Author’s response to reviews

Title: Clinical efficacy of B-mode ultrasound-guided percutaneous transhepatic gallbladder drainage followed by laparoscopic cholecystectomy for acute cholecystitis in high-risk elderly patients

Authors:

Yi-Ren Hu (huyiren2014@163.com)
Jiang-Hua Pan (panjianghua2014@163.com)
Xiao-Chun Tong (tongxiaochun2014@163.com)
Ke-Qin Li (likeqin2014@163.com)
Sen-Rui Chen (chensenrui2014@126.com)
Yi Huang (huangyi1029@126.com)

Version: 6 Date: 20 April 2015

Author’s response to reviews: see over
Response to Reviewers

Dear Reviewers,

Thank you for your review of our manuscript “Clinical efficacy of B-mode ultrasound-guided percutaneous transhepatic gallbladder drainage followed by laparoscopic cholecystectomy for acute cholecystitis in high-risk elderly patients” (Manuscript ID: 8697218301542962). We appreciate the comments and suggestions provided by the reviewers and we have revised our manuscript accordingly. At this time, we have re-submitted the revised MS through the Author Center, and we hope to have an opportunity to publish this paper in “BMC Gastroenterology”.

Please find the revised MS for your approval. In addition, a revised MS with corrected sections marked in red is attached as part of the supplemental material for easier editing and review purposes.

Below, please find our point-by-point responses to the comments of reviewers.

Sincerely yours,

Responds to the reviewers’ comments:

Reviewer 1:

1. Comment: Major compulsory revisions

(1) Please have a look at the uploaded manuscript with highlighted passages which are required to be addressed by the authors adequately and appropriately revised.

Response: We are really sorry that we did not provide a clear description in our initial manuscript. Accordingly, we have revised the highlighted passages. Your suggestion has improved the manuscript. Thank you very much.
(2) Line 185: What is this injection? Why is it being used? Mention the chemical/manufacturing company name/ does it affect the patients’ blood sugar/pressure so rapidly?

Response: Thank you for pointing out the issue. We have revised this as “Patients were intramuscularly injected with Hemocoagulase 1U (Zhaoke Pharmaceutical (Hefei) Co., Ltd., China) for 2 days, each day for 8h. Hemocoagulase is a proteolytic enzyme used as a plasma clotting agent for fibrinogen and for detection of fibrinogen degradation products. Hemocoagulase is a hemostatic drug used to treat primary and secondary bleeding in postoperative period.”

(3) Line 224: The statement is not clear? What is the author trying to imply.

Response: We are sorry for not clearly describing. We revised it as “There were 3 cases of postoperative complications after PTGD surgery. Of the 3 cases, 2 cases had their ducts dislodged and one case involved bleeding.”

(4) Line 244: Mortality rates? Not mentioned.

Response: There was no death in two groups, which was described in Line 207 as “There were no deaths reported in the two groups.”

(2) Need to clarify the selection criteria, criteria for labelling a patient elderly and the process of selection of historical controls.

Response: Thanks for your comments. The inclusion/exclusion criteria are revised as “All subjects in the LC and PTGD + LC groups met the following study inclusion and exclusion criteria. Inclusion criteria: (1) elderly AC patients (> 65 years old) with cardiac, brain and lung comorbidities, and unable to tolerate surgery; (2) patients
with AC and empyema of gall-bladder, failing to respond well to non-surgical therapies; (3) severe AC patients with disease for more than 48-72 h, diameter of gallbladder enlargement 8cm, and gallbladder wall of thickening 4mm. Exclusion criteria: (1) patients with dysfunction in blood coagulation and severe bleeding tendency; (2) patients with massive ascites; (3) patients with gallbladder in free state; (4) patients’ gallbladder with clear or inappropriate puncture route; (5) patients with general peritonitis and suspected perforation of gallbladder.” which is described on Page 5. We also revised the patient information as “This study enrolled 35 elderly (all > 65 years old) and high-risk AC patients who underwent B-mode ultrasound-guided PTGD combined with LC (PTGD + LC group) at the First People’s Hospital of Wenzhou between January 2010 and April 2014. A separate group of 35 elderly and high-risk AC patients were randomly selected from a pool of 186 cases who underwent only LC (LC group) during the same period at the same hospital.” Patients with age of more than 65 years old were defined as elderly in Materials and Methods.

(3) Also need to mention how the skill levels of the operating surgeons were comparable when both the groups were taken into consideration.

Response: Thank you for your instructive comment. We revised to add information as follows “All patients enrolled in this study were informed of the benefits and risks of both interventions. All interventions were provided by an experienced medical team with more than 10 years of clinical and surgical experience. The team included surgeon, an emergency physician and a gastroenterologist”
(4) A table needs to be deleted.

**Response:** Thanks for. We deleted Table 4.

(5) Make sure that the refs are in journal style.

**Response:** Greatly appreciated your reminding. We made corresponding revision to ensure the accuracy of the references according to the specified reference style.

(6) Needs some language corrections before being published

**Response:** We apologize for all the grammatical mistakes in our article. We made corrections and checked our language and expression. The revised manuscript is accordingly much improved, and it was also polished by a native English expert specializing in this study area.

**Reviewer 2: Minor Essential Revisions**

1. **Comment:** Background-45: its a 'disease' and not a disorder

   **Response:** Thank you for the point. We revised it as “*Acute cholecystitis (AC) is an inflammatory gallbladder disease caused by the obstruction and bacterial invasion of the cystic duct, and more than 90% of AC cases are associated with cholelithiasis or gallstones*”.

2. **Comment:** Background-49: 'increased' complication rates than elevated complication rates
Response: After careful consideration, we do believe “increased” complication rates were better than elevated complication rates and we have already revised it. “*Elderly AC patients have higher postoperative mortality and morbidity rates, increased complication rates, longer length of hospital stays and longer recovery times*”.

3. Comment: PTGD treatment-107: need to reformulate entire sentence Anti-infection was carried out according to routine blood return

Response: Thanks for your kindly reminding us of professional expression. We have already reformulate the entire sentence “*Treatments for infections were given if routine blood examination supported such intervention*”.

4. Comment: PTGD treatment-107: please use correct terminology for treatment of hemorrhagic shock and avoid terms like anti-shock therapy

Response: Really appreciate your comments. We went through all related reference material about the treatment of hemorrhagic shock and deleted “anti-shock therapy”. “*the patients with hemorrhagic shock were managed by quickly controlling the source of bleeding and resuscitation (PMID: 23248499)*”.

5. Comment: Discussion-220: Fourth not Forth

Response: Thank very much. We revised it as, “*Fourth, PTGD can be employed for cholangiography, which is crucial for revealing the biliary tract anatomy and for selection of therapy options. Preoperative cholangiography, using PTGD tube, can provide a clear information on the bile duct, cystic duct and gallstone, and*”
additionally intraoperative cholangiography can greatly avoid injury”.

6. Comment: Discussion-228&229: please explain the relevance of statement which holds true for PTBD and not PTGD-However, this procedure is technical difficult when applied to patients without bile duct dilation and ..........the dilated bile ducts

Response: Much appreciate your correction. We sincerely apologize for the misunderstanding. We deleted this statement. Your comment is very constructive, thanks again.

We hope you and the reviewers will agree that we have addressed all the concerns raised by the reviewers in their previous review of the manuscript and that the incorporation of the changes based on reviewers' comments into the revised manuscript has substantially improved the manuscript. Thank you for your re-consideration of our manuscript and we are looking forward to your favorable decision.

Yours sincerely,

Professor Yi Huang

E-mail: huangyi1029@126.com