Detection of buried Barrett glands after Radiofrequency Ablation (RFA) with Volumetric Laser Endomicroscopy (VLE); a histopathology correlation study

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VLE is a feasible imaging technique to detect the presence of glandular structures under the NSE after RFA.

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

Samenvatting

ID

NL-OMON24516

Bron
NTR

Verkorte titel
nVision BB

Aandoening

Barrett's esophagus
Buried Barrett's

Barrett slokdarm

Ondersteuning

Primaire sponsor: AMC Amsterdam
Overige ondersteuning: Ninepoint Medical

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. Presence of structures suggesting BB on VLE;
2. VLE characteristics of buried glands (e.g. sparsely distributed hyposcattering structures underneath NSE with various sizes and shapes) ;
- Number of glands;
- Size of glands ;
- Location of glands from GEJ;
- Depth level of glands
3.Presence of structures suggesting of BB in ER specimens and, if present:
- Number of glands
- Size of glands
- Location of glands from GEJ
- Depth level of glands
4. Histology: Intestinal metaplasia, Dysplasia Correlation of OFDI images with corresponding histology of ER specimen

Toelichting onderzoek

Achtergrond van het onderzoek

Background of the study:

Barrett's esophagus (BE) is a preneoplastic condition in which the normal lining of the esophagus is replaced by columnar epithelium with intestinal metaplasia. Malignant progression in BE develops through a step-wise process from non-dysplastic intestinal metaplasia (IM), low-grade intraepithelial neoplasia (LGIN), high-grade intraepithelial neoplasia (HGIN) to early carcinoma (EC). Patients with HGIN/EC are eligible for endoscopic treatment. Visible lesions, if estimated to be intramucosal, should be removed by endoscopic resection (ER). Residual Barrett's epithelium and flat lesions containing HGIN can subsequently be treated with radiofrequency ablation (RFA). RFA has shown to be an effective treatment with high rates of complete eradication of dysplasia and IM with a favorable safety profile. A known disadvantage of ablation techniques in Barrett's esophagus is the possible occurrence of 'buried Barrett's' (BB): the occurrence of residual Barrett glands hidden under neosquamous epithelium (NSE). These glands may lead to recurrence of Barrett's epithelium after treatment or may progress to dysplasia or cancer while hidden under the NSE. Presence of BB has been described in multiple ablation techniques. Limiting factors in most studies on this subject are the lack of reporting frequency of biopsy sampling of the NSE and that in general most biopsies do not incorporate the lamina propria and BB may, therefore, be missed. For this reason our group performed in 2008 ER and keyhole biopsies from NSE in 22 patients two months after RFA treatment showing no BB in any of the biopsies or endoscopic resection specimens (see the file number of the protocol of this study

under E9a). White light endoscopy (WLE) and/or narrow band imaging (NBI) only image the superficial surface and are not able to detect BB. Optical frequency-domain imaging (OFDI), also known as Volumetric Laser Endomicroscopy (VLE) is a new Optical Coherence Tomography (OCT) technique that is able to visualize underlying layers of the NSE. This technique utilizes optical scattering based on differences in tissue composition to perform high-speed acquisition of large luminal surfaces creating three-dimensional images. OFDI is capable of generating cross-sectional images of the entire circumference of the esophagus over a length of 6 cm with an axial-resolution of up to 10 □m, which is comparable to low-power microscopy. OCT has shown to be a feasible method to differentiate between normal squamous mucosa, Barrett's epithelium and HGIN/EC, with acceptable sensitivity and specificity. In addition, also subsquamous structures such as glands, crypts, cysts and bloodvessels can be distinguished. The mucosa can be investigated in full thickness and over a large area. Due to its high-resolution and high-acquisition rates, VLE is theoretically the ideal technique for assessing the prevalence of buried glands after RFA. It may be a promising tool for investigating the presence of BB and thus for future follow-up of patients treated with RFA. Direct correlation of VLE images with histopathology is needed in order to validate the technique.

Objective of the study:

The aim of this study is to investigate the feasibility of VLE to detect the presence of glandular structures under the NSE after RFA and direct correlation of VLE images with histopathology.

