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Original Article

Utility of controlled attenuation parameter measurement for assessing liver steatosis in Japanese patients with chronic liver diseases

Keiichi Masaki,[1] Shintaro Takaki,[1] Hideyuki Hyogo,[1] Tomoki Kobayashi,[1] Takayuki Fukuhara,[1] Noriaki Naeshiro,[1] Yoji Honda,[1] Takashi Nakahara,[1] Atsushi Ohno,[1] Daisuke Miyaki,[1] Eisuke Murakami,[1] Yuko Nagaoki,[1] Tomokazu Kawaoka,[1] Masataka Tsuge,[1] Nobuhiko Hiraga,[1] Akira Hiramatsu,[1] Michio Imamura,[1] Yoshiiku Kawakami,[1] Hiroshi Aikata,[1] Hidenori Ochi,[1] Shoichi Takahashi,[1] Koji Arihiro[2] and Kazuaki Chayama[1]

Departments of [1]Gastroenterology and Metabolism and [2]Anatomical Pathology, Hiroshima University Hospital, Hiroshima, Japan

Aim: Steatosis is a common histological feature of chronic liver disease, especially alcoholic and non-alcoholic fatty liver disease, as well as chronic hepatitis C. A recent study showed that evaluating the controlled attenuation parameter (CAP) with transient elastography was an efficient way of non-invasively determining the severity of hepatic steatosis. The objective of this study was to prospectively evaluate the utility of CAP for diagnosing steatosis in patients with chronic liver disease.

Methods: One hundred and fifty-five consecutive patients with suspected chronic liver disease underwent steatosis diagnosis using CAP, blood sample analyses, computed tomography for assessing the liver/spleen ratio and liver biopsy. Steatosis was graded according to the percentage of fat-containing hepatocytes: S0, less than 5%; S1, 5–33%; S2, 34–66%; and S3: more than 66%.

Results: The CAP was significantly correlated with steatosis grade, and there were significant differences between the CAP value of the S0 patients and those of the patients with other grades of steatosis. S0 and S1–3 hepatic steatosis were considered to represent mild and significant steatosis, respectively. The CAP values of the patients with mild and significant steatosis were significantly different ($P < 0.0001$). The area under the receiver–operator curve (AUROC) value of the CAP for diagnosing significant steatosis was 0.878 (95% confidence interval, 0.818–0.939), and the optimal CAP cut-off value for detecting significant steatosis was 232.5 db/m. In multivariate analysis, the CAP ($P = 0.0002$) and the liver to spleen ratio ($P = 0.004$) were found to be significantly associated with significant steatosis.

Conclusion: The CAP is a promising tool for rapidly and non-invasively diagnosing steatosis.

Key words: controlled attenuation parameter, FibroScan, liver steatosis, non-invasively diagnose

INTRODUCTION

THE INCIDENCE OF obesity has markedly increased in developed countries in the past few decades. Due to the Westernization of lifestyles in Japan, the frequency of patients presenting with non-alcoholic fatty liver disease (NAFLD) has gradually increased, and NAFLD/non-alcoholic steatohepatitis (NASH) is estimated to affect 10 million people in the general population.[1,2] NAFLD is one of the clinical consequences of obesity and can progress to NASH, ultimately leading to cirrhosis, hepatocellular carcinoma and end-stage liver failure.[3,4]

Liver steatosis is considered to be a risk factor for treatment failure among patients with chronic viral hepatitis, such as that caused by hepatitis B virus (HBV) or hepatitis C virus (HCV).[5] In addition, previous studies demonstrated that the frequency of liver steatosis was significantly lower in hepatitis C patients who

Correspondence: Shintaro Takaki, Hiroshima University Hospital, Gastroenterology and Metabolism, Hiroshima, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8551, Japan. Email: takakiss@hiroshima-u.ac.jp
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achieved a sustained virological response (SVR).[6–11] Although the incidence of liver transplantation for end-stage liver disease is increasing, there is a shortage of organs for living donor liver transplantation.[12,13] Accordingly, it is important to properly estimate the degree of liver steatosis in potential donor livers in order to ensure the success of liver transplantation and donor safety.

