Laparoscopic versus open adhesiolysis for small bowel obstruction - a multicenter, prospective, randomized, controlled trial

Sallinen V¹, Wikström H¹, Victorzon M², Salminen P³, Koivukangas V⁴, Haukijärvi E⁵, Enholm B⁶, Leppäniemi A¹, Mentula P¹

Author details
¹ Helsinki University Central Hospital, Department of abdominal surgery, Haartmaninkatu 4, 00029 Helsinki, Finland. Emails: ville.sallinen@helsinki.fi, heidi.wikstrom@hus.fi, ari.leppaniemi@hus.fi, panu.mentula@hus.fi
² Vaasa Central Hospital, Hietalahdenkatu 2-4, 65130 Vaasa. Email: mikael.victorzon@vshp.fi
³ Turku University Hospital, PL 52, 20521 Turku. Email: paulina.salminen@tyks.fi
⁴ Oulu University Hospital, Kajaanintie 50, 90220 Oulu. Email: vesa.koivukangas@ppshp.fi
⁵ Tampere University Hospital, PL 2000, 33521 Tampere. Email: eija.haukijarvi@pshp.fi
⁶ Päijät-Häme Central Hospital, Keskussairaalankatu 7, 15850 Lahti. Email: berndt.c.enholm@phsotey.fi

Correspondence:
Ville Sallinen
Department of Abdominal Surgery
Helsinki University Central Hospital
Haartmaninkatu 4
00029 HUS
Finland
Tel: +358-9-4711
email: ville.sallinen@helsinki.fi
Abstract

Background
Laparoscopic adhesiolysis is emerging as an alternative for open surgery in adhesive small bowel obstruction. Retrospective studies suggest that laparoscopic approach shortens hospital stay and reduces complications in these patients. However, no prospective, randomized, controlled trials comparing laparoscopy to open surgery have been published.

Methods/Design
This is a multicenter, prospective, open label, randomized, controlled trial comparing laparoscopic adhesiolysis to open surgery in patients with computed-tomography diagnosed adhesive small bowel obstruction that is not resolving with conservative management. The primary study endpoint is the length of postoperative hospital stay in days. Sample size was estimated based on preliminary retrospective cohort, which suggested that 102 patients would provide 80% power to detect difference of 2.5 days in the length of postoperative hospital stay with significance level of 0.05. Secondary endpoints include passage of stools, commencement of enteral nutrition, 30-day mortality, complications, postoperative pain, and the length of sick leave. Tertiary endpoints are the rate of ventral hernias and recurrence of small bowel obstruction in long-term follow-up. Long-term follow-up by letter or telephone interview will take place at 1, 5, and 10 years.

Discussion
This trial is to the best of our knowledge the first one aiming to provide level Ib evidence to support or disprove the use of laparoscopy in the treatment of adhesive small bowel obstruction.

Trial registration
ClinicalTrials.gov identifier: NCT01867528.
Background
Small bowel obstruction (SBO) is a common surgical emergency caused most frequently by adhesions. A large portion of adhesive SBO resolve by nonoperative methods such as fasting and ingestion of an oral contrast-media, while a significant number of patients will need emergency surgery. Open surgery has been the golden standard for decades in treating adhesive SBO. Now that laparoscopic surgery has been established as a first line option in many elective indications such as colorectal operations, fundoplication, and cholecystectomy, to name a few, laparoscopy is also emerging as a viable alternative in emergency surgery.

If SBO is caused by one adhesive band the surgical treatment is straightforward - cutting the band causing obstruction. Laparoscopic approach seems ideal for such a procedure, preventing the morbidity of a laparotomy incision. First publications describing laparoscopic adhesiolysis in SBO are from the 1990’s [1]. Since then several retrospective series have been published, and a recent meta-analysis pooled patients from four studies, including a total of 334 patients [2]. Meta-analysis showed that patients treated by laparoscopic approach had less complications, and bowel function returned faster [2]. However, there are no prospective randomized trials comparing open approach to laparoscopy in treating SBO. Furthermore, previous retrospective studies have selection bias as the easiest cases are selected for laparoscopic approach. One of the drawbacks of laparoscopic approach is the concern for iatrogenic bowel perforation. According to one report, bowel lesion rate in laparoscopic adhesiolysis is 6.6%, while only 84% are acknowledged during the operation [3].

Methods/Design

Objective
The objective of this trial is to compare open surgery to laparoscopic adhesiolysis in patients with computed tomography-diagnosed adhesive SBO that is not resolved by nonoperative means. The hypothesis to be tested is that laparoscopic approach shortens the length of hospital stay without increasing complications.

Ethics and permissions
This study will be conducted in accordance with the principles of the Declaration of Helsinki and ‘good clinical practice’ guidelines. The research plan has been evaluated and approved by the local institutional ethics committee of the main research center (Helsinki University Central Hospital, Ethics Committee, Department of Surgery). The research plan has further been approved by each participating centers’ institutional review board.

