ISRCTN84052649 https://doi.org/10.1186/ISRCTN84052649

Biomarkers for colorectal anastomotic leakage

Submission date
04/10/2018

Recruitment status
No longer recruiting

Registration date
23/10/2018

Overall study status
Completed

Last Edited
31/03/2022

Condition category
Surgery

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
The most important and frustrating complication of rectal surgery is anastomotic leakage. This is when a defect causes the contents of the colon (bowel) to leak into the abdominal and/or pelvic space, leading to peritonitis (infection), abscess (collection of pus) and sepsis that can be fatal. The incidence varies between 3% and 19% and mortality (death) rates vary between 10% and 20%. Anastomotic leakage is a severe complication which prolongs hospital stay by one to two weeks and increases medical costs by as much as $24,000, triple the cost compared to normal recovery. The occurrence of this complication is poorly understood. Fever, abdominal pain and impaired gastrointestinal transit are signs of anastomotic leakage but these are common after rectal surgery and not specific for leakage. Anastomotic leakage is usually detected between day 5 and day 8 after surgery. Early diagnosis is necessary as delayed diagnosis of anastomotic leakage increases mortality. A delay in diagnosis of 2.5 days increases mortality from 24% to 39%. In most cases, CT scanning is required to confirm anastomotic leakage, but with this technique it is impossible to detect anastomotic leakage in at early stage. Therefore, this study aims to find a biomarker in blood or drain fluid to early detect anastomotic leakage after rectal resection (surgery).

Who can participate?
Patients aged over 18 who underwent partial or total mesorectal excision (removal of a significant length of the bowel) with construction of a colorectal anastomosis (cross-connection)

What does the study involve?
All patients receive a pelvic drain during surgery which is kept in place for at least three days after surgery. Drain fluid is collected every morning on the first three days. The drain fluid reservoir is replaced after drain fluid collection. Drain fluid is analysed in batch after including all patients. In addition, C-reactive protein (CRP) is measured in blood samples on the first three days.

What are the possible benefits and risks of participating?
There are no benefits for the participating patients nor will their hospitalization be prolonged. On the other hand there are risks related to the participation of this study. These risks are due to the placement of a drain during colorectal surgery and due to the collection of blood samples.

Despite the fact that a drain is widely used in colorectal surgery, the placement of a drain could cause wound infection. However, the rates of wound infection with and without a drain are similar.

Where is the study run from?
This study is a collaboration between UZ Leuven, Belgium and Erasmus MC Rotterdam, the Netherlands. In total, ten hospitals participated in this study

When is the study starting and how long is it expected to run for?
January 2015 to October 2019

Who is funding the study?
Medtronic

Who is the main contact?
C.L. Sparreboom

Contact information

Type(s)
Public

Contact name
Ms Cloe Sparreboom

ORCID ID
https://orcid.org/0000-0002-4606-6895

Contact details
Wytemaweg 80
Rotterdam
Netherlands
3015 CN

Additional identifiers

Protocol serial number
NL52251.078.15

Study information

Scientific Title
Analysis of predictive parameters for evident anastomotic leakage - II

Acronym
APPEAL-II

Study objectives

This study aimed to find systemic and peritoneal biomarkers for anastomotic leakage after rectal resection. This study will explore combinations of biomarkers as a clinically useful diagnostic tool for early detection of anastomotic leakage after rectal resection.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Belgium: Committee Medical Ethics UZ KU Leuven, 17/07/2015, ref: B322201525195
2. The Netherlands: The Medical Ethical Committee of Erasmus University Medical Center, 24/11/2015m ref: NL52251.078.15

Primary study design
Observational

Study design
International prospective multicenter cohort study

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Anastomotic leakage after rectal resection

Interventions
All patients received a pelvic drain during surgery which will kept in place for at least 3 postoperative days. Drain fluid was collected every morning on the first three postoperative days respecting rules of sterility. The drain fluid reservoir was replaced after drain fluid collection. Drain fluid stored in a -80°C fridge and analysed in batch after including all patients. In addition, C-reactive protein (CRP) was measured in peripheral blood samples on the first three postoperative days according to the hospitals' protocol. Follow-up ended at the first outpatient clinic visit after discharge.

Intervention Type
Other

Primary outcome(s)
Colorectal anastomotic leakage was defined as a clinically manifest insufficiency of the anastomosis, leading to a clinical state requiring treatment. It was confirmed by either endoscopy, CT-scan and/or contrast enema or reoperation. Treatment consisted of therapeutic antibiotics, drainage or a surgical re-intervention. The primary endpoint does not occur at a specific time point since it involves a postoperative complication. Follow-up ends at the first outpatient clinic visit after discharge.

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
01/10/2019

Eligibility

Key inclusion criteria
Patients who underwent partial mesorectal excision (PME) or total mesorectal excision (TME) with construction of a colorectal anastomosis

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
271

Key exclusion criteria
1. Pregnancy
2. Age < 18 years
3. No informed consent
4. No drain
5. Emergency surgery

Date of first enrolment
01/08/2015

Date of final enrolment
31/10/2017

Locations

Countries of recruitment
Belgium

Netherlands

Study participating centre
Havenziekenhuis
Netherlands
3011 TD

Study participating centre
IJsselland Ziekenhuis
Netherlands
2906 ZC

Study participating centre
Reinier de Graaf Gasthuis
Netherlands
2625 AD

Study participating centre
Isala Ziekenhuis
Netherlands
8025 AB

Study participating centre
VU University Medical Center
Netherlands
1081 HV

Study participating centre
University Medical Center Utrecht
Netherlands
3584 CX

Study participating centre
Jeroen Bosch Ziekenhuis
Netherlands
5223 GZ

Study participating centre
OLVG
Netherlands
1091 AC

Study participating centre

University Hospital Leuven
Netherlands
3000

Study participating centre
University Hospital Antwerpen
Netherlands
2650

Sponsor information

Organisation
Universitair Ziekenhuis Leuven

ROR
https://ror.org/0424bsv16

Organisation
Erasmus Medical University Rotterdam

Funder(s)

Funder type
Industry

Funder Name
Medtronic

Alternative Name(s)
Medtronic Inc.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available due to the fact that no ethical approval was obtained to publish the dataset.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		07/11/2021	31/03/2022	Yes	No