Neoplasia at 10-year follow-up screening colonoscopy in a private U.S. practice: comparison of yield to first-time examinations CME

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Background and Aims: Prior studies assessing the yield of a second screening colonoscopy performed 10 years after an initial screening colonoscopy with negative results did not include a control group of persons undergoing a first screening colonoscopy during the same time interval. Our aim was to describe the incidence of neoplasia at a second screening colonoscopy (performed at least 8 years after the first colonoscopy) in average-risk individuals and compare it with the yield of first screening examinations performed during the same time interval.

Methods: Review of a database of outpatient screening colonoscopies performed between January 2010 and December 2015 in an Atlanta private practice.

Results: A total of 2105 average-risk individuals underwent screening colonoscopy, including 470 individuals (53.6% female; mean age ± standard deviation [SD] 64.0 ± 3.9 years) who underwent a second screening examination. In those undergoing second screening, the mean (± SD) interval between examinations was 10.4 years (± 1.1 years, range 8-15 years). At second screening, the polyp detection rate, adenoma detection rate, and advanced neoplasm rate were 44.7%, 26.6%, and 7.4%, respectively. Of 40 advanced neoplasms in 35 individuals, 33 (82.5%) were proximal to the sigmoid colon, and there were no cancers. During the same interval, 1635 individuals (49.4% female; mean age [± SD] 52.6 ± 3.4 years) underwent a first screening colonoscopy. The polyp detection rate, adenoma detection rate, and advanced neoplasm detection rate were 53.5%, 32.2%, and 11.7%, respectively. Of 243 advanced neoplasms in 192 individuals, 152 (62.6%) were proximal to the sigmoid colon, and there were no cancers. After adjustment for age, sex, body mass index, and endoscopist, polyp detection rate, adenoma detection rate, and advanced neoplasm detection rate were all lower at the second screening colonoscopies than at first-time colonoscopies (all $P < .001$).

Conclusions: Despite being 10 years older, persons with a screening colonoscopy with negative results 10 years earlier had lower rates of adenoma and advanced neoplasm at the second screening examination compared with patients in the same practice undergoing a first screening colonoscopy, and they had no cancers. The fraction of advanced neoplasms that were proximal to the sigmoid colon was high in both first and second screenings. These results support the safety of the recommended 10-year interval between colonoscopies in average-risk persons with an initial examination with negative results. (Gastrointest Endosc 2018;87:254-9.)

Abbreviation: BMI, body mass index.

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Since colonoscopy was first endorsed for average-risk screening in 1997,[1] the recommended interval between colonoscopies for average-risk persons who had an initial examination with negative results has been 10 years in all guidelines. Confidence in this recommendation has been undermined in the perspective of some practitioners by the numerous reports of colorectal cancer occurring after a colonoscopy that apparently had cleared the colon of neoplasia.[2-8] Awareness of these interval cancers likely contributes to the performance of screening colonoscopy at 5-year intervals by some practitioners.[9] However, despite the current detailed understanding of the variable detection skills of colonoscopists for both adenomas and serrated lesions[10,11] and the imperfect protection of colonoscopy against colorectal cancer, available evidence suggests that the recommended 10-year interval is safe and appropriate. For example, the yield of advanced lesions and cancers is very low when colonoscopy is repeated in average-risk persons 5 years after an initial examination with negative results,[12,13] and a case-control study found that a screening colonoscopy with negative results provides substantial protection against colorectal cancer for at least 20 years.[14]

A previous single-center observational study described the incidence of neoplasia at a second screening colonoscopy 10 years after an examination with negative results.[15] In that study of 378 individuals, 38.1% had 1 or more conventional adenomas, and only 3.4% had an advanced neoplasm.

In the current study, we extended the observations of the yield of a second screening colonoscopy 10 years after an examination with negative results. Compared with the first study,[15] the current study is larger, describes the yield of second screening in a U.S. private practice rather than an academic institution, and includes a control group of persons undergoing a first screening colonoscopy during the same time period and by the same colonoscopists, thereby allowing a comparison of the yield of first versus second screenings.

