



Multidisciplinary management of HCC

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Hepatocellular carcinoma (HCC) has become the paradigm of complexity in modern oncology, requiring clinicians to weigh liver function, tumour biology, patient frailty, expanding treatment options and sequencing, and rapidly evolving technologies. Historically anchored to rigid staging systems that improved consistency yet increasingly expose their limitations, HCC is no longer adequately represented by static algorithms^[1]. Instead, it is evolving toward a dynamic, multiparametric, and multidisciplinary process in which treatment decisions are continuously refined according to tumour behaviour, patient fitness, biological response, and therapeutic opportunities over time. This evolving vision is reflected in the emerging concept of the Multiparametric therapeutic hierarchy (MTH)^[2,3], which serves as the conceptual backbone of this Special Issue. A central conceptual change captured here is the shift from morphology-based decision making toward biologically integrated medicine: tumour size and number alone no longer capture the heterogeneity of HCC, since patients within the same stage may follow dramatically different oncological trajectories. The incorporation of additional tumour-related variables - biomarkers, inflammatory indices, radiological response patterns, metabolic imaging, and anatomical complexity - has therefore become essential^[4].

In this scenario, biological profiling and advanced imaging are redefining how clinicians estimate tumour aggressiveness and therapeutic potential. The growing use of radiomics, 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT), and new circulating biomarkers reflects the need to move beyond descriptive staging systems toward a more refined interpretation of tumour biology^[4]. This evolution is not merely technological sophistication: it directly affects treatment selection, prediction of recurrence, and survival.

At the same time, the patient has progressively moved to the centre of therapeutic decision making. The Barcelona Clinic Liver Cancer (BCLC) staging system primarily evaluates patient condition through performance status, which, although clinically valuable, only partially reflects the overall functional and physiological reserve of the individual. Modern HCC management increasingly recognises that oncological outcomes are closely linked to broader dimensions of patient fitness. Frailty, sarcopenia, nutritional status, comorbidities, and biological age are critical to



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determine whether a theoretically feasible treatment is also clinically appropriate^[5]. This represents a crucial cultural shift. The question is no longer simply “What treatment is indicated for this tumour?” but rather “What treatment strategy is sustainable and beneficial for this individual patient?”.

Importantly, patient fitness is not a static parameter either. The growing interest in prehabilitation programmes - including nutritional support, physical conditioning, and psychological optimisation - demonstrates that multidisciplinary care extends beyond tumour-directed therapy alone. In many patients, improving functional reserve may directly expand therapeutic possibilities, increasing access to surgery or systemic treatments previously considered too risky^[5].

This dynamic evaluation of treatment options closely parallels another major shift in HCC care: the emergence of therapeutic conversion strategies. Historically, HCC treatments followed a relatively linear hierarchy in which patients progressed from curative to palliative therapies according to disease stage. However, the recent introduction of highly effective systemic therapies, immunotherapy combinations, and advanced locoregional techniques is progressively dismantling this rigid concept^[6].

Today, patients who are initially considered unsuitable for curative approaches may achieve meaningful downstaging, eventually becoming candidates for transplantation, resection or ablation. The therapeutic intent itself has therefore become dynamic. Palliation and cure are no longer strictly separated categories, but interconnected phases within an adaptive treatment continuum. This evolving paradigm has been conceptualised as a “converse therapeutic hierarchy”, in which treatment allocation may dynamically move upward toward curative strategies. Such an approach requires continuous reassessment by multidisciplinary teams (MDT) capable of interpreting radiological response, biological evolution, and liver function changes in real time^[6].

Within this rapidly evolving landscape, another critical dimension emerges: the concept of treatment unfeasibility. Traditionally, therapeutic decision making in HCC has often focused on whether a treatment was theoretically indicated according to oncological criteria. However, real-world experience increasingly demonstrates that the most effective treatment is not always the treatment that can realistically be delivered. Organ shortage, technical complexity, institutional expertise, resource allocation, global disparities, waiting times, financial constraints, and patient preferences and values all contribute to shaping what is truly feasible in real-world settings^[7].

