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Capsule Endoscopy for Screening for Short-Segment Barrett's Esophagus

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BACKGROUND: The rise in the incidence of esophageal adenocarcinoma has led to the development of new methods to screen for the precursor lesion, Barrett's esophagus.

AIM: To evaluate the potential role of esophageal capsule endoscopy in identifying the presence of short-segment Barrett's esophagus.

METHODS: Patients with biopsy-proven short-segment Barrett's esophagus underwent esophageal capsule endoscopy. The images were reviewed by two expert observers with no knowledge of the purpose of the study. The data collected included transit time, quality of image, presence or absence of Z-line, Schatzki's ring, hiatal hernia, and Barrett's esophagus (long or short, definite or suspected).

RESULTS: Twenty patients were studied; in 18, the capsule passed into the stomach. Barrett's esophagus was identified or suspected in eight cases (44%) by one observer and three (16%) by the second ($P = 0.14$). Although the Z-line was seen in the 18 cases that were qualified by both observers, there was an agreement in only six cases as to whether it was regular or irregular. Erosive gastroesophageal reflux disease (GERD) was scored as present in three and absent in six patients by both readers. Nonexisting feline esophagus, varices, and distal esophageal stricture were suspected in one patient each.

CONCLUSIONS: Esophageal capsule endoscopy had a high interobserver variability and a low yield for short-segment Barrett's esophagus. Esophageal capsule endoscopy cannot be recommended for screening for short-segment Barrett's esophagus.

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INTRODUCTION

Barrett's esophagus is thought to be a consequence of chronic gastroesophageal reflux disease (GERD) that results in the replacement of the normal squamous epithelium with specialized metaplastic columnar epithelium. Barrett's esophagus occurs in approximately 15% of the patients with chronic GERD and is considered a serious complication because of its association with a 30- to 60-fold greater risk of developing esophageal adenocarcinoma (1–3). Esophageal adenocarcinoma is estimated to develop in 0.5–1.0% of the patients with Barrett's esophagus per year (4–7).

Screening for Barrett's esophagus is often done in patients with longstanding GERD and appears to be cost-effective in high-risk individuals compared with no screening (8, 9). One issue regarding cost-effectiveness is the relatively low prevalence of Barrett's esophagus in patients with symptomatic GERD, which calls for simple, safe, and effective screening procedures.

Current guidelines for screening for Barrett's esophagus recommend initial screening endoscopy for patients with frequent (*e.g.*, several times per week), chronic GERD for greater than 5 yr (10, 11). Endoscopy with its attendant costs and risks is currently the recommended screening procedure of choice. Newer versions of the video capsule have been introduced, designed specifically to examine the esophagus. The esophageal capsule or "PillCam ESO" (Given Imaging, Yoqneam, Israel) takes seven images per second from both ends of the capsule thus providing 14 images per second as the capsule traverses the esophagus. Various preliminary studies suggested that PillCam ESO provided results comparable to flexible endoscopy in detecting esophagitis, esophageal varices, and long-segment Barrett's esophagus (12–14). As short-segment Barrett's esophagus may carry a risk for malignant transformation comparable to long-segment Barrett's esophagus, an acceptable screening modality must have good sensitivity for the detection of Barrett's esophagus regardless of the length of the epithelium (15). This study evaluated

PillCam ESO for the diagnosis of short-segment Barrett's esophagus.

METHODS

Patients with biopsy-proven short-segment Barrett's esophagus were invited to participate. Short-segment Barrett's esophagus was defined by the presence of specialized intestinal metaplasia of 3 cm or less in the distal esophagus.

Following written informed consent, fasting patients were given 8 oz of water with 2 drops of simethicone (Mylicon® drops, Johnson & Johnson, New Brunswick, NJ)). Patients were instructed to swallow the esophageal capsule in the supine position, flat on their back, with a small pillow under the head followed by raising the patient to an inclination of 30°, 2 min later, followed by raising the patient to a 60° inclination, 1 min later. After swallowing the capsule, the patients were given sips (approximately 10 mL) of water every 15 sec. With this technique, two of the first four capsules did not reach the stomach and the protocol was modified such that the patients reclined on their right sides and swallowed the capsule with a small amount of water. The patients then remained on their right side for 5 min and were given a sip of water every 60 sec for 5 min. They then sat up for an additional 10 min. After 15 min, the leads were removed and the patients were discharged.