Patient evaluation and selection
Patients with computed tomography-confirmed SBO will be evaluated for the study. If no exclusion criteria are met, nasogastric tube is inserted and the patient is admitted to the emergency ward. If the obstruction does not resolve within 12 hours, an oral water-soluble contrast (Gastrografin®) is used. If the contrast has not advanced to the colon within 8 hours and the patient has no signs of spontaneous resolution of obstruction, surgical intervention is deemed necessary and the patient is randomized to either open or laparoscopic surgery. Oral water-soluble contrast has been shown to have 97% sensitivity and 96% specificity in predicting nonoperative resolution of adhesive SBO [4]. Patients can alternatively undergo nonoperative management by fasting and nasogastric tube only if oral water-soluble contrast is contraindicated or not available. If SBO in these patients is not resolved within 48 hours, they are eligible for inclusion in the study.

Inclusion criteria:
- All patients with clinical and computed tomography-diagnosed adhesive small bowel obstruction
- Obstruction is not relieved by conservative methods (nasogastric tube, nil per os) including Gastrografin® is not passed to colon within 8 hours (48-hour conservative treatment without Gastrografin® is allowed if Gastrografin® is contraindicated (e.g. allergy) or not available)

Exclusion criteria:
- Strong suspicion of strangulation or clinical peritonitis thus indicating an urgent operative intervention
- Earlier confirmed or strongly suspected peritoneal carcinoma
- Earlier confirmed wide diffuse adhesions of abdominal cavity
- Earlier open surgery for endometriosis
- Earlier generalized diffuse peritonitis (not including local peritonitis such as appendicitis)
- Active abdominal malignancy or remission less than 10 years
- Earlier abdominal region radiotherapy
- Earlier obesity surgery
- 3 or more earlier open abdominal operations (not including caesarean section(s))
- Suspicion of other cause for obstruction than adhesions in CT-scan
- Earlier abdominal surgical operation within 30 days
- Earlier surgical operation for aorta or iliac vessels performed through laparotomy
- Crohn's disease
- Anesthesiological contraindication for laparoscopy
- Missing informed consent
- Age less than 18 years or over 95 years
- Pregnancy
- Patient living in institutional care (such as health centre ward), not including retirement homes
- Over 1 week of hospital stay directly prior surgical consultation

Randomization procedure
Patients are randomly allocated (1:1) to either laparoscopic or open surgery. Randomization is done using block randomization with randomly varying block size (2-6) stratified by each study center. Cards with participants' randomization number and randomization group are sealed within numbered envelopes. Randomization and sealing within envelopes is done in the main research center (Helsinki) and letters are sent to each participating center at the beginning of the trial. The envelope is opened only after patient fulfills inclusion criteria, none of the exclusion criteria are met, and patient has agreed to participate in the study and has given a written consent. Envelopes are opened in numerical order. Operation is scheduled after randomization.

Intervention

Pre- and perioperative treatment
Fluid balance and electrolyte disturbances are corrected. Cefuroxime 1500mg and metronidazole 500mg are used intravenously as prophylaxis just before incision. An epidural catheter may be placed if recommended by the anesthesiologist. A nasogastric tube is inserted.

Laparoscopic technique
First port is inserted using open approach or by using optic port. Following ports are inserted under vision. Location of the ports is on surgeons discretion. Abdominal cavity is
inspected. Caecum is located and identified. Laparoscopic forceps are used to examine the small bowel starting from the terminal ileum until the transition site is identified. Dilated small bowel is not grasped, but can be mobilized by grasping the mesenterium. Once the transition site is identified, the obstructing adhesions are freed and the bowel is inspected for vitality. Ports are removed under vision, and possible bleeding is primarily controlled by ligatures. Fascia holes of ports over 5 mm are closed. Nasogastric tube is left in place.

Criteria for conversion to open surgery
- Confirmed or suspected small bowel perforation, which is not amenable for laparoscopic suturing
- Transition site is not identified
- Reason for obstruction is not found
- Peritoneal carcinosis
- Widespread diffuse adhesions
- Need for bowel resection - conversion can be made to minilaparotomy to exteriorize the small bowel section needing resection

Open surgical technique
Midline incision is made and abdominal cavity is inspected. Small bowel is examined until transition site is located. Adhesions causing obstruction are freed. Excess fluids within small bowel are pushed into the ventricle and the ventricle is emptied using nasogastric tube. Fascia is closed using continuous or interrupted sutured on surgeon’s discretion.

Postoperative treatment
Nasogastric tube is kept in place until secretion is under 500 ml per 8 hours. After the removal of the nasogastric tube, patient may take peroral fluids 200 ml per 6 hours. If no nausea develops, patient may take fluids per os freely. Proton pump inhibitors are used during the hospital stay. Trombosis profylaxis is commenced 6 hours after surgery, if there is no suspicion of postoperative hemorrhage. Ibuprofen, paracetamol, tramadol, and oxycodone may be used for pain. Pain is evaluated using visual analogue scale daily and before administering pain killers.

Criteria for discharge
- Passage of stools
- Patient tolerates per oral nutrition
- Pain is relieved sufficiently by ibuprofen, paracetamol, and/or tramadol.

