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Research Article

The Prevalence of Fatty Liver Disease Assessed by Controlled Attenuation Parameter (CAP) by Fibroscan in Chronic Liver Disease

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Abstract

Introduction and Aim: The CAP (Controlled Attenuation Parameter) function of FibroScan® is a new non-invasive diagnostic tool that allows the quantification of hepatic steatosis at the same time as elastometry. It calculates the attenuation of ultrasonic signals. The aims of our study are to determine the role of CAP values in predicting liver steatosis in patients with chronic liver diseases, and to determine factors associated with the presence of steatopathy.

Methods: Prospective, cross-sectional study, which was monocentric extending over 1 year. A CAP measurement by compact 530 fibroscan was performed using the M probe, or XL probe in the case of obesity, in all patients with chronic liver disease referred for liver elastometry, whatever its etiology and severity. Liver steatosis is graded based on the percentage of fat within the hepatocytes: grade 0: < 5%, grade 1: 5% -3 3%, grade 2: 34% - 66%, and grade 3: > 66%.

Results: Hepatic steatosis diagnosed by Fibroscan's CAP function is present in 40% of patients referred for evaluation of hepatic fibrosis for all causes of chronic liver disease. Severe hepatic steatosis is present in half of these patients. CAP values were significantly correlated with body mass index ($p < 0.001$), there was no correlation between CAP values and age, sex or etiology of hepatopathy nor with blood glucose, trigylceridemia, cholesterol level and liver enzymes.

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

Keywords: *Controlled Attenuation Parameter; FibroScan; Liver Steatosis; Non-Invasively Diagnose*

Introduction

NAFLD is one of the clinical consequences of obesity and can progress to NASH, that may lead to cirrhosis, hepatocellular carcinoma and chronic liver failure [3,4]. Liver steatosis is regarded to be a poor prognosis factor for treatment failure among patients with chronic viral hepatitis [5]. In addition, previous studies demonstrated that the frequency of liver steatosis was significantly lower in hepatitis C patients who accomplished a sustained virological response "SVR".

Liver biopsy remains the "gold standard" for diagnosing steatosis as well as for establishing the degree of liver fibrosis [3,4,14] however, it is invasive, subject to sampling error and is painful in some patients [15,16]. Several methods have been studied for the assessment of hepatic steatosis by noninvasive means [17]. Due to the impaired propagation of ultrasound by fat, a new ultrasound method has been developed for detection and quantification of steatosis. This novel tool, called the controlled attenuation parameter (CAP) specifically targets liver steatosis using a process based on transient elastography. Although several reports have attested the value of CAP in determining the extent of patient's hepatic steatosis [18-20].

Objective of the Study

The objectives of our study were firstly, to validate the potential of CAP to detect and quantify steatosis, and secondly, to determine the factors associated with the presence of steatopathy in patients with chronic hepatitis due to any cause.

Methods

Study population

Were enrolled between May 2019 and July 2020 two hundred thirty six consecutive patients who present chronic liver disease due to any etiology and who underwent previously an abdominal ultrasound were referred for liver elastometry examination, to calculate CAP and liver stiffness measurement (LSM) values.

LSM and CAP measurement

The tip of the probe transducer will be covered with coupling gel and placed on the skin, between the ribs at the level of the right lobe of the live. All patients had their CAP measured using a standard: The center frequency of the ultrasound waves is 2.5 MHz for the XL probe and 3.5 MHz for the M probe. The LSM (liver stiffness measure) was determined using FibroScan M probe or in case of obesity, XL probe. The fibroscan is a vibration-controlled transient elastography "VCTE" device that measures the stiffness of the liver. The median values of more than ten valid measurements was adopted as the final liver stiffness value used to quantify liver fibrosis and steatosis and was expressed in kPa.

LSM failure was defined as zero valid shots, and unreliable examinations were defined as fewer than 10 valid shots, an interquartile range (IQR)/LSM greater than 30%, or a success rate less than 60%. 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.

Therefore, the LSM and CAP were obtained simultaneously and in the same volume of liver parenchyma. The median of the individual CAP values was used as the final CAP value, which was expressed in dB/m.

The threshold values used for the diagnosis of steatosis were respectively 233/242 dB/m and 291 dB/m for the diagnosis of severe steatosis.

