

Anti-sonic hedgehog immunohistochemistry accurately diagnosis ballooning degeneration in both metabolic dysfunction-associated steatotic liver disease and alcohol-related liver disease

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Background and aims

Ballooning degeneration is a key histological marker of steatotic liver disease (SLD) severity, but it remains difficult to identify reliably and shows poor inter-observer agreement. Sonic hedgehog pathway is involved in ballooning pathogenesis. Our objective was to assess the diagnostic accuracy of anti-SHH immunohistochemistry (IHC) for the diagnosis of ballooning degeneration in SLD.

Method

Recruited participants with a diagnosis of SLD (MASLD or ALD) on imaging and increased liver stiffness (≥ 9 kPa, M probe, Fibroscan[®]) underwent liver biopsy. Four blinded pathologists scored hematoxylin-eosin stained slides for steatosis and activity including ballooning. Anti-SHH IHC was performed on the same liver samples and quantified manually (positive cells per field at 40-fold magnification) by two untrained observers blinded to the pathology score.

Results

Eighty-eight participants with SLD (52 with MASLD, 36 with ALD) were prospectively recruited and underwent liver biopsy. Median self-reported alcohol consumption was 80 units per week in the ALD group. Mean BMI was significantly higher in the MASLD group (34.7 kg/m^2) compared to the ALD group (27.3 kg/m^2 ; $p < 0.0001$). 38% of cases were classified by pathologists as fibrosis grade 0-1 (F0-1), 30% as F2, 26% as F3 and 6% as F4 in the pooled SLD group. 46% of MASLD cases were classified as ballooning grade 0 (B0), 27% as B1 and 27% as B2 while 61% of ALD were classified as B0, 14% as B1 and 25% as B2. The count of SHH positive cells strongly correlated between untrained observers ($r = 0.89$, $p < 0.0001$) across the whole SLD cohort. SHH positive density positively correlated with ballooning grades in MASLD ($r = 0.71$, $p < 0.0001$), ALD ($r = 0.75$, $p < 0.0001$) and pooled SLD ($r = 0.69$, $p < 0.0001$). In particular, the median SHH density was 0.03 for B0, 0.16 for B1 and 0.96 for B2 in the pooled SLD group ($p < 0.0001$). SHH density showed a very high diagnostic accuracy for the diagnosis of ballooning in MASLD (AUC = 0.83, $p < 0.0001$), ALD (AUC = 0.94, $p < 0.0001$) and pooled SLD (AUC = 0.86, $p < 0.0001$).

Conclusion

Anti-SHH IHC is a highly accurate tool for the diagnosis of ballooning by untrained observers in MASLD and ALD highlighting its potential utility in clinical practice and research in the topic of SLD.

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