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Editorial
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Evaluation of Hepatic Steatosis with Controlled Attenuation Parameter (CAP) Technology

Ohkoshi S, Hirono H, Watanabe K and Hasegawa K*

Department of Internal Medicine, Nippon Dental University, Japan

Introduction

In the era of eradication and complete suppression of hepatitis C virus (HCV) and hepatitis B virus (HBV), the most important topic regarding liver diseases is nonalcoholic fatty liver disease (NAFLD). NAFLD is estimated to affect 13% to 32% of the population worldwide [1], and its prevalence is increasing along with the rise in obesity and metabolic syndrome (MetS) [2]. NAFLD is recognized to be closely associated with MetS. Hepatic steatosis is also a symptom of chronic hepatitis C and alcoholic liver injury.

NAFLD is clinically significant because of its progression to nonalcoholic steatohepatitis (NASH), which can result in cirrhosis and hepatocellular carcinoma (HCC).NASH is the most frequent cause of HCC in Western countries [3].

CAP (Controlled Attenuation Parameter) Evaluation for NAFLD

Liver biopsy is the gold standard for the diagnosis of hepatic steatosis. However, it cannot be performed on all patients because of its invasiveness and contraindications. Therefore, non-invasive evaluation techniques for steatosis that can be employed as a population screening tool are urgently needed. In general, diagnosis of NAFLD is made by a combination of laboratory tests such as a spartate aminotransferase (AST), alanine aminotransferase (ALT), and γ-glutamyl transpeptidase (γGTP) levels, and the bright appearance of the liver in regular abdominal echography, which is subjective and not always accurate. Controlled attenuation parameter (CAP) has been recently developed and installed with non-invasive test transient elastography [4,5]. This test estimates the degree of steatosis by evaluating the attenuation of shear wave velocity emitted from the FibroScan® probe at 3.5 MHz. Because this tool is non-invasive and can quantify the level of fatty liver, it is expected to be highly applicable for population screening. Since reported in 2010 [4], there have been many studies demonstrating the validity of this parameter [6,7]. Because the standard evaluation of steatosis has been based on liver biopsies, where the level of steatosis is classified as S0 to S3 [8], the validity of CAP has been based confirmed in comparison to this histological assessment [5,9,10]. In a sub-analysis of 5,323 patients, the area under the receiver operating curve (AUROC) of CAP was reported to be 0.79, 0.84, and 0.84 each for biopsy-proven steatosis of >10%, >33%, and >66%, respectively [7].

CAP and Its Application to Clinical Practice

CAP values have a positive association with parameters of MetS, BMI, waist circumstances, and the presence of DM [7,10,11], possibly correlating with the volume of visceral fat. MetS is closely associated with insulin resistance (IR). Hyperinsulinemia due to IR enhances the transcriptional activity of SRBP (sterol regulatory element-binding protein) 1, which promotes lipid synthesis and the reflux of free fatty acids from adipose tissues into the liver [12]. Consequently, NAFLD can be considered to be another parameter of MetS. Because CAP is installed in FibroScan®, CAP values are obtained along with liver stiffness (LS) values. Some studies showed a positive correlation between LS and CAP values [7,13]. This might indicate that the levels of liver fibrosis could be high in highly steatotic liver, suggesting the possible presence of NASH. However, Petta et al. [14] reported the risk of overestimating LS values in those with high CAP levels. Similarly, Karlas et al. [6] suggested a similar overestimation of CAP values in NAFLD/NASH compared to HCV/HBV/Others and in those with high BMI and diabetes compared to normal. Therefore, precautions should be taken in assessing LS and CAP values. In addition, it is necessary to obtain at least 10 replicate measurements for the evaluation of LS and CAP. The accuracy of CAP decreases when the interquartile range (IQR) of measurements exceeds a 40 dB/m median [15]. Because a regular M-probe cannot accommodate patients with a BMI over 30, an XL-probe should be used instead [16]. Recently, the superior

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Correspondence:
Shogo Ohkoshi, Department of Internal Medicine, School of Life Dentistry at Niigata, Nippon Dental University, 1-8 Hamaura-cho, Chuo-ku, Niigata, 951-8580, Japan, Tel: +81252118243; Fax: +81252671582;
E-mail: okoshi@ngt.ndu.ac.jp

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performance of MRI-based elastography over ultrasound-based CAP and LS in terms of the accuracy of fibrosis and steatosis detection has been shown [17]. However, the convenience and non-invasiveness of LS and CAP for population screening has not lost its appeal, but rather is becoming increasingly necessary. CAP evaluations are expected to efficiently identify NASH patients among those with NAFLD. A recent study revealed that the combination of LS, CAP and ALT values was useful in discriminating NASH patients [18]. Future studies using CAP and LS are expected to more accurately identify patients with NASH at higher risk for cirrhosis and HCC. In addition, longitudinal and prospective studies are needed to elucidate the risk of extrahepatic manifestations of NAFLD, such as cardiovascular and chronic kidney diseases, verifying the pathogenic impact of NAFLD, especially in MetS and even in people with simple obesity [19].

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