A Comparison of Volumetric Laser Endomicroscopy (VLE) and Endoscopic Mucosal Resection (EMR) in Patients with Barrett*s Dysplasia or Intramucosal Adenocarcinoma

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

Summary

ID

NL-OMON40469

Source
ToetsingOnline

Brief title
nVision EMR

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
1) Barrett's oesophagus, 2) early oesophageal cancer

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, Barrett's oesophagus, early neoplasia, endoscopic resection

Outcome measures

Primary outcome

The primary endpoint will be the correlation of features seen on VLE images to

those seen on histopathology from mucosal resection specimens.

Secondary outcome

The secondary endpoint will be the following: The creation of an image atlas,

which will be used to determine the intra and inter observer agreement on VLE

images in correlation with histopathology, resulting in refinement of the

existing VLE image interpretation criteria and the validation of the VLE

classification.

Study description

Background summary

In patients with Barrett oesophagus (BO) malignant degeneration may occur through a series of phenotypic cellular changes detected and graded on microscopy; beginning with non-dysplastic intestinal metaplasia (IM), then low- (LGIN) and high-grade intraepithelial neoplasia (HGIN), and eventually early cancer (EC) may arise1,2. Endoscopic surveillance of patients with BO is, therefore, recommended to detect early neoplasia at a curable stage3. When using standard endoscopy, however, it may be difficult to distinguish areas with early neoplasia (i.e. HGIN a/o EC) within the normal Barrett mucosa4. Thus, in the absence of visible abnormalities random four-quadrant biopsies are obtained every 1-2 cm of the BO, to allow for histological evaluation for the presence of neoplasia (Seattle protocol)4,5. However, random biopsies are

associated with a high rate of sampling error and may miss malignant lesions in the BO6. Moreover, the extensive biopsy protocol poses significant burden on the patient, the endoscopist and the health care system, due to prolonged endoscopy time and high costs. To increase the detection rate of early neoplasia during endoscopic surveillance of BO patients, different imaging techniques have been developed. In this respect, roughly two imaging goals have to be distinguished: first and foremost, suspicious lesions will have to be identified in the BO, which requires a *red flag* imaging modality with the ability to draw attention to a certain area of interest. Second, a differentiating tool will have to be able to distinguish between truly suspicious areas (i.e. HGIN/EC) or false positive areas. The N-Vision pVLE system is a newly developed diagnostic tool that will allow high resolution imaging of the oesophageal mucosa through Optical Frequency Domain Imaging (OFDI), a second generation Optical Coherence Tomography (OCT) technology. OFDI compares backscattered light from tissue to a reference signal, which allows high resolution depth resolved imaging of the investigated tissue. In essence, OFDI is a kind of optical ultrasound imaging. The N-Vision probe based Volumetric Laser Endomicroscopy (pVLE) system incorporates OFDI in a rotating endoscopic probe, that allows for real-time, 3D high resolution imaging of the oesophageal mucosa. The N-Vision system can be used as an additional tool during standard surveillance endoscopy for Barrett's oesophagus or work-up of early neoplasia. The 3D mucosal map that is projected on the screen of the n-Vision system may identify suspicious areas that would otherwise have been overlooked by standard white light endoscopy. VLE is a new technique. Before it can be applied in the clinic, VLE imaging needs to be validated. Therefore, the VLE images have to be correlated to the histopathological features of the imaged tissue. A standardized, ex-vivo set-up will ensure spot-on correlation between the VLE images and the imaged tissue.

Study objective

In patients undergoing surveillance endoscopy for Barrett's oesophagus or work-up and treatment for early neoplasia in Barrett's oesophagus we will evaluate the N-Vision pVLE system for the following items: 1) Correlating the VLE images with the corresponding histology of the biopsy specimen of Barrett's neoplasia in the oesophagus and in the endoscopic biopsy specimen. 2) Correlating the VLE images with the corresponding histology of the biopsy specimen of non-dysplastic Barrett tissue in the oesophagus and in the endoscopic biopsy specimen. 3) To define VLE image characteristics and develope a VLE classification system for the imaging of Barrett's oesophagus. 4) To creating a VLE imaging atlas with corresponding histology. 5) To optimize and validate the VLE classification by independent observers.

