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CARDIOVASCULAR DISEASES AND METABOLIC-ASSOCIATED FATTY LIVER DISEASE: A MODERN PERSPECTIVE ON THE PROBLEM

Parpibayeva D. A.,
Buvamukhamedova N. T.
Tashkent State Medical University

Abstract
The article examines the interrelationship between cardiovascular disease (CVD) and metabolic-associated fatty liver disease (MAFLD), highlighting how MAFLD is an independent cardiometabolic risk factor and emphasizing early detection and integrated management to reduce cardiovascular risk. MAFLD prevalence is high globally and rising, especially among high-risk groups; obesity, type 2 diabetes, dyslipidemia, and hypertension commonly cluster with MAFLD. There is evidence linking MAFLD to subclinical and clinical CVD, with insulin resistance and metabolic syndrome playing important roles; MAFLD may drive adverse myocardial remodeling and diastolic dysfunction. Development of improved non-invasive biomarkers for inflammation and fibrosis is a priority to better predict disease progression and guide treatment.

Keywords: MAFLD, CVD, cardiometabolic disease, insulin resistance, metabolic syndrome, liver fibrosis, ultrasound, non-invasive markers, risk stratification, epidemiology, T2DM, dyslipidemia, obesity.

Introduction

According to the World Health Organization, cardiovascular diseases (CVD) are the most common cause of death worldwide, accounting for 18 million deaths per year [1]. Contemporary Russian literature increasingly discusses the growing role of combined nosologies in internal medicine, with particular emphasis on comorbidity in cardiac pathology [2, 3]. Most patients with CVD in real medical practice are characterized by a combination of two or more diseases and conditions, i.e., cardiovascular comorbidity. This places additional demands on the observation and treatment of this category of patients. There has been a sharp increase in the prevalence of metabolic diseases such as metabolic associated fatty liver disease (MAFLD), type 2 diabetes mellitus (T2DM), and obesity, which often occur as comorbid conditions. When combined with dyslipidemia and hypertension, this quintet constitutes a cardiometabolic disease [4].

Contemporary literature demonstrates a direct link between MAFLD and CVD, indicating that MAFLD should be considered a significant independent risk factor in the absence of traditional cardiovascular risk factors and metabolic syndrome (MS) for subclinical and clinical CVD [5]. Given the clinically significant association between MAFLD and the progression of CVD, early detection of patients with MAFLD plays an important role in practical healthcare.

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MAFLD has become one of the major diseases affecting the population, while also being the most common cause of liver disease in Western countries, accounting for approximately 75% of chronic liver diseases [6]. A recent meta-analysis combining 86 studies with a total sample size of 8,515,431 people showed that the incidence of MAFLD is 25%, with the highest prevalence in the Middle East and South America and the lowest prevalence in Africa [7]. According to the results of the Russian DIREG 1 study (2007), the incidence of MAFLD was 27% [9]. The DIREG 2 study (2015) showed that the prevalence of MAFLD among people seeking outpatient care was already 37.3%, representing a 10% increase over 7 years compared to the DIREG 1 data [8,18].

The prevalence of MAFLD is significantly higher in high-risk patients. Machado et al. combined 12 observational studies involving 1,620 patients with morbid obesity and reported a prevalence of MAFLD in this population of 91% (range: 85-98%) [9]. Two separate studies reported the prevalence of MAFLD based on ultrasound data in patients with diabetes mellitus at 69.4% [10] and 67.8%. However, 22% of patients with MAFLD do not suffer from obesity or diabetes mellitus, and 64% of patients do not meet the minimum criteria for MS, with no MS criteria found in 12% of case. The main risk factors in the MAFLD population in Russia were hypertension (69.9%), abdominal obesity (56.2%), hypercholesterolemia (68.8%), and type 2 diabetes mellitus, which was found in 23.1% of patients [11,19].

