“Considerations in the search for under-reported alcohol consumption in NAFLD”

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Letter to the Editor regarding “Ethyl glucuronide in hair detects a high rate of harmful alcohol consumption in presumed non-alcoholic fatty liver disease”

Title: “Considerations in the search for under-reported alcohol consumption in NAFLD”

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We congratulate Staufer et al for examining a controversial topic in the field (1). Alcohol consumption in NAFLD/MAFLD has definitely been “the elephant in the room” for a long time. This important paper urges the field to include objective alcohol markers as an important quality variable in future cohort studies and treatment trials. However, even though the study is important to the field and highlights the importance of objective alcohol markers, there are some points to be made. First, the “gold standard” definition was based on patient interview using AUDIT-C. This is frequently associated with under-reporting of current and past alcohol consumption, with a risk for non-differential misclassification bias – patients that consume higher levels of alcohol tend to under-report more than patients with a low consumption. The authors confronted patients with “unexpectedly positive” tests, but only those that confirmed under-reporting were counted as positive, which might be an oversimplification. We would trust a specific biomarker such as hEtG, more than self-reported consumption. Nutritional epidemiology, including on alcohol, relies heavily on self-reported data, however, much of this is wrong due to recall bias (2).

Second, a limitation is that the authors did not examine the biomarker Phosphatidyl ethanol (PEth). PEth is a phospholipid that can only be formed in the presence of alcohol (3). Thus, the specificity is 100%. PEth has the clear advantage of being easily measured in blood, in contrast to urine or hair samples, and has a much higher test accuracy compared to other blood-based markers such as CDT (4). A randomized, controlled trial showed that for several candidate biomarkers, PEth alone was able to detect moderate amounts of alcohol consumption (5). PEth performs equally good in categories of age and sex, in contrast to CDT (6). PEth is widely used in the Nordic countries and is an integrated part of every hepatology clinic. We
previously showed that PEth was elevated, corresponding to a more than moderate intake, in approximately 10% of patients with presumed NAFLD (7). These patients had a 3-fold higher risk for having more hepatic fibrosis compared to patients with normal PEth values. All of these reported a low consumption of alcohol and would have been considered having “true” NAFLD in any study not using PEth. We’ve also shown that PEth-values, as a surrogate for alcohol consumption, seems to act synergistically with type 2 diabetes for fibrosis development (8). Thus, it would be highly interesting if the data from Staufer et al could be re-analyzed also considering PEth. Future studies in this field should, in our opinion, strongly consider using PEth, simply since it is superior to other available tests in terms of accuracy and simplicity.

The difficulty in accurately measuring alcohol consumption is a major hurdle in hepatology, perhaps especially when conducting clinical trials. We believe that the days in which it is enough to “know” your patients in NAFLD/MAFLD research are over.

References