

Point-by-point Responses

January, 2022

Dear Editor and Reviewers,

We would like to thank the editor and reviewers for a careful and thorough reading of this manuscript and for the complimentary comments and beneficial suggestions, which helped to improve the value of our manuscript. Each comment has been carefully considered point-by-point and responded. As suggested by the reviewer, this manuscript has been revised by a native English speaker Professor David Y Graham, Baylor College of Medicine, Houston, Texas for language polishing. We hope that you find our responses satisfactory and that the manuscript is now on par with the standard of your prestigious journal. We have also added one additional author Ji-Yu Zhang for his significant contribution in revising, editing, and rearranging the manuscript.

The followings are our point-by-point responses:

All the changes in revised manuscript are shown in **Red**.

REVIEWERS' COMMENTS TO THE AUTHOR:

Reviewer: 1

Comment 1: Interesting topic, experimentation is always welcome, as long as patients are well informed, and it seems that the authors have done so. The manuscript is fluid, well-structured and easy to read. The variables chosen for comparison are acceptable. The figures and tables are of good quality. Most of the references are dated, but there are some quite recent. The supplementary material and the video are of good quality. In my opinion the manuscript can be accepted for publication

Reply: We appreciate the positive feedback from the reviewer. The language edits have been and references have been updated as well in the revised version.

Reviewer: 2

Comments to the Author:

Comment 1:

I reviewed a retrospective study which compared the NOTES with laparoscopic cholecystectomy. The authors matched 95 patients from each group. The study seems very appealing. The title and introduction have been well chosen. I have some comments regarding the methods. The authors found out a high risk of biliary peritonitis in NOTES group (12 patients from 95). Therefore, they change the protocol of NOTES using abdominal irrigation. In my opinion they have 2 options: either they exclude the first 12 patients and included in the study only 82 patients or they assume a high rate of severe complications as biliary peritonitis in NOTES group. If they agree the last option, they should change the results and conclusions.

Reply: Thank you for suggestions. According to your suggestions, we have excluded 9 patients and revised the results and outcomes of the study matching 86 patients pair. All the changes are highlighted in red in the revised version of the manuscript.

Once again, we thank the editors as well as the reviewers for providing very important and constructive feedback; we believe this has enhanced the quality of our work. We hope that the reviewed and refined manuscript is at par with the standards of your prestigious journal.

Sincerely,

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Review's comment

Comment: Well and clearly written paper. I have a small comment: regarding the NOTES technique, please explain how the tip of endoscop was insert in the gallbladder? And how many passes do you need to extract the stones? Please add the median time length spent per NOTES. I did not find any tables or figures attached to the main text.

Reply: Thank you for your positive feedback. A full-thickness longitudinal incision was created in the gallbladder wall using the Hook and IT knives. The tip of endoscope (with transparent cap attached) was inserted into the gallbladder cavity. As the reviewer was unable to access the video of the NOTES technique, so he got confused. We have provided the videos along with manuscript which shows every step clearly including how the tip of endoscope was inserted, after watching the videos. I hope that reviewer will be clear how exactly the procedure was performed. The videos are clear and easily understandable for endoscopist.

The passes depend on the number of stones, if there is only one stone, one pass is enough. If there are more than one stones or muddy stones, more than one passes are needed until the gallbladder cavity is cleared and later flushed with saline.

The median operative time was 119 minutes (IQRs, 95-175) in the NOTES group which was longer then the LC group median time of 60 minutes (IQRs, 48-90), (difference, 59 minutes; $p < .001$). We have added in the manuscript and highlighted in red for your convenience.

Tables and figures was supplied along with manuscript. We aren't sure why you could not access them last time. Please consult EO for this.