Letter to the Editor

Reply to: “Multiple investigations for a very common disorder: Finding the right balance in NAFLD”

To the Editor:

We would like to thank the authors¹ for their interest in our publication and their discussion of the potential risk of overdiagnosis, not just in non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) but in general, which represents a potentially avoidable burden on both patients and healthcare systems.

Current guidelines require the exclusion of other chronic liver diseases to confirm the diagnosis of NAFLD.²⁻⁴ In line with the comment by Kotha and Berry¹ it seems necessary to define metabolic-associated fatty liver disease (MAFLD) by the presence of metabolic dysfunction as recently suggested by an expert panel.⁵,⁶ This definition would allow for identification of “other” liver diseases and would relieve the clinician from searching for a rare cause of fatty liver in an individual with metabolic dysfunction.⁷

Therefore, the algorithm (Fig. 3) proposed in our manuscript addresses this legitimate concern of overdiagnosis by suggesting further workup of rare/secondary causes only for those individuals who do not present with symptoms and signs of metabolic syndrome.⁷ Furthermore, a detailed medical history, clinical examination and abdominal ultrasound will help to identify patients who either have additional causes besides metabolic dysfunction or who may suffer from rare causes of fatty liver disease. Depending on country, dried blood spot testing for glycogen and lysosomal storage diseases as well as lysosomal acid lipase deficiency is broadly available, provided free of charge and allows for efficient diagnosis or in most cases exclusion of these rare diseases.

We would like to emphasize that in contrast to primary NAFLD/MAFLD, patients with secondary causes are amenable to straightforward and in some cases even curative treatment. Thus the "reward" of finding the rare zebra among the horses will not only improve patient outcome but most likely also be cost-effective through prevention of disease progression.

In summary – as clearly stated in our manuscript – workup of secondary causes should be reserved for those patients without symptoms and signs of metabolic dysfunction or in pediatric patients whose liver function tests do not normalize following weight reduction. In these patients, a staged- and presentation-based extended assessment should be initiated as described.²,⁸ Even in times of resource scarcity in healthcare systems, physicians awareness of secondary causes of fatty liver must be raised to ensure that patients are offered the right therapy.

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Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

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Authors’ contributions

VK and TL initiated this work and drafted the response letter. UB contributed pediatric expertise. All authors approved the final version of this letter.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2021.08.032.

References

¹ Kotha S, Berry P. Multiple investigations for a very common disorder: finding the right balance in NAFLD. J Hepatol 2021.
⁸ Hegarty R, Deheragoda M, Fitzpatrick E, Dhawan A. Paediatric fatty liver disease (PeFLD); all is not NAFLD - pathophysiological insights and approach to management. J Hepatol 2018;68:1286–1299.

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