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Review

MASLD and Hepatic & Extrahepatic Malignancies: Epidemiology, Mechanisms, and Clinical Implications

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Abstract

Background: Early-onset cancers are increasingly associated with metabolic risk factors and unhealthy lifestyle patterns. Metabolic dysfunction–associated steatotic liver disease (MASLD), a common chronic liver condition linked to metabolic syndrome, is associated with metabolic and inflammatory alterations linked to carcinogenesis and is associated with both hepatic and extrahepatic malignancies, highlighting its growing public health significance.

Materials and Method: This narrative review summarizes current evidence on MASLD and cancer, focusing on epidemiology and mechanisms. Literature from 2024–2026 was identified through major databases and qualitatively synthesized to provide an integrated overview.

Conclusion: Metabolic dysfunction–associated steatotic liver disease (MASLD) is increasingly associated with both hepatic and extrahepatic malignancies. Its association with hepatocellular carcinoma (HCC) and multiple systemic cancers is driven by interconnected metabolic, inflammatory, and genetic mechanisms. Early risk stratification and appropriate surveillance strategies are essential to improve clinical outcomes.

Keywords: MASLD, Cancer, HCC, Extrahepatic malignancies, Cancer surveillance

Introduction

Early-onset cancers are increasingly reported and have been linked to unhealthy lifestyle patterns and the rising burden of "diabesity," the coexistence of obesity and type 2 diabetes. Diabesity contributes to carcinogenesis through metabolic imbalance, persistent cellular stress, and influences from early-life environmental and microbiome-related exposures. The growing incidence of these cancers carries significant personal, social, and economic consequences, as survivors often experience long-term complications such as infertility, cardiovascular disease, and secondary malignancies.[1]

Metabolic dysfunction–associated steatotic liver disease (MASLD) is defined by hepatic steatosis in the presence of at least one cardiometabolic risk factor, reflecting its systemic metabolic basis rather than an isolated liver condition. Epidemiological studies have linked MASLD with an increased risk of overall and site-specific cancers among younger adults. MASLD is associated with metabolic and inflammatory alterations, including insulin resistance, chronic low-grade inflammation, and oxidative stress, which may contribute to a pro-tumorigenic environment promoting cell proliferation and genomic instability.[1]

MASLD is one of the most common chronic liver diseases in developed regions and encompasses a spectrum ranging from simple steatosis to metabolic dysfunction–associated steatohepatitis (MASH), previously termed non-alcoholic steatohepatitis (NASH). Its increasing prevalence parallels the rising incidence of metabolic syndrome components, including obesity, insulin resistance, and dyslipidaemia, highlighting its importance as a major public health concern with systemic implications.[2]

Progression of MASLD may lead to cirrhosis, a severe condition associated with significant complications, including hepatocellular carcinoma, the most common form of primary liver cancer (LC), often requiring liver transplantation.[2] The most

commonly reported extrahepatic malignancies in individuals with MASLD include endometrial, breast, prostate, colorectal, and lung cancers. While advancing fibrosis and cirrhosis are well-established risk factors for hepatocellular carcinoma (HCC), the association between fibrosis severity and extrahepatic malignancies remains less consistent across studies. With the anticipated rise in MASLD prevalence over the coming decades, the burden of these associated malignancies is also expected to increase.[3]

Materials and Method

This narrative review summarizes current evidence on MASLD and cancer, with a focus on epidemiology, pathophysiological mechanisms, and clinical associations. A literature search was conducted using databases and publisher platforms, including PubMed, Scopus, Google Scholar, ScienceDirect, Wiley Online Library, Taylor & Francis, and MDPI. Search terms included "MASLD," "MASH," "cancer," "early-onset cancer," "insulin resistance," "inflammation," and "hepatocellular carcinoma." Studies published between 2024 and 2026 were prioritized.

Peer-reviewed English-language articles relevant to MASLD and its association with cancer were included. Sources were selected based on relevance to epidemiology, disease mechanisms, and clinical outcomes. Data from the selected literature were reviewed and synthesized qualitatively to provide a structured overview of the current understanding of the relationship between MASLD and cancer.

Discussion

Epidemiology of MASLD

The rising incidence of MASLD parallels the global increase in obesity, which has nearly tripled over recent decades. A meta-analysis reports that MASLD affects approximately 30% of the global population, with the highest prevalence observed in Latin America (44%), followed by Western Europe (25.1%). Current evidence also indicates that 98–99% of individuals previously diagnosed with non-alcoholic fatty liver disease (NAFLD) meet the diagnostic criteria for MASLD.[3]