In case of unresolving obstruction after surgery
If the obstruction if not resolved is spite of surgical treatment, patient may undergo radiological imaging studies and/or surgical exploration (open or laparoscopic) on discretion of the surgeon.

Surgeons
Same surgeons perform the operations in both open and laparoscopic groups. All participating surgeons need to have solid experience and skills of complex laparoscopic procedures, and need to have performed at least two laparoscopic adhesiolysis for small bowel obstruction before operating on patients participating in the trial.

Follow-up
Patients of working age are given sick leave. Lenght of sick leave is on discretion of treating physician, who is taking into consideration patient’s age and type of work (physical or desk job). Follow-up call in scheduled within 30 days, and return to work, possible late
complications and readmissions are inquired. Follow-up questionnaires are sent 1, 5 and 10 years after the randomization, and in case of no response, patients are contacted by telephone. Possible hernias and recurrent bowel obstructions are inquired.

**Primary endpoint**
- Post-operative hospital stay (days)

**Secondary endpoints**
- Passage of stools (post-operative days)
- Commence of enteral nutrition (post-operative days)
- 30-day mortality
- Complications, Clavien-Dindo classification
- Number of participants with iatrogenic small bowel lesions
- Number of participants with readmission(s)
- Number of participant with failure to resolve obstruction
- Pain scores on the Visual Analog Scale
- Length of epidural catheter analgesia (days)
- Total need of opioids in milligrams
- Length of sick leave (days)

**Tertiary endpoints**
- Number of participants who develop ventral hernia
- Number of patient with recurrent adhesive small bowel obstruction

**Data collection and analysis**
Data will be collected by using electronical case report form, and statistically analyzed in the main research center (Helsinki) once the trial is completed. Continuous variables will be compared using t-test or Mann-Whitney-U-test. Categorical variables will be compared using Fischer’s exact-test or Chi-square-test. Groups will be analyzed as intention-to-treat. An interim analysis will be made when 52 patients have been randomized and treated.

**Sample size calculation**
Based on preliminary retrospective analysis on laparoscopic and open adhesiolyis we have estimated standard deviation to be 3.75 days in laparoscopic group and 5 days in open surgery group. Sample size is calculated to be able to demonstrate 2.5 day difference in the post-operative length of stay. 102 patients are needed to achieve 80% power with a significance level of 0.05.

**Registration**
This trial has been registered at ClinicalTrials.gov (Identifier: NCT01867528).

**Discussion**
While laparoscopy has become the treatment-of-choice in acute cholecystitis, acute appendicitis, and perforated peptic ulcer, there are still areas of emergency surgery that are under debate [5, 6]. Purulent peritonitis caused by acute diverticulitis has been proposed to be treated by laparoscopic lavage [7], and randomized studies are on their way to either prove or disprove this approach [8, 9].

As laparoscopic surgery is taking on the field of emergency surgery, adhesive SBO is an evident next target for laparoscopic approach. Although there are several retrospective series, and meta-analyses comparing open approach to laparoscopy, there are no prospective, randomized studies available. A search for ongoing trials reveals that, except
for this trial, there are no other prospective, randomized trials enrolling patients. Although previous retrospective series have shown association of less complications and shorter hospital stay with laparoscopic approach, all previous retrospective series are more or less biased as the easiest cases are selected for laparoscopic approach.

This trial aims to provide level Ib evidence for the use of laparoscopy in the treatment of adhesive SBO. The patients in this trial are selected, and the results will not be applicable to all patients presenting with an adhesive SBO. We have designed the study (i.e. exclusion criteria) so that the likelihood of one occluding adhesion band would be high and likelihood of overwhelming diffuse adhesions would be low. It is evident from experience and earlier studies, that patients with peritoneal carcinosis, peritonitis, strangulated bowel, or dense diffuse adhesions are not good candidates for laparoscopic approach [10]. By excluding such patients from the trial, the conversion rate should remain relatively low.

List of abbreviations
SBO - small bowel obstruction

Acknowledgments
Financial support: Martti I. Turunen Foundation, Finnish Surgical Society, Vatsatautien Tutkimussäätiö Foundation, Mary and Georg Ehrnrooth's Foundation, Governmental competitive research funds (EVO).

Competing interests
None

Authors’ contribution
VS, PM, AL drafted the manuscript. All authors participated in the design of the trial and/or are the main organizing local investigators at the participating hospitals. All authors have read, revised, and approved the final manuscript.

Figures

Figure 1. Flowchart of patients in the trial. CT - computed tomography, NGT - nasogastric tube, NPO - nil per os, SBO - small bowel obstruction.

References


CT-diagnosed adhesive SBO
Accessed for eligibility

Conservative management
(NGT, NPO, Gastrografin)

Randomization
n = 102

Laparoscopic adhesiolysis

Open adhesiolysis

30-day and 1, 5, and 10-year follow-up
Telephone and/or mail questionnaire

Excluded
- exclusion criteria met
- declined to participate
- other reasons

Obstruction resolved

Analyzed as intention-to-treat