Impact of experience with a retrograde-viewing device on adenoma detection rates and withdrawal times during colonoscopy: the Third Eye Retroscope study group

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Background: Colonoscopy has been adopted as the preferred method to screen for colorectal neoplasia in the United States. However, lesions can be missed because of numerous factors, including location on the proximal aspect of folds or flexures, where they may be difficult to detect with the forward-viewing colonoscope. The Third Eye Retroscope (TER) is a disposable device that is passed through the instrument channel of a standard colonoscope to provide a retrograde view that complements the forward view of the colonoscope during withdrawal.

Objective: To evaluate whether experience with the TER affects polyp detection rates and procedure times in experienced endoscopists who had not previously used the equipment.

Design, Setting, Patients: This was an open-label, prospective, multicenter study at 9 U.S. sites, involving 298 patients presenting for colonoscopy, evaluating the use of the TER in combination with a standard colonoscope.

Interventions: After cecal intubation, the 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: Primary outcome measures were the number and size of adenomas and all polyps detected with the standard colonoscope and with the colonoscope combined with the TER. Secondary outcome measures were withdrawal phase time and total procedure time. Each endoscopist examined 20 subjects, divided into quartiles according to the order of their procedures, and results were compared among quartiles.

Results: Overall, 182 polyps were detected with the colonoscope and 27 additional polyps with the TER, a 14.8% increase ($P < .001$). A total of 100 adenomas were detected with the colonoscope and 16 more with the TER, a 16.0% increase ($P < .001$). For procedures performed after each endoscopist had completed 15 procedures while using the TER, the mean additional detection rates with the TER were 17.0% for all polyps ($P < .001$) and 25.0% for adenomas ($P < .001$). For lesions 6 mm or larger, the overall additional detection rates with the TER for all polyps and for adenomas were 23.2% and 24.3%, respectively. For lesions 10 mm or larger, the overall additional detection rates with the TER for all polyps and for adenomas were 22.6% and 19.0%, respectively. The mean withdrawal times in the first and fourth quartiles were 10.6 and 9.2 minutes, respectively ($P = .044$).

Limitations: There was no randomization or separate control group. The endoscopists judged whether each lesion could have been detected with the colonoscope alone by using their standard technique.

Conclusions: Polyp detection rates improved significantly with the TER, especially after 15 procedures, when the mean additional detection rate for adenomas was 25.0%. Additional detection rates with the TER for medium-size and large adenomas were greater than for smaller lesions. These results suggest that, compared with a colonoscope alone, a retrograde-viewing device can increase detection rates for clinically significant adenomas without detriment to procedure time or procedure complications. (Clinical trial registration number: NCT00969124.) (Gastrointest Endosc 2010;71:542-50.)
Colorectal cancer is the second leading cause of cancer death in the United States. Current strategies for reducing the toll from colorectal cancer focus on early detection and removal of potential precancerous lesions.

Colonoscopy is currently regarded as the criterion standard for the detection of polyps and cancers in the colon and is the preferred method of screening for colorectal cancer in the United States. However, evidence shows that polyps and other lesions can be missed during colonoscopy, at least in part because of location on the proximal aspect of flexures, rectal valves, or haustral folds, where they can be difficult to see with the forward-viewing colonoscope.

Therefore, detection rates might be enhanced by an increased ability to visualize areas behind flexures and folds.

BACKGROUND

The Third Eye Retroscope (TER) (Avantis Medical Systems, Inc, Sunnyvale, Calif) is a disposable auxiliary imaging device that is inserted through the instrument channel of a standard colonoscope to provide a retrograde view of the colon during the withdrawal phase of a colonoscopy.

After the colonoscope has been advanced to the cecum in the usual manner, the TER is inserted through the instrument channel. As it emerges from the distal tip of the colonoscope, the TER automatically bends 180 degrees to form a J shape (Fig. 1) so that its sensor and integrated light source are directed back toward the tip of the colonoscope. The device is then withdrawn together with the colonoscope, thus providing a continuous retrograde view to complement the forward view of the colonoscope.

Previous studies showed that the TER can increase detection rates for adenomas and other polyps. Preliminary data also suggested that experience with the TER increases polyp detection rates and procedure efficiency. This study was designed to evaluate whether there is a learning curve for the TER in terms of both efficacy for polyp detection and procedure time.

