

Response to the Editor

Please find enclosed our revised manuscript entitled “Hepatectomy for gallbladder-cancer with unclassified anomaly of right-sided ligamentum teres: Case report”. We greatly appreciate the positive feedback and thoughtful comments from the editorial board and the reviewers of *World Journal of Hepatology*. We have addressed the comments provided by the editor and reviewers. The modified sentences were written in blue text and our revised manuscript was re-checked by American Journal Expert. We hope that the manuscript is acceptable for publication by the *World Journal of Hepatology* editorial board.

Response to Reviewer 1:

We thank the Reviewer 1 for the suggestions and comments, which we address as follows:

1- The reviewer wonders about why we performed an ERCP.

ERCP was performed for four reasons: (1) evaluation of horizontal invasion of the bile duct, (2) placement of an ENBD (endoscopic nasobiliary drainage) tube in the right hepatic duct to prevent obstructive cholangitis, (3) cytological examination of bile obtained from an ERGBD (endoscopic retrograde gallbladder drainage) tube, and (4) execution of “all-in-one” simulation using ENBD tube cholangiography.

Reviewer 3 also asked similar questions about ERCP and cytology, so we have added detailed explanations in the revised manuscript. (Page 6)

2- The reviewer suggests showing clearer portion of segment 5 in liver simulation.

We thank the reviewer for the suggestion regarding simulation. We have modified Figure 3 to clearly show the demarcation line between segments 4 and 5.

3- The reviewer suggests that discussion is too long.

We shortened the discussion section.

4- The reviewer suggests providing a systematic review of cases with RSLT and major hepatectomy.

We agree with your suggestion. However, Ome et al. already conducted a systematic review of hepatectomy in RSLT cases in *World Journal of Hepatology* (Ome Y, Kawamoto K, Park TB, Ito T. Major hepatectomy using the glissonean approach in cases of right umbilical portion. *World J Hepatol* 2016; 8: 1535-1540 [PMID: PMC5143435 DOI: 10.4254/wjh.v8.i34.1535]). The efficacy of preoperative liver simulation was the focus in this manuscript, and it was addressed in the discussion.

5- The reviewer suggests that some references are very old.

Although some references are very old, all the references, including Couinaud’s classification (1957) and Child-Pugh classification (1973), are very important for describing our points and are therefore indispensable in our manuscript.

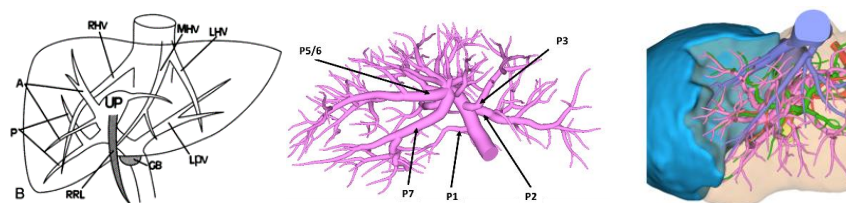
Response to Reviewer 2:

We thank Reviewer 2 for the important comments, which we address point by point as follows:

1- The reviewer wonders if this case looks like a typical “bifurcation type” of RSLT.

We recognize that the ramification pattern of the portal vein was clearly different from the bifurcation type, which Nagai et al. demonstrated. First, no conception of the left portal vein (LPV) trunk and the right portal vein (RPV) trunk was observed in our case. All segmental branches independently ramified from the main portal trunk. Second, in the bifurcation type, P4 runs from the right paramedian branch to the left paramedian area beyond the middle hepatic vein (MHV). However, our case showed that P4 was ramified from the main portal trunk and did not run beyond the MHV.

We show the ramification pattern of the bifurcation type* (left figure), the portal ramification pattern of our case (middle figure), and 3D simulation (right figure). The manuscript was corrected in accordance with this concept. (Page 9)



* Nagai M, Kubota K, Kawasaki S, Takayama T, Bandai Y, Makuuchi M. Are left-sided gallbladders really located on the left side? Ann Surg 1997; 225: 274-280 [PMID: 9060583]

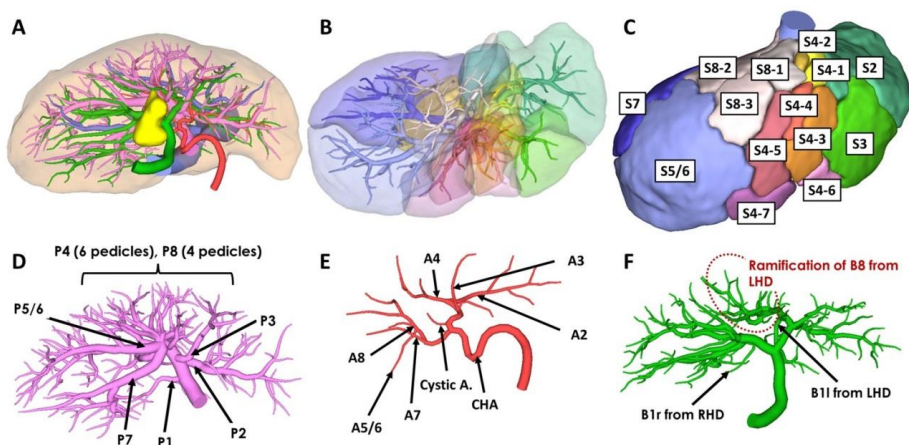
2- The reviewer points out that naming of vascular structure seems inadequate.

