Characterization of three metabolic dysfunction-associated steatotic liver disease clusters in a real-life cohort and their association with liver stiffness evolution

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Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a large spectrum of conditions with possible hepatic and extra-hepatic outcomes. A recent groundbreaking analysis revealed that patients can be classified into three main clusters based on routine clinical data: controls (CTRL), liver-specific steatotic liver disease (LS-SLD) and cardiometabolic (CM-SLD) (Raverdy *et al*. Nat Med. 2024).

Aim

To determine the prevalence and clinical profile of MASLD clusters in a single-center external cohort and assess the association with baseline and follow-up liver stiffness measurement (LSM).

Methods

Patients with MASLD diagnosed by transient elastography were prospectively included and followed. LSM and controlled attenuation parameter (CAP) were recorded at baseline and follow-up. MASLD clusters (CTRL, LS-SLD and CM-SLD) were determined using the clustering tool based on age, body mass index (BMI), glycated hemoglobin (HbA1c; calculated from the latest available blood glucose when HbA1c was missing), alanine aminotransferase (ALT), triglycerides (TG) and low-density lipoprotein-cholesterol (LDL-C). Relative changes in LSM (%) at one- and three-year of standard follow-up (1Y-FU, 3Y-FU) compared to baseline were used to assess longitudinal evolution. Results are presented as median.

Results

438 patients diagnosed with MASLD were recruited. Their median age was 54 years, 51 % were male, with a median BMI of 32.0 kg/m^2, HbA1c of 5.6 %, ALT of 45 IU/L, LDL-c of 105 mg/dL and TG of 150 mg/dL. Median LSM was 7.9 kPa with 55 % having ≥ F2 stage and median CAP was 325 dB/m with 75 % at S3 stage.

MASLD clustering identified 45 % CTRL, 16 % LS-SLD and 8 % CM-SLD. 31 % were non-classified due to missing data. Compared to CTRL and LS-SLD groups, CM-SLD were older (55 vs. 45 vs. 61 years; $p < 0.001$) with similar gender distribution across clusters. Compared with CTRL and LS-SLD, CM-SLD had substantially higher HbA1c (5.5 vs. 5.5 vs. 8.0 %; $p < 0.001$), blood glucose (100 vs. 103 vs. 155 mg/dL; $p < 0.001$) and greater prevalence of type 2 diabetes (32 vs. 31 vs. 92 %; $p < 0.001$). They also showed higher TG (135 vs. 161 vs. 188 mg/dL; $p < 0.001$), prevalence of

dyslipidemia (36 vs. 24 vs. 78 %; $p < 0.05$) and hypertension (49 vs. 31 vs. 89 %; $p < 0.01$). The incidence of past cardiovascular events is also doubled, although this difference is not statistically significant (13 vs. 11 vs. 24 %; $p > 0.05$). CM-SLD also had higher baseline LSM (7.2 vs. 7.9 vs. 11.9 vs.; $p < 0.001$) and higher prevalence of ≥ F2 (48 vs. 53 vs. 87 %; $p < 0.001$). CTRL had lower CAP compared to CM-SLD (317 vs. 330 vs. 344; $p < 0.001$). Compared with CTRL, LS-SLD and CM-SLD presented higher aspartate aminotransferase (26 vs. 48 vs. 41IU/L, $p < 0.001$), γ-glutamyl transferase (42 vs. 77 vs. 62 IU/L; $p < 0.001$) and ALT levels (34 vs. 87 vs. 53 IU/L; $p < 0.001$). In addition, ALT was higher in LS-SLD than CM-SLD.

Follow-up attendance was 62 % at 1Y-FU and 41 % at 3Y-FU. CTRL were more likely to return at 1Y-FU than LS-SLD (69 vs. 56 vs. 65 %; $p < 0.05$). At 3Y-FU, despite similar weight loss across clusters (-2.2 vs. -2.9 vs. -4.0 %, NS), CM-SLD showed greater improvement in LSM than CTRL (-1.4 vs. -12.8 vs. -21.1 %; $p < 0.05$). LS-SLD showed a numerically great improvement in LSM but without reaching statistical significance. Consistently, the proportion of patients improving their LSM ≥ 20 % was higher in LS-SLD and CM-SLD compared with CTRL (23 vs. 46 vs. 53 %; $p < 0.05$).

Conclusion

MASLD clustering is applicable in a real-life single-center cohort and discriminates patients into subgroups. Clinical data non-included in the score and transient elastography confirm that this classification is discriminatory. CTRL patients have lower CAP and CM-SLD patients have higher LSM and hypertension. Longitudinal data show that standard care can reduce the severity of the liver disease in both LS-SLD and CM-SLD clusters. This suggests that this tool could be used in routine practice to better guide patient care.