Letter to the Editor

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Noninvasive Imaging for the Evaluation of Non-Alcoholic Fatty Liver Disease Spectrum

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Dear Editor,

We read the publication "Development and Validation of a Simple Index Based on Non-Enhanced CT and Clinical Factors for Prediction of Non-Alcoholic Fatty Liver Disease" about building a prediction model for the evaluation of non-alcoholic fatty liver disease (NAFLD) with great interest. In that study, the diagnostic efficacy of the clinical-CT index was superior than that of CT_{L-S} or the clinical indices (all $p < 0.05$) based on the pathologic diagnosis of NAFLD as the reference standard (1). This indicates that the clinical-CT index is more accurate than other indices and may have potential clinical application in the evaluation of NAFLD. We would like to share our opinions concerning noninvasive imaging for the evaluation of NAFLD spectrum.

NAFLD is a complicated hepatic disease spectrum, which includes NAFL, borderline non-alcoholic steatohepatitis (borderline NASH), and NASH. Additionally, NAFLD related fibrosis can be detected in borderline NASH or NASH liver, and hepatic steatosis is one of the pathologic characteristics in NAFLD livers. Therefore, different image modalities may have different diagnostic efficacy in the evaluation of NAFLD spectrum. Our previous animal study (2) suggested that multislice computed tomography (MSCT) was better able to differentiate normal or early NAFLD livers from higher severity NAFLD livers compared with ultrasound shear wave elastography (US-SWE). This means that MSCT could be recommended to evaluate or monitor the early stage of NAFLD livers. However, the diagnostic efficacy of US-SWE is superior to MSCT in differentiating NASH from normal or less severe NAFLD. Hence, US-SWE could be recommended for the assessment or follow-up of the dynamic changes in advanced stage NAFLD livers. Thus, the diagnostic efficacies of these two techniques supplement each other in the assessment of NAFLD spectrum (2). In addition, as for hepatic steatosis, the modified Dixon MRI technique is a good method for histological quantification in the assessment of hepatic steatosis (3), as well as intravoxel incoherent motion diffusion-weighted MR imaging for the evaluation of NAFLD spectrum (4).

The present characteristic signs on imaging modalities (e.g., stiffness, attenuation, and signal intensity) do not provide enough diagnostic information to assess or differentiate between the severity of NAFLD livers. Consequently, radiomics and deep learning may be a better way to evaluate NAFLD severity in the near future. Recently, several studies have suggested that it is feasible to use a deep learning method to evaluate the grade of fatty livers based on ultrasonography (5). Deep learning radiomics have a superior diagnostic performance for predicting liver fibrosis severity than 2D-SWE and biomarker evaluation (6).

Noninvasive imaging play an important role in the diagnosis of NAFLD spectrum. Combining multimodality imaging technologies or clinical factors, as well as radiomics and deep learning based on medical images, can improve the diagnostic accuracy of NAFLD spectrum. However, because NAFLD is complicated, the precise diagnostic accuracy in the clinical practice still requires large-scale, long-term research. Deep learning radiomics of multimodality imaging may be a novel way to improve the diagnostic efficacy of NAFLD spectrum in the future.

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Conflicts of Interest
The authors have no potential conflicts of interest to disclose.

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Response

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To the Editor,

Thank you for your comments regarding our article on an index based on non-enhanced CT and clinical factors for the detection of non-alcoholic fatty liver disease (NAFLD) (1). NAFLD is a disease spectrum that includes simple steatosis, nonalcoholic steatohepatitis (NASH), NASH with fibrosis, and cirrhosis. These NAFLD stages are determined by the degree of three major pathologic features, namely steatosis, necroinflammation, and fibrosis (2). Therefore, an ideal examination for NAFLD should distinguish the different disease stages and evaluate the three major pathologic features. However, currently, there are no validated imaging methods that could reliably evaluate necroinflammation and distinguish the early stage of NASH from simple steatosis.

There have been a number of imaging techniques that have been investigated for the assessment of NAFLD. However, there are two clinically available methods that allow for the comprehensive assessment of hepatic steatosis and fibrosis, thus enabling the diagnosis and severity assessment of NAFLD. Transient elastography is an ultrasound-based elastography technique. It generates two quantitative metrics of liver stiffness and a controlled attenuation parameter, which reflects fibrosis and steatosis, respectively. The other method is magnetic resonance (MR)-based proton density fat fraction (PDFF) measurement combined with MR elastography. In terms of diagnostic accuracy, MR-based methods are reported to be superior to transient elastography for assessing both steatosis and fibrosis (3, 4). In addition, PDFF measurement and MR elastography can assess the change in hepatic steatosis and fibrosis in longitudinal follow-up (5). However, the MR-based approach has disadvantages in terms of availability and cost. Thus, MR imaging may be more suitable in clinical trials and longitudinal follow-up than routine clinical practice. Contrastingly, transient elastography is portable and relatively inexpensive. On the other hand, ultrasound-based shear wave elastographic techniques permit both liver imaging and the measurement of liver stiffness. Although the conventional visual grading system based on gray-scale ultrasound suffers from interobserver variability and poor accuracy in steatosis assessment (6), new quantitative ultrasound methods such as the attenuation and backscatter coefficients may allow for the objective and quantitative assessment of hepatic steatosis in the near future.

Liver attenuation measured on non-enhanced CT images has been utilized as a quantitative CT index for assessing hepatic steatosis. Previous studies have shown that the CT index can identify moderate to severe hepatic steatosis with high specificity (7, 8). However, the accuracy of CT in diagnosing mild hepatic steatosis is disappointing, with areas under the receiver operating curve of 0.654–0.735 (6, 7). As such, what could be the actual role of CT in assessing NAFLD in clinical practice or research be? Given the potential radiation hazard of CT, and the availability of better imaging methods for NAFLD assessment than CT, the use of CT solely for the evaluation of NAFLD would not be appropriate. However, CT may suggest the possibility of NAFLD in patients who undergo CT for other purposes. Since CT is widely performed in clinical practice, a CT-based index which reliably screens NAFLD may be used to construct a large cohort of subjects with NAFLD and normal controls using pre-existing retrospective CT data. This retrospective cohort may be used to investigate the natural history and outcomes of NAFLD.

In conclusion, the selection of noninvasive imaging examinations for NAFLD should be tailored by availability, cost, and the purpose of the imaging examination. Currently, MR-based PDFF measurement combined with MR elastography is the most reliable method for the comprehensive evaluation of steatosis and fibrosis associated with NAFLD. Transient elastography could be a practical alternative to the MR-based approach. Given the wide use of CT, a retrospective analysis of preexisting CT data using a CT-based index may be useful for constructing a large cohort of patients with NAFLD for research.

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