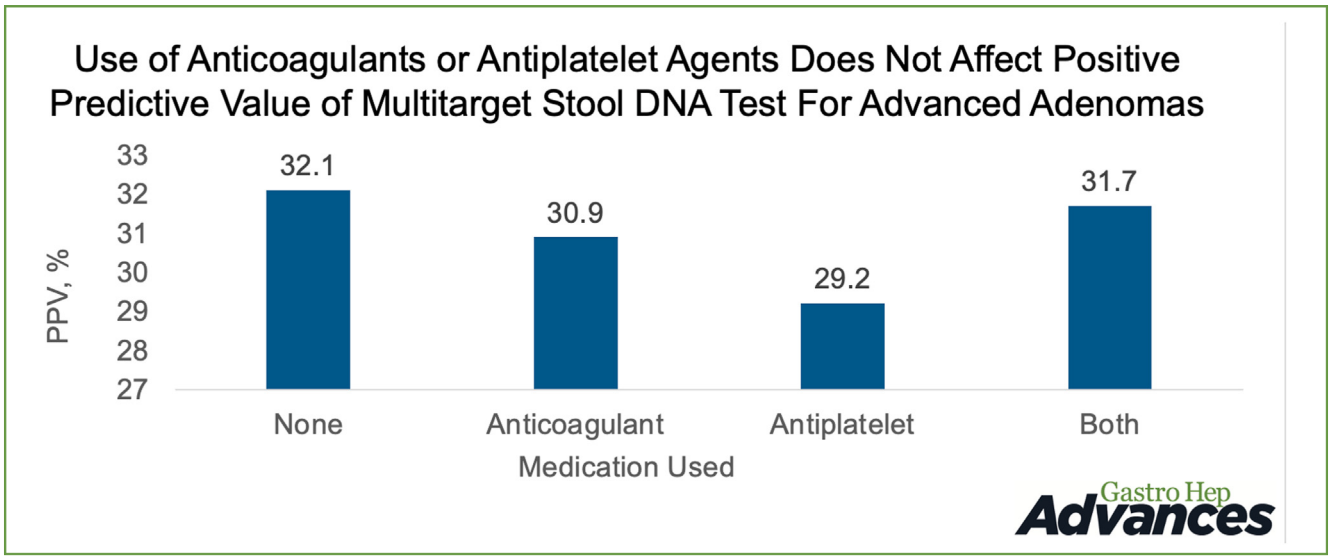
ORIGINAL RESEARCH—CLINICAL

Effects of Oral Anticoagulant and Antiplatelet Agents on Performance of Multitarget Colorectal Cancer Screening Test*

Reilly A. Coombs,[1,2] James L. Adkins,[1,2] Andrew M. Turunen,[2,3] Nadim I. Salfiti,[4] Sahil Khanna,[5] and Sushil Kumar Garg[4]

[1]Research and Innovation, Mayo Clinic Health System – Northwest Wisconsin region, Eau Claire, Wisconsin; [2]School of Medicine, Medical College of Wisconsin – Central Wisconsin, Wausau, Wisconsin; [3]Mayo Clinic Health System – Northwest Wisconsin region, Eau Claire, Wisconsin; [4]Gastroenterology, Mayo Clinic Health System – Northwest Wisconsin region, Eau Claire, Wisconsin; and [5]Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, Minnesota



BACKGROUND AND AIMS: The multitarget stool DNA (mt-sDNA) test is a noninvasive screening tool for colorectal cancer. We aimed to clarify the effects of antiplatelet and anticoagulant medications on the diagnostic performance of this test. **METHODS:** We retrospectively identified patients undergoing mt-sDNA testing from Mayo Clinic sites across the US during a 5-year period. Participants with positive stool testing results and subsequent high-quality colonoscopy were included. Participants were grouped by medication use: antiplatelets, anticoagulants, both, or none of these medications. The primary outcomes were the effects on positive predictive value (PPV) of the test for identifying advanced adenoma by antithrombotic use. **RESULTS:** Of the 11,761 persons with a positive mt-sDNA test result, 8926 persons (age range, 45–91 years) underwent colonoscopy at our institution, of which 7750 were deemed high quality. Among these, 2435 patients were diagnosed with advanced adenomas, for a PPV of 31.4% for detecting advanced adenomas with the mt-sDNA test. The PPVs for advanced adenoma were 32.1% in nonantithrombotic users, 29.2% in antiplatelet users, 30.9% in anticoagulant users, and 31.7% in users of both medications. Additionally, among all patients with positive mt-sDNA testing and subsequent follow-up colonoscopy (n = 8926), colorectal cancer developed in 116 patients, for a notable 1.3% risk of cancer after positive test results and colonoscopy. **CONCLUSION:** In a large retrospective cohort in the US, the PPV of mt-sDNA testing for advanced adenomas was 31.4%. Use of antiplatelet or anticoagulant agents did not affect the PPV for detection of advanced adenomas.

