Author's response to reviews

Title: A multicenter randomized controlled trial evaluating the effect of small stitches on the incidence of incisional hernia in midline incisions (STITCH trial, NCT01132209)

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Author's response to reviews: see over
Dear reviewer,

On behalf of the REPAIR research group of Rotterdam, the Netherlands, I am pleased to answer the questions in your comments on our manuscript: ‘A multicenter randomized controlled trial evaluating the effect of small stitches on the incidence of incisional hernia in midline incisions (STITCH trial, NCT01132209)’

In general, we would like to thank for your comments, which have led to a better and more complete protocol. Please see our revisions in the revised protocol and answers below:

a) The trial is not a double-blinded trial in all aspects: The surgeons and nurses know the technique used. However patients, investigators and radiologists are blinded.

This trial is blinded in all possible aspects. Of course everyone in the OR is informed about the technique. The randomization outcome is not documented in the clinical chart any report or study file. In the follow up, all relevant investigators performing follow-up or documenting details for the CRF/study file are blinded. In the discussion, we state that this trial is at least single blind.

b) The randomization process is not given in detail.

Every patient is randomized approximately 15 minutes before closure to prevent consequences during the operation. Patients are only randomized when the situation is suitable, according to the inclusion and exclusion criteria. Please see our addition in the revised manuscript.

Implementation is not given in detail (see CONSORT guidelines).

In every hospital, the OR nurses, surgeons, gynecologists and residents are instructed before the start of the trial with during presentations and demonstration movies. During at least the first five inclusions the study coordinator will be present in the OR before randomization. Only when the surgeon is familiar with both techniques, the nurses with the counting and measuring of the stitches and suture material and the study, centers are allowed to run the trial. During the study unplanned audits are performed to control quality. Also for every included patient a form with the detailed closing protocol is added to the clinical chart. Please see our addition in the revised manuscript

c) Objective: Primary and secondary endpoints should be given here too and not only in outcome parameters.

Please see our correction in the manuscript

d) Objective: Give details to the meaning of “significant reduction of costs”.
Please see our added economic paragraph.

e) Methods: There are 10 surgical units and only one gynaecological unit: do you not expect a bias?

The risk of bias is minimized by allocation of the patients by center, department, and surgeon/gynecologist or resident; in addition, participants are randomized. Also, we could say that if our guidelines are followed it is really easy to perform both techniques. And the gynecologists are all specialized in oncology and use often midline incisions.

It is also interesting what effect both techniques have in oncological gynecology patients, at the end of this trial we expect to have at least 20% of oncological gynecology research partners. A second oncological gynecological center was added 5 months ago.

f) Trial design: It is not clear, if the surgeons and residents performing the operations are performing the evaluation too.

Surgeons and residents perform the operation and they are responsible for a sufficient closure technique, after an auspicial period. During the first postoperative week, other surgical residents will fill in the case record form. The (blinded) investigator double check the data with the general clinical reports. The operative surgeons/residents are allowed to mention complications and adverse events to the investigator.

After one year, one independent investigator will invite all patients to the local outpatient clinic to physically examine each patient.

g) Trial design/Interventions: How is the instruction of the surgeons, residents, nurses performed?

In every hospital the OR nurses, surgeons, gynecologists and residents are instructed before the operation during presentations and demonstration movies. During at least the first five inclusions the investigator will be present in the OR before randomization. Only when the surgeon is familiar with both the techniques, the nurses with the counting and measuring of the stitches and suture material and the study, centers are allowed to run the trial. During the study unplanned audits are performed to control quality. Please see our addition in the revised manuscript.

h) Trial design/Outcome parameters: What are the specific criteria of the postoperative ultrasonography for incisional hernia?

A specific score list, which was specially designed with our study group radiologist, is used. At ten points, which include 4 measurements, the scar in the abdominal wall is objectified. The conclusion is made at the end by the investigator. Please see our addition in the revised manuscript.

i) Trial design: What are the definitions used for wound infection?
Please see our addition in the revised manuscript

j) Participants: Emergency laparatomies are only included if the patient is able to sign the informed consent. This may give rise to bias as probably sicker patients are not able to sign.

This is an ethical consideration according to the Good Clinical Practice guidelines. In addition, it will also give a bias if you have patients who were not informed consent during inclusion. This may result into a higher loss to follow-up due to less compliance. Therefore, patients who are unable to sign the informed consent will not be included in the study.

k) Outcome parameters: what are the criteria for a clinically detected incisional hernia?

Please see our addition in the revised manuscript. We use the criteria of the European Hernia society.

l) Statistical analysis: Is there a interim analysis planned?

No, since we expect that the inclusion is finished when 50% of patients has completed the primary endpoint at one year follow up. The Adverse Events are intensively reported and analyzed during a predefined time frame of every 3 months.

m) Statistical analysis: How will the predefined, well established predictors recorded?

Before randomization with usage of case record forms. Please see our mentioned parameters in the revised manuscript

n) Monitoring: Who is he sponsor?

The Erasmus University Medical Center, Rotterdam, the Netherlands. Please see our addition in the revised manuscript.

o) According to the GCP guidelines, patients should be enrolled in only one trial.

In general we agree on this point, but after consultation with our Medical Ethical Committee, if it can be guaranteed that studies do not influence each other, it is acceptable. The alternative is to disqualify a large group of academic and oncologic patients. This will introduce a large bias in our study and other studies. The other studies consist in general observational studies.

p) Discussion: See above: How is the standardisation of the two techniques in the many residents and surgeons performing the wound closure performed?
All surgeons and residents have a clear information and controlled starting period. Beside this, if our guidelines are followed decently both techniques are standardized. In every closure, the wound length, the suture length and the amount of stitches is recorded. Also the closure time is measured. After every closure, the suture length wound length is calculated. In every patient we could calculate the precise mean bite size and bite width. We tried to make pictures and movies in a pilot study, but this proved too difficult to implement on a larger scale and it provided less information than ordinary parameters. Because the names of the surgeon and resident are recorded, it will also be possible to analyze the individual suture characteristics. Also for every included patient a form with the detailed closing protocol in added to the clinical chart.

The optimal methodological study is one surgeon in one specific group of patients but this will not give the evidence needed to translate into the daily practice.

Looking forward to your reaction and hopefully a future acceptance in this reliable surgical journal.

On behalf of professor Lange and professor Steyerberg,

Best Regards,

Joris Harlaar