**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:** 2  **Date:** 22 Aug 2019

**Reviewer:** Anthony Bonavia

**Reviewer's report:**

The authors are to be commended for the significant improvement in the quality and clarity of this manuscript, and for addressing many of the reviewer concerns. The grammar is significantly improved but there is still the need for additional grammatical improvement here and there.

**Major comments:**

My main issue with this manuscript is that there appear to be 2 main hypotheses. The first is that "low pressure pneumoperitoneum is superior to standard pressure pneumoperitoneum in terms of inflammatory markers syndecan-1 and VEGFR-2" and the second is that "syndecan-1 and VEGFR-2 are validated markers of renal tubular injury". While this study may validate the first hypothesis, it is insufficient to prove the second. There are still several instances in the manuscript in which the distinction between hypotheses is still unclear. For example: "This study aimed to assess the effect of low intraabdominal pressure on kidney injury prevention." While it is important to identify the renal source of the biomarkers selected in this study in order to justify their reason for looking at kidney immunohistochemistry, the two hypotheses should be kept distinct.

I am very curious as to why the authors went through the trouble to do a randomized trial, using these biomarkers as their primary outcome. Why wouldn't the authors use nGAL, TIMP-2 or other biomarkers that are more established in the literature? The supporting literature for syndecan and VEGF are so sparse.

"In our study, the heart rate in the low-pressure group trended significantly lower than the standard pressure group." - I find this difficult to understand, given that the CI and SV were unchanged. Isn't the cardiac output the product of the SV and the HR? How can the HR be significantly different if the CI and SV are unchanged?

**Minor comments:**

- "Laparoscopic nephrectomy is a preferable technique for living kidney donation." needs supporting reference
"The low-pressure group showed better morphological renal tubule and peritubular capillary ultrastructure" - what does 'better' mean? I would define with histological terms

"It is important to ensure safety and minimize surgical risk to allograft kidney function in both the kidney recipient and donor." - you can delete " to allograft kidney function" in this statement

"The kidneys are at risk of injury induced by increased IAP. A direct correlation of increased IAP secondary to pneumoperitoneum is renal venous congestion and decreased renal blood flow due to compression of the renal vasculature and renal parenchyma" - should be changed to "The kidneys are at risk of injury induced by increased IAP secondary to pneumoperitoneum-induced renal venous congestion and compression of the renal vasculature and parenchyma"

"Exclusion criteria were hemodynamic instability &gt; 25% of baseline despite intervention treatment" - what does this mean? 25% of what?

"Patients were allocated using block randomization of 4." - what does this mean? what were the 4?
"Increased intraabdominal pressure causes mechanical compression of the inferior vena cava, renal vasculature, and parenchyma." - needs reference

**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 recommend additional statistical review

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