Performance of spleen stiffness measurement by vibration-controlled transient elastography to rule out high-risk varices in patients with chronic extrahepatic portal vein obstruction without cirrhosis

Coordinators

Dre Lucile Moga

Hépatologie – Centre de référence des maladies vasculaires du foie

Hôpital Beaujon

Clichy

France

lucile.moga@gmail.com

Dre Aurélie Plessier

Hépatologie – Centre de référence des maladies vasculaires du foie

Hôpital Beaujon

Clichy

France

aurelie.plessier@aphp.fr

Background

Chronic extrahepatic portal vein obstruction (CEPVO) in the absence of cirrhosis refers to a portal vein thrombosis present or persistent for more than 6 months or to a portal cavernoma. Main complications of CEPVO are related to portal hypertension, and probability of having high-risk varices (i.e. large varices, or small varices with red spot signs, or variceal hemorrhage revealing portal cavernoma) is about 55% at baseline endoscopy (1). Plus, probability of developing high-risk varices during follow-up is about 25%.

In patients with cirrhosis, liver stiffness and spleen stiffness are associated with the severity of portal hypertension. According to Baveno VII consensus, liver stiffness measurement by vibration-controlled transient elastography (VCTE) ≥ 25 kPa is sufficient to rule in clinically significant portal hypertension in patients with virus or alcohol-related cirrhosis and non-obese NASH-related cirrhosis. Conversely, cirrhotic patients with a spleen stiffness measurement ≤ 40 kPa have a low probability of high-risk varices (2).

Liver stiffness is usually low in patients with CEPVO without cirrhosis (3), and therefore cannot help to identify patients who have a low probability of having high-risk varices. In patients with CEPVO, splenomegaly is an independent predictor for the presence of varices at baseline endoscopy, which is also true in patients without myeloproliferative neoplasm (1). However, there are currently no data on ability of spleen stiffness measurement by VCTE to rule in or rule out high-risk varices in patients with CEPVO. Baveno VII consensus workshop therefore recommends that all patients in whom thrombosis has not been recanalized should be screened for gastroesophageal varices within 6 months of the acute episode, and that in the absence of varices, endoscopy should be repeated at 12 months, and 2 years thereafter (2).

Aim

- To evaluate the performance of spleen stiffness measurement by VCTE to rule out high-risk varices in patients with chronic extrahepatic portal vein obstruction in the absence of cirrhosis.

Design

Part I: Learning group of patients with CEPVO without cirrhosis

The learning cohort will include patients with CEPVO without cirrhosis who underwent a spleen stiffness measurement by VCTE using FibroScan® since 2013 at Hôpital Beaujon (Clichy, France), and a screening endoscopy. Diagnosis of CEPVO will be based on contrast-enhanced CT or MRI showing a lack of visualization of the portal vein, +/- associated with a cavernoma enhancing after contrast injection. Exclusion of underlying cirrhosis can be based on imaging findings and/or liver stiffness measurement <10 kPa. A liver biopsy can be necessary when an underlying chronic liver disease (cirrhosis or porto-sinusoïdal vascular disorder) is suspected based on abnormal liver morphology and/or increased liver stiffness measurement.

Part II: Validation group of patients with CEPVO without cirrhosis

The validation cohort will include patients CEPVO without cirrhosis from participating VALDIG centers fulfilling the same inclusion criteria.

Inclusion criteria

- Patients with CEPVO (>6 months) diagnosed by radiological imaging;
- Age ≥18 years old
- And available spleen stiffness measurement by VCTE using FibroScan® performed within 2 years before or after endoscopy (or more than 2 years after endoscopy for patients receiving non-selective beta-blockers for primary prophylaxis of variceal bleeding).

Non-inclusion criteria

- Portal vein malignant invasion;
- Cirrhosis;
- Budd-Chiari syndrome;
- Isolated thrombosis of the splenic or superior mesenteric vein with patent portal vein;
- Transjugular intrahepatic portosystemic shunt or history of portal vein recanalisation at the time of SSM – VCTE;
- Tense ascites at the time of SSM – VCTE.

Data collection

Data will be collected from medical records in a dedicated case report form by participating VALDIG members. The following data categories will be retrospectively collected by the local investigators, and sent to the principal investigator of the study:

- demographics data,

- aetiological data,

- clinical presentation,

- laboratory results,

- imaging features,

- upper endoscopic data,

- spleen (and liver if available) stiffness by VCTE, performed within 2 years before or after endoscopy.

Data will be pseudonymized with a number of inclusion assigned to each patient included in the study. Inclusion number will include the number of the center, and the patient's number in the center.

Spleen stiffness measurement by transient elastography will be considered as reliable if:

- performed in fasting condition (≥2 hours);
- interquartile range / median SSM – TE ratio ≤30%;
- ≥10 valid measurements;
- success rate ≥60%;
- performed with a 50 Hz or a 100 Hz probe.

Statistical analysis

Quantitative variables will be expressed as median and interquartile ranges (IQR) and categorical variables as absolute number (percentage). Continuous variables will be compared using the Mann-Whiney test. Comparison of categorical variables will be performed using the Chi-square or Fisher exact test, when appropriate. We will assess the ability of SSM – VCTE to identify high-risk varices in patients with CEPVO without cirrhosis, by calculating area under the receiver operating characteristic curve (AUROC), sensitivity, specificity, positive predictive value, negative predictive value, positive and negative likelihood ratio and diagnostic accuracy of this test. We will test cut-off values already published for patients with cirrhosis (40 kPa). Analyses will be performed both on an intention-to-diagnose (including the entire cohort) and per-protocol (including only patients with valid SSM – TE) basis.

References

1. Noronha Ferreira C, Seijo S, Plessier A, Silva-Junior G, Turon F, Rautou PE, et al. Natural history and management of esophagogastric varices in chronic noncirrhotic, nontumoral portal vein thrombosis. Hepatology. mai 2016;63(5):1640-50.

2. de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C, Baveno VII Faculty. Baveno VII - Renewing consensus in portal hypertension. J Hepatol. avr 2022;76(4):959-74.

3. Sharma P, Mishra SR, Kumar M, Sharma BC, Sarin SK. Liver and spleen stiffness in patients with extrahepatic portal vein obstruction. Radiology. juin 2012;263(3):893-9.