Gluteal turnover flap for closure of the perineal wound after abdominoperineal resection for rectal cancer, BIOPEX 2-study

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Anal and rectal conditions NEC
Study type	Interventional

Summary

ID

NL-OMON52518

Source
ToetsingOnline

Brief title
BIOPEX 2-study

Condition

- Anal and rectal conditions NEC
- Skin and subcutaneous tissue therapeutic procedures

Synonym
rectal cancer, Rectal malignancy

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC, locatie AMC
Source(s) of monetary or material Support: KWF

Intervention

Keyword: Abdominoperineal resection, Flap closure, Rectal cancer, Wound healing

Outcome measures

Primary outcome

The primary endpoint of the study is the percentage of uncomplicated perineal wound healing defined as a Southampton wound score of less than II at 30 days postoperatively.

Secondary outcome

1.) Surgery characteristics (duration of surgery, complications)

2.) Effect of neoadjuvant treatment on PTP-flap healing

3.) Perineal wound healing according to the Southampton wound grading at 14 days, 3, 6 and 12 months postoperatively.

4.) Cosmetic outcome and satisfaction with result .

5.) Incidence of persistent perineal or presacral sinuses, both clinically and by imaging (routine follow-up CT).

6.) Need for re-intervention or re-admission related to pre-sacral abscess or other perineal wound problems.

7.) Length of hospital stay.

8.) Incidence of symptomatic and asymptomatic perineal hernia during follow-up.

9.) Quality of life and urogenital function (EQ 5D-5L, EORTC-QLQ-C30-QL2, EORTC-QLQ-CR29, SF36, UDI6, IIQ7, IIEF, FSDS-R, FSFI).

10.) Postoperative pain score and duration.

11.) Serious adverse events rate.

Study description

Background summary

Colorectal cancer (CRC) is one of the world*s most common forms of cancer. Of which, about 700 patients per year undergo an abdominoperineal resection (APR) for distal rectal cancer (Dutch Colorectal Audit 2016). This procedure entails a radical resection of the rectum with en bloc resection of the anorectal sphincter complex and (part) of the levator muscle with lymphadenectomy according to the total mesorectal excision (TME) principle. Neoadjuvant (chemo)radiotherapy is often used to further improve locoregional control. Morbidity after APR is substantial and mainly consisting of perineal wound problems in about 35% of the patients. If primary healing of the perineal wound after APR doesn*t occur, secondary healing can take up to one year, and there is even a small proportion of patients in whom a chronic perineal wound or fistula persists after one year. During this long period, intensive wound care is necessary. This results in a heavy burden on both patient and health care resources.

Study objective

The high morbidity rate of the perineal wound has resulted in a continuing discussion on how to close the perineal defect after APR. Our research group recently published the BIOPEX-study (NL42094.018.12), in which 104 patients were randomized between primary perineal wound closure and biological mesh closure of the pelvic floor after APR with preoperative radiotherapy for rectal cancer. Similar uncomplicated perineal wound healing rate at 30 days (Southampton wound score < 2) was found: 63% versus 66%, respectively. The hypothesis behind this negative trial result is related to the perineal dead space between the skin and the biological mesh. Fluid will accumulate in this dead space with the risk of secondary contamination and abscess formation, leading to wound dehiscence and purulent discharge. Autologous tissue flaps have been suggested to improve perineal wound healing based on several cohort studies. At least in the Netherlands, these flaps are used only for selected patients with the large defects and highest risk of wound problems, because of the more extensive surgery with added surgical trauma and operative time, and associated donor site morbidity. For these reasons, primary perineal closure (control arm of BIOPEX) is still the standard of care in the Netherlands.
A gluteal turnover flap (GT flap) is a small transposition flap from the unilateral adjacent perineal skin and subcutaneous fat, which is flipped into

the perineal dead space, and stitched with the deepithelialized dermis to the contralateral pelvic floor remnant. Subsequently, the perineal subcutaneous fat and skin are closed over the flap in the midline, thereby not adding a donor site scar. A small pilot study from our group showed that this is a promising solution for routine perineal closure after APR, following the principle of filling perineal dead space.

