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Dear Prof. Shui Qiu

Thank you for reviewing our article for publication. The responses to the comments of the reviewers are as follows.

Reviewer No. 51373:

Table 1 and 2 should be consider putting it together as well as a comparison with the regeneration difference between the right and left hepatectomy.

Response: Thank you for your advice. We putted Table 1 and 2 together to show the regeneration difference between the right and left hepatectomy.

Reviewer No. 2451447:

The authors reported that impaired liver function attenuates liver regeneration and hypertrophy after portal vein embolization.

Comments: 1. The main topic of this paper is impaired liver function. I believe the authors used ICG-R15 to indicate liver function. But the authors did not give any explanation of ICG-R15 in the text, and even not mentioned in the methods of the abstract and main text.

Response: Thank you for your advice. We clarified this point on the Page 7, Line 13-19: “For the measurement of ICG-R15, Indocyanine green (Diagnogreen, Daiichi-Sankyo, Tokyo, Japan) was administered at dose of 0.5 mg/kg by the antecubital vein of the opposite arm. Then, venous peripheral blood samples were collected every 5 minutes for 15 minutes to measure the ICG absorbance. ICG-K and ICG-R15 were calculated by fitting the serum disappearance curve by a single-exponential decay equation.”

2. How ICG-R15 represents liver function? why chose R15 (min) instead of other time points (10min, or 30min)? please explain?

Response: Thank you for your comment. The ICG retention rate at 15min has been used to evaluate preoperative liver function in Japan since the 1980s, and considered as routine guidelines for several Asian countries (Hepatology Research 2009;39:107-116). In addition, not the exact value at 15 min but the disappearance curve at 5, 10, and 15 min is measured as previously described (response to comment 1).

3. Is there any relationship between the ICG-R15 function test and liver enzyme changes (liver injury), such as ALT, AST or AKP? though the authors mentioned bilirubin, etc.

Response: Thank you for your important comment. ICG is secreted uncharged into the bile, therefore ICG-R15 is correlated with bilirubin, but not with ALT, AST or AKP. Since liver resection is limited to patients with normal serum bilirubin level, ICG-R15 is considered to be an independent method to

evaluate bile secretion function of the liver.

4. The authors mentioned the background liver disease in this paper, any of the resected liver with cirrhosis or fibrosis (stage)? Any difference between ICG-R15 test and fibrosis stage?

Response: Thank you for your important comment. There was only one patient with fibrosis, and the ICG-R15 is 12.5%. It is difficult to evaluate the relationship between ICG-R15 and fibrosis.

5. How the authors make sure the readers without the confusion of "liver function" in this paper and general meaning of "liver function" in other literature indicating liver enzymes, INR and platelet numbers?

Response: Thank you for your important comment. We clarified the parameters used for liver function evaluation on the Page 7, Line 10-13: "Preoperative patient characteristics and laboratory data, including platelet count, total bilirubin, and indocyanine green retention rate at 15 min (ICG-R15), were analyzed to identify factors affecting postoperative liver regeneration."

Reviewer No. 187828:

The manuscript entitled "Impaired liver function attenuates liver regeneration and hypertrophy after portal vein embolization" by Yumiko Kageyama et al., is an interesting one. The authors, using 63 patients who underwent major hepatectomy and 13 patients who underwent portal vein embolization, calculated regeneration rate correlated with the remnant liver volume. In conclusion, they found that the

regeneration rate after right hepatectomy and the hypertrophic rate after PVE were attenuated in the presence of impaired liver function. It is a well-written and presented manuscript.

Response: Thank you for your kind comment.

Reviewer No. 1560464:

1) The clinical retrospective study demonstrated that the liver regeneration rate was significantly lower in patients with an ICG-R15 of $\geq 20\%$ in the right hepatectomy group, but not in the left hepatectomy group. The hypertrophic rate after PVE positively correlated with the regeneration rate after hepatectomy. The hypertrophic rate after PVE was significantly lower in patients with an ICG-R15 of $\geq 20\%$ and a serum total bilirubin of ≥ 1.5 mg/dl. 2) The study is very important guidance for selecting the appropriate treatment and extent of resection for liver cancer. 2) I suggest that the study can be published in the form of retrospective study in World J Hepatology.

Response: Thank you for your kind comment.

I hope that you will find our revised manuscript suitable for publication in the *World Journal of Hepatology*. I look forward to hearing from you at your earliest convenience.

Sincerely,

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