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NFS Is Not a Marker of Nonalcoholic Fatty Liver Disease Per Se: What Is the True Relationship With CAD Complexity?

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We read with interest the article by Turan, entitled "The Nonalcoholic Fatty Liver Disease Fibrosis Score Is Related to Epicardial Fat Thickness and Complexity of Coronary Artery Disease."[1] The author investigated the interrelationships between the nonalcoholic fatty liver disease (NAFLD) Fibrosis Score (NFS), epicardial fat thickness (EFT), and the SYNergy between PCI with TAXus and cardiac surgery (SYNTAX) score (a method to quantify the anatomical extent of coronary artery disease). The results of linear regression analysis with backward elimination revealed that the SYNTAX score was independently associated with the NFS ($P = .012$), EFT ($P = .001$), and low-density lipoprotein cholesterol levels ($P < .001$).

Based on the relationship between the SYNTAX score and NFS, the author concluded that "the NFS, as a marker of NAFLD, could identify patients at higher risk of cardiovascular disease."[1] However, this conclusion is not supported by the author's data because NFS has not been properly applied in this study. Accordingly, NFS is not a marker of NAFLD, but instead a noninvasive score to screen for the presence of fibrosis in NAFLD.[2] The test is therefore unable to identify NAFLD per se, but should instead be used to triage patients with NAFLD for their risk of fibrosis.[2] Consequently, we cannot conclude that these "patients with higher risk of cardiovascular disease" truly have a noninvasive diagnosis of NAFLD.

Another problem is the statistical treatment of the NFS. The author analyzed this score as a continuous variable which was entered into a linear regression model after correlation analyses. However, the NFS is not clinically used as a continuous parameter but rather used to identify 3 risk categories for advanced fibrosis based on cutoff values, as follows: NFS < -1.455 (low risk), $-1.455 \leq$ NFS ≤ 0.676 (intermediate risk), and NFS > 0.676 (high risk).[2] Of note, the NFS is a low-sensitivity/high-specificity screening tool.[3] Consequently, it can confidently rule out the presence of advanced fibrosis in patients with NAFLD with a score < -1.455, but it is unable to make a reliable diagnosis of advanced fibrosis in those with a score >0.676.[3] In order to conduct a more meaningful analysis, the author should divide the study patients (n = 159) into the 3 abovementioned NFS categories and report the SYNTAX score values in these risk groups. However, we cannot exclude that the study by Turan[1] could be underpowered to conduct such an analysis because, in general, only 5% of all screened patients fall into the high-risk category.[4] In any case, it should be noted that this analysis would be related to liver fibrosis, not to the risk of NAFLD.

Finally, the reciprocal interrelationships between NFS, EFT, and the SYNTAX score are not surprising. We have previously shown that EFT is increased in patients with biopsy-proven NAFLD, being also the strongest independent variable predicting impaired coronary flow reserve.[5] Moreover, arterial stiffness in patients with NAFLD has been related to both fibrosis stage and EFT.[6]

In summary, it is plausible that the findings by Turan[1] have been chiefly driven by the presence of hepatic fibrosis, not of NAFLD per se.

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References

1. Turan Y. The nonalcoholic fatty liver disease fibrosis score is related to epicardial fat thickness and complexity of coronary artery disease. *Angiology*. 2019;71(1):77-82.
2. Angulo P, Hui JM, Marchesini G, et al. The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology*. 2007;45(4):846-54.
3. Zakeri N, Tsochatzis EA. Steatosis affects the sensitivity but not the specificity of non-invasive fibrosis tests in non-alcoholic fatty liver disease—implications for screening strategies. *Liver Int*. 2018;38(2):224-6.
4. Tsochatzis EA, Newsome PN. Non-alcoholic fatty liver disease and the interface between primary and secondary care. *Lancet Gastroenterol Hepatol*. 2018;3(7):509-17.

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5. Yilmaz Y, Kurt R, Gurdal A, et al. Circulating vaspin levels and epicardial adipose tissue thickness are associated with impaired coronary flow reserve in patients with nonalcoholic fatty liver disease. *Atherosclerosis*. 2011;217(1):125-9.
6. Sunbul M, Agirbasli M, Durmus E, et al. Arterial stiffness in patients with non-alcoholic fatty liver disease is related to fibrosis stage and epicardial adipose tissue. *Atherosclerosis*. 2014;237(2): 490-3.