

Introduction

- Colonoscopy remains the gold standard for colorectal cancer (CRC) screening, but less invasive screening modalities have been employed more recently, including the multitarget stool DNA (MT-sDNA or Cologuard) testing, which combines detection of blood products with genetic markers in the stool.
- Data regarding the false-negative rate of the MT-sDNA test in real-world clinical practice is limited.
- Our primary aim was to determine the rate of false-negative MT-sDNA testing and evaluate for factors associated with higher false-negative rates within our health system.

Methods

- Adults (≥ 18 years old) with a negative MT-sDNA test between 2017 and 2022 and subsequent colonoscopy within three years of the MT-sDNA test, regardless of colonoscopy indication were included.
- Our primary outcome of interest was advanced adenoma (AA) detection rate, defined as adenoma with villous features, size ≥ 1.0 cm, high-grade dysplasia, or early invasive cancer.
- Demographic and procedural variables including age, sex, race, BMI, colonoscopy indication, polyp size, and polyp location were manually extracted from patient charts.
- The two groups (AA vs. no AA) were compared using chi-squared analysis.

		Total		Advanced Adenoma		Non-Advanced Adenoma		p value
		N=370		N=31		N=339		
Male Sex	N (%)	142	38.4%	16	51.6%	126	37.2%	0.114
Age – years	Median (IQR)	66	59-72	67	59-74	66	59-71	0.157
Race	N (%)							0.168
White		300	81.1%	28	90.3%	272	80.2%	
Black		62	16.8%	3	9.7%	59	17.4%	
Other		8	2.2%	0	0.0%	8	2.4%	
BMI – kg/m ²	Median (IQR)	30.1	26-34	30.7	25.6-35.2	30.1	26-34	0.807
Personal History of Colon Cancer	N (%)	3	0.8%	0	0.0%	3	0.9%	0.600
Family History of Colon Cancer	N (%)	32	8.6%	0	0.0%	32	9.4%	0.074
Personal History of IBD	N (%)	3	0.8%	0	0.0%	3	0.9%	0.600
Provider Ordering Test	N (%)							0.971
PCP		332	89.7%	28	90.3%	304	89.7%	
GI		3	0.8%	0	0.0%	3	0.9%	
Other		35	9.5%	3	9.7%	32	9.4%	
Indication for Colonoscopy	N (%)							
GI Bleeding		58	15.7%	10	32.3%	48	14.2%	0.008
Iron deficiency anemia		32	8.6%	4	12.9%	28	8.3%	0.380
Diarrhea		35	9.5%	1	3.2%	34	10.0%	0.216
Constipation		6	1.6%	0	0.0%	6	1.8%	0.457
Weight loss		5	1.4%	0	0.0%	5	1.5%	0.497
Abnormal Imaging		13	3.5%	2	6.5%	11	3.2%	0.355
IBD		0	0.0%	0	0.0%	0	0.0%	
Screening		207	55.9%	14	45.2%	193	56.9%	0.207
Other		14	3.8%	0	0.0%	14	4.1%	0.250
Prep Quality	N (%)							
Poor		26	7.0%	2	6.5%	24	7.1%	0.896
Inadequate		2	0.5%	0	0.0%	2	0.6%	0.669
Fair		89	24.1%	10	32.3%	79	23.3%	0.265
Adequate		37	10.0%	2	6.5%	35	10.3%	0.493
Good		204	55.1%	17	54.8%	187	55.2%	0.972
Excellent		12	3.2%	0	0.0%	12	3.5%	0.288

Table 1. Baseline demographics of patients with negative Cologuard testing and advanced adenoma on colonoscopy (n=31) as compared to patients without advanced adenoma (n=339)

		Total		Advanced Adenoma		Non-Advanced Adenoma		p value
		N=148		n=31		n=117		
# Polyps	Median (IQR)	2	1-2	2	1-4	1	1-2	<0.001
Largest polyp size	Mean (SD)	7.0	4.8	14.1	5.1	5.1	2.2	<0.001
Polyp Location(s)	N (%)							
Terminal Ileum		1	0.3%	0	0.0%	1	0.3%	0.608
Cecum		35	9.5%	8	25.8%	27	8.0%	0.752
Ascending Colon		38	10.3%	10	32.3%	28	8.3%	0.349
Hepatic Flexure		3	0.8%	2	6.5%	1	0.3%	0.050
Transverse Colon		32	8.6%	13	41.9%	19	5.6%	0.002
Splenic Flexure		1	0.3%	0	0.0%	1	0.3%	0.608
Descending Colon		17	4.6%	2	6.5%	15	4.4%	0.326
Sigmoid		44	11.9%	9	29.0%	35	10.3%	0.925
Rectum		26	7.0%	3	9.7%	23	6.8%	0.197
Anal Verge		0	0.0%	0	0.0%	0	0.0%	
Surgery	N (%)	3	0.8%	3	9.7%	0	0.0%	<0.001
Mortality	N (%)	11	3.0%	2	6.5%	9	2.7%	0.235

Table 2. Characteristics of polyps in patients with advanced adenoma (n=31) as compared to all other sub-types (n=117)

Results

- A total of 370 patients met the inclusion criteria, of which 31 (8.4%) were found to have AA and 3 (0.81%) were found to have CRC on colonoscopy within 3 years of negative MT-sDNA test.
- There were no demographic differences between the two groups.
- AA detection rate was significantly higher in patients who underwent colonoscopy for GI bleeding (32.3% vs 14.2%, p=0.008) as opposed to other indications.
- Among patients who had polyps (N=148), AA detection was associated with more numerous polyps (2 [IQR 1-4] vs 1 [IQR 1-2], p < 0.001), and larger polyp size (14 [SD 5.1] vs 5.1 [SD 2.2], p < 0.001).
- AAs were also significantly more frequently found in the hepatic flexure (6.5% vs 0.3%, p=0.050) and transverse colon (41.9% vs 5.6%, p=0.002) compared to other locations.

Discussion

- The results of this study validate the 8% quoted false-negative rate for MT-sDNA testing shown in prior literature.
- Large polyps in the transverse colon and hepatic flexure are more likely to result in a false negative MT-sDNA test and therefore these locations should be examined more carefully during withdrawal.
- A negative MT-sDNA test result should be interpreted with caution and gastroenterologists should have a low threshold to perform a colonoscopy if otherwise clinically indicated.