It is the most common chronic liver disease worldwide and is increasingly recognized as a contributor to HCC, a major cause of cancer-related mortality.[4] Hepatocellular carcinoma accounts for 75–85% of all primary liver cancers and is the fourth leading cause of cancer-related deaths globally. The majority of patients with HCC, up to 90%, have underlying cirrhosis. While viral hepatitis and alcohol-related liver disease (ALD) remain leading causes of cirrhosis and HCC in Europe, MASLD has emerged as the fastest-growing cause of HCC in several regions, including the United States, China, and the United Kingdom. It is estimated that up to 35% of global HCC cases are attributable to MASLD. Notably, nearly 40% of MASLD-related HCC cases occur in the absence of cirrhosis, complicating early detection, as routine surveillance is not recommended for non-cirrhotic MASLD populations.[4]

Data from the Global Burden of Disease 2019 study reported approximately 170,000 new cases of liver cancer associated with MASLD worldwide, accounting for 6.6% of all liver cancer cases related to chronic liver diseases. In the same year, 168,969 deaths were attributed to MASLD-related liver cancer, representing 8.6% of liver cancer mortality from chronic liver diseases. Regional analysis showed that Asia contributed 48.3% of incident cases and 46.2% of deaths, while the Middle East and North Africa (MENA) region accounted for 8.9% of cases and 8.6% of deaths related to MASLD-associated liver cancer.[5]

MASLD affects approximately 38.6% of adults in India, with a markedly higher prevalence of 68.2% among individuals with type 2 diabetes. This burden is associated with increasing obesity, sedentary behaviour, and dietary changes, and MASLD is emerging as a significant cause of cirrhosis and MASLD-related HCC in the Indian population.[5]

A meta-analysis covering the period from 1997 to 2023 reported that the prevalence of MASLD in children (≤18 years) was 13% in the general population, including 15% in males and 10% in females, and 47% among children with obesity, with higher rates observed in males. Studies from Asia reported higher prevalence rates compared to non-Asian regions, with 15% versus 11% in the general population and 53% versus 39% among obese children. The prevalence of MASLD increased with age, irrespective of obesity status, although the highest rates were consistently observed in individuals with obesity, with prevalence rising in parallel with increasing body weight.[5]

These findings indicate a substantial and increasing global burden of MASLD, with particularly high prevalence in Asia. As the incidence of hepatitis B virus (HBV)–related mortality declines due to improved prevention and treatment, mortality

related to MASLD and hepatitis C virus (HCV) is increasing. In parallel, MASLD-related liver cancer continues to rise, with Asia contributing the largest share of incident cases and associated deaths.[5]

Biological Mechanisms Linking MASLD and Cancer

Metabolic dysfunction–associated steatotic liver disease (MASLD) is an established risk factor for HCC. Approximately 20% of individuals with MASH progress to cirrhosis, a major determinant of HCC development, with an estimated annual progression rate to HCC of about 2%. Primary liver cancer ranks as the sixth most commonly diagnosed cancer and the third leading cause of cancer-related mortality worldwide.[6] MASH-related HCC exhibits distinct molecular and immune features and may arise in the presence or absence of cirrhosis, influenced by genetic alterations, environmental exposures, and the immune microenvironment.[7]

The pathogenesis of MASLD-related carcinogenesis involves a complex interaction of metabolic, inflammatory, genetic, and environmental factors, contributing to both hepatic and extrahepatic malignancies.[6] (Fig. 1)

