Prophylactic pectoralis major flap to compensate for increased risk of pharyngocutaneous fistula in laryngectomy patients with low skeletal muscle mass

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We hypothesize that in patients with low SMM the use PMMF as onlay for reinforcement can reduce the PCF rate after TL from 31,0% to 9.9%.

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26043

Bron
Nationaal Trial Register

Verkorte titel
PECTORALIS

Aandoening

Patients who are planned for TL (advanced stage primary laryngeal or hypopharyngeal cancer, salvage patients with recurrent disease after failure of initial organ preserving treatment, dysfunctional larynx)

Ondersteuning

Primaire sponsor: UMC Utrecht
Overige ondersteuning: KWF Kankerbestrijding

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary outcome of this randomized clinical trial is the PCF rate following TL in patients with low SMM with or without PMMF as onlay for reinforcement.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:
In The Netherlands about 160 patients per year undergo total laryngectomy (TL). Postoperative complications including the occurrence of a pharyngocutaneous fistula (PCF) are common and difficult to treat. In a Dutch national study with 324 TL patients the PCF rate was 25.9%. PCF may require additional surgery, prolongs feeding tube dependency, delays or interrupts oral feeding and voice rehabilitation and increases hospital stay and costs. PCF carries a high risk of postoperative infections, wound breakdown and subsequent damage to nearby tissue and structures, including potential carotid artery blowout. PCF may also cause delay of postoperative (chemo)radiotherapy, thus jeopardizing optimal oncological treatment. Surgical closure of PCF, is indicated in half of the cases. Most often a myocutaneous pectoralis major flap (PMMC) is used to restore the mucosal defect. This surgery is associated with complications because of the poor tissue quality due to infection and saliva exposure.
A surgical strategy to minimize PCF development following TL is the transfer of a pectoralis major myofascial flap (PMMF) to the neck as onlay for reinforcement of the pharyngeal closure. Systemic reviews show that a prophylactic PMMF reduces the risk of PCF in TL patients significantly. The use of prophylactic PMMF on the pharyngeal closure for reinforcement is recommended for patients with high risk for PCF.
Low skeletal muscle mass (SMM) has been related to negative outcomes in a variety of tumour types and treatments. In oncological patients, SMM is most commonly assessed on abdominal computed tomography (CT) imaging at the level of the third lumbar vertebra (L3). Abdominal CT imaging is not routinely performed in head and neck cancer patients, and is often only available in a preselected patient group with advanced disease and high risk features for distant metastasis. Recently, a novel SMM assessment method at the level of the third cervical vertebra (C3) was published. Imaging at the level of C3 is almost always available in TL patients, allowing for the routine assessment of SMM without any extra burden for the patient or healthcare-related costs.
Two studies reported that preoperative low SMM is a significant predictor of PCF in patients undergoing TL. Recently we reported on another series of 235 patients undergoing TL either with or without reconstruction of the pharynx with PMMC/PMMF and SMM measured using CT or MRI scans at the level of C3. Low SMM was observed in 109 patients (46.4%). Patients with

low SMM had more frequently PCF than patients with normal SMM (34.9% versus 20.6%, p=0.019) and prolonged hospital stay (median 17 versus 14 days, p<0.001). In multivariate logistic regression analysis low SMM remained significant predictors of PCF (OR 1.950). After exclusion of the patients who received a reconstruction of the pharynx with PMMC or PMMF from the database, the PCF rate in patients with low skeletal muscle mass was 31.0%.
Two systematic reviews of Paleri et al and Sayles et al describe a reduced risk of fistula formation in patients who underwent primary salvage surgery with the prophylactic PMMC or PMMF flap. The incidence of PCF was reduced (47/156 to 11/114), giving a relative risk of 0.32.

