Author’s response to reviews

Title: Influence of anesthesia methods on surgical outcomes and renal function in retrograde intrarenal stone surgery: a prospective, randomized controlled study

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Author’s response to reviews:

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RE: Manuscript revision ID BANE-D-19-00396R1, “Influence of anesthesia methods on surgical outcomes and renal function in retrograde intrarenal stone surgery: a prospective, randomized controlled study”

Dear Editor,

Thank you for the comments on our manuscript. We have revised our previous paper based on the comments made by the reviewers. We hereby submit 2 copies of the revised paper. We are also sending a letter describing our replies to comments of the reviewers in a point-by-point fashion on separate sheets. We would highly appreciate it if you could review this paper again for publication in BMC Anesthesiology.

Sincerely Yours,

Sung Yong Cho, M.D., Ph.D.
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Response to Comments of the Editor

1. We submit one copy of the manuscript that is clean without any changes highlighted.

2. We ensured the following information was included on our title page:
   
a. The identifying institution for each author was listed.

   b. The status of the first author was indicated.

3. We provide a detailed letter describing the exact modifications made to the manuscript and their location within the text.

4. We added a word count of text at title page (2,978 words including 3 tables).

5. All tables and references were cited chronologically.

6. All references included both beginning and end page numbers.

Reply to comments

1. Page 6, lines 1-3: Elaborate on the measurements of the primary and secondary outcomes and how they were determined during the study.
   
   Reply: Thank you for your comment. We revised the sentence as following;

   Primary outcome is renal function change, and secondary outcome is performance of operator. And, primary outcome is renal function change assessed by estimated glomerular filtration rate and separate renal function evaluated by nuclear medicine test. And, secondary outcome is performance of operator evaluated by one experienced surgeon.

2. Page 6, lines 46-56: Mention explicitly the primary outcome and the statistical test that was used to determine the sample size. Also, mention the magnitude and the units of the effect size that was used for such determination.
   
   Reply: Thank you for constructive review.

   Primary endpoint was difference of renal function recovery rate and the difference was 6.5% from previous investigations. Predicted standard deviation was 9.0%, target power is 80%, and target significance level is 0.05. As we commented at method section, we planned study of experimental subjects with one control(s) per experimental subject. Under the above conditions,
our study needed 31 patients in each GA and SA group. Considering dropout rates about 10%, we decided to include total 70 patients (35 patients each).

We revised the paragraph as following:
We planned a study of experimental subjects with one control(s) per experimental subject. In a previous pilot study, the response within each subject group was normally distributed with standard deviation 9. If the true difference in the previous investigations between the experimental and control means is 6.5%, we will need to study 31 experimental subjects and 31 control subjects to be able to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) 0.8 (non-inferiority test). The Type I error probability associated with this test of this null hypothesis is 0.05. Considering dropout rates about 10%, we decided to include total 70 patients (35 patients each).

3. Table 2: Use the Bonferroni correction factor to determine the statistical significance for the following parameters: Visual analogue scale, Stone composition, Intraoperative events, Postoperative complications, Relative renal function data, and Postoperative 3 months. Also, change the results and the discussion and conclusion according to the new findings after using the Bonferroni correction factor. (See Reviewer #2 previous comments).

Reply: Thank you for your helpful review. However, Bonferroni correction as post hoc analysis is used to compare more than 3 groups. But this study compares parameters between 2 groups, so Bonferroni correction is inappropriate for this study. If you have give some recommendation, we, authors, would appreciate it.

4. Table 3: Patients who had spinal anesthesia with sedation cannot be presented as a separate group because they were not randomized to receive spinal with sedation, spinal without sedation, or general anesthesia. Therefore, this table has to be deleted or presented with only two groups: General anesthesia or Spinal anesthesia group as shown in table 2. The finding that sedation can improve the maneuverability and accessibility may be mentioned as an incidental finding in the results section.

Reply: Thank you for your constructive and helpful review. We reconstructed table 3 as you recommended.

5. Start the discussion section with a paragraph clearly showing a summary of the results particularly the primary outcome.

Reply: Thank you for your constructive review.

According to your comments, we reconstructed first paragraph as following:
Urologists routinely prefer GA for RIRS in patients with renal stones. Under GA, surgeons can be more comfortable due to decreased patient movement by controlling breathing [21]. Some studies reported that surgeries under regional anesthesia could show reduced major complications (for example, mortality, morbidity, and myocardial infarction) than those under GA [2-4]. The present study compared, for the first time, changes in renal function using renogram after GA with those after SA in RIRS for renal stones. Postoperative pain after GA was higher than after SA on the first postoperative morning; however, the pain scores were similar prior to discharge. There was no difference in postoperative change in serum creatinine between the GA and SA groups. However, the difference in separate renal function between the operative and contralateral sites increased significantly in patients under GA than those under SA 3 months postoperatively. This study also evaluated maneuverability and accessibility during surgery, and SA with sedation showed better maneuverability and accessibility than GA.

The present study compared, for the first time, changes in renal function using renogram after GA with those after SA in RIRS for renal stones. There was no difference in postoperative change in serum creatinine level and estimated glomerular filtration rate between the GA and SA groups. However, patients of SA group showed improvements in separate renal function recovery. The difference in separate renal function between the operative and contralateral sites increased significantly in patients under GA than those under SA 3 months postoperatively. Postoperative pain after GA was higher than after SA on the first postoperative morning; however, the pain scores were similar prior to discharge. In addition, some studies reported that surgeries under regional anesthesia could show reduced major complications (for example, mortality, morbidity, and myocardial infarction) than those under GA [2-4]. In general, urologists routinely prefer GA for RIRS in patients with renal stones. Under GA, surgeons can be more comfortable due to decreased patient movement by controlling breathing [21]. This study also evaluated maneuverability and accessibility during surgery, and SA with sedation showed better maneuverability and accessibility than GA.

6. Page 12, lines 7-10: Delete the sentence starting with ‘We believe…’..
Reply: Thank you for your kind comment. We deleted that sentence.

7. Add an appendix to the manuscript describing the equations used to determine the glomerular filtration rate.
Reply: Thank you for your constructive review. We added Appendix at the end of manuscript.

Modification of Diet in Renal Disease (MDRD) Study equation [1]
GFR - 186×(serum creatinine)-1.154×(age)-0.203×(0.742 if female)

Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine-based Equation [2] is based on the same four variables as the MDRD Study equation, but uses a 2-slope spline to model the relationship between estimated GFR and serum creatinine, and a different relationship for age, sex and race.
Reference)


We highly appreciate your invaluable comments and helpful suggestions.

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