



## Monitoring of Liver Function in Patients with Fatty Liver Disease in combination with Coronary Heart Disease and type 2 Diabetes Mellitus

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### ABSTRACT

The aim of the study was to examine the liver detoxification function by comparing a <sup>13</sup>C- methacethine breath test, with a Forns formula and with liver transaminases in patients with coronary heart disease and type 2 diabetes mellitus in combination with nonalcoholic fatty disease. Comparisons of the rates of metabolism ( $p < 0.01$ ) between cumulative dose at 40 minutes ( $p < 0.01$ ) with those at 120 minutes ( $p < 0.01$ ), in two groups of patients displayed more signs of steatohepatitis than signs of steatosis. Use of the <sup>13</sup>C-methacethine test to diagnose pathological changes in the liver in the early stages of NAFLD (steatosis, steatohepatitis) is positively correlated with the Forns formula. It is likely to find fibrosis of the liver when Forns formula is over 4.25, <sup>13</sup>C-breath test at least 10%, lower levels of ALT and bilirubin, and elevated triglycerides contrary.

**Keywords:** nonalcoholic fatty liver disease, steatosis, steatohepatitis, fibrosis, <sup>13</sup>C- methacethine breathe test, Forns formula, ultrasonography

### INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is diagnosed in a significant proportion of coronary artery disease and type 2 diabetes patients, exacerbating the underlying disease. It is frequently associated with abdominal obesity, diabetes mellitus, arterial hypertension, age over 45 years and the ratio of transaminase activity [10, 6]. Although this disease often comes across asymptomatic, the progression of steatosis to steatohepatitis is found in almost half of cases and in not less than 1/6 of patients fibrosis of liver develops. It is also known that 72% of patients with coronary heart disease combined with type 2 diabetes are diagnosed with NAFLD [3, 4, 6]

The problem of the development and progression of NAFLD in addition to coronary heart disease and type 2 diabetes mellitus is one of the most important and urgent tasks of internal medicine, since it leads to the worsening of comorbid diseases [1].

Patients with NAFLD are usually asymptomatic, high values of liver enzyme tests being the most common find-

ing [6, 10]. The definitive diagnosis of NAFLD is based on liver biopsies, which show inflammatory infiltrates, Mallory bodies and signs of fibrosis [5, 7, 2]. Although liver biopsy is the current gold standard for diagnosis of NAFLD, it is not a practical screening tool given the cost, time-consuming nature and potential morbidity of this procedure [2, 3, 10].

However, more attention is paid to early diagnosis of NAFLD by using either special sets of designed formulas with biochemical parameters, data Fibroscan, or respiratory tests with <sup>13</sup>C-methacethine (C13-MBT) and <sup>13</sup>C-aminopyrine [3, 5, 7].

The aim of the study was to examine the liver detoxification function by comparing a <sup>13</sup>C- methacethine breath test, with a Forns formula and with liver transaminases in patients with coronary heart disease and type 2 diabetes mellitus in combination with nonalcoholic fatty disease.

### MATERIAL AND METHODS

The study involved 52 patients with type 2 diabetes (male 48, female 83, aged 43 to 82 years, mean age  $60.94 \pm 0.82$  years). Among them, 32 patients with type 2 diabetes (mean age  $64.5 \pm 1.58$ ) and 20 patients with coronary

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artery disease, stable angina and II FC (mean age  $54.60 \pm 2.74$ ).

Biochemical tests were taken for the presence of the functional state of liver disorders, including total bilirubin, AST, ALT, AST/SLT and lipidogram.

Studies for the presence of fibrotic changes were conducted by calculating a Forns formula:  $7.811 - 3.131 \ln(\text{platelets}) + 0.781 \ln(\text{GGTP}) + 3.467 \ln(\text{age}) - 0.014(\text{cholesterol, mg/dl})$ . Result less than 4.2 corresponded to absence of fibrosis.

To determine the degree of liver injury all patients underwent a 13C-MBT. These antitoxic function were evaluated on the basis of the total concentration of 13CO<sub>2</sub>, 40 and 120 minutes [5].

