A retrograde-viewing device improves detection of adenomas in the colon: a prospective efficacy evaluation (with videos)

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Background: Colonoscopy may fail to detect neoplasia located on the proximal sides of haustral folds and flexures. The Third Eye Retroscope (TER) provides a simultaneous retrograde view that complements the forward view of a standard colonoscope.

Objective: To evaluate the added benefit for polyp detection during colonoscopy of a retrograde-viewing device.

Design: Open-label, prospective, multicenter study evaluating colonoscopy by using a TER in combination with a standard colonoscope.

Setting: Eight U.S. sites, including university medical centers, ambulatory surgery centers, a community hospital, and a physician's office.

Patients: A total of 249 patients (age range 55-80 years) presenting for screening or surveillance colonoscopy.

Interventions: After cecal intubation, the disposable TER was inserted through the instrument channel of the colonoscope. During withdrawal, the forward and retrograde video images were observed simultaneously on a wide-screen monitor.

Main Outcome Measurements: The number and sizes of lesions (adenomas and all polyps) detected with the standard colonoscope and the number and sizes of lesions found only because they were first detected with the TER.

Results: In the 249 subjects, 257 polyps (including 136 adenomas) were identified with the colonoscope alone. The TER allowed detection of 34 additional polyps (a 13.2% increase; $P < .0001$) including 15 additional adenomas (an 11.0% increase; $P < .0001$). For lesions 6 mm or larger, the additional detection rates with the TER for all polyps and for adenomas were 18.2% and 25.0%, respectively. For lesions 10 mm or larger, the additional detection rates with the TER for all polyps and for adenomas were 30.8% and 33.3%, respectively. In 28 (11.2%) individuals, at least 1 additional polyp was found with the TER. In 8 (3.2%) patients, the polyp detected with the TER was the only one found. Every polyp that was detected with the TER was subsequently located with the colonoscope and removed. For all polyps and for adenomas, the additional detection rates for the TER were 9.7%/4.1% in the left colon (the splenic flexure to the rectum) and 16.5%/14.9% in the right colon (the cecum to the transverse colon), respectively.

Limitations: There was no randomization or comparison with a separate control group.

Conclusions: A retrograde-viewing device revealed areas that were hidden from the forward-viewing colonoscope and allowed detection of 13.2% additional polyps, including 11.0% additional adenomas. Additional detection rates with the TER for adenomas 6 mm or larger and 10 mm or larger were 25.0% and 33.3%, respectively. (Clinical trial registration number: NCT00657371.) (Gastrointest Endosc 2010;71:551-6.)

Abbreviation: TER, Third Eye Retroscope.

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Colonoscopy is the criterion standard for colorectal polyp and cancer detection. However, even meticulous colonoscopy misses substantial numbers of colorectal polyps,[1-6] and complete colonoscopy can be followed by the development of colorectal cancer after only short intervals.[7-14]

Colonoscopy may miss lesions because they are located on the proximal side of the ileocecal valve, haustral folds, flexures, or rectal valves,[5,15] because they are too flat to be easily visualized,[16] because of poor bowel preparation,[17,18] or because of poor technique.[19]

The Third Eye Retroscope (TER) (Avantis Medical Systems, Inc, Sunnyvale, Calif) is an auxiliary imaging device that is passed through the working channel of a colonoscope and provides a retrograde image of the colon during colonoscope withdrawal. The device has proved effective in improving polyp detection on the proximal sides of folds in models[20] and has proved safe in humans.[21]

In this study, we investigated the impact of the TER on polyp and adenoma detection in a prospective human trial.

Capsule Summary

What is already known on this topic

- Colorectal polyps may be missed on colonoscopy because they are located on the proximal side of haustral folds and flexures, where they can be difficult to detect with the forward-viewing colonoscope.

What this study adds to our knowledge

- In a prospective, multicenter study, use of the Third Eye Retroscope, a retrograde-viewing imaging device, in conjunction with a standard colonoscope resulted in the detection of 34 additional polyps of all sizes, including 15 adenomas, compared with the colonoscope alone.
- With the retrograde-viewing device, additional detection rates for adenomas larger than 6 mm and larger than 10 mm were 25.0% and 33.3%, respectively.

MATERIALS AND METHODS

Fourteen experienced endoscopists at 8 U.S. sites, including 4 university hospital outpatient endoscopy centers, 2 ambulatory surgery centers, a community hospital, and a physician's office, participated in this multicenter study. Patients underwent bowel preparation according to the standard regimens used at each site. Permission to perform the study was granted by the institutional review board at each site, and all subjects provided informed consent.

