Reviewer’s report

Title: Hypoxia preconditioning attenuates lung injury after thoracoscopic lobectomy in patients with lung cancer: a prospective randomized controlled trial

Version: 0 Date: 10 May 2019

Reviewer: Hynek Riha

Reviewer's report:

MAJOR COMMENTS

1. Major limitation of the study is the choice of primary outcome parameters. PaO2/FiO2 is a good parameter but probably more measurements (i.e., not only 30 min after the start of OLV and 7 days after the surgery, but more often; it could be extremely interesting to see the values just before and after HPC intervention). The same apply for parameters from spirometry. How were 7-days values obtained in the patients discharged before 7 days (see Table 4 for postoperative hospital stay)?

Moreover, it is strange that no difference in morbidity translated into significant difference in hospital length of stay. Furthermore, the patients were excellently fit (see spirometry values in Table 1, i.e., before the surgery), and this should be listed also as limitation of the study.

2. I would suggest to modify the title of the manuscript, e.g., HPC attenuates lung injury after …

3. P4/L2. The authors state that there is little clinical evidence regarding protective effect of HPC on lung injury - still it should be cited and discussed here, i.e., what research has been done until now with appropriate references. Moreover, the authors should explain how this limited evidence currently available influenced the design of their clinical study.

4. In Methods section, there is detailed description of anesthesia provided, followed by the description of intervention (HPC). The intervention should be certainly described with more details, e.g., how was the other lung ventilated during HPC (OLV to non-operated lung) - was the same protocol used as described in methods as general approach to all patients, or where there any differences? Precise specification of tidal volume, FiO2, PEEP, concentration of sevoflurane etc. for HPC is needed as it represents the crucial part of the study.

5. The authors stated that mechanical ventilation during the surgery was provided without PEEP - was it really the case? The duration of OLV was approx 2.5 h in both groups thus one could expect problems with desaturation (i.e., decrease in SpO2 values) during OLV in some patients. Was FiO2 1.0 only measure needed to keep the patients adequately oxygenated or other measures to improve oxygenation were used (e.g., CPAP to non-dependent lung)?

6. There is no information about extubation, duration of postoperative ventilation, early postoperative care, time in ICU/standard ward etc.

7. P10/L219: I would suggest to mention only „prevention", not „treatment" of lung unjury (as HPC is a preventive measure certainly).

MINOR COMMENTS

1. In Figure 1, 6 patients were excluded due to open thoracotomy - it was realized probably during the surgery (in inclusion criteria there was thoracoscopic procedure) thus should be moved below
randomization (?).

2. P5/L110. A little bit more detail about thoracic paravertebral block could be provided.

3. Table 1. I would suggest to divide „Smoking” to 3 categories: non-smoker, ex-smoker, current smoker.

4. Table 1. The values depicted as „Predicted FVC and FEV” should be marked as measured values expressed as % of predicted values (depending on patient's characteristics).

TECHNICAL COMMENTS

1. Table 3. The columns for Control and HPC groups should be exchanged to follow the pattern of other three tables where first column is for HPC group.

   **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?**
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