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REVIEW

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Advances in multi-omics studies of microvascular invasion in hepatocellular carcinoma

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Abstract

Microvascular invasion (MVI) represents a pivotal independent prognostic factor for the recurrence of hepatocellular carcinoma (HCC) after surgery. It contributes to early intervention for potentially recurrent HCC to enhance patient outcomes and increase survival rates. Traditionally, the diagnosis of MVI has relied on postoperative pathological analysis, and accurate preoperative detection methodologies are lacking. Recent research suggests that multi-omics strategies play a role in definitively diagnosing MVI before surgery and offering personalized selection for clinical decision-making in HCC management. This review meticulously examines a multi-omics approach for the preoperative prediction of MVI in HCC patients, aiming to innovate diagnostic paradigms to anticipate postsurgical recurrence, thereby facilitating earlier and more personalized therapeutic strategies.

Keywords Hepatocellular carcinoma, Microvascular invasion, Multi-omics, Preoperative prognosis

Background

Hepatocellular carcinoma (HCC) ranks as the fifth most prevalent malignancy globally and has emerged as the third most common cause of cancer-induced mortality [1]. Despite surgical interventions such as lobectomy or segmental resection being standard treatments for early-stage HCC, the recurrence rate after surgery remains high, with 50–70% of patients experiencing recurrence within five years, leading to a dismal long-term prognosis [2]. Consequently, preoperatively identifying the factors associated with postoperative recurrence in patients with HCC can substantially refine the clinical diagnosis and treatment needed to carry out precise treatment.

Vascular invasion critically influences the prognosis and likelihood of early recurrence in HCC, with distinctions between macrovascular and microvascular invasion (MVI). MVI is histologically characterized by the presence of tumor cell clusters within endothelial-lined microvessels (e.g., portal or hepatic vein branches) in peritumoral liver parenchyma [3]. This phenomenon is intricately linked to the degree of tumor malignancy, and the dismal prognosis of MVI has been recognized as a potent indicator for the prediction of tumor recurrence following liver transplantation and surgical resection, underscoring its prognostic significance. Currently, the definitive diagnosis of MVI is contingent upon postoperative histopathological examination, with needle biopsy posing risks of inadvertent bleeding and implantation metastasis [4]. Consequently, a pressing demand exists

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for noninvasive methodologies capable of accurately predicting MVI presence preoperatively in HCC patients.

Multi-omics research delves into the intricate interplay among various molecular entities within a biological system, encompassing genomics, transcriptomics, proteomics, metabolomics, and microbiomics. In addition, radiomics has emerged as a powerful and innovative tool for extracting mineable high-throughput data by analyzing digital computed tomography (CT) and magnetic resonance imaging (MRI) images [5], enabling the quantification of tumor spatial heterogeneity [6]. It has been extensively applied in both research and clinical settings across various cancer types, demonstrating substantial value in early tumor detection, precise staging, treatment response evaluation, and prognosis prediction [5–7]. Multi-omics analysis approaches have recently surfaced as innovative tools for detecting MVI in HCC patients. These methodologies can holistically evaluate imaging features, mutated genes, dysregulated proteins, and altered metabolites. This article highlights the forefront of research advancements in imaging, genomics, proteomics, and metabolomics for assessing MVI status in HCC patients and aims to synthesize the current knowledge and prospects of multi-omics strategies in predicting MVI, with the goal of identifying the most efficacious prediction models. This review aims to refine clinical decision-making processes and guide more targeted and personalized therapeutic interventions for HCC (Fig. 1).

Radiomics of the current status of MVI status assessment in HCC patients

Magnetic resonance imaging

MRI, which is esteemed for its exceptional sensitivity, spatial resolution, enhanced soft-tissue contrast, and absence of ionizing radiation, has established itself as a pivotal technique for clinically assessing hepatobiliary disorders. The traditional evaluation of MVI by tumor size and margin status is susceptible to subjective interpretation, limiting its predictive reliability. Therefore, swift advancements in imaging technology have introduced more sophisticated modalities for prognosticating MVI in HCC patients. Within the realm of MRI diffusion imaging, parameters such as the apparent diffusion coefficient [8], the mean diffusion kurtosis [9], and the diffusion coefficient value [10] have been validated as independent predictors for MVI status, heralding a new era in diagnostic precision.