Clinical and biological evaluations

Different parameters were assessed during the follow-up in consultation: The following data were collected: age, sex, etiology, body mass index (BMI); liver function tests, lipid profile test, hemoglobin A1c (HbA1c) levels, and finally blood count.

All blood sample were taken in our hospital laboratory.

Statistical analysis

A multivariate analysis was developed to investigate potential relationships between LSM, CAP and histological parameters (activity grade, fibrosis stage, and steatosis grade). Box plots were used to assess the utility of the non-invasive methods for differentiating between each grade of steatosis. Statistical analyses of the present study was analyzed by using the IBM SPSS software ver 24.0. the results obtained with a p-value less than 0.05 (typically ≤ 0.05) were statistically significant.

Results

Patient characteristics

Out of 236 patients referred for fibrosis evaluation during this period, 101 were diagnosed with hepatic steatosis (42%). The mean age was 50,2 years (range 24 - 91), and 62,5 patients were female. Etiologies of chronic liver diseases were chronic hepatitis B in 37,6% of cases (n = 38), chronic hepatitis C in 25,7% (n = 26), NASH in 30,6% (n = 31), auto immune hepatitis AIH in 3,9% of cases (n = 4), and primary biliary cholangitis in 2% (n = 2). None of our patients had HVC-HVB coinfection.

42.5% were overweight (BMI ≥ 25 kg/m^2) and 40% were obese (BMI ≥ 30 kg/m^2). The use of the M-probe allowed reliable results to be obtained in 100% of cases. The use of the XL probe was necessary in 27.5% of patients (n = 11).

The median CAP and LSM values were 281.8 dB/m (± 58.7) and 8.4 kPa respectively.

Variable	NAFLD (n=101)
Age(yr)	50,2 (23 - 75)
Sex (male/female), % female	39/62, 61%
BMI, median (range, kg/m^2)	29,4 (19,9 - 40,1)
BMI > 25 kg/m^2	83 (82,5%)
Etiologies, number(B/C/Nash/Others)	38/26/31/6
HbA1c	6,1(4,9 - 9,8)
HDL cholesterol (mg/l)	0,42(0,4 - 2)
Triglycerides (g/l)	1,4(0,3 - 4)
LDL cholesterol (mg/dl)	1,1(0,8 - 2)
ASAT (U/L)	31(7 - 150)
ALAT (U/L)	33(10 - 299)
Platelet (*104/mL)	22.5 (6.8 - 54.1)
Liver Stiffness (range, Kpa)	8,4(3,4 - 32,1)
CAP (db/m)	281,8 (± 58,7)

Table 1: *Demographical, clinical, biochemical and histological characteristics of 101 patients with nonalcoholic steatohepatitis.*

The median (quartiles 25 - 75%) CAP values for each grade of steatosis were: 201.9 dB/m for S0, 248.5 dB/m (range, 180 - 401) for S1, 273.7 dB/m (range, 159 - 356) for S2 and 331.0 dB/m (range, 291 - 346) for S3 (Figure 1).

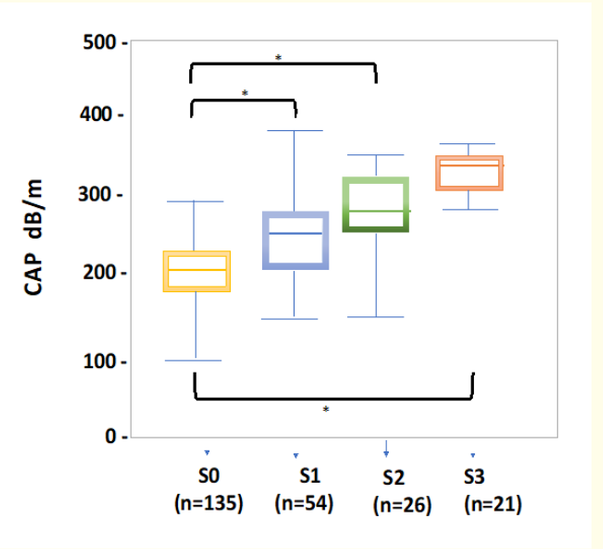

Figure 1: *Distribution of controlled attenuation parameter (CAP) for each steatosis grade. The bottom and top of each box represent the 25th and 75th percentiles, giving the interquartile range. The line through the box indicates the median, and the error bars indicate the 10th and 90th percentiles.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

As observed on the box plot, 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). Severe steatosis was noted in 20% of our patients. Patients initially referred with the diagnosis of NASH (6 patients) had steatosis also diagnosed by CAP in 83.3% of cases. This steatosis was severe in 66.6% of cases (n = 4).