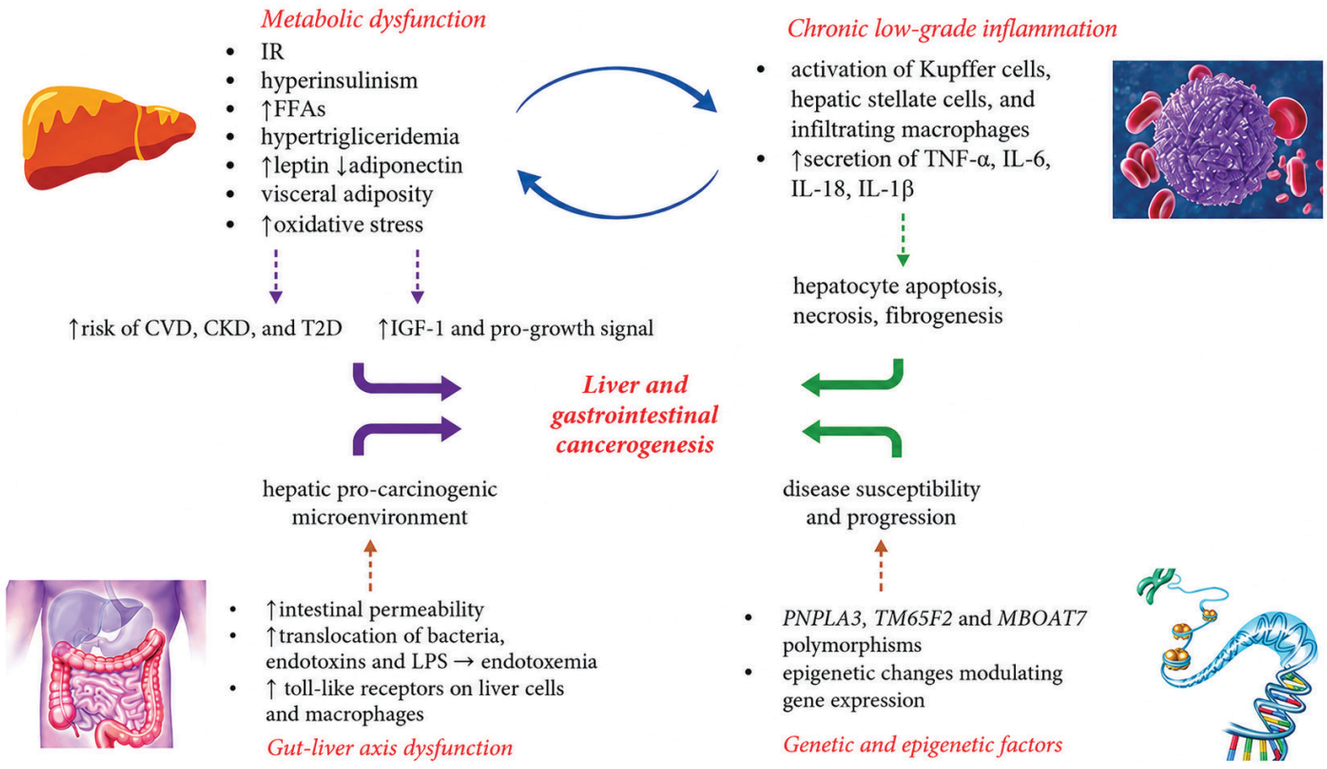

Fig 1. Interplay of metabolic, inflammatory, genetic, epigenetic, and environmental pathophysiological mechanisms linking MASLD to oncogenesis.[8]

Chronic inflammation and oxidative stress

Chronic inflammation is a central driver in the progression of MASLD from steatosis to MASH, cirrhosis, and HCC. Hepatic lipid accumulation leads to immune cell infiltration and activation, with Kupffer cells, neutrophils, macrophages, and lymphocytes releasing pro-inflammatory cytokines that perpetuate liver injury.[6] Activation of hepatic stellate cells (HSCs), mediated by signals such as damage-associated molecular patterns (DAMPs), transforming growth factor-β (TGF-β), and inflammasome activation, promotes fibrosis and architectural distortion of the liver.[6]

Excessive accumulation of free fatty acids (FFAs) results in lipotoxicity, increasing the production of ceramides, sphingolipids, and cholesterol, all of which contribute to cellular stress. Oxidative stress leads to mitochondrial dysfunction, DNA damage, and impaired DNA repair mechanisms, facilitating oncogenic transformation.[6] Chronic inflammation and fibrosis create a microenvironment that supports tumour initiation and progression through pathways such as signal transducer and activator of transcription 3 (STAT3) activation.[6]

During progression to HCC, inflammatory mediators including tumour necrosis factor-α (TNF-α) and interleukin-6 (IL-6) promote oncogenic signalling. Accumulation of genetic mutations, including those involving telomerase reverse transcriptase, β-catenin, and TP53, further contributes to malignant transformation. The patatin-like phospholipase domain-containing 3 (PNPLA3) variant is strongly associated with increased susceptibility to MASH-related HCC.[6]

MASH-related HCC develops within a pro-inflammatory environment in early stages, which later transitions to an immunosuppressive tumour microenvironment characterized by pro-tumorigenic immune cells and reduced immune surveillance. This distinct immune profile has implications for therapeutic response.[8]

Insulin resistance and hyperinsulinemia

Insulin resistance (IR) is a central feature of MASLD and drives increased lipolysis, resulting in elevated free fatty acid flux to the liver and subsequent hepatic steatosis.[8] Progressive fat accumulation promotes oxidative stress and triggers inflammatory cascades involving cytokines such as TNF-α, IL-6, interleukin-1β (IL-1β), and interleukin-18 (IL-18), leading to hepatocyte injury, apoptosis, and fibrosis.[8]

IR also activates intracellular signalling pathways, including phosphoinositide 3-kinase (PI3K)/Akt and mammalian target of rapamycin (mTOR), contributing to metabolic dysregulation, inflammation, and carcinogenesis.[9] The coexistence of IR and MASLD amplifies pro-inflammatory and pro-fibrotic pathways, accelerating progression to HCC and contributing to distinct metabolic characteristics in MASLD-related HCC.[9]

Visceral adipose tissue dysfunction further contributes to disease progression through the release of pro-inflammatory adipokines. Altered adipokine profiles, including increased leptin and reduced adiponectin, promote cell proliferation, insulin resistance, and tumour development.[8]

Gut–liver axis disruption also contributes to carcinogenesis, with increased intestinal permeability allowing translocation of endotoxins such as lipopolysaccharides, which enhance hepatic inflammation and fibrosis.[3] Genetic and epigenetic factors, including variants in PNPLA3, Transmembrane 6 Superfamily Member 2 (TM6SF2), and Membrane-Bound O-Acyltransferase Domain-Containing Protein (MBOAT7), influence susceptibility to MASLD progression and HCC development.[3]