Study design:

This is a single centre, single arm, observational trial which will take place at the department of Gastroenterology of the AMC which is a tertiary-care referral centre for patients with a Barrett's esophagus and the detection and treatment of early Barrett's neoplasia. Endoscopic procedure: the esophagus will first be examined in overview with white light endoscopy (WLE). In order to localize possible BB underneath the NSE, 4 reference markers will be made with an electrocoagulation device. Two markers 5 mm above the GEJ, in neutral position at the 12 o'clock position (1 dot) and at the 6 o'clock position (2 dots), subsequently at 4 cm above the GEJ an additional 2 mark sets will be made at the 12 o'clock position (1 dot) and at the 6 o'clock position (2 dots). The Nvision guidesheath and probe will be introduced through the working channel of a therapeutic endoscope and positioned in the distal esophagus including the GEJ. Once the correct position is obtained, a full scan will be performed. Based on this scan the most likely area containing OCT-structures suspicious for buried glands will be identified and localized in the esophagus according to 4 reference markers. Subsequently, the probe and balloon are removed from the endoscope. The area of interest with a maximum diameter of 15 mm will be delineated with an additional set of electrocoagulation markers according to the following protocol: The proximal margin (top most) of the area will be marked by two proximal reference markers, in the 12 o'clock position of the lesion and single markers at 3, 6 and 9 o'clock positions. When no structures are seen suspicious for buried glands, the second set of coagulation markers will be placed at a random location at

the discretion of the endoscopist including the GEJ. After placement of the second set of coagulationmarkers an additional VLE-scan of the distal esophagus will be performed to allow optimal correlation between the in-vivo VLE-image and the area of interest delineated with the second coagulationmarker set. After imaging is completed the selected area will be resected en-bloc including the coagulationmarkers per standard clinical practice, using the ER-cap method. After ER, the ER-specimen will be obtained and additional ex-vivo VLE imaging will be performed. After ER and VLE imaging four random biopsies will be obtained under the NSE in the GEJ (<5mm) and repeated in all 4 quadrants every 2 cm, according to standard follow-up protocol.

Doel van het onderzoek

VLE is a feasible imaging technique to detect the presence of glandular structures under the NSE after RFA.

Onderzoeksopzet

VLE scan will take place 6 or 12 months after last RFA treatment with 100% endoscopic regression. There will be no follow-up VLE.

Onderzoeksproduct en/of interventie

The study uses the VLE catheter to examine and scan the distal Barrett's esophagus. VLE is an advanced imaging technique that has the potential to visualize subsquamous structures in Barrett's esophagus. These subsquamous structures (so-called Buried Barrett's) are not certain to be really existing below the newly formed squamous epithelium in the distal esophagus that has been treated with RFA. In order to research if these structures are present in patients that have received RFA and reached 100% endoscopic regression of their Barrett's esophagus, we will use VLE to examine. VLE, in other words, is not a treatment but a diagnostic technique. The intervention is that the balloon (containing the VLE catheter) will be guided through the working channel of the endoscope and will be brought into the distal esophagus where scanning is performed. With the VLE areas suspicious of "buried Barrett's" are attempted to be identified, if applicable these areas will be marked. Hereafter, an EMR of a suspicious lesion (or when no suspicious structures are seen, an at random area near the gastro-esophageal junction) will be performed in order to obtain the histological substrate of the VLE scans in-vivo as well as ex-vivo of the EMR specimen. The scan(s) take about 2 minutes each and the esophagus will be scanned twice (before and after identifcation and marking of suspicious areas), so about 4 scans per patient will be performed, depending of scanning results. The procedure will take about 30-45 minutes longer than normal, considering the time to look at the in-vivo VLE scans searching for suspicious structures. This is a pilot study with only 10 patients and no controls, all patients have had RFA in the past for early neoplasia in Barrett's esophagus, but have reached 100% endoscopic regression.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age > 18 – 80 years;

2. Patients post RFA treatment with 100% endoscopic regression of Barrett’s epithelium;

3. Minimum circumferential Barrett’s extent of 2 cm prior to ablation therapy;

4. Signed informed consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Presence of significant stenosis;

2. Presence of erosive esophagitis;

3. Inability to undergo ER and/or obtain biopsies (e.g. due to anticoagulation, coagulation

disorders, varices);

4. Unable to provide signed informed consent.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	12-07-2013
Aantal proefpersonen:	10
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	01-07-2013
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	NL3894
NTR-old	NTR4056
Ander register	NL44441.018.13 : 2013/097
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A