Response to letter: Multiparametric magnetic resonance imaging in patients with nonalcoholic fatty liver disease

Schaapman, J.J.; Coenraad, M.J.; Lamb, H.J.

Response to letter: Multiparametric magnetic resonance imaging in patients with nonalcoholic fatty liver disease

Jelte J. Schaapman, MD,[1,2*]
Minneke J. Coenraad, MD, PhD,[2] and
Hildo J. Lamb, MD, PhD[1]

We appreciate the interest in our review article on multiparametric magnetic resonance (MR) methods in patients with nonalcoholic fatty liver disease[1] (NAFLD) and value the authors' letter expressing their concern that, based on the currently available evidence, it is not clear which role iron-corrected T_1 mapping (cT_1) may play in the management of NAFLD.

Our primary goal was to review the utility and limitations of multiparametric quantitative imaging of the liver for the diagnosis and management of patients with NAFLD. We agree that liver fibrosis stage is shown to be an important predictor for overall and disease-specific mortality in patients with NAFLD.[2] Liver biopsy is the reference standard for assessment of fibrosis but has an inherent risk of complications, therefore noninvasive biomarkers are needed. For the quantification of fibrosis with MR, we chose to discuss magnetic resonance elastography (MRE), a method that is already extensively studied, and cT_1 as a relatively novel MR method. The authors raise an important point: cT_1 alone is not suitable for the assessment of fibrosis grade of the liver. Contrary to what has been alleged in their letter to the editor, we fully agree with this statement and in our review this limitation is briefly addressed.

Studying the present literature carefully, we concluded that cT_1 shows potential to distinguish simple steatosis from nonalcoholic steatohepatitis (NASH) and cirrhosis.[3,4] However, a major limitation of cT_1 is the difficulty to distinguish between active inflammation and fibrosis in the liver, because both processes increase the liver T_1 relaxation time. In our proposed clinical algorithm, we show clearly that elevated cT_1 values are indicative for fibrosis and/or inflammation and not fibrosis alone. It should be noted that cT_1 shows good diagnostic accuracy for identifying patients with NASH and fibrosis.[5] Furthermore, while cT_1 cannot dissociate the signal from inflammation and fibrosis, it does remain linearly related to both. The same cannot be said for MRI proton density fat fraction, which decreases with increasing fibrosis,[6] highlighting the potential of cT_1 as a NASH specific biomarker.

We agree that further studies are necessary to fully assess the diagnostic potential of cT_1 in the evaluation of patients with suspected high-risk NAFLD. It is interesting to await the results of the Radical 1 study,[7] a multicenter randomized controlled phase 4 trial, designed to investigate the use of multiparametric MR methods as a standardized diagnostic test in comparison to routine methodical assessment for patients with suspected NAFLD in Europe.

In summary, we agree that cT_1 alone cannot yet differentiate between various stages of liver fibrosis and inflammation. MRE is highly accurate in the detection of fibrosis; however, the need for additional hardware limits its wide application in clinical practice. Therefore, it is necessary to discuss the utility and limitations of novel techniques, such as cT_1, for the assessment of patients with suspected NAFLD. We will await the results of further studies to assess the role of cT_1 in the management of NAFLD.

Conflict of interest

The authors declare no conflict of interest.

[1]*Department of Radiology, Leiden University Medical CenterLeiden, The Netherlands*
[2]*Department of Gastroenterology and Hepatology, Leiden University Medical CenterLeiden, The Netherlands*

References

1. Schaapman JJ, Tushuizen ME, Coenraad MJ, Lamb HJ. Multiparametric MRI in patients with nonalcoholic fatty liver disease. J Magn Reson Imaging. 2020. https://doi.org/10.1002/jmri.27292. Online ahead of print.
2. Ekstedt M, Hagstrom H, Nasr P, Fredrikson M, Stål P, Kechagias S, et al. Fibrosis stage is the strongest predictor for disease-specific mortality in NAFLD after up to 33 years of follow-up. Hepatology. 2015;61(5):1547–54.
3. Banerjee R, Pavlides M, Tunnicliffe EM, Piechnik SK, Sarania N, Philips R, et al. Multiparametric magnetic resonance for the non-invasive diagnosis of liver disease. J Hepatol. 2014;60(1):69–77.
4. Pavlides M, Banerjee R, Tunnicliffe EM, Kelly C, Collier J, Wang LM, et al. Multiparametric magnetic resonance imaging for the assessment of non-alcoholic fatty liver disease severity. Liver Int. 2017;37(7):1065–73.
5. Dennis A, Mouchti S, Kelly M, Fallowfield JA, Hirschfield G, Pavlides M, et al. A composite biomarker using multiparametric magnetic resonance imaging and blood analytes accurately identifies patients with non-alcoholic steatohepatitis and significant fibrosis. Sci Rep. 2020;10(1):15308.
6. Wildman-Tobriner B, Middleton MM, Moylan CA, Rossi S, Flores O, Chang ZA, et al. Association between magnetic resonance imaging-proton density fat fraction and liver histology features in patients with nonalcoholic fatty liver disease or nonalcoholic steatohepatitis. Gastroenterology. 2018;155(5):1428–35.e2.
7. Tonev D, Shumbayawonda E, Tetlow LA, Herdman L, French M, Rymell S, et al. The effect of multi-parametric magnetic resonance imaging in standard of care for nonalcoholic fatty liver disease: protocol for a randomized control trial. JMIR Res Protoc. 2020;9(10):e19189.

DOI: 10.1002/jmri.27510

Level of Evidence: 5
Technical Efficacy Stage: 2