Lipotoxicity and metabolic dysregulation

Lipotoxicity plays a critical role in MASLD progression. Hepatocyte injury results in the release of DAMPs, which activate the NLR family, pyrin domain-containing 3 (NLRP3) inflammasome in Kupffer cells and promote the release of pro-inflammatory cytokines.[6] Nuclear factor-κB (NF-κB) signalling further amplifies inflammation and recruits immune cells, sustaining hepatic injury.[6]

Oxidative stress induced by lipotoxicity leads to mitochondrial dysfunction and increased susceptibility to cell death. This process contributes to fibrosis and chronic liver inflammation, extending beyond the liver to systemic inflammation and increasing the risk of neoplasia.[3]

Fibrosis and cirrhosis-mediated oncogenesis

Fibrosis and cirrhosis are major drivers of oncogenesis in MASLD, creating a persistent pro-inflammatory and pro-fibrotic environment that promotes HCC development. Although cirrhosis remains the strongest risk factor, HCC can develop in earlier stages of fibrosis or in non-cirrhotic MASLD.[10]

Hepatic stellate cell activation is central to fibrosis development, driven by hepatocyte injury, immune dysregulation, and metabolic stress. Progressive fibrosis results from sustained inflammatory signalling and cellular injury, ultimately altering liver architecture and function.[10] (Fig. 2)

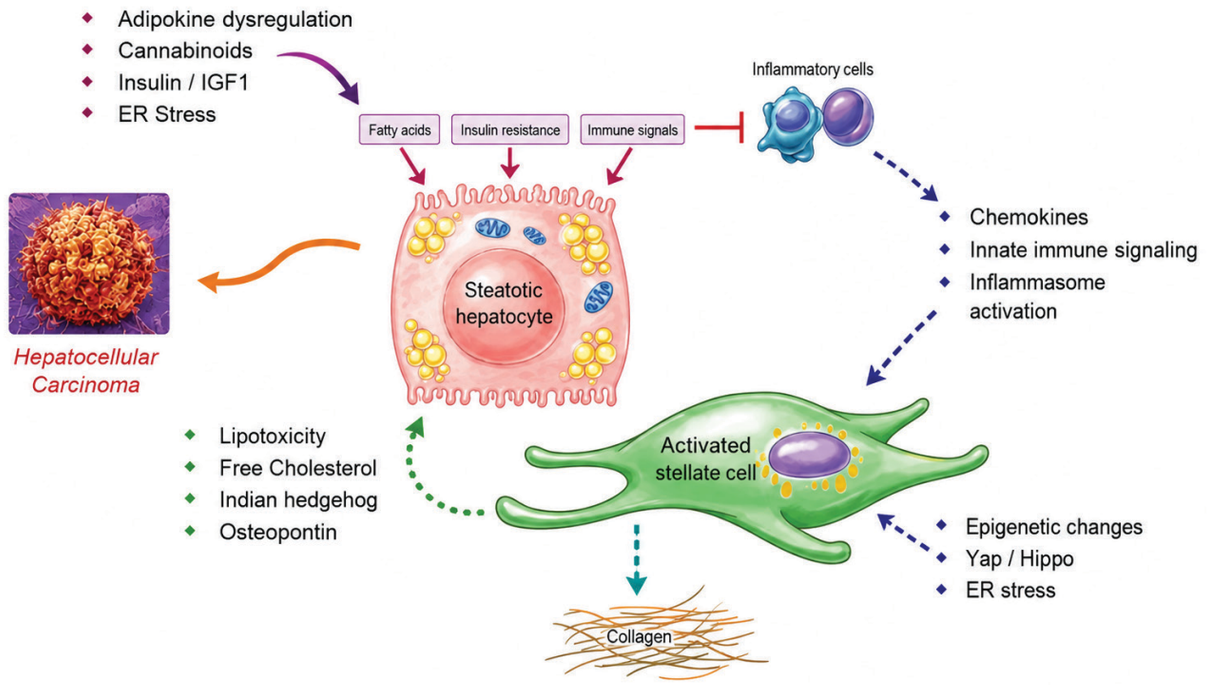

Fig 2. Hepatic drivers of MASLD and fibrosis.[10]

Type 2 diabetes mellitus is a major risk factor for MASLD progression and fibrosis, with strong clinical associations supporting routine screening for MASLD in affected individuals using non-invasive assessment tools. Improved metabolic control has been associated with beneficial effects on disease progression.[10]

Fibrosis severity remains a key determinant of clinical outcomes in MASH, reflecting the cumulative effects of metabolic dysfunction, chronic inflammation, and sustained hepatocellular injury.[10]

Hepatic Malignancies Associated with MASLD

Primary liver cancer includes HCC, which accounts for approximately 80% of cases, and intrahepatic cholangiocarcinoma, representing around 15%.[6] MASLD is increasingly recognized as a major contributor to HCC development, although the precise etiopathogenic mechanisms remain incompletely defined.[3]