Keywords: Advanced Adenomas; mt-sDNA; Positive Predictive Value; Stool Testing

***Mayo Clinic does not endorse specific products or services included in this article.**

Abbreviations used in this paper: **CRC, colorectal cancer; FIT, fecal immunochemical test; mt-sDNA, multitarget stool DNA; OR, odds ratio; PPV, positive predictive value.**

Most current article

2772-5723
https://doi.org/10.1016/j.gastha.2024.100610

Introduction

Colorectal cancer (CRC) is the fourth most prevalent cancer in the United States and the second most lethal for men and women combined. With an estimated 153,020 new cases and 52,550 fatalities in 2023,[1] CRC is a serious public health challenge.[2] The US Preventive Services Task Force recommends several screening methods for CRC and advanced adenomas, including colonoscopy as a comprehensive option, as well as noninvasive tests such as the guaiac fecal occult blood test, fecal immunochemical test (FIT), and the multitarget stool DNA (mt-sDNA) test (Cologuard; Exact Sciences), which was approved by the US Food and Drug Administration in August 2014.[3,4]

The mt-sDNA test is a noninvasive test designed to detect hemoglobin, sequence variations in *KRAS*, and methylation of *BMP3* and *NDRG4* promoter regions from abnormal colon mucosa cells in stool, any of which may indicate the presence of abnormal growths.[5] If an mt-sDNA test is positive, the US Preventive Services Task Force advises follow-up colonoscopy.[6] The introduction of mt-sDNA technology marked a substantial advancement in noninvasive CRC screening.[4,7] mt-sDNA testing has been shown to have increased adherence compared with FIT, as well as increased test performance in head-to-head comparisons in real-world practice.[8]

In real-world settings, it is possible that certain medications, such as those that increase the risk of bleeding, may affect the performance of noninvasive tests. An association between the regular use of antiplatelet and anticoagulation medications and the incidence of bleeding has been well documented, especially among persons aged 45 years and older—a demographic that aligns with the target population for CRC screening.[9–12] This heightened risk of bleeding could possibly affect the performance of the mt-sDNA test, potentially altering its positive predictive value (PPV), the proportion of positive tests that are corroborated by the detection of advanced adenomas and CRCs in subsequent colonoscopies.

Although antiplatelet and anticoagulant use in the setting of mt-sDNA testing currently is not well described in literature, these drugs could indeed have several possible effects; existing research indicates that these drugs exert differential effects on the PPV of FIT.[9,13] These medications may induce bleeding from nonadvanced lesions or increase the susceptibility of colonic mucosa to bleeding, possibly decreasing the PPV for advanced pathologic processes. Conversely, they may enhance the detection of advanced adenomas and CRCs through increased bleeding, thereby potentially increasing the PPV of this diagnostic test. Of note, current studies of this test have not required any medication restrictions before enrollment.[14] Some potential interfering substances have been evaluated for their effects on safety and effectiveness of the mt-sDNA test; anti-inflammatory agents were noted to not interfere with the hemoglobin assay portion of the test.[15] Furthermore, current guidelines do not require medication changes before mt-sDNA testing.[6]

The primary aim of this study was to determine the PPV of the mt-sDNA test for identifying advanced adenomas and assess the influence of antiplatelet and anticoagulant medications on the PPV. We also aimed to delineate the range of pathologic processes identified in patients after a positive mt-sDNA test result.

