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The liver as a thermometer of cardiometabolic health: time to prioritize MASLD in Global Health Policy

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Over the past decades, the fight against hepatitis C has become one of the most remarkable public health successes of our time.[1] Once a disease with profound clinical, social, and economic consequences, hepatitis C is now approaching elimination in countries like Spain.[2] This achievement reflects the powerful convergence of scientific innovation, effective health policies, and a sustained collective effort by healthcare professionals, affected individuals, institutions, and civil society. It stands as a compelling demonstration that when scientific knowledge, political will, and civic engagement align, transformative and enduring progress is not only possible, it is inevitable.

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Today, we are witnessing the consolidation of a new global health challenge affecting millions of people worldwide: metabolic dysfunction-associated steatotic liver disease (MASLD). A recent systematic review estimated its global prevalence at 32.4% (95% CI: 29.9–34.9).[3] Strongly associated with metabolic conditions such as obesity, insulin resistance, or type 2 diabetes, approximately 20% of MASLD cases progress to metabolic dysfunction-associated steatohepatitis (MASH), carrying a significant risk of progression to cirrhosis and hepatocellular carcinoma (HCC).[4,5] As a result, MASLD has become the most common chronic liver disease and a leading cause of liver-related morbidity and mortality worldwide.[3] Beyond the liver, MASLD is increasingly recognized as a multisystemic disease, closely linked to extrahepatic conditions such as cardiovascular disease and various types of cancer. Notably, the degree of liver fibrosis has been independently associated with all-cause mortality.[6,7] MASLD has been implicated in a broad spectrum of comorbidities, including heart failure with preserved ejection fraction, arrhythmias, cardiac conduction defects, subclinical atherosclerosis, and elevated incidence of cancers beyond HCC, particularly breast and colorectal cancer.[8,9] The typically silent clinical course of MASLD complicates early detection, often delaying timely intervention. Importantly, the health and societal impact of this condition is no longer a future projection, it is a present-day reality already transforming hepatology and primary care practice, with forecasts that paint an even more alarming picture.[10]

According to the *Global Burden of Disease Study 2021*, published in The Lancet in 2024, chronic liver disease ranked 18th in mortality and 14th in disability-adjusted life years (DALYs) when considering both sexex and all age groups combined.[11] Its presence in both of the GBD's major rankings underscores its growing relevance and the urgent need to prioritize liver disease in public health strategies. Despite its, MASLD remains underrecognized in public health agendas and largely underestimated in health planning. The clinical focus continues to center disproportionately on cirrhosis and its complications, often neglecting the earlier, reversible stages of the disease.[12] This oversight is

particularly concerning given that validated, accessible, reproducible, simple, and cost-effective non-invasive diagnostic tools are available to detect liver fibrosis without biopsy. Yet, these tools remain significantly underused, even though early detection and preventive strategies could prevent nearly 300,000 deaths annually across Europe.[13]

Lifestyle modification remains the cornerstone of MASLD management. Sustained weight loss of 7–10% has been shown to improve hepatic steatosis and reduce liver fibrosis.[14] Integrated care models that provide individualized monitoring and multidisciplinary support are increasingly being implemented, reflecting a shift toward more patient-centered approaches. Alongside these strategies, a promising therapeutic landscape is emerging. In 2024, the approval of resmetirom marked a pivotal milestone as the first pharmacological treatment specifically indicated for MASH with stages F2-F3 fibrosis.[15] More recently, results from a phase 3 trial of semaglutide at a 2.4 mg dose demonstrated significant improvements not only in steatohepatitis but also in fibrosis.[16] Additional candidates are in advancing through late-stages clinical development, including fibroblast growth factor 21 (FGF21) analogues (pegozafermin, efruxifermin, efimosfermin alpha), pan-peroxisome proliferator-activated receptor (PPAR) agonist (lanifibranor), and dual incretin receptor agonists (tirzepatide, survodutide)[17,18], Collectively, these advances are paving the way for personalized, multi-targeted therapies capable of addressing both hepatic pathology and systemic metabolic dysfunction.

In this evolving therapeutic landscape, endoscopic metabolic therapy (EMT) is gaining recognition as an effective, safe, and minimally invasive option for patients with metabolic disease[19]. These minimally invasive procedures are designed to comprehensively address obesity and its associated metabolic comorbidities, including MASLD, and are particularly beneficial for patients requiring rapid weight reduction due to severe comorbidities or limited access to pharmacologic treatments[20,21] .Among its modalities, endoscopic sleeve gastroplasty (ESG) has shown sustained weight loss and significant improvement in both metabolic and hepatic parameters[22] .EMT is not only

valuable as a rescue intervention when conservative strategies fail, but also holds promise as a synergistic approach alongside pharmacotherapy, or even as a frontline option in selected clinical phenotypes[23]. Recent clinical evidence supports the efficacy of EMT in MASLD management. Our group recently conducted and published the first multicenter, randomized, placebo-controlled trial specifically evaluating the impact of ESG on MASH[24] .After 72 weeks, participants in the intervention arm achieved a mean weight loss of 9.47% (±9.38), compared to 3.91% (±5.43) in the control group ($p < 0.05$). This was accompanied by significant reductions in liver stiffness and steatosis, as well as a marked decrease in NAS scores among patients who achieved ≥10% weight loss. These findings underscore the potential of EMT to induce clinically meaningful hepatic improvements. As precision medicine continues to shape the future of hepatology, it is imperative that proven technologies such as EMT are no longer confined to experimental settings or remain out of reach in routine clinical practice.

Institutional recognition of this evolving paradigm is essential. The National Liver Health Plan (Reto 2032), promoted by the Spanish Association for the Study of the Liver, outlines a comprehensive strategy that prioritizes MASLD.[24] The plant champions preventive hepatology and adopts the "Food is Medicine" framework, shifting from a solely pharmacological model to a more integrative approach in which nutrition serves as a key instrument for health equity[26]. This is particularly relevant given that food insecurity constitutes a major metabolic, psychosocial, and structural determinant in the onset and progression of MASLD[27-29] .Moreover, the plan calls for the strengthening of the role of primary care, the development of context-adapted diagnostic algorithms, increased investment in professional training, and guarantee of equitable access to both diagnostic and therapeutic tools. Central to its vision is the creation of interdisciplinary functional units, bringing together hepatology, endocrinology, internal medicine, nutrition, psychology, and family medicine, to ensure a truly person-centered, continuous and integrated model of care.

Given the increasing clinical complexity of MASLD patients, who often present with multiple comorbidities, a longitudinal, compassionate, and evidence-based approach is not only desirable but essential. Equity in access must serve as a guiding principle, eliminating preventable delays that fuel health disparities and accelerate disease progression. We are at a pivotal moment, one that offers a rare opportunity to redefine the future of hepatology. The knowledge, the technology, and the strategic framework are already in place. What remains is to summon the collective will to act. Because the liver is becoming the thermometer of our cardiometabolic health. And we cannot afford to wait.

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