## RESULTS

According to the ultrasonography of patients with coronary artery disease and type 2 diabetes there was a diffuse increase in the echogenicity of the liver parenchyma a slight increase in its size, which is consistent with steatosis: liver echogenicity was significantly higher than the echogenicity of a normal kidney or psoas. In other patients hyperechogenic liver parenchyma and a slight enlargement of the portal vein (more than 13 mm in diameter), was observed which is more typical of steatohepatitis. For the group of fibrosis patients these items were characteristic: some rough inner echostructure, periportal fibrosis, echogenic membrane lesions (fibrotic transformation of branches of portal vessels, echogenic strips) and signs of portal hypertension. Groups were formed based on the ultrasound information, which showed their clinical NAFLD stage. Among them, 10 patients were found with steatosis, 12 – with steatohepatitis, 5 – with fibrosis and in 5 patients NAFLD was not found.

Comparison of biochemical parameters in patients with type 2 diabetes in combination with coronary artery disease, found that levels of bilirubin, AST, ALT and AST/ALT were significantly different from that of patients without NAFLD ( $p < 0.05$ ).

The difference between TG was unreliable in the fibrosis group ( $p < 0.05$ ) and a group without NAFLD ( $p < 0.01$ ). However, as in previous results, indicator lipidogram did not exceed normal limits, despite the presence of NAFLD.

Use of a Forns formula revealed in subgroups of clinical forms of NAFLD functional and morphological changes in the liver. This formula clearly indicated the absence of fibrosis in groups of steatosis, steatohepatitis and fibrosis ( $< 4.25$ ), and clearly showed its presence at a value 5.26 in patients with fibrotic changes. The reliability of the difference was between groups of patients with steatohepatitis and fibrosis ( $p < 0.05$ ), between groups steatohepatitis and group of liver without NAFLD ( $p < 0.05$ ). A strong negative relationship was marked between the Forns formula

and ALT levels ( $r = -0.944$ ) and bilirubin ( $r = -0.967$ ) in patients with fibrosis.

As a result of 13C-MBT, patients without NAFLD indexed antitoxic liver function beyond the norm ( $20.44 \pm 0.66\%$ ). Patients with steatosis from steatohepatitis showed a moderate reduction in liver function, respectively, ( $10.94 \pm 1.22\%$ ) and ( $11.69 \pm 0.48\%$ ). A significant difference between the rates of two subgroups were found, while fibrosis was almost three times lower than other indicators and meant a marked reduction in the antitoxic function of the liver ( $6.32 \pm 1.47\%$ ).

Analyse of liver transaminases and data-13C methacetin tests showed a higher metabolic rate correlated with higher cumulative doses 40 and 120 minutes and normal ALT levels ( $p < 0.05$ ).

A reduction in the rate of metabolism and cumulative doses 40 and 120 minutes was observed with increasing levels of ALT ( $p < 0.05$ ).

Comparisons of the rates of metabolism ( $p < 0.01$ ) between cumulative dose at 40 minutes ( $p < 0.01$ ) with those at 120 minutes ( $p < 0.01$ ), in two groups of patients displayed more signs of steatohepatitis than signs of steatosis.

## DISCUSSION

1. When monitoring the hepatic function in patients with coronary artery disease and type 2 diabetes it is desirable to include data from the ultrasound of the liver examination of hepatic transaminases and the evaluation a 13C-methacetin test which shows the metabolic rate and the cumulative dose percent. This data reflects deviations in the functional state and the initial manifestations of fibrotic changes in the liver parenchyma.
2. The result of the Forns formula calculation must be more than 4.25 to diagnose the fibrosis as clinical stage NAFLD.
3. Use of the 13C-methacetin test to diagnose pathological changes in the liver in the early stages of NAFLD (steatosis, steatohepatitis) is positively correlated with the Forns formula.
4. It is likely to find fibrosis of the liver when Forns formula is over 4.25, 13C-breath test at least 10%, lower levels of ALT and bilirubin, and elevated triglycerides contrary.

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