A Randomized Trial comparing Surveillance with Radio-Frequency Ablation of Barrett’s Esophagus with Low-Grade Dysplasia; the SURF-study.

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Radiofrequency ablation (RFA) will lead to permanent and complete eradication of Barrett's epithelium. This will prevent development of high grade intraepithelial neoplasia (HGIN) or early carcinoma and may eliminate the need for endoscopic...

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20984

Bron
NTR

Verkorte titel
SURF

Aandoening

The most important risk factor for developing esophageal adenocarcinoma (EAC) is the presence of a Barrett esophagus (BE), a condition in which, due to chronic gastro-esophageal reflux, the epithelium of the distal esophagus has been replaced by columnar epithelium containing specialized intestinal metaplasia. Patients with low grade intraepithelial neoplasia (LGIN) are therefore kept under more close observation and/or undergo more frequent endoscopic surveillance (every 6 to 12 months). Endoscopic surveillance for BE is uncomfortable to the patient and cost-effectiveness is not evidence-based.

Ondersteuning

Primaire sponsor: Academic Medical Center (AMC) Amsterdam
Overige ondersteuning: Maag-Lever-Darm-Stichting (MLDS)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Rate of high-grade intraepithelial neoplasia and early cancer during two year follow-up.

Toelichting onderzoek

Achtergrond van het onderzoek

Background:

In the last three decades the incidence of esophageal adenocarcinoma (EAC) has increased almost fourfold, making it the most rapidly rising cancer in the Western world. EAC carries a poor prognosis when diagnosed in symptomatic patients. The most important risk factor for developing EAC is the presence of a Barrett esophagus (BE), a condition in which, due to chronic gastro-esophageal reflux, the epithelium of the distal esophagus has been replaced by columnar epithelium containing specialized intestinal metaplasia. Patients with a BE are kept under endoscopic surveillance to detect malignant progression in their esophagus at an early and curable stage.

Patients with low-grade intestinal neoplasia (LGIN) in their Barrett esophagus are considered to have a significantly increased risk for development of esophageal cancer (i.e. synchronous cancer). Patients with LGIN are therefore kept under more close observation and/or undergo more frequent endoscopic surveillance (every 6 to 12 months).

Endoscopic ablation therapy is used for treatment of selected patients with high-grade intraepithelial neoplasia (HGIN) and early cancer in a Barrett’s esophagus. Radiofrequency ablation (RFA) is a new promising endoscopic ablation technique. In RFA, the Barrett’s segment is ablated by radiofrequency ablation through a specially designed balloon or electrode-cap. Balloons with different diameters and lengths of electrodes are available.

Aim:

to perform a randomized trial comparing RFA with endoscopic surveillance for patients with a Barrett’s esophagus containing low-grade intraepithelial neoplasia. This study will also progression and development of genetic oncogenetic abnormalities.

Hypothesis:

RFA will lead to permanent and complete eradication of Barrett's epithelium. This will prevent development of HGIN or early carcinoma and may eliminate the need for endoscopic surveillance.

Patients and methods:

Patients are eligible if they have LGIN in biopsies obtained from the Barrett’s esophagus in the preceding 12 months and after revision of the pathology slides by at least one of the study pathologists. At inclusion, patients are randomized to RFA or standard endoscopic surveillance. Patients randomized to RFA will have complete removal of all Barrett epithelium in one or multiple treatment sessions. RFA will be performed using the HALO-360 balloon. For additional RFA-treatment the HALO-90 device will be used. After complete eradication of BE, patients will are scheduled for endoscopic surveillance annually. Patients randomized to standard surveillance will undergo upper endoscopies every 6 months the first year and annually from the second year. In the surveillance arm, cyto-brushes will be performed at all endoscopies for analysis of genetic oncogenetic alterations using FISH.
Primary outcome parameter is the rate of high-grade intraepithelial neoplasia and early cancer during two year follow-up. Quality of life will be compared in the two groups using questionnaires.
A sample size of 120 patients will allow detection of a difference between the groups, assuming that 25% of these patients may be expected to develop high-grade intraepithelial neoplasia or early cancer during two years of follow-up.

Doel van het onderzoek

Radiofrequency ablation (RFA) will lead to permanent and complete eradication of Barrett's epithelium. This will prevent development of high grade intraepithelial neoplasia (HGIN) or early carcinoma and may eliminate the need for endoscopic surveillance.