METHODS

Fifteen experienced endoscopists at 9 U.S. sites participated in an open-label, prospective study to determine polyp detection rates and procedure time while performing colonoscopy by using a standard colonoscope (CF-Q160AL, CF-Q180AL, or CF-H180AL; Olympus America, Inc, Center Valley, Pa) with the addition of the TER, a retrograde-viewing auxiliary imaging device, during the withdrawal phase. The participating endoscopists had no previous experience with the TER other than a training session with an anatomical model.

Subjects were invited to participate in the study if they were undergoing colonoscopy for colorectal neoplasia screening, for polyp surveillance, or for diagnostic workup (including anemia, abdominal pain, abnormal imaging) and if they were able to understand and provide written consent for the procedure.

Exclusion criteria included history of colon resection, known inflammatory bowel disease, polyposis syndrome, radiation therapy to abdomen or pelvis, suspicion of chronic stricture potentially precluding complete colonoscopy, presence of diverticulitis or toxic megacolon, and concurrent enrollment in another clinical investigation.

The study was approved by the institutional review board of each participating institution, and all patients signed an informed consent. Between January and June
Figure 1. After insertion through the instrument channel, the TER assumes a J shape so that its sensor and light source are directed back toward the tip of the colonoscope, providing a retrograde view to complement the forward view of the colonoscope.

Because the TER reduces suction capacity approximately 50% when it is in the channel, endoscopists were advised to lavage and suction any residual stool and pools of fluid during colonoscope insertion. The Ottawa Bowel Preparation Quality Scale was used to grade the bowel of fluid during colonoscope insertion. The Ottawa Bowel Advisory to lavage and suction any residual stool and pools of fluid. Approximately 50% when it is in the channel, endoscopists were advised to lavage and suction any residual stool and pools of fluid if necessary.

During each procedure, the colonoscope was advanced to the cecum in the usual manner and its position was documented with photographs of the ileocecal valve, appendiceal orifice, or terminal ileum. Polyps that were found during colonoscope insertion were immediately removed and counted as having been found with the colonoscope.

After water irrigation of the instrument channel of the colonoscope, the TER was inserted through the channel, much as one would insert a polypectomy snare or biopsy forceps. During withdrawal, the forward and retrograde video images were observed simultaneously side by side on a wide-screen monitor (Fig. 2). When necessary, the colonoscope water jet was used to clean the lens of the TER. When a polyp was seen, the endoscopist indicated whether it could have been seen with the colonoscope alone by using a routine degree of deflection of the tip of the colonoscope or whether it was found only because it was detected with the TER (Fig. 3). When a polyp was seen both with the colonoscope and the TER, the colonoscope was credited with finding it.

For each polyp, the endoscopist indicated its size, its distance from the anal verge, and the segment of the colon in which it was found. When a polyp was seen during withdrawal, the TER was removed while maintaining the colonoscope in place. The polyp was then removed by using the tip of the colonoscope or the instrument (snare or biopsy forceps). Because each polyp was removed at the time that it was found, there was no possibility that a lesion could be counted twice.

Total procedure time started with colonoscope insertion and ended when the colonoscope was withdrawn past the anal verge. Withdrawal time began when the endoscopist began to withdraw the colonoscope and TER together through the colon and ended when both were withdrawn through the anal verge. Any pauses for polypectomies, biopsies, or extensive bowel cleansing were subtracted so that the withdrawal time would represent the time that was devoted to examining the colon mucosa. A research assistant was present during the procedure to record findings and procedure times as directed by the endoscopist.

Primary outcome measures were the number and size of the polyps detected with the colonoscope, and the number and size of the additional polyps that were found only because they were first detected with the TER. Secondary outcome measures were the withdrawal phase time and total procedure time.

Statistical analysis
The 20 subjects who were enrolled by each endoscopist were divided into quartiles, ie, the first 5 constituted the first quartile, the second 5 the second quartile, and so on. The learning curve was evaluated by comparing results among quartiles. The exact binomial test was used to determine the significance of the increased detection rates by using the TER.

Differences in withdrawal times, total procedure times, and the size of polyps detected with the colonoscope and with the TER were evaluated by using analysis of variance. Differences in polyp detection between the left and right side of the colon were determined by using the Fisher exact test. For statistical purposes, the numbers of polyps were analyzed independently of whether a patient had more than 1 polyp detected. No corrections were made for the multiplicity of tests performed.

RESULTS
Of the 328 subjects who were enrolled, 30 (9.1%) were withdrawn per protocol for inadequate bowel preparation (n = 15), inability to reach the cecum (n = 9), previously unrecognized diseases in which use of the TER was considered by the endoscopists to be a potential risk factor (colitis, polyposis, severe diverticulosis; n = 3), technical error (incorrect cap placed on the colonoscope; n = 1), and protocol violation (n = 2).