Study design

Endoscopic procedure: During standard endoscopy for surveillance or work-up,

the oesophagus will first be examined with white light endoscopy, recording all marks, distances and possible suspicious areas. Subsequently, the N-Vision probe will be deployed through the working channel of the endoscope, the balloon inflated and the inner lining of the oesophagus imaged. Areas suspicious for early neoplasia identified on the N-Vision 3D image will be recorded. Mapping with the N-Vision is followed by standard biopsies: all suspicious areas and random four-quadrant biopsies, as required by the official guidelines. The endoscopist will remove the system after performing this. If there is an abnormality, this will be marked by electrocoagulation according to the guidelines, followed by endoscopic resection of the abnormality by the Cap-technique according to the guidelines. When indicated, biopsies will follow of other (suspected) abnormalities. All abnormalities will be visualised with the N-Vision VLE system. After the procedure the biopsy specimen will be placed in an especially constructed mold and the second pVLE imaging will take place. Afterwards diagnostic work up will be done on the specimen by the pathology department. All histological evaluation is done by both a junior and a senior pathologist. All histology will be reviewed by a GI-expert pathologist. The histological data will be correlated to the N-Vision data. These images and histology results will be used to create an image atlas and to develop and validate a VLE classification system for imaging and reviewing Barrett's mucosa and neoplasia in the oesophagus. The study will be done in 2 phases: 1) First phase is a single-centre pilot study, in which set up and logistics of the system will be optimalised, the VLE image characteristics will be defined and the VLE classification determined. In this phase,10 patients will be included: 5 patients with Barrett's oesophagus without dysplasia and 5 patients with an early neoplastic abnormality of Barrett's oesophagus. 2) In the second phase, up to 30 patients will be included in 1 centre (the AMC); the first 15 inclusions will be patients with an early neoplastic abnormality of Barrett's oesophagus. After the first 15 an evaluation will be performed to determine the number of additional patients (maximum of 15), these can be dysplastic and non-dysplastic. In this phase, the image-atlas will be created and the VLE classification optimized and validated by indepent observers.

Study burden and risks

Endoscopic treatment is standard policy in patients with an early neoplastic lesion in Barrett's oesophagus. An endoscopic resection is prefered because of the diagnostic and therapeutic value. During this study patients will undergo a nVision pVLE procedure before and after endoscopic resection. The resection specimen will 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 performance of an ER in patients in the dysplastic group does not pose additional risks, given the fact that these patients undergo an endoscopic resection as a regular therapy for carcinoma or high-grade dysplasia. The additional risc is associated with the application of nVision VLE (mucosal laceration due to the extension of the balloon). In the non-dysplastic group, a

regular follow-up endoscopy will be performed, with standard biopsy sampling. Additionally, an endoscopic resection will be performed by using the cap-technique. Minor bleeding may occur in 6% of the cases, usually easily managed with endoscopic hemostatic techniques. During this study non-dysplastic patients will undergo a nVision pVLE procedure before and after endoscopic resection. The resection specimen will 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 30 minutes longer compared to the standard endoscopy. The additional risc is associated with the application of nVision VLE (mucosal laceration due to the extension of the balloon). Moreover, patients in the non-dysplastic group undergo an extra intervention (ER), which may mean an extra burden and risk for these patients, compared to normal surveillance endoscopy.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Males and females over the age of 18 years. - Patients with either suspected or confirmed Barrett*s-associated dysplasia or intramucosal adenocarcinoma presenting for endoscopy likely requiring EMR. - Patients with non-dysplastic Barrett*s oesophagus - Eligible for endoscopic resection of Barrett mucosa. - Ability to provide written, informed consent.

Exclusion criteria

- patients with a condition precluding full distension of the N-Vision balloon, such as strictures or a mass - inability to obtain biopsies and/or EMR (e.g. due to antocoagulation therapie, coagulation disorder, varices) - eosophillic oesophagitis - oesophagitis > LA grade A - pregnancy - 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):	13-05-2013
Enrollment:	50
Type:	Actual

Medical products/devices used

Generic name:	nVision pVLE system
Registration:	No

Ethics review

Approved WMO Date:	18-03-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-09-2014
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	NL43663.018.13