Materials and Methods

Study Design and Populations

The study adhered to ethical guidelines, and the protocol was considered exempt by the Mayo Clinic Institutional Review Board. All patient information was anonymized before analysis to ensure confidentiality and compliance with health-care privacy regulations. We retrospectively identified all mt-sDNA tests conducted at Mayo Clinic sites from January 1, 2018, through October 12, 2023. We did not include patients who had not authorized their records for research. For patients who had at least 1 positive result, data from colonoscopies performed at Mayo Clinic within 1 year after the positive test were abstracted. If multiple colonoscopies were performed during this time frame, the examination showing the most advanced pathology was selected for analysis, after accounting for completion of examination based on cecum extent reached and adequate bowel preparation. *Advanced adenomas* were defined as tubulovillous or villous adenomas, adenomas with high-grade dysplasia, and tubular adenoma or sessile serrated adenomas/polyps 10 mm or larger. *CRC* was defined as adenocarcinoma of the colon or rectum. The use of medications by each patient at the time of the mt-sDNA test was carefully assessed and categorized as use of antiplatelet agents (aspirin, clopidogrel, cilostazol, dipyridamole, ticagrelor, or prasugrel), anticoagulants (warfarin, apixaban, rivaroxaban, dabigatran, or edoxaban), both types of medication, or neither.

Patients with suboptimal bowel preparation, indicated by a Boston Bowel Preparation Score[16] of less than 2 in any segment, were excluded, as were records lacking detailed information about the quality of the bowel preparation. Furthermore, we excluded patients for whom *complete colonoscopy*, defined as reaching the intended extent, was not achieved. All other patients were deemed as having a high-quality colonoscopy and were included in the study.

Data Extraction

Our analysis involved extracting data from more than 8000 pathology reports. To extract data contained in free-text reports, we used a tool developed internally at Mayo Clinic which runs the custom prompt on each pathology report independently. The tool runs a request to an instance of the Google Gemini 1.0 large language model through a protected health information–safe application programming interface call provided by Google Inc to Mayo Clinic. We used a custom prompt (Appendix) and the following application programming interface settings: temperature = 0, TopP = 0.7, TopK = 30, and MaxTokens = 1024. In addition to histology information, we extracted data from colonoscopy reports on the quality of bowel preparation, the extent of the colon examined, and polyp size using ProVation software. Polyp size from the colonoscopy report was matched with pathology data to determine if the

