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A pilot study of capsule endoscopy after a standard meal for the detection and grading of oesophageal varices in cirrhotic patients

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ABSTRACT

Background: Capsule endoscopy has been proposed as an alternative to fibreoptic endoscopy for oesophageal varices evaluation in cirrhotics. However, it shows only moderate sensitivity compared to fibreoptic endoscopy.
Aim: To compare post-meal capsule endoscopy to fibreoptic endoscopy, based on the hypothesis that meal-induced increase of portal pressure can enhance its sensitivity.
Methods: Twenty-five patients were submitted to fibreoptic endoscopy and, after a standard meal, capsule endoscopy.
Results: Post-meal capsule endoscopy detected varices in the 18 patients in whom fibreoptic endoscopy detected varices plus 3 more subjects (sensitivity 100%, specificity 70%); large varices in the 4 patients in whom fibreoptic endoscopy graded varices as large, plus 5 more subjects; red markers in the 5 patients in whom fibreoptic endoscopy detected red markers, plus 3 more subjects. High-risk varices were identified in 11 patients by post-meal capsule endoscopy and in 10 by fibreoptic endoscopy (sensitivity 100%, specificity 93.8%).
Conclusions: Post-meal capsule endoscopy identified more varices, large varices and red markers than fibreoptic endoscopy. The two methods detected similar proportions of high-risk varices. These data suggest that a standard meal can enhance the sensitivity of capsule endoscopy in the detection and grading of oesophageal varices in cirrhotics.

1. Introduction

In liver cirrhosis, a major cause of morbidity and mortality is variceal haemorrhage, occurring each year in 12–15% of patients with gastro-oesophageal varices [1]. Although the mortality rate for variceal haemorrhage declined over the past 20 years, it still approximates to 20% for each episode [1]. Therefore, in order to promptly identify subjects at high-risk for variceal haemorrhage, current guidelines for the treatment of portal hypertension recommend that all patients with liver cirrhosis should undergo endoscopic screening at diagnosis [2,3] and that in those who do not need immediate prophylaxis a programme of endoscopic surveillance should be started [2].

The gold standard for the detection and grading of gastro-oesophageal varices is fibreoptic endoscopy (FE). FE is widely available, but it often requires conscious sedation and is not well tolerated by several patients [4]. Since 2004, when a specifically designed device was developed to image the oesophagus, capsule endoscopy (CE) has been evaluated in several studies as a possible alternative to FE for the diagnosis of varices in patients with liver cirrhosis. This procedure has some practical advantages over FE: it is better tolerated by patients [5] and it does not require sedation, avoiding potentially dangerous drugs in patients with advanced liver disease and preserving the ability to pursue daily activities in well-compensated ones. However, despite these favourable characteristics, oesophageal CE failed to gain a wide diffusion in

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clinical practice, due to the only moderate sensitivity for the detection of varices, especially small ones [6,7], that raises the concern of a possible deferred prophylaxis.

In liver cirrhosis, meal-induced changes in splanchnic blood flow transiently increase blood pressure in the portal system [8–12]. We hypothesized that a standard meal given to patients shortly before the procedure can enlarge varices, enhancing the sensitivity of CE for their detection and grading.

In order to assess the sensitivity of CE performed after a standard meal (post-meal CE, PCE) for the detection of varices, we conducted a prospective study comparing the results of PCE with those of FE in a group of cirrhotic patients screened for oesophageal varices.

2. Methods

This pilot study was carried out in our liver unit enrolling all patients evaluated at the time of diagnosis of liver cirrhosis from January 2010 to February 2011.

Patients who accepted to participate into the study were submitted to fibreoptic endoscopy and immediately after, following the ingestion of a standard meal, were submitted to capsule endoscopy.

Liver cirrhosis was diagnosed based on clinical, instrumental (ultrasound, transient elastography, computed tomography), or histological findings.

None of these patients presented one of the following conditions: implanted medical devices, dysphagia, known Zenker's diverticulum, known or suspected intestinal obstruction, pregnancy, prior abdominal surgery of the gastro-intestinal tract (other than uncomplicated appendectomy or cholecystectomy), and life-threatening conditions.

All patients eligible for the study were required to sign an informed consent.

After at least eight-hour fasting, patients were submitted to FE. All FE were performed and reviewed by the same experienced endoscopist (CS), who was blinded to clinical data and to the results of capsule endoscopies.