Of the 298 subjects who completed the study, 144 (48.3%) were men and 154 (51.7%) were women, and their mean age was 56.8 years (standard deviation 11.3; range 22-90 years). The indications were screening in 164
(55.0%) subjects, polyp surveillance in 62 (20.8%), and diagnostic in 72 (24.2%).

In the 298 subjects, 182 polyps were detected with the colonoscope. An additional 27 polyps were detected with the TER, a 14.8% increase ($P < .001$). Of the polyps found with the colonoscope, 100 were adenomas. An additional 16 adenomas were detected with the TER, a 16.0% increase ($P < .001$) (Table 1).

For all polyps, the additional detection rates for the TER were 17.8% in the first quartile and 17.0% in the fourth ($P = .84$). For adenomas, the additional detection rates for the TER increased from 15.4% in the first quartile to 25.0% in the fourth ($P = .48$) (Table 1).

For individual investigators, the additional detection rates for all polyps with the TER ranged from 0.0% to 33.3% overall and from 0.0% to 66.7% in the fourth quartile. The individual additional detection rates for adenomas with the TER ranged from 0.0% to 100.0% overall and from 0.0% to 66.7% in the fourth quartile.

The mean estimated size of all polyps detected with the TER was 6.5 mm (range 2–13 mm) compared with 5.5 mm (range 1–40 mm) for those detected with the colonoscope alone ($P = .37$). The TER allowed detection of 23.2% additional polyps 6 mm or larger ($P < .001$) and 22.6% additional polyps 10 mm or larger ($P < .001$) (Table 2).

The mean estimated size of adenomas detected with the TER was 6.8 mm (range 2–13 mm) compared with 6.5 mm (range 1–40 mm) for adenomas found with the colonoscope ($P = .87$). The TER allowed detection of 24.3% additional adenomas 6 mm or larger ($P < .001$) and 19.0% additional adenomas 10 mm or larger ($P < .001$) (Table 2).

Of the total of 182 polyps seen with the colonoscope, 80 were in the right side of the colon (cecum to transverse colon) and 102 were in the left side of the colon (spleenic flexure to rectum). The additional detection rates for all polyps with the TER were similar in the 2 sides of the colon at 14.7% in the left side of the colon and 15.0% in the right side of the colon ($P = .88$). For adenomas, the...
additional detection rates for the TER were 21.4% in the left side of the colon and 12.1% in the right side of the colon ($P = .28$) (Tables 3 and 4).

Overall detection rates for all polyps were 0.61 per patient with the colonoscope alone and 0.70 per patient with the colonoscope and TER. Overall detection rates for adenomas were 0.34 per patient with the colonoscope alone and 0.39 per patient with the colonoscope and TER.

In 27 subjects (9.1%), at least 1 additional polyp was found with the TER, and in 10 subjects (3.4%), the polyp detected with the TER was the only one found.

Mean withdrawal times in the first and fourth quartiles were 10.6 and 9.2 minutes, respectively ($P = .044$). Total

### TABLE 1. Additional detection with the Third Eye Retroscope of all polyps and adenomas by quartile

<table>
<thead>
<tr>
<th>Quartile</th>
<th>All polyps with COLO</th>
<th>Additional polyps with TER</th>
<th>% Additional polyps with TER</th>
<th>Adenomas with COLO</th>
<th>Additional adenomas with TER</th>
<th>% Additional adenomas with TER</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>45</td>
<td>8</td>
<td>17.8</td>
<td>26</td>
<td>4</td>
<td>15.4</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
<td>4</td>
<td>8.5</td>
<td>26</td>
<td>1</td>
<td>3.8</td>
</tr>
<tr>
<td>3</td>
<td>37</td>
<td>6</td>
<td>16.2</td>
<td>16</td>
<td>3</td>
<td>18.8</td>
</tr>
<tr>
<td>4</td>
<td>53</td>
<td>9</td>
<td>17.0</td>
<td>32</td>
<td>8</td>
<td>25.0</td>
</tr>
<tr>
<td>Total</td>
<td>182</td>
<td>27</td>
<td>14.8</td>
<td>100</td>
<td>16</td>
<td>16.0</td>
</tr>
</tbody>
</table>

COLO, Colonoscope; TER, Third Eye Retroscope.