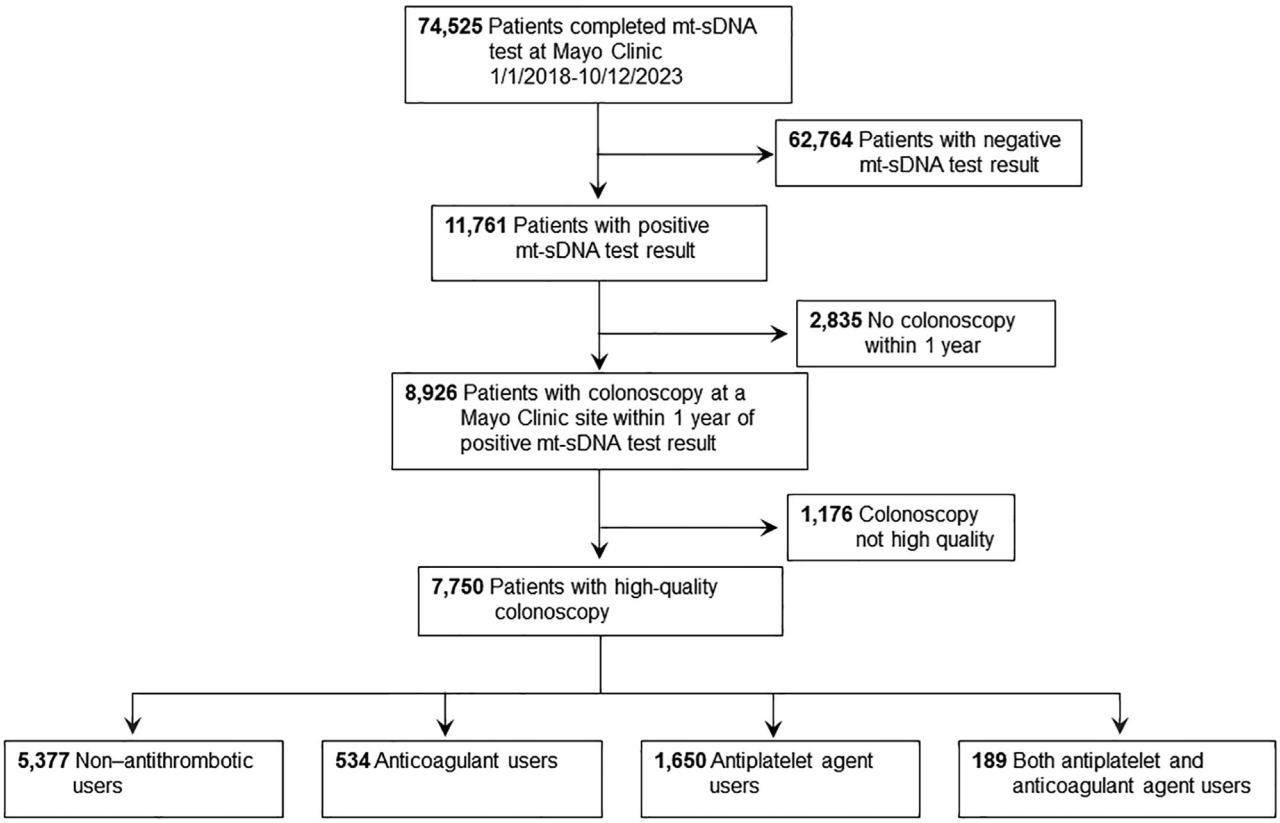


Figure. Flowchart of study participants.

patient had an advanced adenoma. We conducted manual verifications for all patients identified with adenocarcinoma, tubulovillous adenomas, and high-grade dysplasia. Additionally, for the remaining reports, we manually reviewed a random sample of 1000 pathology reports, which confirmed that the automated extraction achieved a 99% accuracy rate.

Analysis

Demographic characteristics of patients were abstracted from the health records: age, weight, sex, race and ethnicity, smoking status, presence of diabetes, hemorrhoid categorization, bowel preparation quality, and medication usage categorized by anticoagulant agents, antiplatelet agents, both, or none. Continuous and categorical variables were encoded as factors with specified reference levels for meaningful comparisons and were assessed for patients with and without advanced adenoma. PPV of the mt-sDNA test for detecting advanced adenoma was calculated for the study cohort overall and for the different anticoagulant groups. Differences in PPV on the basis of anticoagulant usage were analyzed with c^2 tests.

To examine the association of individual predictors (mt-sDNA test, sex, weight, smoking status, hemorrhoid categorization, bowel preparation quality, and medication usage [anticoagulant agents, antiplatelet agents, both, or none]) with the likelihood of advanced adenoma, we conducted logistic regression analysis. The logistic regression models provided estimates of the log odds of the outcome for each level of the predictor compared with the reference level. These log odds were exponentiated to obtain odds ratios (ORs) and 95% confidence intervals (CIs), facilitating an interpretable measure of the effect size and direction. A P value less than .05 was considered statistically significant.

Results

Among 74,525 patients who had an mt-sDNA test during the study period, 11,761 (15.8%) received at least 1 positive result (Figure). Among these patients with a positive result, 8926 (75.9%) had follow-up colonoscopy at our institution within 1 year; 7750 colonoscopies were deemed high quality and included in the study. Participants were aged 45–91 years, and more than half were women (53.2%) (Table 1). A total of 2435 patients were diagnosed with advanced adenoma, for a PPV of 31.4% for detecting advanced adenoma with the mt-sDNA test. Table 1 shows the characteristics of these patients and the 5315 patients without advanced adenoma.

Pathologic findings of high-quality colonoscopies at our institution showed that 8 patients had neuroendocrine tumors, 168 had high-grade dysplasia, 522 had tubulovillous or villous adenomas, 4439 had tubular adenomas, and 2228 had sessile serrated adenomas/polyps (Table 2). Various patients had a combination of these findings.

In our cohort of 7750 patients, 5377 were non-antithrombotic users, 1650 were antiplatelet users, 534 were anticoagulant users, and 189 were antiplatelet and

Table 1. Characteristics of Patients With Positive mt-sDNA Test Results Undergoing High-Quality Colonoscopy (N = 7750)

