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SUMMARY OF THE CONNECTION BETWEEN DIABETES MELLITUS TYPE 2 AND NON-ALCOHOLIC FATTY LIVER DISEASE

Abstract: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in Western countries and is expected to become the most common indication for liver transplantation by 2030. Over the past decade, it has been shown that the clinical significance of NAFLD is not limited to increased morbidity and mortality associated with liver disease. More and more studies indicate that NAFLD is multisystemic, affecting other organs as a result of multiple pathological pathways. In particular, NAFLD increases the risk of developing type 2 diabetes mellitus (DM), cardiovascular diseases, and chronic kidney disease [1].

Key words: Non-alcoholic fatty liver disease, metabolic syndrome, liver inflammation, diabetes mellitus

NAFLD is a pathological condition characterized by excessive accumulation of adipose tissue in the liver, accompanied by insulin resistance and fatty degeneration of more than 5% of hepatocytes, detected by morphological examination of liver tissue or proton magnetic resonance spectroscopy. In this case, it is necessary to exclude other secondary causes, as well as alcohol consumption (more than 30 g of ethanol per day for men and 20 g for women) [2]. Additionally, criteria such as an increase in waist circumference (more than 94 cm in men and more than 80 cm in women), the presence of hypertension or persistent increase in blood pressure over 130/85 mm Hg, the presence of type 2 diabetes or hyperglycemia over 5.6 mmol/l, increased triglyceride levels (more than 1.7 mmol/l), and a decrease in high-density lipoprotein levels (less than 1 mmol/l in men and 1.3 mmol/l in women), according to the results of a biochemical blood test can be used to diagnose NAFLD [2]. An obligatory factor of NAFLD is insulin resistance, the formation of which is associated with an increase in the production of proinflammatory cytokines in response to the development of a chronic inflammatory process caused by various factors (changes in the qualitative and quantitative composition of microflora, obesity, sedentary lifestyle, arterial hypertension). In response to such stimulation, the body excessively transmits cytokine suppressors (SOCS), which block and destroy insulin receptors in proteosomal oxidation reactions [8]. The formation of insulin resistance leads to hyperinsulinemia and excessive accumulation of glucose in the liver, as well as to the activation of lipolysis in adipocytes and the flow of fatty acids into hepatocytes. In turn, in the liver, as a result of insulin resistance, the expression of sterol-sensitive element binding protein (SREBP-1) and carbohydrate-sensitive element binding protein (ChREBP) is triggered, which activates lipogenesis processes leading to the synthesis of fatty acids from excess glucose. The increase in the formation of fatty acids, which is a consequence of the above processes, inhibits their transport to the mitochondria as a result of an increase in the content of malonyl-CoA, which causes increased esterification of fatty acids and the accumulation of formed triglycerides in the liver. NAFLD and metabolic syndrome (MS) are closely related entities. Due to their strong bidirectional association, it has been recently proposed to change the term “NAFLD” to “fatty liver disease associated with metabolic dysfunction-MAFLD” [5]. Insulin resistance (IR), one of the main components of MS, plays a key role in the pathophysiology of NAFLD, promoting the progression of simple steatosis to liver inflammation and fibrosis . Moreover,

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the presence of NAFLD may contribute to hepatic IR and therefore increases the risk of subsequent T2DM [2]. The homeostatic model assessment of insulin resistance (HOMA-IR) indirectly assesses hepatic IR and is widely used in daily clinical practice and proposed in clinical algorithms for NAFLD and T2DM [2].

Furthermore, T2DM is a well-known risk factor for NAFLD [1]. The prevalence of NAFLD among patients with T2DM reaches 60–80%, and T2DM has been consistently shown to act as a trigger, promoting NAFLD progression and progressive liver fibrosis [4]. In the last decade, several genetic risk factors have been associated with susceptibility to NAFLD and development of progressive disease [3].The presence of diabetes is consistently a key predictor of NAFLD and advanced fibrosis in NAFLD. Several experts have recommended liver biopsy in selected patients with NAFLD and diabetes [3]. In this era of responsible healthcare and increasing cost constraints, it is not appropriate to recommend liver biopsy in all patients with diabetes and NAFLD. For this reason, we aimed to identify the most reliable factors associated with NAFLD or advanced fibrosis in patients with diabetes and NAFLD to identify patients who should undergo liver biopsy first and/or be referred to a hepatologist for further evaluation.

