ISRCTN66787074 https://doi.org/10.1186/ISRCTN66787074

CLosure of acute colonIc Perforations: endoscoPic OTSC closurE versus suRgical closure

Submission date
17/06/2011

Recruitment status
No longer recruiting

Registration date
30/01/2012

Overall study status
Completed

Last Edited
08/08/2014

Condition category
Surgery

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims

The large intestine (colon) is part of the digestive system of the body. The partially digested food passes through the colon where water is extracted. In the colon defects such as polyps can be found. These abnormalities can be examined during a procedure which is called a colonoscopy. This is an examination of the colon with an endoscope. An endoscope is a flexible tube with a small lamp and camera at the tip. Through this tube the doctor can exchange tools to perform certain operations. However, in one of 1000-5000 patients who undergo a colonoscopy, a perforation or opening in the intestine may arise during the procedure. When a perforation of the intestinal wall occurs, it must be closed quickly so that the intestinal contents do not leak into the abdominal cavity, which can result in a life-threatening infection of the abdominal wall or a blood infection. A colon perforation following a colonoscopy is a rare condition. This makes it difficult to conduct research on the condition and its treatment. Because a perforation can cause a life-threatening infection of the abdominal wall or a blood infection, it is important to investigate whether the treatment can be improved. It might be possible to decrease the incidence of adverse events (complications) and to achieve a faster recovery after treatment.

The current treatment for a perforation of the intestinal wall is a laparoscopic operation or open surgery performed by a surgeon in the operating room. For laparoscopy, the surgeon uses a special video camera, the laparoscope and other special instruments. The camera and instruments are inserted into the abdominal wall through 3-5 small incisions of 0.5 to 3 cm. The perforation is closed and the abdominal incisions are closed with hand sutures. This operation is always performed under general anaesthesia. In some cases it is not possible to do a laparoscopy and open surgery needs to be performed. For open surgery larger abdominal incisions are made to close the perforation. The incisions are sutured. After treatment the patient is admitted to the hospital. Sometimes, due to the perforation, the intestinal tissue surrounding the perforation is also affected and a part of the intestine needs to be removed. In some cases this may mean that a stoma should be made (an opening to the outside of the abdomen through which stool is collected in a bag).

Recently a new endoscopic technique has been developed for the treatment of an intestinal perforation. For this new method a specially designed clip is used to immediately close the

perforation during the procedure. An endoscopic bowel examination is performed under mild sedation, which means that the patient is less conscious. Using a special small grasper the edges on both sides of the perforation are pulled into the clip after which the clip closes the defect. By treating patients with this clip patients may recover faster and the chance of unfavourable side effects might be smaller compared to the standard surgical operation because no abdominal incisions need to be made. The aim of this study is to find out this new technique is as successful and safe as surgical closure, but with fewer side effects, improved appearance, and lower costs.

Who can participate?
Patients aged 18 years and older with an acute perforation of the colon that was caused during colonoscopy.

What does the study involve?
To compare the two treatments, the patient with a colon perforation will be randomly allocated to one of two groups. One group receives the standard treatment, which is to surgically close the intestinal perforation. In the other group, patients will be treated endoscopically with a clip to close the perforation. Colonoscopy is always done with mild sedation which means that an anaesthetic and analgesic is administered through a drip in your hand. With this medication your consciousness is reduced. Therefore we cannot ask you if you want to participate in the study. It is important to treat the perforation as soon as possible. This means that you do not have sufficient time to decide whether you want to participate. Because the new treatment shows good results in earlier studies with patients, we think that you will be well treated with both techniques. We have therefore chosen to randomly allocate the treatment immediately after we knew a perforation was made and you will know after you wake up from the sedation what way you were treated. Because we are interested in your general health, we will ask you to complete two short questionnaires.

What are the possible benefits and risks of participation?
If you are treated with the standard surgical treatment it means that you have no additional advantages that could be a consequence of your participation in the study. For this standard treatment it means that no additional risks are expected for you than those known for this standard treatment: the risk of bleeding during or after surgery and the risk of an infection of the abdomen or the surgical wounds. If you are treated with the endoscopic clip there is a small chance that it is not possible to adequately close the perforation with the new clip. If this occurs the gastroenterologist can decide to treat the perforation with the standard surgical procedure. It is also possible that the bowel contents may leak into the abdominal cavity prior to closure of the perforation. This can mean that an abdominal infection can develop. Regarding these problems it can mean that you have to stay in hospital longer than expected or that additional treatment or procedures have to take place. Because you do not have surgical wounds you could experience less pain after treatment. It can also mean that you can sooner return to your normal daily activities. Additionally, you have less chance to develop infections of the abdominal wounds and because of absence of abdominal incisions you will not have abdominal scars.

Where is the study run from?
It is being organised by Academic Medical Center, University of Amsterdam in Amsterdam. Several centers are participating, including:
1. Cliniques Universitaires Saint-Luc, Brussels, Belgium
2. Erasme University Hospital, Brussels, Belgium
3. Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany
4. Medizinische Klinik, Evangelisches Krankenhaus Düsseldorf, Germany
5. GastroZentrum Hirslanden Zürich, Switzerland
6. Universitätsspital Zürich, Switserland

7. Catholic University of Rome, Italy
8. Erasmus Medical Centre Rotterdam, the Netherlands
9. St. Antonius Hospital, Nieuwegein, the Netherlands
10. Catharina Hospital Eindhoven, the Netherlands:
11. Sint Lucas Andreas ziekenhuis, Amsterdam, Netherlands
12. Onze Lieve Vrouwe Gasthuis hospital, Amsterdam, the Netherlands
13. University Medical Centre Utrecht, the Netherlands
14. University Medical Centre Groningen, Groningen, the Netherlands
15. Academical hospital Maastricht, Maastricht, the Netherlands
16. Flevoziekenhuis, Almere, the Netherlands

When is the study starting and how long is it expected to run for?
The study will start in January 2012 and will run until January 2015.

