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## Editorial

# Management of hepatocellular carcinoma in China: Seeking common grounds while reserving differences

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Hepatocellular carcinoma (HCC) is a serious and life-threatening form of cancer that is highly prevalent in China due to the high prevalence of hepatitis B virus (HBV) infection. Other risk factors for HCC include hepatitis C virus (HCV) infection, exposure to aflatoxins, excessive alcohol consumption, and tobacco smoking. In China, neonatal HBV vaccination programs and effective anti-viral agents have contributed to a significant decline in HCC incidence, especially for those below 40 years old.<sup>1</sup> However, the increasing prevalence of HCV, diabetes mellitus, obesity, non-alcoholic fatty liver disease (NAFLD), and other risk factors for HCC is concerning and could lead to an increase in the number of cases of HCC in the future.<sup>2</sup> The review article by Xie et al.<sup>3</sup> gives a comprehensive introduction of Chinese clinical practice guidelines and real-life practice for the management of HCC, which has an important guiding significance for clinicians.

Prevention and early detection of HCC are important in order to reduce the burden of this disease. The aMAP score (prognostic score involving age, male, albumin-bilirubin and platelets) is recommended in the 2022 Chinese guidelines to predict HCC occurrence,<sup>4</sup> and the China liver cancer (CNLC) staging system proposed in the 2017 guideline is the standard model for staging.<sup>5</sup> Multi-modal and high-intensity strategies treatments, including the addition of immunotherapy-based systemic treatment to local therapies such as liver resection, local ablation, and intra-arterial therapies, have been adopted in real-life practices in China. The treatment options for HCC vary depending on the stage of the disease. According to the Bridge to Better Outcomes in HCC (BRIDGE) study, unfortunately, only 36% of Chinese cases were initially diagnosed at an early stage and eligible for curative treatments, including liver resection, local ablation and liver transplantation, while the remaining 9% and 55% were at intermediate and advanced stages, respectively.<sup>6</sup>

HCC surveillance is an important tool for early detection

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and improved long-term survival, yet adherence to surveillance protocols is low even in high-risk patient populations. This is due to a variety of factors, including poor access to medical care, higher prevalence of comorbidities, etiology of liver disease, and less favorable socioeconomic status.<sup>7</sup> It is essential that physicians assess patients holistically when making decisions on the appropriateness and necessity for HCC surveillance, taking into account all known risk factors, including demographics, co-morbidities, environmental factors, fibrosis stage, medications, serologic tests and genetic polymorphisms.<sup>4,7</sup>

Multidisciplinary treatment (MDT) is essential for the successful management of HCC, as it allows for the integration of different medical specialties to provide comprehensive care for patients.<sup>8</sup> MDT is beneficial in providing a holistic approach to the diagnosis and treatment of HCC, and it is also important in helping to identify the most appropriate treatment option for each individual patient.<sup>9</sup> However, due to too many patients with newly diagnosed HCC every year, it is difficult to provide MDT for every patient with HCC, especially in China. Due to the involvement of multiple departments in the MDT of HCC, including hepatobiliary surgery, liver transplantation, interventional therapy, radiation therapy, digestive medicine, oncology, infectious diseases, minimally invasive ablation, and even traditional Chinese medicine, there is currently a situation of competition among departments for HCC patients in many Chinese hospitals. As we believe, similar situations also exist to a greater or lesser extent in other countries and regions worldwide. The availability of low-cost treatments for HCC in China is encouraging, but the high prevalence of advanced and end-stage disease in rural areas means that many patients are unable to access these treatments in time.<sup>10</sup> Furthermore, the long-term, continuous, and comprehensive nature of HCC treatment means that some patients are unable to continue treatment due to the cost. It is therefore important to ensure that all patients have access to affordable and effective treatments for HCC.

The CNLC system incorporates tumor characteristics, liver function and performance status, similar to the Barcelona Clinic of Liver Cancer (BCLC) system.<sup>5</sup> Each stage of BCLC 0/A,

B, and C is divided into two substages in the CNLC system, including stages Ia, Ib, IIa, IIb, IIIa and IIIb, with CNLC stage IV equivalent to BCLC stage D. The CNLC system is a treatment allocation method for decision-making purpose, while the Japan Integrated Staging (JIS) score and its variants focus on the prognostic predictive function. The modified Union for International Cancer Control (mUICC) system adopted in Korea is characterized by more detailed treatment allocation and is applied on the premise of Child-Pugh A function, no portal hypertension and performance status (PS) scoring 0–1. The CNLC system has been widely used in real-life practices in China, although the BCLC systems continues to be the main stratification factor for clinical trial designing.

With regard to the patterns of hepatic resection for HCC, including patient characteristics, candidate selection, operative techniques, and surgical practice, etc., distinct differences between those hepatic surgical centers in the East and the West have been widely acknowledged. However, those studies providing meaningful direct comparisons have been lacking, especially for their surgical safety and long-term efficacy – that is, which one side is superior to the other side is little based on the evidence till now.<sup>11</sup> In our previous study, there were many significant differences in patient characteristics and operative variables for their patients undergoing liver resection for HCC between two large hepatic surgical centers in the East (Eastern Hepatobiliary Surgery Hospital of Shanghai) and the West (Mount Sinai Hospital of New York), but no any difference was revealed in their hospital mortality and morbidity rates (both overall and major), as well as their long-term survival and recurrence. In other words, the present study demonstrates that the safety and efficacy of liver resection for HCC are comparable between these two centers which could be regarded as representative ones from the East and the West.<sup>12,13</sup>

BCLC intermediate and advanced stage (BCLC stage B and C) HCC is a heterogeneous population, and that PS and tumor features should be taken into account when determining the best treatment for each patient. PS1 alone is not sufficient to include a patient into either of these two stages, and that new patient-tailored therapeutic indications are needed in order to improve overall survival rates.<sup>14,15</sup>

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#### Abbreviations:

HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NAFLD, non-alcoholic fatty liver disease; CNLC, China liver cancer; MDT, multidisciplinary treatment; BCLC, Barcelona Clinic of Liver Cancer; JIS, Japan Integrated Staging; mUICC, modified Union for International Cancer Control

China is making significant efforts to tackle HCC, with the Ministry of Health investing heavily in viral hepatitis and HCC research and the Chinese Academy of Sciences setting up a national tumor research center in Shanghai.<sup>1</sup> These initiatives have already led to an increase in the number of Chinese research papers on HCC, but more international cooperation is needed to further upgrade China's scientific research in HCC and improve prevention and treatment of the disease. For all clinicians of the world, whether from China or elsewhere, "seeking common ground while reserving differences", this is the core of objective and unbiased academic attitude we need to set up when facing the issue of HCC management.

### Authors' contribution

All the authors were responsible for the interpretation of findings, the drafting, and critical revision of the editorial for important intellectual content. All authors approved the final version of the article.

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### Conflicts of Interest

The authors have no conflicts to disclose.

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