# Multi-Interventional program for prevention and early Management of Anastomotic leakage after total mesorectal excision in Rectal cancer patIents, IMARI-trial

Published: 14-08-2019
Last updated: 15-05-2024

To increase the one year anastomotic integrity rate in patients undergoing total mesorectal excision (TME) for rectal cancer by the routine and quality controlled implementation of a multi-interventional program, which includes:1. MBP with oral...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Gastrointestinal neoplasms malignant and unspecified |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON55903

**Source**
ToetsingOnline

**Brief title**
IMARI-trial

### Condition

- Gastrointestinal neoplasms malignant and unspecified
- Gastrointestinal therapeutic procedures

**Synonym**
Rectal cancer

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** B. Braun Surgical, S.A.,KWF kankerbestrijding heeft een beurs toegekend aan de IMARI. Door de industrie (Stryker European BV en B. Braun Surgical).,Stryker European BV

## Intervention

**Keyword:** Anastomotic leakage, Anastomotic salvage, Prevention, Total Mesorectal Excision

## Outcome measures

### Primary outcome

The primary endpoint of the IMARI-trial is anastomotic integrity at one year

postoperative.

### Secondary outcome

Secondary endpoints

The most important secondary aim is to determine the impact on the incidence of

AL within 30 and 90 days and one year post-operation.

Other secondary aims include:

1. Quality of life and functional outcomes pre-op, 90 days post-op and one year

after operation.

2. Protocol compliance to any intervention

3. Compliance in association to AL

4. Changes in rectal microbiome and correlation to AL

5. Change in management due to FA using ICG

i. Site of proximal bowel division used for anastomosis

ii. Redo anastomosis or reinforcement of anastomosis after construction

anastomosis

iii. Decision for diverting stoma

iv. Decision for Hartmann or abdominoperineal resection rather than restorative

procedure

6. Diagnostic accuracy of CRP for AL

7. Efficacy of EVAC with early transanal closure of the anastomotic defect

8. Permanent stoma rate

9. Temporary stoma rate and stoma duration

10. Operative and post-operative complications within 30 days of operation

(using the Clavien-

Dindo classification of surgical complications)

11. Death

12. Hospital stay

13. Reintervention rate

14. Overall and stoma-related readmission

15. Local recurrence at one year post-operation

16. Cost analysis of AL and EVAC therapy

# Study description

**Background summary**

Problem:
Anastomotic leakage (AL) is one of the most feared complications after rectal cancer surgery. AL leads to a significant increase of postoperative morbidity, long-term surgical complications, negative impact on quality of life, higher permanent stoma rates and impaired oncological outcome.
Our research group recently published a cross-sectional study of outcomes after

rectal cancer surgery in the Netherlands with a long-term incidence of AL of 20%. The current management of AL usually involves a deviating ileostomy, if not performed primarily, in combination with *passive* drainage of the abscess cavity via transanal or transcutaneous route. The cross-sectional study showed that almost half of the leaks do not heal and may require major salvage surgery.

Solution:
Numerous risk factors have been identified for AL. Modifiable surgical factors include tension on the anastomosis and anastomotic perfusion. A more recently described pathophysiological mechanism relates to the intestinal microbiome. Given the multifactorial etiology, a multi-interventional program is required for the prevention of AL. Mechanical bowel preparation (MBP) with oral antibiotics can lead to a reduction in AL by reduction of
the fecal bulk and bacterial load. Splenic flexure mobilization (SFM) optimizes a tension-free anastomosis, particularly for the most distal rectal cancers. Intraoperative real-time fluorescence angiography (FA) using indocyanine green (ICG) assesses perfusion, thereby enabling precise
delineation of bowel transection and final anastomotic vitality. Routine use of this technology has been associated with reduced AL rates.
If AL occurs, early diagnosis and *active* treatment allows for optimal control of pelvic sepsis, anastomotic healing and stoma reversal. No international consensus exists on a diagnostic pathway for early detection of AL, even though evidence is building for the use of C-reactive protein (CRP) in the early postoperative period. Considering *active* treatment our research group investigated the impact of endoscopic vacuum-assisted drainage (EVAC) of the abscess cavity in combination with early transanal closure of the anastomotic defect. In the IMARI-trial we want to address all the interventions mentioned above within existing institutional enhanced recovery programs and prehabilitation initiatives (i.e. correction of anemia, optimization of nutritional status, cessation of smoking).