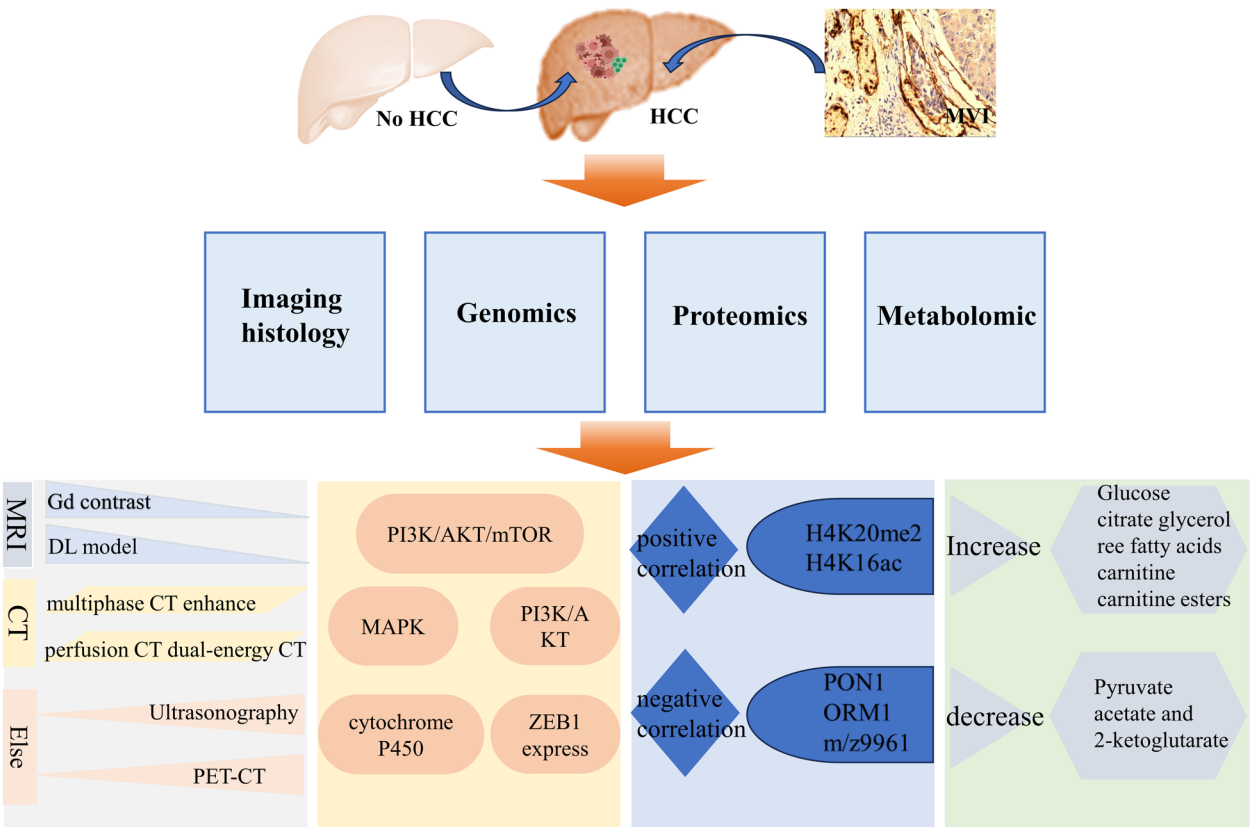

Fig. 1 Diagnostic schematic of multi-omics data

Gadoxetic acid disodium is an innovative hepatocyte-specific contrast agent. This agent facilitates the detailed assessment of blood supply patterns of hepatic lesions through dynamic enhancement scanning while also enabling the evaluation of hepatocyte function via signal fluctuations in the hepatobiliary phase [11]. These findings provide crucial functional and morphological insights for accurately identifying early-stage HCC and performing differential diagnosis. Specific imaging features, including peritumoral low-signal intensity in the hepatobiliary phase, nonsmooth tumor margins, irregular arterial-phase enhancement, and peritumoral arterial enhancement [12], have been identified as significant preoperative indicators for MVI prediction.