Objective:
With this prospective randomized clinical trial, we aim to investigate if the use of prophylactic PMMF on the pharyngeal closure for reinforcement in TL patients under high risk for PCF because of low (SMM), can reduce the risk of PCF to a level of TL patients without low SMM. We
hypothesize that in patients with low SMM the use PMMF as onlay for reinforcement can reduce the PCF rate after TL from 31.0% to 9.9%. Study design: In a multicenter randomized clinical trial patients who are planned for TL without PMMC for reconstruction of the mucosal defect will be asked to participate in this study. SMM is measured on pre-treatment CT or MRI scans at the level of C3 using a previously published method. One hundred twenty-eight patients with low SMM will be randomized between prophylactic PMMF at the time of TL or not. Incidence of PCF will be scored for the three groups: patients with low SMM with PMMF as onlay for reinforcement, patients with low SMM without PMMF and patients without low SMM. In a part of the low SMM patients group' shoulder- and neck function, swallowing function, and voice quality with their consequences on quality of life will be investigated. Patients' experience of the oncological treatment and rehabilitation will be explored by qualitative research with semi-structures interviews. A cost-effectiveness analysis will be performed.

Study population:
Patients will be recruited in head and neck centers of the Dutch Head and Neck Society. Patients eligible for this study, are 18 years of age or older, are scheduled for TL are able to understand Dutch, and do not meet any of the exclusion criteria. Patients who are planned for TL without PMMC for reconstruction of the pharynx and without previous chemoradiation of the head and neck will be asked to participate in this study. SMM is measured on pre-treatment CT or MRI scans at the level of C3 using a previously published method. One hundred twenty-eight patients with low SMM will be randomized between prophylactic PMMF at the time of TL or not.

Intervention:
PMMF in TL patients with low SMM who are randomized for intervention arm.

Main study parameters/endpoints:
The primary outcome of this randomized clinical trial is the PCF rate following TL in patients with low SMM with or without PMMF as onlay for reinforcement. Secondary outcomes of this study are hospital stay, shoulder- and neck function, swallowing function, voice quality, quality of life, patients' perspective, and costs.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
Burdens: Patients in the intervention arm will receive PMMF with potential shoulder morbidity. Patients with low SMM will be asked to complete questionnaires before and 6 months after TL. The EQ-5D-5L will be filled out 3 months after TL also. Shoulder function tests, voice recording and videofluoroscopic swallowing study (VFSS) will be performed dependent on the ability in each participating study and consent of patient. The shoulder function test will be performed before and 6 months after TL. VFSS and voice recording only 6 months after TL. Radiation dose during VFSS will be <1.5 mSv, which is a lot less than a routinely performed CT thorax (4 mSv).It is estimated that it takes 50 minutes to fill out all questionnaires at one time point. Function tests will take 45 minutes. The questionnaires and function tests will be conducted during a routine consultation. Additional operation time for harvesting the PM flap will take 30 minutes. It is expected that the use of PMMF will result in less and limited (duration and extent) PCF, shorter hospital stay, less delay in adjuvant treatment, lower costs and improved quality of life. PMMC for fistula closure is probably associated with more morbidity than prophylactic PMMF. For TL patients, this study may serve as a basis for a reduction of PCF, which is a difficult problem to manage and is associated with severe complications and reduction of quality of life. Prevention of PCF is essential in the management of TL patients.

Doel van het onderzoek

We hypothesize that in patients with low SMM the use PMMF as onlay for reinforcement can reduce the PCF rate after TL from 31,0% to 9.9%.

Onderzoeksopzet

Baseline, operation, 6 months follow up (postoperative)

Onderzoeksproduct en/of interventie

Patients with low SMM are centrally randomized to use of prophylactic myofascial pectoralis major flap (PMMF) or not

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Planned for TL.
- Eighteen years of age or older, and able to exercise their free will.
- Sufficient understanding of the Dutch language to give informed consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Planned for TL with PMMC for reconstruction of the pharynx.
- Major CT or MRI artefacts, impeding accurate muscle tissue identification on CT imaging.
- Interval between TL and imaging > 2 months.
- Concurrent treatment with chemotherapy for a previously diagnosed head and neck carcinoma.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-06-2020
Aantal proefpersonen:	276
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	11-05-2020
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 52422
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8605
CCMO	NL72319.041.20
OMON	NL-OMON52422

Resultaten

Samenvatting resultaten
N.A.