

Dear Editors and Peer-reviewers:

We are truly grateful to your thoughtful suggestions and three reviewers' comments. Those comments are all valuable and very helpful for revising and improving our paper. Based on Editors and Peer-Reviewers' comments and advises, we have made careful modifications on the original manuscript. In addition, below you will find our point-by-point responses to the comments/ questions: Each of the points raised by the peer-reviewers has been revised as follows:

Replies to peer-reviewer (code: 03023594)

COMMENTS : Major concern: 1.The selection whether a patient will underwent ENBD or ERBD is not randomly, therefore, to calculate the significance between two group with respect to their demography and clinical characteristics did not stand on a solid base. 2.As the mean length of biliary stricture in the ENBD group was significantly shorter than that in ERBD group, I did not agree that EBD method and length of biliary stricture are independent risk factors for development of deep abdominal infection after PD. The authors should re-analyze and re-interpret the results. Minor concern: EBD is performed prior to PD. However, I saw in several paragraphs, there are descriptions; such as following PD or after PD, seemed to be illogical.

Response: We express our gratitude for your careful review and comments.

Major concern1: In this paper, we had retrospectively reviewed 178 patients with malignant distal biliary obstruction who had

undergone EBD prior to PD in the First Affiliated Hospital of Nanchang University from January 2009 to July 2016 . Due to the retrospective study, there were indeed some drawbacks, such as Non - randomness and research bias.

Thank for your suggestions, we re-design the study to minimize research bias and eliminate differences in baseline parameters between two groups; we perform the 2:1 ratio matching design, the ENBD group is still 102 patients as control group, According to patient demographic and clinical characteristics in ENBD group, 51 of the 76 patients who had undergone ERBD prior to PD are matched in ERBD group. Finally, the total 153 patients are included in re-designed study (in revised manuscript page 6, third passage).

Major concern2: In this paper, we analyzed the difference of clinical characteristics and the postoperative complications of PD between the two groups, The data showed that the mean length of biliary stricture in the ENBD group was shorter than that in the ERBD group (1.55 ± 0.84 and 1.90 ± 0.99 , $P=0.012$) and the incidence of deep abdominal infection after PD was significantly lower in the ENBD group than in the ERBD group (24.5% vs 39.5%, $P=0.033$). Furthermore, we performed univariate and multivariate logistics analyses with odds ratios (ORs) and 95% confidence intervals (95% CIs) to identify the risk factors for deep abdominal infection after PD,

there showed that Male gender (OR=2.76; 95% CI, 1.30-5.83; P=0.008), soft pancreas texture (OR=3.02; 95% CI, 1.45-6.27; P=0.003), length of biliary stricture (≥ 1.5 cm) (OR=3.46; 95% CI, 1.64-7.32; P=0.001) and ERBD method (OR=2.07; 95% CI, 1.00-4.28; P=0.049) were independent risk factors for deep abdominal infection after PD.

Special thanks to you for your good comments, we re-analyze our data and have found that our center more preferred to perform ERBD for the patients with severe biliary stricture or long length of biliary stricture, this preference accounts for the mean length of biliary stricture in the ENBD group was shorter than that in the ERBD group and cause the research bias.

Via matching, we eliminate the difference in the mean length of biliary stricture between the two groups (1.55 ± 0.84 and 1.58 ± 0.83 , P=0.849) (in revised manuscript table 1). The specific method is as follows: Firstly, we evaluated the patient distribution ratio of different length of the biliary stricture (≥ 1.5 or < 1.5 cm) in ENBD group, then we match the patients in ERBD group according to the patient distribution ratio in ENBD group.

After eliminated differences in baseline parameters between two groups, we furtherly analyzed the difference in the postoperative complications of PD, the re-designed study still shows that the incidence of deep abdominal infection after PD was significantly lower in the ENBD group than in the ERBD group

(24.5% vs 43.1%, $P=0.019$) (in revised manuscript table 3). Furthermore, we performed univariate and multivariate logistics analyses with odds ratios (ORs) and 95% confidence intervals (95% CIs) to identify the risk factors for deep abdominal infection after PD. The data still show that gender (male), length of biliary stricture (≥ 1.5 cm), pancreas texture (soft) and ERBD method were significant factors and found that the diameter of pancreatic duct (≤ 3 mm) was also a significant factor. Then, the independent risk factors of deep abdominal infection were identified by multivariate logistic regression analysis. Male gender (OR=3.92; 95% CI, 1.63-9.47; $P=0.002$), soft pancreas texture (OR=3.60; 95% CI, 1.37-9.49; $P=0.009$), length of biliary stricture (≥ 1.5 cm) (OR=5.20; 95% CI, 2.23-12.16; $P=0.000$) and ERBD method (OR=4.08; 95% CI, 1.69-9.87; $P=0.002$) were independent risk factors for deep abdominal infection after PD (in revised manuscript table 4).

After matching design to eliminated differences in baseline parameters, our data still suggest that ERBD method and length of biliary stricture are independent risk factors for the deep abdominal infection after PD. We all agree with the retrospective study may not be fully convincing and it need a prospective randomized trial to identify ERBD method and length of biliary stricture as risk factors for infectious complications after PD (in revised manuscript page 14); We intend to perform a prospective randomized trial to study

the efficacy of preoperative endoscopic biliary drainage for the malignant distal biliary obstruction prior to pancreaticoduodenectomy and we trustly hope that you can give some proposals for us.

Minor concern: The language errors had been modified.

Lastly, we appreciate your warm work earnestly again and hope the modifications and interpretation will meet with your approval.

Replies to peer-reviewer (code: 03026750)

COMMENTS: Good work and well written manuscript

Response: We are very grateful to you for your careful review and high evaluation. The minor language errors have been modified.

Replies to peer-reviewer (code: 02537509)

COMMENTS: This study is well written and worthy of publication in the World Journal of Gastroenterology. Some drawbacks: Retrospective and non-randomized design. However, your publication may be useful.

Response: We are very grateful to your kind advices and high evaluation.

The drawbacks you have pointed out will improve our understanding of the clinical research .

Best regards,

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