Reviewer’s report

Title: Effects of Low Versus Standard Pressure Pneumoperitoneum on Renal Syndecan-1 Shedding and VEGF Receptor-2 Expression in Living-donor Nephrectomy: A Randomized Controlled Study

Version: 4 Date: 05 Dec 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses one or several testable research questions? (Brief or other article types: is there a clear objective?)

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with sufficient technical rigor to allow confidence in the results?

Yes - experiments and analyses were performed appropriately

STATISTICS - Is the use of statistics in the manuscript appropriate?

Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

Yes - the author's interpretation is reasonable

OVERALL MANUSCRIPT POTENTIAL - Has the author addressed your concerns sufficiently for you to now recommend the work as a technically sound contribution? If not, can further revisions be made to make the work technically sound?
Maybe - with major revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: The authors did a great job in adapting the paper to the reviewers' comments.

Unfortunately, I did not see the previous version of the paper being invited to review only the present one. So, I have some further comments which need to be addressed.

ADDITIONAL REQUESTS/SUGGESTIONS:

Specific comments:

Introduction: extremely well written.

Materials and methods: extremely well written.

Results - lines 298-9: i think "comparable" is not enough. I would change into "non-statistically significant differences in...".

Results: I would specify in the text if the pneumoperitoneum pressure was kept stable along the whole procedures or if temporary increase were necessary to keep up with surgical needs. Although live donor nephrectomy is not a bloody procedure, pneumoperitoneum pressure increases is common practice during specific steps of other procedures associated significant bleeding (e.g, tumor resection in minimally-invasive partial nephrectomy or DVC section and suture in minimally-invasive radical prostatectomy). Clarification is needed. The fact that the patients were randomized to pressure of 8 or 12 mmHg does not mean that that pressure was not increase due to specific reasons during the procedure due to surgical needs.

Results: intraoperative and postoperative overall and high grade complication rates should be reported somewhere in one of the table.

Results: level of precision of the results is inaccurate. Please, see https://doi.org/10.1016/j.eururo.2014.06.024.

Results: I am not familiar with the CO2 insufflator produced by Olimpus and used in the present study but the vast majority of the insufflator that I saw/used in Europe do not allow the keep the intraabdominal pressure always stable during the procedure, especially whenever suction is needed or laparoscopic instruments are inserted. To my knowledge, the only device working in a different way is the AirSeal System by Conmed. This pressure barrier insufflator works by creating and maintaining a forced gas pressure barrier in the proximal end of the trocar with a system of continuous pressure flow (inflow and outflow) to create a valveless pressure curtain rather than the standard one-way valve system. This new generation of valve-less and barrier-
free surgical trocars are typically associated with extremely stable pneumoperitoneum pressure along the procedures, despite suction and instruments insertion. Clarification is needed on this issue. The fact that the patients were randomized to pressure of 8 or 12 mmHg does not mean that that pressure was stable at that values during the procedure. It should be reported if such variations were recorded or that should be disclosed as a limitations.

Discussion: still too long and wordy. A paragraph with the study limitations should be included at the end. The authors data are very elegant but renal function at follow-up was similar in both groups. So, either all the observed differences are not clinically significant in the long term or the study is underpowered to detect such differences.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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