Phosphatidylethanol in Steatotic Liver Disease: Unveiling Alcohol Use and Enhancing Diagnostic Precision

Author: *Nikolaj Torp[1]
1. Odense University Hospital, Denmark
*Correspondence to nikolaj.torp@rsyd.dk

Citation: EMJ Hepatol. 2025;13[1]:24-26.
https://doi.org/10.33590/emjhepatol/ILRJ2155

ACCURATELY discerning the contribution of alcohol intake to the pathogenesis of steatotic liver disease (SLD) is fundamental to its classification, management, and prognosis. As the field transitions toward a refined taxonomy, including metabolic dysfunction-associated SLD (MASLD), alcohol-associated liver disease (ALD), and the hybrid phenotype metabolic dysfunction and alcohol-related liver disease (MetALD), the role of objective biomarkers becomes increasingly crucial. At the European Association for the Study of the Liver (EASL) Congress 2025, three pivotal studies illustrated the emerging clinical value of phosphatidylethanol (PEth), a blood-based biomarker that directly quantifies alcohol intake over a ~4-week window, proving an important supplement to the self-reported history.

DISCORDANCE BETWEEN SELF-REPORT AND PHOSPHATIDYLETHANOL QUANTIFICATION

The study by Bech et al.[1] evaluated PEth concentrations in 2,925 individuals undergoing screening for SLD. The investigators highlighted significant discrepancies between self-reported alcohol consumption and PEth-based measurements.

Despite an Alcohol Use Disorders Identification Test-C (AUDIT-C) score indicative of hazardous drinking in 71% of the cohort, the median PEth concentration (40.8 ng/mL) revealed underestimation.

Correlation coefficients between PEth and self-reported alcohol intake were modest at best (r=0.400 for past-week intake) and poor for average intake over 3 months (r=0.131). Notably, among individuals classified with MASLD who were ostensibly free of harmful alcohol use, 8% had PEth levels ≥200 ng/mL (indicative of heavy intake), and 31% had levels consistent with significant intake (≥20 ng/mL).

This substantial misclassification raises concerns regarding diagnostic precision in both clinical and research contexts. Here, PEth may prove to be an important aid in the subclassifications of patients across the spectrum of steatotic liver disease.

PROSPECTIVE VALIDATION IN A COMMUNITY-BASED COHORT

Building on this, Tavaglione et al.[2] conducted a prospective, population-based study assessing under-reported alcohol use via PEth in 556 community-dwelling adults, 391 of whom had MRI-confirmed SLD. Using established PEth thresholds (≥25 ng/mL for MASLD and ≥200 ng/mL for MetALD), the authors found that 16% of patients were misclassified based on self-report alone.

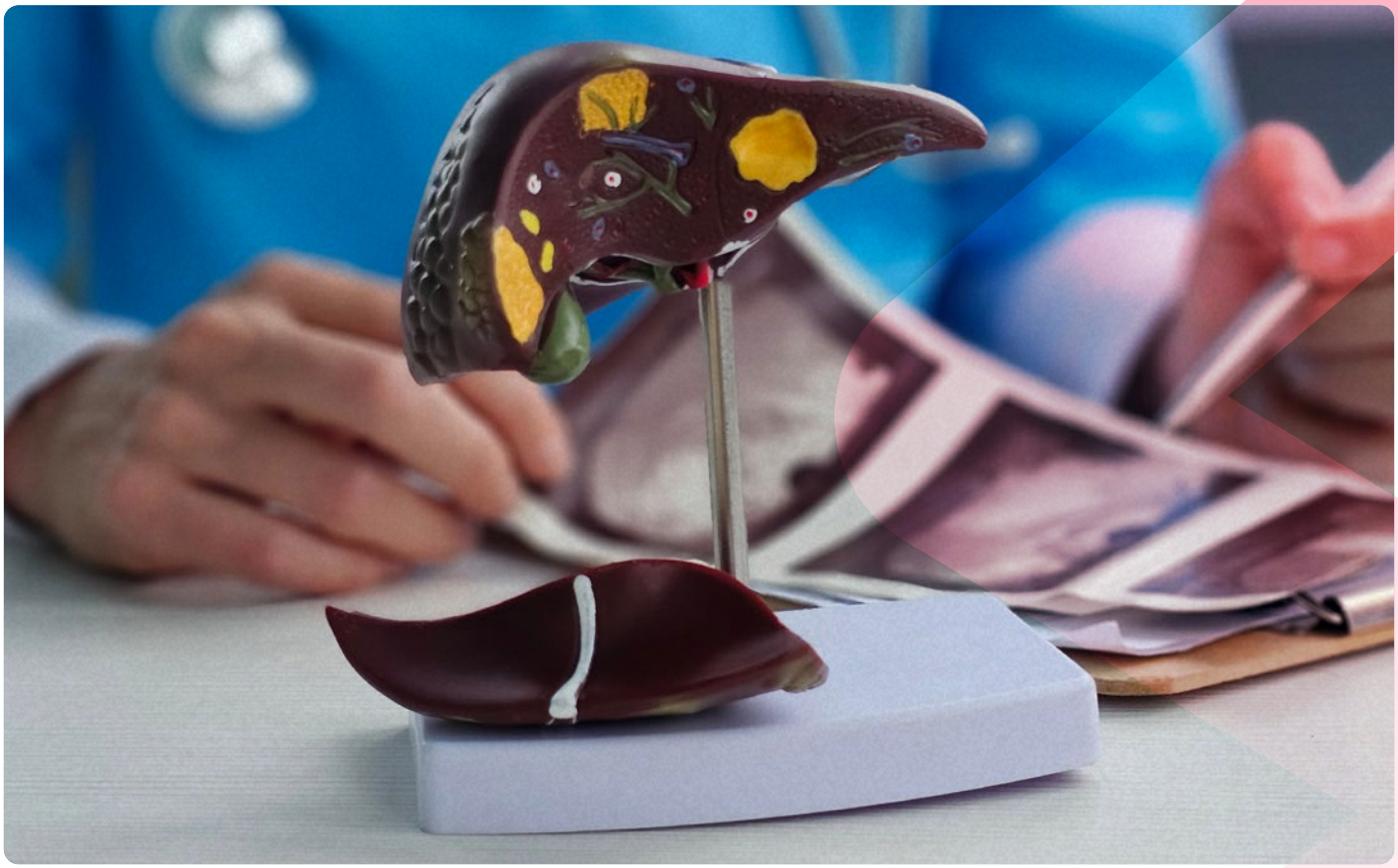
These data have immediate clinical ramifications: reliance on tools such as AUDIT or Lifetime Drinking History (LDH) may inadvertently categorise individuals into inappropriate SLD subtypes, thereby affecting therapeutic strategy and prognosis. Multivariable analysis showed that under-reporting was more common among male, Caucasian participants without diabetes.

