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

Douglas K Rex 1
Prasanna Ponugoti 1
Cynthia S. Johnson 2
Lisa Kittner 3
Randy Yanda 3

1 Division of Gastroenterology/Hepatology; Indiana University School of Medicine, Indianapolis, IN
2 Department of Biostatistics, Indiana University School of Medicine, Indianapolis, IN
3 Digestive Healthcare of Georgia, Atlanta GA

Address correspondence to:

Douglas K Rex MD

Indiana University Hospital 4100

550 North University Hospital

Indianapolis, IN

46202

Phone: 317-948-8741

Fax: 317-944-5449

Email: drex@iu.edu

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Johnson: statistical analysis, review and revision of the manuscript
Kittner: collection of data, review and revision of the manuscript
Yanda: study conception, collection of data, review and revision of the manuscript

Abstract:

Background and Aims: Prior studies assessing the yield of a second screening colonoscopy performed 10 years after an initial negative screening colonoscopy did not include a control group of persons undergoing their 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 64.0 ± 3.9 years) who underwent a second screening examination. In those undergoing second screening, the mean interval between examinations was 10.4 years (±1.1; range 8-15 years). At second screening, the polyp detection rate (PDR), adenoma detection rate (ADR) and advanced neoplasm rate (ANR) 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 52.6 ± 3.4 years) underwent their first screening colonoscopy. The PDR, ADR and ANR 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, gender, body mass index, and endoscopist, PDR, ADR, and ANR were all lower at the second screening colonoscopies than at first-time colonoscopies (all $p<0.001$).

Conclusions: Despite being 10 years older, persons with a negative screening colonoscopy 10 years earlier had numerically lower rates of adenomas and advanced neoplasms at their second screening examination compared with patients in the same practice undergoing their first

screening colonoscopy, and they had no cancers. The fraction of advanced neoplasms that were proximal to the sigmoid 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 negative examination.

Introduction:

Since colonoscopy was first proposed for average-risk screening in 1997 (1), the recommended interval between colonoscopies for average-risk persons with an initial normal examination 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 negative examination (12,13), and a case-control study found that a negative screening colonoscopy 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 a negative examination (15). In that study of 378 individuals, 38.1% had one or more conventional adenomas, and only 3.4% had an advanced neoplasm.

In the current study we extend the observations of the yield of a second screening colonoscopy 10 years after a negative examination. 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 their 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 subjects were at least 50 years of age at their baseline examination, had screening listed as the indication, had a complete examination to the cecum with the bowel preparation listed as fair, good, or excellent and/or with Boston Bowel Preparation Scores of 6 to 9. Because the data were acquired in Atlanta and de-identified for analysis, the Institutional Review Board at Indiana University waived review of the study.

All of the procedures in the study were performed at one ambulatory surgery center (ASC). The patient population served by the ASC 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 ASC 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 de-identified 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 11 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 (SSP; synonymous with sessile serrated adenoma), and traditional serrated adenomas (TSA). Advanced neoplasms were defined

as adenomas with villous elements, high-grade dysplasia, or size ≥10 mm, SSPs ≥10 mm in size or with cytological dysplasia and TSAs ≥10 mm in size. The database for the study recorded age, gender, polyp findings (size, location, and pathology), and body mass index (BMI).

Statistical Methods:

Chi-squared tests were used to compare polyp, adenoma, and advanced neoplasm rates between the groups. Wilcoxon rank sum t-test was done to compare adenomas per colonoscopy between the groups. Multivariable logistic and linear regression was used to determine if the groups differences persisted after adjusting 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 underwent a second screening colonoscopy at least 8 years after their initial examination and 1635 individuals underwent their first screening examination. Of the 470 individuals undergoing a second screening, 440 had no polyps at their baseline examination and 30 had only distal colon (rectum and/or sigmoid) hyperplastic polyps <10 mm in size.

Second screening group

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

There were 35 individuals (17 females) with 40 advanced neoplasms at the second examination, of which 33 (82.5%) were proximal to the sigmoid colon. The overall polyp detection rate (PDR), adenoma detection rate (ADR), adenomas per colonoscopy (APC), and advanced neoplasm detection rate (ANR) at the second examination were 44.7%, 26.6%, 0.44 and 7.4%, respectively. ADR was 25.7% in subjects 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 PDR, ADR, APC and ANR were 46.6%, 27.8%, 0.47, and 8.0%, respectively.

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

Initial screening group

Among 1635 subjects who underwent initial screening colonoscopy (the screening colonoscopy control group) during the study period, the mean (SD) age was 52.6 (3.4) (range 50-81) years and 808 (49.4%) were women. The mean (SD) BMI was 26.9 (5.0) (Table 1). The PDR, ADR, APC, and ANR were 53.5%, 32.2%, 0.54, and 11.7%, respectively (Table 2). There were 192 individuals (85 females) with 243 advanced neoplasms of which 152 (62.6%) were proximal to the sigmoid. There were no cancers.

On multi-variable 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 gender, 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 subjects in an attempt to identify a subgroup with either zero or an extremely low risk of advanced neoplasia at the second colonoscopy. Although age, gender, and BMI were all associated with neoplasia, we did not identify any such subgroup (data not shown).

