EDITORIAL

Noninvasive diagnosis of hepatic steatosis in patients with severe obesity: a clinically challenging issue

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In the 21st century, the current epidemic in the field of hepatic diseases is associated with nonalcoholic fatty liver disease (NAFLD). The diagnosis of NAFLD is established based on the presence of triglycerides in the hepatic parenchyma in the amount exceeding 5%, defined as steatosis, in the absence of secondary causes of chronic liver injury, such as chronic viral hepatitis, excessive alcohol consumption, or the use of steatogenic medications.[1] NAFLD can progress to nonalcoholic steatohepatitis (NASH), which is characterized by the additional emergence of hepatocyte ballooning, inflammation, hepatocyte injury, and can be accompanied by fibrosis.[2] Obesity, defined as having body mass index (BMI) above 30 kg/m^2, and especially morbid obesity (BMI ≥40 kg/m^2 or BMI ≥35 kg/m^2 and at least 1 serious obesity-related health condition) is a strong risk factor for the development of NAFLD and its progression to NASH and liver cirrhosis.[3] The prevalence of NAFLD and NASH among patients with morbid obesity can be as high as 95% and 56%, respectively.[4] Therefore, screening for NAFLD, especially in the subgroup of patients with obesity, is of great importance. The current gold standard for the diagnosis and staging of NAFLD is liver biopsy. However, its invasive nature, the sampling variability, increased morbidity as well as high cost substantially limit its feasibility. In recent years, European guidelines have proposed the use of magnetic resonance spectroscopy (MRS) or magnetic resonance imaging (MRI) as alternative methods for the detection of liver fat.[1] Nonetheless, those imaging modalities are characterized by limited availability for a mass screening on a large population scale due to their high cost, and thereby cannot be routinely implemented in clinical practice.

To this end, several noninvasive, imaging- or laboratory-based tools such as the Hepatic Steatosis Index (HSI),[5] NAFLD logit score[6] and the Hepatorenal index (HRI)[7] have generated a lot of interest among researchers for the detection of liver steatosis. However, data regarding their effectiveness in evaluation of steatosis in patients with severe obesity, who make up a significant proportion of NAFLD patients, remain relatively scarce.

In this issue of *Polish Archives of Internal Medicine,* Byra et al[8] compared the diagnostic performance of HRI, HSI, and NAFLD logit score in the detection of hepatic steatosis in 162 individuals with severe obesity (BMI >40 kg/m^2; NAFLD, n = 106; controls, n = 56), referred for bariatric surgery between 2016 and 2019. They showed that the performance of HRI (area under the curve [AUC] of 0.879) and NAFLD logit score (AUC of 0.825) was relatively lower than the corresponding AUCs found in the literature (ranging from 0.92 to 0.996 for HRI, and 0.87 for NAFLD logit score). More precisely, the authors determined the optimal cutoff value of HRI at 1.12 for NAFLD diagnosis, much lower than that proposed in the literature for the general population.[7] That discrepancy can be attributed to the fact that Byra et al[8] enrolled only individuals with morbid obesity (mean BMI >43 kg/m^2 in patients and controls), in whom the efficacy of ultrasound-based techniques and the resolution of ultrasound images are significantly lower than in the general population.[9] Secondly, they used the XL (2.5 MHz) probe, which is a recommended diagnostic tool for obese individuals, instead of the M or S probe used in most similar studies.[7,10] Nonetheless, ultrasound and, as expected, ultrasound-based tools exhibit limited sensitivity in detection of steatosis below 20%,[11] and thus the argument of the authors that inclusion of NAFLD patients with lower liver fat content could ameliorate the diagnostic performance of the HRI is questionable. In addition, the number of patients for whom HRI was not feasible due to

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their morbid obesity would be of importance to be reported in the study.

As for the laboratory-based indices, the authors showed that NAFLD logit score displayed a good performance, achieving an AUC value of 0.825, using higher cutoff values than those reported in the literature.[6] Consistently, for the optimal classification accuracy of HSI, increased cutoffs were needed (56.9), as compared with those originally reported for HSI (36). We shall point out though, that the initial cutoffs were designed for the general population rather than patients with morbid obesity. To this end, the necessity for higher cutoff values of HSI was supported by the findings of Parente et al[12] (cutoff of 53), Coccia et al[13] (cutoff of 52), Garteiser et al[14] (cutoff of 55), and Ooi et al[15] (cutoff of 67). However, despite the higher cutoffs used by Byra et al,[8] the classification performance of HSI was relatively poor (AUC of 0.599), drastically lower than the AUC value (0.812) first described for the general population. The authors attributed this finding to the enrolment of only patients with morbid obesity. Nonetheless, significantly higher AUC values were reported by Parente et al[12] (0.777) and Coccia et al[13] (0.76), who had also enrolled patients with severe obesity. Although the sample size in those studies was smaller than in the work by Byra et al,[8] a fact that mitigates their statistical power, a recent large study including 182 patients with morbid obesity (mean BMI, 45.1 kg/m^2) also showed that HSI had a relatively low diagnostic accuracy in hepatic steatosis, achieving an AUC of 0.491.[15] Therefore, the diagnostic utility of HSI in the detection of hepatic steatosis in the patients with morbid obesity needs further assessment.

