PHaLIR

Prevent Hernia after Loop Ileostomy Reversal

A randomized controlled study comparing standard closure of the abdominal wall in loop ileostomy closure with a retro muscular mesh at the stoma site.

Karolina Eklöv
Södersjukhuset
1 mars 2018

INNEHÅLLSFÖRTECKNING

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CONTENT

1. Introduction

This is a multicenter, blinded randomized controlled study comparing standard closure of the abdominal wall in loop ileostomy reversal, after low anterior resection for rectal cancer, with a retro muscular mesh at the stoma site.

1.1 Protocol committee

Jonas Nygren, MD, Ass professor, Department of Surgery and clinical research, Ersta Hospital and KIDS Stockholm., Sweden
Karolina Eklöv, MD, PhD student, Department of Surgery and clinical research, South General Hospital, Stockholm, Sweden
Sven Bringman, MD, Ass professor, Department of Surgery Södertälje Hospital and dep of clinical research KIDS, Stockholm, Sweden
Åsa Hallqvist Everhov, MD, PhD, Department of Surgery and clinical research, South General Hospital, Stockholm, Sweden

1.2 Writing committee

The results of the study are planned to be published in a peer reviewed international medical journal and be part of a doctoral thesis. The members of the protocol committee are responsible for the writing. The final decision on participating in the writing committee will be left to the protocol committee based on the researchers contributing to the study.

1.3 Principal investigator

Åsa Hallqvist Everhov, MD, Colorectal surgeon, Department of Surgery and clinical research, South General Hospital, Stockholm., Sweden

2. Background

Colorectal cancer is one of the world's most common forms of cancer and the third most common cancer in Sweden. [1] When operating colorectal cancer, ostomies are sometimes placed, either temporarily or permanently. Ostomies can reduce quality of life by causing leakage, parastomal hernia and prolapse, why stoma reversal is prioritized. [2-6]

A temporary loop ileostomy is widely used when operating rectal cancer.[7] The ostomy is then reversed in a separate operation. Morbidity of stoma reversal is significant, but not clearly defined. One complication in connection with stoma closure is development of hernia at the former stoma site. [8-10]

A hernia is a weakening of the muscular layers and the connective tissue of the abdominal wall, which may cause pain and discomfort, as well as an inconvenient bulge. A hernia could also cause more serious complication of obstructed or strangulated bowel. According to international studies, the incidence of hernia at the ostomy site varies between 7% and 35% [5, 11-18] Many of the studies are heterogenic and some of them include both colostomies and ileostomies. Among studies that focus on reversal of ileotomies the hernia incidence varies between 11-15%. [14, 16].Preliminary results from a retrospective study here in Stockholm indicates a frequency of 7,4%.

The best method to avoid hernia after stoma closure is not known. Most commonly surgeons tend to close the fascia in one layer with monofilament suture. In our study mentioned above 90% of the operations were done with one-layer monofilament, mostly PDS. Use of prophylactic mesh in the abdominal wall has been proposed [19-22] but there is currently insufficient scientific evidence to recommend it as a routine.

In this trial we focus on loop ileostomy closure after rectal cancer. We want to have a non-heterogenous group of ostomies to see if we can evaluate the operation method and lower the incidence of hernia in this group. If this study can detect a decreased frequency of hernia when using prophylactic meshes, it may lead to new recommendations for this patient group.

3. Objectives and purpose

This is a non-commercial clinical trial with the purpose of trying to find an operating method that could benefit the patients that undergoes loop ileostomy closure and lower their incidence of hernias without increasing other complications.

3:1 Primary aim

To study if a retro muscular mesh at the stoma site prevents development of hernia

3:2 Secondary aim

To compare operation time, length of stay, pain and risk of complications, in patients exposed and not exposed to retro muscular mesh placement.