Insulin resistance and related metabolic dysregulation contribute to hepatocarcinogenesis through proliferative and pro-inflammatory signalling pathways.[3] Oxidative stress contributes to MASLD-related hepatocarcinogenesis through reactive oxygen species (ROS)-mediated lipid peroxidation, mitochondrial dysfunction, inflammation, and fibrogenesis. Hyperinsulinemia and altered iron metabolism may further enhance oxidative injury and promote tumour development.[3] Gut microbiota alterations and disruption of the gut–liver axis may further contribute to hepatic inflammation and hepatocarcinogenesis.[3] Genetic susceptibility variants such as PNPLA3 have also been associated with increased HCC risk in MASLD.[3]

Epidemiology

Primary liver cancer is the sixth most common cancer globally and the third leading cause of cancer-related mortality. HCC accounts for 75–85% of these cases, with the highest incidence reported in Asia and Africa, where viral hepatitis remains a major etiological factor.[3]

Among individuals with MASLD, approximately 20–30% progress to metabolic dysfunction–associated steatohepatitis (MASH), and 10–20% of these individuals develop cirrhosis. In MASLD-related cirrhosis, the annual incidence of HCC ranges from 0.5% to 2.6%. With the global rise in MASLD prevalence, HCC attributable to MASLD is increasing, while cases related to viral hepatitis are declining due to improved preventive and therapeutic strategies.[3]

Cirrhosis remains the primary risk factor for HCC in MASLD, although HCC can occur in non-cirrhotic individuals. The risk is higher in patients with decompensated cirrhosis. Metabolic syndrome components, particularly central obesity and type 2 diabetes mellitus, are strongly associated with increased HCC risk through persistent inflammation and oxidative stress. Duration of diabetes further influences risk, with a higher incidence observed over time.[3]

A prospective study comparing individuals with steatosis due to MASLD, metabolic dysfunction–associated alcohol-related liver disease (MetALD), and alcohol-related liver disease with those without steatosis demonstrated a higher risk of HCC in patients with steatosis, particularly in MetALD.[3] (Fig. 3)

Fibrosis severity has been consistently associated with increased risk of HCC, with higher fibrosis-4 (FIB-4) index values correlating with a greater likelihood of cirrhosis and HCC development, supporting its role in hepatic cancer risk stratification.[2]

MASLD has also been associated with other hepatobiliary and systemic malignancies. Evidence indicates its role as a risk factor for biliary tract cancers, particularly in the presence of coexisting metabolic conditions such as diabetes. In addition, associations with metastatic liver involvement, including colorectal cancer metastases, have been reported, reflecting the broader systemic impact of MASLD.[2]

