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Yield of repeat forward-view examination of the right side of the colon in screening and surveillance colonoscopy

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Abstract

Background and Aims—Colonoscopy is less protective for right-sided colon cancers than distal colon cancers. Repeat right-sided examination has been suggested to increase adenoma detection and right-sided protective effect. Our prospective study assessed the yield of a second forward-view examination of the right colon done immediately after the initial examination.

Methods—All men, age 50 to 75 years, undergoing screening or surveillance colonoscopy at the West Haven Veterans Affairs Medical Center were invited to participate. A second forward-view examination was performed if the Boston Bowel Preparation Scale score was 8 to 9 (scale = 0 – 9) with right-colon-segment score 2 to 3 (scale = 0 – 3). The primary outcome was per-patient detection rate of adenomas (including sessile serrated polyps) on repeat right-colon examination, defined as number of patients with 1 adenoma on the second right-sided colon examination divided by total number of patients. An increase in the adenoma detection rate (ADR) was a secondary outcome.

Results—Repeat right-sided colon examination, performed in 280 patients, revealed additional adenomas in 43 patients (15.4%; 95% CI of difference, 11.3%–21.0%). Overall ADR increased by 3.2% (95% CI, 1.1%–5.3%) after the second right-sided colon examination; right-sided colon ADR increased by 6.7% (95% CI, 3.8%–9.7%). Ten (3.6%) patients had a change in their screening/surveillance interval with the addition of findings on the repeat right-sided colon examination.

Conclusions—A substantial 15.4% of patients had additional adenomas detected on repeat forward-view examination of the right side of the colon, whereas overall ADR increased significantly by 3.2%. Given the lack of additional training or equipment required, repeat forward-view examination of the right side of the colon is a simple, readily available method to achieve a modest improvement in ADR.

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INTRODUCTION

Screening and surveillance colonoscopy decreases the incidence of colorectal cancer, but interval cancers, which develop before the next scheduled colonoscopy, remain a concern and account for up to 10.5% of colorectal cancers.[1–6] Furthermore, a number of studies indicate that the protective effect of colonoscopy is significantly less for right-sided cancers than for distal cancers.[5, 7–9]

Potential explanations for this reduced protection include poorer bowel preparation in the right side of the colon, different biological behavior of right-sided neoplasms, and a greater number of flat lesions such as sessile serrated polyps (SSP) that are more difficult to visualize in the right side of the colon. A variety of methods are being considered to potentially increase the detection of right-sided neoplastic lesions including repeat examination, retroflexed examination, mechanical fold-flattening, and increased colonoscopic field of view.

Retroflexed examination of the right side of the colon after standard forward examination was suggested to potentially allow for a greater detection of adenomas, especially those on the back side of folds. A 2011 cohort study of 1000 patients identified additional adenomas in 4.4% of patients with an increase in the adenoma detection rate (ADR) of 2.2%, whereas a second cohort study in 1341 patients found additional polyps in 5.0% (proportion with additional adenomas not provided) and an increase in ADR of 1.8% [10, 11]. However, subsequent trials indicated that the increase in detection of adenomas was comparable with a second examination in the retroflexed or forward position [12, 13].

These results have led some experts to recommend a second examination of the right side of the colon, especially when polyps are detected on initial examination [14, 15]. A repeat forward-viewing examination of the proximal colon may be the simplest method to improve the yield of adenomas and potentially decrease interval cancer. No additional equipment is required and the additional risk, time, and expense related to performing the second examination and any additional polypectomies are relatively minor. However, despite these recommendations, evidence to support repeat forward examination of the right side of the colon is limited. A prospective trial examined the yield of repeat forward-view examination of the proximal colon (hepatic flexure to cecum) in 400 patients and found that the ADR was increased by 2.3% and screening/surveillance intervals were changed in only 3.3% of patients [13].

Determining whether the yield of repeat examination of the right side of the colon is clinically meaningful and justifies routinely incorporating a second examination is important to inform endoscopists and guideline panels deciding on optimal methods for colonoscopic screening and surveillance. We therefore performed a prospective study in patients undergoing screening or surveillance colonoscopy to determine the yield of a second forward-view examination of the right side of the colon done immediately after completing the initial examination.