Colonoscopy was performed by using standard (adult) Olympus colonoscopes (CF-Q160AL, CF-Q180AL, or CF-H180AL; Olympus America Inc, Center Valley, Pa).

The TER is a single-patient use, flexible endoscope with an integrated camera and light source that is passed through the working channel of a standard colonoscope after the colonoscope reaches the cecum. As the TER emerges from the colonoscope channel, it automatically retroflexes 180 degrees (Video 1; available online at www.giejournal.org). A polarizing filter cap preloaded on the colonoscope prevents the high-intensity light guides of the colonoscope from creating glare that would blind the TER's view. Electronic circuitry in a separate video processor unit prevents the light source near the tip of the TER from creating glare that would affect the colonoscope's image. The outer diameter of the camera (135-degree angle of view) at the tip is 3.5 mm, with the remainder of the shaft being 2.5 mm. During colonoscope insertion, pools of fluid are suctioned from the colon because fluid aspiration during withdrawal is reduced approximately 50% by the presence of the TER in the channel.

During the withdrawal phase, the forward view of the colonoscope and the retrograde image from the TER are observed simultaneously on a wide-screen monitor in a side-by-side configuration (Fig. 1). A lock mechanism may be used to maintain the tip of the TER at 2.5 cm from the tip of the colonoscope, but it may be placed 1 to 5 cm from the colonoscope lens. If debris obscures the TER's view, the water jet from the colonoscope serves to clean the TER lens.

For each polyp visualized, the endoscopist indicated whether it could be seen with the colonoscope view alone or whether it could be seen with the colonoscope only after it was first detected with the TER. Thus, polyps that were visualized simultaneously with the forward view and the TER or that were initially viewed with the TER but then were readily apparent on the forward view with the colonoscope were not considered additional polyp detections by the TER. Therefore, additional polyp detections by the TER constituted a group of polyps that, in the best judgment of the investigators, would not have been detected by the forward-viewing colonoscope (Fig. 2, Video 2; available online at www.giejournal.org). Once any polyp was detected, the TER was withdrawn from the colonoscope, the polyp was removed by using standard techniques, and the TER was reinserted before continuing withdrawal.

It was noted that there was more than 1 polyp in some patients. However, for the purposes of applying statistical techniques to data related to polyps, it was assumed that individual polyps constituted statistically independent observations. We based the sample size on an estimated gain in detection of 12% provided by the TER and a goal of measuring the gain in detection to within ±3.75% with a 95% confidence interval. Assuming an average of 1.2 polyps per subject, the required sample size was 241 subjects. Assuming that approximately 15% of subjects would not be assessable (eg, because of poor bowel preparation), a total of 284 subjects were planned for enrollment.

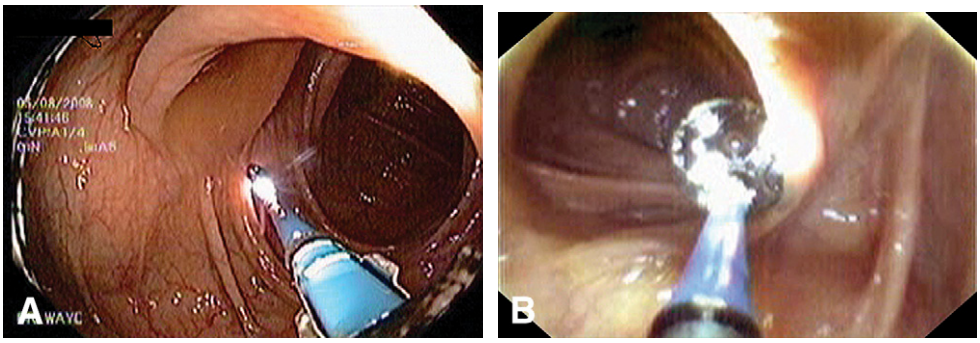

Figure 1. The colonoscope's forward view is displayed on the left side of the split-screen monitor, with the retrograde view on the right.

Increased detection using the TER was evaluated by using the exact binomial test. Differences in polyp size detected by colonoscopy and by the TER were evaluated by using the Student *t* test. Additional detections by using the TER were compared for the right and left side of the colon by using the Fisher exact test.

Although there was multiple testing of outcome data arising from individual patients and polyps, correction by the Bonferroni method would not have removed significance from any findings; therefore, all *P* values are presented uncorrected for multiple testing.

This study was initiated by the sponsor, Avantis Medical Systems, which provided the equipment and reimbursed the investigators and facilities for expenses incurred as a result of their participation in the study. The study was designed by the investigators.