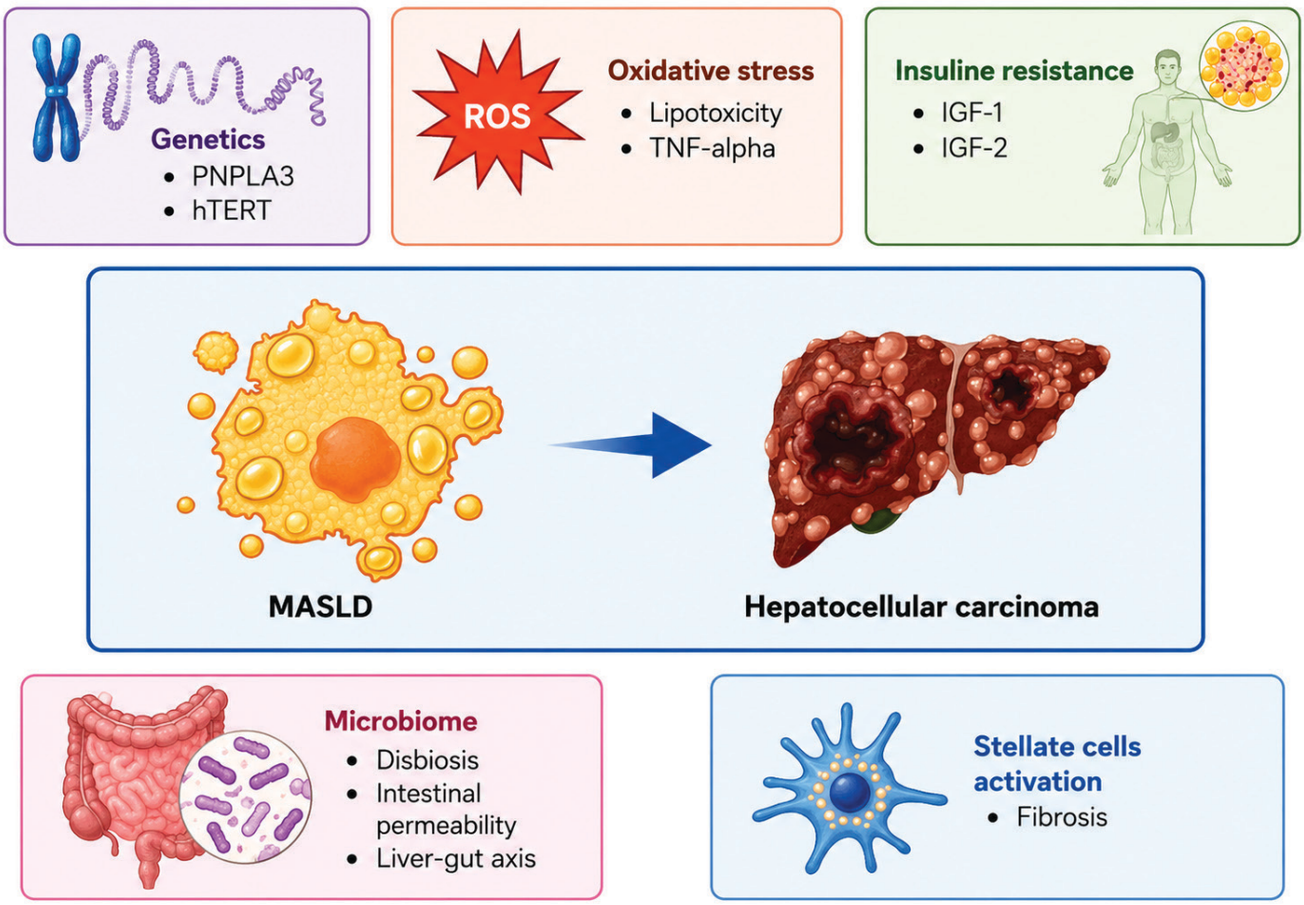

Fig 3. Etiopathogenic pathways from hepatocellular carcinoma (HCC) to MASLD.[3]

The incidence of MASLD-related HCC varies across populations. In Western cohorts, the annual incidence of MASH-related cirrhosis is approximately 2.6%, whereas higher rates of up to 11.3% have been reported in Asian populations.[2]

Population-based data indicate a rising contribution of MASLD to HCC burden. In a large European cohort, MASLD-related HCC incidence increased substantially over time, becoming a leading cause of HCC, while cases related to viral hepatitis declined. Patients with MASLD-related HCC were typically older, had a higher burden of metabolic comorbidities, and were less likely to have cirrhosis compared to other etiologies.[4]

Age-specific trends show a higher incidence in older populations, particularly those aged 70 years and above. Overall incidence rates remain lower in certain European regions compared to global averages, although the proportion of MASLD-related HCC continues to increase.[4]

Extrahepatic Malignancies Associated with MASLD

Evidence from cohort studies indicates an increased risk of multiple cancers in individuals with persistent MASLD. The most commonly reported extrahepatic malignancies include endometrial, breast, prostate, colorectal, and lung cancers. With the rising prevalence of MASLD, the burden of these associated malignancies is also increasing.[3]

Colorectal cancer is the most extensively studied extrahepatic malignancy in MASLD. Insulin resistance and chronic low-grade inflammation play central roles in its pathogenesis by promoting cellular proliferation and inhibiting apoptosis. Several studies have reported an increased prevalence of adenomas and colorectal cancer in individuals with MASLD, with MASLD identified as an independent risk factor for the development of colonic polyps. The risk of adenomatous polyps has been reported to be approximately threefold higher compared to the general population, with a higher likelihood of multiple lesions, right-sided distribution, and high-grade dysplasia. Cohort and prospective studies have demonstrated an association between MASLD and increased risk of colorectal cancer and adenomatous polyps.[3]

The association between MASLD and other malignancies involves similar metabolic and inflammatory pathways. Insulin resistance and hyperinsulinemia lead to elevated levels of insulin-like growth factor-1, which promotes cell proliferation and inhibits apoptosis. Increased levels of insulin-like growth factor-1 have been associated with cancers of the prostate, colorectal region, lung, and breast. Alterations in gut microbiota and dysbiosis have also been implicated in carcinogenesis. A meta-analysis of cohort studies reported that MASLD is associated with a 1.5–2-fold increased risk of gastrointestinal cancers and a 2.5-fold increased risk of thyroid cancer, along with a modest increase in the risk of breast, lung, urinary, and gynaecological malignancies. Obesity, a key component of MASLD, is also associated with cancers of the oesophagus, pancreas, breast, and thyroid.[3]

Persistent MASLD has also been linked to increased risk of site-specific cancers, including hepatic, pancreatic, renal, colorectal, biliary, and gynaecologic malignancies. A meta-analysis including multiple cohort studies demonstrated increased risks of gastric, colorectal, pancreatic, biliary tract, thyroid, urinary system, breast, and female genital cancers in individuals with MASLD. Advanced fibrosis is a recognized determinant of hepatic malignancy risk, particularly HCC. However, the association between fibrosis severity and extrahepatic malignancies remains inconsistent across studies. A cohort study conducted in the United States reported that MASLD was associated with a significantly higher overall cancer risk compared to matched controls, while extrahepatic cancer and cardiovascular mortality were more pronounced in individuals with MASLD-related cirrhosis compared to those without cirrhosis.[11]

