ABSTRACT

INTRODUCTION: Metabolic dysfunction-associated steatotic liver disease (MASLD) is now the most common cause of non-infectious hepatitis worldwide with a prevalence of 25-30%. It is rising constantly over the years in proportion to the global increase in obesity and metabolic syndrome. MASLD is divided into simple steatoisis (MASL), metabolic dysfunction-associated steatohepatitis (MASH) and cirrhosis. It is diagnosed when hepatic steatosis is present (in imaging tests or liver biopsy) excluding other potential causes of steatosis with the presence of at least one criteria of cardiovascular or metabolic disorders. Patients with MASH with fibrosis stage F2-F4, referred to as "at risk" MASH, prestent a higher risk of morbidity and mortality associated with the development of cirrhosis and its complications. The gold standard for the diagnosis of MASLD, especially MASH, remains liver biopsy. However, non-invasive tests for liver fibrosis assessment are becoming more widely used in clinical practice.

AIM: The aim of the study was to retrospectively analyze clinical, biochemical and imaging studies in patients with MASLD confirmed by liver biopsy and to compare non-invasive makers of liver fibrosis.

STUDY GROUP AND METHODS: The study included 80 patients (25 females, 55 males) with MASLD confirmed in liver biopsy, hospitalized in the Department of Internal Medicine and Hepatology of the National Medical Institute of the Ministry of Internal Affairs and Administration in Warsaw from 1.01.2018 to 30.06.2023. The analysis of medical history, laboratory, imaging tests and liver biopsy was performed. Two groups were distinguished according to the stage of fibrosis in the liver biopsy: with minor fibrosis (F0-F1) and with significant fibrosis (≥F2). Also, the most common markers of insulin resistance (HOMA-IR, QUICKI-IR, TyG index, TG/HDL ratio), non-invasive tests of hepatic steatosis (Hepatic Steatosis Index, controlled CAP suppression parameter) and liver fibrosis (AST/ALT ratio, FIB-4, APRI, NAFLD Fibrosis Score, BARD scale, Fibroscan) were assessed and compared with the results of liver biopsy. The ROC curves were drawn for each non-invasive test of liver fibrosis and new cutoff points in the diagnosis of significant fibrosis using the Youden index were determined.

RESULTS: According to liver biopsy, significant fibrosis (≥F2) was found in 32 patients, and non-significant fibrosis (<F2) in 48 patients. The group of patients with ≥F2 fibrosis

had higher BMI [30,91 (27,91-34) kg/m^2 vs. 28,08 (25,99-31,12) kg/m^2, p=0,017], lower total cholesterol [172 (148-208) mg/dl vs.189 (166,5-214) mg/dl, p=0,019], non-HDL cholesterol [129 (104-157) mg/dl vs. 143 (120-170) mg/dl, p=0,029] and triglycerides [125,5 (99-167,5) mg/dl vs. 164 (119-203) mg/dl, p=0,022], lower platelets [210 (190,5-242) x10^3/uL vs. 258,5 (210-302) x10^3/uL, p=0,001], higher creatinine [0,92 (0,82-1) mg/dl vs. 0,85 (0,76-0,95) mg/dl, p=0,017] and lower eGFR [82 (68,5-97) ml/min/1,73m^2 vs. 91 (83,5-110) ml/min/1,73m^2, p=0,002], lower TyG index [8,72 (8,43-8,94) vs. 8,84 (8,57-9,14), p=0,039) and higher AST [61,5 (44-99) U/l vs. 47,5 (37,5-59,5) U/l, p=0,02] compared to the group with <F2 fibrosis. The group with ≥F2 fibrosis was more likely to present with hypertension (62,5% vs. 37,5%, p=0,03), type 2 diabetes (50% vs. 10,42%, p<0,001), obesity (56,25% vs. 33,33%, p=0,04) and metabolic syndrome (62,07% vs. 38,10%, p=0,05). The percentage of steatosis in the liver biopsy correlated with body weight (R=0,254, p=0,023), BMI (R=0,279, p=0,012), leukocyte count (R=0,251, p=0,024), ALT (R=0,337, p=0,002) and AST (R=0,373, p=0,001) activity, controlled attenuation parameter (CAP) in Fibroscan (R=0,415, p=0,014), fasting insulin concentration (R=0,447, p=0,017), HOMA-IR (R=0,411, p=0,033) and inversely correlated with QUICKI (R=-0,411, p=0,033). There was a positive correlation between the steatosis grade and AST (R=0,345, p=0,002) and ALT (R=0,367, p<0,001) activity, between the lobular inflammation and AST (R=0,275, p=0,013), and between the fibrosis stage and AST (R=0,272, p=0,015). In logistic regression, it was found that the higher fibrosis stage in the liver biopsy significantly increased the risk of hypertension (OR=2,16; p=0,006; 95% CI=1,25-3,76) and metabolic syndrome (OR=1,89; p=0,024; 95% CI=1,09-3,29), while higher hepatocyte ballooning stage increased the risk of metabolic syndrome (OR=2,25; p=0,043; 95% CI=1,03-4,95). All non-invasive methods for assessing liver fibrosis positively correlated with the fibrosis stage in the liver biopsy, with the BARD score showing the highest correlation coefficient (R=0,626, p<0,001). The largest area under the ROC curve was obtained for Fibroscan (AUROC=0,832), while tests including biochemical parameters showed similar diagnostic accuracy with minor superiority for FIB-4 and NAFLD Fibrosis Score. The combination of tests presented an increase in their diagnostic accuracy. The new optimal cutoff points of each non-invasive test based on the Youden index in order to identify patients with ≥F2fibrosis were lower than those previously presented in the literature, which was associated with an increase in their sensitivity and negative predictive value.

CONCLUSION: MASLD is strongly associated with metabolic syndrome, therefore the patients with obesity, hypertension, dyslipidemia and diabetes should be closely monitored for hepatitis and liver fibrosis. Non-invasive liver fibrosis assessment tests based on medical history and biochemical tests appear to be useful in assessing the fibrosis stage. They become particularly important with the appearance of the treatment and the FIB-4 or NAFLD Fibrosis Score seem to be the most effective. The best non-invasive test for assessing liver fibrosis is liver stiffness measurement in Fibroscan. While using non-invasive tests to diagnose F2-F4 liver fibrosis, a lower cut-off point or using two methods simultaneously in patients with MASLD should be considered. The liver biopsy remains gold standard in the cases of non-specific clinical picture or rapidly progressive fibrosis.

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