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Liver function tests in NAFLD: Changes in upper normal limits, does it really matter?

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Background and aims: Non-Alcoholic Fatty Liver Disease (NAFLD) is the commonest cause of abnormal liver function tests (LFTs). The current Upper Normal of Limit (UNL) of LFTs was derived from an apparently "healthy" population, where a high rate of undiagnosed NAFLD and chronic viral hepatitis may be suspected. We aimed to evaluate potential implications of changes in UNL of ALT in patients with NAFLD.

Method: We retrospectively assessed consecutive first referrals with a clinical or histological diagnosis of NAFLD from 2010 to 2017. The high UNL of ALT was set at 45 IU/L for men and 34 IU/L for women, while the low UNL of ALT was set at 30 IU/L for men and 19 IU/L for women. The UNL of AST was 40 IU/L for both men and women. Liver biopsies were scored according to the NASH CRN Scoring System. All patients underwent Liver Stiffness Measurement (LSM).

Results: 436 patients were enrolled; of these, 288 underwent liver biopsy. Lowering the UNL of ALT reduced the percentage of patients who had liver fibrosis or NASH despite normal ALT from 10% to 4% and from 28% to 4% respectively. However, the percentage of those with increased ALT and no evidence of liver fibrosis or NASH increased from 27% to 33% and from 3% to 19% respectively. There were no differences in terms of demographic, anthropometric and metabolic features.

Conclusion: Liver function tests might both under- and overestimate NASH-related liver disease. Reducing the UNL might not beneficial and lead to an increase in overall healthcare burden. Risk stratification in NAFLD should rely on a combination of risk factors, not on LFTs alone.