Author’s response to reviews

Title: REDUCING KIDNEY MOTION: OPTIMIZING ANESTHESIA AND COMBINING RESPIRATORY SUPPORT FOR RETROGRADE INTRARENAL SURGERY: A PILOT STUDY

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Author’s response to reviews:

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Dear Editor,

Thank you for your expeditious and favorable review of our manuscript entitled "REDUCING KIDNEY MOTION: OPTIMIZING ANESTHESIA AND COMBINING RESPIRATORY SUPPORT FOR RETROGRADE INTRARENAL SURGERY: A PILOT STUDY". We appreciate the constructive criticism provided by the reviewers and feel the requested revisions have made the manuscript stronger. Before addressing each comment below, all of the contributing authors would like to thank the reviewers for the time, efforts and subsequent comments regarding our manuscript. Below please find our detailed response to the reviewers’ comments.
In this study, the Authors evaluated a peculiar general anesthesia protocol in order to minimize kidney movement during RIRS. The study and its results look interesting, however some major remarks need to be addressed:

Q1: “Subjective assessment via the questionnaire scale point values varied significantly before and after the application of CRS and were 2.1 2.3 2.6 and 3.7 3.8 4.0 respectively”; please simplify and make it more clinically understandable; the scale was never introduce before, therefore it is difficult to understand in the abstract

A1: We thank the reviewer for the comment. We made the changes to reflect the suggestion you made.

Q2: Spell out abbreviations (HFJV and SVMV)

A2: We thank the reviewer for the comment. We made the changes to reflect the suggestion you made.

Q3 Briefly synthetize what the new anesthesia consists of in the abstract

A3: We thank the reviewer for the comment. We made the changes to reflect the suggestion you made.

Q4 Please provide Table 1 with patients and stones characteristics, including results cited in the text

A4: We thank the reviewer for the comment. We have provided the table with patients and stone characteristics.
Q5 Please detail stone position in the kidney in table 1

A5: We thank the reviewer for the comment. Provided table 1 includes information on the stone position

Q6 Was URS possible in every case?

A6: We thank the reviewer for the comment. Yes, URS was possible in every case, and we made the change to reflect the point.

Q7 Was UAS used?

A7: We thank the reviewer for the comment. Yes, UAS was used in 2 cases and we made the change to reflect the point in the «material and methods» section

Q8 How long can this anesthesia be used safely?

A8: We thank the reviewer for the comment. The longest time under CRS in our study was 32 minutes. In patients with multiple stones who were out of the study protocol CRS lasted for 124 minutes without any negative sequelae.

Q9 Please justify statistical tests used in the methods section, clearly specifying what measures (means? Medians? Proportions?) are being compared

A9: We thank the reviewer for the comment. Modern nonparametric resampling, permutation and randomization procedures (bootstrap and Monte Carlo) as the most reliable and robust statistical procedures implemented in PAST software were used. Statistical significance of the observed effects was justified by the p-values for the paired t-test and confidence intervals (CIs) for the mean differences (effect sizes), d = Mb - Ma, where Mb and Ma are the mean values before and after the application of the CRS technique, respectively.

Mahesh R Desai, MS, FRCS, FRCS, FACS (Reviewer 2):

This article is about the feasibility of change in anesthesia parameters for reduction in motion during RIRS
Q1 Complications of anesthetic technique not assessed in detail (effect of HFJV on trachea)

A1: We thank the reviewer for the comment. We did not experience any CRS associated complications as stated in the study but knowing of possible complications of HFJV the following preventive measures were undertaken:

- the insufflation catheter was inserted through a sealed adapter into the tracheal tube thus, direct contact of the catheter with the trachea was excluded.

- the effect of high gas jet on the tracheal mucosa during HFJV with the possible development of tracheitis described in the literature is more attributed to the use of devices without gas conditioning option and the use of high pressure. We used “ZisLINEJV-100” machine with the air conditioning option and small working pressure of 0.3 – 0.6 bar. Besides heat and moisture filter was used in a sealed respiratory circuit anesthetic apparatus. In the postoperative period, there were no clinical signs of tracheal mucosa lesion. We made the change to reflect the given question in the “discussion” section.

