

# Multi-disciplinary treatment for hepatocellular carcinoma in primary hospitals in China during the COVID-19 epidemic

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## Abstract

Hepatocellular carcinoma (HCC) is a common malignant tumor in the Chinese population. Due to its high degree of malignancy, rapid progression, and poor prognosis, it mainly requires multi-disciplinary treatment (MDT) in the clinic. In December 2019, COVID-19, a novel coronavirus pneumonia, broke out in Wuhan, China. It has rapidly spread across the country, with various places launching a level I response to major public health emergencies and traffic being restricted. Most patients with HCC were only able to attend primary hospitals, while the MDT model for HCC in provincial hospitals was restricted. Therefore, it was a huge task for clinicians in primary hospitals to ensure MDT was given to patients with HCC during the level I response to major public health emergencies. How to formulate a reasonable MDT mode for patients with HCC according to local conditions was worthy of consideration by hepatobiliary surgeons in primary hospitals.

Received: 10 June 2020  
Revised: 15 July 2020  
Accepted: 4 August 2020

**Key words:** COVID-19; primary hospital; hepatocellular carcinoma; multi-disciplinary treatment

In December 2019, COVID-19, a novel coronavirus pneumonia, broke out in Wuhan, China<sup>[1]</sup>. The epidemic spread across the country with unprecedented momentum, with various places launching a level I response to major public health emergencies and traffic being restricted, which caused challenges for primary hospitals. HCC is a common malignant tumor in the Chinese population. Due to the high degree of malignancy and rapid progression, most patients with HCC are already in the mid-late stages when diagnosed and prognosis is poor. In recent years, the rapid development of biomedicine, imaging medicine, interventional medicine, and surgical technology, has promoted the birth of new model treatment for HCC, multi-disciplinary treatment (MDT)<sup>[2]</sup>.

During the level I response to major public health emergencies, most patients with HCC were only able to attend primary hospitals, while the MDT model for HCC in provincial hospitals was restricted. In addition, HCC patients were susceptible to COVID-19 due to their low immunity. Therefore, it was a huge task for clinicians in

primary hospitals to ensure the MDT mode was given to HCC patients during this level I response to major public health emergencies. The formulation of a reasonable MDT mode for patients with HCC according to local conditions was worthy of consideration by hepatobiliary surgeons in primary hospitals.

## Particularity of patients with HCC during the COVID-19 epidemic

Patients with HCC are susceptible to COVID-19 due to their low immunity. It was shown that a history of cancer was the highest risk factor for COVID-19, resulting in a patient's condition deteriorating more quickly once infected by COVID-19<sup>[3]</sup>. Moreover, patients who have recently received chemotherapy or surgery have a higher risk of serious illness than those who have not received treatment. Patients with cancer will consume more nutrients than the healthy population due to the coexistence of tumor cells and the ability to fight pathogens

is relatively weak. Moreover, the immune function of these patients has been in a state of immunodeficiency for a long period of time due to surgery, chemotherapy, biological agents, immunosuppressive therapy, and so on, meaning the defense ability against pathogens has been significantly reduced. In addition, most patients with HCC have a background of viral hepatitis and cirrhosis, and therefore the outcome may be worse than the general population once infected by COVID-19 [4]. Hence, it is very important to strengthen personal protection.

### MDT model for HCC in primary hospitals of China during the COVID-19 epidemic

It is feasible to wait for a short period of time for patients with HCC in very early stage of the disease, then surgical resection (SR) or radiofrequency ablation (RFA) can be performed after the epidemic situation is stable. As HCC presents as asymptomatic with a single lesion less than 2 cm in diameter, without vascular invasion and distant metastasis [5], the efficacy of treatment will not be effected by a short postponement.

The early stage of HCC refers to a single cancer nodule with a diameter less than 5 cm or no more than 3 cancer nodules each with a diameter less than 3 cm [6]. For patients with early HCC (Child-Pugh A or B) and good hepatic reserve function, the choice of treatment depends on the degree of liver dysfunction, portal hypertension, as well as the systemic state of the patient. RFA should be considered for the patients with tumors smaller than 3 cm as the overall survival (OS) and cancer-specific survival (CSS) have been reported to be similar between patients receiving RFA and SR [7]. RFA also has a lower incidence of complications and requires a shorter hospital stay, which is a good option during the epidemic period. For patients with a single tumor lesion and no portal hypertension, SR should be considered after excluding COVID-19. One randomized clinical trial comparing RFA and SR for early-stage HCC showed that RFA is not superior to hepatic resection in terms of tumor recurrence, overall survival, and disease-free survival [6]. SR may be a superior treatment option with better long-term outcomes compared to RFA in patients with tumors measuring 3.1–5 cm [7]. The protection of patients during the perioperative period is very important. RFA can be selected for patients with tumors which cannot be resected.

Patients with compensated liver cirrhosis, no tumor symptoms, no vascular infiltration, but a single large lesion or multiple lesions are considered to have middle-stage HCC. Transcatheter arterial chemoembolization (TACE) is a good choice for these individuals [8]. TACE is one of the most safe, effective, and commonly used interventional

therapies at present and is widely recommended by domestic and foreign guidelines for the treatment of HCC [9]. Compared to conservative treatment, the 2-year survival rate with TACE can be increased by 20% to 25%. Furthermore, it is also suitable for the epidemic situation due to the advantages of reduced trauma, quick recovery, and the convenient and short operation time. In addition, TACE should be combined with molecular-targeted agents and PD-1/PD-L1 in the early phases of disease, which can result in improved survival benefits for patients [10].

Patients with mild tumor-related symptoms, vascular invasion, or extrahepatic tumor metastasis are considered to be in the late stage of disease and are no longer suitable for more aggressive treatments. In recent years, studies have found that hepatic artery infusion chemotherapy (HAIC) for the treatment of advanced liver cancer shows great advantages [11]. HAIC not only has an improved objective remission rate and longer survival benefits, but can also significantly reduce the size of the tumor and reduce the stage of disease, providing a new option for the treatment of advanced HCC [12]. In addition, the approval of molecular-targeted agents and PD-1/PD-L1 has brought new hope to these patients [10].

End-stage HCC is often accompanied by liver failure, vascular invasion, extrahepatic tumor spread, and so on. The 1-year survival rate is less than 10% and they are unable to benefit from the above treatment [13]. For patients with ruptured liver cancer, emergency SR, RFA, and TACE can be used when required, and the secondary protection from COVID-19 must be done well.

The conventional MDT mode for HCC has been greatly affected during the epidemic period, and primary hospitals should play a practical role in the whole process of diagnosis and treatment of HCC. Primary hospitals are duty-bound not only to do a safe job in the prevention and control of COVID-19, but also to give effective MDT treatment to patients with HCC.

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**DOI 10.1007/s10330-020-0436-6**

**Cite this article as:** Wu Q, Wen SQ. Multi-disciplinary treatment for hepatocellular carcinoma in primary hospitals in China during the COVID-19 epidemic. *Oncol Transl Med*, 2020, 6: 233–235.