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● *Original Contribution*

POINT SHEAR WAVE ELASTOGRAPHY OF THE SPLEEN: ITS ROLE IN PATIENTS WITH PORTAL HYPERTENSION

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Abstract—The goals of the study described here were to evaluate the feasibility and reproducibility of measuring spleen stiffness (SS) using point shear wave elastography in a series of cirrhotic patients and to investigate whether SS, liver stiffness (LS) and other non-invasive parameters are correlated with the presence of esophagogastric varices (EVs). Fifty-four cirrhotic patients with low-grade EVs or without EVs at esophago-gastro-duodenoscopy were enrolled. They underwent abdominal ultrasound and Doppler ultrasound of hepatic vessels simultaneously with p-SWE of the liver and spleen. In 42 patients, the accuracy of LS and SS, as well as of platelet count and spleen longitudinal diameter, in predicting the presence of EVs was evaluated. The technical success was 90.74% for LS (49/54 patients) and 77.78% for SS (42/54 patients). Inter-observer agreement for SS measurement was high. Both LS and SS correlated with esophago-gastro-duodenoscopy: LS had the highest accuracy in predicting the presence of EVs (area under the receiver operating characteristic curve [AUROC] = 0.913); SS had the lowest accuracy (AUROC = 0.675); platelet count and spleen diameter had intermediate accuracy (AUROC = 0.731 and 0.729, respectively). SS did not have an advantage over LS in predicting low-grade EVs and cannot be proposed as a useful tool in the diagnostic process of cirrhotic patients who require screening esophago-gastro-duodenoscopy. (E-mail: natalie.lucchina@hotmail.it) © 2017 World Federation for Ultrasound in Medicine & Biology. All rights reserved.

Key Words: Portal hypertension, Esophagogastric varices, Point shear wave elastography, Liver stiffness, Spleen stiffness.

INTRODUCTION

A hepatic venous pressure gradient (HVPG) > 10 mm Hg in cirrhotic patients is a major risk factor for the development of esophagogastric varices (EVs) and defines clinically significant portal hypertension (CSPH) (Berzigotti and Piscaglia 2011). Variceal hemorrhage occurs when the HVPG increases over 12 mm Hg, so this threshold is closely related to the presence of decompensating events and defines severe portal hypertension (SPH), which carries a high risk of death (D'Amico et al. 2006; Garcia-Tsao et al. 2010). Therefore, cirrhotic patients should undergo periodic surveillance for portal hypertension (PH) and EVs, as strongly recommended by the guidelines of the American Association for the Study of Liver Diseases (De Franchis 2010).

The gold standard for PH assessment is measurement of the HVPG by means of hepatic vein catheterization, whereas the diagnosis of EVs requires esophago-gastro-duodenoscopy (EGD) (Berzigotti and Piscaglia 2011). Both techniques are invasive, can lead to complications and entail high costs. Furthermore, HVPG measurement requires specific training and equipment and is routinely performed only in expert centers; EGD is poorly accepted by patients, who may refuse further follow-up (Castera et al. 2012).

There is thus a need for simple methods able to predict the progression of PH toward CSPH (Castera et al. 2012). Several non-invasive methods have been introduced, but none has spread to clinical practice because of insufficient accuracy (Baik et al. 2006; De Franchis 2010; Kim et al. 2012; Thabut et al. 2007).

Elastography is emerging as a promising tool for risk stratification of patients with PH. It has the advantages of

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being easy to perform, time saving and well tolerated by patients (Carrión et al. 2006; Kazemi et al. 2006). Shear wave elastography (SWE) encompasses three techniques: transient Elastography (TE), point SWE (p-SWE) and SWE imaging. To predict the degree of PH, p-SWE appears to be more applicable than TE by measuring both liver stiffness (LS) and spleen stiffness (SS). As for the measurement of LS, p-SWE exhibits some advantages over TE: First, the rate of unsuccessful TE was reported to be as high as 18.9%, mostly because of obesity, ascites and narrow intercostal spaces (Piscaglia et al. 2016); p-SWE is not limited by these conditions, and the rate of unsuccessful results was reported to be 2.9% overall (Park et al. 2015). Furthermore, p-SWE is superior in terms of convenience because it is integrated into a conventional ultrasonography system; in addition, with the positioning of the region of interest (ROI), nearby interfering structures, such as blood vessels, can be avoided, minimizing measurement error (Castera et al. 2010; Friedrich-Rust et al. 2012; Park et al. 2015; Piscaglia et al. 2016).