MATERIALS AND METHODS

This was a retrospective review of colonoscopies performed at an outpatient endoscopy unit in a private practice in Atlanta between January 2010 and December 2015. Eligible patients were aged at least 50 years at the baseline examination, had screening listed as the indication, and had a complete examination to the cecum with the bowel preparation listed as fair, good, or excellent and/or with Boston Bowel Preparation Scale scores of 6 to 9. Because the data were acquired in Atlanta and were deidentified for analysis, the Institutional Review Board at Indiana University waived review of the study.

All of the procedures in the study were performed at 1 ambulatory surgery center. The patient population served by the ambulatory surgery center is approximately 15% African American, and the remainder of the patients are largely white. The patients are uniformly insured (either private insurance and/or Medicare). The database was created retrospectively by technical support personnel in Atlanta for quality assessments. Provation (Provation Medical, Minneapolis, Minn) was introduced in the ambulatory surgery center in 1999 as the endoscopic report generating system for the center. Provation was searched by its key word search function to identify screening procedures. Endoscopist, patient demographics, and polyp findings were determined from Provation reports. When a patient was identified, the patient's chart was reviewed to identify polyp pathology. The nurse's notes documented the patient's height and weight. These were entered into bmi-calculator.net to determine body mass index (BMI). The deidentified database was coded for endoscopist and sent to Indianapolis for analysis.

Individuals undergoing a second screening examination during the study period had undergone a baseline screening examination in the same practice between January 2002 and December 2007 and had either no colorectal polyps or had only hyperplastic polyps <10 mm in size in the rectum or sigmoid colon identified during the baseline colonoscopy. The second examination occurred a minimum of 8 years after the first examination. The same 12 gastroenterologists performed both the first and the second screenings.

Conventional adenomas included tubular, tubulovillous, and villous adenomas. Serrated class lesions included hyperplastic polyps, sessile serrated polyps (synonymous with sessile serrated adenomas), and traditional serrated adenomas. Advanced neoplasms were defined as adenomas with villous elements, high-grade dysplasia, or size ≥10 mm or sessile serrated polyps ≥10 mm in size or with cytologic dysplasia, or traditional serrated adenomas ≥10 mm in size. The database for the study recorded age, sex, polyp findings (size, location, and pathology), and BMI.

Statistical methods

Chi-square tests were used to compare polyp, adenoma, and advanced neoplasm rates between the groups. A Wilcoxon rank sum t test was done to compare adenomas per colonoscopy between the groups. Multivariable logistic and linear regression was used to determine whether the groups' differences persisted after we adjusted for age, BMI, and endoscopist. Because the number of adenomas per colonoscopy is highly positively skewed, the square root of number of colonoscopies was used in the multivariable linear regression. Although the square root is still positively skewed, the residuals were examined and were approximately normally distributed.

RESULTS

A total of 2105 individuals underwent screening colonoscopy during the study interval, of which 470 individuals

TABLE 1. Patient demographics

	Second screening group			
	Patients without polyps at baseline examination	Patients with distal hyperplastic polyps at baseline examination	Total	Initial screening group
	n = 440	n = 30	n = 470	n = 1635
Sex, no. (%)				
Male	205 (46.6)	13 (43.3)	218 (46.4)	827 (50.6)
Female	235 (53.4)	17 (56.7)	252 (53.6)	808 (49.4)
Age at initial colonoscopy, mean (± SD), range, y	53.5 (± 3.6), 50-67	54.3 (± 4.1), 50-66	53.5 (± 3.7), 50-67	52.6 (± 3.9), 50-81
Age at second colonoscopy, mean (± SD), range, y	63.9 (± 3.8), 59-80	64.3 (± 4.3), 59-76	64.0 (± 3.9), 59-80	N/A
Interval between colonoscopies, mean (± SD), range, y	10.5 (± 1.0), 8.0-15.0	10.0 (± 1.1), 8.0-12.6	10.4 (± 1.1), 8.0-15.0	N/A
BMI, mean (± SD), range	26.3 (± 2.2), 16.9-43.5	27.3 (± 4.5), 17.0-36.9	26.4 (± 4.4), 16.9-43.5	26.9 (± 5.0), 16.6-57.5