This perspective is particularly relevant in HCC, where liver transplantation - the most comprehensive functional and oncological treatment - simultaneously represents one of the most effective and least universally accessible options. Accordingly, access to transplantation cannot rely solely on theoretical eligibility, but should be reserved for patients expected to derive the greatest transplant benefit, particularly when the alternative therapeutic strategies are represented by progressively less curative options^[8].

The paradox of modern HCC care is therefore that therapeutic superiority may coexist with practical unfeasibility. Recognising this reality requires a more mature and transparent decision-making process capable of integrating not only biological appropriateness, but also ethical, logistical and social dimensions^[7]. In this context, treatment unfeasibility should not be interpreted as therapeutic failure, but rather as a multidimensional variable that must be explicitly acknowledged during MDT discussions. The challenge for modern tumour boards is no longer limited to identifying the theoretically best treatment, but to identifying the best achievable treatment for a specific patient within a specific healthcare environment. Such an

approach reinforces the need for expert MDT evaluation, where clinical judgement extends beyond guidelines and incorporates equity of access, resource availability, institutional capability, and patient values^[7].

Within this framework, multidisciplinary tumour boards assume an even more central role. Their value no longer resides solely in applying guideline-based decisions, but in integrating heterogeneous layers of information into individualised treatment pathways. Surgeons, hepatologists, oncologists, interventional and diagnostic radiologists, pathologists, epidemiologists, nutritionists, geriatricians, and increasingly data scientists are now collectively contributing to decision-making processes that have become too complex for isolated expertise^[3]. In particular, the contribution of population-based epidemiological studies is essential, as the systematic monitoring of high-risk populations enables earlier detection and timely referral, thereby feeding the multidisciplinary process from its earliest stage.

The integration of artificial intelligence (AI) into HCC management further emphasises this transformation. AI-based systems are demonstrating promising results in radiological interpretation, recurrence-risk stratification, treatment-response assessment and histopathological analysis. Machine-learning models may eventually help clinicians navigate the enormous amount of biological, radiological, and clinical information generated during multidisciplinary evaluations^[9].

However, AI should not be interpreted simply as an instrument of automation. Its greatest potential may lie in augmenting multidisciplinary intelligence rather than replacing clinical judgement. In HCC, where uncertainty and biological heterogeneity remain dominant, the combination of human expertise and computational support may become particularly valuable. Nevertheless, enthusiasm must remain balanced by caution: data harmonisation, external validation and ethical governance remain critical prerequisites before widespread implementation can occur safely and equitably^[9].

These same principles of personalisation and integration are also reshaping surveillance strategies. Conventional surveillance protocols have traditionally adopted a relatively uniform approach for all at-risk patients. Nonetheless, precision surveillance models are emerging with the aim of tailoring screening intensity according to personalised risk stratification. Risk-stratified and precision surveillance may also represent the earliest step of the multiparametric framework^[10].

The incorporation of abbreviated magnetic resonance imaging (MRI) protocols, biomarkers, and predictive algorithms may significantly improve early detection while simultaneously optimising healthcare sustainability. Importantly, surveillance itself increasingly becomes part of the multidisciplinary continuum rather than an isolated hepatology activity. Earlier detection, more accurate biological characterisation, and faster referral may substantially increase access to curative opportunities^[10].

This closing Editorial synthesises the seven contributions of the Special Topic and outlines how they collectively refine the MTH framework [Table 1].

The Special Topic also reveals important areas that remain insufficiently resolved. Among them, the integration of liver function into dynamic treatment allocation, the prospective validation of MDT-based decision models, and the harmonisation of AI-supported tools across institutions remain priorities for future research.

Collectively, the studies included in this Special Issue suggest that HCC management is progressively evolving toward a new conceptual framework in which treatment decisions are determined not exclusively by stage-migration rules, but by the dynamic interaction among therapeutic efficacy, technical feasibility, biological aggressiveness, patient fitness, and future therapeutic opportunities^[3].