Moreover, integrating radiomics, mainly through analyzing intratumoral and peritumoral regions in gadoxetic acid disodium-enhanced MR images, has emerged as an effective predictive model for MVI [13]. With artificial intelligence, intense deep learning (DL) has been gradually applied to the preoperative prediction of MVI in HCC patients. DL distinguishes itself by extracting features directly from raw images through an advanced hierarchical neural network and convolutional operations, surpassing traditional radiomic methods' efficiency and predictive accuracy capabilities. Song et al. [14] built a DL model incorporating preoperative dynamic contrast-enhanced MR images and clinical parameters to predict the MVI status and grade of HCC patients. This model exemplifies the predictive performance of the synergy between DL and clinical parameters, with an area under the curve of 0.931.

CT

CT is an intuitive, rapid method that can meticulously reorganize tumors across multiple directions and planes, elucidating their morphological features with exceptional clarity. This capability has rendered CT an indispensable tool in the early screening and diagnosis of HCC lesions. The application of dynamic-enhanced CT, in particular, offers vivid depictions of lesion vascularity and has become a staple in clinical practice. Features such as irregular tumor margins, a halo sign, and internal arterial structures have been identified as independent predictors of MVI [15].

Furthermore, multiphase CT-enhanced texture analysis, a noninvasive technique capable of quantitatively capturing medical image characteristics, has demonstrated that tumor size, nonsmooth tumor margins, and intratumoral arteries serve as imaging findings for predicting MVI in HCC patients [16]. Advanced modalities such as perfusion and dual-energy CT show significant potential in noninvasively assessing tumor attributes, offering additional quantitative parameters. Perfusion CT, a relatively novel imaging technique, can vividly reveal in vivo microvascular alterations associated with tumor angiogenesis. Its quantitative CT perfusion parameters enable the quantification of tumor vasculature and angiogenesis in HCC, aiding in the differentiation between benign and malignant neoplasms. Notably, the permeability surface area has emerged as a singularly significant parameter for predicting recurrence risk [17], reflecting tumor invasiveness and serving as a prognostic indicator.

The advent of dual-energy CT has increased image quality and expanded the quantitative analytical toolkit available to clinicians. Among these innovations, dual-energy CT iodine quantification stands out for offering objective, precise assessments of lesion iodine uptake, thereby shedding light on the tumor's blood supply, hemodynamic properties, and microcirculatory characteristics [18]. Kim et al. [19] discovered that the normalized iodine concentration in the peritumoral region within 2 mm of the tumor margin is an independent predictive factor for MVI. This finding underscores the utility of quantifying the iodine volume in the peritumoral region during the arterial phase as a method for the preoperative prediction of MVI via dual-energy CT.

Building on these advancements, Wang et al. [20] pioneered an end-to-end DL approach based on CT radiomics. This innovative method integrates raw data preprocessing, automatic segmentation of interest regions, and MVI prediction, achieving optimal predictive outcomes during the arterial phase. Compared with conventional models, the designed convolutional neural network exhibited superior accuracy (0.8678), effectively addressing the inefficiencies associated with manual delineation of interest regions and thereby conserving human and material resources.

Ultrasound and PET–CT

Ultrasonography, recognized for its affordability, ability for real-time monitoring, noninvasive nature, and absence of radiation exposure, has been endorsed by multiple guidelines as an essential first-line screening tool for populations at high risk for HCC. Studies have identified tumor diameter, echo intensity, the extent of peritumoral enhancement in the arterial phase, and the degree of enhancement in the portal venous phase [21], alongside higher acoustic radiation values and lower minimum gray values [22], as substantial independent predictors of MVI. Ultrasonography has evolved into a sophisticated imaging modality, offering insights into tumor perfusion, with enhancement patterns in the portal and delayed phases, outflow timing, and differences in tumor margin echogenicity that are critical for MVI prediction [23]. The prognostic accuracy improves when ultrasonographic findings are integrated with clinical parameters [24].