Q2 This new method was not compared with routine ventilation in separate patients

A2: We thank the reviewer for the comment. In this pilot study we did not compare CRS technique with other methods since at first, it was more important to understand the safety of this method and get an impression of feasibility.

We are on our way of conducting such a comparative study. Results will be presented as soon as they will be ready.

Q3 the effect on duration of surgery should have been explained

A3: We thank the reviewer for the comment. The longest time under CRS in our study was 32 minutes without any complications. In patients with multiple stone who were out of the presented study protocol CRS lasted for 124 minutes without any negative sequelae. The combination of the SVMV with HFJV in closed respiratory circuit allows maintaining the necessary minute ventilation and adequate gas exchange.

Q4. The parameters assessed was only a subjective assessment scale of movements. It is inadequate

A4: We thank the reviewer for the comment. We agree on that point - our study lacks objective criteria for evaluation such as operating or fragmentation and dusting rates. However, we have
deliberately simplified our study protocol due to the fact that variables such as fragmentation and dusting rates are inherently dependent on factors such as stone size, stone density, renal anatomy, the surgeon’s expertise, where the main factor being assessed in this study was operative field stability.

Mario Sofer (Reviewer 3):

Q1: Background: delete first sentence. Correct to: "One of the greatest challenges presented with RIRS is the potential for movement of the stone within the operative field associated with diaphragm and chest respiratory excursions due to mechanical ventilation. To overcome this challenge, we propose in this pilot study a new general anesthesia technique combining HFJV with SVMV. Data regarding safety, feasibility and surgeons’ impression was assessed."

A1: We thank the reviewer for the comment. We made the changes to reflect the suggestion you made.

Q2 Methods: describe the technique, inly the name of it is mentioned!

A2: We thank the reviewer for the comment. We made the changes to reflect the suggestion you made.

Q3 Conclusions: soften the statement. "…appears to provide better and…"  

A3: We thank the reviewer for the comment. We made the changes to reflect the suggestion you made.

Q4: The content of first paragraph is routinely used in many articles. The second sentence is confusing, dealing with RIRS in regards of unfavorable factors for SWL.

I suggest beginning this section from the second paragraph deleting the first one.

- add "mechanical ventilation" when first using in the text followed by abbreviation (MV).

A4: We thank the reviewer for the comment. We made the changes to reflect the suggestion you made.
Q5: The aim of the study is to optimize RIRS. Therefore change to "...high frequency jet ventilation (HFJV) during RIRS..."

A5: We thank the reviewer for the comment. We made the changes to reflect the suggestion you made.

Q6: move to Discussion section: "Popiolek et al. was the first to present HFJV in RIRS during the 2017 World Congress of Endourology, demonstrating the true necessity of stabilization of the operative field." And correct the references list accordingly.

A6: We thank the reviewer for the comment. We made the changes to reflect the suggestion you made.

Q7. "Therefore, HFJV remains a suboptimal approach toward anesthesiology support during RIRS." This statement is an assumption of the authors without support in the literature. Fact that HFJV has clinical use. Please delete it.

A7 We thank the reviewer for the comment. We truly believe that HFJV is suboptimal for RIRS due to mentioned in the text factors but we made the changes to reflect your suggestion

Q8 Efficacy was not assessed. Please delete it.

A8. We thank the reviewer for the comment. We made the changes to reflect your suggestion

Q9 Consider re-editing the last paragraph in: In order to further improve monitoring and safety during anesthesia as well as intraoperative conditions for performing effective RIRS we propose a modified technique of GA, referred to as combined respiratory support (CRS). It implies HFJV with small volume mechanical ventilation (SVMV). We present here a pilot study to assess efficacy, safety and feasibility of CRS during RIRS.

A9. We thank the reviewer for the comment. We made the changes to reflect your suggestion

Q10 How reference 6 is related to any of the statements in the first paragraph? Please delete it from here.
A10. We thank the reviewer for the comment. Reference 6 explains what means experienced in ureteroscopic surgery although participating urologists in our study have >100 cases each.

Q11 In the background effectiveness is also mentioned as an aim of the study. Please add it as a primary outcome purpose or delete it from background section.