Characteristic	Presence of advanced adenoma[a] No (n = 5315)	Yes (n = 2435)
Age, y	n = 5306	n = 2434
<50	380 (7.2)	232 (9.5)
50–64	2095 (39.5)	1088 (44.7)
65–79	2599 (49.0)	1036 (42.6)
≥80	232 (4.4)	78 (3.2)
Weight, kg	n = 4201	n = 1976
<50	83 (2.0)	36 (1.8)
50–74.9	1461 (34.8)	562 (28.4)
75–89.9	1090 (26.0)	539 (27.3)
≥90	1567 (37.3)	839 (42.5)
Sex		
Women	2929 (55.1)	1191 (48.9)
Men	2386 (44.9)	1244 (51.1)
Race	n = 5306	n = 2434
Black or African American	49 (0.9)	19 (0.8)
Other	137 (2.6)	74 (3.0)
White	5120 (96.5)	2341 (96.2)
Ethnicity	n = 5306	n = 2434
Hispanic or Latino	92 (1.7)	48 (2.0)
Not Hispanic or Latino	5214 (98.3)	2386 (98.0)
Smoking status	n = 5306	n = 2434
Current smoker	540 (10.2)	365 (15.0)
Former smoker	1943 (36.6)	923 (37.9)
Never smoker	2823 (53.2)	1146 (47.1)
Diabetes	956 (18.0)	412 (16.9)
	n = 5306	n = 2434
Hemorrhoids	n = 5056	n = 2341
None	3959 (78.3)	1874 (80.0)
Small	1055 (20.9)	453 (19.4)
Large	42 (0.8)	14 (0.6)
Bowel preparation quality		
Excellent	2809 (52.9)	1380 (56.7)
Good	1467 (27.6)	580 (23.8)
Fair	1039 (19.6)	475 (19.5)
Antithrombotic used		
None	3649 (68.7)	1728 (71.0)
Anticoagulant	369 (6.9)	165 (6.8)
Antiplatelet	1168 (22.0)	482 (19.8)
Both	129 (2.4)	60 (2.5)

[a]Values are No. of patients (%).

Table 2. Pathologic Findings in Patients Undergoing High-Quality Colonoscopy After Positive mt-sDNA Testing

Variable	Number N = 7750 (%)
Tubular adenoma	4439 (57%)
Hyperplastic polyp	2471 (32%)
Sessile serrated adenoma/polyp	2228 (29%)
Low-grade dysplasia	1846 (24%)
Tubulovillous adenoma or villous adenoma	522 (7%)
Traditional serrated adenoma	244 (3%)
High-grade dysplasia	168 (2%)
Colitis	150 (2%)
Inflammatory polyp	138 (2%)
Neuroendocrine tumor	8 (0.1%)

anticoagulant users. The PPV of the mt-sDNA test for advanced adenoma was 32.1% (1728 of 5377) in non-antithrombotic users, 29.2% (482 of 1650) in antiplatelet users, 30.9% (165/534) in anticoagulant users, and 31.7% (60/189) for both antiplatelet and anticoagulant users. On univariate analysis using c^2 tests, the PPV for advanced adenoma detection in the antiplatelet group was significantly different from that of the nonantithrombotic group ($P = .03$), but the PPVs for the anticoagulant group ($P = .59$) and the group using both medications ($P = .97$) were not significantly different. However, on multivariate analysis, the use of antiplatelets ($P = .08$), anticoagulants ($P = .49$), or both ($P = .75$) did not significantly affect the PPV for advanced adenoma detection.

Table 3 shows regression analysis for predictors of advanced adenomas. The only negative predictor of advanced adenomas was older age at mt-sDNA test: patients aged 65–79 years (OR, 0.76 [95% CI, 0.62–0.94]; $P = .01$) and patients aged 80 years and older (OR, 0.70 [95% CI, 0.48–1.00]; $P = .05$) were both at lower risk. The only positive predictor of advanced adenomas was current and previous smoking: former smokers were at increased risk (OR, 1.17 [95% CI, 1.04–1.32]; $P = .009$) and current smokers were at even greater risk (OR, 1.56 [95% CI, 1.31–1.85]; $P < .001$).

To calculate the risk of CRC (adenocarcinoma), we used the findings of all colonoscopies, not just the high-quality colonoscopies. After a positive mt-sDNA test result and follow-up colonoscopy (n = 8926), CRC developed in 116 patients. Of these CRC diagnoses, 108 patients were diagnosed within 1 year; 8 were diagnosed more than 1 year after the positive mt-sDNA test because of delayed follow-up (n = 1), an incomplete examination due to poor bowel preparation (n = 1), and negative colonoscopy findings leading to a delayed CRC diagnosis (n = 6). For patients with a positive mt-sDNA test result and subsequent colonoscopy, the prevalence of cancer in this study group is 1.3%.

