**Peer Review File**

**Reviewer A**

This study demonstrates the usefulness of the E-PASS system in evaluating the prognosis after hepatectomy. Studies on the evaluation of the postoperative prognosis of the E-PASS system and CRS have been widely reported in gastrointestinal surgery, spinal surgery, and other orthopedics surgeries. This study reports on the role and usefulness of CRS in liver resection in patients with primary liver cancer.

It is a well-known fact that factors such as old age and underlying diseases affect the prognosis and complications after surgery.

In every research about the E-pass system for predicting prognosis after surgery, a poor prognosis with high CRS is a predictable outcome.

It is expected that there are more surgical factors that can be considered additionally in liver resection, and I think that it would have been a better study if other factors were added to the CRS of the existing E-PASS system to show the results. From the point of view of an HBP surgeon, it could not show the results of a study on a score appropriate for liver surgery. Although there are no new findings and the results are not different from expected, we believe that this paper will be meaningful in that there are not many studies on the usefulness of CRS for liver cancer or hepatectomy patients in existing studies.

A few additional things I want to mention

**Comment1:** Table 1 I think it would be better to show a demographic finding of CRS low/high rather than a comparison with or without complications.
**Reply1:** Thanks for bringing this to our attention. We made a new table to show characteristics between CRS high and low group (according our cut-off value 0.126), and we found that most of the factors that differ are those contained in the E-PASS system. So, we wonder if we can add this new table (as Table 3 in revised manuscript) without deleting our Table 1.
**Changes in the text:** We added a Table 3 in our revised manuscript (Page27) and some content in the results (Page11, Line1-8).

**Table3**: Characteristics between low CRS group and high CRS group

| Characteristic | CRS<0.126(N=153) | CRS≥0.126(N=83) | P |
|---|---|---|---|
| Age | 57.3±10.8 | 64.2±10.1 | <0.001 |
| Gender(male/female) | 129/24 | 70/13 | 0.096 |

| | | | |
|---|---|---|---|
| Weight(kg) | 65.1±10.4 | 63.4±10.5 | 0.259 |
| BMI (kg/m$^2$) | 23.2±3.0 | 23±3.1 | 0.590 |
| Hypertension(with) | 47(30.7%) | 36(43.4%) | 0.052 |
| Diabetes mellitus (with) | 18(11.8%) | 21(25.3%) | 0.008 |
| Hemoglobin(g/L) | 142.6±15.5 | 134.6±17.8 | <0.001 |
| Lymphocyte count(×10^9/L) | 1.5±0.7 | 1.4±0.6 | 0.103 |
| Neutrophils count(×10^9/L) | 3.3±1.3 | 3.3±1.5 | 0.891 |
| Platelet(×10^9/L) | 148.3±55.7 | 145.0±67.2 | 0.701 |
| Albumin(g/L) | 41.0±4.8 | 39.3±4.7 | 0.009 |
| Total bilirubin(μmol/L) | 16.7±7.4 | 16.2±7.9 | 0.634 |
| PT | 13.8±1.0 | 13.8±0.9 | 0.604 |
| ALBI | −2.7±0.4 | −2.6±0.4 | 0.014 |
| PNI | 48.7±6.4 | 46.3±6.0 | 0.004 |
| CRP (mg/L) | 1.2(0.1-46.6) | 2.2(0.1-86.2) | <0.001 |
| AFP (ng/mL) | 27.5(1.0-114971.0) | 16.2(1.2-251299.0) | 0.581 |
| HBV surface antigen(with) | 127(83.0%) | 59(71.1%) | 0.032 |
| Cirrhosis(with) | 107(69.9%) | 54(65.1%) | 0.443 |
| Child-Pugh grade A | 148(96.7%) | 78(94%) | 0.328 |
| Maximum tumor diameter(cm) | 3.2(0.7-15) | 5.4(1.0-15.5) | <0.001 |
| PRS | 0.289(0.144-0.670) | 0.454(0.216-1.224) | <0.001 |
| Performance Status (0 or 1) | 151(98.7%) | 59(71.1%) | <0.001 |
| ASA (1or 2) | 150(98.0%) | 70(84.3%) | <0.001 |
| SSS | −0.182(−0.297-0.292) | 0.204(−0.267-1.118) | <0.001 |
| Estimated blood loss(ml) | 200(30-1500) | 500(50-4000) | <0.001 |
| Operation time(min) | 180(60-400) | 250(100-650) | <0.001 |
| Laparoscopy | 145(94.8%) | 31(37.3%) | <0.001 |
| CRS | −0.154(−0.421-0.124) | 0.301(0.129-1.159) | <0.001 |
| BCLC (0/A/B/C) | 38/89/18/8 | 12/54/10/7 | 0.258 |
| TNM (I/II/III) | 124/17/12 | 62/6/15 | 0.049 |

**Comment2:** Table 2 does not seem to have much meaning.
**Reply2:** Thank you for your helpful advice. We agree it and deleted our Table2 in previous manuscript.
**Changes in the text:** We deleted our table2 in previous manuscript.

**Comment3:** Does table 3 also apply to all complications? I think it would be better to

describe it like table 5. The description of other factors is lacking.