In this analytical study, the CAP values were significantly correlated with body mass index (p < 0.001), FBS (P = 0.046), and with HbA1c (P = 0.039), In contrast, CAP values were not correlated with blood glucose, triglyceridemia, cholesterol, and liver enzymes, total cholesterol (P = 0.065), triglyceride (P = 0.052), ALT (P = 0.255), alkaline phosphatase (P = 0.472), GGT (P = 0.078),white blood cell (P = 0.539), platelet count (P = 1.000).

85% of patients with steatosis and 55% of patients with severe steatosis by CAP, didn't have steatosis on ultrasound. In addition, 97% of patients without hepatic steatosis by CAP didn't have either steatosis on ultrasound.

Discussion

In recent years, Nonalcoholic fatty liver disease (NAFLD) has gradually become one of the most common chronic liver diseases worldwide, this is mainly due to the increase in obesity and diabetes rates but also to the modernisation of lifestyles [1].

NAFLD progresses in about one third of cases to a more severe form: NASH, which leads to more advanced fibrosis and eventually to cirrhosis [2].

Hepatic steatosis is considered a factor in treatment failure and also in infection in patients with chronic viral hepatitis [3].

Liver biopsy is currently the gold standard for the evaluation of both steatosis and other histological lesions [4-6]; however, it is an invasive, painful method that can lead to serious complications. Moreover, its reliability is subject to possible sampling errors (a liver biopsy examining only 1/50,000 of the liver mass) [7,8]. Taking these difficulties into account, several non-invasive methods have been developed to assess liver histological lesions [9,10]. Steatosis can also be diagnosed by non-invasive radiological means: CT scan, magnetic resonance imaging (MRI), or ultrasound, with the latter being the most commonly used method [11,12]. However, these conventional imaging techniques have several constraints: they are operator dependent, expensive, and sometimes difficult to obtain [10,12,13].

Thus, CAP was designed to get ahead of these obstacles and to have immediate results independent of the operator's device [14].

Especially since the LSM and CAP values measured by FibroScan have been shown to be accurate for both steatosis and fibrosis in the liver [20,21].

Many studies have demonstrated the good performance of the CAP for assessing the severity of steatosis [15-19].

Importantly, CAP detects steatosis independent of liver fibrosis stage [22].

In our study, CAP was correlated with the grade of steatosis and is therefore a non-invasive way to detect steatosis in our Moroccan patients.

In our study, the factors associated with steatosis were represented by diabetes and obesity with a highly significant p value, this is consistent with previous studies where high BMI has been reported as one of the factors associated with liver steatosis [23,24].

For other non-invasive methods, abdominal Ultrasound (AUS) is the most used imaging tool for the initial assessment and diagnosis of steatosis as it is a non-invasive, available and not expensive, however, AUS has limited sensitivity and doesn't reliably detect steatosis when it is < 20% or when patients have a high body mass index (BMI) (> 40 kg/m^2) [3].

Ultrasound is also limited in patients with small amounts of liver fat, Indeed, in patients with < 20% of hepatic steatosis on histology, the sensitivity of ultrasound is estimated at 55%.

In addition, hepatic fibrosis may increase liver echogenicity to a similar degree to steatosis and that of steatosis and therefore a liver with severe fibrosis without steatosis may be indistinguishable from severe steatosis without fibrosis.

In our study, 85% of patients with steatosis and 55% of patients with severe steatosis by CAP, didn't have steatosis on ultrasound. In addition, 97% of patients without hepatic steatosis by CAP didn't have either steatosis on ultrasound.

This study had several limitations. One limitation is that the population size is relatively small, which may make our results imprecise. and also partly because of the difficulty of obtaining valid measurements of CAP in obese patients. In the future, it will be desirable to realized more studies to develop a CAP algorithm for such patients.

Conclusion

CAP has been shown to be good to excellent non-invasive tool, in the clinical management of patients with chronic liver disease for the detection and the quantification of hepatic steatosis and has several advantages: It provides immediate results at the same time as the CAP and is inexpensive compared to other measurement modalities.

In our study, CAP was mainly influenced by BMI, but is not found to be associated with liver fibrosis.

Further studies are desirable to validate our results in larger cohorts and to define optimal WTP thresholds.

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