18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET)/CT is a cornerstone of molecular imaging. It furnishes vital data on malignant tumor recurrence and metastasis and aids in the staging and prognostic evaluation of HCC patients. Typically, malignant tumors exhibit heightened 18F-FDG uptake, allowing for the preoperative prediction of MVI when the standardized uptake value exceeds 3.2 [25]. Li et al. [26] incorporated 80 patients with BCLC 0-A HCC who underwent preoperative 18F-FDG PET/CT into their study. They devised a radiomic nomogram integrating radiomic and clinical features and discovered that a combination of five PET features and six CT texture features was a potent predictor of MVI. A nomogram that integrates Rad scores with clinical predictors yielded the highest efficacy in MVI detection [27].

Radiomics is a noninvasive approach for the preoperative prediction of MVI status in HCC patients. Presently, CT and MR radiomics models outperform ultrasound-based models in terms of predictive accuracy. Compared with focusing on the tumor alone, incorporating various sequences enhances predictive capabilities, and segmentation of the tumor and peritumoral regions offers superior predictive value [28]. Nevertheless, the manual extraction of image features is a complex, labor-intensive task with limited repeatability, potentially affecting the consistency of imaging histology feature measurements. The advent of artificial intelligence, particularly the integration of DL with imaging histology and the inclusion of biological markers, promises to substantially increase prediction performance.

Genomics identifies genes associated with MVI status in HCC patients

The advent of genomics has heralded a transformative era in targeted medicine, primarily fuelled by advancements in next-generation sequencing technologies. Illumina second-generation sequencing, a hallmark of this evolution, has significantly increased sequencing throughput and reduced costs. This technological leap has shifted genomics research from focusing on a select few genes to conducting extensive whole-genome, multi-omics, and pancancer analyses. The continual refinement of sequencing technologies has been pivotal in catalyzing the rapid expansion of cancer genomics research [29].

In HCC, the genetic underpinnings contributing to MVI—a critical factor affecting patient prognosis—are yet to be fully deciphered. Unravelling the driver genes responsible for MVI could unveil novel therapeutic targets, thereby enhancing patient outcomes. Preliminary investigations pinpoint several genes, such as ARID2, IGF2R, DENND5A, PIK3CA, IL6ST, and ABCG2, as critical genes in the MVI mechanism [30]. Various signaling pathways, including those mediated by growth factors, Wnt/β-catenin, and RAS/RAF/MAPK, may play roles in the development of MVI in HCC patients [31]. Moreover, the TSC2 gene is a crucial regulator of the PI3K/AKT/mTOR pathway upstream of signal transduction. It is significant in HCC and metastasis and has been shown to be strongly correlated with MVI in recent studies [32].

Integrating bioinformatics with genomics sequencing technologies has become a cornerstone in investigating various tumors, offering valuable insights into tumorigenesis, progression, and metastasis mechanisms. The calcium-binding protein S100P is known for its abnormal expression in several cancers, including breast, ovarian, prostate, and colon cancers. CD44 has been shown to play a significant role in MVI development within HCC, mainly through the upregulation of CD44 expression, highlighting its potential as a preoperative predictor of MVI status in HCC patients [33].

Further efforts to identify biomarkers indicative of early recurrence in MVI and HCC patients have led to studies such as that by Xin et al., who enrolled 41 patients who underwent hepatectomy for suspected HCC. Through high-throughput targeted sequencing, the study identified mutations in genes such as KEAP1, TP53, HIST1H3D, NFKBIA, PIK3CB, and WRN, which were more prevalent in patients with both MVI and early recurrence than in those without recurrence. Rap1 and Ras signaling pathway alterations are significantly more common in MVI patients [34].

The Tumor Genome Atlas program and its expansive database have become indispensable resources in oncology research, facilitating the identification of overexpressed genes such as HOXD9, HOXD10, and PPP2CA in patients with MVI [35, 36]. Additionally, a study conducted on formalin-fixed paraffin-embedded surgical biopsies of HCC samples revealed that six genes (ROS1, UGT2B7, FAS, ANGPTL7, GMNN, and MKI67) correlated with MVI, achieving 82% accuracy in identifying MVI in HCC patients [37].