Discussion

In this report we demonstrate that the yield of a second screening colonoscopy in 470 persons who had a negative screening colonoscopy 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 negative colonoscopy 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 negative examinations is safe and appropriate. For both first and second screening colonoscopies the majority of advanced lesions were in the proximal colon, increasing

the rationale for screening by colonoscopy. This finding was also observed for second screening examinations in the prior published study (15).

Our data suggest that females with normal BMI are a candidate group to evaluate in larger studies of second screening examinations because they might be candidates for colonoscopy examinations at intervals >10 years after an initial negative examination. 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 negative baseline examination 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 negative examination 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 a negative initial baseline screening colonoscopy 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 positive fecal blood test, 36.5% had symptoms or positive screening tests 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 a negative index colonoscopy found that the rate of advanced lesions in patients undergoing repeat colonoscopy at 6 to 10 years was 3.6%, which was not different than the incidence of 7% for repeat colonoscopies at 5 years (p=0.15). 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 those undergoing a first screening colonoscopy, suggesting that selection bias might result in important differences between the two 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, gender, 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 first-time screenees, 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 non-steroidal 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 the study ASC 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 negative screening colonoscopy have a lower rate of colorectal neoplasia than first-time screenees who are 10 years younger.

In conclusion, our study demonstrates that the yield of a second screening colonoscopy 10 years after an initial negative examination 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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Table 1: Patient demographics

	Second screen group			Initial screening group
	Subjects without polyps at baseline exam	**Subjects with distal hyperplastic polyps at baseline exam**	**Total**	
	n=440	**n=30**	**n=470**	**n=1635**
	n (%)	**n (%)**	**n (%)**	**n (%)**
Sex				
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)
	Mean (SD) Range	Mean (SD) Range	Mean (SD) Range	Mean (SD) Range
Age at initial colonoscopy	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	63.9(3.8) 59-80	64.3(4.3) 59-76	64.0 (3.9) 59-80	-
Interval between colonoscopies (years)	10.5 (1.0) 8.0-15.0	10.0 (1.1) 8.0-12.6	10.4 (1.1) 8.0-15.0	-
BMI	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

Table 2: Yield of screening colonoscopy in the first and second screening groups: number of patients with at least one lesion of different types and total number of lesions detected according to histology

	Second screen group			**Initial screening group**
Number of patients	**Subjects without polyps at baseline exam**	**Subjects with distal hyperplastic polyps at baseline exam**	**Total**	
	n=440	**n=30**	**n=470**	**n=1635**
Yield by patient	n (%)*	n (%)	n (%)	n (%)
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)
Males with ≥1 adenoma (n=218)	65 (31.7)	6 (46.2)	71 (32.6)	309 (37.4)
Females with ≥1 adenoma (n=252)	48 (20.4)	6 (35.3)	54 (21.4)	217 (26.9)
Total number of lesions detected	**n=334**	**n=33**	**n=367**	**n=1718**
Histology of lesions detected	n (%)**	n (%)	n (%)	n (%)
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)

- * number of patients (%)
- ** number of lesions with designated pathology (% of all lesions detected with designated pathology)

Table 3: Within group multivariable associations with conventional adenoma and advanced neoplasm

	2nd Screening Group – Conventional Adenoma		
	OR	95% CI	*P* value
Age (10-year increase)	2.52	(1.44 - 4.42)	0.001
Sex (M vs F)	1.79	(1.12 - 2.88)	0.015
BMI (5-point increase)	1.44	(1.12 - 1.84)	0.005
	Initial Screening Group – Conventional Adenoma		
Age (10-year increase)	1.09	(1.06 - 1.13)	<0.001
Sex (M vs F)	1.58	(1.26 - 1.98)	<0.001
BMI (5-point increase)	1.26	(1.13 - 1.41)	<0.001
	Initial Screening Group – Advanced Neoplasm		
Age (10-year increase)	1.10	(1.06 - 1.14)	<0.001
Sex (M vs F)	1.29	(0.93 - 1.78)	0.127
BMI (5-point increase)	1.20	(1.03 - 1.39)	0.020

M: male

F: female

BMI: Body Mass Index

Table 4: Between group comparisons of lesion yields in patients undergoing second versus initial screening colonoscopies

	Second screening patients (n=470)	Initial screening patients (n= 1635)	OR (95% CI) Initial vs 2nd	Univariate group *P* value	Multivariable group *P* value
PDR	44.7%	53.5%	2.99 (2.00 - 4.45)	<0.001	<0.001
ADR	26.6%	32.2%	3.09 (2.07 - 4.63)	0.021	<0.001
APC	0.44	0.54	-	0.024	<0.001
ANR	7.4%	11.7%	4.55 (2.61 - 7.91)	0.008	<0.001

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)

PDR	Polyp Detection Rate
ADR	Adenoma Detection Rate
ANR	Advanced Neoplasm Rate
SSP	Sessile Serrated Polyps
TSA	Traditional Serrated Adenoma
BMI	Body Mass Index
APC	Adenomas per Colonoscopy
SD	Standard Deviation
CI	Confidence Interval
OR	Odds Ratio