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Improvement of the verification of liver fibrosis using new minimally invasive markers in patients with metabolic-associated steatotic liver disease

Yu.M. Stepanov, V.I. Didenko, I.A. Klenina, O.M. Tatarchuk, O.P. Petishko

SI "Institute Gastroenterology of the National Academy of Medical Sciences of Ukraine"
96, Slobozhanskyi Ave., Dnipro, Ukraine, 49074
inklenina@gmail.com

Background. Improvement of the verification of early-stage liver fibrosis using new minimally invasive markers in patients with metabolic-associated steatotic liver disease (MASLD) is a topical issue today. **Aim.** To identify new minimally invasive serum markers of fibrotic liver changes in patients with MASLD and compare them with well-known fibrosis diagnostic indices. **Methods.** We examined 108 patients with MASLD with a mean age of (48,0±1,84), of whom 84 were without fibrosis and 24 had fibrosis that was confirmed morphologically. The concentration of TNF-α, IL-10, insulin, and α1-acid glycopeptide in the blood serum was determined by ELISA, and the activity of enzymes (ALT, AST, GGTP, ALP), hemostatic system, lipid, carbohydrate, and protein metabolism in the blood were measured to calculate fibrosis indices: Forns index, APRI, FIB-4 AAR. Correlation analysis was performed according to Spearman (r), and ROC analysis was used to assess the diagnostic efficiency of the indicators with the determination of the area under the ROC curve (AUC) and its 95% confidence interval (CI) to determine the quality and reliability of the diagnostic model (p). **Results.** In patients with MASLD, the liver stiffness was found to be in a direct correlation with the HOMA-IR index ($r = 0.710$; $p < 0.05$), which was 1.7 times higher in the patients with liver fibrosis than without fibrosis. A direct correlation was found between the liver stiffness index and α1-acid glycopeptide ($r = 0.693$; $p < 0.05$), which was 1.4 times ($p < 0.05$) higher in patients with liver fibrosis than without fibrosis, and with the TNFα/IL-10 ratio ($r = 0.637$; $p < 0.05$), which was 5.6 times ($p < 0.05$) higher in the patients with liver fibrosis than without fibrosis. According to the results of ROC analysis, the diagnostically significant risk markers for the development of liver fibrosis in patients with MASLD are TNFα/IL-10 values of more than 0.77 (sensitivity — 63.6%, specificity — 79.4%), NOMA-IR values of more than 6.4 (sensitivity — 71.4%, specificity — 88.5%), and α1-acid glycopeptide content of more than 0.43 g/l (sensitivity — 75.5%, specificity — 82.5%). Taking into account the area under the ROC curves for TNFα/IL-10 ($AUC = 0.778$; $p < 0.0001$), NOMA-IR ($AUC = 0.796$; $p < 0.0001$) and α1-acid glycopeptide ($AUC = 0.799$; $p < 0.0001$), it is possible to assert the good quality of these diagnostic criteria. According to the results of the ROC analysis of the generally accepted fibrosis assessment indices, it was found that the best result was obtained with the AAR index at a threshold value of > 0.85, $AUC = 0.762$ ($p < 0.001$), but its validity was lower relative to TNFα/IL-10, α1-acid glycopeptide and HOMA-IR. **Conclusions.** Comparison of the diagnostic value of biological markers obtained in our study with well-known fibrosis scores showed that TNFα/IL-10, NOMA-IR, and α1-acid glycopeptide content are more sensitive and specific. New possible biomarkers for predicting the development of liver fibrosis in patients with MASLD were obtained. A largest cogort and additional studies are needed to validate the proposed biomarkers panel.

Keywords: metabolically associated fatty liver disease, fibrosis of liver, cytokines, biochemical markers.