

Minshan Chen: combination of TACE and RFA can improve the treatment of HCC

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Transcatheter arterial chemoembolization (TACE) is the most widely used therapy for mid-stage hepatocellular carcinoma (HCC), while radiofrequency ablation (RFA) is commonly used as a therapy for early-stage HCC. This study combines RFA with TACE for the treatment of HCC. So where did this idea come from? Is there any plan for a follow-up research?

RFA is a relatively fast-developing treatment for HCC in recent years, currently considered as the third major therapy for HCC following surgery and interventional treatment. It is minimally invasive, easy to operate, and can be used repeatedly. Several studies have demonstrated that it has similar curative effect for early HCC with surgical resection, and it is generally considered as a major alternative treatment for nonresectable small HCC. However, now some studies show RFA can be used as a first-line treatment for resectable small HCC.

TACE is now regarded as the main therapy for advanced HCC and several studies have demonstrated TACE can improve therapeutic effect in patients with advanced HCC. But this does not mean that TACE cannot be used to treat small HCC. Although surgical resection and RFA have much better efficacy than TACE alone for small HCC, this study is a combination therapy rather than a single therapy. The combination therapy can detect and treat some small lesions that were not found before, thus benefiting the implementation of subsequent RFA. The design of this study is based on the limitations of both TACE and RFA because neither of them can result in adequate control of medium or large HCC.

The combination of TACE with RFA is considered as the most complementary treatment. It is now the research

focus at home and abroad for three reasons: first, to perform TACE before RFA can decrease blood flow to the liver tumor, enlarging the ablation range, as there is less heat loss in the process of subsequent RFA; second, the heat generated during radiofrequency ablation can exert the effect of chemotherapeutic agents injected during TACE; third, performing TACE before RFA can detect and control possible microsatellitic lesions around the liver tumor, thereby improving the efficacy of treatment.

Our previous retrospective study showed that performing TACE before RFA is superior to RFA alone in regard to the treatment effect, and several retrospective studies reached the same conclusion. We intend to further study the therapeutic effect of the combination of TACE-RFA with molecular targeting agents in hopes of finding more suitable therapeutic regimens for HCC and further improve the therapeutic effect for HCC.

The participants of this study were selected out of 2,256 patients with HCC, so what are the entry criteria and how were the criteria made?

We set strict entry criteria: aged 18 to 75 years; a solitary HCC ≤ 7.0 cm in diameter, or multiple (three or fewer) HCC lesions, each ≤ 3.0 cm in diameter; no hepatic venous and portal vein tumor thrombus or extrahepatic metastases; with safe puncture pathway; an Eastern Cooperative Oncology Group (ECOG) performance status of 0; no previous treatment; and Child-Pugh class A or B. We also developed exclusion criteria: severe coagulation disorders; evidence of refractory hepatic ascites, hepatic encephalopathy, or esophageal or gastric venous bleeding; and history of allergic reactions to standard chemotherapy

drugs in TACE. The criteria were based on our study of previous literature and domestic treatment of HCC, similar to most of the current research standards, but a bit more advanced.

The paper mentions that this is a single-center and non-double blind study. What is the clinical significance of the study results? What are the specific guiding functions for clinicians?

It is significant in two aspects: on one hand, it provides a new effective treatment combination for HCC; before adopting radiofrequency or other ablations (such as microwave coagulation) in future clinical treatment, if the tumor is large (HCC ≥ 7.0 cm in diameter) or there are multiple tumors, TACE can be used before RFA so as to increase the efficacy. On the other hand, the study also provides clinical evidence that TACE can improve the efficacy of locoregional therapy in HCC by altering the tumor microenvironment and blocking tumor capillaries. Of course, it will be more convincing and have stronger evidence in evidence-based medicine if it is a multi-center study conclusion.

Until now, there has been no universally accepted standard for treatment of HCC. In your opinion, what is the main reason behind this?

This problem does exist. Now there is no universally accepted standard for treatment of HCC at home and abroad, including protocols for the treatment of HCC of Barcelona Clinic Liver Cancer (BCLC), Japan, Italy, and China. The main reason is that the pathobiology of hepatocellular carcinoma (over 95% of the general called primary hepatic cancers are hepatocellular carcinomas, HCC) is rather special, unlike other tumors.

The specificity of HCC expresses in the following three aspects: first, most patients suffer from chronic hepatitis,

cirrhosis, and ultimately HCC caused by hepatitis viruses, so there will be “three diseases in one person”, which means that each patients with HCC gets three kinds of hepatic disease of chronic hepatitis, cirrhosis, and HCC, greatly increasing the difficulty of treatment. Second, there are many more factors affect HCC prognosis than that of any other tumors, including the size, number and location of the tumor; venous cancerous embolus, lymph nodes, and distant metastasis; combined hepatitis, liver cirrhosis; hepatitis virus quantity and activity, etc. Therefore, clinical staging of HCC has not been unified internationally over the years. At present the criteria of international clinical stagings commonly used are those of Union for International Cancer Control (UICC), Barcelona Clinic Liver Cancer (BCLC), Japan, Italy, and Hong Kong. Third, the treatment for HCC is different from that of other tumors whose three main treatments depend on surgery, radiotherapy, chemotherapy, while for HCC they are surgery, intervention (TACE) and ablation therapy (giving prior to radiofrequency). Radiotherapy and chemotherapy are not the common and effective treatment for HCC.

Due to the specificity of HCC mentioned above, especially the dispute in clinical staging, it is difficult to develop universally accepted treatment standard for HCC. Taking the entry criteria of this study as an example, we cannot adopt a certain clinical staging standard of HCC to selected patients, but only design entry criteria on the basis of actual clinical situation and the commonly used standards instead of writing “IIa” or “IIb” alone. Of course, it is generally approved by famous foreign journals as long as the entry criteria are reasonable designed.

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