Discussion

To our knowledge, this is the most extensive real-world estimation of the PPV of the mt-sDNA test for advanced adenomas, which was 31.4% in our study. This value aligns closely with previously reported PPVs ranging from 27.3% to 42.4% in earlier studies.[14,17] Other recent studies have aimed to evaluate predictive values in second-round testing, the value of the mt-sDNA result in average-risk screening examinations, and the PPV for any colorectal neoplasia.[18–20]

This study, to our knowledge, is also the first to describe the effects of antiplatelet and anticoagulant medications on mt-sDNA testing. A critical aspect of estimating the efficacy

Table 3. Regression Analysis for Predictors of Advanced Adenoma[a]

Predictor	OR (95% CI)	*P* Value
Age, y		
<50	Ref	
50–64	0.93 (0.76–1.15)	.51
65–79	0.76 (0.62–0.94)	.01
≥80	0.70 (0.48–1.00)	.05
Men (vs women)	1.10 (0.97–1.24)	.13
Weight, kg		
<50	Ref	
50–74.9	0.87 (0.57–1.32)	.50
75–89.9	1.06 (0.69–1.62)	.80
≥90	1.09 (0.71–1.67)	.71
Smoker		
Never	Ref	
Former	1.17 (1.04–1.32)	.009
Current	1.56 (1.31–1.85)	<.001
Hemorrhoids		
None	Ref	
Small	1.03 (0.77–1.37)	.86
Large	0.90 (0.56–1.43)	.64
Bowel preparation quality		
Fair	Ref	
Good	0.92 (0.77–1.09)	.32
Excellent	1.08 (0.93–1.25)	.29
Anticoagulant use		
None	Ref	
Anticoagulant	1.08 (0.86–1.36)	.49
Antiplatelet	0.88 (0.76–1.01)	.08
Both	1.06 (0.74–1.51)	.75

CI, confidence interval; Ref, reference category.
[a]Advanced adenoma includes tubulovillous adenoma, villous adenomas, high-grade dysplasia, and sessile serrated adenomas/polyps ≥10 mm.

of the mt-sDNA test as a CRC screening tool is its PPV for advanced adenomas. Knowing the PPV is essential for assessing the tool's utility in reducing unnecessary colonoscopies while maintaining effective screening. We found that the PPV for advanced adenomas was significantly lower in antiplatelet users than in nonantithrombotic users ($P = .03$) on univariate analysis, but on multivariate analysis there were no significant differences between groups.

Age was inversely associated with the development of advanced adenomas, with patients aged 65–79 years and those 80 years and older exhibiting a lower risk. This finding contrasts with current literature, which suggests that advancing age is a significant risk factor for CRC development.[21–23] However, this discrepancy is likely due to the decreased specificity of mt-sDNA tests in older populations.[3] Other possible, though less likely, explanations include the relatively recent introduction of mt-sDNA testing. Specifically, older patients currently undergoing mt-SDNA screening may possess lower risk factors, while younger patients using mt-sDNA may represent a more average-risk population. Additionally, Strum[24] reported that 15% of patients newly diagnosed with CRC are younger than 50 years.

Our regression analysis also showed that both former and current smokers were at increased risk for advanced adenomas, with current smokers being at greater risk. In one study, Figueiredo et al[25] reported that cigarette smoking (current and former) was associated with a significantly increased risk of advanced polyps, specifically serrated polyps. Thus, our findings are consistent with the existing literature, but our data may indicate a stronger correlation. Although we identified no previous studies on the efficacy of mt-sDNA testing in antiplatelet and anticoagulant users, some studies have aimed to understand the effects of these drugs on FIT performance. One study by Randel et al[9] showed that the PPV of FIT for CRC was lower in both aspirin and direct-acting oral anticoagulant users compared with nonusers. Specifically, Randel et al[9] found that there was a 2.6% reduction in the PPV for CRC and a 5.4% reduction in the PPV for advanced adenomas aspirin users vs matched nonusers. Additionally, for direct-acting oral anticoagulant users vs matched nonusers, they found a 5.5% reduction in the PPV of CRC and a 11.9% reduction in the PPV for advanced adenomas, respectively.[9] Similarly, a review article by Jung et al[26] showed aspirin, antiplatelet agent, and oral anticoagulant use to result in significantly lowered PPV of FIT for detecting advanced colorectal neoplasia, suggesting that these drugs may increase the false positive rate of FIT.