4. Hypotheses

- We estimate that at least 12% of the patients who undergoes a closure of loop ileostomy are at risk to develop hernia at the former stoma site.
- Synthetic mesh can prevent hernia development
- Synthetic mesh is not carrying more risks for the patient that normal closure

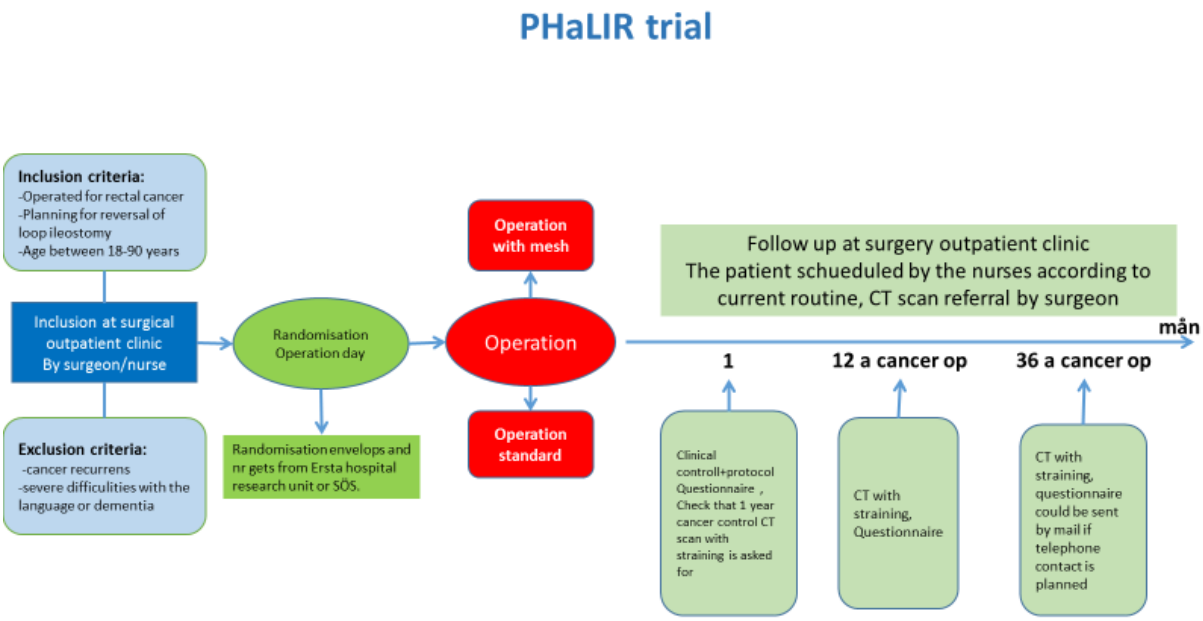
5. Study design

PHaLIR is a prospective, double-blinded randomized study in which patients planned for stoma reversal after rectal cancer surgery will be randomized between retro muscular mesh Ultrapro-Advanced™ or standard treatment without mesh. Operating time, complications, LOS, pain, infections and postoperative hernia are to be studied. The patients will be identified and asked about participation when they come for postoperative control after rectal cancer operation and are planned for the ileostomy reversal after check of the rectal anastomosis. They will be given oral and written information and signed informed consent is required from all patients.

At operation the operation-protocol should be filled in. The operation notes will be written in a blinded way and the original version will be stored on paper until after the study is finished and then added to the patient chart.

At discharge from the surgical ward the patient should be planned for a follow up at the surgical clinic at 30 days postoperatively. The doctor at the follow up visit should be another than the operating surgeon. The patients should then fill in a questionnaire and the surgeon should note the postoperative complications in the 30-days follow up form. At the 30-day follow up the surgeon checks that the one-year follow up after the cancer operation is commissioned. Normally this is a CT thorax and abdomen with contrast. For the study-patients it should be complemented with the question of hernia and the CT scan shall be a CT with straining. The CT scan shall be performed first in a native phase without contrast and then as usual scan with intravenous contrast. The normal 1-year follow up for the cancer will

be the follow up for the ileostomy reversal also. That means that in most cases it will take place 6-9 months after the reversal. Sometimes the clinician chooses to postpone the 1-year cancer control because an additional CT scan might have been performed to check the anastomosis. If so the 1-year control will be around 1 year after the ileostomy reversal which is even more preferable, but the routines for each clinic should be followed not to do extra controls for the sake of the trial. At this control and at the three years control (after cancer operation) the patient will be given or send a questionnaire (the same as the 30-day questionnaire). The follow up by doctor could be done either with a clinical visit or a telephone call according to the routines of the particular clinic in their follow up program for cancer patients. At three years follow up after cancer operation patients will also get the same questionnaire and the CT scan follow up at three years will also be with straining.