Liver biopsy is the current gold standard for evaluating steatosis and other histological lesions;[3,4,14] however, it is invasive, subject to sampling error and is sometimes painful.[15,16] To avoid unnecessary biopsy examinations, various non-invasive methods have been developed for the assessment of hepatic steatosis.[17] As fat affects ultrasound propagation, a novel attenuation parameter has been developed to detect and quantify steatosis. This parameter, which is called the controlled attenuation parameter (CAP) because it specifically targets the liver, is based on the ultrasonic properties of the reflected radio frequency signals acquired by the FibroScan M probe (Echosens, Paris, France). Although many reports have demonstrated the utility of the CAP to determine the extent of a patient's liver steatosis,[18–20] its utility for assessing chronic liver disease in Japanese patients is unknown.

The primary objective of our study was to validate the ability of the CAP to detect and quantify steatosis. The secondary objective was to determine whether steatosis could be assessed simultaneously using the FibroScan M probe in patients with biopsy-proven chronic hepatitis due to any cause.

METHODS

Study population

ONE HUNDRED AND fifty-five consecutive patients with suspected chronic hepatitis due to any etiology who underwent liver biopsy and an ultrasound examination with the FibroScan M probe on the same day to calculate their CAP and liver stiffness measurement (LSM) values were enrolled. The patients were recruited at our institution between April and December 2012.

LSM and CAP measurement

After performing conventional ultrasonography to search for hepatocellular carcinoma, the tip of the transducer probe was placed on the patient's skin between the ribs over the right lobe of the liver with the patient lying in the dorsal decubitus position. All patients had their CAP measured using a standard 3.5-MHz M probe. In a preliminary retrospective study, in which the CAP was assessed in 115 patients with chronic liver disease due to various etiologies, the CAP performed well during the detection and semiquantification of steatosis.[18] The LSM was determined using a FibroScan M probe, a Vibration-Controlled Transient Elastography (VCTE; Echosens) device that is designed to measure liver stiffness. Briefly, the VCTE system generates a 50-Hz shear wave that is longitudinally polarized along the ultrasound axis.[21,22] The median value of 10 measurements performed at depths ranging 25–65 mm was adopted as the final liver stiffness value and was expressed in kPa. Only results derived from five valid shots and displaying an interquartile range (IQR)/median liver stiffness ratio of less than 30% were included. The CAP was designed to measure liver ultrasonic attenuation (along the go and return path) at 3.5 MHz using the signals acquired by the FibroScan M probe.[18] The CAP uses a sophisticated guidance process based on VCTE. In brief, the CAP is based on validated measurements, which are subject to the same criteria as the LSM and are obtained from the same signals. Therefore, the LSM and CAP were obtained simultaneously and in the same volume of liver parenchyma (i.e. at depths of between 25 and 65 mm). The median of the individual CAP values was used as the final CAP value, which was expressed in dB/m. The ratio of the IQR of the CAP values to the median CAP value (IQR/Mcap) was calculated as an indicator of variability.[18–20]

Clinical and laboratory evaluations

Biological and clinical parameters were assessed during liver biopsy. The following data were recorded: age; sex; etiology; height; bodyweight; body mass index (BMI); aspartate aminotransferase, alanine aminotransferase (ALT), γ-glutamyltransferase (GGT), total bilirubin, albumin, triglyceride, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, fasting glucose (FBS) and hemoglobin A1c (HbA1c) levels; prothrombin time; and platelet count. All blood sample analyses were performed in our hospital laboratory. Liver density was assessed using the ratio of the mean computed tomography (CT) attenuation value of the liver (in Hounsfield units; HU) to that of the spleen (L/S ratio), which was evaluated using abdominal CT.

Liver biopsy

Liver biopsy was performed by senior surgeons using a 1.2 mm/1.6 mm diameter Menghini needle (Surecut needle, Create Medic Co. Ltd, Japan). The liver speci-

mens measured more than 20 mm in length and were fixed, embedded in paraffin, and then stained with hematoxylin and Masson-trichrome. One experienced pathologist analyzed all of the biopsies independently without knowledge of the clinical data. Steatosis was graded according to the method of Kleiner *et al.*[23] as: S0, steatosis in less than 5% of hepatocytes; S1, 5–33%; S2, 34–66%; and S3, more than 66%

Statistical analyses

The relationships between the CAP and clinical or morphological parameters were evaluated using Spearman's rank correlation coefficient. Multivariate analysis was performed using multiple linear regression to investigate the effects of fibrosis stage, activity grade and steatosis grade on liver stiffness and the CAP. Box plots were used to assess the utility of the non-invasive methods for differentiating between each grade of steatosis. Area under the receiver–operator curve (AUROC) values were computed as well as their 95% confidence intervals (CI) using the Mann–Whitney *U*-test statistic according to the method proposed by Hanley and McNeil.[24] The cut-off value that maximized the accuracy, sensitivity, and negative and positive predictive values of the CAP for diagnosing significant steatosis was computed. All statistical analyses were performed using the SPSS software ver. 18 (SPSS, Chicago, IL, USA). Statistical results associated with *P*-values of less than 0.05 were considered significant.