Onderzoeksopzet

Study: in case randomized to RFA (t= number of months after first RFA-treatment).

1. T=0 months: first RFA-treatment (HALO-360 RFA balloon).

2. T=2 months: endoscopy ± RFA. For isolated islands with a maximum length of 2 cm and less than 50% of the circumference RFA will be performed with the HALO-90 RFA device. For larger areas of residual Barrett’s mucosa, RFA will be performed using the HALO-360 RFA balloon. It is expected that the majority of patients will require some form of additional RFA.

3. T=4 months: endoscopy ± RFA. For isolated islands with a maximum length of 2 cm and

less than 50% of the circumference RFA will be performed with the HALO-90 RFA device. For larger areas of residual Barrett's mucosa, RFA will be performed using the HALO-360 RFA balloon. It is expected that the minority of patients will require some form of additional RFA and that this mainly will be done using HALO-90 RFA device.

4. T=6 months: high-resolution endoscopy with lugol staining and biopsies from neosquamous epithelium (4QBx/2 cm, standard biopsy forceps). In case biopsies are obtained from areas with visible Barrett's mucosa, additional treatment using the catheter based RFA device is allowed.

5. T=12 months: endoscopy with lugol staining and biopsies from neosquamous epithelium (4QBx/2 cm, standard biopsy forceps). From the second year: annual endoscopy with lugol staining and biopsies from neosquamous (4QBx/2 cm, standard biopsy forceps).

Study: in case randomized to surveillance (t=number of months after last endoscopy prior to inclusion)

1. T=6 months: endoscopic surveillance using high-resolution endoscopy with biopsies according to the Seattle protocol (4QBx/2 cm, standard biopsy forceps) and cyto-brushes.

2. T=12 months: endoscopic surveillance using high-resolution endoscopy with biopsies according to the Seattle protocol (4QBx/2 cm, standard biopsy forceps) and cyto-brushes.

3. T=24 months: endoscopic surveillance using high-resolution endoscopy with biopsies according to the Seattle protocol (4QBx/2 cm, standard biopsy forceps) and cyto-brushes.

From the second year: annual endoscopic surveillance using high-resolution endoscopy with biopsies according to the Seattle protocol (4QBx/2 cm, standard biopsy forceps) and cyto-brushes.

Study: quality of life (t= number of months after randomization).

In both groups quality of life questionnaires (QoLq) will be completed at parallel time points: T= before randomization: QoLq1, T=2 months after randomization when the RFA-group will have been treated with RFA one time: QoLq2, T=9 months after randomization when the control-group will have had the first surveillance endoscopy within the study and the RFA-group will have been treated multiple times QoLq3, T=14 months after randomization when the surveillance group will have had the second surveillance endoscopy within the study: QoLq4, T=26 months after randomization during the time interval between control endoscopies in both groups: QoLq5, T=38 months after randomization as final measurement: QoLq6.

Onderzoeksproduct en/of interventie

Radiofrequency ablation of the Barrett’s segment.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Patients in the age of 18-85 years with LGIN in a Barrett’s esophagus;

2. Last high resolution endoscopy with biopsies performed within 6 months prior to inclusion;

3. LGIN in biopsies obtained from the Barrett's esophagus in the preceding 18 months and after revision of the pathology slides by at least one of the study pathologists;

4. No endoscopically visible abnormalities during at least one high resolution endoscopy within 12 months prior to inclusion;

5. In case of endoscopic resection of visible abnormalities, the resection specimen may at the

utmost contain LGIN, after revision by at least one of the study pathologists;

6. Informed written consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Any endoscopic visual abnormality detected by high-resolution white light endoscopy;

2. High-grade intraepithelial neoplasia or invasive cancer, confirmed by at least one of the study pathologists, in any of the biopsies obtained at endoscopies within 12 months prior to inclusion;

3. Any prior endoscopic treatment of HGD or invasive cancer in Barrett's esophagus, confirmed by at least one of the study pathologists;

4. Any known secondary malignancy in active disease stage;

5. Estimated life-expectancy < 2 years;

6. Patients unable to give informed consent.

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-06-2007
Aantal proefpersonen:	120
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	25-01-2008
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1155
NTR-old	NTR1198
Ander register	- : MEC 06/188
ISRCTN	ISRCTN wordt niet meer aangevraagd

Resultaten

Samenvatting resultaten
N/A