

## **Response to Reviewer Comments**

### **Comment:**

#### **General considerations:**

Nowadays the prevention of one of the most severe complications of portal hypertension, that is, upper gastrointestinal hemorrhage due to variceal rupture (esophageal or gastric), is one of the goals in patients with hepatic cirrhosis. Large varices and the presence of red signs are considered the most valuable objective signs of risk for variceal rupture leading to the administration of preventive treatment with vasoactive drugs and endoscopic treatments such as variceal ligation. Upper GI endoscopy is considered the gold standard method for assessing the presence of varices, their size and red markings. Elective UGI endoscopy is currently considered easily available, speedy and safe and provides excellent tolerance under deep sedation (midazolam or propofol). The main inconvenience is the price, which varies greatly depending on the countries. As stated by the authors, many indexes had been proposed on suspicion of the presence of large sized varices induced by portal hypertension, avoiding the use of upper GI endoscopy with an acceptable accuracy. However, the inverse objective seems to be more important, because endoscopy is considered an important tool for preventing variceal hemorrhage with the use of endoscopic band ligation in patients with large varices. Nevertheless, if an accurate index ensuring the absence of varices or even the presence of risky varices were available, this index would be very useful for avoiding upper GI endoscopy. The authors have

exhaustively studied a series of patients with HVC hepatic cirrhosis A and B Child, including a CT scan to build a non-invasive diagnostic model for screening large esophageal varices. The use of continuous variables makes it easy to obtain the best results in regard to accuracy in determining the most adequate sample size, but the authors do not consider the sample size calculation, which is due probably to the retrospective nature of this study in a series of patients.

**Specific remarks:**

The mortality rate induced by esophageal varices rupture has significantly reduced in the last years (*Baveno*) as compared with the mortality rate cited in the paper. The side effects and severe complications induced by elective upper GI endoscopy is widely considered to be very low, and in the Introduction the authors consider that this is a risky procedure. This aspect should also be addressed. The rise of accuracy in assessing the presence of varices by CT-scan is modest as compared with the previous indexes used which are easily obtained, and require less technological complexity. It seems that with an adequate number of patients the accuracy of the model could be enhanced. In fact, CT-scan or magnetic resonance is considered adequate when investigating hepatocellular carcinoma, but in these cases esophageal and gastric varices in the form of venous submucosal dilatations can also be accurately assessed. In the Discussion, the second and third paragraph contains similar information to that included in Patients and Methods and Results and should be omitted.

**Response:**

To date, esophagogastroduodenoscopy (EGD) is considered the gold standard tool for the diagnosis of esophageal varices. Therefore, high-risk patients require EGD to be repeated every 1-2 year. In addition, upper endoscopy is associated with many complications either related to the sedation or to the maneuver itself (*Eisen GM et al, 2002; Kevin R Palmer, 2007; Harris MD and Ells PF, 2009*), in addition to the invasive nature of the procedure and lack of patient compliance restricting its use.

The present study involved a significant number of cirrhotic patients who underwent upper gastroscopy followed by CT imaging in addition to a series of simple inexpensive investigations to determine values for APRI, FIB-4, and PC/SD ratio. Patients undergoing the latter procedures were much more willing to comply when compared to consenting for endoscopy, giving further support that endoscopy, in spite of its established benefits, remains a costly uncomfortable procedure for many patients who prefer to avoid this invasive maneuver in any way possible, particularly when other accurate diagnostic tools are readily available.

Data from this study suggest that CT scanning may afford an adequate alternative to endoscopy in diagnosis of esophageal varices in cirrhotic patients. In addition, parameters easily detectable by CT, such as PC/SD ratio and PVD, form the basis for the model proposed by this study group.