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Original Article

Elevated body mass index is a risk factor associated with possible liver cirrhosis across different etiologies of chronic liver disease

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Liver cirrhosis;
Metabolic risk factor;
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Background/Purpose: Metabolic risk factors are associated with liver fibrosis. Whether or not metabolic risk factors affect the severity of liver fibrosis in patients with chronic hepatitis B (CHB), chronic hepatitis C (CHC), or risk factors associated with non-alcoholic fatty liver disease (NAFLD) remains unclear. We aimed to investigate this by transient elastography.

Methods: In this cross-sectional study, we enrolled 1513 patients who presented with chronic liver disease (CLD) at a tertiary hospital. Liver stiffness measurement (LSM) >13 kPa was used as a cutoff suggesting possible liver cirrhosis (LC).

Results: Possible LC was noted in 7.8% of the CHB patients, 19.9% of the CHC patients, and 11.9% of the patients with risk factors associated with NAFLD. After adjustments for biochemical and virological factors were made, BMI (per 1 kg/m^2 increase) (OR: 1.17, 95% CI: 1.06–1.29, P = 0.002) was found to be an independent factor associated with possible LC in CHB patients; BMI (per 1 kg/m^2 increase) (OR: 1.15, 95% CI: 1.07–1.24, P < 0.001) and diabetes mellitus (DM) (OR: 2.32, 95% CI: 1.25–4.30, P = 0.008) were found to be independent factors associated with possible LC in CHC patients; and BMI (per 1 kg/m^2 increase) (OR: 1.19, 95% CI: 1.07–1.32, P = 0.002) and DM (OR: 10.35, 95% CI: 2.95–36.32,

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$P < 0.001$) were found to be independent factors associated with possible LC in patients with risk factors associated with NAFLD.
Conclusion: Elevated BMI was an independent risk factor associated with possible LC across the three different etiologies of CLD. As such, weight loss may be beneficial in these patients.

Introduction

Chronic hepatitis B virus (HBV) and chronic hepatitis C virus (HCV) infections both lead to progressive liver fibrosis, and such infections are the leading causes of chronic liver disease (CLD).[1,2] In addition, as the incidence of obesity increases in the general population, non-alcoholic fatty liver disease (NAFLD) is also emerging as a disease of significant concern, with NAFLD affecting more than 30% of adults in developed countries.[3] Coexistent steatosis is common in chronic HCV infections and chronic HBV infections and is also strongly associated with more advanced liver disease.[4]

Metabolic risk factors associated with NAFLD, including obesity, diabetes mellitus (DM), and hyperlipidemia, have recently emerged as potential cofactors in the development of fibrosis in cases of chronic HCV and HBV.[5–7]

Consequently, hepatic fibrosis evaluation is highly important in the management of patients with CLD. The extent of any hepatic fibrosis has classically been determined by histological assessment, which is currently the reference standard. However, the accuracy of hepatic fibrosis evaluations is limited by both sampling variability and inter-observer variability between pathologists.[8] In addition, liver biopsy is associated with patient discomfort and the risk of serious complications.[9] Therefore, the use of liver biopsy as a screening tool for liver fibrosis is unlikely to be widely accepted.

In contrast, liver stiffness measurement (LSM) using transient elastography (TE) is considered the non-invasive standard for the measurement of liver fibrosis, with LSM values being strongly associated with the histological stages of liver fibrosis.[10] As such, we sought in this study to use LSM to investigate the relationship between metabolic risk factors and the risk of liver cirrhosis in different etiologies of CLD.

Materials and methods

Patients

Between January 2013 and April 2014, all the patients who presented with CLD in the hepatology department of Kaohsiung Chang Gung Memorial Hospital were enrolled consecutively. The patients with chronic viral hepatitis received regular follow-up for liver disease, while the patients without chronic viral hepatitis were referred from endocrinologists to be tested for NAFLD; all these patients had at least one risk factor associated with NAFLD, such as obesity, type 2 DM, dyslipidemia, or hypertension.[11]

The exclusion criteria were as follows: use of drugs known to induce steatosis, excessive alcohol consumption (>21 drinks per week in men and >14 drinks per week in women over the preceding 2-year period),[11] technical issues (i.e., LSM failure or unreliable LSM values),[12] hepatic malignancy, and decompensated liver disease. Patients with HIV infection or hepatitis B and C co-infection were also excluded. All procedures followed were in accordance with the ethical standards of the responsible committees on human experimentation (institutional and national) and in accordance with the Helsinki Declaration of 1975, as revised in 2008. This retrospective study was approved by the human research committee of our institution (IRB number: 201601042B0). The requirement for informed consent was waived by the IRB. The data were analyzed anonymously.

Liver stiffness and control attenuated parameter measurements

LSM and control attenuated parameter (CAP) measurements were performed with the FibroScan device (Echosens, Paris, France) by two experienced operators. In all patients, these measurements were performed using the 3.5 MHz standard M probe. Only results with 10 valid shots and an IQR/median liver stiffness ratio <30% were included. The principles of liver stiffness and CAP measurements have been described elsewhere.[13] LSM > 13.0 kPa was taken as the cutoff suggesting possible liver cirrhosis.[14] LSM ≥8.0 kPa was used as a cutoff suggesting clinically relevant fibrosis.[15]

Ultrasound

Ultrasound (US) scans were performed by hepatologists in our department with five different ultrasound machines including an SSA-580A Nemio XG Color doppler ultrasonic (TOSHIBA, Japan), an Aplio XU MdlSSA-700A (TOSHIBA, Japan), a Xario™XG SSA-680A (TOSHIBA, Japan), a Hitachi Hi Vision Preirus Ultrasound Machine (Japan), and a Philips/ATL HDI 5000 ultrasound (Netherlands). Predefined criteria were used to determine the severity of hepatic steatosis. These included the presence of bright echoes or increased hepatorenal contrast for steatosis grade 1 (S1) (mild steatosis); the presence of both bright echoes and increased hepatorenal contrast, as well as vessel blurring, for

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