In this study, 32% (2835) patients with a positive mt-sDNA test did not undergo a high-quality colonoscopy at Mayo Clinic within 1 year. However, our analysis was limited to colonoscopies performed within our system, and it is possible that some patients had follow-up procedures outside the Mayo Clinic Network. This limitation highlights the need for more comprehensive data integration across health systems to accurately track patient follow-up. Patient-related barriers, such as fear of the procedure, misunderstanding of test results, or financial concerns likely played a role. Additionally, the COVID-19 pandemic likely exacerbated these delays, as many elective procedures, including colonoscopy, were postponed, and patients were reluctant to seek care due to infection risks. Further studies should incorporate data from multiple health-care systems to better assess and improve follow-up after positive mt-sDNA results.

Our analysis also detailed the diverse pathologic processes found after a positive mt-sDNA test and subsequent colonoscopy. Additionally, CRC was detected in 116 patients who underwent colonoscopy after a positive mt-sDNA test, indicating a cancer prevalence rate of 1.3% among those who received a follow-up colonoscopy.

Our study has numerous strengths. Our large sample size gave the study enough power to allow analyses on individual drug classes for antiplatelets and anticoagulants. Additionally, medication information extracted from patient records was entered by physicians and other medical team members during the time of the patient's mt-sDNA test. Our study also has some limitations. We included drug information only for those with a known positive mt-sDNA test

and included only patients who attended follow-up colonoscopy at our institution. We also did not consider the duration or dosage of the antithrombotic medications, which limits our analysis. In addition, we are not able to confirm that patients were truly at average risk with respect to prior polyp history and family history. Data obtained for this study were extracted from a large database and not extracted manually directly from the electronic health record. Finally, we did not include detailed information on other medications such as nonsteroidal anti-inflammatory drugs or proton pump inhibitors.

In this large, retrospective cohort in the US, the PPV of the mt-sDNA test for detecting advanced adenomas was 31.4%. Furthermore, antiplatelet, anticoagulant, or combined agents do not affect the PPV of mt-sDNA testing based on multivariate analysis. Current guidelines do not recommend that antiplatelets or anticoagulants be halted at the time of fecal testing.[6] Our results from a large, multisite, tertiary medical center suggest that this practice should be continued.

Supplementary Materials

Material associated with this article can be found in the online version at https://doi.org/10.1016/j.gastha.2024.100610.

