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Hepatology highlights

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de Oliveira AC, *et al.* Utility and limitations of APRI and FIB4 to predict staging in a cohort of nonselected outpatients with hepatitis C

de Oliveira AC, *et al.* in this issue of Annals of Hepatology focus on the usefulness of AST-to-platelet ratio index (APRI) and Fibrosis-4(FIB4) values as predictive algorithms in patients with C hepatitis.[1,2]

Chronic hepatitis C virus infection (CHC) is currently the leading cause of liver cirrhosis, hepatocellular carcinoma and represents an of indication for liver transplantation. CHC therefore represents a major burden of care worldwide. Due to elevated costs of new antiviral agents, a careful stadiation of liver injury is required in the treatment decision making process, which is still mainly based on liver histology from biopsy specimens during an invasive procedure which carries some risks and sampling errors and is not well accepted by patients. Therefore, the identification of noninvasive markers is being actively investigated. At this aim, WHO suggests the use of simple algorithms, i.e. APRI and FIB4 (AST, ALT, platelet count, and patient age) score for staging CHC, in view of their convenience, easy access, and validated accuracy in developing countries. Fibrotest®, and transient elastography, although perform well, are costly techniques not yet diffused in low- and middle-income countries.

In this paper, the authors assessed the value of APRI and FIB4 tests in identifying fibrotic livers in a cohort of non-selected CHC patients (798 adult outpatients analyzed retrospectively) who underwent a prior liver biopsy and histology (Metavir) in a referral center at São Paulo, Brazil. The predominant form (> 71%) was genotype 1. At histology, 288 patients (36%) had no fibrosis or showed early-stage fibrosis (F0 - F1), 64% of patients had significant fibrosis (> F2) with 44% showing advanced fibrosis and 28% cirrhosis.

Using the recommended cut off values, approximately 30 - 40% of the patients could not be correctly classified. In the remainder, either APRI or FIB4 alone correctly diagnosed 80 - 85% of cases (the AUROC for significant fibrosis, advanced fibrosis, and cirrhosis were 0.809, 0.819, and 0.815, respectively for the APRI test and 0.803, 0.836 and 0.852, respectively for FIB4). As reported, FIB4 performed better for advanced fibrosis, APRI lower and upper values performed better for diagnosis of cirrhosis, although a better AUROC was obtained by FIB4 test. Sequential use of the APRI and FIB4 tests did not provide a further advantage. However, combined application of the tests improved their discriminant ability for the different degrees of hepatic fibrosis and reduced the number of incorrectly diagnosed cases.

In conclusion, de Oliveira, *et al.* show that APRI or FIB4 tests for detection of hepatic fibrosis may be a viable alternative to liver biopsy in routine practice and in referral centers in low- and middle-income countries to select CHC patients who are candidate for treatment. Despite relatively good accuracy, approximately one-third of patients could not be assessed by both methods as the obtained values were not located between the given cutoff points. This subgroup of CHC patients would require additional diagnostic methods to assess liver fibrosis and to decide for treatment option.

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Barros RK, *et al.* Nonalcoholic steatohepatitis in severely obese subjects: coffee consumption *vs.* disease severity

Barros RK, *et al.* in this issue of *Annals of Hepatology,* assessed the correlation between the degree of liver steatosis at histology, insulin resistance (IR) and coffee consumption in a group of obese patients living in Brazil.

Obesity is a major emerging public health problem worldwide, and is associated with a progressively increasing prevalence rates of related metabolic diseases including nonalcoholic fatty liver disease (NAFLD). NAFLD occurs in 90 to 100% of severely obese individuals. One of the main factors responsible for the severity of liver injury in NAFLD patients is the ongoing development of chronic inflammatory status and IR with increased accumulation of intrahepatic triglycerides.[1] Intracellular events will induce progressive mitochondrial dysfunction and oxidative stress, which, when combined with genetic predisposition,[2] favor the progression to more advanced forms of nonalcoholic steatohepatitis, and significant liver fibrosis and cirrhosis.

Coffee consumption has been associated with reduced progression of liver fibrosis in both hepatitis C infection and NAFLD; however, few data are available in severely obese individuals.