The continuous evolution of genomic databases and high-throughput analysis technologies remains critical in elucidating the complex mechanisms underlying MVI, paving the way for more precise and practical approaches in cancer treatment. Despite these advancements, the field faces several challenges, including incomplete database data on MVI status in HCC patients, the need for further clinical validation of preoperative MVI risk prediction, and the limitations posed by small sample sizes and the absence of large-scale, multi-center validation (Fig. 2).

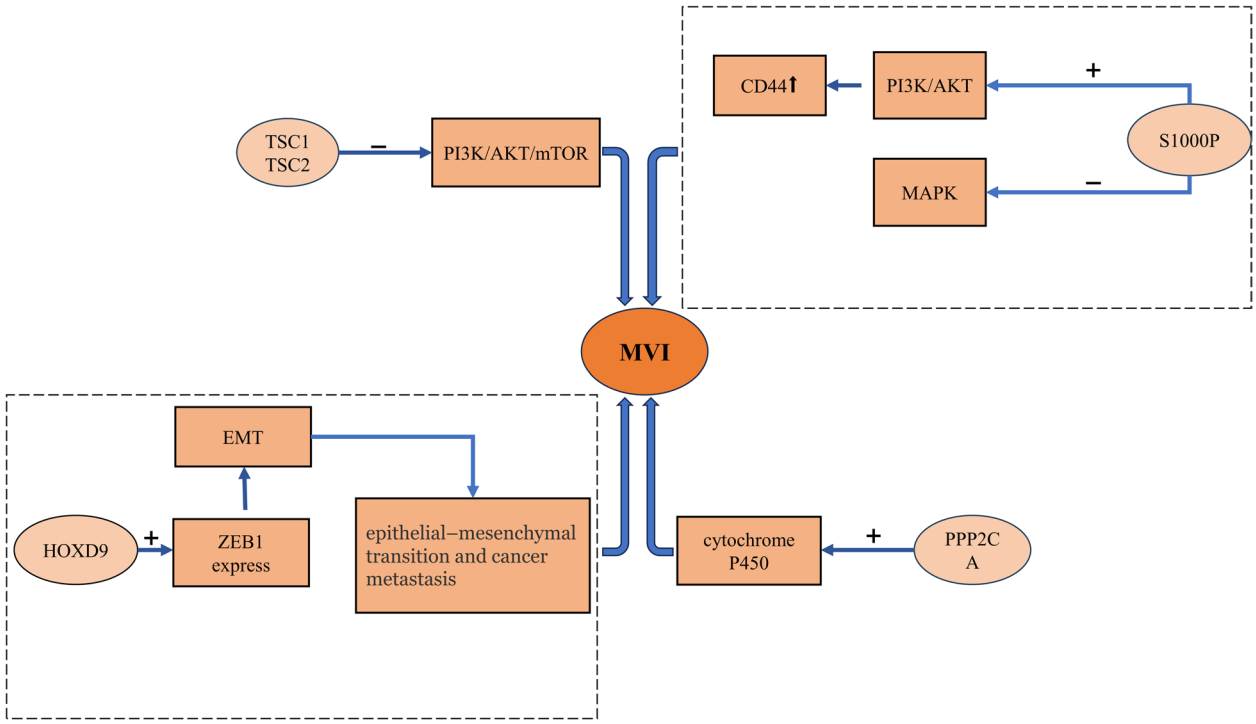

Fig. 2 Relevant genes and signaling pathways leading to MVI

Proteomics search for biomarkers of MVI status in HCC patients

While genomic and transcriptional analyses shed light on the nature and potential implications of genomic alterations, proteomics offers more direct insights into protein-mediated regulation and response mechanisms to these changes. Proteomics can reveal the specifics of the tumor microenvironment and cellular signal transduction levels. Alpha-fetoprotein (AFP), currently the most widely recognized biomarker for HCC, serves as an independent indicator of recurrence risk and poor prognosis [38]. However, the diagnostic efficacy of AFP is undermined by its low sensitivity and specificity, rendering its utility in monitoring HCC a subject of ongoing debate.