3- The reviewer wonders about the umbilical portion of our case.

4- The reviewer wonders if a common trunk of segment 5 and 6 branches cannot happen embryologically.

We thank Reviewer 2 for the important comments about liver anatomy. First, simulation was performed based on 2D-CT images and was verified by 4 liver surgeons independently. We also verified the vascular structure during laparotomy by observation, ultrasonography, and the demarcation line after clamping each vascular pedicle. Therefore, the simulation revealed the true structure. Of course, we named each portal branch based on its correlation to the hepatic veins using Couinaud's definition. For an easier understanding, we have added and changed two images (B & C) in Figure 2, with coloring of each subsegment.

批注 [SE1]: Please update the page numbers/line numbers in this manuscript after our edits and suggestions have been considered.



Yellow: Segment 1 (S1), Deep green: S2, Light green: S3, Pink: S4, Light blue: S5/6, Deep blue: S7, White: S8

Second, as the reviewer pointed out, our case had an unknown vessel structure as reported. Usually, the umbilical portion is located in the right medial portal vein and the ligamentum teres runs between S5 and S6 in RSLT patients. However, in our case, the ligamentum teres originated from the main portal trunk and ran between S4-6 and S4-7, as shown in Figure 2. This structure was confirmed clearly in Figure 7. We have added this explanation to Figure 7.



Figure 7 Final view after hepaticojunostomy.

As Reviewer 2 pointed out, a common trunk of the branches of segments 5 and 6 cannot manifest embryologically. We strongly agree with this comment. During the operation, however, a common trunk of P5/6 was observed and the ischemic region of S5/6 was confirmed by clamping one targeted portal vein (Figure 6). We have emphasized this anomaly in Figures 2 and 6.

Response to Reviewer 3:

We thank Reviewer 3 for the valuable comments that we address point by point as follows:

1- The reviewer wonders if operative procedures should be more summarized.

The operative procedure was further summarized as suggested.

2- The reviewer suggests discussing the necessity of major hepatectomy in this patient.

We recognized that the gallbladder cancer penetrated the serosa and was suspected to invade the

right hepatic duct. No apparent lymphoid swelling or distant metastasis was observed. For T3 advanced gallbladder cancer, extended resection should be performed as reported in ref. 9. The patients had no other significant diseases except for cancer and had good exercise tolerance. Therefore, we decided to perform extended hepatectomy including the right hepatic duct dominant area. We have described the patient's surgical eligibility in the revised manuscript. (Page 5)

3- The reviewer suggests providing preoperative assessment of T-stage.

The preoperative stage was cStage III A (T3; right bile duct, N0, M0). We added this information in the revised manuscript.

4- The reviewer suggests providing results of preoperative cytology and pathological pictures of resected specimens.

We thank the reviewer for the suggestion regarding pathological findings. The process of preoperative diagnosis and planning of the surgical strategy are described in more detail in the revised manuscript. In brief, CT scanning demonstrated a severely atrophying gallbladder with tumor-like localized wall thickness enhanced by contrast medium, strongly suggesting the possibility of gallbladder cancer. ERGBD was performed for cytological examination of bile in the gallbladder, not in the bile duct, and adenocarcinoma was detected twice (Figure 1F). To prevent obstructive jaundice and to evaluate horizontal extension of the tumor along the bile duct, ERGBD was switched to ENBD one week later. Two ENBD tubes were placed both in the right and the left hepatic ducts. ENBD tube cholangiography demonstrated a severe stenotic change of the right hepatic duct, and based on these findings, the patient was diagnosed with advanced gallbladder cancer with direct infiltration of the right hepatic duct. We finally determined that right-sided major hepatectomy with resection of the right hepatic duct drainage territory was required.

Pathological examinations demonstrated well-differentiated tubular adenocarcinoma of the gallbladder with direct invasion of the liver parenchyma and extrahepatic bile ducts, including the right hepatic duct. Gross and histological images were added to the revised manuscript (Figure 8). We have included detailed explanations in the revised manuscript. (Pages 5-6 and 8)

Response to Reviewers 4 & 5

We thank the reviewers for the positive comments. No suggestions were provided for our manuscript.