COLOR III: A multicentre randomised clinical trial comparing transanal versus laparoscopic total mesorectal excision for rectal cancer.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON47551

Source
ToetsingOnline

Brief title
COLOR III trial.

Condition

- Gastrointestinal therapeutic procedures

Synonym
Rectal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: rectal cancer, TaTME, total mesorectal excision, transanal

Outcome measures

Primary outcome

The primary endpoint is the percentage of patients with local recurrence after 3-years follow-up.

(defined as local macroscopic tumour assessed by colono- or proctoscopy, (PET-)CT-scan or MRI of the pelvis)

Secondary outcome

Pathological

• Quality of specimen (as proposed and published by Quirke et al.)

• Involved circumferential resection margin

• Distal resection margin (defined as distance in cm from distal border of the tumour to distal resection surface)

• Translational research will be performed on predictive/prognostic biomarkers and imaging methods.

Clinical

• Length of hospital stay postoperatively (calculated as time from surgery to discharge in days)

• Morbidity within 28 days after surgery and within 90 days (graded by Clavien-Dindo Classification)

• Mortality within 28 days after surgery and within 90 days

• Local recurrence at three and five years (defined as cancer recurrence within the pelvic and perineal area)

• Disease-free survival at three and five years (calculated as time from surgery to last follow- up or date of recurrence)

• Overall survival at three and five years (calculated as time from surgery to last follow- up or death)

Quality of life

• Percentage of sphincter saving procedures (defined as colostomy percentage at 1 year postoperatively)

• Postoperative health related quality of life (quality adjusted life years) and functional outcome (measured with EORTC QLQ-CR29 and C30, EQ5D and LARS score).

Study description

Background summary

The quality of rectal cancer surgery has improved during the last decades with the total mesorectal excision (TME) technique, adaptation of laparoscopic surgery and extralevatory approach for abdominoperineal resection (APR). Nevertheless, surgery for mid and low rectal cancer is associated with relative high rates of incomplete mesorectal excisions and relative high rates of circumferential resection margin (CRM) involvement resulting in significant number of local recurrences. Moreover, patients with mid and low rectal cancer suffer from high rates of morbidity, permanent colostomies and significant impairment of quality of life.
The transanal TME (TaTME) has been developed with use of laparoscopic single port platforms to improve the quality of the TME procedure in mid and low rectal cancer. In TaTME, the tumour is distally approached through the anus with laparoscopic instruments.
Published cohort studies have shown that the TaTME procedure is safe and is

associated with low conversion rate and less permanent colostoma. Before adaptation of the TaTME as standard surgical therapy for mid an low rectal cancer, a well-designed study is essential to demonstrate its oncological efficacy and safety in a multicentre randomised setting.

Study objective

In attempt to improve the quality of the TME procedure in low rectal cancer and further improve morbidity the TaTME has been developed, in which the rectum is dissected transanally according to TME principles. First series have been described since 2010 and although randomised evidence is still lacking this new technique has shown to be feasible and safe. The rectum including the total mesorectum is mobilised transanally in a reversed way with minimally invasive surgery including high quality imaging techniques.
The TaTME technique for mid and low rectal cancer has shown to have potential benefits: less conversions in the majority of patients and more sphincter saving rectal resections without compromising oncological outcomes.
We propose to evaluate the TaTME technique compared with conventional laparoscopic rectal resection for patients with mid and low rectal cancer in an international randomised trial: the COLOR III trial.

Study design

The COLOR III trial is an international multicentre, non-inferior, randomised study comparing short- and long term outcomes of TaTME and laparoscopic TME for rectal cancer.
The study will include a quality assessment phase before randomisation to ensure required competency level and uniformity of the new TaTME technique and the laparoscopic TME. During the trial the clinical data will be reviewed centrally to ensure uniform quality.

In laparoscopic TME the percentage of local recurrence is estimated 5%. A local recurrence increase of 4% is believed to be inferior. Based on this difference, sample size calculation has been done with a one-sided level of significance of 2,5% and a power of 80%.A total of 1104 patients is needed, 735 patients in the TaTME arm and 369 patients in the laparoscopic TME arm.
In this sample size calculation, additional postrandomisation analyses (drop-out, cross-over total 5%), is taken into account.

Randomisation will be stratified for
T3a and less / T3b and more
Downstaged with chemoradiotherapy: yes / no / NA
Preoperative radiotherapy: yes / no
Height of the tumour: 0-2.0cm / 2.1-5.0cm / 5.1-10cm
Gender: male / female
BMI <= 30.0 / BMI > 30.0

The randomisation will be executed in such a way that concealment of allocation for the indicating surgeon is guaranteed.

Intervention

Transanal Total Mesorectal Excision.

Study burden and risks

Patients participating in this study have low burden and low risk on complications related to the trial. The follow-up scheme is almost similar to the regular scheme after rectal cancer surgery, except from the questionnaires. An pelvic CT or pelvic MRI is needed at 3 years conform international guidelines.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

1) Solitary adenocarcinoma rectal cancer within 10 cm from anal verge defined by MRI
2) Stage 1-3 based on AJCC classification including downstaged tumours
3) Intention for LAR with colorectal anastomosis or with coloanal anastomosis
4) Suitable for elective laparoscopic surgical resection
5) Informed consent according to local requirements

Exclusion criteria

1) T3 tumour with margins less than 1 mm to the mesorectal fascia or T4 tumour, determined by MRI-scan (staged after (chemo)radiotherapy if applicable)
2) Intention for complete intersphincteric APR with coloanal anastomosis
3) Malignancy other than adenocarcinoma at histological examination
4) Patients under 18 years of age
5) Pregnancy
6) Previous prostate or rectal surgery (excluding local excision)
8) Signs of acute intestinal obstruction
9) Multiple colorectal tumours
10) Familial Adenomatosis Polyposis Coli (FAP), Hereditary Non-Polyposis Colorectal Cancer (HNPCC), active Crohn*s disease or active ulcerative colitis
11) Planned synchronous abdominal organ resections
14) Other malignancies in medical history, except adequately treated basocellular carcinoma of the skin or in situ carcinoma of the cervix uteri
15) Absolute contraindication to general anaesthesia or prolonged pneumoperitoneum, as severe cardiovascular or respiratory disease (ASA class > III)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-01-2017
Enrollment:	690
Type:	Actual

Ethics review

Approved WMO Date:	17-02-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-08-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-12-2019
Application type:	Amendment

Review commission: METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
CCMO	NL54598.029.15