

November 13, 2020

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Company Editor-in-Chief

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Dear Sir,

We would like to thank you and the reviewers of *World Journal of Gastroenterology* for taking the time to review our article. We have made some corrections and clarifications in the manuscript after going over the reviewers' comments. The changes are summarized below:

Responses to reviewers' comments

Reviewer #1:

Comment 1: This is an interesting study looking at the value of post-operative nutritional support in patients with extrahepatic cholangiocarcinoma and malignant obstructive jaundice undergoing radical resection in a prospective, randomised study design. Patients are randomised into a control arm with post-op TPN versus a treatment arm on early enteral nutrition and augmented parenteral nutrition. Whilst the authors mention this is a single-blind study as treating doctors will be aware of which arm is chosen, the patients would be aware too as there is an element of enteral feeding via NJ tube in one but not the other, unless the control group also had NJ tubes placed which was not mentioned in the manuscript.

Our response: Thanks for the comment. The two groups both had NJ tubes placed. The included patients had no knowledge of the treatment allocation, but the treating physicians had knowledge of it, this study is considered a single-blind clinical trial.

Comment 2: The inclusion and exclusion criteria is clear and appropriate. There was no mention of pre-operative nutritional support given nor the timing to surgery from presentation. The inclusion criteria mentioned a need to have a drop in bilirubin before surgery but it was not mentioned

how this was done e.g. ERCP or PTCD, and for what duration prior to surgery.

Our response: Thanks for the comment. Preoperative parenteral nutrition was given according to the patient's nutritional status. Patients with preoperative total bilirubin greater than 200 $\mu\text{mol/L}$ were treated with preoperative biliary drainage therapy, such as percutaneous transhepatic cholangial drainage (PTCD) or endoscopic nasobiliary drainage (ENBD). The bilirubin of patients with cholangiocarcinoma dropped to around 200 $\mu\text{mol/L}$, and patients with Child-Pugh liver function was class A or B, so surgical treatment can be considered.

Comment 3: The study size is 56 over 3 years with 26 in the treatment and 30 in the control group. There is no mention on statistical calculation before the study on the adequacy of power of this sample size.

Our response: Thanks for the comment. The standard deviation of IgA in the literature was 0.5 ($\sigma=0.5$), and the mean value was 2.2g/L ($\mu_0=2.2$ g/l). It was estimated that the mean level of IgA (μ_1) in the experimental group was 0.4g/L higher than that of the control group ($\delta = 0.4\text{g/l}$). Generally, $\alpha=0.05$ and Z value was two-sided, then $Z_\alpha=1.96$. When β was unilateral, the test efficiency was $1-\beta=0.9$, then $Z_\beta=1.28$, the sample size of the experimental group is N_1 , and the sample size of the control group is N_0 . The formula: $N_1=N_0=[(Z_\alpha+Z_\beta)*\sigma/\delta]^2*2=[(1.96+1.28)*0.5/0.4]^2*2=33$, $N=N_1+N_0=66$. Finally, a total of 66 samples were collected.

Comment 4: There was also no information on the 2 that dropped out from the treatment arm to explain the reasons for the dropout and if this was indeed due to issues arising from early enteral feeding.

Our response: Thanks for the comment. There were 2 patients who dropped out for adverse reactions of early enteral feeding, as shown in **Figure 1**.

Comment 5: There seems to be a higher proportion of pancreaticoduode

nectomy in the control arm although not statistically significant but this might account for differences in the two groups based on severity/magnitude of the procedure with resultant higher stressors to the patient. Otherwise the data from the CD studies are interesting. There is a need for major language polishing.

Our response: Thanks for the comment. We have neglected the psychological impact of high proportion of pancreaticoduodenectomy in the control arm on patients. That's an interesting question, then it will be discussed in the discussion section.

Reviewer #2:

Comment 1: Thank you for giving opportunity to me to review this article. Authors compared the nutrition methods in the patients who underwent operation for cholangiocarcinoma. Study points out the importance of the early enteral nutrition on the recovery status of the patients. It should be considered for publication in your journal as it is. Thank you.

Our response: Thanks for reviewers' comments. Your encouragement is the biggest motivation for us to move forward.

Science editor:

- This is an interesting study looking at the value of post-operative nutritional support in patients with extrahepatic cholangiocarcinoma and malignant obstructive jaundice undergoing radical resection in a prospective, randomized study design. There was no mention of pre-operative nutritional support given nor the timing to surgery from presentation. The inclusion criteria mentioned a need to have a drop in bilirubin before surgery but it was not mentioned how this was done.

Our response: Thanks for the comment. Preoperative parenteral nutrition was given according to the patient's nutritional status. Patients with preoperative total bilirubin greater than 200 $\mu\text{mol/L}$ were treated with preoperative biliary drainage therapy, such as percutaneous transhepatic cholangial drainage (PTCD) or endoscopic nasobiliary drainage (ENBD). The bilirubin of patients with cholangiocarcinoma dropped to around 200 $\mu\text{mol/L}$, and patients with Child-Pugh liver function was class A or B, so surgical treatment can be considered.

- The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement.

Our response: As the editor pointed out, we have uploaded the PDF version of the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement.

- (1) I found the language classification was grade C. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Our response: As the editor recommended, we have made major language polishing at the professional English language editing companies again.

- (2) I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s)

Our response: As the editor pointed out, we have uploaded the PDF version of the approved grant application forms and funding agency copy of any approval documents.

- (3) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Our response: As the editor pointed out, we provided the decomposable figure of all the figures and submit as "59038-Figures.ppt" on the system.

We hope the revised manuscript will better meet the requirements of your journal for publication. We thank the editor and the reviewers of *World Journal of Gastroenterology* once again for the constructive review of our paper.

Sincerely yours,

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