A11. We thank the reviewer for the comment. We made the changes to reflect your suggestion.

Q12 Since converting from MV to HFJV implies changing the connections within airways, it would be interesting to assess the anesthesiologist impression with this technique in comparison to the standard GA. Anesthesiologists are not servants but part of the team.

A12. We thank the reviewer for the comment. Combined respiratory support (CRS) was developed by anesthesiologists and urologists to reduce the respiratory mobility of kidney in order to achieve accurate, rapid and continuous lithotripsy without the risk of hypoxia and hypoventilation of the patient. Of course, CRS in comparison to MV requires some efforts from anesthesiologists but they do it once at the beginning and then every switching to CRS is made just with one button. In the process of replying to your comments, I asked our anesthesiologists of what do they think about CRS - they highly value our work.

Q13 if performing dusting we cannot talk about fragments 9. Maybe change to: …a fragment was deliberately left to be extracted for calculi composition analysis.

A13. We thank the reviewer for the comment. We made the changes to reflect your suggestion.

Q14 mention if the procedures were performed with UAS and which

A14. We thank the reviewer for the comment. We made the changes to reflect your suggestion.

Q15 delete "…and included.."

A15. We thank the reviewer for the comment. We made the changes to reflect your suggestion.

This section is really somewhat laconic, but I understand that according to the study design there is no much to add.
Q16 "…after the application of CRS (2.1 2.3 2.6 and 3.7 3.8 4.0, p<0.0001, respectively) (Table 2)." The data in the parentheses is not understandable.

A16 We thank the reviewer for the comment. We made the changes to reflect your suggestion.

Q17 Since we are anesthesiologists it is not clear to us what is the significance of changes in the ventilation monitoring between the standard and CRS methods. I'm not sure that all these data is needed at all.

A17 We thank the reviewer for the comment. Ventilation parameters were included in the article deliberately - if get published hopefully urologist will share it with anesthesiologist so they could read it together properly.

Q18 Please add stone free rates and how they were assessed.

A18 We thank the reviewer for the comment. We didn’t include stone free rates of patients since we sought only to assess the feasibility and safety of reducing respiratory kidney motion and thus providing better conditions for intracorporeal lithotripsy. But we made the changes to reflect your suggestion.

Q19 delete "due to advancements in endoscopic technology". This is not the sole reason.

A19 We thank the reviewer for the comment. We made the changes to reflect your suggestion.

Q20 All the second paragraph is a repetition from the Background section. It should be deleted either from here or from Background section!! I suggest leaving it only here and starting the Discussion section with it.

A20 We thank the reviewer for the comment. We made the changes to reflect your suggestion.

Q21 "The periodic apnea technique has been proven..." No, it was not proven! Reference 3 is only a presentation of the technique, with no comparison, no outcomes in terms of successful treatments. We just may say that it was proposed.

A21 We thank the reviewer for the comment. We made the changes to reflect your suggestion.
Q22 correct: "The technique of general anesthesia with… was previously described by Kourmpetis et al……… LV was associated with better fragmentation, removal, and processing rates but not operating rate. Although end-tidal CO2 in the LV group was 50 mmHg this finding was not associated with clinical side effects. However, this level of end-tidal CO2 is defined as mild hypercapnia and may cause possible negative health consequences.21

A22. We thank the reviewer for the comment. We made the changes to reflect your suggestion

Q23 Discuss the disadvantage of using HFJV: ex. expensive ventilation machines, demanding effort of an anesthesiologist, etc.

A23. We thank the reviewer for the comment. We made the changes to reflect your suggestion

Q24 Discuss the MOSES technology in the context of stabilizing stones during processing.

A24. We thank the reviewer for the comment. Unfortunately, we don't have experience with MOSES technology.

Q25 correct: "Our impression is that According to the urologist assessment the novel combined respiratory approach consisting of HFJV and SVMV provides better conditions for stone dusting through reduced respiratory kidney motion and is not associated with adverse health effects or complications. Further larger sample studies are needed to confirm these findings and elucidate its effect on stone free rates."

A25. We thank the reviewer for the comment. We made the changes to reflect your suggestion