Author’s response to reviews

Title: RCT to estimate reduction in pain after laparoscopic surgery when using a combination therapy of intraperitoneal normal saline and the pulmonary recruitment maneuver.

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Author’s response to reviews:

The authors'response letter has been included as a supplementary file.

Comments from the editorial board:

1. We recommend that you ask a native English speaking colleague to help you copyedit the paper.

We appreciate your recommendation. The current version of the paper has been revised by a professional copyeditor.

Comments from reviewer #1:

1. Background section, page 5, line 89 sentence would read better as "A combination of the techniques described above has been shown to reduce.... pain"....

Thank you for this suggestion. This sentence has been changed accordingly.

2. Considering the potential impact of BMI, should randomization also be stratified by two or three BMI categories?

This is a very interesting question. See background section, page 5, lines 89-90 and method section, page 7, lines 139–143. We only stratified by hospital, not for BMI categories. This is
because we do not expect BMI to have an influence on how patients experience pain. Two systematic reviews showed no relation between BMI and post-operative pain. Some isolated studies found an association, especially with morbid obesity; however, the association did not reach statistically significant values1-2. One study found no statistically significant relationship between postoperative pain and body mass index in women with a hysterectomy and bilateral salpingo-oophorectomy3. However, the weight of patients is important to calculate the amount of normal saline for intraperitoneal use. The mean body weight in Dutch women is expected to be higher than the mean body weight in Asian women in which the combination treatment we want to study has been shown to reduce post-laparoscopic pain4. No adjustments have been made in the text.

3.Interventions section, page 8, line 162, control group: is there any time limit involved in the application of abdominal pressure (to standardize this)?

Thank you for this interesting question. There is no time limit involved in the application of abdominal pressure. The purpose is to remove as much carbon dioxide as possible with gentle abdominal pressure and passive exsufflation through the port sites with the sleeve valves open. We use a standardized method in laparoscopic surgery and this passive exsufflation at the end of the surgery is part of that standardized method. No adjustments have been made in the text.

4.Sample size section, page 8, line 176. More information re these "inputs" would be helpful. Is 48 hours the timepoint expected to show the maximum pain difference between groups?

We have adjusted this section to clarify. See sample size section, page 8, lines 176–185. Our two primary outcomes are the incidence of pain and the intensity of pain which are determined using the VAS scores. In according with Tsai et al., we measured pain intensity using the preliminary data of the 24-hour and 48-hour pain scores4. Post-laparoscopic pain is most common and evident in the first 48 hours after surgery, after that period the pain declines. That is why we have chosen to look at the 48-hour pain score.

5.Data analysis section, pages 8,9: I expected pain incidence to be evaluated by a distribution-based test such as chi-squared or similar, and pain intensity to be evaluated by a two-way repeat measures ANOVA (or similar general linear model).

Thank you for this feedback. We have discussed this issue and decided to classify patients as having pain or not having pain using the questionnaires the patients fill in after surgery. Comparing the incidence of pain between the intervention and control groups the Pearson’s Chi-squared statistic will be used. For those who do experience pain, we will compare the average pain scores between groups. We will use T-tests for pain scores that are normally distributed. We adjusted the text of the data analysis section, namely page 9, lines 193–197.

Comments from reviewer #2:

1.There are some Grammatical errors however given that the authors are not native English speakers I think they have done well.
Thank you for this suggestion. The current version of the paper has been revised by a professional copyeditor.

2. They need also to spell fully all the acronyms as they first use them.

We appreciate your comment and have now fully spelled out all acronyms.

Page 6, lines 114–115: American Society of Anesthesiologists physical status classification of I-II (ASA classification)

Page 6, line 120: nonsteroidal anti-inflammatory drugs (NSAIDs)

Page 6, line 121: chronic obstructive pulmonary disease (COPD)

Page 8, line 170: body mass index (BMI)

3. They need to mention how the randomization will take place with special reference to the stratification process as to what factors they controlled for by stratified randomization.

Thank you for your helpful critique. We have adjusted the text of the randomization section; see randomization section, page 7, line 139–143.

This study is a multicenter trial. Therefore randomization will be stratified by hospital to get an equal distribution of patients between the two groups (control group and intervention group) per hospital. For randomization we used an Excel sheet that randomly assigned 200 patients (two lists of 100 patients, one for each hospital) to either the intervention or control group.

However, after randomization we included 56 patients in the control group and 71 patients in the intervention group. The unequal randomization was caused by the use of the incorrect method, as we should have used a block randomization method. To correct the unequal distribution, we requested an amendment which was approved by the ethics committee. We wanted to include 200 women, resulting in 100 women in each arm. To reach this number of inclusions, we had to include an additional 29 women in the intervention group and an additional 44 women in the control group. See results section, page 10, lines 200–206.

4. They are using a combination of instillation of normal saline and pulmonary recruitment maneuver however in their analysis they have not specified how they will differentiate which of the two had the major effect on reducing postoperative shoulder tip pain, if it at all does. I believe that will be difficult unless they introduce two more groups that has either instillation of saline or pulmonary recruitment maneuver alone so that they can establish if the combination or any of the two procedures was more effective in reducing pain.

Thank you for your comment. Tsai et al. has shown that the combination of intraperitoneal saline and the pulmonary recruitment maneuver is the most effective method of reducing pos-laparoscopic pain4. In this study we do not aim to assess which of the two had the major effect.
The purpose of our study is to confirm the results of Tsai et al. in a Dutch population of women having gynecologic surgery.

References


