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: 1 Date: 08 Jan 2019

Reviewer: Anthony Bonavia

Reviewer's report:

Unfortunately, while a lot of effort has gone into this manuscript, there are some major flaws that preclude publication in my view.

1. First and foremost, the scientific premise of the study is very weak. The biomarkers that have been proposed are not standard (or widely accepted) biomarkers of renal tubular injury, and the articles referenced in support of these biomarkers have not influenced the prevailing standard of care. This reviewer is familiar with the scientific literature regarding renal biomarkers, and there is sparse data for syndecan-1 or VEGFR-2 as biomarkers of early renal injury, compared with nGAL, [IGFBP-7]xTIMP2 and others. The author's primary outcome measures for early kidney injury are therefore erroneous, and the authors cannot make any conclusions regarding the effect of pneumoperitoneum on early kidney injury based on these measures alone.

2. where is the data regarding the duration of pneumoperitoneum? duration of surgery is not the same as duration of pneumoperitoneum. If all patients having standard pressure also had pneumoperitoneum of twice the duration, then you cannot separate the effect of either variable on the outcome

3. the discussion section is far too long and circuitous, and the conclusions made are not sufficiently backed up by the data (especially given the sample size). For example (p.19): "Shear stress will stimulate the synthesis of endothelial nitric oxide, which will activate the NF-KB signaling pathway through VEGFR-2". This statement contains several hypotheses which are not backed up by data or references. The liberal use of the word "will" is unsubstantiated by data in most instances in the discussion.

4. how was the sample size calculated?

5. what about the intraoperative hemodynamics in each group? What was the mean arterial pressure in each? Were vasopressors used (if so, how much)? All these factors can affect the development of postoperative AKI

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

No
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.

No

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

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