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ORIGINAL ARTICLE

# Does transient elastography (FibroScan®) have a role in decision making in hepatocellular carcinoma?

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## Abstract

**Objectives:** Portal hypertension has been reported as a negative prognostic factor and a relative contraindication for liver resection. This study considers a possible role of fibrosis evaluation by transient elastography (FibroScan®) and its correlation with portal hypertension in patients with cirrhosis, and discusses the use of this technique in planning therapeutic options in patients with hepatocellular carcinoma (HCC).

**Methods:** A total of 77 patients with cirrhosis, 42 (54.5%) of whom had HCC, were enrolled in this study during 2009–2011. The group included 46 (59.7%) men. The mean age of the sample was 65.2 years. The principle aetiology of disease was hepatitis C virus (HCV)-related cirrhosis (66.2%). Liver function was assessed according to Child–Pugh classification. In all patients liver stiffness (LS) was measured using FibroScan®. The presence of portal hypertension was indirectly defined as: (i) oesophageal varices detectable on endoscopy; (ii) splenomegaly (increased diameter of the spleen to $\geq$12 cm), or (iii) a platelet count of <100 000 platelets/mm$^3$.

**Results:** Median LS in all patients was 27.9 kPa. Portal hypertension was recorded as present in 37 patients (48.1%) and absent in 40 patients (51.9%). Median LS values in HCC patients with and without portal hypertension were 29.1 kPa and 19.6 kPa, respectively ($r = 0.26$, $P < 0.04$). Liver stiffness was used to implement the Barcelona Clinic Liver Cancer algorithm in decisions about treatment.

**Conclusions:** The evaluation of liver fibrosis by transient elastography may be useful in the follow-up of patients with cirrhosis and a direct correlation with portal hypertension may aid in the evaluation of surgical risk in patients with HCC and in the choice of alternative therapies.

## Keywords

portal hypertension, hepatocellular carcinoma, liver fibrosis, transient elastography, liver stiffness, Barcelona Clinic Liver Cancer (BCLC)

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## Introduction

Underlying liver cirrhosis is the strongest predisposing factor for hepatocellular carcinoma (HCC) and is found in 80% of HCC patients.[1] However, up to 40% of HCC patients are suitable for consideration for potentially curative interventions. Excluding liver transplantation, which may resolve both conditions, the treatment of HCC and cirrhosis is complex because of the simultaneous needs for radical oncological treatment and the preservation of hepatic parenchyma. In patients with HCC and underlying cirrhosis, the correct estimation of the future hepatic reserve is crucial to ensure patients are correctly selected for surgical resection.[2,3] The Barcelona Clinic Liver Classification (BCLC) scheme is considered the most used staging system and therapeutic

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algorithm for patients with HCC; however, in this classification portal hypertension and increased bilirubin are contraindications for liver resection, but the severity of portal hypertension is only indirectly defined.[1] Portal hypertension and hepatic fibrosis are generally considered poor prognostic factors in patients with HCC undergoing liver resection[4] and the pathophysiology of liver fibrosis and portal hypertension are directly correlated.[5] In fact, the initial event in portal hypertension is increased vascular resistance to portal flow, primarily caused by structural changes such as fibrotic scar tissue and regenerative nodules that compress portal and central venules in which stellate cells are involved in the regulation of the liver microcirculation and portal hypertension.[5]

Transient elastography (FibroScan®; Echosens SA, Paris, France) is a non-invasive method that uses measurements of liver stiffness (LS) to assess hepatic fibrosis in patients with chronic liver disease. It is easily performed, gives immediate results and has good reproducibility. A mechanical pulse is generated at the skin surface and is propagated through the liver. The velocity of the wave is measured by ultrasound (US). The velocity is directly correlated to the stiffness of the liver, which, in turn, reflects the degree of fibrosis.[6] The aim of this study was to investigate the relationship between LS as a surrogate measure of hepatic fibrosis and portal hypertension.[4,7,8]