International guidelines state that, in cases of suspected MAFLD, the initial diagnostic examination should include the results of a biochemical blood test and a non-invasive imaging study to confirm the presence of steatosis. Non-invasive assessment should be aimed primarily at identifying MAFLD among patients with metabolic risk factors, and then at monitoring disease progression and response to treatment, identifying patients with the worst prognosis. Experts agree that normal liver enzyme levels cannot rule out MAFLD, as they are insensitive screening tests. Due to its wide availability and low cost, ultrasound (US) is the preferred initial test for assessing fatty liver infiltration. US has sufficient accuracy in the diagnosis of MAFLD, with a sensitivity of 60-94% and a specificity of 66-97%. However, its sensitivity decreases in patients with morbid obesity (BMI > 40 kg/m²) and when the fat content in the liver is less than 20% [12].

Liver biopsy is still the gold standard for diagnosing and assessing the progression of MAFLD. However, due to the high prevalence of MAFLD, the costs of performing a liver biopsy on every patient with this disease are enormous. In addition, liver biopsy often requires hospitalization, which leads to temporary disability. Furthermore, biopsy can lead to complications, including bleeding and mortality. Therefore, repeat biopsy is not the method of choice for assessing treatment efficacy and monitoring disease progression. Biopsy samples represent only 1/50,000 of the liver tissue, which must be taken into account, as this increases the likelihood of sampling error. Therefore, non-invasive methods of diagnosing liver damage in MAFLD are currently preferred; however, liver biopsy is the gold standard for diagnosing steatogepatitis [13,17].

With the exception of the recommendations of the UK National Institute for Health and Care Excellence (which do not contain specific guidelines on which patients should undergo liver biopsy), all other guidelines agree that confirmatory liver biopsy is not necessarily required in all patients with MAFLD. It should be performed when progressive liver disease associated with MAFLD is suspected and in situations where competing etiologies of chronic liver disease cannot be ruled out based solely on laboratory tests, medical history, and noninvasive test results. Currently, the lack of a highly

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specific and sensitive non-invasive marker predicting inflammation and fibrosis has generated considerable interest in identifying new markers of MAFLD progression and developing clinical indicators of disease severity [14, 16].

Metabolic syndrome (MS) is an important risk factor predisposing to the development of type 2 diabetes and CVD. A recent study conducted in 19 European centers demonstrated a link between decreased insulin sensitivity and an increased incidence of cardiovascular disease in patients with MAFLD. These results were also confirmed by a recently published meta-analysis demonstrating the association of MAFLD with insulin resistance and type 2 diabetes. There is evidence of hepatocardiac links involving changes in the geometry and structural and functional parameters of the myocardium, diastolic dysfunction in patients with MAFLD, which may lead to the development of left ventricular remodeling in the form of hypertrophic variants (eccentric, concentric LV hypertrophy), which are prognostically unfavorable. In patients with MAFLD, a Russian study comparing groups of patients with CHF and combined CHF, MAFLD, demonstrated a more severe course of CHF, more pronounced changes in the myocardium and vascular wall in the form of greater myocardial mass, increased heart chamber size, and thickening of their walls. The fatty liver index (FLI) correlated with the thickness of epicardial fat, the thickness of the left ventricular posterior wall, the thickness of the interventricular septum, and the mass of the left ventricular myocardium. Despite the available data, the mechanisms that determine changes in the cardiovascular system remain poorly understood.

Mortality among patients with MAFLD is significantly higher than in the general population. Patients with MAFLD with progressive fibrosis or cirrhosis (> F3 stage of fibrosis) have the highest risk of liver-related death, while cardiovascular events and malignancies are the most common complications in patients with early-stage MAFLD (< F3).

Identifying patients with early-stage MAFLD is important for determining individuals at high cardiometabolic risk who need treatment aimed at preventing the progression of MAFLD and CVD [15,20].

Summary

The data presented indicate the need for better risk stratification, earlier diagnosis, and treatment of MAFLD in order to reduce the short- and long-term burden of this disease on public health. Given the lack of research on the relationship between MAFLD and cardiovascular disease, the potential mechanisms underlying this association, and their relationship to insulin resistance, obesity, and metabolic syndrome in the context of increased cardiovascular risk, the available data is contradictory, and a comprehensive assessment of the clinical and functional status of MAFLD patients with concomitant cardiovascular disease is urgently needed.

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