

Biomarkers for colorectal anastomotic leakage

Submission date 04/10/2018	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 23/10/2018	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 31/03/2022	Condition category Surgery	<input type="checkbox"/> 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

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ORCID ID

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Contact details

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3015 CN

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

Study design

International prospective multicenter cohort study

Primary study design

Observational

Secondary study design

Cohort study

Study setting(s)

Hospital

Study type(s)

Diagnostic

Participant information sheet**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 measure

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.

Secondary outcome measures

There are no secondary outcome measures

Overall study start date

01/01/2015

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

Age group

Adult

Sex

Both

Target number of participants

300

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

Sponsor details
Herestraat 49
Leuven
Belgium
3000

Sponsor type
Hospital/treatment centre

Website
<https://www.uzleuven.be/en>

ROR
<https://ror.org/0424bsv16>

Organisation

Erasmus Medical University Rotterdam

Sponsor details

Wytemaweg 80
Rotterdam
Netherlands
3015 CN

Sponsor type

Hospital/treatment centre

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**Publication and dissemination plan**

Planned publication in a high-impact peer reviewed journal.

Intention to publish date

01/10/2019

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