### TABLE 2. Additional detection with the Third Eye Retroscope of all polyps and adenomas by size

<table>
<thead>
<tr>
<th></th>
<th>All polyps</th>
<th>Adenomas</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any size</td>
<td>≥6 mm</td>
</tr>
<tr>
<td>No. detected with standard COLO</td>
<td>182</td>
<td>56</td>
</tr>
<tr>
<td>No. additional detected with TER</td>
<td>27</td>
<td>13</td>
</tr>
<tr>
<td>% additional detected with TER</td>
<td>14.8</td>
<td>23.2</td>
</tr>
<tr>
<td>$P$ value</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

COLO, Colonoscope; TER, Third Eye Retroscope.

### TABLE 3. Location of all polyps and adenomas by segment of colon

<table>
<thead>
<tr>
<th>Segment of colon</th>
<th>All polyps</th>
<th>Adenomas</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Detected with COLO</td>
<td>Detected with TER</td>
</tr>
<tr>
<td>Cecum</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>Ascending colon</td>
<td>29</td>
<td>5</td>
</tr>
<tr>
<td>Hepatic flexure</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Transverse colon</td>
<td>17</td>
<td>6</td>
</tr>
<tr>
<td>Splenic flexure</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Descending colon</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>Sigmoid colon</td>
<td>55</td>
<td>8</td>
</tr>
<tr>
<td>Rectum</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>182</td>
<td>27</td>
</tr>
</tbody>
</table>

COLO, Colonoscope; TER, Third Eye Retroscope.
procedure times in the first and fourth quartiles were 25.8 and 22.6 minutes, respectively ($P = .046$) (Table 5).

No colon malignancies were diagnosed. There were no device-related adverse events and no complications such as perforation, bleeding, and postprocedural hospital admission.

**DISCUSSION**

Colonoscopy is the best available method for evaluating the colon because of its diagnostic and therapeutic capabilities, but extensive research has demonstrated that significant lesions can be missed during standard colonoscopy procedures.

Rex et al performed same-day, back-to-back (or tandem) colonoscopies on 183 patients and reported an overall adenoma miss rate of 24% (range 17%-48%). In a meta-analysis of 6 studies in which patients had undergone 2 same-day colonoscopies, Van Rijn et al reported a 22% miss rate for polyps of any size. More recently, Heresbach et al performed tandem colonoscopies in 286 patients and reported miss rates during the first examination of 28% for all polyps and 20% for adenomas.

When compared with CT colonography, Pickhardt et al found that colonoscopy had a miss rate of 12% for polyps 10 mm or larger. Pabby et al determined that 23% of patients in whom colon cancer developed were diagnosed within 30 months of a previous colonoscopy during which no lesion had been found in that area of the colon. Postic et al compared resected colon specimens with the results of colonoscopies performed within 5 months of surgery and found that 23.3% of the lesions in the specimens had been missed during colonoscopy, including 2 cancers measuring greater than 1.0 cm.

Factors contributing to colonoscopy miss rates include poor bowel preparation, 20-22 performing a rapid withdrawal, 23-26 and inability to visualize some sections of the colon wall. 13 Although each of these factors is important, it is clear that some polyps are missed because they are located on the proximal aspect of haustral folds and flexures where they can be hidden from the forward view of the colonoscope despite the best efforts to improve colon visualization. This is supported by Pickhardt et al, who mapped locations of nonrectal neoplasms that were detected by CT colonography but were missed by colonoscopy and found that 67% of missed lesions were on the proximal aspect of folds.

The TER was designed to improve polyp detection by providing a retrograde view of the colon that reveals the areas behind haustral folds, rectal valves, flexures, and the ileocecal valve (Fig. 4).

The potential effectiveness of the TER was first demonstrated in a randomized, controlled preclinical study using anatomical models in which a prototype TER allowed endoscopists to detect 81% of simulated polyps located behind haustral folds compared with 12% when using the colonoscope alone.

In a first human use pilot study of 24 patients, Triadafilopoulos and Li found the TER allowed detection of 11.8% additional polyps compared with the colonoscope alone.

Waye et al examined 249 subjects with the TER in conjunction with a standard colonoscope and found additional detection rates with the TER of 13.2% for all polyps and 11.0% for adenomas. For adenomas 6 mm or larger, the additional detection rate with the TER was 25.0% and for adenomas 10 mm or larger, it was 33.3%.
The current study was designed to determine the amount of experience required to achieve maximal proficiency with the TER. We found that even during their initial 5 procedures using the TER, endoscopists who had no previous experience with the device could detect a mean of 15.4% additional adenomas compared with the standard colonoscope. In the last quartile, after they had completed 15 procedures, their mean additional adenoma detection rate with the TER was 25.0%. Although this increase was not statistically significant, it suggests a trend toward improvement with greater experience. The variation in the results among the endoscopists suggests that they learned the basic mechanical skills after only a few procedures, but that they required varying amounts of experience to develop optimal technique.

