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Quantitative Assessment of Steatosis in Liver Tissue Using Controlled Attenuation Parameter

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Hepatic steatosis (or fatty liver) is a common histological finding in patients with metabolic syndrome, alcoholic hepatitis, or hepatitis C, or those who receive certain drugs such as steroids and amiodarone. The complication of hepatic steatosis in patients with other liver diseases such as hepatitis C leads to the progression of liver fibrosis and poor treatment response. Therefore, an accurate evaluation of hepatic steatosis is essential for clinical decision making and prognosis assessment. Abdominal ultrasonography is a highly accurate and commonly used tool for diagnosing fatty liver. The diagnostic criteria of this technique include the following: brightness contrast between the liver parenchyma and the right renal cortex; masking of the portal vein, hepatic vein, and gallbladder wall; and ultrasound attenuation in deep liver tissues. However, ultrasound has low sensitivity in diagnosing mild steatosis and is prone to the operator’s subjective opinion. Although computed tomography and magnetic resonance imaging play a certain role in diagnosing fatty liver, these techniques are limited by availability and radiation exposure. Computed tomography is suitable only for detecting steatosis with >30% fat accumulation. Although magnetic resonance imaging offers outstanding accuracy, it is less suited for regular screening for fatty liver because it is both complex and expensive. Currently, the gold standard for steatosis assessment is liver biopsy; however, it is invasive, costly, prone to sampling bias, and risks potential serious complications. Furthermore, in the clinical setting, repeated biopsies are not a feasible method for following up on the status of steatosis. To overcome these limitations, Fibroscan (© 502 Touch by Echosens (Paris, France)), a technology based on liver fibrosis, has been developed.

The measurement of ultrasound attenuation during transmission through biological tissues has multiple useful biomedical applications. Ultrasound attenuation, the energy loss when the sound wave passes through a medium, depends on: (1) the frequency of the ultrasound; and (2) the nature of the transmission medium. The standard ultrasound attenuation rates at 3.5 MHz in different human tissues are as follows: 175–630 dB/m in fat, 40–70 dB/m in liver, 315–385 dB/m in tendons, and 105–280 dB/m in soft tissues. Based on ultrasound attenuation principles and the effect of fat on attenuation, researchers developed a new method, named controlled attenuation parameter (CAP), to quantify the degree of steatosis in liver tissue [1]. This technology uses Vibration-Controlled Transient Elastography (VCTE), which emits ultrasound at a fixed center frequency of 3.5 MHz and traces the velocity of shear waves to measure liver firmness. In addition, CAP uses the frequency data collected from the same examination area to assess the total attenuation of the ultrasound signal, including the paths from and to the probe. The result is expressed in dB/m, ranging from 100 dB/m to 400 dB/m (a
higher value represents a larger proportion of steatosis). The CAP technology is noninvasive, is easy to use, and provides real-time surveillance. Furthermore, because the procedure can monitor an area 100 times that of liver biopsy, it eliminates operator sampling bias. Fibroscan allows the clinician to evaluate and quantify steatosis while assessing fibrosis, thus facilitating post-treatment comparison through follow ups.

Myers et al [2] analyzed 153 patients who received liver biopsy and CAP-coupled Fibroscan simultaneously. They found that patients with a higher degree and proportion of steatosis confirmed by liver biopsy also had higher CAP scores. A recent large-scale study (comprising 5323 tests) found CAP scores associated with clinical disease presentation and blood test values. Researchers found that patients with fatty liver-triggering conditions such as metabolic syndrome, alcoholism, hypertriglyceridemia, large abdominal circumference, diabetes or hypertension, and high body mass index ($>30$ kg/m$^2$) had increased CAP values accordingly. CAP areas under the receiver operating characteristic curve were $0.79$ [95% confidence interval (CI), $0.74–0.84$; $p < 0.001$], $0.84$ (95% CI, $0.80–0.88$, $p < 0.001$), and $0.84$ (95% CI, $0.80–0.88$, $p < 0.001$) in patients with $>10\%$, $>33\%$, and $>66\%$ steatosis, respectively [3]. Other clinical studies also showed CAP examination to be free from operator bias. In a prospective study, two independent operators performed CAP examinations on 118 patients. The results revealed good consistency between the CAP data from the two operators, with an intraclass correlation coefficient of $0.84$ (95% CI, $0.77–0.88$) [4]. In addition, CAP can be used to diagnose fatty liver regardless of etiology. One study recruited 146 patients with chronic hepatitis B, 180 with chronic hepatitis C, and 63 with nonalcoholic fatty liver; all 389 patients received liver biopsy and CAP examination. CAP showed areas under the receiver operating characteristic curve of $0.683$, $0.793$, and $0.841$ in chronic hepatitis B patients with $>6\%$, $>33\%$, and $>66\%$ steatosis, respectively. In addition, the accuracy of diagnosing fatty liver did not differ significantly between groups [5].

Fibroscan coupled with CAP shows promise as a noninvasive tool for assessing liver fibrosis and steatosis. Specifically, as this technology provides longitudinal data, it can be effectively used to evaluate treatment outcomes and prognosis in patients with chronic viral hepatitis, nonalcoholic fatty liver disease, or alcoholic hepatitis, as well as other chronic liver diseases.

References


