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Are there any reliable predictors of unreported alcohol consumption in MAFLD patients?

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To the Editor,

We have read with positive interest the study by Staufer et al. dealing with a very interesting topic that is the role of alcohol consumption in metabolic-dysfunction associated fatty liver disease (MAFLD) (1). This study assessed and compared the accuracy of five tests - ethylglucuronide in hair (hEtG) and urine (uEtG), carbohydrate deficient transferrin (CDT), mean corpuscular volume (MCV), gamma-glutamyl transferase (GGT) - and two scores, Alcohol Use Disorders Identification Test - Consumption (AUDIT-C), and ALD/NAFLD – Index (ANI) - for diagnosing regular moderate or excessive ethanol intake. The Authors claim that hEtG shows “an excellent accuracy to identify repeated moderate to excessive ethanol consumption in patients with fatty liver disease at risk for alcoholic liver damage” (1).

We have some concerns about the conclusions. First of all, we found some apparent inconsistencies among the results (Table 3) that might impact on the reliability of the conclusions. The diagnostic assessment of the index tests has not been reported in adherence to the Standards for Reporting of Diagnostic Accuracy Studies (STARD) initiative (2) and with sufficient detail to allow replication. In particular, as the number of participants undergoing the different tests varies, it is not possible to build up the two-by-two tables and replicate the results. In Table 3, we found some inconsistencies between sensitivity, specificity, and predictive values. Some tests show a negative predictive value (NPV) of 100% (i.e. zero false negatives) with a sensitivity lower than 100% (i.e. a number of false negatives). For example, it is highly unlikely that carbohydrate deficient transferrin (CDT) with a sensitivity of only 8.3% could have a NPV of 100%. The same comment applies to hEtG which could not have NPV=100% with the reported sensitivity of 85.4%.

Is there any chance that the columns of positive predicting values (PPV) and that of negative predictive values (NPV) might have been swapped?
Furthermore, Authors stated that “patients whose alcohol marker test results were unexpectedly positive, thus contradictory to the quantitative ethanol amount reported and quantified by Systematic Inventory of Alcohol Consumption (SIAC), were confronted with the test results. Only biomarkers that were positive, as confirmed by the patient after confrontation, were counted as true positive”. This choice aims reducing the false-positive results, but actually introduces a differential verification bias, as the participants underwent a further verification only in the case that the Index Tests (hETg or other biomarkers) were positive (3). Accordingly, the tests sensitivity has possibly been overestimated.

Also, the definition of new cut-off values instead of using the predefined ones (at least when available) has possibly over-estimated the tests accuracy (4). In case a new definition was needed, the choice of the cut off value with the lowest negative likelihood ratio would be more appropriate, as these tests are mainly used to rule out ethanol consumption. The Youden index is used to define the optimal cut off value only when false negative and false positive results can be considered equivalent in term of downstream consequences (4, 5). Anyway, it is unclear why, for diagnosing excessive EtOH consumption, the MCV cut off value of 98.0 fl was chosen: no participants showed values higher than 98. Only for this reason, the sensitivity was 0% and the specificity was 100%

Finally, the ROC curve and the area under the curve (AUC) have been inappropriately calculated, as only one cut-off value has been considered in the analysis. A comprehensive assessment of the diagnostic accuracy using the ROC approach requires the use of data of all the possible cut-off values.

We agree with Authors that “accurate estimates of the sensitivity and specificity of the available biomarkers are needed for an early diagnosis of patients with potentially harmful alcohol consumption” but the results of the present study, at least as shown in this paper, seem unable to
achieve such an objective. Before suggesting the use of AUDIT-C, uEtG and hEtG for screening alcohol consumption in patients with fatty liver disease, consistent data on their diagnostic accuracy should be made available.

References


