

Point-by-Point Response:

Reviewer 1:

Thank you very much for your support and advices, I have revised the content according to your opinion, the details are as follow:

1.It appears to me that the authors sometimes change between patients with HCC metastases with and without Liver transplantation. This needs to be clarified in the text. For example the citation of Hiraki et al.. Here it is not clear of what kind of patient we are dealing with (transplanted or not transplanted).

Response:

The manuscript has been revised according to your correction. Thank you.

“It has been demonstrated to be a safe and valuable treatment option and is accepted as the best therapeutic choice for patients with unresectable pulmonary metastases after LT for HCC, RF ablation therapy improves survival in patients with limited lung metastatic disease^[29]. Lencioni et al reported that radiofrequency ablation yields high proportions of sustained complete responses in properly selected patients with pulmonary malignancies, and was associated with acceptable morbidity^[30]. Hiraki et al found that radiofrequency (RF) ablation for 83 pulmonary metastases resulting from HCC was effective and safe in selected patients, the effectiveness rate was 92% and survival rate was improved significantly^[31].” has been revised to “RFA has been demonstrated to be a safe and valuable treatment option and is accepted as the best therapeutic choice for patients with unresectable HCC pulmonary metastases. Lencioni et al reported that RFA results in a high proportion of sustained complete responses in properly selected patients with pulmonary malignancies, and is associated with acceptable morbidity^[37]. Hiraki et al found that RFA for 83 pulmonary metastases resulting from HCC was effective and safe in selected patients, where the effectiveness rate was 92% and survival rate was significantly improved^[38]. Therefore, RFA improves survival in patients with limited metastatic lung disease^[39].”

2. Please change “mole cular” to molecular in the chapter “targeted drugs”.

Response:

The manuscript has been revised according to your correction. Thank you.

Reviewer 2:

Thank you very much for your support and advices, I have revised the content according to your opinion, the details are as follow:

- 1. Any discussion of post transplantation HCC recurrence is incomplete without a detailed analysis of immunosuppression.**

Response:

The contents has been added:

Immunosuppression

More and more studies have confirmed that immunosuppressants (e.g. mammalian target of rapamycin inhibitors, m-TORi) have anti-transplant rejection and multiple anti-tumor effects after LT for HCC^[28,29]. Kawahara et al found that m-TORi can decrease the risk of recurrence after LT for HCC and have lower drug toxicities^[30]. Cholongitas et al also showed that patients on m-TORi had significantly lower recurrence rates following LT for HCC, thus m-TORi may represent an alternative immunosuppressive regimen with antineoplastic effects^[31]. Moreover, the early use of m-TORi can significantly prolong survival time and delay tumor progression after LT^[32]. Klintmalm et al indicated that m-TORi may have benefits in the oncology setting and in relation to HCV-related allograft fibrosis, metabolic syndrome, neurotoxicity, and survival time^[33]. However, clinical studies have demonstrated that immunosuppressive agents can cause serious adverse reactions in patients such as pneumonia and thrombocytopenia^[34]. In patients with pulmonary metastases after LT for HCC, most were in poor physical condition and were unable to tolerate further treatment. Therefore, further research on reducing the side effects of m-TORi and controlling further progression with combination therapy for pulmonary metastases after LT for HCC, will have significant clinical value.

- 2. Any discussion of post transplantation HCC recurrence is incomplete without a detailed analysis of the characteristics of the primary tumor.**

Response:

The contents has been added:

However, due to extrahepatic organ micrometastases, which cannot be found by

imaging and cancer cells present in the blood circulation before LT, the characteristics of liver cancer (microvascular invasion, low differentiation, allelic imbalance, genetic diversity), the stage (super Milan criteria) and the administration of immunosuppressive agents during and after LT^[4].

3.The references should be cited according to the instructions to the authors.

Response:

The references has been revised according to your correction. Thank you.