

## Title:

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Pilot study on the assessment of unrecognized alcoholic liver disease in patients with metabolic dysfunction-associated steatotic liver disease using the ANI score

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Dear Editor,

The EASL-EASD-EASO guidelines on Steatotic Liver Disease (1) emphasize the importance of distinguishing between metabolic dysfunctionassociated steatotic liver disease (MASLD) and MASLD with moderate (increased) alcohol consumption (MetALD). This distinction is crucial due to the adverse prognostic implications associated with the concurrent presence of both harmful factors (2,3). The guidelines recommend systematically recording alcohol consumption and/or using validated biomarkers to detect alcohol consumption in all patients (1). However, patient-reported alcohol consumption could underestimate actual intake,



and there is currently no effective, widely available standardized biomarker (4). Nevertheless, the ALD/NAFLD index (ANI) score has shown the ability to identify patients at high risk of alcoholic liver disease based on routine analytical parameters (5).

To investigate this further, we conducted a retrospective single-center pilot study to identify potential cases of unrecognized MetALD in patients with MASLD using the ANI score. Patients attending Digestive Diseases consultations during May and June 2024 were included. MASLD was defined as the presence of hepatic steatosis with alcohol intake of <20 g/day for women and <30 g/day for men, along with at least one cardiovascular risk factor and no other discernible cause (1). Patients with suspected advanced chronic liver disease were excluded. MetALD probability was defined as an ANI>0 (indicating a probability >50%) (5). Sociodemographic variables, alcohol consumption over the last 12 months, liver fibrosis (Kpa) and the Controlled Attenuation Parameter by transient elastography were recorded. These variables were compared between the ANI>0 and ANI<0 groups, with statistical significance set at p<0.05.

We included 85 patients, with a mean age of  $61.8\pm9.7$  years, of whom 52.9% were male. Alcohol consumption was documented in the clinical history for 63.3% (54/85) of cases, among whom 53.4% (29/54) reported not consuming alcohol. According to the ANI score, 21.2% (18/85) had a probability of MetALD (ANI>0), with half (9/18) having a probability >90%. Table 1 shows that alcohol consumption of 10-30 g/day was significantly higher in the ANI > 0 group, all of whom were male. Liver fibrosis was higher in this group (7.6±3.6 vs 5.9±1.7), although this difference did not reach statistical significance.



Even though the ANI score is not validated to differentiate between MASLD and MetALD, our percentage of unrecognized alcoholic liver disease observed is notable. Therefore, it could be a useful tool to enhance diagnostic accuracy, reducing the bias of classifying as MASLD patients who underreport their alcohol consumption. To validate these findings, a prospective study with a significantly larger sample size is underway.

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**Table 1**: Comparison of ANI>0 and ANI<0 groups. Percentages and means</th>with standard deviations are shown. Statistical analysis was based on Chi-Square/Fisher's test and Mann-Whitney U test for qualitative andquantitative variables, respectively. CAP: Controlled AttenuationParameter

	ANI>0 (n = 18)	ANI<0 (n=67)	Odds ratio	p-value
Age (years)	62.2±9.4	61.8±9.8		0.97
Male	100% (18/18)	40.3% (27/67)	Infinity	<0.001
Body mass index	28.7±3.9	31.7±4.6		0.02
Arterial hypertension	61.1% (11/18)	59.7% (40/67)	1.06	0.86
Diabetes mellitus	50% (9/18)	40.3% (27/67)	1.48	0.64
Dyslipidemia	38.9% (7/18)	53.7% (36/67)	0.55	0.39
Recorded alcohol consumption:	72.2% (13/18)	61.2% (41/67)	1.71	0.51
0 gr/week	23.1% (3/13)	63.4% (26/41)	0.17	0.01
10-20 gr/week	15.4% (2/13)	12.2% (5/41)	1.31	0.54
30-60 gr/week	7.7% (1/13)	4.9% (2/41)	1.65	0.57
10-20/30 gr/day (female/male)	53.9% (7/13)	19.5% (8/41)	4.85	0.03
Fibrosis (Kpa)	7.6±3.6	5.9±1.7		0.18
САР	292.7±46.6	305.6±51.9		0.41
AST (U/L)	46.7±35.7	34.1±15.9		0.08
ALT (U/L)	38.9±33.6	39.1±23.9		0.39