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● *Original Contribution*

USING ULTRASONIC TRANSIENT ELASTOMETRY (FIBROSCAN) TO PREDICT ESOPHAGEAL VARICES IN PATIENTS WITH VIRAL LIVER CIRRHOSIS

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Abstract—The correlation between liver stiffness (LS), measured by ultrasonic transient elastometry (FibroScan), and the presence and severity of esophageal varices (EV) in patients with viral cirrhosis of the liver has not been well documented to date. The study described here investigated the value of using FibroScan to predict EV. Patients with cirrhosis (200 patients: 167 cases caused by hepatitis B virus and 33 cases caused by hepatitis C virus) underwent both upper gastrointestinal endoscopy and FibroScan. Demographic, clinical, biochemical and endoscopic data and FibroScan-obtained LS parameters were collected. The mean LS value in patients with EV (33.2 kPa) was significantly higher than the mean LS value in patients without EV (18.6 kPa) ($p < 0.05$). The mean LS value in patients with grade 2 and 3 EV (38.3 kPa) was significantly higher than that in patients with grade 1 EV (24.8 kPa) ($p < 0.05$). Overall, FibroScan was 86.4% sensitive and 72.2% specific in predicting the presence of EV, with an area under the receiver operating characteristic curve (AUROC) of 0.84. The sensitivity and specificity for the patients with grade 2 or 3 EV were 84% and 73% (AUROC = 0.86). When FibroScan was combined with platelet count, the overall sensitivity and specificity of prediction increased to 84% and 80% (AUROC = 0.88), respectively, and 84% and 75% (AUROC = 0.89), respectively, in patients with grade 2 and 3 EV. FibroScan alone or combined with platelet count might predict the presence and severity of EV in patients with hepatitis B or C-related viral cirrhosis. (E-mail: xiaopingtangcn@163.com)

Key Words: **Esophageal varices, Liver cirrhosis, FibroScan, Transient elastography.**

INTRODUCTION

Progressive hepatic fibrosis caused by the accumulation of collagen in the extracellular matrix is characteristic of almost all chronic liver diseases (Bataller and Brenner 2005). Liver cirrhosis is the final phase of the hepatic fibrosis process, combining extensive fibrosis and regenerative nodules. In the East, chronic infection with hepatotropic viruses is a predominant problem (Margolis et al. 1991; Wang et al. 2014). Approximately 10%–20% of patients infected with chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) present with cirrhosis at their first clinical examination. As many as 20%–30% of patients who do not present with cirrhosis at that initial visit will develop cirrhosis within at least a decade (Benvegnù et al. 2004; Di Marco et al. 1999; Ikeda et al. 1998; Niederau et al. 1998). Major complications of cirrhosis include liver failure, portal hypertension (PHT), hepatorenal syndrome and esophageal varices (EV), all of which are poor prognostic indicators (Ginès et al. 2004). Up to 90% of patients with cirrhosis develop EV, which may bleed. The incidence of bleeding EV is around 5% in patients with small EV (SEV) and up to 15% in patients with large EV (LEV) (Jensen 2002). Mortality per bleeding episode is around 10%–20% (Carbonell et al. 2004). Therefore, screening for EV in patients with cirrhosis is strongly recommended across guidelines and consensus statements (de Franchis 2005).

Accordingly, it is generally recommended that patients with cirrhosis undergo active surveillance for