References

1. National Cancer Institute. Cancer stat facts: colorectal cancer. https://seer.cancer.gov/statfacts/html/colorect.html. Accessed April 16, 2024.
2. Sifaki-Pistolla D, Poimenaki V, Fotopoulou I, et al. Significant rise of colorectal cancer incidence in younger adults and strong determinants: 30 years longitudinal differences between under and over 50s. Cancers (Basel) 2022;14(19):4799.
3. U.S. Food and Drug Administration. Premarket approval (PMA). https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=p130017. Accessed April 16, 2024.
4. Lin JS, Perdue LA, Henrikson NB, Bean SI, Blasi PR. Screening for colorectal cancer: updated evidence report and systematic review for the US preventive services task force. JAMA 2021;325(19):1978–1998, Erratum in: JAMA. 2021 Jul 20;326(3):279. doi: 10.1001/jama.2021.10417. PMID: 34003220.
5. What is cologuard? https://www.cologuard.com/what-is-cologuard. Accessed April 16, 2024.
6. U. S. Preventive Services Task Force, Davidson KW, Barry MJ. Screening for colorectal cancer: US preventive services Task Force recommendation statement. JAMA 2021;325(19):1965–1977.
7. Onieva-Garcia MA, Llanos-Mendez A, Banos-Alvarez E, et al. A systematic review of the clinical validity of the cologuard genetic test for screening colorectal cancer. Rev Clin Esp 2015;215(9):527–536.
8. Ebner DW, Kisiel JB. Stool-based tests for colorectal cancer screening: performance benchmarks lead to high expected efficacy. Curr Gastroenterol Rep 2020;22(7):32.
9. Randel KR, Botteri E, Romstad KMK, et al. Effects of oral anticoagulants and aspirin on performance of fecal immunochemical tests in colorectal cancer screening. Gastroenterology 2019;156(6):1642–1649.e1.
10. Holster IL, Valkhoff VE, Kuipers EJ, et al. New oral anticoagulants increase risk for gastrointestinal bleeding: a systematic review and meta-analysis. Gastroenterology 2013;145(1):105–112.e15.
11. Gullov AL, Koefoed BG, Petersen P. Bleeding during warfarin and aspirin therapy in patients with atrial fibrillation: the AFASAK 2 study. Atrial Fibrillation Aspirin and Anticoagulation. Arch Intern Med 1999;159(12):1322–1328.
12. Loffredo L, Perri L, Violi F. Impact of new oral anticoagulants on gastrointestinal bleeding in atrial fibrillation: a meta-analysis of interventional trials. Dig Liver Dis 2015;47(5):429–431.
13. Bujanda L, Lanas A, Quintero E, et al. Effect of aspirin and antiplatelet drugs on the outcome of the fecal immunochemical test. Mayo Clin Proc 2013;88(7):683–689.
14. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitarget stool DNA testing for colorectal-cancer screening. N Engl J Med 2014;370(14):1287–1297.
15. FDA summary of safety and effectiveness data (SSED). https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130017b.pdf. Accessed April 16, 2024.
16. Lai EJ, Calderwood AH, Doros G, et al. The boston bowel preparation scale: a valid and reliable instrument for colonoscopy-oriented research. Gastrointest Endosc 2009;69(3 Pt 2):620–625.
17. Multi-target colorectal cancer screening test for the detection of colorectal advanced adenomatous polyps and cancer (DeeP-C). 2015. https://clinicaltrials.gov/study/NCT01397747. Accessed April 16, 2024.
18. Eckmann JD, Ebner DW, Bering J, et al. Multitarget stool DNA screening in clinical practice: high positive predictive value for colorectal neoplasia regardless of exposure to previous colonoscopy. Am J Gastroenterol 2020;115(4):608–615.
19. Ebner DW, Burger KN, Mahoney DW, et al. Neoplasia diagnosis after multi-target stool DNA is enhanced among lowest baseline detectors. Dig Dis Sci 2023;68(9):3721–3731.
20. Voss JK, Ebner DW, Burger KN, et al. Multitarget stool DNA testing has high positive predictive value for colorectal neoplasia on the second round of testing. Clin Gastroenterol Hepatol 2023;21(9):2399–2406.
21. Lewandowska A, Rudzki G, Lewandowski T, et al. Risk factors for the diagnosis of colorectal cancer. Cancer Control 2022;29:10732748211056692.
22. O'Sullivan DE, Sutherland RL, Town S, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 2022;20(6):1229–1240.e5.
23. Sninsky JA, Shore BM, Lupu GV, et al. Risk factors for colorectal polyps and cancer. Gastrointest Endosc Clin N Am 2022;32(2):195–213.
24. Strum WB. Colorectal adenomas. N Engl J Med 2016;374(11):1065–1075.
25. Figueiredo JC, Crockett SD, Snover DC, et al. Smoking-associated risks of conventional adenomas and serrated

polyps in the colorectum. Cancer Causes Control 2015; 26(3):377–386.
26. Jung YS, Im E, Park CH. Impact of antiplatelet agents and anticoagulants on the performance of fecal immunochemical tests: a systematic review and meta-analysis. Surg Endosc 2022;36(6):4299–4311.

Received August 16, 2024. Accepted December 30, 2024.

Correspondence:
Address correspondence to: Sushil Kumar Garg, MBBS, Gastroenterology, Mayo Clinic Health System – Northwest Wisconsin region, 1221 Whipple Street, Eau Claire, Wisconsin 54703. e-mail: garg.sushil@mayo.edu.

Acknowledgments:
The Scientific Publications staff at Mayo Clinic provided editorial consultation, proofreading, and administrative and clerical support. Presented at Digestive Disease Week, Washington, DC, May 18, 2024.

Authors' Contributions:
Reilly A. Coombs: Data curation, Investigation, Writing – original draft. James L. Adkins: Data Curation. Andrew M. Turunen: Data curation. Nadim I. Salfiti: Writing – review & editing. Sahil Khanna: Writing – review & editing. Sushil Kumar Garg: Conceptualization, Formal analysis, Methodology, Writing – review & editing.

Conflicts of Interest:
The authors disclose no conflicts.

Funding:
The authors report no funding.

Ethical Statement:
The study adhered to ethical guidelines, and the protocol was considered exempt by the Mayo Clinic Institutional Review Board.

Data Transparency Statement:
All relevant data supporting the findings of this study are reported within the article or are available from the corresponding author upon reasonable request.

Reporting Guidelines:
STROBE.