Sex-Specific Differences in MASLD-Related Cancer Risk

Sex-related differences influence the development and progression of MASLD and its associated malignancies. These differences are mediated by hormonal, genetic, and metabolic factors that affect fat distribution, insulin sensitivity, and oxidative stress.[12]

Men have a higher overall risk of HCC, while women exhibit a comparatively lower risk during reproductive years. This difference is partly explained by hormonal and immunological factors. In contrast, postmenopausal women demonstrate accelerated progression of fibrosis and increased susceptibility to HCC, along with reduced therapeutic response, highlighting the influence of hormonal changes on disease progression.[12]

Sex-specific variations are also observed in cancer risk patterns. In MASLD populations, the relative risk of liver cancer is higher in men compared to women, whereas the risk of extrahepatic cancers is higher in women. Reported relative risks for liver cancer are 3.16 in males and 1.25 in females, while for extrahepatic cancers, the relative risks are 1.01 in males and 1.44 in females. These findings indicate a comparatively greater predisposition to extrahepatic malignancies in women with MASLD.[12]

Sex hormones play a central role in these differences. Estrogens regulate glucose and lipid metabolism, reduce inflammation, and support hepatocellular regeneration. Loss of estrogen after menopause is associated with an increased prevalence of MASLD and a higher risk of fibrosis, with risk correlating with the duration of estrogen deficiency.[12]

Androgens also influence hepatic metabolism. Reduced androgen levels in men are associated with increased risk of MASLD and metabolic dysfunction, while excess androgens in women contribute to disease progression. These hormonal imbalances affect lipid metabolism and insulin sensitivity, thereby influencing MASLD severity and associated cancer risk.[12]

Genetic and chromosomal factors further contribute to sex-based differences. Variations in sex chromosome composition and hormone levels influence metabolic regulation and susceptibility to liver disease.[12]

Sex-based differences are also evident in clinical outcomes. Women have a higher incidence of cirrhosis, whereas men have higher rates of hepatic decompensation, HCC, cardiovascular disease, chronic kidney disease, and non–sex-specific cancers. Specifically, women have a 9% higher risk of cirrhosis, while men have an 11% higher risk of hepatic decompensation and more than double the risk of HCC. Additionally, men have increased risks of cardiovascular disease, chronic kidney disease, and overall cancer incidence compared to women.[13]

Cancer surveillance strategies in MASLD

Cancer surveillance in MASLD primarily focuses on early detection of HCC in high-risk individuals, particularly those with cirrhosis. Current strategies recommend biannual abdominal ultrasound, with or without alpha-fetoprotein (AFP) measurement.[14]

Given the increasing recognition of HCC risk in non-cirrhotic individuals with advanced fibrosis, risk-stratified surveillance approaches are being considered. Non-invasive scoring systems such as fibrosis-4 (FIB-4) are used to identify individuals at higher risk. Clinical guidelines support this approach, with recommendations suggesting that selected non-cirrhotic patients with advanced fibrosis may be considered for surveillance based on individualized risk assessment. Cost-effectiveness analyses indicate that surveillance is most appropriate in populations with an annual HCC incidence of approximately 1% or higher, a threshold not consistently reached in non-cirrhotic MASLD populations.[14]

Ultrasound-based surveillance has limitations in MASLD, particularly in individuals with obesity, where increased subcutaneous fat reduces image quality and sensitivity. Studies report that ultrasound may miss a substantial proportion of HCC cases in this population.[14]

Alternative imaging modalities, including computed tomography (CT) and magnetic resonance imaging (MRI), provide improved detection but are limited by cost, accessibility, and contrast-related concerns. Abbreviated MRI protocols have demonstrated improved detection rates compared to ultrasound, including in patients with hepatic steatosis. However, current guidelines do not recommend CT or MRI as first-line surveillance tools, reserving them for cases where ultrasound is inadequate.[14]

Biomarkers for Early Detection

Several biomarkers have been evaluated to improve the early detection of HCC. Due to the heterogeneity of HCC, single biomarkers have limited sensitivity, and combined biomarker approaches are increasingly utilized. The GALAD score, which incorporates age, sex, AFP, lens culinaris agglutinin-reactive fraction of alpha-fetoprotein (AFP-L3), and des-gamma-carboxy prothrombin (DCP), has demonstrated high accuracy for early HCC detection in MASLD populations, including those without cirrhosis.[14]

Circulating cell-free DNA (cfDNA) and circulating tumor DNA (ctDNA) have also been investigated as potential diagnostic tools. Methylation-based marker panels have shown high sensitivity and specificity for early-stage HCC detection in clinical studies. However, these approaches require further validation, particularly in MASLD-specific cohorts.[14]