Who is funding the study?
The study is an investigator-initiated study. When possible, Ovesco (Tuebingen, Germany) will provide the Over-The-Scope-Clip and associated materials.

Who is the main contact?
Tessa Verlaan (PhD student)
t.verlaan@amc.uva.nl

Contact information

Type(s)
Scientific

Contact name
Prof Paul Fockens

Contact details
Meibergdreef 9
Amsterdam
Netherlands
1105 AZ
p.fockens@amc.uva.nl

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
January 2011/02/34159

Study information

Scientific Title
CLosure of acute colonIc Perforations: endoscoPic OTSC closurE versus suRgical closure: a randomised controlled trial

Acronym
CLIPPER II

Study objectives
Endoscopic closure of acute colonic perforations following a colonoscopy with the Over-the-Scope-Clip (OTSC) is as successful and safe as surgical closure, but with less procedure-related morbidity, better cosmesis and procedure-related costs.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Medical Ethics Committee of the Academic Medical Centre Amsterdam, 03/03/2011, ref: 10/246

Study design
Randomised controlled multi-centre trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Acute colonic perforation

Interventions
Surgical closure (gold standard) vs endoscopic closure with Over-the-Scope-Clip

Treatment of the iatrogenic colonic perforations will be either endoscopic with the Over-The-Scope-Clip or with surgical closure. The Over-The-Scope-Clip system (OTSC) is an endoscopic device that consists of a large nitinol clip pre-loaded on a transparent plastic cap. The cap is mounted on the tip of an endoscope and the clip can be released by rotating a wheel, which is attached to the shaft of the endoscope. To approximate both sides of the perforation, a twin grasper is deployed through the working channel of the endoscope.
The twin grasper has one fixed middle branch and two independently movable lateral branches, which enable grasping of both perforation edges separately. The tissue is approximated and

gently pulled into the cap while applying continuous suction. The OTSC is released by pulling on a wire that is led through the working channel of the endoscope.

Surgical closure of the perforation will consist of a preferably laparoscopic procedure according to the standard operating procedure of the respective study center within 6 hours after the perforation occurred. The perforated colon will be explored and the perforation will be repaired surgically with primary closure (suturing), resection with primary anastomosis or resection with diversion (stoma) at the surgeons preference.

Intervention Type
Procedure/Surgery

Phase
Not Applicable

Primary outcome measure
1. Closure-related morbidity, defined as clinical leakage or leakage seen on CT with enteral contrast requiring surgical intervention or radiological drainage within 30 days after the closure procedure
2. Clinical leakage, defined as abdomninal wall rigidity and tenderness associated with relative temperature rise, leucocytosis and relative C-reactive protein (CRP) rise

Secondary outcome measures
Any adverse event that leads to death, additional intervention or prolonged hospital stay within 30 days after the procedure
1. Hospital stay (days) following closure of colonic perforation (solid diet should be started within 12 hours following the procedure) the patient will be discharged from the hospital in case of adequate pain control with oral medication and patients acceptance to be discharged. These discharge criteria should be checked daily
2. Procedure and hospital stay related costs (direct and indirect costs)
3. Number of days needing analgetics (preferably, the patient should indicate whether analgetics are needed so that the (minimal) use and type of analgetics can be scored)
4. Day of return to normal daily activities
5. Closure time defined as time starting from introduction of the endoscope with the OTSC or the first surgical incision, until adequate closure
6. Quality of life as measured by SF-36 questionnaire at day 1, 3, 8 and 14

Overall study start date
01/07/2011

Completion date
01/07/2013

Eligibility

Key inclusion criteria
1. Documented colonic perforation: clear view of the peritoneum or other visceral organs documented by endoscopic picture or video. In case of doubt a plain abdominal X-ray or computerised tomography (CT) can be taken to detect intraperitoneal air
2. Etiology
3. Endoscope perforation during colonoscopy

4. Perforation during polypectomy, endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD)
5. Perforation size 1-3 cm in diameter as can be estimated with the jaws of an open biopsying forceps (8 mm)
6. Colon prepared for colonoscopy with good or excellent result and no solid stool remaining
7. Detection of perforation within 3 hours of the procedure

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
54

Key exclusion criteria
1. Tumour perforation
2. Suspicion of severe contamination of the abdominal cavity with digestive organ content
3. Sepsis
4. American Society of Anesthesiologists (ASA) class IV or V

Date of first enrolment
01/07/2011

Date of final enrolment
01/07/2013

Locations

Countries of recruitment
Belgium

Denmark

France

Germany

Italy

Netherlands

Switzerland

Study participating centre

Meibergdreef 9
Amsterdam
Netherlands
1105 AZ

Sponsor information

Organisation
Academic Medical Centre Amsterdam (Netherlands)

Sponsor details
Meibergdreef 9
Amsterdam
Netherlands
1105 AZ

Sponsor type
Hospital/treatment centre

Website
http://www.amc.nl/

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Academic Medical Center Amsterdam (Netherlands)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration