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Role of EUS evaluation after endoscopic eradication of esophageal varices with band ligation

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Background and Aims: Variceal recurrence after endoscopic band ligation (EBL) for secondary prophylaxis is a frequent event. Some studies have reported a correlation between variceal recurrence and variceal rebleeding with the EUS features of paraesophageal vessels. A prospective observational study was conducted to correlate EUS evaluation of paraesophageal varices, azygos vein, and thoracic duct with variceal recurrence after EBL variceal eradication in patients with cirrhosis.

Methods: EUS was performed before and 1 month after EBL variceal eradication. Paraesophageal varices, azygos vein, and thoracic duct maximum diameters were evaluated in predetermined anatomic stations. After EBL variceal eradication, patients were submitted to endoscopic examinations every 3 months for 1 year. We looked for EUS features that could predict variceal recurrence.

Results: Thirty patients completed a 1-year endoscopic follow-up. Seventeen patients (57%) presented variceal recurrence. There was no correlation between azygos vein and thoracic duct diameter with variceal recurrence. Larger paraesophageal varices predicted variceal recurrence in both evaluation periods. Paraesophageal varices diameters that best correlated with variceal recurrence were 6.3 mm before EBL (52.9% sensitivity, 92.3% specificity, and .749 area under the receiver operating characteristic curve [AUROC]) and 4 mm after EBL (70.6% sensitivity, 84.6% specificity, and .801 AUROC).

Conclusions: We conclude that paraesophageal varices diameter measured by EUS predicts variceal recurrence within 1 year after EBL variceal eradication. Paraesophageal diameter after variceal eradication is a better recurrence predictor, because it has a lower cut-off parameter, higher sensitivity, and higher AUROC. (*Gastrointest Endosc* 2016;84:400-7.)

The current recommendation for secondary prophylaxis of variceal bleeding is endoscopic band ligation (EBL) combined with oral beta-blockers.¹⁻⁶ Eradication of esophageal varices with EBL is successful in over 90% of patients.

Abbreviations: AUROC, area under the receiver operating characteristic curve; EBL, endoscopic band ligation; ROC, receiver operating characteristic.

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However, variceal recurrence can be as high as 50% within the first year after eradication.⁷⁻¹¹ The rebleeding rate from recurrent varices increases significantly 1 year after variceal eradication.¹⁰ This justifies endoscopic surveillance for variceal recurrence, and the current recommendations are to perform endoscopy 1, 3, and 6 months after variceal eradication.¹²⁻¹⁴ However, it is unclear if endoscopy alone may predict this outcome and which patients will present with a rebleeding episode.

EUS is used as a noninvasive method that can provide anatomic high-resolution images and hemodynamic features of collateral vessels surrounding the distal esophagus and upper stomach in patients with portal hypertension.¹⁵⁻²³ Previous studies performed EUS analysis of paraesophageal varices and reported correlation between their number or diameter with rebleeding episodes and variceal recurrence after endoscopic treatment.^{21,22,24} Leung et al²² compared recurrence and rebleeding rates

in patients with small paraesophageal collaterals after endoscopic variceal ligation against larger varices and found that recurrence (46% compared with 93% within 1 year) and rebleeding rates (12% compared with 43%) were higher in the latter patient group. However, in a review article²⁵ the authors concluded that most angiographic and EUS studies indicate that extravariceal collaterals, including paraesophageal varices, may prevent the recurrence of esophageal varices by reducing the portal pressure after EBL. These contradictory findings may be one reason why these echoendoscopic patterns have never been used in clinical practice and never had an impact on follow-up in patients with cirrhosis.

To clarify the correlation between paraesophageal anatomic structures and esophageal varices recurrence, we conducted a prospective study via echoendoscopic evaluation observing paraesophageal varices, azygos vein, and thoracic duct characteristics in patients with cirrhosis after their first episode of bleeding. Unlike prior studies, we analyzed these structures before and after esophageal varices eradication. By adopting this approach we aimed to correlate EUS findings with variceal recurrence and propose a better period for EUS evaluation, either before or after esophageal varices eradication with EBL.

METHODS

The study was conducted in a tertiary hospital after institutional review board approval. From May 2011 to August 2013 all cirrhotic patients with portal hypertension referred to our endoscopic unit for secondary prophylaxis of variceal bleeding were invited to participate in this study. Each enrolled patient provided informed consent.

Inclusion criteria were patients over age 18 years at their first bleeding episode from esophageal varices. Patients were excluded based on the following criteria: under age 18; Child-Pugh class C cirrhosis; contraindication or intolerance to oral beta-blockers; and previous endoscopic, pharmacologic, or surgical treatment for variceal bleeding.

Esophageal varices were graded by their maximum diameter into small (<3 mm), medium (3-6 mm), and large (>6 mm) diameter, according to the Palmer and Brick classification.²⁶ All included patients received sessions of EBL performed by endoscopy fellows under the supervision of a senior endoscopist at monthly intervals until all varices were eradicated. The treatment used a multiband ligator (Wilson-Cook Medical, Winston-Salem, NC), and the number of endoscopic sessions and band ligations deployed to achieve eradication per patient was recorded. Variceal eradication was defined as no endoscopic visualization of varices or the presence of small, whitish variceal columns, with no red spots, in which band ligation could not be performed.

EUS evaluation of paraesophageal varices, azygos vein, and thoracic duct was performed both before and 1 month

after variceal eradication with a radial echoendoscope (EUG Radial, Fujinon System 7000, Fujinon, Japan). This stage was determined by 4 senior echoendoscopists, each with over 1000 EUS examinations. The index EUS was performed immediately before the first endoscopic session of band ligation for secondary prophylaxis of bleeding, under the same sedation. This session occurred after patients were discharged from the hospital as an outpatient procedure. It was performed not less than 4 weeks after the bleeding episode. During this evaluation the paraesophageal varices, azygos vein, and thoracic duct were scanned upward from the gastroesophageal junction, and the azygos vein was measured at its proximal aspect, immediately before it assumed the typical arch shape. Their largest diameters were considered for this study.

During the first year after variceal eradication, a researcher blinded to the EUS findings performed 3 monthly endoscopic examinations to assess variceal recurrence. Recurrence was defined as the presence of esophageal varices that could undergo a new endoscopic treatment, such as band ligation or sclerosis, or a new episode of variceal bleeding. At the end of the study patients were divided into groups of recurrent and nonrecurrent esophageal varices.

Statistical analysis between these 2 groups was performed using clinical, endoscopic, and echoendoscopic features. The Fisher test was used to analyze categorical variables such as gender, cirrhosis etiology, and Child-Pugh stage. For continuous variables, a Student *t* test or Wilcoxon test was used to compare differences between groups. Once a parameter was considered a predictive factor for variceal recurrence, a receiver operating characteristic (ROC) curve was performed to ascertain optimal cut-off values, sensitivity, specificity, and the area under the ROC curve (AUROC). Internal validation of the prediction of variceal recurrence was performed by bootstrap regression (100 repetitions). If 2 or more parameters were considered a predictive factor for variceal recurrence, the results were combined to test their combined accuracy. All calculations were performed using the R-package,²⁷ and statistical significance was considered at $P < .05$.

RESULTS

From May 2011 to August 2013, 317 patients with cirrhosis were referred for endoscopic treatment of esophageal varices. Of those, 282 were excluded on the basis of the exclusion criteria, such as primary prophylaxis, previous endoscopic treatment, Child C cirrhosis, and contraindication for beta-blockers. A total of 35 patients were included in our study (Fig. 1). Of those, 1 patient underwent orthotopic liver transplantation, and 4 died during the endoscopic treatment with band ligation (2 had a new episode of bleeding and 2 died from other adverse events

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