Crucially, PEth enabled correction of this misclassification, supported a data-driven transition away from purely subjective assessments toward integrative, biomarker-based diagnosis in liver clinics.

RISK STRATIFICATION AND FIBROSIS IN METABOLIC DYSFUNCTION AND ALCOHOL-RELATED LIVER DISEASE

In the third key presentation, Diaz et al.[3] examined a cohort of 617 overweight or obese adults, identifying 97 individuals at risk of MetALD. The risk was defined based on either self-reported alcohol intake within MetALD thresholds or lower reported intake but with PEth ≥25 ng/mL.

Using a tiered screening approach, beginning with fibrosis index based on four factors (FIB-4) followed by VCTE, the researchers demonstrated that non-invasive testing effectively identified individuals with significant fibrosis (defined as magnetic resonance elastography ≥3.14 kPa or VCTE ≥7.6 kPa). The diagnostic performance was robust (FIB-4 area under the receiver operating characteristic curve=0.78; VCTE area under the receiver operating characteristic curve=0.85) and importantly, this strategy maintained a false negative rate as low as 2% when applied sequentially.



These findings reinforce the utility of PEth not only for diagnostic classification but also for augmenting fibrosis risk assessment when coupled with established non-invasive tests. Such strategies are indispensable for efficient triage and resource allocation in hepatology care pathways.

CLINICAL IMPLICATIONS

Together, these studies paint a compelling picture of PEth as an indispensable tool for modern hepatology practice. Key implications include:

- Improved diagnostic precision: PEth overcomes recall and social desirability bias, thereby enabling more accurate phenotypic categorisation among MASLD, MetALD, and ALD.
- Impact on clinical trials: misclassification due to reliance on self-report can distort eligibility criteria and confound outcomes in therapeutic studies. PEth incorporation into trial screening protocols could enhance external validity and reproducibility.
- Potential for risk stratification: beyond classification, PEth may have prognostic relevance, particularly when integrated with non-invasive fibrosis markers such as FIB-4 and VCTE.

CONCLUSION

As hepatology embraces a precision medicine paradigm, PEth emerges as a robust biomarker that bridges the gap between subjective history and objective phenotyping. Its value lies not only in detecting under-reported alcohol consumption but also in refining diagnostic classification and guiding individualised care. The EASL Congress 2025 marks a turning point in the endorsement of PEth as a standard adjunct in the diagnostic armamentarium for SLD.

References

1. Bech K et al. Discrepancies between self-reported alcohol intake and phosphatidylethanol in 2,925 individuals at risk of steatotic liver disease. Abstract OS-030-YI. EASL Congress, 7-10 May, 2025.
2. Tavaglione F et al. Prospective study of phosphatidylethanol as a quantitative, objective biomarker to detect under-reported alcohol use in steatotic liver disease. Abstract SAT-482-YI. EASL Congress, 7-10 May, 2025.
3. Diaz LA et al. Stratification of liver fibrosis in individuals at-risk of metabolic dysfunction and alcohol-associated liver disease (MetALD). Abstract SAT-495. EASL Congress, 7-10 May, 2025.