RESULTS

Patient characteristics

THE BASELINE CHARACTERISTICS of the 155 patients are shown in Table 1. The median age was 55.0 years (range, 24–91), and 92 patients were male. Etiologies of chronic liver diseases were chronic hepatitis B ($n = 17$), chronic hepatitis C ($n = 58$), NASH ($n = 40$), unknown etiology ($n = 35$) and normal liver ($n = 5$). Their median BMI was 24.4 kg/m^2 (range, 15.4–39.2). The patients' median CAP value was 231.0 dB/m (range, 100–400) and their median LSM was 10.7 kPa (range, 2.60–75.0). CT examinations were available in 97 patients, and the median L/S ratio of these patients was 1.05 (range, −0.144 to 2.03).

Table 1 Bioclinical and historical characteristics of the patients

Characteristics	Patient data
No. of patients	155
Age (years)	55.0 (24–91)
Sex (male/female)	92/63
Etiology (B/C/NASH/others)	17/58/40/40
Height (m)	1.61 (1.40–1.79)
Bodyweight (kg)	64.0 (39.5–117.2)
Body mass index (kg/m^2)	24.4 (15.4–39.2)
AST (IU/L)	52.0 (14–467)
ALT (IU/L)	64.2 (7–657)
Total bilirubin (mg/dL)	1.0 (0.3–9.3)
Serum albumin (g/dL)	4.2 (2.8–5.4)
Prothrombin (%)	93.7 (43–140)
Platelet count (×104/μL)	19.3 (6.2–54.3)
Triglycerides (mg/dL)	113.5 (23–479)
Total cholesterol (mg/dL)	182.9 (68–336)
High-density lipoprotein cholesterol (mg/dL)	60.5 (12–179)
Low-density lipoprotein cholesterol (mg/dL)	113.6 (26–204)
Fasting blood sugar (mg/dL)	108.9 (21–179)
HbA1c (NGSP, %)	6.0 (4.8–10.1)
Controlled attenuation parameter (CAP, dB/m)	231.0 (100–400)
Liver stiffness measurements (LSM, kPa)	10.7 (2.60–75.0)
L/S ratio	1.05 (−0.144 to 2.03)

All data are median (range).
ALT, alanine aminotransferase; AST, aspartate aminotransferase; B, HBs antigen positive; HbA1c, hemoglobin A1c; C, HCV antibody positive; L/S, liver/spleen; NASH, non-alcoholic steatohepatitis; NGSP, National Glycohemoglobin Standardization Program.

CAP values for steatosis assessment

The CAP values of each steatosis grade are shown in Figure 1. The median (25–75% quartiles) CAP values for each steatosis grade were: 202.1 dB/m (range, 100–298) for S0, 279.5 dB/m (range, 179–400) for S1, 297.7 dB/m (range, 162–367) for S2 and 323.0 dB/m (range, 290–345) for S3. There were significant differences between the CAP values for S0 and S1 ($P < 0.0001$), S0 and S2 ($P < 0.0001$), and S0 and S3 ($P < 0.0001$). A box plot of the CAP values of the patients with mild (steatosis affecting <5% of hepatocytes) and significant (steatosis affecting ≥5% of hepatocytes) hepatic steatosis is shown in Figure 2. The median CAP value for mild hepatic steatosis was 202.1 dB/m, and that for significant hepatic steatosis was 285.1 dB/m. There was a significant difference between the CAP values for mild and significant hepatic steatosis ($P < 0.0001$).

The AUROC of the CAP for differentiating between mild and significant steatosis is shown in Figure 3. The

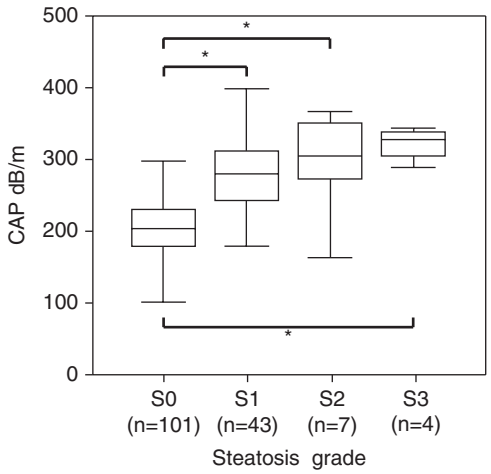


Figure 1 Distribution of controlled attenuation parameter (CAP) for each steatosis grade. The bottom and top of each box represent the 25th and 75th percentiles, giving the interquartile range. The line through the box indicates the median, and the error bars indicate the 10th and 90th percentiles. *$P < 0.0001$.

CAP displayed an AUROC value of 0.878 (95% CI, 0.818–0.939) for diagnosing significant hepatic steatosis. The optimal CAP cut-off value for differentiating between mild and significant hepatic steatosis was 232.5 dB/m, which produced sensitivity and specificity values of 87.0% and 77.2%, respectively, as well as a positive predictive value (PPV) of 75.2% and a negative predictive value (NPV) of 87.0%. The AUROC based on the individual etiologies were shown in Supporting Information Figure S1.

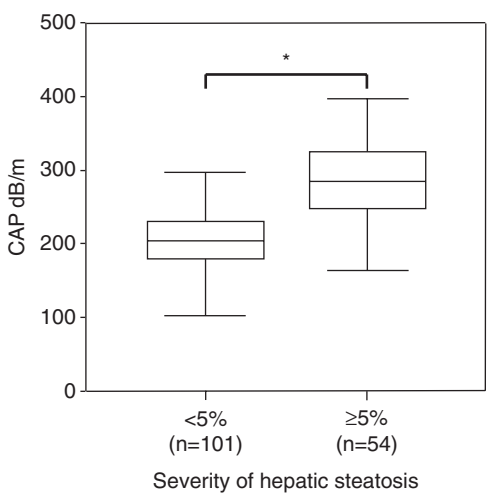
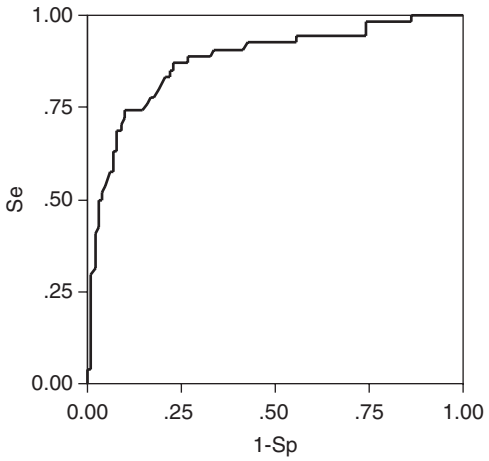


Figure 2 Box plot of controlled attenuation parameter (CAP) in hepatic steatosis according to severity <5% and ≥5%. There is significant correlation between CAP and frequency of steatosis. *$P < 0.0001$.



AUROC (95%CI)	0.878 (0.818-0.939)
Cut-off	232.5
Se/Sp	87.0%/77.2%
PPV/NPV	75.2%/87.0%

Figure 3 AUROC to compare the diagnostic accuracy of liver steatosis (<5% and ≥5%) assessed by controlled attenuation parameter. AUROC, area under the receiver–operator curve; NPV, negative predictive value; PPV, positive predictive value; Se, sensitivity; Sp, specificity.

The results of our univariate analysis of the factors associated with significant steatosis are shown in Table 2. Among the analyzed factors, BMI, cholinesterase, the CAP value and L/S ratio displayed the most significant associations with significant steatosis ($P < 0.0001$). ALT ($P = 0.0001$), triglyceride ($P = 0.002$), HbA1c ($P = 0.002$), alkaline phosphatase ($P = 0.007$), white blood cell ($P = 0.020$), platelet count ($P = 0.020$), GGT ($P = 0.028$), FBS ($P = 0.036$) and total cholesterol ($P = 0.043$) also displayed significant associations with significant hepatic steatosis. In the multivariate analysis, only the CAP value (odds ratio, 27.656; 95% CI, 4.762–160.622; $P = 0.0002$) and L/S ratio (odds ratio, 10.881; 95% CI, 2.101–56.361; $P = 0.004$) were significantly associated with significant steatosis (Table 3).

DISCUSSION

IN JAPAN, MUCH attention has been paid to HBV/HCV-infected patients over the past few decades because there are high numbers of carriers of these viruses in Japan, and most cases of cirrhosis and hepa-

Table 2 Factors associated with steatosis ≥5% on liver biopsy (univariate analysis)

Variable		Severity of hepatic steatosis				*P*-value
		<5%		≥5%		
		n	Mean ± SD	*n*	Mean ± SD	
Age	<60/≥60	50/51	45.8 ± 9.8/66.6 ± 6.1	34/20	44.7 ± 10.3/65.6 ± 4.8	0.129
Sex	Female/male	44/57		19/35		0.391
BMI (kg/m^2)	<25/≥25	74/27	21.6 ± 2.0/26.8 ± 1.9	18/36	23.1 ± 2.0/29.3 ± 4.0	<0.0001
AST (IU/L)	<33/≥33	50/51	25.1 ± 5.0/90.9 ± 99.5	19/35	24.1 ± 5.6/49.2 ± 17.7	1.000
ALT (IU/L)	<35/≥35	51/50	24.0 ± 7.0/113.8 ± 114.0	12/42	24.9 ± 8.0/65.0 ± 22.7	0.0001
ALP (IU/L)	<359/≥359	68/33	223 ± 60/587 ± 243	47/7	222 ± 55/525 ± 189	0.007
GGT (IU/L)	<41/≥41	53/48	23.4 ± 8.6/281 ± 522	18/36	26.0 ± 9.6/103 ± 73	0.028
Cholinesterase (IU/L)	<300/≥300	69/32	224 ± 58/339 ± 35	16/38	228 ± 56/381 ± 50	<0.0001
Total bilirubin (mg/dL)	<1.2/≥1.2	83/18	0.74 ± 0.19/2.48 ± 1.9	47/7	0.73 ± 0.19/1.51 ± 0.38	0.498
Serum albumin (mg/dL)	<4.3/≥4.3	51/50	3.73 ± 0.39/4.50 ± 0.26	24/30	3.97 ± 0.26/4.64 ± 0.31	0.503
Prothrombin (%)	<70/≥70	5/96	59.8 ± 10.5/94.7 ± 12.8	2/52	57.5 ± 5.0/96.4 ± 10.9	1.000
White blood cell (/μL)	<4000/≥4000	25/76	3318 ± 578/6143 ± 1806	5/49	3522 ± 485/6929 ± 2836	0.020
Platelet count (/μL)	<22×10^4/≥22×10^4	75/26	15.4 ± 4.1/27.4 ± 5.2	30/24	15.4 ± 4.1/27.4 ± 6.6	0.020
Triglyceride (mg/dL)	<149/≥149	81/13	85.9 ± 28.7/182 ± 46.5	32/19	82.5 ± 29.7/236 ± 83.8	0.002
Total cholesterol (mg/dL)	<179/≥179	56/45	149 ± 25/213 ± 33	20/34	162 ± 15/212 ± 22	0.043
FBS (mg/dL)	<109/≥109	65/33	97.7 ± 6.6/141.8 ± 37.0	25/27	99.3 ± 6.7/133.9 ± 32.0	0.036
HbA1c (NGSP, %)	<6.2/≥6.2	63/14	5.6 ± 3.7/6.5 ± 0.6	26/21	5.2 ± 0.3/6.9 ± 1.3	0.002
CAP (dB/m)	<232.5/≥232.5	76/25	182 ± 34/263 ± 31	7/47	196 ± 24/298 ± 41	<0.0001
LSM (kPa)	<10.7/≥10.7	77/24	6.0 ± 1.8/29.0 ± 22.0	36/18	6.1 ± 2.1/15.5 ± 4.6	0.255
L/S ratio	≥1.1/ < 1.1	40/11	1.27 ± 0.16/1.01 ± 0.07	13/33	1.18 ± 0.08/0.74 ± 0.29	<0.0001

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; FBS, fasting blood sugar; CAP, controlled attenuation parameter; GGT, γ-glutamyltransferase; HbA1c, hemoglobin A1c; L/S, liver/spleen; LSM, liver stiffness measurement; NGSP, National Glycohemoglobin Standardization Program; SD, standard deviation.

tocellular carcinoma in Japan are associated with persistent HBV or HCV infection.[25] In recent years, NAFLD has become a major social problem in Japan due to the Westernization of lifestyles and the increasing rates of obesity and diabetes.[26] Approximately 30% of NAFLD patients are considered to progress to NASH, a more severe form of NAFLD, which leads to more advanced fibrosis and ultimately cirrhosis.[27] Among chronic viral hepatitis patients, liver steatosis is a risk factor for infection and treatment failure.[5] Chronic HCV infection is associated with fatty liver changes, and HCV patients display a higher incidence of fatty changes than patients with other chronic liver dysfunctions.[28,29] Furthermore, Okanoue *et al*. demonstrated that the frequency of liver steatosis was significantly lower in hepatitis C patients who achieved an SVR.[11] Therefore, it is important to diagnose and evaluate the severity of steatosis to improve its treatment and prognosis. Liver biopsy is the current gold standard for evaluating steatosis and other histological lesions;[3,4,14] however, liver biopsy can be affected by sampling error,[15,16] is an invasive and often painful procedure, and can result in severe complications.[30,31] Moreover, the repetition of liver biopsy to monitor changes in steatosis is difficult. In light of these obstacles, various non-invasive methods have been developed for the assessment of hepatic histology, particularly fibrosis.[17,32] Steatosis can also be diagnosed by non-invasive means and is mainly diagnosed using conventional imaging techniques, for example, CT, multiple resonance imaging (MRI), magnetic resonance

Table 3 Factors associated with steatosis ≥5% on liver biopsy (multivariate analysis)

Variable	Odds ratio	95% confidence interval	*P*-value
CAP ≥232.5 (dB/m)	27.656	4.762–160.622	0.0002
L/S ratio <1.1	10.881	2.101–56.361	0.004

Factors: body mass index, ≥25; alanine aminotransferase, ≥35; alkaline phosphatase, ≥359; γ-glutamyltransferase, ≥41; cholinesterase, ≥300; white blood cell, ≥4000; platelet count, ≥20 × 10^4; triglyceride, ≥149; total cholesterol, ≥179; fasting blood sugar, ≥109; hemoglobin A1c, ≥5.7; controlled attenuation parameter (CAP), ≥243.5; liver/spleen (L/S) ratio <1.1.

spectroscopy or ultrasonography, with the latter being the most commonly used method.[33,34] However, these techniques suffer from various pitfalls; namely, they are costly, not easily available, operator-dependent and/or display poor sensitivity.[32,34,35] Moreover, existing methods cannot simultaneously assess hepatic fibrosis and steatosis. To overcome these limitations, the CAP, which was designed to produce immediate results and be reproducible and operator- and device-independent, was developed.[36] Previous studies have shown the utility of the CAP for assessing the severity of steatosis.[18–21,23,37,38]

In our study, we have demonstrated that the CAP is correlated with steatosis grade and can be used to non-invasively identify steatosis in Japanese patients. The AUROC of the CAP for detecting significant steatosis (≥5% of hepatocytes affected) was 0.878 (95% CI, 0.818–0.939), and a CAP threshold of 232.5 dB/m demonstrated 87.0% sensitivity and 77.2% specificity for detecting significant steatosis. This study is the first to report the utility of the CAP in Japanese subjects. A previous study reported similar findings in a study of 153 patients with chronic liver disease due to any etiology, in whom the CAP displayed an AUROC of 0.81 for diagnosing significant stenosis, and a CAP threshold of 283 dB/m demonstrated 76% sensitivity and 79% specificity for significant steatosis.[20] Sasso *et al*. studied 115 patients with various liver disorders. As a result, they found that the CAP displayed an AUROC of 0.91 for detecting significant steatosis, and a CAP threshold of 238 dB/m exhibited 91% sensitivity and 81% specificity for significant steatosis.[18,19] The discrepancies between these studies may be related to differences in the study populations including in their disease etiologies, the prevalence of obesity and the extent of subcutaneous adiposity, the severity of the patients' steatosis and racial differences, all of which could influence CAP performance because of spectrum bias. Further studies in larger cohorts would help to refine the patient data characteristics of the CAP.

In some patients, steatosis can progress to cirrhosis and end-stage liver disease.[39] Furthermore, liver transplantation is the only treatment option for end-stage liver failure. In such cases, it is important to select an appropriate donor in order to achieve good donor and recipient outcomes. The implantation of donor livers with severe fatty infiltration is associated with a high incidence of severe ischemic damage, resulting in primary dysfunction and/or primary non-function after liver transplantation.[40–44] To reduce the risk of progressive liver disease and achieve a successful liver transplantation, it is important to estimate the extent of liver steatosis. A few reports have suggested that there is a risk associated with mild macrovascular steatosis after right hepatectomy in living donors.[45,46] Goldaracena *et al*. reported that the liver pool can be safely expanded using extremely marginal liver grafts. It is considered that steatosis should not affect more than 30% of such grafts;[12] therefore, most centers only accept donor livers from individuals in whom hepatic steatosis affects 20% or less of the liver.[47–49] In this study, we thought that we could detect steatosis more strictly by using a 5% cut-off value according to Kleiner *et al*.[23] Accordingly, we selected 5% as the cut-off value. When we selected a 10% cut-off value, the result was similar (AUROC, 0.878 [95% CI, 0.810–0.947]; CAP threshold, 258.0 dB/m; sensitivity, 81.8%; specificity, 87.4%).

Imaging studies such as ultrasonography, CT and MRI can depict the characteristic features of fatty liver.[30–34,39] In particular, CT has proven to be useful for diagnosing and quantifying liver fat non-invasively. The HU attenuation value of the liver on CT scans is usually higher than that of the spleen. However, the presence of fat in the liver will reduce its HU attenuation value. Thus, an L/S ratio of less than 1.0 can be used to effectively diagnose the presence of liver fat, and studies also have shown that liver HU attenuation values of less than 40 HU represent a liver fat content of more than 30%.[34,39] Furthermore, Oliva *et al*. reported that the use of an L/S ratio of less than 1.2 resulted in all cases of fatty liver being detected, whereas some authors reported cut-off values of 1.0 or 1.1 for fatty liver.[49]

In our study, significant hepatic steatosis was significantly associated with a CAP of 232.5 dB/m or more and an L/S ratio of less than 1.1. These results demonstrate that the CAP accurately predicts the degree of steatosis. Furthermore, the CAP is an easier and cheaper procedure than CT and does not involve radiation exposure.[47,49,50]

This study had several limitations. One limitation was that our study involved a relatively small population, which limited the precision of our results. Second, although a correlation was observed between the degree of steatosis and the CAP ($r = 0.517$, $P < 0.0001$, Pearson product-moment correlation coefficient), our study population was highly selected; namely, it included patients with mild hepatic steatosis, which also limited the precision of our results. Third, our sample size was limited in part because of the difficulty of obtaining valid CAP measurements in obese patients using the FibroScan M probe. Further studies are necessary to develop a CAP algorithm for such patients. Finally, selection bias was another limitation of this study

because we did not examine patients who displayed clinical evidence of hepatic decompensation.

In conclusion, the CAP can be used for steatosis detection and semiquantification and possesses several advantages; namely, it is non-invasive, easy to perform, provides immediate results and is inexpensive in comparison with other measurement modalities. Moreover, the CAP can provide an immediate assessment of steatosis and be obtained at the same time as the LSM, which is used to stage hepatic fibrosis. Further studies are necessary to validate our findings in larger cohorts and to define optimal CAP thresholds. If these results are confirmed, the CAP could be useful for the diagnosis of steatosis, not only in chronic liver disease, but also in liver graft evaluations, longitudinal monitoring of disease progression or the response to therapy, population-based epidemiological or observational studies, and drug discovery.

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SUPPORTING INFORMATION

ADDITIONAL SUPPORTING INFORMATION may be found in the online version of this article at the publisher's website:

Figure S1 (a) AUROC to compare the diagnostic accuracy of liver steatosis (<5% and ≥5%) assessed by CAP in HBV patients. (b) AUROC to compare the diagnostic accuracy of liver steatosis (<5% and ≥5%) assessed by CAP in HCV patients. (c) AUROC to compare the diagnostic accuracy of liver steatosis (<5% and ≥5%) assessed by CAP in NASH patients. (d) AUROC to compare the diagnostic accuracy of liver steatosis (<5% and ≥5%) assessed by CAP in patients of other etiologies. AUROC, area under the receiver–operator curve; CAP, controlled attenuation parameter; HBV, hepatitis B virus; HCV, hepatitis C virus; NASH, non-alcoholic steatohepatitis; NPV, negative predictive value; PPV, positive predictive value; Se, sensitivity; Sp, specificity.