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*Letter to the Editor*

# Hepatic artery resistive index as surrogate marker for fibrosis progression in NAFLD patients: A clinical perspective

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**Abstract**

Ultrasound (US) can reveal the presence of steatosis in non-alcoholic fatty liver disease (NAFLD), but its diagnostic accuracy to reveal signs of fibrosis is low except in advanced stages of disease (e.g. cirrhosis). Current guidelines suggest the use of clinical algorithms, such as the NAFLD fibrosis score, and elastography to predict the progression of fibrosis, and the integration of elastography improves the detection accuracy of liver stiffness. However, there is a lack of evidence about the correlation between clinical algorithms and conventional US, and elastography is limited by the relative low diffusion, necessity of training, and loss of diagnostic accuracy in patients with high body mass index (BMI), waist circumference, or increased thickness of parietal walls, with consequent significant rates of failure of measurement of liver stiffness. Recently, the measurement of hepatic artery resistive index (HARI) has demonstrated a significant positive correlation with fibrosis degree, as measured with NAFLD fibrosis score, suggesting that the fibrous tissue accumulation may result in increased arterial rigidity and, therefore, in a rise of resistance to flow, and that the different tissue composition of the liver (adipose versus fibrous) can influence HARI differently. These issues should be further investigated because some aspects are still unknown. The limited data currently justify the need of larger, prospective studies aimed at assessing whether HARI correlates with elastography results. In view of their effect on weight loss, serum lipid concentration, and hepatic arterial flow hemodynamics, it could be interesting to evaluate if lifestyle and diet changes can influence significantly HARI values in NAFLD patients.

**Keywords**

fatty liver disease, fibrosis, hepatic artery resistive index, non-alcoholic fatty liver disease, score, steatosis

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## Clinical perspective

Non-alcoholic fatty liver disease (NAFLD) is a common worldwide disorder characterized by imaging or histological evidence of steatosis occurring in patients with predisposing risk factors such as diabetes, hypertension, and hypercholesterolemia. Patients should have no specific etiology of liver disease such as viral hepatitis and alcohol abuse.[1,2]

Instrumental evaluation of NAFLD is made with conventional ultrasound (US), an inexpensive and

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largely diffused technique, which is reliable to reveal the presence of hepatic steatosis. Because of low cost, simple, and rapid execution for skilled operators, US is effective to detect several hepatic and extrahepatic disorders, and can be useful in almost all body organ and tissues.[3–6] However, US is limited in several clinical conditions, such as low compliance, high degree of meteorism, and non-fasting patients. US diagnostic accuracy is improved by the use of ultrasound contrast agents (UCAs), a relative novel class of drugs which has demonstrated a diagnostic efficacy not only in liver diseases, by differentiating benign from malignant lesions according to the contrast washout in portal venous and late phases,[7,8] but also in several extra-liver conditions, including other focal tumors,[9–11] rare disorders, and vascular malformations.[11,12] Their use has diffused in clinical practice, and contrast enhancement ultrasound (CEUS) can be considered a valid alternative to traditional imaging techniques such as contrast enhancement computed tomography and contrast enhancement magnetic resonance imaging (CECT and CMRI, respectively) for several clinical indications, with the advantage of absence of radiation exposure and nephrotoxicity. However, some limits are the same of conventional US such as low patient compliance and high degree of meteorism.[8]

Despite advances in the diagnosis of focal liver disorders, the diagnostic accuracy of conventional US to reveal signs of fibrosis progression is low except in advanced stages of the disease (e.g. cirrhosis). Current guidelines suggest the use of clinical algorithms such as NAFLD fibrosis score (NFS) and fibrosis-4 (FIB-4) calculator which have been validated in ethnically different NAFLD populations and have demonstrated a high accuracy to predict significant overall cardiovascular (CV) and liver-disease mortality.[13–18] In particular, NFS is a simple scoring system, including routine demographic, clinical, and laboratory variables, such as body mass index (BMI), platelet count, albumin, and aspartate aminotransferase/alanine aminotranferease (AST/ALT) ratio.[14] In particular, Angulo et al. found that a cutoff score of −1.455 can exclude the presence of advanced fibrosis with high accuracy (negative predictive value (NPV) of 93% groups), avoiding an unnecessary liver biopsy in 75% of patients.[14]

The use of elastography has further improved the evaluation of liver stiffness measurement also in NAFLD patients.[15–17] Main limits of elastography are that patients with high BMI ($\geqslant 30\,kg/m^2$), waist circumference $\geqslant 102\,cm$, or increased thickness of parietal walls are associated with significant rates of failure of measurement of liver stiffness.[17,18] Elastography requires moreover specific training and is not available everywhere, and there is a lack of data about the correlation between clinical algorithms (e.g. NFS) and US findings (both conventional examination and elastography).[18] Different approaches were evaluated to identify patients at high risk of significant fibrosis. Previously, the measurement of hepatic artery resistive index (HARI) demonstrated an inverse correlation with the US severity of steatosis (mild versus moderate versus severe, and all groups versus controls), suggesting different physiopathological mechanisms influencing the hepatic arterial resistance in the different NAFLD populations.[19] In a recent study, HARI has demonstrated a significant positive correlation with fibrosis degree, as measured with NFS. HARI exceeded the range of controls for patients with NFS greater than 0.675 (mean HARI value $= 0.98 \pm 0.02$ of NAFLD patients versus $0.88 \pm 0.03$ of controls, $P < 0.05$), suggesting that the fibrous tissue accumulation may result in increased arterial rigidity and, therefore, in a rise of resistance to flow, and that the different tissue composition of the liver (adipose versus fibrous) in the two hepatic disorders can influence HARI differently.[19]

These data support the hypothesis that the increased liver stiffness can affect globally US parameters, and suggest that the arterial resistance is differently influenced, depending on the prevalent tissue.

However, in view of the limited data, these issues should be further investigated with larger prospective trials because some aspects are still unknown. Further studies should evaluate also whether these parameters correlate with those from elastography. In view of their effect on weight loss, serum lipid concentration, and hepatic arterial flow hemodynamics,[20] it could be also interesting to evaluate whether lifestyle and diet changes can influence significantly HARI in NAFLD patients.

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