonoscopy
- colorectal cancer
- colorectal neoplasms
- stool-based screening

Introduction

Colorectal cancer (CRC) is the second most common cause of cancer-related death globally, with an estimated incidence of 153,020 new cases and estimated mortality of 52,550 cases in the United States in 2023.[1–3] However, the incidence rate has shown a steep decline over the past two decades (46%; from 66.2 per 100,000 in 1985 to 35.7 per 100,000 persons in 2019), owing largely to a shift to earlier stage diagnosis with participation in population-based screening methods.[2] For instance, with Medicare coverage for colonoscopy screening

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expanding to all beneficiaries in 2001, colonoscopy prevalence tripled (20% in 2000 to 61% in 2018 among adults aged ≥50 years) with corresponding decline in annual incidence of CRC by 3 to 5%.[2,4] Indeed, colonoscopy is considered the gold standard screening tool, offering high sensitivity for both cancer and all classes of precancerous lesions.[5] It is also generally well known that increasing adenoma detection rate (ADR), defined as the proportion of screening colonoscopies that detect at least one adenoma, is inversely correlated to incidence of interval CRC.[5–8] Concordantly, in 2006 the American Society for Gastrointestinal Endoscopy Task Force recommended an ADR target of 20% in female patients and 30% in male patients for primary screening colonoscopies, accounting for an average ADR of 25%.[9,10]

Currently, several noninvasive colorectal screening tests have been approved by the U.S. Food and Drug Administration to increase patient compliance with screening participation.[11] Among these, stool-based screening tests including the guaiac-based fecal occult blood test (FOBT), fecal immunochemical test (FIT), and the fecal DNA testing (FIT-DNA) have received widespread uptake. These tests detect fecal biomarkers of CRC and precancerous lesions prompting further evaluation with colonoscopy for a positive test.[11] Given wide adoption of this sequential screening approach, recent evidence supports higher ADR targets in patients who have a positive stool test.[9,12–14] For example, findings from Wisse et al[9] in a multicentered Dutch CRC screening program suggested a median ADR of 67% in FIT-positive colonoscopies and an inverse relationship to interval CRC. Specifically, the authors reported that among endoscopists having ADRs of 65 versus 55%, the occurrence of interval postcolonoscopy colorectal cancers (PCCRCs) was almost halved. Indeed, multiple expert groups, including the United States Preventive Services Task Force, have proposed ADR of around 40% in colonoscopies evaluating FIT positivity as a new quality metric; however, the quality of evidence to support this has been low.[15,16]

We aimed to assess the ADR in all patients with stool-positive screening at a U.S. tertiary care center, and determine whether there is any relationship to the development of interval cancers. These findings will help elicit the generalizability of the previously reported results and inform endoscopists of ADR targets that will optimize health outcomes in this demographic.

Materials and Methods

All persons undergoing FOBT, FIT, and FIT-DNA who received a positive test result and who underwent a first colonoscopy between January 1, 2017 and December 31, 2021 at MedStar Georgetown University Hospital, a U.S. academic tertiary care center, were included. FOBT and FIT positivity cutoff of 20 µg of hemoglobin and FIT-DNA cutoff of 100 ng of hemoglobin per gram of feces were used. Participants were excluded if aged less than 18 years and if they had received diagnosis of CRC within 6 months of the first colonoscopy. A retrospective chart review was performed to determine the ADR (number of procedures completed with detection of at least one adenoma divided by the total number of procedures done during the time period) and interval colon cancers. The latter is defined by the World Endoscopy Organization and United States Preventive Services Task Force as any CRC diagnosed more than 6 months after the first colonoscopy in which no CRC had been diagnosed and before the next recommended surveillance colonoscopy. Secondary outcomes measured were the serrated polyp detection rate (SPDR), including any identified sessile serrated adenomas or polyps, traditional serrated adenomas, and hyperplastic polyps. All polyps confirmed on histopathology. Colonoscopy quality indicators including sufficient bowel preparation (based on the Boston Bowel Preparation Scale) and the rate of sufficient colonic withdrawal time (CWT) were also measured. Ancillary aids including artificial intelligence systems were not used during colonoscopy assessment. One-way analysis of variance testing was used to compare outcomes between stool-based tests.

