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A METHOD OF DIAGNOSING NON-ALCOHOLIC FATTY LIVER DISEASE WITH THE CALCULATION OF THE STEATOSIS INDEX

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СПОСОБ ДИАГНОСТИКИ НЕАЛКОГОЛЬНОЙ ЖИРОВОЙ БОЛЕЗНИ ПЕЧЕНИ С РАСЧЕТОМ ИНДЕКСА СТЕАТОЗА

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Objective. To work out the index for diagnosing non-alcoholic fatty liver disease (NAFLD) in women with metabolic syndrome (MS) in postmenopause using generally available markers.

Materials and methods. 62 females with NAFLD and MS in early postreproductive period took part in the study. They were compared to 24 relatively healthy females not suffering from obesity in postmenopause. The average age of the patients was $49,9 \pm 1,1$. Hepatic steatosis was diagnosed by ultrasound examination. The

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mathematic model of hepatic steatosis index (HSI) calculation included: body mass index (BMI), waist size (WS), triglycerides and low-density lipoproteins (LDL).

Results. BMI and WS in patients with MS and NAFLD in postmenopause were considerably more than in relatively healthy women. Hypertriglyceridemia and an increase of LDL in blood serum were noted in patients with steatosis. Biometric and laboratory data were included in the mathematical formula which allows to calculate HSI. With HSI 0,5 and more NAFLD is diagnosed in women in post menopause, when HSI is lower than 0,5 it is not diagnosed. Indicators of sensitivity and specificity of the method were 98,4 % and 95,85 % respectively.

Conclusions. The minimally invasive method suggested above allows to reveal hepatic steatosis in females with MS in early postreproductive period. High diagnostic characteristics of the method are worth mentioning, as well as the possibility to be widely used thanks to simple biometric and laboratory data employed.

Keywords. Non-alcoholic fatty liver disease, hepatic steatosis, steatosis index, menopause.

Цель. Разработать индекс для диагностики неалкогольной жировой болезни печени (НАЖБП) у женщин с метаболическим синдромом (МС) в постменопаузе с использованием общедоступных маркеров.

Материалы и методы. В исследовании приняли участие 62 пациентки с НАЖБП и МС в раннем пострепродуктивном периоде, средний возраст $49,9 \pm 1,1$ года, и 24 относительно здоровые женщины без ожирения в постменопаузе, которые составили группу сравнения. Диагноз стеатоза печени был поставлен методом ультразвукового исследования. В математическую модель расчета индекса стеатоза печени (ИСП) печени были включены следующие параметры: индекс массы тела (ИМТ), объем талии (ОТ), триглицериды (ТГ) и липопротеиды низкой плотности (ЛПНП).

Результаты. ИМТ и ОТ у пациенток с МС и НАЖБП в постменопаузе были значимо выше, чем в группе сравнения ($p = 0,001$ и $p = 0,001$ соответственно). Также у женщин со стеатозом регистрировалась гипертриглицеридемия и повышение ЛПНП в сыворотке крови. Исследуемые биометрические и лабораторные показатели были включены в математическую формулу, позволяющую рассчитать ИСП. При значении ИСП, равном 0,5 и более, диагностируют наличие НАЖБП у женщин в постменопаузе, при ИСП менее 0,5 – отсутствие. Показатели чувствительности и специфичности метода составили 98,4 и 95,8 % соответственно.

Выводы. Предложенный малоинвазивный метод позволяет выявить стеатоз печени у женщин с МС в раннем пострепродуктивном периоде. Стоит отметить высокие диагностические характеристики предлагаемого метода и его доступность для широкого применения, так как используются простые биометрические и лабораторные показатели.

Ключевые слова. Неалкогольная жировая болезнь печени, стеатоз печени, индекс стеатоза, менопауза.

INTRODUCTION

Metabolic syndrome (MS) and associated nonalcoholic fatty liver disease (NAFLD) present pathologic manifestations and diagnosis that are in the area of interest of almost every therapeutic specialist. The presence of MS and/or obesity

signs in a patient indicates a high NAFLD risk, and therefore, routine screening examination of this group of patients is recommended to identify NAFLD. Postmenopausal women, especially those not taking hormone replacement therapy, are at risk for NAFLD. Hypoestrogenism leads to obesity, which is recorded in more than half of

postmenopausal women [1–3]. Liver steatosis is detected in 60 %–75 % of patients aged 40–50 years with metabolic disorders. Some reports showed that postmenopausal women develop liver fibrosis faster than premenopausal women and men [4].

According to the clinical guidelines for the management of NAFLD patients, ultrasound is used for detecting liver steatosis [5; 6]. Ultrasound was found to detect steatosis in only 12 %–20 %, and its accuracy may decrease in morbidly obese patients [7]. Moreover, liver biopsy with a morphological study of the specimen may be conducted to diagnose steatosis. However, the use of this method in widespread clinical practice is limited owing to its invasiveness and risk of complications. Currently, non-invasive and minimally invasive diagnostic methods of NAFLD using laboratory markers are preferred [5; 8].

