2nd GLOBAL LIVER HEALTH FORUM

HEPATIC STEATOSIS IN MAFLD – IMPORTANCE OF EARLY INTERVENTION

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Resources

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NAFLD/MAFLD disease progression

NAFLD includes the following histological subtypes: isolated steatosis, steatosis with mild inflammation, and NASH. NASH is associated with hepatocyte injury and ballooning, is recognized as a progressive form of fatty liver disease and has been documented to have the potential to progress to cirrhosis, HCC and end-stage liver disease.[1,2,3]

A retrospective cohort study was conducted to examine incidence rates for cirrhosis and HCC, and to evaluate the risk of cirrhosis and HCC. The results of this study showed that patients with hepatic steatosis with persistently normal ALT were at lower risk for cirrhosis and HCC (though the risk is not non-existent) compared with those with steatosis and elevated ALT, and not different from the risk in a clinical cohort without steatosis.[4]

DTA of tools available for the diagnosis of NAFLD/MAFLD

Liver biopsy is the gold standard for diagnosis of NAFLD, but it is invasive and subject to sampling error.[5] Several non-invasive tests have been suggested as alternatives to liver biopsy for assessing the severity of liver scarring (fibrosis) and steatohepatitis in patients with NAFLD. These include the liver enzyme, CGT,[6] ultrasound,[7] CT without contrast,[8] MRI,[9] and MRS,[10] but these are not without limitations.

A systematic review and meta-analysis showed that when elastography index tests are acquired successfully, they have acceptable diagnostic accuracy for advanced fibrosis and cirrhosis.[11]

Quantitative assessment of MRI-PDFF had the highest diagnostic accuracy for stage 1 detection (HSROC 0.97); the diagnostic accuracy was the same for detecting ≥S2 and ≥S3 with HSROC values of 0.93 and 0.91, respectively.[12] Quantitative assessment of liver fat by TE with CAP (FibroScan®) had the highest diagnostic accuracy for detecting steatosis stage ≥S1, with HSROC 0.85. The diagnostic accuracy was relatively lower for S3 detection, with HSROC 0.79.[12]

Artificial intelligence (AI) applications may help physicians in implementing a complete automated NAFLD diagnosis and staging. A systematic review showed that deep-learning index demonstrated the best diagnostic ability to distinguish between moderate and severe NAFLD (AUC 0.958). Extreme learning machine (ELM, a class of Symtosis) had a diagnostic accuracy of 96.75%, AUC 0.97. Support vector machines had a diagnostic accuracy of 89.01%, AUC 0.91.[13]

Lifestyle modifications for NAFLD/MAFLD

Evidence from a network meta-analysis that assessed the comparative benefits and harms of different lifestyle interventions in the treatment of NAFLD indicates considerable uncertainty about the effects of the lifestyle interventions compared with no additional intervention (to general public health advice) on any of the clinical outcomes after a follow-up period of 2–24 months in patients with NAFLD. Accordingly, high-quality randomized clinical trials with adequate follow-up are needed.[14]

Indications for EPL administration in steatosis, and clinical evidence of their use in NAFLD/MAFLD

The MANPOWER study examined the real-world effects of EPL on steatosis and transaminases. This was an observational, multicenter study of EPL treatment in NAFLD patients with cardiometabolic comorbidities for 24 weeks.[15–17] As per available data, simple steatosis was reported in 74.9% of the 2843 patients included in this study. EPL administered as adjunctive therapy in patients with NAFLD with metabolic comorbidities improved the ultrasonographic features of NAFLD, particularly regarding liver echogenicity and structure.[17] Significant decreases in ALT, AST and GGT ($P<0.05$) were observed following 3 and 6 months of treatment with EPL.[16]

In a study of EPL in 147 patients with NAFLD and/or viral hepatitis (HBV/HCV), 12 weeks of EPL paste 600 mg TID resulted in improvements in general and gastrointestinal symptoms. Significant improvements in patient-reported outcomes were recorded in Weeks 4, 8 and 12.[18]

The Russian clinical guidelines on MAFLD recommend screening by St-index for liver steatosis, and ultrasound as a routine liver steatosis diagnostic tool. Recommended therapeutic options include weight reduction, physical activity, and EPL.[19]

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ALT, alanine aminotransferase; CAP, controlled attenuation parameter; CT, computed tomography; DTA, diagnostic test accuracy; ELM, extreme learning machine; EPL, essential phospholipids; GGT, gamma-glutamyl transferase; HBV, hepatitis B; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HSROC, hierarchical summary receiver operating characteristic curves; MAFLD, metabolic-associated fatty liver disease; MRI, magnetic resonance imaging; MRI-PDFF, magnetic resonance imaging-proton density fat fraction; MRS, magnetic resonance spectroscopy NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; transient elastography; S, stage; TID, three times a day.

Learning objectives:

- Explore prognostic scenarios of steatosis in MAFLD
- Become familiar with the DTA of tools available for the diagnosis of MAFLD
- Understand the effects of lifestyle modifications for MAFLD
- Understand the effects of EPL administration in steatosis, and clinical evidence of their use in MAFLD

Main takeaways:

- Liver biopsy is currently the gold standard for NAFLD/MAFLD diagnosis; however, it is invasive and subject to sampling error, highlighting the need for accurate, alternative diagnostic techniques
- Early intervention appears to improve long-term outcomes in patients with NAFLD/MAFLD, albeit the best time to start the intervention is still in debate
- There is uncertainty around the effects of lifestyle modification in patients with NAFLD/MAFLD
- EPL treatment as adjunctive therapy can improve clinical outcomes in patients with NAFLD/MAFLD, and have been recommended in clinical guidelines

DTA, diagnostic test accuracy; EPL, essential phospholipids; MAFLD, metabolic-associated fatty liver disease.

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