MATERIALS AND METHODS

Study Population

All men, age 50 to 75 years, undergoing colonoscopy for an indication of screening or surveillance at the West Haven Veterans Affairs Medical Center were invited to participate prospectively. Exclusion criteria included the following: prior resection of any portion of the colon or rectum, active anti-thrombotic therapy preventing polypectomy, American Society of Anesthesiologists Class 3 or higher, familial polyposis syndrome, inflammatory bowel disease, inability to achieve cecal intubation, a total Boston Bowel Preparation Scale (BBPS) score of 0 (solid stool covering all segments of colon), or inability to completely remove a polyp. Eligible patients were recruited before their scheduled procedure and informed consent was obtained. This study was approved by the institutional review board of the West Haven Veterans Affairs Medical Center in November 2013 with continuing review approval in November 2014.

Study Design

All colonoscopies had to be performed by 1 of 4 study endoscopists, who were attending gastroenterologists on the faculty at Yale School of Medicine. Eligible patients who consented to participation underwent their planned colonoscopy by 1 of the 4 study endoscopists, who was performing procedures that day per normal standard of care. The colonoscope was passed to the cecum, the colonoscope was withdrawn with washing and aspirating of colonic contents as needed to optimize visualization of colonic mucosa, the mucosa was carefully examined, and all polyps that were identified were removed, as would be done for any other screening or surveillance examination. All procedures were performed using Olympus (Tokyo, Japan) EVIS Exera II high-definition colonoscopes. Narrow band imaging could be used at the discretion of the endoscopist. Each polyp was submitted for histological assessment per usual standard of care.

After completing the colonoscopy, the endoscopist rated the adequacy of bowel preparation using the BBPS[16, 17], scoring the left side of the colon, transverse colon, and right side of the colon segments as 0 (mucosa not seen due to solid stool or thick liquid stool that cannot be cleared), 1 (areas of the colon segment not well seen due to staining, residual stool and/or opaque liquid), 2 (minor amount of residual staining, small fragments of stool and/or opaque liquid but mucosa seen well), or 3 (entire mucosa of the colon segment seen well). If a patient had a total BBPS score of 8 to 9 (scale 0–9), including a right-sided colon segment score of 2 or 3, and the endoscopist rated the prep as adequate (defined as able to identify polyps >5 mm), then the colonoscope was not removed, and a different study endoscopist immediately performed a second examination of the colon. We did not mandate specific aspects of colonoscopic technique, such as equal withdrawal times, for the first and second colonic examinations. In order to minimize the burden on the endoscopy center, we limited enrollment of of same-day repeat examinations to no more than 2 in 1 day.

Age of the patient, indication for colonoscopy (screening, surveillance), and study endoscopist were recorded. In addition, the size of polyps was categorized at the time of colonoscopy as 5 mm, 5 to 9 mm, or 10 mm. Endoscopists were asked to estimate sizes

using visual comparison with forceps of known dimension. Visualization of the polyp after retrieval could be used for confirmation if the polyp was removed in one piece.

Outcome Definitions

Primary Outcomes—For the predefined analysis of repeat examination of the right side of the colon, we assessed the findings from the second examination of the right side of the colon. The right colon was defined as the cecum and ascending colon, per the definition from the validated bowel prep scoring system, BBPS, used for our study [17]. Polyps detected on the second examination were defined as missed polyps. The primary outcome was the per-patient detection rate of right-sided colon adenomas (including SSP as discussed below) on repeat examination, defined as the number of patients with at least one adenoma identified on the second examination divided by the total number of patients completing both initial and second examination.

Secondary Outcomes—We examined the increase in per-patient ADR and right side of the colon ADR (defined by the increase in ADR when including polyps found on the second examination) because ADR is considered the primary quality metric for colonoscopy, given its correlation with interval cancers. We also determined the per-patient detection rate for each of the following polyp types: adenomas >5 mm, diminutive (<5 mm) adenomas, advanced adenomas, and SSP, calculated as described for all adenomas. An advanced adenoma was defined by any of the following features: size ≥ 1 cm, high-grade dysplasia, villous architecture, or carcinoma. Only sessile-serrated adenomas/polyps and traditional serrated adenomas were included in our definition of SSP as defined histologically by histopathologists using standard definitions [18]. Polyps that were classified as hyperplastic polyps were not included in our definition of SSP given their lack of malignant potential [18]. In addition to being listed separately, SSP were also included in the adenoma results because in clinical practice the implication of detecting SSP is similar to the implication of finding an adenoma with respect to intervals for repeat colonoscopy and risk of colorectal cancer.