The images were reviewed by two experienced observers: one with more than 1,000 small bowel capsule studies and less than 10 esophageal capsule studies, and the other with approximately 125 small bowel capsule and 25 esophageal capsule studies. Neither had the knowledge of the purpose of the study. They were given data collection sheets that did not provide clues as to the finding sought; the data collected included: transit time defined as the time elapsed from the first esophageal image to the first gastric image; quality of the image as poor, fair, or good; the percentage of Z-line seen (graded as not seen, <25%, 26–50%, 51–75%, 75–98%, and approximately 100%), as well as regular or irregular or could not tell, the presence or absence of a Schatzki's ring or hiatal hernia (graded as not present, suspected, or definite); or Barrett's esophagus (defined as long- or short-segment and as definite or suspected Barrett's). The readers were asked to record the presence of esophageal varices, feline esophagus, and any gastric abnormalities seen.

The protocol was approved by the local institutional review boards and all patients provided written informed consent.

STATISTICAL ANALYSES

The data were summarized using descriptive statistics. The parameters were analyzed using standard parametric statistics for numerical data (*e.g.*, age and transient time) and using nonparametric statistics for categorical data.

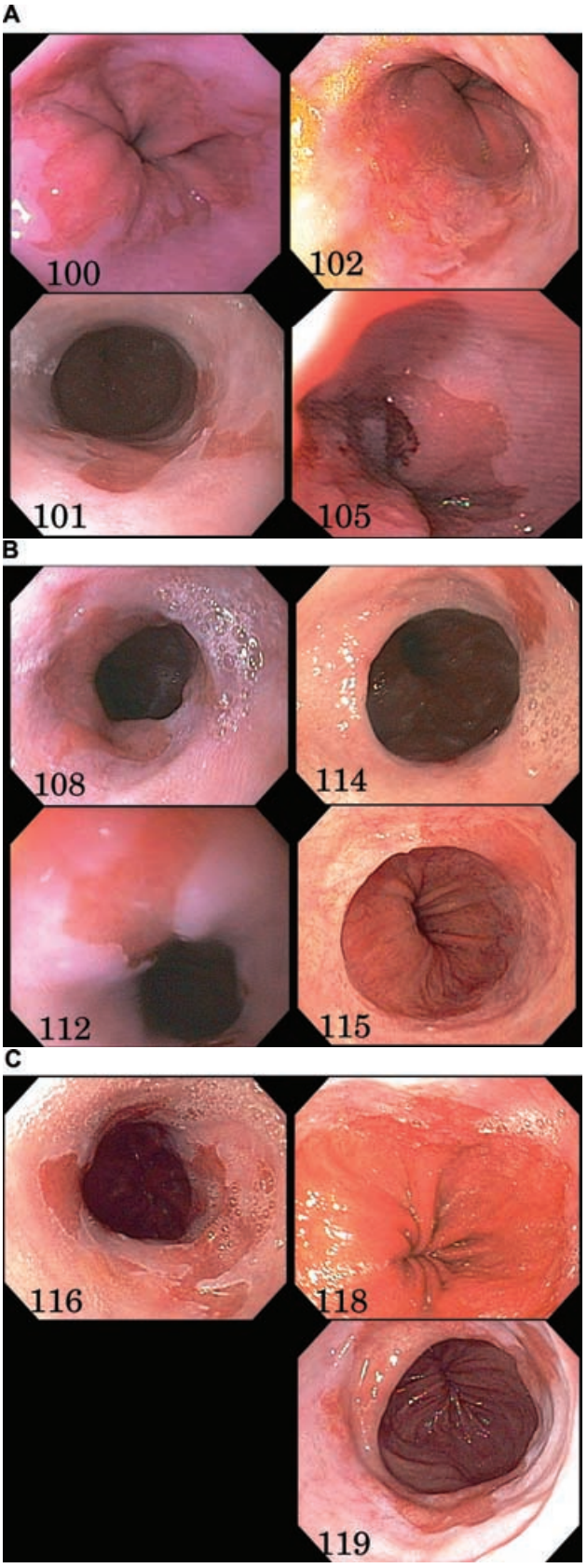

Figure 1. Endoscopic photographs of the gastroesophageal junction showing examples of 11 of the cases of short-segment Barrett's in the study. The case number is shown in each example.