**Study objective**

To increase the one year anastomotic integrity rate in patients undergoing total mesorectal excision (TME) for rectal cancer by the routine and quality controlled implementation of a multi-interventional program, which includes:
1. MBP with oral antibiotics
2. Tailored full SFM
3. Intraoperative FA using ICG
4. Routine CRP-measurement at day three postoperatively, CT-scan with rectal contrast on
indication
5. EVAC with early transanal closure of the anastomotic defect

**Study design**

This is a multicenter prospective clinical effectiveness trial, whereby current local practice (control cohort) will be evaluated, and subsequently compared to the results after implementation of the multiinterventional program (intervention cohort). Hospitals that apply up to three interventions in the routine care pathway comprise the control cohort. After finishing accrual of the control cohort, the full multi-interventional program will be implemented and checked for quality over a three month period in all participating hospitals, followed by accrual in the intervention cohort. Anastomotic integrity at one year will be determined by a CT-scan in all included patients. In the setting of a classical randomized controlled trial, contamination is likely to occur in the control arm. We consider this also as a downside of a stepped wedge cluster randomized trial design. For this reason, a comparative cohort design has been chosen.

**Intervention**

The quality controlled implementation of a multi-interventional program to increase the one year anastomotic integrity rate in patients undergoing total mesorectal excision (TME) for rectal cancer, includes:
1. MBP with oral antibiotics
2. Tailored full SFM
3. Intraoperative FA using ICG
4. Routine CRP-measurement at day three postoperatively, CT-scan with rectal contrast on
indication
5. EVAC with early transanal closure of the anastomotic defect

Of this program, fluorescence angiography using ICG is an intraoperative tool and an investigational intervention.

**Study burden and risks**

Patients are asked to fill in questionnaires before surgery and 90 days and 1 year after the operation. Furthermore, patients are asked to submit faecal material for microbiota-analysis before surgery, and 4 days post-operative. Drain fluid will be collected on day 1 postoperative (when a postoperative drain is placed during surgery) and each subsequent day until the drain is removed. Drain fluid collection will only be performed in Amsterdam UMC locations and OLVG. Blood samples will be taken peri-operatively and on day 3 after surgery. When patients develop AL, an additional swab will be taken from the presacral cavity.

At one year a CT-scan will be performed to assess the primary endpoint

# Contacts

**Public**
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
**Scientific**
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

Patients with primary rectal cancer and scheduled for a total mesorectal excision with planned restoration of bowel continuity or for completion total mesorectal excision after previous local excision or regrowth in a watch and wait protocol.

## Exclusion criteria

Patients not undergoing colorectal/-anal anastomosis;
Local recurrent rectal cancer, or redo surgery;
Locally advanced rectal cancer requiring extended or multi-visceral excision.

# Study design

## Design

| | |
|---|---|
| Study type: | Interventional |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Prevention

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 11-02-2020 |
| Enrollment: | 488 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Generic name: | Fluorescence Angiography using Indocyanine Green |
| Registration: | Yes - CE intended use |

# Ethics review

| | |
|---|---|
| Approved WMO Date: | 14-08-2019 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 04-11-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 30-01-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

| | |
|---|---|
| Approved WMO Date: | 24-02-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 02-06-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-12-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-02-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 26-02-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-01-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 02-08-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 20-01-2023 |
| Application type: | Amendment |
| Review commission: | MEC Academisch Medisch Centrum (Amsterdam)<br>Kamer G4-214<br>Postbus 22660<br>1100 DD Amsterdam |

| | |
|---|---|
| | 020 566 7389 |
| | mecamc@amsterdamumc.nl |
| Approved WMO Date: | 21-04-2023 |
| Application type: | Amendment |
| Review commission: | MEC Academisch Medisch Centrum (Amsterdam) |
| | Kamer G4-214 |
| | Postbus 22660 |
| | 1100 DD Amsterdam |
| | 020 566 7389 |
| | mecamc@amsterdamumc.nl |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

ID: 26456
Source: NTR
Title:

## In other registers

| Register | ID |
|---|---|
| CCMO | NL67600.018.18 |
| OMON | NL-OMON26456 |