In the quest for more reliable biomarkers, proteins such as PIVKA-II, GPC3, GP73, AFU, GGT, and SCCA [39] have been identified and incorporated into clinical practice. However, these markers lack limitations concerning specificity and sensitivity, underscoring the critical need to identify novel biomarkers. Proteomics analysis technology has emerged as a beacon of hope in this context. With the ability to analyze thousands of proteins simultaneously, identify and characterize hundreds of biomarkers in a single sample, and conduct large-scale quantification and validation, proteomics is a potent tool for identifying new tumor markers and therapeutic targets. PON1 is a serum antioxidant protein that plays a crucial role in regulating oxidative metabolism and thus inhibits tumor invasion. It acts as a protective agent against vascular invasion and metastasis. Huang et al. [40] discovered a negative correlation between PON1 expression in tumor cells and the extent of vascular invasion through iTRAQ-based proteomic analysis, suggesting that the serum PON1 concentration is a novel preoperative biomarker for MVI in HCC.

Furthermore, ORM1, which is known to facilitate tumor necrosis factor-induced angiogenesis, is expressed at varying levels across different cancers. Its reduced expression in HCC cells, in contrast with elevated levels in vascular-invasive tumor cells, can be quantified in plasma and other bodily fluids, positioning ORM1 as a prime candidate for the dynamic monitoring of disease progression [41]. Mass spectrometry, a cornerstone of proteomics research, is celebrated for its sensitivity, precision, and high throughput. Investigations utilizing mass spectrometry have highlighted the significant correlation between MVI presence and low expression of m/z9961 and increased expression of H4K20me2 and H4K16ac [42, 43].

The advancement of proteomics is intrinsically linked to the swift progression of proteomics analysis technology. When synergistically combined with bioinformatics, proteomics becomes a powerful strategy for identifying specific biomarkers indicative of MVI in patients

with HCC. Despite these technological strides, contemporary research in this domain is often encumbered by challenges such as limited sample sizes, lack of standardization in laboratory techniques, and variability in the bioinformatic processing of data. These obstacles considerably impede the clinical application of identified biomarkers. Nonetheless, it is anticipated that with ongoing technological refinement and maturation, the screening of biomarkers leveraging proteomics data will evolve into a routinely employed tool in cancer analysis.

Metabolomic analysis of metabolites related to the MVI status of HCC patients

Metabolomics is an emergent science that facilitates the concurrent quantification of myriad metabolites within biological fluids and tissues. This field has garnered application across oncology and diverse disease spectra to evaluate alterations in pathological states. This approach surpasses traditional histological methods by offering insights into metabolites directly generated in response to endogenous and exogenous influences. Given its role as the metabolic epicenter, the liver hosts an extensive array of lipids and water-soluble metabolites more than any other human organ does. It is capable of modulating the expression levels of numerous metabolites. Notably, shifts in metabolic profiles precede radiographic diagnosis in HCC patients [44], emphasizing the importance of metabolomic perspectives in HCC research. Metabolomic analyses have revealed specific changes in the hepatic metabolite landscape of HCC patients, including reductions in glucose, citrate, and glycerol 3-phosphate and increases in pyruvate, signaling aberrant metabolic activities.

In contrast to the traditional understanding that tumors synthesize fatty acids from citrate through acetyl coenzyme A, recent metabolomics data from HCC research indicate increased fatty acid β-oxidation; increased levels of acetate and 2-ketoglutarate (carnitine precursors); and decreases in free fatty acids, carnitine, and carnitine esters. These findings suggest metabolic reprogramming within HCC, characterized by the Warburg effect and increased fatty acid catabolism [45]. Additionally, anomalies in bile acid, lysophosphatidylcholine, free fatty acid, and hypoxanthine concentrations have been observed in HCC patients [46]. Despite these advances, explorations into potential metabolites capable of predicting MVI in HCC patients remain scarce. Lee et al. [47] undertook plasma metabolic profiling via 1H-nuclear magnetic resonance spectroscopy in HCC patients slated for hepatic resection. Their findings highlighted formate as a particular and selective biomarker for predicting MVI presence. Moreover, integrating formate levels with tumor size and AFP metrics notably enhances predictive accuracy.