Table 1. Summary of the Scores of Endoscopic Capsule Endoscopy by Two Observers

	Image Quality		Z-Line (%)		Barrett's Esophagus†		Erosive GERD	
Number	B1	B2	B1	B2	B1	B2	B1	B2
100*	F	G	–	–	–	–		
101	F	G	51–75	51–75	S-LS		Yes	Yes
102	F	G	51–75	51–75	S-SS	D-SS	Yes	
103	P	G	26–50	75–98	S-SS			
104*	F	G	–	–	–	–		
105	F	G	26–50	<25				
106	F	G	51–75	75–98				Yes
107	F	G	51–75	75–98	S-SS		Yes	Yes
108	F	F	75–98	26–50			Yes	
109	G	G	75–98	51–75				Yes
110	G	G	75–95	26–50	D-SS		Yes	
111	G	G	51–75	51–75				
112	G	G	75–98	100	S-LS	D SS		
113	F	G	100	100			Yes	Yes
114	P	F	75–98	51–75				Yes
115	F	G	26–50	51–75				Yes
116	F	F	51–75	75–98	S-SS			Yes
117	F	F	51–75	75–98				
118	F	G	75–98	75–98				
119	F	F	51–75	51–75	S-SS	D-SS	Yes	

*Patient in whom the capsule did not pass into the stomach during the study period.
†Barrett's score graded as absent.
S-SS = suspected short segment; D-SS = definite short segment; S or D-LS = suspected or definite long-segment Barrett's; B1 & B2 = blinded observers.

RESULTS

Twenty patients, all male veterans with a mean age of 63.7 yr (range 46–78 yr) with previously endoscopically and histologically diagnosed short-segment Barrett's esophagus entered the study. Of these 20 patients, 16 were white, 3 Hispanic, and 1 black. In two patients, the capsule failed to reach the gastroesophageal junction such that only 18 patients completed the study. All had tongues of Barrett's epithelium, examples of which are shown in Figure 1.

Table 1 summarizes the data obtained in all 20 patients. The mean transit times through the esophagus were similar with the two observers, being 28.5 and 26.7 sec, respectively. The median quality of the images was poor, good, and fair for the two blinded observers and the one unblinded observer. All three agreed in 7 and two of the three agreed in 11 cases. Barrett's esophagus, either long or short segment, was identified or suspected in eight cases (44.4%) by one observer and three cases (16.6%) by the second. There was agreement in three of the 18 cases (16.6%) with regard to the presence of Barrett's esophagus.

Although the Z-line was recorded as having been seen in 18 patients by both observers, there was agreement in only six (33%) cases as to whether it was regular or irregular. When asked what percentage of the Z-line was seen, again there was agreement in only six of the 18 (33%) cases. Hiatal hernia was scored as present in three (definite in 1 and suspected in 2) by one observer and two (definite in 1 and suspected in 1) by the second observer with only one agreement (the definite hiatal hernia). Erosive GERD was scored as present in three and absent in seven patients by both readers in the same patients (agreement in 10 of 18 or 55%). With regard to Schatzki's rings, in 17 of 18 cases (94%), it was agreed that there was no ring.

Feline esophagus, varices, and distal esophageal stricture were suspected in one patient each although none were present.

DISCUSSION

Previous attempts to screen for Barrett's esophagus without endoscopy have included the use of orally introduced balloons, brushes, mesh catheters, and sponge-in-a-capsule techniques, but none were proved clinically useful (16–18). Other recent approaches have included transnasal endoscopy and video capsule endoscopy including traditional video capsules tethered to a string to allow the capsule to reliably remain in the region of the squamocolumnar junction and to be retrieved and reused after appropriate disinfection (19, 20). Clearly, a cheap and reliable way to screen for Barrett's esophagus could have a major impact on how we manage the disease.

The populations at highest risk for Barrett's esophagus are of white men older than 50 yr and those with nocturnal reflux (10). Other risk factors include smoking, body mass index >25, and working in a stooped posture (21). The true prevalence remains unknown and is likely to be below 15%, but will depend on age, sex, and ethnic group. For example, one study of 6,215 patients referred for an endoscopy reported

an overall prevalence of Barrett's esophagus of 8.4% (22). The prevalence was 14% in the subpopulation with erosive esophagitis compared with 2.3% among those with nonerosive GERD (22). A recent study from Sweden reported a prevalence of 2.3% for Barrett's esophagus among patients with reflux symptoms (23). The other end of the spectrum was a 23% prevalence reported in male veterans with reflux symptoms (24). Recent studies in the general community have reported Barrett's esophagus in 6.8% of 961 patients undergoing esophagoscopy at the time of colon cancer screening; 1.2% had long-segment Barrett's esophagus (25). Ward *et al*. evaluated patients presenting to a colonoscopy-screening clinic. Each patient was asked to complete a GERD questionnaire and undergo upper endoscopy. Barrett's esophagus was present in 16.7% (50 of 300). GERD symptoms were present in 106 (35%) and Barrett's esophagus was found in a similar proportion in those with and without GERD symptoms (19.8% *vs* 14.9%, respectively) (26). It is therefore difficult to reliably identify the "high-risk" patient for endoscopy. Capsule endoscopy, however, offers an opportunity for mass screening.

