

World journal of Hepatology revise

We appreciate the reviewers' suggestions and comments. We believe that they have helped us greatly improve our manuscript.

Reviewer #1:

Comments to the Author

The authors have conducted an interesting study to compare the invasiveness of the open and laparoscopic liver resection. I have following comments regarding the manuscript:

1. Why TSP-1 was considered as a measure of invasiveness. The authors should provide appropriate reasons in the Introduction or Discussion along with references as they have done for IL-6.

We agree with this comment. However, we already mentioned it in the Introduction. Kuroki and colleagues reported the relationship between TSP-1 and the magnitude of the invasiveness using mouse models and 30 patients who performed partial liver resection.

2. Please mention whether there is any biological process to explain the inverse correlation between IL-6 and TSP-1.

Our study can't reveal the relationship between IL--6 and TSP-1. Furthermore, there are no reports about any biological process between two factors. We added the following sentences to the Discussion section (Page 19, Lines 14 to 16).

“Secondly, this study can't reveal the biological process to explain the relationship between IL-6 and TSP-1. There are no reports on it, and this is a future issue.”

3. The sample size of the study is very small. Please check with the statistician whether it is meaningful to perform multivariate analysis for such small sample size.

As reviewer mentioned, We are aware that this is a preliminary study with a small number of cases. However, the number of factors used in the multivariate analysis is only two, which we believe is not statistically problematic in our study with a total of 30 cases.

4. The incidence of complications in this study was high. Please provide the details about the major and minor complications in both the groups and compare them.

I'm sorry. I had mistaken it. Yes and No were listed in reverse order. I fixed it. The actual incidence of complications in this study was not high with 3 cases (bile leakage, refractory ascites, and surgical site infection). We added the following sentences to the Result section (Page 12, Lines 3 to 5).

“The postoperative complications included one case of bile leakage, one case of refractory ascites, and one case of surgical site infection.”

5. Please discuss whether major complications affected the postoperative IL-6 and TSP-1 levels.

Thank you for your valuable comment. Although complications was included in the univariate analysis of factors that related with higher level of IL-6 on POD1 and lower level of TSP-1 on POD3, complication was not identified.

We added the following sentences to the Discussion section (Page 19, Lines 7 to Lines 10).

“Complication was not observed in the univariate analysis of the factors that related with higher level of IL-6 on POD1 in 30 patients who has undergone hepatectomy. In present study, complications were not affected higher level of IL-6 on POD1.”

We added the following sentences to the Discussion section (Page 19, Lines 4 to Lines 6).

“Complication was not observed in the univariate analysis of the factors that related with lower level of TSP-1 on POD3. In present study, complications were not affected lower level of TSP-1 on POD3.”

6. CRP is also an useful marker of invasiveness. I believe that CRP along with IL-6 and TSP-1 should be included in this study as a marker of invasiveness.

Thank you for your valuable comment. We also believe that CRP is one of the reasons why laparoscopic surgery is minimally invasive. CRP is synthesized in the liver by stimulation of IL-6, since CRP is likely to be affected by liver function, IL-6 may be more appropriate than CRP in assessing the degree of invasiveness of hepatic resection.

7. Why TSP-1 on POD3 and not POD5 was used for univariate and multivariate analysis in Table 5.

We sincerely appreciate the reviewer's beneficial comment. Kuroki et al. reported perioperative changes on plasma TSP-1 levels in 30 patients who underwent partial liver resection. In that report, plasma TSP-1 levels was measured up to POD7, with improvement to baseline at POD3, and no significant change in TSP-1 after POD5. That's why we used TSP-1 levels up to POD3 in present study. We added the following sentences to the Methods section (Page 8, Lines 11 to Lines 13).

“Blood samples taken up to POD3 were used because previous studies had not found significant changes in TSP-1 levels after POD5.”