The burgeoning domain of metabolomics heralds substantial promise for precision medicine's future, underpinned by metabolic analysis and phenotyping. This avant-garde approach aims to tailor patient treatment strategies to their unique molecular aberrations. Metabolomics has demonstrated its ability to identify potential biomarkers pivotal for cancer diagnosis, surveillance of metastasis, anticipation of recurrence, and formulation of targeted treatment strategies. Nonetheless, the current landscape of metabolomics research is not devoid of challenges and limitations. A fundamental question pertains to discerning whether metabolic alterations are directly attributable to the diagnosed condition. Variabilities among patients, the analogous nature of diseases, and methodological discrepancies further muddle the reliability of findings. This underscores the imperative for more exhaustive investigations to capture the entirety of the metabolic perturbations involved.

Most metabolomics research on HCC has focused predominantly on metabolic profiling, often neglecting the integration of comprehensive data across other biological dimensions, such as genomics, transcriptomics, and proteomics. This realization has sparked a progressive shift towards harmonizing metabolomics insights with data derived from upstream genomic technologies. Metabolomics, the nascent branch of histological sciences, has already started to shed light on novel discoveries and insights into liver disease mechanisms, revealing potential therapeutic targets. It is believed that metabolomics will eventually pave the way for novel therapeutic modalities (Table 1).

Summarizing and looking forward

HCC is highly malignant and prone to recurrence after surgery, and preoperative clarification of the presence of MVI is highly important for patients. Genomics, proteomics, metabolomics, and radiomics studies provide us with information from DNA, proteins, metabolites, and imaging. It bridges the gap from the micro to the macro level to understand a living organism fully and explains the entire process of change in a living organism from microscopic DNA molecules to the secretion of small-molecule metabolites. Multi-omics studies of MVI can provide early assessment and precise prediction and offer a basis for elucidating the mechanism of MVI, drug targets, individualized treatment, and prognosis assessment. Currently, imaging studies focusing on HCC MVI are relatively comprehensive, and most of the proposed clinical prediction models are highly accurate and can provide specific reference values for clinicians. This review establishes a pivotal framework for advancing HCC management: Multimodal MRI and PET–CT enable dynamic tumor microenvironment monitoring,

Table 1 Preoperative assessment of HCC in the presence of MVI multi-omics studies

Serial no.	Title	Author	Date of publication	Journal	Page	Number	Method	Type
1	Using preoperative radiomics to predict the microvascular invasion of hepatocellular carcinoma based on Gd-EOB-DTPA enhanced MRI [7]	Xin-Yu Lu	2022 Sep	Randomized Controlled Trial	1–13	165	*D* value	Radiomics
2	A radiomics nomogram for preoperative prediction of microvascular invasion risk in hepatitis B virus-related hepatocellular carcinoma [12]	Jie Peng	2018 May–Jun	Diagn Interv Radiol	121–127	304	Tumor margins not smooth, halo sign, presence of internal arteries	Radiomics
3	S100P as a novel biomarker of microvascular invasion and portal vein tumor thrombus in hepatocellular carcinoma [30]	Lu-Nan Qi	2021 Feb	Hepatol Int	114–126	826	S100P overexpression	Genomics
4	A predictive and prognostic model for hepatocellular carcinoma with microvascular invasion based TCGA database genomics [32]	Jin Wang	2021 Dec	BMC Cancer	1–11	260	HOXD9, HOXD10overexpression	Genomics
5	The effect of PPP2CA expression on the prognosis of patients with hepatocellular carcinoma and its molecular biological characteristics [33]	Jingchang Liang	2021 Dec	J Gastrointest Oncol	3008–3021	128	PPP2CAoverexpression	Genomics
6	Gene expression signature as a surrogate marker of microvascular invasion on routine hepatocellular carcinoma biopsies [34]	Aurélie Beaufrère	2022 Feb	J Hepatol	343–352	178	ROS1, UGT2B7, FAS, ANGPTL7, GMNN, MKI67 gene mutation	Genomics
7	Quantitative proteomic analysis identified paraoxonase 1 as a novel serum biomarker for microvascular invasion in hepatocellular carcinoma [37]	Cheng Huang	2013 Apr	J Proteome Res	1838–46	90	Serum PON1 protein concentration	Proteomics
8	ORM 1 as a biomarker of increased vascular invasion and decreased sorafenib sensitivity in hepatocellular carcinoma [38]	Jiangning Gu	2022 Oct	Bosn J Basic Med Sci	949–958	35	Increased ORM1 expression levels	Proteomics
9	SELDI-TOF MS Analysis of Hepatocellular Carcinoma in an Australian Cohort [39]	Steven M Schlichtemeier	2019 Jun	J Surg Res	127–136	30	m/z9961low	Proteomics
10	Contribution of virtual biopsy to the screening of microvascular invasion in hepatocellular carcinoma: A pilot study [40]	Nicolas Poté	2018 Apr	Liver Int	687–694	106	Increased H4K20me2, H4K16acexpression levels	Proteomics

