

We have revised the manuscript according to the comments of reviewers. We believe this would satisfy the reviewers' comments. We look forward to your favorable consideration.

Answer the following:

Comments of Reviewer 1

Gastric cancer is one of the common leading cancers in the world, especially in China. Helicobacter pylori infection, an important factor associated with the occurrence and development of gastric cancer. The mechanism of H.pylori infection in the invasion and metastasis of GC is still unknown. The authors studied 99 patients with gastric cancer. They found that H. pylori infection is not only the primary factor involved in gastric cancer but is also involved in proliferation, invasion and metastasis of gastric cancer by upregulating HPA expression, which is likely mediated via activation of the MAPK signalling pathway. Preoperative H.pylori infection affects the prognosis of patients. All postoperative cases were followed up for 3 - 60 months in this study. What is the status of H.pylori infection of the patients after operation? Whether it can improve the prognosis of postoperative patients with H.pylori infection by eradication treatment?

Thank you for your comments.

The objective of this study was to observe the relationship and mechanism between H.pylori infection and heparanase in patients with gastric cancer, therefore, the study of H.pylori radical cure was not involved. Moreover, during the follow-up, only telephone follow-up was conducted to see whether the patient was recurrence or death, and the detection of H.pylori was not performed. While it was suggested that positive cases of H.pylori infection in postoperative recovery of gastric cancer should administrate a radical cure of H.pylori after discharge, patient compliance were so poor that most patients were no treatment, 10 patients made triple therapy (but no testing for eradication, 1 case recurred, 4 cases died), 6 patients made triple therapy (C13 breathing test is negative, no recurrence, 1 case died) in the

process of follow-up. Although there were a lot of above indefinite factors, it seemed to reduce mortality after giving eradication treatment. Obviously, it need large samples and control studies to be verified in the future.

Comments of Reviewer 2

This is an interesting study to demonstrate H. pylori may promote the proliferation, invasion and metastasis of GC by increasing HPA expression that may associate with MAPK activation, And this study also show that the HPA was association with the survival time of patients, Thanks for submitting it. After carefully reviewing your paper this reviewer has some comments regarding your paper. Please note below;

- 1. Our previous studies have shown the heparanase expression via the PI3K/Akt/NF- κ B signaling pathway for gastric cancer metastasis, whether H. pylori increased HPA expression also associate with via the PI3K/Akt/NF- κ B signaling pathway.**
- 2. The grammar needs further retouching**
- 3. The artical show H. pylori infection and positive expression of HPA were both associated with lymph node metastasis and invasion in vivo experiment. So I suggest the invasion and metastasis of cell in vitro experiment should be added.**

Thank you for your comments. 1. This is a good idea, so the next step of our study could be specifically designed to verify whether H. pylori increased HPA expression is related to the PI3K/ Akt/ NF- κ B signaling pathway. 2. The grammar is modified accordingly. 3. Invasion and metastasis have been done in vitro experiments, and have been added in the paper (figure 2G-J).