Results

A total of 120 patients were identified, including 32 (26.7%) FOBT-positive, 43 (35.8%) FIT-positive, and 45 (37.5%) FIT-DNA-positive screening participants. Among these patients, 58 (48.3%) were males and 62 (51.7%) were females. Eighty-one participants (67.5%) were Caucasians. The most common comorbidities were hypertension (51.7%) and hyperlipidemia (37.5%).

Colonoscopies were performed by 22 different endoscopists. Forty-two of the colonoscopies detected at least one adenoma leading to the average ADR of 35% (►**Table 1**). A

Table 1 Comparison of ADR, SPDR, and total precancerous polyp detection rates between screening tests

Stool-based screening method	Adenoma detection rate (%)	Advanced adenoma detection rate (%)	Serrated polyp detection rate (%)	Total polyp detection rate (%)
Fecal occult blood test ($n = 32$)	25.0 (8/32)	0	31.2 (10/32)	56.2 (18/32)
Fecal immunochemical test ($n = 43$)	11.6 (5/43)	4.7 (2/43)	51.2 (22/43)	62.8 (27/43)
Fecal immunochemical test–DNA ($n = 45$)	64.4 (29/45)	4.4 (2/45)	11.1 (5/45)	75.5 (34/45)
Total average ($n = 120$)	35.0 (42/120)	3.3 (4/120)	30.8 (37/120)	65.8 (79/120)

Abbreviations: ADR, adenoma detection rate; SPDR, serrated polyp detection rate.

significant difference in ADR was noted between stool-testing groups ($F = 14.9$; $p < 0.0001$). Tukey's honestly significant difference (HSD) test confirms that FIT-DNA has better detection of precancerous adenomas than FIT ($Q = 6.93$; $p < 0.0001$) and FOBT ($Q = 5.53$; $p = 0.00033$).

Nonadvanced polyps (adenomas without high-grade dysplasia, and/or <25% villous histology, and/or size <10 mm) were most identified adenomas at 78.6% (33/42). Advanced adenomas were noted in two FIT-positive and two FIT-DNA-positive participants and were not detected in any FOBT-positive patients. In comparing SPDR between groups, a significant difference was noted ($F = 7.3$; $p = 0.001$) with mean SPDR between FIT and FIT-DNA of notable distinction ($Q = 5.08$; $p = 0.00138$). Overall, there was no significant difference in the total polyp detection rate between groups ($F = 0.73$; $p = 0.48$). Additionally, no interval cancers were identified within our sample.

Assessment of other quality indicators revealed Boston Bowel Preparation Scale ≥6 points in 92.8% of procedures and colonoscopy withdrawal time ≥6 minutes in 95.4% of procedures (►**Fig. 1**).

Discussion

It is well known that the ADR, a metric describing the proportion of screening colonoscopies in which one or more adenomas are identified, is a robust colonoscopy quality indicator.[9] In one study conducted by Waldmann et al,[17] it was observed that colonoscopies performed by endoscopists whose ADR was less than 25% resulted in a higher CRC mortality rate for patients with high-risk adenomas. This was in contrast to endoscopists with an ADR exceeding 25%, where the adjusted hazard ratio was 2.25 compared with 1.35 for endoscopists with an ADR of less than 25%, respectively. Several other studies have further demonstrated an inverse correlation between the ADR and postcolonoscopy CRC risk.[5–8] The ADR is therefore a key measure of the technical performance of colonoscopy in detection of premalignant lesions and as such, the current benchmark for primary screening colonoscopy is a combined ADR of at least 25%.[9,10] Higher ADR targets for colonoscopies performed in patients with positive stool screening have been proposed, yet the quality of evidence supporting this remains inadequate.[9,12–14]