This study evaluated the potential role of the wireless esophageal capsule for the detection of short-segment Barrett's epithelium. The study was designed to simulate the "real-life" situation when patients with GERD would be screened for possible Barrett's esophagus, and thus the reviewers were blinded to the endoscopic and histologic diagnosis. As no string was attached to the capsule, the capsule was free to move with esophageal peristalsis, which limited the observer to the images taken in a single pass. We found that short-segment Barrett's esophagus could not be reliably diagnosed with the current version of capsule endoscopy designed for examination of the esophagus. We also recorded a high level of interobserver variability in the readings.

The study design reduced the potential biases that may occur when observers are aware that the population is enriched with patients with the desired findings. We did not include a control group without short-segment Barrett's esophagus, as this was a pilot study to define the value of the technique among those with the condition. If the technique had proven to be potentially useful, a follow-up study would have compared patients with and without Barrett's esophagus, which would have provided data about the false-positive results not obtainable in our study. However, the results clearly showed that experienced observers could not reliably detect short-segment Barrett's esophagus using current capsule endoscopy equipment. Blinded studies of Barrett's esophagus of different lengths are needed to identify the minimum length that can be reliably identified. Our approach of using completely blinded observers allowed an objective evaluation of a new device using a minimal number of expensive capsules and allowed us to make a "go" *versus* "no go" decision regarding expanding a study from a pilot study to a full study.

STUDY HIGHLIGHTS

What Is Current Knowledge

- Barrett's esophagus (BE) occurs in approximately 15% of patients with chronic gastroesophageal reflux disease (GERD) and is associated with a 30- to 60-fold greater risk of developing esophageal adenocarcinoma.
- Current guidelines recommend initial screening endoscopy for patients with frequent (*e.g.,* several times per week), chronic GERD for greater than 5 yr.
- The incidence of esophageal adenocarcinoma is rising.
- Flexible upper endoscopy is the current method for diagnosing BE.

What Is New Here

- New versions of capsule endoscopy have been introduced to allow detailed examination of the esophagus.
- This is the first prospective study of the role of this device for detection of short-segment BE.
- The observers were completely blinded with regard to the questions to be addressed to reduce bias.
- Esophageal capsule endoscopy had a high interobserver variability and a low yield for short-segment BE and cannot be recommended.

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REFERENCES

1. Cameron AJ, Ott BJ, Payne WS. The incidence of adenocarcninoma in columnar-lined (Barrett's) esophagus. N Engl J Med 1985;313:857–9.
2. Hage M, Siersema PD, van Dekken H, et al. Oesophageal cancer incidence and mortality in patients with long segment Barrett's oesophagus after a mean follow-up of 12.7 years. Scand J Gastroenterol 2004;39:1175–9.
3. Solaymani-Dodaran M, Logan RF, West J, et al. Risk of oesophageal cancer in Barrett's oesophagus and gastroesophageal reflux. Gut 2004;53:1070–4.
4. O'Connor JB, Falk GW, Richter JE. The incidence of adenocarcinoma and dysplasia in Barrett's esophagus: Report on the Cleveland Clinic Barrett's Esophagus Registry. Am J Gastroenterol 1999;94:2037–42.
5. Shaheen NJ, Crosby MA, Bozymski EM, et al. Is there publication bias in the reporting of cancer risk in Barrett's esophagus? Gastroenterology 2000;119:333–8.
6. Jankowski JA, Provenzale D, Moayyedi P. Esophageal adenocarcinoma arising from Barrett's metaplasia has regional variations in the west. Gastroenterology 2002;122:588–90.
7. Bytzer P, Christensen PB, Damkier P, et al. Adenocarcinoma of the esophagus and Barrett's esophagus: A

