EDITORIAL

MASLD—A Gateway for ASCVD: A Call for Early Intervention and Multidisciplinary Care

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Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as nonalcoholic fatty liver disease (NAFLD), has emerged as a significant public health concern, affecting approximately 25% of the global population with its prevalence rising from 22% in 1991 to 37% in 2019.[1] While the hepatic consequences of MASLD, such as steatohepatitis, fibrosis, and cirrhosis, are well documented, its systemic implications are increasingly coming to light. While traditionally viewed as a hepatic disorder, growing evidence highlights MASLD as a multisystem disease with profound implications on cardiovascular health. Atherosclerotic cardiovascular disease (ASCVD) has now been recognized as the leading cause of mortality in patients with MASLD, surpassing liver-related complications. MASLD is present in up to 75% of patients with type 2 diabetes mellitus (T2DM). Notably, MASLD is linked to a higher risk of cardiovascular diseases (CVD), including arrhythmia, atherosclerotic heart disease, heart failure, and CVD-related mortality.[2] The association between MASLD and ASCVD is particularly alarming, positioning MASLD as a critical gateway for cardiovascular morbidity and mortality.

Metabolic dysfunction-associated steatotic liver disease and ASCVD share common pathophysiological underpinnings, including insulin resistance, chronic inflammation, dyslipidemia, and endothelial dysfunction. These overlapping mechanisms suggest that MASLD is not merely a liver-specific condition but a multisystem disorder with far-reaching consequences. Emerging evidence indicates that individuals with MASLD are at a significantly higher risk of developing ASCVD, independent of traditional cardiovascular risk factors.[3] This association underscores the need for a paradigm shift in how we perceive and manage MASLD, moving beyond hepatology to embrace a more holistic, multidisciplinary approach.

The MASLD–ASCVD Nexus: A Pathophysiological Continuum

The relationship between MASLD and ASCVD is bidirectional and synergistic. On one hand, MASLD exacerbates cardiovascular risk by promoting atherogenic dyslipidemia, systemic inflammation, and oxidative stress. On the other hand, the metabolic dysregulation driving ASCVD—such as obesity, type 2 diabetes, and hypertension—also fuels the progression of MASLD. This vicious cycle highlights the importance of early detection and intervention in MASLD to mitigate its cardiovascular sequelae.

Recent studies have demonstrated that the severity of liver fibrosis in MASLD is a strong predictor of cardiovascular outcomes.[4] Patients with advanced fibrosis are at a markedly increased risk of coronary artery disease, heart failure, and arrhythmias. These findings emphasize the need for risk stratification in MASLD patients, with a focus on identifying those at highest risk for ASCVD. A major concern is that MASLD often remains undiagnosed, as hepatic steatosis is frequently silent until advanced stages. This diagnostic gap results in a missed opportunity for early cardiovascular risk stratification and intervention. Given that MASLD affects nearly a quarter of the global population, the implications for ASCVD prevention are substantial.

Reframing MASLD as a Cardiovascular Risk Factor

Given the strong association between MASLD and ASCVD, it is imperative to incorporate hepatic health into cardiovascular risk assessment frameworks. Current guidelines emphasize traditional risk factors such as hypertension, diabetes, and dyslipidemia, but MASLD remains largely overlooked. Emerging data suggest that advanced MASLD, especially in the presence of fibrosis [metabolic dysfunction-associated liver fibrosis, or metabolic dysfunction-associated steatohepatitis (MASH) with fibrosis], confers an independent risk for cardiovascular events.[3] A shift toward proactive screening strategies in high-risk individuals, such as those with type 2 diabetes, obesity, or metabolic syndrome, is warranted. Incorporating noninvasive tools like, liver stiffness measurements, and serum biomarkers into routine cardiovascular evaluations can aid in early risk identification.

A Call for Early Intervention and Integrated Management

Given the strong link between MASLD and ASCVD, early intervention is paramount. Lifestyle modifications, including weight loss, dietary changes, and increased physical activity, remain the cornerstone of MASLD management. These interventions not only improve liver health but also reduce cardiovascular risk. Pharmacological therapies targeting metabolic dysfunction show promise in addressing both MASLD and ASCVD offering a dual benefit. Drugs like Vitamin E, pioglitazone and saroglitazar has been used in treatment of MASLD for quiet sometime but recently Resmetirom and injectable semaglutide has also been approved for treatment of MASLD by US FDA. Sodium-glucose cotransporter 2 (SGLT2) inhibitors have also shown encouraging results in its treatment. Moreover, the integration of cardiovascular risk assessment into the routine care of MASLD patients is essential. Hepatologists, cardiologists, endocrinologists, consultant physicians, and primary care providers must collaborate to develop comprehensive care plans that address both hepatic and extrahepatic manifestations of MASLD. Noninvasive tools, such as transient elastography and cardiovascular risk scores, can aid in risk stratification and guide therapeutic decisions.

The Role of Research and Public Health Initiatives

Despite the growing recognition of the MASLD–ASCVD connection, significant gaps remain in our understanding of the underlying mechanisms and optimal management strategies. Large-scale, longitudinal studies

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are needed to elucidate the causal pathways linking MASLD to ASCVD and to identify biomarkers that can predict cardiovascular outcomes in MASLD patients. Additionally, public health initiatives aimed at raising awareness of MASLD and its systemic implications are crucial for early detection and prevention.

Conclusion

Metabolic dysfunction-associated steatotic liver disease is no longer just a liver disease; it is a multisystem disorder with profound implications for cardiovascular health. The recognition of MASLD as a cardiovascular risk amplifier necessitates a paradigm shift in clinical practice. Moving beyond the liver-centric approach and integrating MASLD into ASCVD risk prediction models can significantly enhance preventive strategies. The strong association between MASLD and ASCVD underscores the need for early intervention, multidisciplinary care, and a renewed focus on research and public health initiatives. By addressing MASLD as a gateway for ASCVD, we can not only improve liver outcomes but also reduce the global burden of cardiovascular disease. The time has come to view MASLD not just as a hepatic disorder but as a sentinel warning of impending cardiovascular disease. By addressing this link proactively, we have the opportunity to mitigate ASCVD burden and improve long-term patient outcomes. The time to act is now, before the ripple effects of MASLD become a tidal wave of cardiovascular morbidity and mortality.

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