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early detection of EV *via* upper gastrointestinal (GI) endoscopy; however, endoscopic examination can be considered an unnecessary burden for both patients and doctors. Approximately half of patients with cirrhosis will not develop EV in the 10 y after the initial cirrhosis diagnosis (Addley et al. 2012). A common consequence of virus-related chronic liver disease is PHT, which results in EV. The hepatic venous pressure gradient (HVPG) is considered the gold standard for assessing PHT in patients with cirrhosis; however, assessments using this parameter are invasive and not routinely performed (Thabut et al. 2011). More non-invasive methods have been proposed as alternatives to endoscopy for EV screening. Measurement of liver stiffness (LS) with ultrasonic transient elastometry has been recognized as a rapid, non-invasive technique in which the measurement correlates well with the underlying stage of fibrosis. A particularly strong correlation has been observed between LS measured by FibroScan (Echosens, Paris, France), the first tool introduced to assess fibrosis through LS (Echosens, Paris, France), and HVPG. Thus, FibroScan has potential to be used for the non-invasive evaluation of EV (Castera et al. 2012). Although the value of FibroScan in assessment of the degree of LS in patients with chronic HCV infection has been well documented, few studies have been conducted on the use of FibroScan for patients with chronic HBV infection (Castéra et al. 2005; Cui et al. 2013; Dolmazashvili et al. 2008; Marcellin et al. 2009; Ziol et al. 2005). Moreover, few studies have focused on the relationship between LS and the presence and severity of EV, especially in patients with HBV infection. This is concerning, as the most common cause of cirrhosis with high mortality in China is HBV infection (Calvaruso et al. 2013; Castéra et al. 2009; Kazemi et al. 2006). In addition, the results of different studies still lack sensitivity and specificity (Calvaruso et al. 2013). The aim of this study was to investigate the relationship between degree of LS and EV and to assess the use of FibroScan to predict the presence and severity of EV.

METHODS

Participants

Between July 2007 and October 2012, 200 consecutive inpatients from Guangzhou No. 8 People's Hospital, China, were initially included. Patients were older than 18 y, included both sexes, had chronic HBV- or HCV-related liver cirrhosis, had undergone upper GI endoscopy, and agreed to a FibroScan examination. Cirrhosis of the liver was diagnosed using the criteria from the Chinese Association of Liver Diseases practice guidelines, which, in turn, are adapted from the American Association for the Study of Liver Diseases guidelines (Runyon 2013).

The diagnosis was based mainly on abdominal ultrasonic findings combined with medical history, clinical symptoms and laboratory results. If the diagnosis was unclear from these parameters, liver biopsy was considered a secondary diagnostic measure. In this study, 22 patients underwent liver biopsy. Serologic detection of hepatitis B surface antigens and hepatitis C antibodies was used to diagnose HBV or HCV infection. Patients were excluded from this study if they were infected with both HBV and HCV, reported heavy alcohol intake (defined as $>$40 g of alcohol/d for $\geq$5 y), or had comorbid chronic liver diseases, aspartate aminotransferase (AST)/alanine aminotransferase (ALT) levels greater than three times the normal upper limit, hepatocellular carcinoma, acute liver failure or decompensated congestive heart failure.

The clinical parameters collected from each patient were: age, sex, history of ascites, bleeding varices, spontaneous bacterial peritonitis, hepatic encephalopathy, organic kidney failure, or hepatorenal syndrome. Collected biological parameters included a complete blood count and levels of AST, ALT, alkaline phosphatases, total bilirubin, albumin, gamma globulins, prothrombin time (PT), creatinine, urea and α-fetoprotein.

The research protocol was approved by the ethics committee of Guangzhou No. 8 People's Hospital. Written informed consent was obtained from each participant. The study was registered in the Chinese Clinical Trial Registry.

Endoscopy

All patients underwent upper GI endoscopy (Fujinon EG-590 WR, Japan). Varices were graded according to their size and appearance by an endoscopic physician experienced in the following grading scale (Chinese Medical Association 2003): grade 0 = no varices; grade 1 = small, straight EV; grade 2 = enlarged, tortuous EV occupying less than one-third of the lumen; and grade 3 = large, coil-shaped EV occupying more than one-third of the lumen.

Liver stiffness measurement

FibroScan was used to measure LS during the same week the patients underwent endoscopic examinations. An experienced doctor blinded to the patients' clinical data and endoscopic results performed all measurements. The FibroScan device was equipped with a probe that included a vibrating component. The vibrator transmitted vibrations to the tissues, inducing an elastic shear wave that propagated through the tissue. The propagation was followed by pulse-echo ultrasound acquisitions. Their velocity, directly related to tissue stiffness, was then measured (Friedrich-Rust et al. 2010; Sandrin et al.