RESULTS

There were 288 subjects enrolled in the study, of whom 39 were withdrawn (poor bowel preparation [n = 15], device-related reasons [n = 13], previously undiagnosed colitis [n = 1], unable to intubate the cecum [n = 5], polyposis [n = 3], protocol violation [n = 2]).

Of the 249 patients included in the study, 132 (53%) were men. The indication was screening in 145 (58%) and polyp surveillance in 104 (42%) subjects. The mean age was 63.1 (standard deviation 6.5) years (range 55-80 years).

Table 1 shows the increase in polyp and adenoma detection by using the TER. The increase in detection of all polyps by using the TER (13.2%) and the increase in adenoma detection (11.0%) were significant ($P < .0001$) (Table 1).

The additional detection rates of all polyps by the TER were 9.7% in the left side of the colon (the splenic flexure to the rectum) and 16.5% in the right side of the colon (the cecum through the transverse colon) ($P = .20$). Of the 22 polyps detected with the TER in the right side of the colon, 2 were in the cecum, 10 in the ascending colon, 1 in the hepatic flexure, and 9 in the transverse colon. In the left side of the colon, 2 were in the splenic flexure, 1 in the descending colon, 3 in the sigmoid colon, and 6 in the rectum.

The additional detection rates of adenomas with the TER were 4.1% in the left side of the colon and 14.9% in the right side of the colon ($P = .09$) (Table 1). Of the 13 adenomas detected with the TER in the right side of the colon, 1 was in the cecum, 8 in the ascending colon, and 4 in the transverse colon. In the left side of the colon, 1 was in the splenic flexure and 1 in the sigmoid colon.

There were 28 individuals (11.2%) having at least 1 additional polyp found with the TER, and 8 patients (3.2%) in whom the polyp detected with the TER was the only polyp found. All polyps detected with the TER were subsequently located with the colonoscope and removed.

The mean size of all polyps detected with the TER was 4.6 mm (range 2–12 mm) compared with 4.2 mm (range 1–15 mm) for those detected with the colonoscope ($P = .42$). Of the 34 polyps detected with the TER, 10 (29.4%) were 6 mm or larger and 4 (11.8%) were 10 mm or larger. Of the 257 polyps detected with the colonoscope, 55 (21.4%) were 6 mm or larger and 13 (5.1%) were 10 mm or larger. The TER allowed detection of 18.2% additional polyps 6 mm or larger and 30.8% additional polyps 10 mm or larger (Table 2).

The mean size of adenomas detected with the TER was 5.2 mm (range 2–12 mm) compared with 4.4 mm (range 1–15 mm) for adenomas detected with the colonoscope ($P = .41$). Of the 15 adenomas detected with the TER, 8 (53.3%) were 6 mm or larger and 3 (20.0%) were 10 mm or larger. Of the 136 adenomas detected with the colonoscope, 32 (23.5%) were 6 mm or larger and 9 (6.6%) were 10 mm or larger. The TER allowed detection of 25.0% additional adenomas 6 mm or larger and 33.3% additional adenomas 10 mm or larger (Table 2).

The mean withdrawal time during colonoscopy was 10.9 minutes, and the mean total procedure time was 26 minutes.

DISCUSSION

In this prospective study, we found that a retrograde-viewing device allowed detection of 13.2% more polyps

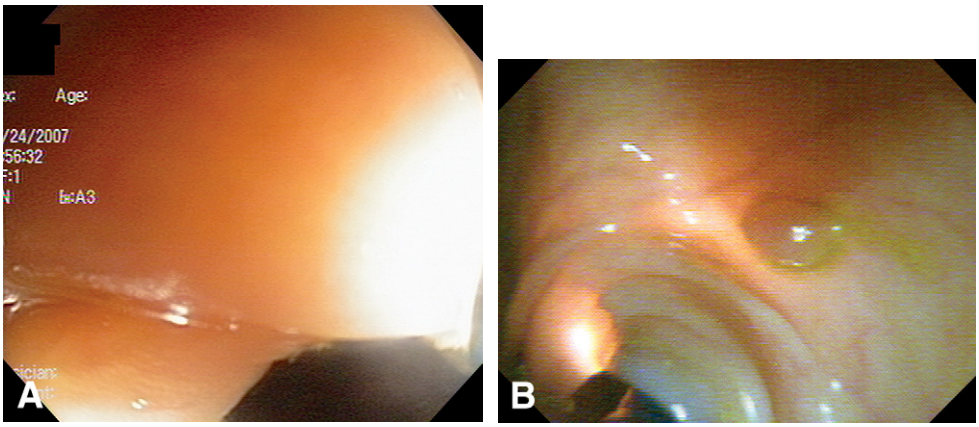

Figure 2. This polyp was detected in the retrograde view but was hidden from the forward view of the colonoscope by a large haustral fold.