**Reply3:** We apologize for our unclear representation. By referring to our Table1, we selected several variables that differ between the complication group and non-complication group for multivariate logistic regression analysis. Although there were several variables with statistical differences, considering that some of that were parameters of the E-PASS system, we finally selected CRS, Maximum tumor diameter and total bilirubin in revised-manuscript Table2. In revised-manuscript Table 4, we also detailed postoperative complications of these patients. However, because it was a retrospective study with a limited sample size, some complications were not recorded, which is the limitation of our research.

Changes in the text: none

**Comment4:** Table 5: Is there any reason to show HCC recurrence? It is thought that tumor-specific factors such as size, number, and vascular invasion mainly influence the oncologic outcome, but it is questionable whether CRS has any significance. If the author wants to show HCC recurrence, it would be good to do subgroup analysis in patients with similar stages.

**Reply4:** Thank you for your question. We agree that tumor-specific factors can influence the oncologic outcome. We can only show survival analysis result, but cannot give convincing reasons to explain it currently. At the time we hypothesized that the CRS might be indirectly altered by the size of the tumor, but the statistical analysis did not show difference. Perhaps changing the cut-off value of the CRS could make a difference. This is the weakness of our study. According to your advice, we select patients in TNM I for further analysis, but the result was similar. Thanks again for your suggestion.

Changes in the text: We updated our Figure2(added figure2C and 2D) and we described it in results (Page11, Line12-15).
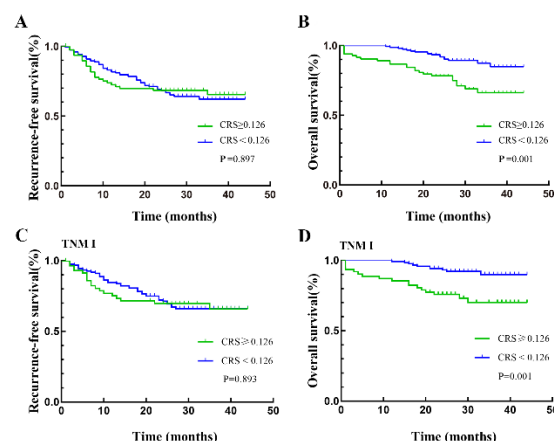


**Comment5:** Why did you add meta-analysis? What is the key you want to talk about in this thesis? Is it "the postop outcome is not good in High CRS"? It is not a new finding at all. Nevertheless, a sufficient explanation is needed to explain why this paper is more valuable than the existing papers.

**Reply 5:** We appreciate your suggestion. We agree that the meta-analysis is odd. Meanwhile, we revised our introduction to describe the highlights of this study. Changes in the text: We removed all content about meta-analysis in our manuscript. There are a few relevant studies on the predictive power of E-PASS system for HCC patients after hepatectomy, and we also think our research included a considerable number of cases.

I think the emphasis of the article with physiological ability is interesting - and I think it is something we will see more of in the literature. There are however several major concerns with article.

**Comment1:** Introduction:
The introduction is way too long, and there is lack of focus. No red thread can be followed. Part of the problems are grammatical, and that the language is not of sufficient standard. There are several sentences, which don't add any explanation, such as "The treatment for HCC patients depends on the disease staging, expected benefits of interventions and patients' physical characteristics especially the liver function". A much better take would be a short description of how patient's diagnosis is determined (often with imaging). That the treatment follows an algorithm, which places surgery first, provided that there is no cirrhosis, etc.. Other sentences, which lack linguistic rigour, and are very difficult to understand are: "It's extremely matters to evaluate the patient's physiological condition comprehensively before surgery to obtain a better prognosis and maintain a higherquality of life." "Therefore, the purpose of this research was to verify whether the E-PASS system can predict occurrence of postoperative complication and is related with long-term prognosis in HCC patients. We also compared with previous similar studies by meta-analysis to verify the worthy of E-PASS system".
**Reply1:** We regret the poor writing in the introduction of our original manuscript. Therefore, we have carefully revised and simplified the content of this part. Thanks again for your advice. If the manuscript needs further revision, we will send it to be polished.
Changes in the text: We revised our Introduction. We changed our added some content and deleted inappropriate content. (Page4, Line4-6); (Page4, Line13-15); (Page4, Line18-Page5, Line2); (Page5, Line7-14) and (Page5, Line16-19)

**Comment2:**
Method:
Is not sufficiently described. How was the multivariable (!) (not multivariate) analysis performed. Entry and exit criteria? Do the authors suggest that a change in bilirubin (within normal level, 19 vs 15) increase the risk of a complication? This is highly unlikely. When I read the article I fail to see follow the argument along the way, and

the inclusion of a meta-analysis appears a bit odd. Why not focus on what your main findings are? There is no information about the patients that were excluded. This is paramount to include.

**Reply2:** We are guilty of the confusion caused by our vague expression. We added entry and exit criteria, described more detail information and corrected inappropriate expressions in our method. As for bilirubin change, we only considered statistical differences and did not correlate it with the clinical situation. It was our negligence indeed. Furthermore, we appreciate your helpful suggestion about meta-analysis, we deleted all this content.

Changes in the text: We added inclusion and exclusion in method(Page6, Line3-11).We also removed all content about meta-analysis in our manuscript.