The development of new accessible diagnostic methods for NAFLD continues, which should facilitate screening for liver steatosis in patients primarily from risk groups including women of post-reproductive age.

The study aimed to develop an index for diagnosing NAFLD in postmenopausal women with MS using publicly available markers.

MATERIALS AND METHODS

The study included 62 post-reproductive patients with NAFLD and MS, with

a mean age of 49.9 ± 1.1 years, and 24 relatively healthy nonobese postmenopausal women who comprised the comparison group. Written informed voluntary consent was obtained from all study participants. Liver steatosis was diagnosed by ultrasound.

The mathematical model for calculating the hepatic steatosis index (HSI) included the following parameters: body mass index (BMI), waist circumference (WC), triglyceride (TG) levels, and low-density lipoproteins (LDL). The blood serum concentrations of TG and LDL were determined using a Landwind LW C200i analyzer (Shenzhen Landwind Industry Co., Ltd., China) with kits from Vector-Best (Novosibirsk, Russia).

The constant and coefficients for this equation were calculated using the multiple regression method. The indicator of the presence of liver steatosis according to liver ultrasound was used as the dependent variable.

RESULTS AND DISCUSSION

BMI and WC in postmenopausal patients with MS and NAFLD were significantly higher than those in the comparison group ($p = 0.001$ and $p = 0.001$, respectively). Hypertriglyceridemia and increased LDL in the blood serum were recorded in women with steatosis. Various studies have reported dyslipidemia in 50 %–80 % of NAFLD patients [7; 9].

The studied biometric and laboratory indicators were included in the following equation used to calculate HSI¹:

$$\text{HSI} = -1.4672 + 0.0096 \cdot \text{BMI} + 0.0151 \cdot \text{WC} + 0.0157 \cdot \text{TG} + 0.1406 \cdot \text{LDL}$$

NAFLD is diagnosed in postmenopausal women when the HSI value is ≥ 0.5 , whereas an HSI of < 0.5 indicates that NAFLD is absent. The predictive value of each model parameter was assessed using the area under the ROC curve (AUC) scale (Figure).

The sensitivity and specificity of the method were 98.4 % and 95.8 %, respectively.

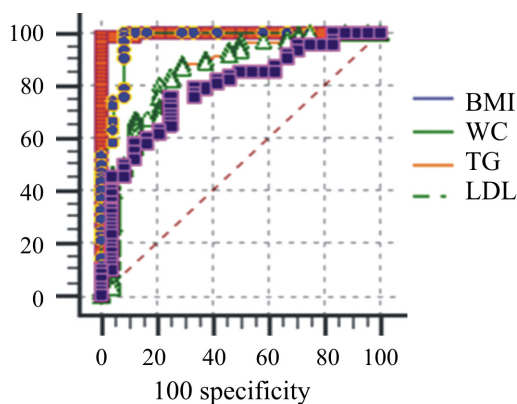


Fig. ROC curve for liver steatosis index scores

In recent decades, several tests (indices) for diagnosing NAFLD have been proposed, and biochemical, clinical, and biometric indicators are used for their

calculation. For example, HSI is calculated using sex, presence/absence of diabetes, BMI, and transaminase ratio. The sensitivity and specificity of HSI are 93.1 % and 92.4 %, respectively. Another example is the fatty liver index (FLI), which includes TG and gamma glutamine transferase concentrations, BMI, and WC. If FLI is < 30 , nonalcoholic hepatic steatosis is ruled out; an FLI between 30 and 60 indicates possible nonalcoholic hepatic steatosis; and an FLI > 60 confirms nonalcoholic hepatic steatosis. The method has good diagnostic sensitivity (87 %), but low specificity (64 %). Furthermore, the SteatoScreen test has good diagnostic characteristics, and its calculation equation includes 10 blood parameters and biometric data, which limits its use in clinical practice [5; 6; 10]

The threshold values of the tests included in the mathematical model were determined to rule out NAFLD: 25.8 for BMI, 79 cm for WC, 0.95 mmol/l for TG, and 3.15 mmol/l for LDL. The proposed minimally invasive method can be used to detect liver steatosis in women of early post-reproductive age with MS. The high diagnostic characteristics and availability for widespread use of the proposed method should be noted, since simple biometric and laboratory indicators are used.

CONCLUSIONS

1. An index has been developed for diagnosing NAFLD in postmenopausal

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women using publicly available markers (BMI, WC, TG, and LDL) and showed high diagnostic characteristics. The presence of NAFLD is confirmed in postmenopausal women when the HSI is ≥ 0.5 and its absence with HSI < 0.5 .

2. The threshold values of tests included in the mathematical model were calculated to rule out NAFLD in this category of patients.

3. The use of the proposed minimally invasive and accessible method will ensure early detection of fatty changes in the liver in this risk group, enabling prompt treatment.

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