Study design

In this multicenter single blinded study, eligible patients will be randomized between pelvic floor reconstruction using a GT flap (intervention arm) and primary closure of the perineal defect (standard arm). The perineal wound healing will be evaluated at 14 days and 1, 3, 6 and 12 months postoperatively using the Southampton wound scoring system by an independent observer. In addition, CT scan of the pelvis as usually performed during oncological follow-up, will be reviewed with respect to presacral or perineal sinuses and perineal herniation. Quality of Life questionnaires will be administered to the patient at each follow-up interval. In addition, the nature and severity of any wound event, all medical or surgical interventions and or re-operations will be collected.

Intervention

Surgery can start with the abdominal or the perineal phase. The abdominal phase of the APR can be performed via either laparoscopic or open surgery. The perineal phase of the APR will be performed according to the principles of a complete or limited extralevator APR, which means that the levator muscles will be transected laterally in order to leave a muscular cuff around the resection specimen or only at the site of the tumor. The coccyx will not be routinely resected, but only if indicated based on surgical exposure or oncological principles. The extent of excision of perineal skin will be as limited as oncologically justified. An omentoplasty will not be standardly being performed. A transabdominal drain will be placed and removed after 4 days or when the drain production is beneath 100cc/24hours. Perineal closure will be performed by a surgeon experienced with the PTP-flap. When this experience is not sufficiently present at the local participating hospital, an experienced surgeon from the Amsterdam UMC will perform or supervise the perineal phase at the local participating hospital. The patient will be positioned either in prone or lithotomy position as preferred by the operating surgeon. A shallow semicircular incision is made in the right or left gluteal skin with a maximum distance of about 2.5 centimeter from the adjacent perineal defect. The half-moon shaped skin island is deepithelialized. The subcutaneous fat is transected lateral from the perforator(s) down to the gluteal fascia in a 45 degree angle. Thereafter, the subcutaneous flap is placed into the perineal defect and fixed to the pelvic floor remnants with Vycril 2.0 sutures. The ischioanal fat is sutured together using interrupted 2.0 Vicryl sutures.

Afterwards, the subcutaneous fat will be closed using interrupted 2.0 Vicryl sutures. A Redon drain (CH10) will standardly be placed between these layers and removed after 14 days or when the production is beneath the 30cc/24hours. Subsequently, the skin will be closed using interrupted Vycril 3.0 sutures. Dry gauze will be placed against the wound and will be changed two times a day. Postoperatively the ERAS protocol will be followed and the sutures will be removed after 14 days at the outpatient clinic.

Study burden and risks

The potential benefit resulting from participation of the study in patients randomized for GT flap closure may be a higher chance of uncomplicated perineal wound healing and lower perineal hernia rate. The potential risks of a GT flap are experiencing more pain than usual after the operation. In addition, it may be that the GT flap does not heal and becomes necrotic after the operation. These previously mentioned complications usually do not require any major treatment. In exceptional cases, it may be necessary to remove the flap partially or completely. This will then be performed through a local operation. The use of a GT flap will not affect the strength or size of the buttocks.

Contacts

Public
Amsterdam UMC, locatie AMC

Meibergdreef 9
Amsterdam Zuidoost 1105AZ
NL
Scientific
Amsterdam UMC, locatie AMC

Meibergdreef 9
Amsterdam Zuidoost 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

(1) Resection of primary or recurrent rectal carcinoma by abdominoperineal resection.
(2) Age of 18 years or older.
(3) Ability to return for all scheduled and required study visits.
(4) Written informed consent.

Exclusion criteria

(1) The patient will undergo an intersphincteric abdminoperineal resection.
(2) Total pelvic exenteration or sacral resection above level S4/S5.
(3) Severe systemic diseases affecting wound healing except diabetes (i.e. renal failure requiring dialysis, liver cirrhosis, and immune compromised status like HIV).
(4) Collagen disorders (i.e. the syndrome of Marfan).
(5) Enrolment in trials with overlapping primary endpoint.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Prevention

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	11-06-2019
Enrollment:	160
Type:	Actual

Ethics review

Approved WMO Date:	14-05-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-11-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2022

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	NL65461.018.18