We also compared the increased per-patient detection rate of right colon adenomas on a second examination in patients who had at least one polyp in the entire colon compared with patients with no polyps identified on the initial examination for the following outcomes: all adenomas, adenomas >5 mm, adenomas ≤ 5 mm, overall ADR, and right-sided colon ADR. Increased yield of adenomas per colonoscopy was calculated as the total number of adenomas found on second look of the proximal colon divided by the total number of patients examined. The per-adenoma miss rate was calculated as the number of adenomas found on the second-look examination of the right side of the colon divided by the total number of adenomas found on the first and second look examination of the right side of the colon combined. A per-SSP miss rate was defined similarly.

Finally, using current guideline recommendations [19] for timing of repeat colonoscopy in a patient with adequate prep (based on number, size, and histology of polyps identified), we determined the proportion of patients who would have a change in screening/surveillance

interval based on the findings of the second-look right colon examination plus the initial entire colon examination versus the findings of the initial entire colon examination alone.

Statistical Analyses

Proportions, differences in proportions, and 95% confidence intervals (CI) were calculated using the exact method for binomial proportions. Hypothesis testing of differences in proportions was performed using 2-sample proportion testing. Multivariate analysis to assess the impact of potential confounding factors (age, indication (screening vs surveillance), BBPS score (2 vs 3), endoscopist, and presence or absence of polyp on initial examination) on the primary outcome of detection of adenoma on second right-sided colon examination was performed by using a logistic regression model. Analyses were performed using Stata 13.1 (StataCorp, College Station, Tex). This study was a pre-specified part of a larger prospective study and the population represents a subset of the larger study's population[20]. The sample size for this larger trial was designed to enroll 450 colon segments with a BBPS = 2 and 450 colon segments with a BBPS = 3. No separate hypothesis-guided sample size calculation was performed for this study."

RESULTS

Patients

Two hundred eighty patients had BBPS scores of 8 to 9, underwent a repeat examination of the right colon by a second blinded endoscopist, and thus were included in our analysis. All of the patients were male, with a mean age of 62.3 ± 6.7 years. One hundred fifty (53.6%) of the colonoscopies were done for screening and 130 (46.4%) for surveillance.

Colonoscopy Findings

Initial examination of the right side of the colon identified adenomas in 134 (47.9%) patients (Table 1). Fifty-three patients (18.9%) had adenomas >5 mm whereas 108 (38.6%) had diminutive adenomas (≤ 5 mm). Fifteen (5.4%) patients had advanced adenomas and 23 patients (8.2%) had SSPs. A second examination of the right side of the colon revealed adenomas in 43 additional patients, resulting in an increased per-patient detection rate of right-sided colon adenomas of 15.4% (95% CI of difference, 11.3%-20.1%). The per-patient detection rates of right-sided colon adenomas on second examination for the 4 individual endoscopists were 5/43 (11.6%), 13/72 (18.1%), 14/74 (18.9%), and 11/91 (12.1%). The proportion of patients with additional findings on second examination of the right colon was 3.9% for adenomas >5 mm, 12.9% for diminutive adenomas, 1.1% for advanced adenomas, and 3.2% for SSPs (Table 1).

The initial examination ADR was 71.8%, which was increased to 75.0% after adding the second examinations of the right side of the colon for an increase of 3.2% (95% CI of difference, 1.1%–5.3%) (Table 2). Right-sided colon ADR was 47.9% for the initial examination and 54.6% for the combined first and second examinations for an increase of 6.7% (95% CI of difference, 3.8%–9.7%). The initial examination ADRs for screening versus surveillance were 98/150 (65.3%) versus 103/130 (79.2%) for the entire colon and 68/150 (45.3%) versus 66/130 (50.8%) for the right side of the colon. The mean number of

additional adenomas on second examination was 0.20 (55/280). The per-adenoma miss rate for the first examination was 16.1% (55/341). The per-SSP miss rate for the right side of the colon was 10/43 (23.3%).

Thirty-eight (16.2%) of the 234 patients who had a polyp on initial examination were found to have an additional adenoma on the second examination, whereas 5 (10.9%) of the 46 patients without a polyp on initial examination were discovered to have an additional adenoma on repeat examination (Table 3). The increase in overall ADR with a second right-sided colon examination was 3.8% in patients with a polyp on initial colon examination and 10.9% in patients without a polyp on initial colon examination (Table 3).

Ten (3.6%) of the 280 patients had a change in their screening/surveillance interval with the addition of the findings on the repeat right-sided colon examination. Two (0.7%) patients had a change from no-risk or low-risk adenoma to high-risk adenoma necessitating repeat colonoscopy in 3 years, whereas the remainder changed from no adenoma to low-risk adenoma.