The use of stool-based testing for CRC screening has been validated by several randomized clinical trials.[18] The FOBT, which detects color change from an oxidative reaction with hemoglobin in stool, has a reported sensitivity of 62 to 79%, with specificity ranging from 87 to 96%.[18,19] Given the lack of differentiation of diet or drug mimickers from gastrointestinal bleeding, FOBT has largely been replaced by the FIT, which uses antibodies targeting human hemoglobin in stool samples. The FIT has a reported sensitivity of 73 to 92% and specificity of 91 to 97%.[18,19] Most recently, the FIT-DNA was developed, which combines the assessment of DNA biomarkers and a hemoglobin immunoassay to determine the likelihood of tumorigenesis among cells in a stool sample.[18] The sensitivity of FIT-DNA has been shown to be 92.3% with specificity at 89.8%.[20]

Research indicates that individuals hesitant about colonoscopy often find noninvasive screening tests more acceptable, leading to better adherence to national screening initiatives.[21] In regions without screening programs, categorizing patients based on risk assessments (such as the Cleveland Clinic and National Cancer Institute (NCI) tests) and recommending stool testing could aid in designing population-wide screening efforts.[11] By focusing on those who stand to gain the most, such an approach can be cost-effective and address challenges related to the demand and capacity for colonoscopies.

Indeed, with the rapid uptake of stool-based CRC screening, the population-based cohort study performed by Wisse et al[9] aimed to assess any difference in ADR in this setting compared with primary screening colonoscopies. Data collected from 300 endoscopists performing more than 110,000 colonoscopies in FIT-positive patients showed a median ADR of 67% and an inverse association between ADR and interval CRC risk. Our results further demonstrate higher average

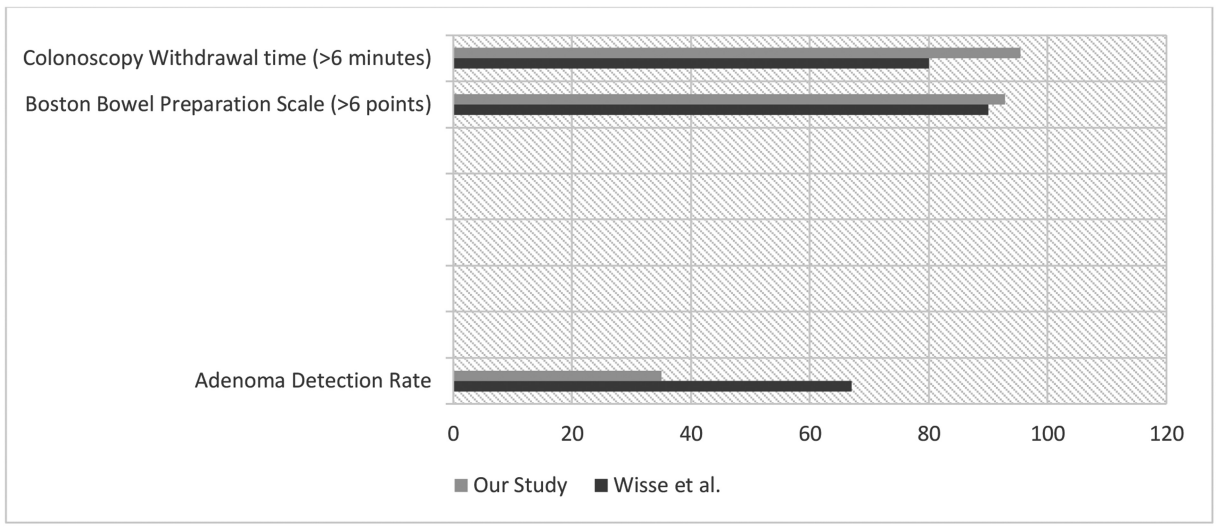

Fig. 1 Comparing adenoma detection rate (ADR), bowel cleanliness, and inspection time between endoscopies included within our study and Wisse et al.[9] The goal thresholds are based on the European colorectal cancer (CRC) screening guideline.