The additional polyps detected behind folds with the TER varied in size, as did the polyps found with the colonoscope. It is possible that a smaller polyp that was missed with the colonoscope because it was hidden behind a fold would grow large enough to be seen with the colonoscope at a subsequent surveillance examination. However, even if the patient were fully compliant with recommended surveillance intervals, 10 to 15 years might elapse before the lesion could be detected and removed with the colonoscope. Moreover, a subset analysis of our data showed that the TER was able to detect 19.0% additional adenomas that were at least 1 cm in diameter, lesions that most would agree are high risk and should be removed as soon as possible.

The mean withdrawal time in the study was longer than the 6- to 10-minute (exclusive of time for biopsy and polypectomy) minimum proposed as a quality measure for colonoscopy, and although it decreased with experience, the change was not statistically significant. Although previous colonoscopy withdrawal times were not investigated for the endoscopists, it is possible that use of the TER or awareness of participation in a study might have increased their withdrawal times. Although increased withdrawal time by itself could improve detection rates with the colonoscope, the detection rates were further enhanced by use of the TER.

The additional detection rate with the TER for adenomas in the left side of the colon was nonsignificantly higher than that in the right side of the colon, a trend that differs from a previous study of the TER.

The polyps that were detected with TER were located on the proximal aspect of haustral folds. Some were very near the edge of the fold, whereas others were farther back from the edge. Still others were located in rather deep "pockets" behind folds, where they would have been difficult to detect with the colonoscope even if the endoscopist were extremely conscientious and spent the time required to flatten every fold in 4 quadrants with the tip of the colonoscope.

Whenever polyps were detected during withdrawal, the endoscopists noted landmarks that could assist in locating the lesions and then removed the TER to allow insertion of the polypectomy snare or biopsy forceps. As they flattened the folds with the tip of the colonoscope to remove the polyps, the endoscopists were free of any impairment that the TER might have caused. This provided them with a second opportunity to determine whether they could have detected the polyp with the colonoscope alone by using their standard technique.

Overall adenoma detection rates were 0.34 per patient with the colonoscope alone and 0.39 per patient with the colonoscope and TER. These rates are within the range reported in previous studies. However, several factors might have contributed to lowering the overall adenoma detection rate in this study, including the relatively equal distribution by sex (many studies involve predominantly male subjects who generally have more polyps than women) and a lower average subject age. The subjects in this study also had a broad spectrum of indications, with fewer surveillance and diagnostic procedures compared with many colonoscopy studies.
Limitations of the study included the lack of randomization or blinding and the lack of a separate control group. Determinations regarding adequacy of bowel cleansing and whether each polyp could have been detected with the colonoscope alone involved a judgment by the endoscopist. However, to prevent an unfair advantage for the TER, polyp detection was biased toward the colonoscope. Increased cleansing during intubation likely enhanced detection by the colonoscope before the TER was inserted, and the endoscopists were instructed to remove such lesions immediately. If a polyp was found with both the colonoscope and TER, it was counted as detection with the colonoscope.

Especially before they gained experience in observing both sides of the split-screen video display, some endoscopists might have focused more on the novel TER image on the right side of the screen, resulting in failure to detect some lesions in the colonoscope view on the left side of the screen. However, such an effect would be expected to exaggerate the additional detection rate for TER in the earlier quartiles more so than in the later quartiles, and that would be counter to the trend shown in the study results. Also, observation of multiple views has not adversely affected endoscopy efficacy in other gastroenterological modalities such as capsule endoscopy.30

CONCLUSIONS

Experienced endoscopists new to the TER were able to detect a mean of 15.4% additional adenomas during their first 5 procedures. After completing at least 15 procedures with the device, their mean additional detection rates with the TER compared with the colonoscope alone were 17.0% for all polyps and 25.0% for adenomas of all sizes. Additional detection rates with the TER for medium-size and large adenomas were greater than those for smaller lesions. Procedure times did not vary significantly as more procedures were performed.

These results suggest that, compared with routine colonoscopy, a retrograde-viewing device can increase detection rates for clinically significant adenomas without detriment to procedure time or procedure complications.

REFERENCES


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