TABLE 1. Increase in detection of all polyps and adenomas with Third Eye by location

	All polyps			Adenomas		
	Entire colon	Right colon	Left colon	Entire colon	Right colon	Left colon
Standard colonoscope*	257	133	124	136	87	49
Third Eye Retroscope†	34	22	12	15	13	2
Additional with Third Eye Retroscope, %	13.2	16.5	9.7	11.0	14.9	4.1

*Detected with the colonoscope.
†Detected with the Third Eye Retroscope (located behind folds and found with the colonoscope only because they were first detected with the Third Eye Retroscope).

TABLE 2. Increase in detection of all polyps and adenomas with Third Eye by size

	All polyps			Adenomas		
	Any size	≥6 mm	≥10 mm	Any size	≥6 mm	≥10 mm
Standard colonoscope	257	55	13	136	32	9
Third Eye Retroscope	34	10	4	15	8	3
Additional with Third Eye Retroscope, %	13.2	18.2	30.8	11.0	25.0	33.3
P value	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001

and 11.0% more adenomas of all sizes than could be seen with the colonoscope alone.

The gains in detection with the TER were greater for larger lesions. For lesions 6 mm or larger, the additional detection rates with the TER for all polyps and for adenomas were 18.2% and 25.0%, respectively. For lesions 10 mm or larger, the additional detection rates with the TER for all polyps and for adenomas were 30.8% and 33.3%, respectively.

Thus, we identified a potential clinical role for a simultaneous retroflexed view in improving adenoma detection during colonoscopy, and our results support previous observations that polyps may be located in areas difficult to detect by forward-viewing colonoscopy.[5,15] Given that recent guidelines for colorectal cancer screening and surveillance triage patients into a wide range of follow-up intervals based on whether polyps were found and their characteristics[22-25] and that colonoscopy has imperfect protection against colorectal cancer,[7-14] the need to identify all the neoplasias in the colon has assumed increased importance.[26,27]

We found numerically higher detection rates with the TER in the right side of the colon compared with the left side of the colon, although this difference did not reach statistical significance. This finding may have clinical importance, given recent studies that found that

colonoscopy is not as protective in the right side of the colon as it is in the left side of the colon.[14,28]

This study has multiple limitations. First, the study colonoscopists were obviously not blinded to the presence of the TER. Although we created reasonable rules for determining whether polyps were only detected with the TER, these rules were subject to an element of interpretation and the study results could have been affected by biases among the investigators.

Second, we have not established an optimal method of viewing simultaneous images, and the viewing method was not specified or controlled in the study. Until they have gained proficiency in observing both screens simultaneously, some endoscopists could be distracted by the novelty of the Third Eye image. Thus, we cannot guarantee that time and attention spent viewing the forward colonoscopy image was adequate or meets current recommended standards for forward-viewing.[29]

Third, the study was not designed with detection of large polyps or adenomas as an endpoint. The large gains in large adenoma detection reported here should be viewed with caution because they are based on a very small number of polyps, they substantially exceed previously measured large polyp miss rates of colonoscopy by either tandem colonoscopy studies[1,2] or studies with CT colonography as the criterion standard,[5,6] they are subject to size measurement error, and we do not know the baseline adenoma detection rates of all the study colonoscopists. Thus, the device might increase adenoma detection more in poor adenoma detectors than in high adenoma detectors.

The overall total number of adenomas per colonoscopy (136 adenomas/249 subjects = 0.55 adenomas per colonoscopy) (Table 2) is in the mid range of reported rates[26] and well below the highest rates reported.[30] Thus, poor adenoma detectors could have been present among the study colonoscopists because experience in colonoscopy is no guarantee of high levels of detection.[31,32]

Finally, the trend toward higher gains in large compared with small polyp detection could reflect that the image quality with the version of the TER used in the study is not as good as the forward-viewing colonoscopes used, and thus small polyps were perhaps not as easily seen with the TER. A planned second-generation TER with improved image quality may reverse this trend, if it is real, and even if the issue of image quality affected the ratio of large to small polyp detection in this study, it would not account for the high rates for detection of additional large adenomas and other large polyps with the TER in comparison with the colonoscope.

In summary, our results suggest a potential role for a retroflexed view and the TER in improving adenoma detection during colonoscopy. Additional study of the impact of this device on colonoscopy is warranted.

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