Table 2 Number of stool-positive screeners segmented by recommended surveillance interval and the completed surveillance interval (in years) during the study period

Stool-based screening method	Recommended surveillance interval (y)							Completed surveillance interval (y)						
	None	<1	1–3	3–5	5	5–10	≥10	None	<1	1–3	3–5	5	5–10	≥10
Fecal occult blood test	5	4	4	0	12	2	1	1	3	3	0	1	1	0
Fecal immunochemical	1	1	10	1	12	12	0	0	0	2	0	0	0	0
Fecal immunochemical test–DNA	9	4	13	0	12	2	4	0	0	3	0	0	0	0

Note: The surveillance intervals refer to the suggested time frame within which follow-up colonoscopy should occur after initial screening colonoscopy. The completed follow-up interval identifies the number of patients who completed follow-up within their recommended surveillance period and within our study period.

ADR targets in positive stool-screening participants than the current benchmark for primary screening colonoscopy (35 vs. 25%, respectively). A markedly higher ADR was noted particularly among the patients who were FIT-DNA positive with an ADR of 64.4%. Interestingly, among the FIT-positive patients only 5 out of 43 colonoscopies were able to detect at least 1 adenoma, leading to an ADR of 11.6%, which is significantly lower than the median ADR of 67% reported by Wisse et al.[9] Differences in sample sizes and longitudinal study designs could account for the discrepancy in ADR.

Approximately 51.2% (22/43) of the FIT-positive colonoscopies instead detected serrated polyps, which are not included in the ADR (vs. 3.4% [3,511/103,900] reported by Wisse et al[9]). Among the serrated polyps, the sessile serrated adenomas/polyps and the traditional serrated adenomas have a high malignant potential.[22] The current benchmark for clinically significant SPDR (defined as any serrated polyp >1 cm anywhere in the colon) is 7% and that for proximal SPDR (serrated polyp of any size proximal to the sigmoid colon) is 11%.[22] However, there is wide variation in the current literature regarding achieving these targets, largely attributed to differences in observations and interpretations between endoscopists and pathologists given the ambiguous morphology of serrated lesions.[22,23] Our data suggest that FIT testing may raise the threshold for the endoscopic detection of serrated polyps and therefore endoscopists should proceed with a higher index of suspicion when approaching these cases. Interestingly, previous studies have shown that FIT-DNA exhibits greater sensitivity in detecting serrated polyps compared with FIT.[24] This enhanced detection capability has largely been attributed to the identification of methylated pathway aberrations and the absence of bleeding from these lesions, which limits detection with FIT. The smaller sample size in our study might explain the differences observed compared with previous research. Our data further suggest a trend toward increasing total polyp detection rate from FOBT to FIT to FIT-DNA screening. These results are consistent with the known sensitivity of these tools.[18–20]

Despite no interval cancers identified, endoscopists within our institution had similarly sufficient bowel preparation and colonoscopy withdrawal times to endoscopists in the Dutch screening program.

Limitations

Our study period may have limited data collection on interval colon cancers in patients with longer surveillance recommendations (►**Table 2**). Further data collection with an extended study time period and across affiliated institutions may be better able to showcase a correlation with interval CRC and ADR. Identifying the ADR of primary colonoscopies performed by our endoscopists will also be a useful baseline measure to determine suitable ADR targets after positive stool-based screening tests.

Conclusions

Overall, the data highlight that ADR after positive stool testing is higher than current targets for primary screening colonoscopy. FIT-DNA testing shows higher ADRs than FIT and FOBT. Institutional tracking of ADRs in the setting of positive stool tests may be a helpful measure to ensure high-quality colonoscopy.

Previous Presentation
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Statement of Ethics
Approval from the Institutional Review Board was obtained before conducting the chart review.

Author Contributions
T.D. was responsible for planning of the study, collecting and interpreting of data, as well as drafting and editing of the manuscript. R.H. was responsible for collecting data and drafting of the manuscript. S.M.W. was responsible for planning of the study, data analysis, as well as editing of the manuscript. T.L. and J.J. were involved with planning of the study and revision of manuscript. All the authors have approved the final draft of the manuscript submitted.

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Conflict of Interest
None declared.

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