In this paper, the authors performed a cross-sectional cohort study to assess the association between coffee consumption, IR (HOMA-index) and histological NAFLD severity in 112 severely obese patients undergoing bariatric surgery and liver biopsy during surgery. The amount of ingested coffee per week was estimated by questionnaire and patients were classified into three groups according to their weekly consumption, i.e. 0.0 - 239.9 mL, 240 - 2099.9 mL and over 2,100 mL. A constant consumption of coffee was reported by 72.3% of patients. There were no statistical differences between groups regarding the presence of IR (84.8% *vs.* 74.2% *vs.* 75.9%). Percent of patients with normal liver histology increased as coffee consumption increased (14.7%, 21.9%, 24.3%, respectively). Percentages of patients with steatohepatitis (NASH) were 65.7%, 70.3%, 57.5% in the 3 groups of coffee consumption, respectively, and tended to be lower in patients reporting higher coffee consumption. This study shows that severely obese individuals who reported greater coffee consumption had a less frequent histological diagnosis of NASH with and without fibrosis and a higher percentages of normal livers.

The potential protective role of coffee against the appearance and progression of liver diseases is a topic which has gained attention in the literature. Caffeine, triacylglycerol, tocopherols, chlorogenic acid, cafestol, kahweol are contained in coffee which also displays antioxidant and anti-inflammatory properties. A beneficial metabolic effect is therefore anticipated, at least in theory. Since the rate of IR did not differ and the presence of metabolic syndrome was comparable in the three classes of patients, it is conceivable that the protective effect afforded by coffee consumption relies on its antioxidant properties and mitochondria protection.

Further studies are needed to better establish the hypothesis of a protective effect of coffee on liver steatosis and its variants and to strengthen the promising results of the study by Barros, *et al.* Moreover, differences in coffee consumption patterns, preparation and contents need to be carefully addressed in future studies.

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Ferraioli G, *et al.* Liver stiffness assessed by transient elastography in patients with β thalassaemia major

Ferraioli G, *et al.* in this issue of *Annals of Hepatology*, studied the liver stiffness by transient elastography (TE) in patients with β thalassemia major (βTM) with and without hepatitis C virus (HCV) infection, compared to healthy controls.

βTM is a leading cause of liver iron overload, both as a consequence of recurrent transfusion and of increased iron absorption. Hepatic iron overload can lead to the development of liver fibrosis. Liver biopsy with histology is the gold standard both for the evaluation of liver fibrosis and hepatic iron content; however, the procedure is invasive, not totally risk-free, can have sampling errors and is not well accepted by patients. Additional markers of hepatic iron overload are serum ferritin levels, although values can be influenced by inflammation and malignancies.

Liver iron concentration is critical to determine clinical outcome in patients with bTM.[1] Therefore, non-invasive methods for detecting iron overload, such as T2 star magnetic resonance imaging (MRI T2*) and superconductive quantum interference device (SQUID) liver susceptometry, are being employed. However, such techniques do not provide accurate information on the presence and extent of hepatic fibrosis. Some recent studies have addressed the potential usefulness of TE to assess liver fibrosis in a small cohort of patients with βTM.[2]

The authors investigated the influence of iron overload on TE values by FibroScan in a large series of patients with βTM (n = 119) with (n = 41) or without (n = 78) HCV infection, and in n = 183 control healthy subjects enrolled in a cross-sectional multicenter study in Italy. Secondary aim was to assess potential correlation between βTE, serum ferritin, MRI T2* or liver iron concentration (LIC) assessed with SQUID susceptometry.

A significant fibrosis was registered in 40/119 βTM patients: 23/40 were HCV positive and 17/40 HCV negative. A significantly higher TE values was noted in TM patients with HCV infection compared with those without. When adjusted for age and sex, patients negative for HCV showed a significantly higher liver stiffness than controls ($p < 0.0001$). Liver stiffness positively correlated with ferritin values ($r = 0.49$, $p < 0.0001$) whereas no correlation existed between TE values and MRI T2* or SQUID susceptometry. As βTM patients had a significant increase in TE values also in the absence of HCV infection, iron accumulation is the cause of such finding.

The results of this study are promising but more evidences are needed to correlate the values of TE with total liver iron content in liver specimens. The use of TE to compare βTM with additional control groups, i.e. HCV infected patients without βTM would extend the results of this study.

CONFLICTS OF INTEREST

None.

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