5.1 CRF

- Written consent and patient information will be given at surgical outpatient clinic at the follow up visit after rectal cancer surgery
- Operation-protocol will be filled out in connection to the operation and the operating notes blinded according to appendix 4
- 30-days questionnaire will be filled out at 30 days follow up
- 30-days follow up form will be filled up by the doctor which should be another than the operating surgeon.
- Questionnaire in connection with 1 and 3-year follow up for the cancer (that will be around 3-9 month after stoma reversal) should be filled out by the patient either at the clinical visit or sent by mail and followed up by telephone call. In connection with the questionnaire the doctor shall fill in the answer from the CT scan.

5.2 Exposure

On the operation day the patient will be randomized to either regular abdominal wall closure which in most cases will be closure with PDS 2/0 monofilament in one layer, but should be to the surgeon's normal preference, or placement of retro muscular mesh. The mesh should be standardized, and we have chosen Ultrapro Advanced. The size shall be 5x5 cm. The operation method should be as follow:

Preop antibiotic: po Bactrim Forte 1 tabl, po Metronidazol 400 mg, 3 tabl

1. Circular incision around the stoma
2. Detach the stoma in the normal standardized way, do a hand sewn anastomosis with 4/0 PDS one layer, seromuscular suture
3. Put bowel back in abdominal cavity
4. Free the posterior rectus aponeurosis or the peritoneum depending on the level of the stoma and suture with PDS 2/0 running suture with start and stop knot.
5. Put the mesh in the retro-muscular space. Use Ultrapro Advanced, 5 x 5 cm. It should fill the width of the sheath of the rectus muscle.
6. If there are technical difficulties; widening of the incision crosswise is permitted
7. Close the anterior fascia with 2/0 Prolen. Start and stop knot.
8. Close the skin with intracutaneous tobacco pouch suture with Prolen 3/0 or 2/0. If the incision is extended, close the side first with Monocryl.
9. Local anesthetics subcutaneously with Marcain/Adrenalin 5 mg/ml 20 ml

If the patient is randomized to a standard closure the closure will take place after point 3 with in most cases closure of anterior fascia with 2/0 PDS.

6. Patient selection

All patients from the including centers, whom fulfil the inclusion criteria shall be evaluated for participation in the study. Even the patients who are not included in the study should be registered in the screening log with information as to why they were not included. Patients are given written and oral information before signed written consent. When they have given their consent, they will be given a code with the hospital name first, for example Sös-001. Patient will be given a note in the file system about participating in the trial.

6.1 Inclusion criteria

- Patients operated for low anterior resection for rectal cancer with a diverting loop ileostomy and planned for stoma reversal with suture of the aponeurosis according to the actual routines of the clinic
- Age 18-90 years

6.2 Exclusion criteria

- Language barrier or cognitive disability
- Recurrent cancer

7. Randomization

Randomization will take place in batches of 10. Closed envelopes will be used. Each center will get their envelopes sent from Ersta research unit or Södersjukhuset. The randomization envelope will be placed together with the operation-protocol and the instructions for the operation and placed in a location convenient for each center. On the operation day the envelop will be opened and the operation-protocol filled out during and after the operation. After the operation the note with the randomization from the envelope should be replaced in the envelope and given to the research-nurse together with the operation protocol. The operation notes should be written from the instructions. Appendix 4. See point 8. The randomization number will be noted in the patients file by the nurse.

8. Blinding

- No 1. The operation note will be blinded in the file. The blinded part is the closure of the abdominal wall. The surgeon will dictate as usual regarding the first part of the operation with the opening, the bowel anastomosis and so on. When the bowel is replaced in the abdominal cavity the dictate will be as follow:

  "The patient has been randomized and the closure of the abdominal wall is according to the arm he/she has been giving in the PHaLIR protocol"

  After that, the surgeon dictates a short amendment containing the method of the abdominal wall closure that took place in the particular case, ie either with or without mesh, and the secretary will write it down on a separate Word document and give to the research nurse who will store it together with the operation protocol and the randomization envelope after the operation.

  To break the code in an emergency situation the responsible physician for the actual unit shall be contacted and the list of the code shall be located in a locked place in the research unit or the surgical outpatient unit.

  When the study is finished after three years the "true" operation note will be written in the file.

- No 2. When patient comes for postoperative controls the doctor shall be another than the operating surgeon.