NAFLD can be combined with alcoholic liver disease in patients with metabolic syndrome when consuming alcohol more than 60 g/day for men and more than 40 g/day for women, which can lead to a more aggressive course of the disease [6]. The prevalence of NAFLD in diabetes mellitus was studied in a small number of studies and amounted to 69% according to ultrasound data (10 and 65% according to proton MR spectroscopy) [7]. Due to the fact that in recent years there has been an increase in the incidence of NAFLD in various carbohydrate metabolism disorders, the search for cause-and-effect relationships between these comorbid diseases, new directions for their diagnosis and treatment methods has become especially relevant.

There is now compelling evidence that NAFLD often precedes the development of T2DM. The idea that NAFLD is simply a “liver manifestation” of metabolic syndrome is outdated. NAFLD can be considered as an early predictor and a decisive factor in the development of diabetes and other clinical manifestations of metabolic syndrome [5]. In 2016, a systematic review was published on the relationship between NAFLD and the risk of developing T2DM. According to the studies included in this review, there is now compelling evidence that the presence of NAFLD is associated with an increased risk of developing T2DM, as well as new compelling evidence that the risk varies with the severity of NAFLD. However, further research in this area is needed due to the fact that almost all studies were conducted on various Asian populations [3]. However, a recently published analysis of the Multinational Atherosclerosis Study, which included more than 3,000 Americans without T2DM, confirmed that NAFLD diagnosed by CT scan was independently associated with a two-fold increased risk of developing T2DM [4]. The presence of NAFLD allows the clinician to suspect various disorders of carbohydrate metabolism, which develop specific metabolic changes and macro- and microvascular complications. Given that patients with diabetes are more often diagnosed with NAFLD than the general population, and that diabetes is a factor in the progression of the disease to NASH and cirrhosis, this pathological process should be given special attention.

References:

1. Byrne CD NAFLD: A multisystem disease. J. Hepatol., 2016, Vol. 62, No. 1, pp. 47–64.

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Volume: 11, Issue 11, November-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

2. 2. EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J. Hepatol., 2016, Vol. 64, No. 6, pp. 1388–1402, doi:10.1016/j.jhep.2015.11.004.

3. Targher G, Marchesini G, Byrne CD. Risk of type 2 diabetes in patients with non-alcoholic fatty liver disease: Causal association or epiphenomenon? Diabetes Metab. 2016 Jun;42(3):142-56. doi: 10.1016/j.diabet.2016.04.002. Epub 2016 Apr 30. PMID: 27142870.

4. Lonardo A, Ballestri S, Guaraldi G, Nascimbeni F, Romagnoli D, Zona S, Targher G. Fatty liver is associated with an increased risk of diabetes and cardiovascular disease - Evidence from three different disease models: NAFLD, HCV and HIV. World J Gastroenterol. 2016 Nov 28;22(44):9674-9693. doi: 10.3748/wjg.v22.i44.9674. PMID: 27956792; PMCID: PMC5124973.

5. Lonardo A, Ballestri S, Marchesini G, Angulo P, Loria P. Nonalcoholic fatty liver disease: a precursor of the metabolic syndrome. Dig Liver Dis. 2015 Mar;47(3):181-90. doi: 10.1016/j.dld.2014.09.020. Epub 2014 Nov 18. PMID: 25739820.

6. Ekstedt M, Franzén LE, Holmqvist M. Alcohol consumption is associated with progression of hepatic fibrosis in non-alcoholic fatty liver disease. Scand J Gastroenterol. 2009;44(3):366-374. doi: 10.1080/00365520802555991

7. Doycheva I, Cui J, Nquyen P, et al. Non-invasive screening of diabetics in primary care for NAFLD and advanced fibrosis by MRI and MRE. Aliment Pharmacol Ther. 2016;43(1):83-95. doi: 10.1111/apt.13405

8. Sun W, Zhang D, Sun J, et al. Association between non-alcoholic fatty liver disease and autonomic dysfunction in a Chinese population. QJM 2015;108(8):617-624.