Capsule Endoscopy Is Not as Accurate as Esophagogastroduodenoscopy in Screening Cirrhotic Patients for Varices

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BACKGROUND & AIMS: Esophagogastroduodenoscopy (EGD) is the standard technique for screening cirrhotic patients for high-risk varices and other significant upper gastrointestinal lesions (HRVLs). We investigated whether esophageal capsule endoscopy (ECE) is as convenient and accurate as EGD for the detection of HRVLs. **METHODS:** We analyzed data from 65 cirrhotic patients without prior upper gastrointestinal bleeding who were examined for varices and HRVLs by ECE and EGD (both procedures were performed on the same day). EGD was performed by 2 physicians (75% of patients were unsedated) who used standard grading for esophageal and gastric varices, portal hypertensive gastropathy, and HRVLs. Coded capsule tracings were read by 2 investigators, blinded to the EGD findings, using standard grading. **RESULTS:** The median procedure time for EGD (with or without biopsy collection) was 3 minutes, compared with 20 minutes for ECE. The overall accuracy for diagnosis of esophageal varices was 63.2% ± 5.9%; for detection of esophageal varices red marks was 68.8% ± 5.4%; and for diagnosis of other HRVLs was 51.5% ± 4.2%. The interobserver agreement in the diagnosis of esophageal varices was 90.8%; in the detection of esophageal varices red marks was 86.2%; and in the diagnosis of other HRVLs was 7.3%. **CONCLUSIONS: ECE is not as accurate as EGD in the diagnosis of esophageal varices and red markings or in grading esophageal varices. Moreover, ECE had poor accuracy in grading portal hypertensive gastropathy and detecting ulcers, gastric varices, and other significant upper gastrointestinal lesions. It took significantly longer to perform ECE and interpret the results than for EGD. These findings do not support ECE as a preferred tool for screening esophageal varices and HRVLs.**

Keywords: Detection; Surgery; Esophagus; Cirrhosis; Hepatitis.

At least two-thirds of cirrhotic patients develop esophageal varices (EVs) during their lifetime. Besides EVs, gastric varices (GVs), portal hypertensive gastropathy (PHTG), and peptic ulcer also are common causes of acute upper gastrointestinal (UGI) bleeding in cirrhotic patients.[1] Despite having effective treatment, the mortality rate of first variceal bleeding remains high (20%–35%).[2] Therefore, screening of cirrhotic patients for high-risk varices and other significant UGI lesions (HRVLs) and prophylactic therapies (either medical or endoscopic) have been recommended.[1–4] These have the potential of preventing the initial variceal bleeding and offer the promise of reducing mortality, morbidity, and associated health care costs.[1–3]

Esophagogastroduodenoscopy (EGD) is the gold standard method for examining the UGI tract of cirrhotic patients with no prior UGI bleeding to screen for HRVLs. However, this procedure may be unpleasant, some patients may require conscious sedation, and EGD may be associated with an increased potential for complications. Esophageal capsule endoscopy (ECE) is a sedationless alternative to EGD for evaluating esophageal lesions and potentially other UGI lesions. Currently, it is controversial whether ECE is as convenient and accurate as EGD for detection of HRVLs. If the ECE procedure was as accurate as EGD, it could play an important role in improving screening rates of cirrhotic patients.

Our purposes were to assess the accuracy and convenience of ECE versus EGD for the diagnosis and grading of EVs, and the detection of other clinically significant UGI lesions in cirrhotic patients without prior screening. This was a blinded, prospective study comparing accuracies and convenience to the patient and staff of ECE with EGD for diagnosis and grading of portal hypertensive-related lesions and other clinically significant UGI lesions in cirrhotic patients without prior UGI bleeding.

Methods

Study Population

This study was registered with ClinicalTrials.gov (ID: 01-11-047-12). Seventy-four patients who met clinical entry criteria were referred by the hepatologist co-investigators for study (S.H.H., F.D., and S.S.) after they determined that these patients required screening and potentially treatment if HRVLs were detected. Nine of these patients were not included in the final analysis because they did not complete the capsule ingestion and were screened by EGD alone. Reasons for not being included in the study were as follows: 2 patients refused to swallow the capsule; 3 patients refused to participate in the ECE study; 1 patient vomited the capsule out after swallowing it (but had no stricture on EGD); and 3 patients swallowed the capsule but images were not recorded. These 9 patients had EGD screening, but were not included in this comparative study.

Abbreviations used in this paper: ECE, esophageal capsule endoscopy; EGD, esophagogastroduodenoscopy; EVs, esophageal varices; GVs, gastric varices; HRVLs, high-risk varices and other significant upper gastrointestinal lesions; PHTG, portal hypertensive gastropathy; UGI, upper gastrointestinal.

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Sixty-five cirrhotic patients provided written informed consent and completed this study for same-day screening for EVs and other HRVLs with ECE and EGD. They had both procedures performed at the University of California Los Angeles Medical Center or the VA Greater Los Angeles Healthcare System between June 2006 and February 2008.