9. Data to be collected

The following data will be collected and evaluated:

- Age operation protocol, surgeon
- Gender operation protocol, surgeon
- Length operation protocol, surgeon or anesthetist nurse

- Weight — operation protocol, surgeon or anesthetist nurse
- ASA class — operation protocol, surgeon or anesthetist nurse
- Smoking — operation protocol, surgeon
- Immunosuppression — operation protocol, surgeon
- Diabetes — operation protocol, surgeon
- Collagenous disease — operation protocol, surgeon
- Parastomal hernia preop — operation protocol, surgeon
- Operating time — operation protocol, surgeon
- Time for abdominal wall closure — operation protocol, surgeon
- Bleeding — operation protocol, surgeon or anesthetist nurse
- Bowel injury — operation protocol, surgeon
- Complication — 30-days follow up, doctor
- SSI — 30-days follow up, doctor
- Postop hernia — 30-days follow up, doctor, 1 year, 3 years, CT
- Pain and inconvenience — patient, nurse, doctor on follow up, questionnaires

10.Statistics

Primary outcome: Occurrence of hernia within 1year (3-9 month) and 3 years, (clinical diagnosis or radiological findings of hernia) time to first hernia.

Secondary outcome: Operation time, time for abdominal wall closure, length of stay, postoperative pain, 30-day complications, including SSI.

Occurrence of hernia (yes / no) 1 and 3 years after the cancer operation will be compared between the group operated with and without retro muscular mesh. Preliminary power analysis based on international studies (see background): If we assume a cumulative hernia incidence of 12%, 208 patients (104 in each arm) need to be randomized to detect a reduction of hernia from 12% to 3% (double-sided test, p-value 0.05 with 80% power).

11. Ethical considerations

The study is approved by the ethical committee in Stockholm. Reference no 2007/1693-31/2

The operations will take place under general anesthesia with careful, standardized routines for sterilization. The per-and postoperative period for the two methods are expected to be equivalent. The operation with mesh is expected to take maximum 30 minutes longer than the standard procedure. The operation, regardless of method, carry risks of complications, mainly infection and postoperative ileus and in rare cases bleeding and bowel injury. Participation in the study is not expected to increase these risks. The length of stay is expected to be the same with the two methods.

CT scans carry a risk for ionizing radiation. We are therefore going to use the ordinary follow up program for cancer control with 1 and 3 years follow up with CT scan and complement it with a phase with straining.

The patients are cared for according to clinical routines meaning postoperative monitoring until patient is adequately pain relieved and had passed flatus. The patients are followed up regarding possible complications. The patients in the study will be followed even more actively than the standard treatment for these patients today.

12. Time schedule

The trial starts 1 March 2018. Inclusion is planned for at least two years. The first follow up at one year after the cancer surgery (ie 3-9 month after ileostomy reversal) will be the first publication and the second will be after 3 years follow up.

13. Administration

The Surgical clinic and department for clinical research at Södersjukhuset and the research unit at Ersta Hospital will be responsible for the coordination with dr Karolina Eklöv, dr Jonas Nygren and research nurse Nina Blommé at Ersta and nurse Anna Rantanen, Södersjukhuset as the principal contact persons.

For every participating hospital a principal physician and nurse will be responsible for the study. The protocol committee is responsible for problems that may arise during the time of the study.

14. Significans

This study contributes to better knowledge around complications after loop ileostomy reversal. If the study can show a reduction of hernias for this patient group, it can affect the routines for these operations. If the study also can show comparable post operatively symptoms for the patient with and without mesh it will increase the flexibility to put mesh even in connection with bowel operations. Hopefully we can also identify risk groups who benefit more of the mesh.

14. Appendices (Swedish)

1) Patient information and consent

2) Questionnaire 30 d, 1 year, 3 year

3) Operation protocol

4) Operation description and blinding

5) 30-day protocol

6) Flow chart

7) Reminder in short

8) Screening log

9) Subject enrolment

10) Examples on file notes for Take care

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Ongoing studies:

Anastomosis and stomas- the persiut of technical perfection, Postoperative complications after closure of a diverting ileostoma- differences according to closure technique, P Gustavsson, Ulrik Lindforss, KS

Mesh Reinforcemanet During Temporary Stoma Closure after Spincter-Saving Rectal cancer surgery(MEMBO), Hopitaux de Paris,

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Prophylaxis of Ileostomy Closure Site Hernia by Placing Mesh (ILEOCLOSE), Hospital Universitari Vall d'Hebron Research Institute