A good correlation between LS values and HVPG was initially reported by Carrión et al. (2006), but other studies found that although the correlation was excellent for HVPG values below 10–12 mm Hg, it hardly reached statistical significance for values >12 mm Hg (Castera et al. 2012). This observation suggests that beyond a certain degree of portal pressure, the development of PH becomes at least partially independent of the simple accumulation of fibrillar extracellular matrix responsible for the increase in LS because several extrahepatic factors contribute to the rise of portal pressure.

Although the pathogenesis of splenic modifications is not yet completely understood, a causal link has been postulated between spleen changes and PH. Splenomegaly in cirrhosis is characterized by enlargement and hyperactivation of the splenic lymphoid tissue, as well as increased angiogenesis and fibrogenesis, in addition to passive congestion. Together, these changes are likely to result in increased SS, suggesting the possibility of using this marker to monitor PH (Bolognesi et al. 2002; Colecchia et al. 2012).

Published data regarding SS assessment by p-SWE to predict and stage PH and EVs reveal controversial results; from 2010 to 2016, nine studies involving more than 1700 patients were published. Some authors reported significantly higher values in patients with EVs than in those without EVs (Park et al. 2016; Rizzo et al. 2014; Takuma et al. 2013, 2016; Ye et al. 2012); others (Bota et al. 2010, 2012; Mori et al. 2013; Vermehren et al. 2012) did not report significantly different values between the two groups. It should be noted that in these studies, there was no differentiation between patients with low-grade EVs and those with high-grade EVs.

Another explanation may lie in the heterogeneity of the methods used. Most of the studies used EGD as a reference, but although EGD is regarded as the standard for assessing EVs, there is significant inter-observer variability, which limits its value as a gold standard. To date, only one study has carried out HVPG to evaluate the degree of PH (Takuma et al. 2016), and it found that SS has better diagnostic performance than LS.

In our opinion, the most important topic to clarify is the stage of the disease at which p-SWE measurements are most useful; because we believe that the method should be directed to the evaluation of low-grade EVs, when to use tailored management is most important.

To the best of our knowledge, our study is the first to evaluate the utility of SS in this setting. The main aims of this study were to evaluate the feasibility and reproducibility of measurement of SS using p-SWE in a series of cirrhotic patients and to investigate whether SS, LS and other non-invasive parameters (*i.e.,* platelet count and spleen diameter) are correlated with the presence of low-grade EVs.

METHODS

Patients and study design

We used the information system of the Gastroenterology Department to identify patients who had undergone EGD and serologic tests within a mean of 5 mo (range: 1–8 mo) before US and p-SWE examination. The inclusion criteria were as follows:

- Liver cirrhosis of various etiologies (30 patients affected by hepatitis C virus [HCV+], 8 by alcohol-related cirrhosis, 2 by non-alcoholic fatty liver disease [NAFLD], 10 by HCV-HIV co-infection, and 2 by autoimmune, 1 by cryptogenic and 1 by primary biliary cirrhosis) previously diagnosed by combined clinical and laboratory findings or by former liver histology in selected cases (n = 6).
- Endoscopic detection of low-grade EVs (grade F1, according to Beppu classification) (Beppu et al. 1981) or normal endoscopic findings.

The exclusion criteria were endoscopic detection of large EVs (grade ≥F2); history of treatment for PH; and presence of hepatocellular carcinoma.

Between April 2014 and May 2016, we enrolled 54 patients (41 males, 13 females, mean age: 63.8 y, range: 42–87) who met the inclusion criteria. All patients underwent upper abdominal US with a 1- to 5-MHz convex transducer (iU22, Philips Healthcare, Bothell, WA, USA) and Doppler ultrasound of hepatic vessels. They simultaneously underwent p-SWE of the liver and spleen with a convex broadband probe using the ElastPQ technique. The shear wave velocity was displayed in meters per second