

## Peer Review File

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### Reviewer A

This article collected clinicopathological data of HCC patients who received 2 surgery procedures and observed the effects of Huaier granule on liver inflammation, liver fibrosis, postoperative recurrence. The results showed that Huaier granule may reduce post-operative relapse by inhibiting liver inflammation and fibrosis. Therefore, this Chinese medicine is beneficial to HCC patients, and this conclusion was verified from clinical work. We thank all the authors for their efforts. However, this article also needs to be further modified in the following aspects.

1. You divided HCC patients into two groups based on whether Huaier granules were taken. So, would patients in group A be willing to take the drug? Were patients in Group B given a placebo after surgery?

Reply 1: We collected clinicopathological data through a retrospective study, so patients according to taking/not taking Huaier granule after the first hepatectomy were divided into Group A and B.

2. Please explain whether blind method was used in this research. Was there a lost follow-up?

Reply 2: We collected clinicopathological data through a retrospective study, so this research was not used blind method.

3. In line 208, the legends of the picture are not appropriate. “A and B are the liver inflammation grades in the distant cancer tissue of the first and the second operations of case 1, showing improvement in liver inflammation in this patient (G2 becomes G1)”. You could modify this sentence into “Figure A and B showed the liver inflammation grades in the .....” And there are similar problems in your paper, please revise them.

Reply 3: we have modified our text as advised (see Page 10-11, line 205 208 211 220 221 223 225 226)

4. In the section of introduction, Paragraph 2, you mentioned that “Hepatic resection, ablation, and liver transplantation are the main curative treatment options for patients with HCC”. In addition to these methods you mentioned, chemotherapy is also a powerful tool for HCC treatment. Please add these references into your essay.

Chinese expert consensus on conversion therapy for hepatocellular carcinoma (2021 edition) (doi: 10.21037/hbsn-21-328)

Downstaging and resection of hepatocellular carcinoma in patients with extrahepatic metastases after stereotactic therapy. (doi: 10.21037/hbsn-21-188)

Reply 4: we have modified our text as advised (see Page 5, line 98-99)

## Reviewer B

1. Please provide the full names of “BCLC” “SD” “HE” in the main text. Please also check through your article to make sure **all** the abbreviated terms have been defined when they **FIRST** appear in the Abstract and the main text.

Reply: we have modified our text as advised.

2. Please recheck the full name of “HBV-DNA load”, “GS”.

liver function, alpha-fetoprotein (AFP), hepatitis B virus deoxyribonucleic acid (HBV-DNA load), tumor size, tumor number, BCLC stage, recurrence interval, independently reassessed by two pathologists. Gleason grade (GS grade) was

Reply: we have modified our text as advised (see Page 9, line 192,195-196).

3. Please check if any reference should be added since you mention “studies”.

“Many **studies** has shown that it can promote tumor cell apoptosis, regulate body immunity, reverse drug resistance, and inhibit angiogenesis, etc(24).”

“Basic experimental **studies** have also shown that Huaier granule have the effect of improving liver cirrhosis(16).”

Reply: we have modified our text as advised (see Page 13, line 285; Page 14,289).

4. Figures and Tables

- **All abbreviations** in figures/tables and legends should be explained. “HBV” “HCC” “TACE” in Figure 1, and “GS” “SD” in Table 3 for example. Please check all abbreviations and provide the full names in the corresponding figure legend/table foot.
- Please provide an **editable** version of Figure 1 as a stand-alone **WORD/PPT** file, so that the editor can slightly and properly adjust the lines and structures, and text during the editing.
- The scale bar is not clear in Figures 2-3. Please provide Figures 2-3 in higher resolution.
- Please revise “p-value” to “P value” in Table 1-3.
- There is no “IQR” in Table 1, 2, while it is explained in Table 1, 2 footnote.
- Please revise “HBVDNA” to “HBV-DNA” in Table 1, 2.
- Please recheck the data in Table 1, whether it should be “88.2%” “11.8%” “84.3%” respectively after rounding.

Tumor number		
Solitary	92 (86.0%)	45 (88.3%)
Multiple	15 (14.0%)	6 (11.7%)

**BCLC stage**

0/A 88 (82.2%) 43 (84.4%)

- Please recheck the data in Table 3.

Unchanged 63 (58.9%) 31 (60.7%)

**Liver cirrhosis**

Improved 22 (20.5%) 17 (33.4%) 5 (8.9%)  
Unchanged 77 (72.0%) 32 (62.7%) 45 (80.4%)  
Deteriorated 18 (16.8%) 2 (3.9%) 6 (10.7%)

Reply: we have modified our text as advised.