The inclusion criteria were as follows: (1) age at least 18 years and younger than 86 years at the time of consent; (2) clinically evident or biopsy-proven cirrhosis; (3) no previous documented UGI bleeding; (4) no previous endoscopic or radiologic treatments for variceal bleeding or ascites; and (5) probable life expectancy of at least 24 months without liver transplantation and have a Model for End-Stage Liver Disease score of 29 or less.

In addition, patients were excluded from the study if they had any of the following clinical findings: (1) severe comorbid illness; (2) cancer with less than a 24-month expected survival and/or cancer on active treatment with chemotherapy and/or radiation therapy; (3) esophageal motility disorder, esophageal stricture, or esophageal diverticulum, causing dysphagia or requiring dilatation; (4) gastrointestinal obstruction or partial obstruction (by history or imaging); (5) symptomatic gastrointestinal stricture or pseudo-obstruction that may prevent passage of the capsule; or (5) potentially reversible portal hypertension such as alcoholic hepatitis, acute viral hepatitis, untreated autoimmune hepatitis, or chronic hepatitis B or C on viral therapy.

Institutional review boards reviewed the study and approved it at both medical centers before initiation of the study and annually. These patients were all being screened for high-risk varices and later potential primary prophylactic medical or endoscopic treatment to prevent first esophageal variceal bleeding as previously described.[3]

Hepatologists referred all patients, continued follow-up evaluations, and later treated those with high-risk EVs or GVs with β-blockers or rubber band ligation for EVs; β-blockers for severe PHTG; and proton pump inhibitors and/or *Helicobacter pylori* eradication for ulcers, esophagitis, or gastroduodenal erosions. All patients were followed up at 24 to 72 hours after the procedure, 2 weeks later by telephone, and had liver clinic follow-up evaluations within 30 to 60 days with their hepatologist.

Esophageal Capsule Endoscopy

The PillCam ESO (Given Imaging, Ltd, Yoqneam, Israel) was used for all ECEs. Two cameras on the ECE each transmit 14 color images per second. No sedation was used before or during ECE. When the 20 minutes of recording was completed, images were downloaded on a computer workstation for interpretation. Coded capsule images were read by 2 experienced ECE physicians, blinded to EGD findings, using a modified Japanese grading system (none, no varices seen; small, the esophageal varices were small and nontortuous and not compromising the lumen; medium, the esophageal varices were tortuous, raised, and occupied less than one-third of the distal esophageal lumen; large, esophageal varices were large, raised, tortuous, compromising the lumen, and occupied more than one-third of the distal esophagus).

Standardization of Esophageal Capsule Endoscopy

Before interpreting the capsule images of all study patients, the ECE investigators reviewed the manufacturer's tutorial for EV grading. They also completed a separate CURE hemostasis tutorial of both EGD and ECE images of 20 selected patients with different grades of EV, UGI lesions, and PHTG, based on our recent reports.[1,3] Discrepancies in interpretations of capsule grading in these tutorials were reconciled before starting this study. Supplementary Figures 1 and 2 show different grades of EV and PHTG.

Esophagogastroduodenoscopy

Two very experienced endoscopists performed all the EGDs with diagnostic-sized Olympus (Center Valley, PA) or Pentax (Montvale, NJ) endoscopes. Seventy-five percent of the patients chose not to receive intravenous sedation and received a 5% lidocaine gargle instead. Standard grading for EV, GV, and PHTG was used.[1,5] All major findings were recorded on video and digital pictures and any discrepancies were reconciled and then reported as the EGD findings.

Data Collection

Data were recorded on standard forms by research coordinators. All missing data were identified and retrieved from the medical records, investigators, or patients in accordance with institutional review boards and Health Insurance Portability and Accountability Act regulations. A data manager entered all de-identified, coded data into an electronic study database.

Convenience, Medical Personnel Time, and Incremental Cost Estimate

We describe the convenience to the patient of ECE versus unsedated EGD as determined by the patients. After the procedures, we asked each patient to rate the convenience of ECE versus EGD as more, less, or as convenient. For the convenience to the medical personnel, this was described in terms of total time for screening patients and interpreting results with ECE versus unsedated EGD. We also estimated the incremental direct costs. For convenience to the patient, we asked all cirrhotic patients who had been referred for screening whether they had a successful ECE or not as well as all patients who had both ECE and EGD. For the physician time (for performance of procedure and interpretation) and other medical personnel (for recording or medical procedure time), we used the actual median times spent by these personnel for performance and interpretation of either ECE or EGD for patients who had both procedures.

For the incremental direct cost estimate, we assumed that the endoscopic equipment and ECE workstation and recorders were available and that the capsules ($450 each) would need to be purchased.

Statistical Analysis

Comparisons were made by the statistician (J.A.G.) for each ECE interpreter and those combined for sensitivity, specificity, and accuracy of their ECE readings versus EGD (as the gold standard) for EV; EV red marks; and detection of any other HRVLs. Overall accuracy was calculated for each capsule interpreter using EGD as the gold standard. The Spearman correlation scores were calculated for ordered comparisons (EV size and PHTG grade) whereby complete accuracy was indicated by a correlation near 1.0. The weighted κ statistic was used to measure interobserver variability.