Immediately after, patients were required to fully ingest within 10 min a standardized liquid nutrition solution (5 mL/kg b.w. of flavoured Fresubin® original DRINK; Fresenius-Kabi, Bad Homburg, Germany), followed by 250 mL of tap water. Thirty minutes later they were submitted to CE (PillCam® ESO II; Given Imaging, Yokneam, Israel). Patients were asked to drink 100 mL of tap water and then to lie in bed on their left side with the head on a pillow. The capsule was swallowed in the supine position with a small amount of water. The patients remained in this position for 8 min drinking a small sip of water every 30 s. After 8 min in this position, patients were free to sit or walk for 20 min, without drinking or eating anything until the end of the procedure. All the recordings were viewed by the same endoscopist experienced in capsule endoscopy (MER), who was blinded to clinical data and to the results of fibreoptic endoscopies.

One week following the procedures, all patients were contacted to confirm elimination of the capsule in the stools and asked for adverse events.

Following the classification proposed by de Franchis et al. [13], the varices detected with PCE were graded according to the proportion of the circumference of capsule picture frame occupied by the largest varix present. Varices are divided into 3 grades: C0, no varices; C1, <25% of the picture frame circumference (small varices); C2, >25% of the picture frame circumference (large varices).

Following the classification of the Italian Liver Cirrhosis Project [14], the varices detected with FE were graded according to the proportion of the radius of the oesophagus occupied by the largest varix present at full insufflation of the oesophagus.

Table 1
Characteristics of patients ($N = 25$) enrolled in the study.

Variables	N (%)
Mean age, years	58.1 ± 11.2 (37–83)
Male gender	15 (60)
Aetiology of cirrhosis	
Hepatitis C	13 (52)
Alcohol	7 (28)
Hepatitis B	4 (16)
Nonalcoholic steatohepatitis	1 (4)
Child–Pugh class	
A	12 (48)
B	10 (40)
C	3 (12)
Mean MELD score	11.0 ± 3.8 (range 7–22)

MELD, model for end stage liver disease.

Varices are divided into 4 grades: F0, no varices; F1, <33% of the radius of the oesophagus; F2, 33–66% of the radius of the oesophagus; F3, >66% of the radius of the oesophagus. In order to compare FE findings with those of CE, F1 were considered as small varices, F2 and F3 as large varices.

The red colour signs on varices viewed by both FE and CE were recorded.

Patients requiring primary prophylaxis as indicated by current guidelines [2,3] were identified solely on the basis of FE findings.

The study was approved by the Ethics Committee of our Institution and conducted according to guidelines of the International Conference on Harmonization for Good Clinical Practice. The study was designed, conducted, and the results were analyzed without any financial support from the producers of the endoscopic instruments used.

PCE was compared with FE for the detection of oesophageal varices, large varices, red markers and for the indication to primary prophylaxis calculating true and false positive and true and false negative results and sensitivity, specificity, positive and negative predictive values.

3. Results

Twenty-five consecutive patients evaluated at the time of diagnosis of liver cirrhosis accepted to be enrolled in the study.

Baseline characteristics of the 25 patients enrolled in the study are reported in Table 1.

All patients enrolled in the study completed both FE and PCE and no adverse events were registered during the procedures and in the following seven days.

Overall, FE identified oesophageal varices in 18 patients and PCE identified oesophageal varices in 21 patients. PCE detected oesophageal varices in all the 18 patients in whom FE detected varices and in 3 of the 7 patients in whom FE did not detect varices. PCE graded the varices as large in all the 4 patients in whom varices were considered large by FE and also in 5 of the 14 patients in whom varices were considered small by FE. PCE detected red colour signs in 8 patients and FE in 5 patients. PCE detected red colour signs in all the 5 patients in whom they were also detected by FE. On the whole, the FE and PCE findings were concordant in 17 patients, while PCE provided a more severe grading of varices in 8 patients (Figs. 1–3).

Based on FE findings, primary prophylaxis was prescribed in 10 of the 25 patients enrolled in the study. According to Child–Pugh class, PCE findings (variceal size and red colour signs) would lead to primary prophylaxis in all patients in whom FE findings indicated the need of prophylaxis and in one more patient.

True and false positive and true and false negative results for oesophageal varices and indication to prophylactic treatment with