Table 1 (continued)

Serial no.	Title	Author	Date of publication	Journal	Page	Number	Method	Type
11	Serum metabolites may be useful markers to assess vascular invasion and identify normal alpha-fetoprotein in hepatocellular carcinoma undergoing liver resection: a pilot study [44]	Chao-Wei Lee	2020 Jun	World J Surg Oncol	1–12	57	Carboxylic acid ester	Proteomics

circumventing limitations of conventional histopathology to accelerate clinical translation of precision oncology. Furthermore, radiogenomics-integrated imaging analyses noninvasively decode tumor microenvironment molecular heterogeneity, offering quantifiable biomarkers for personalized therapeutic strategies. Notably, miR-510-3p targets VEGFA and inhibits phosphorylation of PI3K, AKT, eNOS, and mTOR, which are important regulators of angiogenesis and vasodilation [48].Furthermore, functional characterization reveals that miR-21 plays a pivotal role in maintaining mesenchymal stem cell pluripotency, as evidenced by the significant impairment of osteogenic and adipogenic differentiation following miR-21 knockdown experiments [49]. This is an important guideline for microRNA refinement of MVI-related pathways for targeted therapy. The dual regulatory mechanisms involving angiogenesis inhibition through miR-510-3p/VEGFA axis modulation and stem cell differentiation potentiation via miR-21 expression maintenance provide novel insights into precision medicine approaches for vascular remodeling disorders. However, other omics studies of MVI are still in their infancy, and multi-omics still needs to be integrated. It does not provide a strong predictor for the occurrence of MVI. Technology development still limits current multi-omics research. More unified process specifications, large-sample validation, multi-center studies, and prospective studies are needed. However, in the future, with the continuous development of multi-omics technology, continuous intermingling of multi-omics technologies, deep mining of clinical data, and continuous upgrading of artificial intelligence and deep learning methods, we can gain a deeper understanding of HCC, establish MVI prediction models with the best predictive performance, and ultimately play an essential role in exploring individualized and precise treatments.

Abbreviations

MVI	Microvascular invasion
HCC	Hepatocellular carcinoma
MR	Magnetic resonance
DL	Learning
CT	Computed tomography
PET	Positron emission tomography
18F-FDG	18F-fluorodeoxyglucose
AFP	Alpha-fetoprotein

Author contributions

Wang Lili, Xu Hanxin and Wang Rui wrote the main manuscript text, Zhang Fachang, Deng Diandian and Zhu Xiaoyang prepared Figs. 1, 2. Tan Qi and Yang Heng prepared Table 1. All authors reviewed the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study has been approved by Ethics Committee of the First Hospital of Lanzhou University (Approval number: LDYYLL2022-251). Patient informed consent was waived.

Competing interests

The authors declare no competing interests.

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