Risk stratification and screening approaches

Risk prediction models have been developed to identify individuals at higher risk of HCC. The Toronto HCC Risk Index (THRI) and age-male sex-ALBI (Albumin-bilirubin)-platelets (aMAP) score incorporate clinical and laboratory parameters to stratify patients into different risk categories. Additional models integrating liver stiffness measurements and biochemical markers have demonstrated moderate predictive performance in MASLD populations.[14]

Emerging approaches include genetic and molecular risk stratification. Polygenic risk scores incorporating variants such as PNPLA3, TM6SF2, MBOAT7, and Glucokinase Regulatory Protein (GCKR) have been associated with increased HCC risk. Gene expression signatures have also shown potential in predicting long-term HCC development, although further validation is required before clinical application.[14]

Multidisciplinary management

HCC remains a major cause of cancer-related mortality, with MASLD increasingly recognized as a contributing etiology. Early detection and accurate risk assessment are essential for improving clinical outcomes.[15]

Management strategies for MASLD-related HCC follow established staging systems such as the Barcelona Clinic Liver Cancer (BCLC) classification. Early-stage disease (BCLC 0 and A) may be managed with curative approaches, including surgical resection, liver transplantation, or ablation. Advanced stages require systemic therapies based on disease extent and patient factors. (Fig. 4) Treatment approaches are not currently differentiated based on underlying etiology, including MASLD.[15]

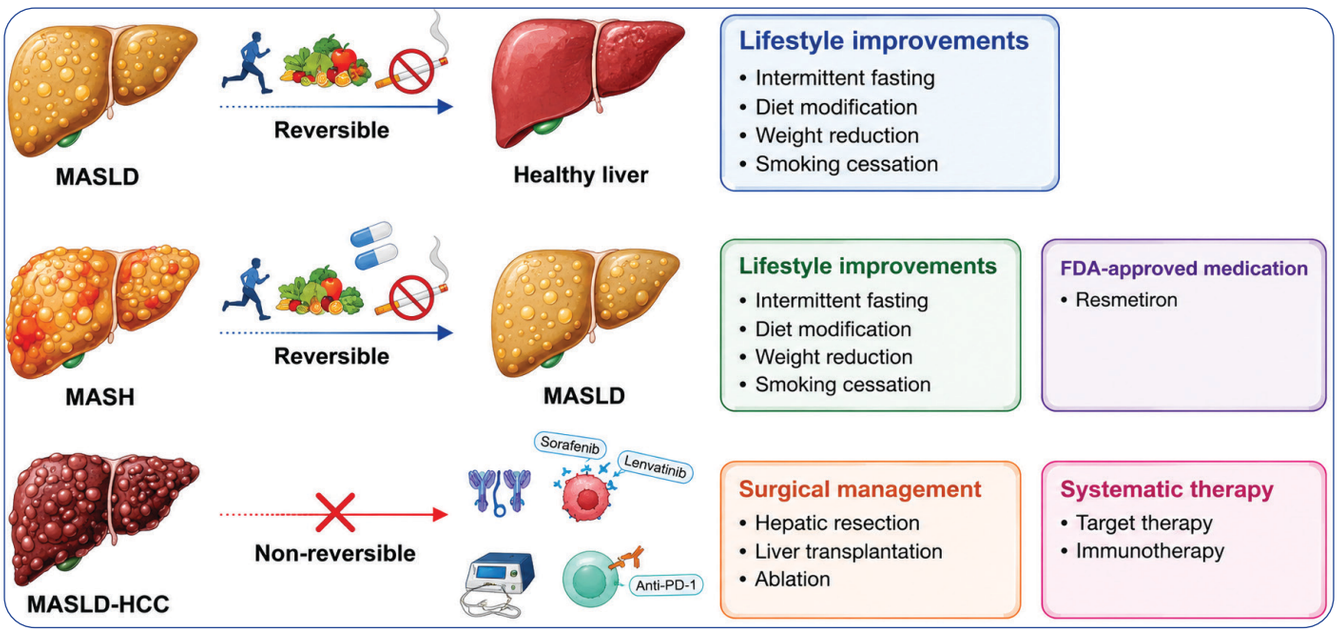

Fig 4. Clinical management for MASLD/MASLD-HCC patients.[15]

Conclusion

Metabolic dysfunction–associated steatotic liver disease represents a significant and growing contributor to the global cancer burden, particularly HCC, while also being associated with a spectrum of extrahepatic malignancies.

The association between MASLD and malignancy is linked to metabolic and inflammatory alterations, including insulin resistance, chronic inflammation, oxidative stress, gut–liver axis alterations, and genetic susceptibility.

Disease progression, especially the development of fibrosis and cirrhosis, remains a key determinant of cancer risk, although malignancies may also arise in non-cirrhotic stages. Sex-specific differences further influence disease patterns and outcomes.

Given the rising prevalence of MASLD, there is an increasing need for effective risk stratification, improved surveillance tools, and early detection strategies. A multidisciplinary approach integrating clinical, biochemical, and emerging molecular markers is essential for optimizing management and reducing MASLD-related cancer morbidity and mortality.

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