SD, Standard deviation; *BMI,* body mass index; *N/A,* not applicable.

underwent a second screening colonoscopy at least 8 years after the initial examination, and 1635 individuals underwent their first screening examinations. Of the 470 individuals undergoing a second screening, 440 had no polyps at their baseline examinations, and 30 had only distal colon (rectum and/or sigmoid colon) hyperplastic polyps <10 mm in size.

Second screening group

The second screening group was 53.6% female, had a mean (± standard deviation [SD]) age of 64.0 (± 3.9) years (range 59-80 years). The mean (± SD) BMI was 26.4 (± 4.4). The mean (± SD) interval between examinations was 10.4 (± 1.1) years (range 8.0-15.0 years) (Table 1).

There were 35 individuals (17 female) with 40 advanced neoplasms at the second examination, of which 33 (82.5%) were proximal to the sigmoid colon. The overall polyp detection rate, adenoma detection rate, adenomas per colonoscopy, and advanced neoplasm detection rate at the second examination were 44.7%, 26.6%, 0.44, and 7.4%, respectively. The adenoma detection rate was 25.7% in patients with no baseline polyps and 40.0% in patients with distal colon hyperplastic polyps at the baseline colonoscopy (Table 2). No cancers were identified. Among 363 patients with at least 10 years between examinations, the polyp detection rate, adenoma detection rate, adenomas per colonoscopy, and advanced neoplasm detection rate were 46.6%, 27.8%, 0.47, and 8.0%, respectively.

Multivariable logistic regression showed that a higher BMI was associated with a higher risk of adenoma at a second screening colonoscopy (odds ratio [OR] 1.44; 95% confidence interval [CI], 1.12-1.84) for each 5-point increase in BMI (Table 3).

Initial screening group

Among 1635 patients who underwent initial screening colonoscopy (the screening colonoscopy control group) during the study period, the mean (± SD) age was 52.6 (± 3.4) years (range 50-81 years), and 808 (49.4%) were women. The mean (± SD) BMI was 26.9 (± 5.0) (Table 1). The polyp detection rate, adenoma detection rate, adenomas per colonoscopy, and advanced neoplasm detection rate were 53.5%, 32.2%, 0.54, and 11.7%, respectively (Table 2). There were 192 individuals (85 female) with 243 advanced neoplasms, of which 152 (62.6%) were proximal to the sigmoid colon. There were no cancers.

On multivariable analysis, BMI was significantly associated with the presence of adenomas. For each 5-point increase in BMI in the first screening colonoscopy group, the odds for adenoma increased by 1.26 (95% CI, 1.13-1.41). Each 5-point increase in BMI was associated with a 1.20 increased risk of advanced neoplasm (95% CI, 1.03-1.39) (Table 3).

Group comparisons

Univariate analysis of the yield of polyps, adenomas, advanced neoplasms, and adenomas per colonoscopy indicated that each of these endpoints was higher in the control group undergoing first-time screening compared with patients undergoing second screening. These differences all persisted after logistic regression to control for the effects of sex, age, BMI, and endoscopist (10 of the 12 endoscopists with >50 procedures were included in the analysis) (Table 4).

We qualitatively examined multiple subpopulations of second screening patients in an attempt to identify a subgroup with either zero or an extremely low risk of advanced neoplasia at the second colonoscopy. Although age, sex, and BMI were all associated with neoplasia, we did not identify any such subgroup (data not shown).