Table 1. The seven contributions of the Special Issue and their position within the MTH framework

Article (<i>Hepatoma Research</i>)	Position within the MTH framework and key message
Vitale <i>et al.</i> 2025;11:26 (Opinion) ^[3]	Introduces the MTH as the conceptual backbone of the issue: a tri-axial model that separates prognostic staging from treatment allocation, combining an ordinal hierarchy of therapies ranked by survival benefit, a multiparametric feasibility assessment, and a converse hierarchy allowing upward, dynamic reallocation toward curative intent
Lai <i>et al.</i> 2025;11:14 (Review) ^[4]	Critical tumour features beyond morphology: tumour location, AFP and emerging markers (DCP/PIVKA-II, liquid biopsy), inflammation-based indices, radiological response and FDG-PET, integrated into multiparametric, biology-driven decision-making
Masarone <i>et al.</i> 2025;11:21 (Review) ^[5]	Patient fitness as a decisive, dynamic parameter: frailty, sarcopenia, comorbidity and biological age move beyond performance status, with prehabilitation able to expand therapeutic eligibility
Tovoli <i>et al.</i> 2026;12:6 (Review) ^[6]	Converse therapeutic hierarchy and conversion therapy: high response rates of systemic and locoregional treatments can downstage initially non-curable patients toward resection, ablation or transplantation, reframing every treatment as a potential gateway to cure
Govoni <i>et al.</i> 2026;12:10 (Review) ^[7]	Treatment unfeasibility as a multidimensional construct (technical feasibility, resources, equity, values and acceptability), adapting the GRADE Evidence-to-Decision framework to individual care and exposing the inverse relationship between efficacy and feasibility
Abdelhamed and El-Kassas 2025;11:8 (Review) ^[9]	Artificial intelligence in multidisciplinary HCC care: opportunities across screening, diagnosis, recurrence-risk stratification and response assessment, with data harmonisation, external validation and ethical governance as prerequisites for safe implementation
Lani <i>et al.</i> 2025;11:9 (Review) ^[10]	Risk-stratified and precision surveillance: tailoring screening intensity and modality (abbreviated MRI, biomarkers such as GALAD) to individual risk to improve cost-effectiveness, early detection and access to curative options through the tumour board

AFP: Alpha-fetoprotein; DCP: des-gamma-carboxy prothrombin; PIVKA-II: protein induced by vitamin K absence II; GRADE: Grading of Recommendations Assessment, Development and Evaluation; MRI: magnetic resonance imaging; MTH: Multiparametric Therapeutic Hierarchy; FDG-PET: 18F-fluorodeoxyglucose positron emission tomography/computed tomography; HCC: hepatocellular carcinoma.

This perspective better reflects the reality of contemporary clinical practice, where treatment sequencing, conversion strategies, and longitudinal reassessment increasingly influence survival outcomes. More importantly, it embraces the principle that HCC management should remain adaptable over time. A patient's trajectory is no longer fixed at diagnosis but may evolve according to biological response, functional optimisation, and technological innovation.

Ultimately, this Special Issue highlights that the future of HCC care will not depend on a single breakthrough therapy or technology. Rather, progress will derive from the ability to integrate multiple dimensions of care into patient-centred strategies. Biological data, advanced imaging, AI, patient-fitness assessment, and multidisciplinary expertise are not competing paradigms, but complementary components of the same evolving scenario.

In many ways, HCC has become the ideal model for precision oncology because it forces medicine to move beyond reductionism. The modern clinician is no longer asked simply to treat a tumour, but to interpret a complex interaction between cancer biology, chronic liver disease, patient resilience, and therapeutic adaptability.

The challenge ahead will therefore not simply be to expand the therapeutic arsenal, but to construct integrated decision-making systems capable of selecting the right treatment, for the right patient, at the right moment, while continuously adapting to disease evolution. In this context, multidisciplinary management is no longer an organisational accessory to HCC care: it becomes its intellectual and clinical foundation.

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Authors' contributions

The author contributed solely to the article.

Availability of data and materials

Not applicable.

AI and AI-assisted tools statement

During the preparation of this manuscript, the AI tool Claude (Anthropic, version Opus 4.8, released 2026-05-28) was used solely for language editing and grammar. The tool did not influence the study design, data collection, analysis, interpretation, or the scientific content of the work. The author takes full responsibility for the accuracy, integrity, and final content of the manuscript.

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Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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