On multivariate analysis, factors such as age (OR=1.02, 0.97–1.08), screening versus surveillance examination (OR = 1.11, 0.55–1.25), initial BBPS score of 2 versus 3 (OR = 1.05, 0.54–2.05), and the presence of a colon polyp on initial examination (OR = 1.56, 0.57–4.29) were not significant predictors of an adenoma on the second examination of the proximal colon.

DISCUSSION

In this prospective study assessing the potential benefit of a second examination of the right side of the colon immediately after the initial evaluation, 15.4% of patients had an additional adenoma detected on repeat forward-view examination. Overall ADR increased by 3.2% and right-sided colon ADR increased by 6.7% with repeat examination of the right side of the colon. However, screening/surveillance intervals were shortened in only 3.6% of patients after incorporating the findings of the second right-sided colon examination. The benefit of a second examination of the right side of the colon was not greater in those with a polyp on initial examination. In fact, the increase in ADR was greater in those without a polyp on initial examination of the colon.

Given the lower protective effect of colonoscopy against right-sided colon cancer, reexamination of the right side of the colon in a different orientation using retroflexion was proposed as a method to improve polyp detection. Although detection rates did increase with retroflex examination of the right side of the colon [10, 11], prospective randomized trials revealed that the yield was comparable to repeat examination in the forward view [12, 13].

A prior prospective trial of repeat forward-view examination of the transverse and right side of the colon in 48 patients identified an additional 14 adenomas on repeat examination (0.29 adenomas per repeat examination)(12). However, because it included repeat examination of the transverse colon, it is not directly applicable to the question regarding utility of repeat examination of the right side of the colon, and information on ADR and screening/surveillance intervals was not provided. More recently, Kushnir et al performed a

prospective study of repeat forward examination of the right side of the colon (hepatic flexure to cecum) in 400 patients and found that 10.5% of patients had an additional adenoma in the proximal colon on repeat forward examination, with a mean of 0.12 additional adenomas per repeat examination [13]. These results are slightly lower than our findings of 15.4% of patients with additional adenomas and a mean of 0.20 additional adenomas per repeat examination despite the fact that our repeat examination did not include the hepatic flexure. The difference is most likely related to differences in population: our study consisted only of male veterans whereas over half of the patients from Kushnir et al were female; the mean age and the proportion undergoing surveillance rather than screening colonoscopy were also somewhat higher in our population.

Kushnir et al reported that adenomas identified on initial examination and older age were significant independent factors associated with detecting adenomas on repeat examination. We did not find age, bowel prep quality (BBPS 2 vs 3) or indication (screening vs surveillance) to be predictors of finding additional adenomas on repeat examination of the right side of the colon. In addition, we felt that polyps on initial examination were a more clinically relevant variable to examine than adenomas on initial examination because at the time of colonoscopy the endoscopist does not know the histologic diagnosis of the polyp. We found that finding polyps on the initial examination of the colon did not predict finding adenomas on the repeat examination. Over 10% of patients with no polyps on the initial examination had adenomas detected on repeat examination of the right side of the colon, resulting in a substantial 7% increase in ADR for these patients. Thus, although repeat examination of the right colon has been recommended especially in those with a polyp on initial examination, our results suggest that if performed, repeat examination is warranted regardless of the findings on initial examination.

Although the fact that 15% of patients had additional adenomas found on repeat examination of the right side of the colon suggests a major benefit at first glance, the characteristics of the additional adenomas and the implications of our findings need to be considered. Eighty-four percent of the additional adenomas detected were ≤ 5 mm and only 1.1% were advanced adenomas. The ADR increased by 3.2% whereas the screening/surveillance intervals were changed in only 3.6% of patients on the basis of the repeat examination of the right side of the colon, similar to the 2.3% change in ADR and 3.3% change in intervals identified by Kushnir et al in their prospective study of repeat forward examination of the proximal colon [13]. If the increases in larger or advanced adenomas and changes in screening/surveillance intervals occur in only a small proportion of patients, one may question if the additional time and expense for repeat examination or use of other modalities will be justified. Nevertheless, ADR is the primary metric for colonoscopy quality due to its documented correlation with interval cancers, and even small improvements in ADR appear to be clinically significant: a 3% decrease in colorectal cancer risk is reported to occur with every 1% increase in ADR [20].

Other modalities also have been developed in an effort to increase polyp detection, including methods designed to increase the field of view (eg, retro-viewing camera, wide-angle colonoscopy) or to flatten folds (eg, balloon-assisted colonoscopy, caps)[22–24]. However,

no study has compared the use of one of these modalities to repeat examination of the right side of the colon.

