ROUND 1

Dear Reviewers,

Many thanks for your critical comments and thoughtful suggestions. We have carefully evaluated the critiques and recommendations and revised the manuscript again. And the manuscript was also revised substantially and edited for proper English language using the Premium Editing service from MedE Editing Service. Our point-by-point response to your comments is attached below. We hope that you will be pleased with this version. Thank you.

Yours sincerely,

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Reviewers 1:

1. Page 6 line 88: The two clinic cohorts included were: Some data is missing please add more details about the cohorts that have been included.

RESPONSE: We sincerely appreciate these valuable suggestions. The missing part of details of the cohorts was added in our revised manuscript. The revised version was "The study was based on data from two cohorts of ICC patients who underwent curative resections from August 2012 to October 2019. The two clinic cohorts included were: The First Affiliated Hospital of Wenzhou Medical University, China, and Qilu Hospital of Shandong University, China." Please find changes in Page 6 the second paragrap line 2-4 in our revised manuscript.

2. Page 10 line 158-159 How did you calculate the best cut-off value?

RESPONSE: We sincerely appreciate this thoughtful recommendation. The optimal sex-specific cut-off value of DROSD was selected by the *survminer* package in R software. We had added it in ***Statistical analysis*** of the method part in the revised manuscript. Please find changes in Page 8 the third paragrap line 10-11 in our revised manuscript.

3. Figure 4, 5 and 6 Please replace the figures. It is not clear enough and it is hard to read it.

RESPONSE: Thank you for your kind suggestion. We should have provide figures with enough quality for readers, we have replaced the Figure 4, 5 and 6 in our resubmission. Please find high quality version of Figure 4, 5 and 6 in our revised version.

4. How did you measure portal hypertension? Was this based on HVPG?

RESPONSE: Thank you very much for this helpful recommendation. Though the gold standard for portal hypertension diagnosis is based on HVPG, HVPG was not measured in this study for the reason that HVPG was rarely measured preoperatively in cancer patients. The diagnosis of portal hypertension in this article is based on preoperative CT imaging features of splenomegaly, gastric fundus varices, preoperative blood routine features of thrombocytopenia, intraoperative ascites and varicose vessels.

5. According to table 1 – 24 patients had Child-Pugh B but only 4 patients had Portal Hypertension. How is it possible to have a decompensated liver cirrhosis (here Child B) and no portal hypetension? In the same table it is mentioned that 32 patients had liver cirrhosisbut 143 had Child Pugh A cirrhosis. How is it possible to have only 4 patients with portal hyperthenison out of 143. Please explain how many had portal hypertension. All the results must be rechecked keeping in mind the above mentioned details. I would expect to see different spleen density in patients with cirrhosis compared to those without. At least these are my taughts. How could it be possible to have similar spleen density in patients with portal hypertension compared to those without? Please explain.

RESPONSE: We sincerely appreciate this thoughtful recommendation. To answer this question, we check our data thoroughly. For 167 patients selected from 2 centres, 8 out of 32 patients with hepatocirrhosis were evaluated as Child-Pugh B and the other as Child-Pugh A. In other 135 patients without hepatocirrhosis, there are also 16 patients evaluated as Child-Pugh B (Table 1). It is noteworthy that the diagnosis of hepatocirrhosis was based on pathology and histology on para-cancerous tissues.

Therefore, some mild hepatocirrhosis with histological confirmation was diagnosed as hepatocirrhosis as well even they were without clinical manifestations. 4 out of 8 hepatocirrhosis patients with Child-Pugh B classification were with portal hypertension. However, the other 4 patients were not marked as portal hypertension because they showed no sign of portal hypertension such as thrombocytopenia, a manifestation of splenomegaly and ascites on CT images.

Secondly, as we briefly mentioned above, hepatocirrhosis was diagnosed based on histology feature. Further, early-stage hepatocirrhosis may not influence the portal venous system so that the density of the spleen may not change in this way. Based on this theory, it is simply that no significant difference was found between hepatocirrhosis and DROSD in our data. And it may worth further exploration. Thank you for your advice.

Thirdly, we measured the spleen density of the patients with portal hypertension again. And the results were still similar to the data in the table. However, the data volume was not large enough since only 4 cases in our data had portal hypertension. Thus, from a statistical point of view, in this case, patients with portal hypertension have the same splenic density as patients without portal hypertension. We have doubts about this conclusion as well, and we believe that patients with portal hypertension should have a higher spleen density than patients without portal hypertension, but the statistic showed in that way. Thank you again for your advice, which points out the direction for my further research. Many patients with liver cancer are complicated with cirrhosis portal hypertension. Therefore, we are going to conduct a study on the correlation between spleen density in patients with and without portal hypertension in liver cancer.

Table 1

Live Cirrhosis	n (%)	Portal Hypertension, n	Child-Pugh grde, n(%)
Yes	32(19.2)	4	A 24 (75.0) B 8 (25.0)
No	135(80.8)	0	A 119 (88.1) B 16 (11.9)

ROUND 2

Reviewers 2:

In table 1 that you have attached to the document " Point to point response" Child-Pugh B - 8 patients and 16 patients. In total 24 patients. Once again - Child-Pugh B means -clinically significant portal hypertension for certain HVPG (even though it was not measured) is higher than 10 mmHg. You had 24 patients with portal hypertension. Now I think the data volume might be large enough. Meaning you have to do the maths once again. But this time consider that 24 patients have portal hypertension and not 4!!!!!! How is it possible to do not have cirrhosis but to have a Child-Pugh class? Child-Pugh class is used only for patients with cirrhosis.

RESPONSE: We sincerely appreciate these valuable suggestions and your rigorous review of our manuscript. In our study, we use Child-Pugh class to evaluate all surgical patients to reflect the liver function reserve of these surgical patients. we did not comprehensively consider that the Child-Pugh class is used only for patients with cirrhosis, thus, the data showed in Table 1 which Child-Pugh class was used to reflect the evaluation of liver function reserve of all patients is not rigorous. Therefore, we carefully reviewed the relevant data and consulted relevant information again and remanded Table 1 in our manuscript, and the Child-Pugh class indicator was removed for the reason above.

The number of patients with portal hypertension should be 11, including 4 cases in the DROSD group and 7 cases in the non-DROSD group. Comparison between the two groups showed no difference (see Table 1). We believed that the data amount was still small, and some results might be obtained after increasing the data amount. However, the relationship between portal hypertension and spleen density was not reflected in our cohort. This is also one of the limitations of our study. After data correction, relevant statistical analysis was conducted again, and it was found that portal hypertension was not a factor influencing patients' OS and RFS. Fig. 4 and Fig. 5 were revised again. As for the question that 24 patients with portal hypertension in our cohort you pointed out, our reexamined data showed Child-Pugh B-16 patients were patients without cirrhosis, which we have indicated in our last reply. Out of the 167 patients in this cohort, only 32 had cirrhosis, with 8 columns of Child-Pugh grade B in liver function. The modification in the revised manuscript are highlighted. We are sorry that we gave you incorrect information and the inconvenience caused to you in reviewing the manuscript. Finally, thank you again for your

valuable advice on our paper.