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

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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.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Observational invasive

Summary

ID

NL-OMON38462

Source
ToetsingOnline

Brief title
nVision BB

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
1) "Buried Barrett's" 2) Occult buried glandular mucosa

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

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

Intervention

Keyword: advanced imaging, buried Barrett glands, endoscopic resection, histopathology correlation

Outcome measures

Primary outcome

Presence of structures suggesting BB on VLE;

- 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

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

- Histology: Intestinal metaplasia, Dysplasia

Correlation of OFDI images with corresponding histology of ER specimen

Secondary outcome

-

Study description

Background summary

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.

Study objective

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.

Study burden and risks

Endoscopic follow-up is standard policy in patients that underwent RFA treatment for Barrett's esophagus with an early neoplastic lesion. General risks associated with a gastroscopy are: mild irritation of the throat due to introduction of the endoscope, difficulties swallowing and retrosternal pain. The ER, performed using the ER cap-technique, is an additional procedure that is not routinely done during standard follow-up in patients post RFA treatment. The ER cap-technique is widely used and a safe technique, serious complications such as severe bleeding and perforation are rare (<3%). Perforations when occur can mostly be handled conservatively without the need of surgery. Minor complications, such as minor bleeding, occur in 9% of the cases and usually are easily managed with endoscopic hemostatic techniques. Yielding an additional ER specimen for diagnostic and histology correlation purposes was done before in studies by our group in 2008 (See protocol with file number NL21978.018.08, ABR form 21978 and also in another protocol: NL35326.018.11, ABR form 35326). During this study patients will undergo an nVision pVLE procedure before and after endoscopic resection. The resection specimen will also be imaged in a standardized ex-vivo set-up with pVLE. The regular diagnostic and therapeutic proces is not influenced by these extra procedures. The endoscopy will take 15 minutes longer compared to the standard endoscopy. The nVision pVLE System is non-invasive in nature. The type of light delivered by the optical probe is equivalent in intensity to the standard light source used and delivered by a standard endoscope; the excitation of tissue by the light energy delivered by the optical biopsy system is non-damaging and does not result in any thermal effects on tissue. The additional risk associated with the application of nVision VLE is mucosal laceration due to the extension of the balloon. In very rare occasions perforation of the esophagus can happen when inflated above maximum allowed pressure. A safety valve is included in the design of the balloon to avoid this problem. In patients with an esophageal stricture, the risk of laceration increases, and these patients are therefore excluded from participation in this trial.

Contacts

Public
Academisch Medisch Centrum

Kendall Square 1
Cambridge MA02139
NL
Scientific
Academisch Medisch Centrum

Kendall Square 1
Cambridge MA02139
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age > 18 * 80 years;
- Patients post RFA treatment with 100% endoscopic regression of Barrett*s epithelium;
- Minimum circumferential Barrett*s extent of 2 cm prior to ablation therapy;
- Signed informed consent.

Exclusion criteria

- Presence of significant stenosis;
- Presence of erosive esophagitis;
- Inability to undergo ER and/or obtain biopsies (e.g. due to anticoagulation, coagulation disorders, varices);
- Unable to provide signed informed consent.

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-07-2013
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	nVision pVLE system
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	20-06-2013
Application type:	First submission
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	NL44441.018.13