DISCUSSION

In this report, we demonstrated that the yield of a second screening colonoscopy in 470 patients who had a

TABLE 2. Yield of screening colonoscopy in the first and second screening groups*

	Second screening group			
	Patients without polyps at baseline examination	Patients with distal hyperplastic polyps at baseline examination	Total	Initial screening group
No. of patients	**n = 440**	**n = 30**	**n = 470**	**n = 1635**
Yield by patient, no. (%)†				
Patients with ≥1 polyp	192 (43.6)	18 (60.0)	210 (44.7)	875 (53.5)
Patients with ≥1 adenoma	113 (25.7)	12 (40.0)	125 (26.6)	526 (32.2)
Patients with ≥1 advanced neoplasm	34 (7.7)	1 (2.9)	35 (7.4)	192 (11.7)
Men with ≥1 adenoma	65 (31.7)	6 (46.2)	71 (32.6)	309 (37.4)
Women with ≥1 adenoma	48 (20.4)	6 (35.3)	54 (21.4)	217 (26.9)
Total no. of lesions detected	n = 334	n = 33	n = 367	n = 1718
Histology of lesions detected, no. (%)‡				
Tubular adenoma	185 (55.4)	20 (60.6)	205 (55.9)	839 (48.8)
Tubulovillous adenoma	2 (0.6)	0 (0.0)	2 (0.5)	38 (2.2)
Hyperplastic polyp	66 (19.8)	9 (27.3)	75 (20.4)	387 (22.5)
Benign mucosa	31 (9.3)	2 (6.1)	33 (9.0)	211 (12.3)
Sessile serrated polyp	46 (13.8)	2 (6.1)	48 (13.1)	218 (12.7)
Other polyp	4 (1.2)	0 (0.0)	4 (1.1)	14 (0.8)
Traditional serrated adenoma	0 (0.0)	0 (0.0)	0 (0.0)	11 (0.6)

*No. of patients with at least 1 lesion of different types and total number of lesions detected according to histology.
†No. of patients (%).
‡No. of lesions with designated pathology (% of all lesions detected that had the designated pathology).

TABLE 3. Within-group multivariable associations with conventional adenomas and advanced neoplasms

	OR	95% CI	*P* value
Second screening group—conventional adenoma			
Age (10-y increase)	2.52	(1.44-4.42)	.001
Sex (men vs women)	1.79	(1.12-2.88)	.015
BMI (5-point increase)	1.44	(1.12-1.84)	.005
Initial screening group—conventional adenoma			
Age (10-y increase)	1.09	(1.06-1.13)	< .001
Sex (men vs women)	1.58	(1.26-1.98)	< .001
BMI (5-point increase)	1.26	(1.13-1.41)	< .001
Initial screening group—advanced neoplasm			
Age (10-y increase)	1.10	(1.06-1.14)	< .001
Sex (men vs women)	1.29	(0.93-1.78)	.127
BMI (5-point increase)	1.20	(1.03-1.39)	.020

OR, Odds ratio; *CI,* confidence interval; *BMI,* body mass index.

screening colonoscopy with negative results at least 8 years and an average of 10.4 years earlier was 0% for cancer and lower for adenomas and advanced neoplasms than first-time screening colonoscopies. This was true even though patients were 10 years older than first-time screening patients, and increasing age is strongly associated with colorectal adenomas and cancer. Thus, patients with a colonoscopy with negative results appear to be selected for a lower risk of colorectal neoplasia. Our results indicate that the current recommendation for colonoscopy every 10 years in persons with initial examinations with negative results is safe and appropriate. For both first and second screening colonoscopies, the majority of advanced lesions was in the proximal colon, increasing the rationale for screening by colonoscopy. This finding also was observed for second screening examinations in a previously published study.[15]

Our data suggest that women with normal BMIs are a candidate group to evaluate in larger studies of second screening examinations because they might be candidates

TABLE 4. Between-group comparisons of lesion yields in patients undergoing second versus initial screening colonoscopies

	Second screening (n = 470)	Initial screening (n = 1635)	OR (95% CI) initial vs second screening	Univariate group *P* value	Multivariate group *P* value
PDR	44.7%	53.5%	2.99 (2.00-4.45)	< .001	< .001
ADR	26.6%	32.2%	3.09 (2.07-4.63)	.021	< .001
APC	0.44	0.54	–	.024	< .001
ANR	7.4%	11.7%	4.55 (2.61-7.91)	.008	< .001

