Reviewer's report

Title: BIOLAP: Biological versus synthetic mesh in laparo-endoscopic inguinal hernia repair: Study protocol for a randomized multicenter, self-controlled clinical trial

Version: 0 Date: 15 Aug 2018

Reviewer: Willem Zwaans

Reviewer's report:

Overall a very interesting and relevant research question which is especially of interest nowadays as more patients refuse the use of (permanent) foreign body material. The self-controlled design of the study makes it unique and less prone to bias. The methods for this study, however, should definitely be described more comprehensive and this section should be revised. Please find my recommendations and remaining questions below.

Background

Page 4 line 96: the purpose should be to investigate instead of to show, it indicates a preference of outcomes

Page 4 line 106: Simultaneous laparoscopic repair instead of simultaneous laparoscopic operation

Page 5 line 110: surgical hernia repair instead of herniae repair

Page 5 line 115: please add reference of the single study on biological versus synthetic meshes

Page 5 line 115: a favourable outcome for biological mesh

Page 5 line 117: please clarify which mesh implant resulted in a higher recurrence rate

Page 5 line 117: please remove the double space before "However..."

Page 5 line 122: randomized instead of prospective?

Page 5 line 125: randomized study is desirable?
Methods/Design

1. Please separate the 'aim of the study' section from the 'primary and secondary outcomes' section.

2. Why is the time point of six months chosen as a primary outcome for pain?

3. Are data on other pain syndromes (e.g. headache, (lower) back pain etc) also collected?

4. How is the sequence generation determined and allocation concealment secured?

5. Who is called for the randomization and how is this randomization performed (by computer, by person)?

6. Is block randomization performed (e.g. by centre)? I would suggest a separate section for description of the randomization, random sequence generation and allocation concealment.

7. Since the study is already running, any suggestions for methodological issues are not given.

8. Is the type of hernia also documented, as this may influence the chances on a recurrence?

9. I assume pain as an outcome measure is a quantitative measure on the level of an individual patient instead of a qualitative (binary) outcome measure (yes/no), as the VAS scale is used to quantify pain. Consequentially, the primary outcome measure is not the incidence but for example, the mean or median pain intensity in the group?

10. If you will use pain as a continuous outcome measure (quantitative) you will use the paired t-test or the Wilcoxon signed ranks test? If so, please adapt the sentence of page 7, line 188.

11. Please clarify the second paragraph in the 'Statistical analysis and power calculation' section. Do you have any literature or references to assume that the standard deviation of pain at different end points is different? I understand that pain at later follow-up points may be lower, but this does not automatically mean that the standard deviation is different.

12. You can only state that data are not normally distributed if calculated by, for example, skewness and kurtosis. Please analyze the data for its distribution before choosing the appropriate statistical test.

13. Why do you expect the biological mesh to have a lower recurrence rate? Based on what data c.q. theory?

14. Perhaps you can consider to perform a subanalysis for different types of meshes (i.e. different types of biological meshes and different types of synthetic meshes) and for endoscopic (TEP) versus laparoscopic (TAPP) repair. Previous studies have shown differences in recurrence rates and adverse events of different types of meshes.
Page 5 line 130: laparoscopic or endoscopic repair, i.e. by TAPP or TEP or both?

Page 5 line 131: 'Primary OUTCOMES represent...' instead of 'primary aims represent...'

Page 5 line 132: local pain at six months measured by ...?

Page 6 line 136: diagnostic confirmation by ultrasound, ...

Page 6 line 137: ...as left/right, and which type of mesh is used on which side will be kept sealed...

Page 6 line 139: Secondary outcome measures are ....

How is patient satisfaction measured?

Page 6 line 140: please remove 'in time'.

Page 6 line 142: I think you mean any somatosensory alterations/disturbances instead of paraesthesia here. Paraesthesia is defined as an on-painful ongoing sensation (e.g. ant crawling, tingling) and sensory disturbances after hernia repair may include hypoesthesia, hyperesthesia, allodynia etc.

Page 6 line 145: please remove the word prospective; a prospective, randomized study is a pleonasm

Page 6 line 146: trial instead of study.

Page 6 line 155: please remove the word main

Page 6 line 157 fully legally competent

Page 6 line 159: Six trial visits are planned to assess the outcome measures: ...

Page 6 line 160/161: follow-up instead of follow up; please be consistent

Page 6 line 163: ultrasound instead of ultra sound, MRI instead of MR

Page 7 line 165: please remove 'the therapeutich effect of'

Page 7 line 174: 'Randomization of mesh (biologic or synthetic)' ...

Page 7 line 184: please remove '<'.

Page 8 3rd paragraph: total paragraph can be deleted as all information is provided previously in the manuscript.
Page 8 line 210: normally distributed instead of symmetrically distributed?

Page 8 line 215: The use of pain medication could not be directly related to the left... > please remove whole sentence.

Page 9 line 225: repetition of previous (page 6 line 142)

Page 9 line 231: the study instead of a study

Discussion

1. Please discuss some of the assumptions in the method section with up-to-date literature.

Page 10 line 257/258: Please add a reference to the statement that 30% of patients suffer from bilateral herniae.

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Please indicate how interesting you found the manuscript:

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