population-based study. Am J Gastroenterol 1999;94:86–91.
8. Inadomi JM, Sampliner R, Lagergren J, et al. Screening and surveillance for Barrett's esophagus in high-risk groups: A cost-utility analysis. Ann Intern Med 2003;138:176–86.
9. Gerson LB, Groeneveld PW, Triadafilopoulos G. Cost-effectiveness model of endoscopic screening and surveillance in patients with gastroesophageal reflux disease. Clin Gastroenterol Hepatol 2004;2:868–79.
10. Sampliner RE. Updated guidelines for the diagnosis, surveillance, and therapy of Barrett's esophagus. Am J Gastroenterol 2002;97:1888–95.
11. Hirota WK, Zuckerman MJ, Adler DG, et al. ASGE guideline: The role of endoscopy in the surveillance of premalignant conditions of the upper GI tract. Gastrointest Endosc 2006;63:570–80.
12. Eliakim R, Yassin K, Shlomi I, et al. A novel diagnostic tool for detecting oesophageal pathology: The PillCam oesophageal video capsule. Aliment Pharmacol Ther 2004;20:1083–9.
13. Eliakim R, Sharma VK, Yassin K, et al. A prospective study of the diagnostic accuracy of PillCam ESO esophageal capsule endoscopy versus conventional upper endoscopy in patients with chronic gastroesophageal reflux diseases. J Clin Gastroenterol 2005;39:572–8.
14. Eisen GM, Eliakim R, Zaman A, et al. The accuracy of PillCam ESO capsule endoscopy versus conventional upper endoscopy for the diagnosis of esophageal varices: A prospective three-center pilot study. Endoscopy 2006;38:31–5.
15. Rudolph RE, Vaughan TL, Storer BE, et al. Effect of segment length on risk for neoplastic progression in patients with Barrett's esophagus. Ann Intern Med 2000;132:612–20.
16. Fennerty MB, DiTomasso J, Morales TG, et al. Screening for Barrett's esophagus by balloon cytology. Am J Gastroenterol 1995;90:1230–2.
17. Rader AE, Faigel DO, Ditomasso J, et al. Cytological screening for Barrett's esophagus using a prototype flexible mesh catheter. Dig Dis Sci 2001;46:2681–6.
18. Qureshi WA, El-Zimaity HMT, Green LK, et al. Screening for Barrett's esophagus: Searching for a new technique. Am J Gastroenterol 2002;97:1565–6.
19. Ramirez FC, Shaukat MS, Young MA, et al. Feasibility and safety of string wireless capsule endoscopy in the diagnosis of Barrett's esophagus. Gastrointest Endosc 2005;61:741–6.
20. Halum SL, Postma GN, Bates DD, et al. Incongruence between histologic and endoscopic diagnoses of Barrett's esophagus using transnasal esophagoscopy. Laryngoscope 2006;116:303–6.
21. de Jonge PJ, Steyerberg EW, Kuipers EJ, et al. Risk factors for the development of esophageal adenocarcinoma in Barrett's esophagus. Am J Gastroenterol 2006;101:1421–9.
22. Malfertheiner P, Lind T, Willich S, et al. Prognostic influence of Barrett's oesophagus and *Helicobacter pylori* infection on healing of erosive gastro-oesophageal reflux disease (GORD) and symptom resolution in non-erosive GORD: Report from the ProGORD Study. Gut 2005;57:746–51.
23. Ronkainen J, Aro P, Storskrubb T, et al. Prevalence of Barrett's esophagus in the general population: An endoscopic study. Gastroenterology 2005;129:1825–31.
24. Gerson LB, Shelter K, Triadafilopoulos G. Prevalence of Barrett's esophagus in asymptomatic individuals. Gastroenterology 2002;123:461–7.
25. Rex DK, Cummings OW, Shaw M, et al. Screening for Barrett's esophagus in colonoscopy patients with and without heartburn. Gastroenterology 2003;125:1670–7.
26. Ward EM, Wolfsen HC, Achem SR, et al. Barrett's esophagus is common in older men and women undergoing screening colonoscopy regardless of reflux symptoms. Am J Gastroenterol 2006;101:12–7.

CONFLICT OF INTEREST

Guarantors of the article: Waqar A. Qureshi, M.D., Suhaib Abudayyeh, M.D., and David Y. Graham, M.D.

Specific author contributions: The three Baylor authors, Waqar A. Qureshi, Suhaib Abudayyeh, and David Y. Graham, were all involved in the study design, in writing the protocol, in identifying and contacting the patients, in data analysis, and in writing the manuscript. Suhaib Abudayyeh performed all the capsule studies. The non-Baylor investigators, Justin Wu and Daniel DeMarco, interpreted each of the studies blindly and recorded their findings on a predesigned data collection form. They also assisted in writing the manuscript and approved the final version.

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