## Materials and methods

The current study enrolled patients with cirrhosis between November 2009 and August 2011. Patients with portal vein thrombosis were excluded from the study. Data were collected on age, sex, disease aetiology, liver function, presence of portal hypertension, Model for End-stage Liver Disease (MELD) score, alpha-fetoprotein values and tumour characteristics (single or multi-nodular HCC). Cirrhosis diagnoses were based on clinical, laboratory and US findings.[9] Liver function was assessed using the Child–Pugh classification. The presence of portal hypertension was indirectly defined according to current guidelines as: (i) oesophageal varices detectable on endoscopy; (ii) splenomegaly (increased diameter of the spleen to ≥12 cm), or (iii) a platelet count of <100 000 platelets/mm$^3$.[10] Direct measurements of the hepatic venous pressure gradient (HVPG) were not performed in this series. In all patients, LS was measured using FibroScan® 502 in the right lobe of the liver, through the intercostal space, with the patient lying in the dorsal position and the right arm in maximal abduction. The tip of the transducer probe was covered with coupling gel and placed on the skin between the ribs at the level of the right lobe of the liver.

In patients with HCC, sonographic evaluation was used to assess non-tumour liver parenchyma before FibroScan® LS values were obtained. Ten validated measurements were obtained in each patient. The success rate was calculated as the number of validated measurements divided by the total number of measurements. The results were expressed in kilopascals (kPa). A success rate of ≥60% and an interquartile range (IQR) of ≥20–30% of the median value were considered reliable.[6] Liver stiffness was considered as absent or mild for LS values of 0.0–7.0 kPa; LS values of >12.5 kPa were considered indicators of cirrhosis.[11] Liver stiffness values of 12.5–17.6 kPa were considered to represent low–moderate LS and values of >17.6 kPa were considered to indicate high LS, in line with Vizzutti *et al.*[12]

Possible relationships among LS value, portal hypertension, Child–Pugh class and MELD score were evaluated.

### Statistical analysis

Quantitative data are given as the median and IQR. Qualitative data are given in percentages. Differences between the groups (with and without HCC, respectively) were tested using the sign test for quantitative data and chi-squared test (or Fisher's exact test, as appropriate) for qualitative data. The association between LS and portal hypertension was evaluated using the Wilcoxon two-sample test. The association between LS and Child–Pugh class was tested using the Kruskall–Wallis test. Correlations between quantitative variables were computed using Spearman's correlation test. Boxplots were furnished to illustrate median and IQR LS values according to portal hypertension and Child–Pugh class.

## Results

The current study enrolled 77 patients with cirrhosis, 42 (54.5%) of whom had HCC, between November 2009 and August 2011. The mean age of the patient cohort was 65.2 years (range: 45–86 years) and the group included 46 (59.7%) men. Demographics, underlying aetiology, level of hepatic dysfunction and tumour characteristics are shown in Table 1. The presence of portal hypertension according to Child–Pugh class and tumour characteristics in HCC patients is shown in Table 2. Median LS in all patients was 27.9 kPa (IQR 19.8–31.5 kPa), confirming severe fibrosis (F4, Metavir score 4, Ishak score 5–6). Median LS in HCC patients with portal hypertension (29.1 kPa, IQR 19.1–39.3 kPa) was higher than that in patients without portal hypertension (19.6 kPa, IQR 14.9–32.5 kPa) ($r = 0.28$, $P < 0.04$) (Fig. 1). A direct correlation between LS and Child–Pugh class was found: patients in Child–Pugh classes B and C presented the highest levels of LS ($P < 0.005$) (Fig. 2). However, LS measurements correlated with MELD scores: the median LS value in patients with MELD scores of >10 was 29.1 kPa, whereas that in patients with MELD scores of ≤10 was 22.9 kPa ($r = 0.26$, $P = 0.02$) (Fig. 3).

Treatment decisions were evaluated according to the BCLC algorithm and LS was used to provide a better evaluation of portal hypertension and to predict surgical risk. In this series, of 20 patients with Child–Pugh class A status with a single HCC, eight patients were submitted to liver resection, nine to radiofrequency ablation and three to percutaneous ethanol injection (Table 3). Patients who underwent liver resection presented normal bilirubin values, MELD scores of <10, performance status of 0–1 and Okuda stage I. Four patients displayed no portal hypertension,