Of note, the authors acknowledged that they did not evaluate the performance of other noninvasive tests, such as fatty liver index or lipid accumulation product index, or other unmentioned tests such as NAFLD liver fat score, SteatoTest and Controlled Attenuation Parameter. Some of those indices require measuring of anthropometric parameters such as BMI and, more importantly, waist circumference, which may not be evaluated and registered in a plethora of real-life data sources. Despite their large sample size, the lack of evaluation of anthropometric measurements is a common issue in several electronic medical registries. Moreover, as the authors mentioned and we agree, the use of more advanced imaging modalities for the detection of steatosis, such as MRI/MRS, would drastically reduce the cost-effectiveness of a screening program, even if it targeted only the population of patients with morbid obesity. Further to that, the procedure of MRI or MRS would be technically difficult to implement in individuals with morbid obesity. Importantly, the study by Byra et al[8] is, to our knowledge, the only one that evaluated the NAFLD logit score in the patients with morbid obesity. The authors also reported on 3 noninvasive scores, and they used wedge liver biopsy as a reference for the evaluation of liver steatosis. We shall point out that in the future, given the availability of patients' liver biopsy data, it would be highly interesting if the authors evaluate the diagnostic utility of noninvasive inflammation and fibrosis scores, such as Fibrosis-4 and NAFLD fibrosis score in the patients with morbid obesity.

In conclusion, this important study adds to the growing body of literature suggesting that different cutoffs for several noninvasive tools and biomarkers might be needed for proper and more accurate classification of the degree of steatosis in the patients with severe obesity. Nonetheless, it was a single-center study with limited sample size that included only Caucasian patients, and therefore further studies in large samples, optimally with a prospective design, are needed to evaluate and establish new thresholds to detect hepatic steatosis in the patients with morbid obesity.

ARTICLE INFORMATION

DISCLAIMER The opinions expressed by the author(s) are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

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REFERENCES

1 European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hepatol. 2016; 64: 1388-1402.

2 Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018; 67: 328-357.

3 Sarwar R, Pierce N, Koppe S. Obesity and nonalcoholic fatty liver disease: current perspectives. Diabetes Metab Syndr Obes. 2018; 11: 533-542.

4 Vernon G, Baranova A, Younossi ZM. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. Aliment Pharmacol Ther. 2011; 34: 274-285.

5 Lee JH, Kim D, Kim HJ, et al. Hepatic steatosis index: a simple screening tool reflecting nonalcoholic fatty liver disease. Dig Liver Dis. 2010; 42: 503-508.

6 Yip TC, Ma AJ, Wong VW, et al. Laboratory parameter-based machine learning model for excluding non-alcoholic fatty liver disease (NAFLD) in the general population. Aliment Pharmacol Ther. 2017; 46: 447-456.

7 Webb M, Yeshua H, Zelber-Sagi S, et al. Diagnostic value of a computerized hepatorenal index for sonographic quantification of liver steatosis. AJR Am J Roentgenol. 2009; 192: 909-914.

8 Byra M, Szmigielski C, Kalinowski P, et al. Ultrasound- and biomarker-based assessment of hepatic steatosis in patients with severe obesity. Pol Arch Intern Med. 2023; 133: 16343.

9 Ryan CK, Johnson LA, Germin BI, et al. One hundred consecutive hepatic biopsies in the workup of living donors for right lobe liver transplantation. Liver Transpl. 2002; 8: 1114-1122.

10 Isaksen VT, Larsen MA, Goll R, et al. Hepatic steatosis, detected by hepatorenal index in ultrasonography, as a predictor of insulin resistance in obese subjects. BMC Obes. 2016; 3: 39.

11 Saadeh S, Younossi ZM, Remer EM, et al. The utility of radiological imaging in nonalcoholic fatty liver disease. Gastroenterology. 2002; 123: 745-750.

12 Parente DB, Perazzo H, Paiva FF, et al. Higher cut-off values of non-invasive methods might be needed to detect moderate-to-severe steatosis in morbid obese patients: a pilot study. Sci Rep. 2020; 10: 15007.

13 Coccia F, Testa M, Guarisco G, et al. Noninvasive assessment of hepatic steatosis and fibrosis in patients with severe obesity. Endocrine. 2020; 67: 569-578.

14 Garteiser P, Castera L, Coupaye M, et al. Prospective comparison of transient elastography, MRI and serum scores for grading steatosis and detecting non-alcoholic steatohepatitis in bariatric surgery candidates. JHEP Rep. 2021; 3: 100381.

15 Ooi GJ, Earnest A, Kemp WW, et al. Evaluating feasibility and accuracy of non-invasive tests for nonalcoholic fatty liver disease in severe and morbid obesity. Int J Obes (Lond). 2018; 42: 1900-1911.