Endoscopists and payors will need to determine what level of increased detection justifies repeat examination of the right side of the colon and/or use of other modalities to improve visualization of the right colon. Other modalities will need to be assessed in direct comparisons with forward-view repeat examination. Additional factors, such as time, cost, availability, training, and risk, will also need to be considered. Repeat forward examination has the advantage of being the most readily available modality, requiring no additional equipment, training, or expense. The major drawback to repeat examination of the right side of the colon is time. The additional time to examine a right-sided colon segment that has already been washed and remove any additional polyps detected should be minimal. However, we acknowledge that even a couple of minutes per colonoscopy over a full day in a very busy, rapid-throughput endoscopy unit could approach the time required to perform an additional colonoscopy.

Our study had limitations. Different endoscopists performed the first and second examinations of the colon, which does not reproduce what occurs in standard clinical practice. Potential disadvantages of separate endoscopists are that they do not have identical withdrawal techniques and baseline adenoma detection rates. Moreover, the advantage of 2 endoscopists is that it eliminates the potential bias that may be seen in tandem studies performed by the same endoscopist. For example, endoscopists may not use the same effort to detect adenomas if they know they will be performing a second evaluation or they already performed a careful initial examination. In addition, our study population consisted of male veterans, potentially limiting generalizability to populations including women.

In a population with a lower ADR, and thus lower adenoma prevalence, we would expect less of an increase in per-patient detection of right-sided colon adenomas with the second examination, but we would not necessarily expect less of an absolute increase in ADR. The higher prevalence of adenomas in our population should increase the number of additional adenomas found on repeat examination but minimize the increase in ADR because so many patients have adenomas detected on the first examination. In contrast, fewer patients in a lower adenoma prevalence group will have an adenoma detected on their initial examination, so the ADR may be more likely to increase when an adenoma is detected on the second examination.

In conclusion, our prospective study found that a repeat forward-viewing examination of the right side of the colon detects additional adenomas in a substantial 15.4% of patients and results in a 3.2% increase in ADR. Decisions regarding the incorporation of repeat forward-view examination of the right side of the colon or other modalities designed to improve adenoma detection require assessment of study results together with consideration of factors such as cost and risk by endoscopists, patients, guideline panels, and payors. Whether other modalities will increase adenoma detection significantly more than repeat forward-view colonoscopy and justify their use will require future study. Given the lack of additional training or equipment required, repeat forward-view examination of the right side of the colon is a simple and readily available method to achieve a modest improvement in ADR.

Abbreviation List

ADR	adenoma detection rate
SSP	sessile serrated polyps
BBPS	Boston bowel preparation scale

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Table 1

Proportion of patients with findings on first and second examinations of the right side of the colon

	Combined first and second examination (N = 280)	First examination (N = 280)	Proportion of patients with additional finding on 2nd examination (95% CI)
All adenomas	177 (63.2%)	134 (47.9%)	15.4% (11.3 – 20.1%)
Adenomas >5 mm	64 (22.9%)	53 (18.9%)	3.9% (2.0 – 6.9%)
Adenomas ≤ 5 mm	144 (51.4%)	108 (38.6%)	12.9% (9.2 – 17.3%)
Advanced adenoma	18 (6.4%)	15 (5.4%)	1.1% (0.2 – 3.1%)
Sessile serrated polyp	32 (11.4%)	23 (8.2%)	3.2% (1.5 – 6.0%)

Table 2

Adenoma detection rates (ADRs) with first and second examinations of the right side of the colon

	Combined first and second examination	First examination	Increase in ADR (95% CI)
Overall ADR	210 (75.0%)	201 (71.8%)	3.2% (1.1 – 5.3%)
Right side of colon ADR	153 (54.6%)	134 (47.9%)	6.7% (3.8 – 9.7%)

Table 3

Findings on second examination based on presence or absence of polyp on first examination

	Polyp on first examination (N = 234)	No polyp on first examination (N = 46)	Difference (95% CI)
Proportion of patients with adenomas on second examination			
All adenomas	38 (16.2%)	5 (10.9%) (−8.8 – 14.1%)	5.4%
Adenomas >5 mm	10 (4.3%)	1 (2.2%) (−8.9 – 6.3%)	2.1%
Adenomas ≤ 5 mm	32 (13.7%)	4 (8.7%) (−8.6 – 12.3%)	4.9%
Increase in ADR after second examination			
Overall ADR	9 (3.8%)	5 (10.9%) (−19.3 – −0.1%)	−7.0%
Right side of colon ADR	14 (5.9%)	5 (10.9%) (−17.2 – 2.3%)	−4.9%