DOI: 10.1111/apt.16034

LETTER TO THE EDITORS

AP&T Alimentary Pharmacology & Therapeutics WILEY

Letter: the use of Fibrosis-4 score in primary care and diabetology practices—Occam's razor applied to advanced fibrosis screening

EDITORS,

We read with interest the recent review by Younossi et al,[1] in which they discussed the optimal strategies for identifying high-risk patients with non-alcoholic fatty liver disease (NAFLD)-related advanced fibrosis in nonspecialist settings (primary care and diabetology practices), and linking them to specialised hepatology care. Currently, hepatology consultations from nonspecialist settings are still mainly motivated by abnormal liver enzyme levels.[2] However, relying on abnormal transaminase levels alone would significantly underestimate the risk of advanced fibrosis in patients with NAFLD.[3,4] Several non-invasive tests (NITs)—including Fibrosis-4 (FIB-4) score and NAFLD fibrosis score (NFS)—have been proposed as screening tools for advanced fibrosis.[4-7] Unfortunately, it remains challenging for primary care and diabetology physicians to interpret the results of established NITs for identifying fibrosis, and to integrate them into their risk stratification process. One of the main issues with NITs lies in their frequent use of dual cut-offs (ie a low cut-off with high sensitivity and a high cut-off with high specificity).[8] When the two cut-offs are used, a significant proportion of patients will ultimately fall into an indeterminate risk category (a 'grey zone') for which referral to specialised hepatology care might not be obvious.[8] Interestingly, the consensus recommendation from Younossi et al[1] is to risk-stratify patients based on the presence of a FIB-4 score ≥1.3. We entirely endorse this approach for at least two reasons. First, determination of FIB-4 is simpler than that of NFS owing to the lower number of parameters included in the calculation.[7] Second, the use of a single cut-off allows an easier interpretation of test results without resorting to an indeterminate risk category.[5] This is a good example of Occam's razor applied to advanced fibrosis screening. Named after 14th-century English logician William of Ockham, the Occam's razor, put simply, states that 'the simplest solution is almost always the best'.

We have recently demonstrated that FIB-4 should be recommended for screening for advanced fibrosis in both diabetic and nondiabetic patients with NAFLD.[5] Notably, the cut-off values proposed in our study (>1.275 for patients with diabetes and >1.210 for those without)[5] are in line with those reported by Shah et al[9] and with the value suggested by Younossi et al.[1]

The implementation of the recommendations proposed by Younossi et al[1] will be essential to future significant advances in the field of fibrosis screening in four different ways, including the opportunity to refer more at-risk patients from a nonspecialist to a specialist setting, the identification of 'missing cases' of fibrosis that will never have the opportunity to be referred to a hepatologist if not screened outside of the hepatology clinic,[10] the availability of a more representative general NAFLD population in the hepatology clinic (which is currently enriched with the most severe cases—potentially also creating a selection bias in phase 3 clinical trials), and the possibility to target liver biopsies to a lower number of cases.

ACKNOWLEDGEMENT

Declaration of personal interests: None.

LINKED CONTENT

This article is linked to Younossi et al and Younossi & Henry papers. To view these articles, visit https://doi.org/10.1111/apt.15830 and https://doi.org/10.1111/apt.16091

Yusuf Yilmaz[1,2]
Eda Kaya[3]
Fatih Eren[2,4]

[1]*Department of Gastroenterology, School of Medicine, Marmara University, Istanbul, Turkey*
[2]*Institute of Gastroenterology, Marmara University, Istanbul, Turkey*
[3]*Department of Internal Medicine, Helios Hospital Schleswig, Academic Educational Hospital of Luebeck and Kiel Universities, Schleswig, Germany*
[4]*Department of Medical Biology, School of Medicine, Marmara University, Istanbul, Turkey*
Email: dryusufyilmaz@gmail.com

ORCID

Yusuf Yilmaz https://orcid.org/0000-0003-4518-5283
Eda Kaya https://orcid.org/0000-0002-9293-2811
Fatih Eren https://orcid.org/0000-0001-8126-2413

AP&T correspondence columns are restricted to letters discussing papers that have been published in the journal. A letter must have a maximum of 500 words, may contain one table or figure, and should have no more than 10 references. It should be submitted electronically to the Editors via http://mc.manuscriptcentral.com/apt.

 © 2020 John Wiley & Sons Ltd

REFERENCES

1. Younossi ZM, Corey KE, Alkhouri N, et al. Clinical assessment for high-risk patients with non-alcoholic fatty liver disease in primary care and diabetology practices. *Aliment Pharmacol Ther*. 2020;52:513-526.
2. Degertekin B, Tozun N, Demir F, et al. Determination of the upper limits of normal serum alanine aminotransferase (ALT) level in healthy Turkish population. *Hepatology Forum*. 2020;2:44-47.
3. Ulasoglu C, Enc FY, Kaya E, et al. Characterization of patients with biopsy-proven non-alcoholic fatty liver disease and normal aminotransferase levels. *J Gastrointestin Liver Dis*. 2019;28:427-431.
4. Kaya E, Bakir A, Eren F, et al. The utility of noninvasive scores in non-alcoholic fatty liver disease patients with normal and elevated serum transaminases. *Hepatology Forum*. 2020;1:8-13.
5. Alkayyali T, Qutranji L, Kaya E, et al. Clinical utility of noninvasive scores in assessing advanced hepatic fibrosis in patients with type 2 diabetes mellitus: a study in biopsy-proven non-alcoholic fatty liver disease. *Acta Diabetol*. 2020;57:613-618.
6. Jafarov F, Kaya E, Bakir A, et al. The diagnostic utility of fibrosis-4 or nonalcoholic fatty liver disease fibrosis score combined with liver stiffness measurement by fibroscan in assessment of advanced liver fibrosis: a biopsy-proven nonalcoholic fatty liver disease study. *Eur J Gastroenterol Hepatol*. 2020;32:642-649.
7. Kaya E, Bakir A, Kani HT, et al. Simple noninvasive scores are clinically useful to exclude, not predict, advanced fibrosis: a study in Turkish patients with biopsy-proven nonalcoholic fatty liver disease. *Gut Liv*. 2020;14:486-491.
8. Patel K, Sebastiani G. Limitations of non-invasive tests for assessment of liver fibrosis. *JHEP Rep*. 2020;2:100067.
9. Shah AG, Lydecker A, Murray K, et al. Comparison of noninvasive markers of fibrosis in patients with nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol*. 2009;7:1104-1112.
10. 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.