OR, Odds ratio; *CI,* confidence interval; *PDR,* polyp detection rate (% of patients with ≥ 1 polyp); *ADR,* adenoma detection rate (% of patients with ≥ 1 adenoma); *APC,* adenomas per colonoscopy; *ANR,* advanced neoplasm rate (% of patients with ≥ 1 advanced neoplasm).

for colonoscopy examinations at intervals >10 years after an initial examination with negative results. Additional study is needed to evaluate this suggestion.

The main result in our study is that the observed incidence of adenomas and advanced neoplasms at a second screening 10 years after a baseline examination with negative results is lower than the yield of first-time screening colonoscopy, even though patients are 10 years older. A previous single-center report in 378 persons undergoing screening colonoscopy after an initial examination with negative results found an incidence of advanced neoplasms of 3.4% but did not include a control group of patients undergoing initial screening colonoscopy during the same time interval.[15] A study from the Clinical Outcomes Research Initiative database reported that the incidence of polyps >9 mm at 7 to <10 years after an initial baseline screening colonoscopy with negative results was 4.4%. However, 42.3% of the population had a family history of colorectal cancer or polyps, 13.6% initially underwent colonoscopy for a fecal blood test with positive results, 36.5% had symptoms or screening tests with positive results as the indication for the second colonoscopy, and there was no control group undergoing first-time screening in the same time period.[16] A small study of patients with an index colonoscopy with negative results found that the rate of advanced lesions in patients undergoing repeat colonoscopy at 6 to 10 years was 3.6%, which was not different from the incidence of 7% for repeat colonoscopies at 5 years ($P = .15$). However, no control group of patients undergoing first-time screening colonoscopy in the same time interval was included.[17]

This study has several limitations. First, the number of persons undergoing a second screening colonoscopy was lower than that of those undergoing a first screening colonoscopy, suggesting that selection bias might result in important differences between the 2 groups of patients. Thus, patients presenting for a second colonoscopy might lead a healthier lifestyle and generally interact more frequently with the health care system. However, in screening studies, patient age, sex, smoking status, and obesity are the main determinants of adenoma prevalence.[18] Willingness to undergo screening has never been shown to be a predictor of neoplasia prevalence. Second, the study is underpowered to evaluate some relevant outcomes, particularly colorectal cancer, and to evaluate predictors of advanced lesions in a multivariable regression. The overall lower rates of adenomas and advanced lesions at the second examination compared with the first screening colonoscopy, despite the older age at the second screen, seems to be the relevant result of the study. Increasing age has always been a powerful predictor of colorectal neoplasia in screening populations. The low rate of neoplasia in the second screening group in this study, despite their older age compared with patients undergoing a first-time screening, is evidence of the powerful negative predictive value of a normal colonoscopy. Additional studies to evaluate specific predictors of advanced lesions at a second screening colonoscopy will be needed. Third, as a single-center study, generalizability of the results is uncertain. Fourth, we did not have data on a number of factors that might predict the incidence of precancerous lesions at a second screening colonoscopy, including use of aspirin and nonsteroidal anti-inflammatory drugs, family history, smoking status, bowel preparation scores at the baseline colonoscopy, or comorbidities such as diabetes. Finally, we did not have complete follow-up of the initial cohort, and patients may have developed cancer detected at earlier symptomatic examinations at outside centers or had second screening colonoscopies at other centers. This does not negate the important observation that patients remaining asymptomatic 10 years after an initial screening colonoscopy with negative results have a lower rate of colorectal neoplasia than patients who are 10 years younger and are undergoing a first-time screening.

In conclusion, our study demonstrates that the yield of a second screening colonoscopy 10 years after an initial examination with negative results is lower than the yield of first-time screening and supports the current recommendation of screening colonoscopy at 10-year intervals.

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