Autofluorescence endoscopy and spectroscopy for detection of early Barrett's neoplasia: the AFI-III study

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Study phase 1: In patients with BO undergoing work-up endoscopy for early neoplasia, we aim to develop a classification to evaluate fluorescence spectroscopy of neoplastic and non-neoplastic lesions in Barrett epithelium, as used in phase 2.Study...

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

Summary

ID

NL-OMON34541

Source
ToetsingOnline

Brief title
the AFI III study

Condition

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

Synonym
1) Barrett 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,deels uit de Europese

Unie;deels uit restgelden van eerdere projecten

Intervention

Keyword: autofluorescence, Barrett, imaging, spectroscopy

Outcome measures

Primary outcome

Phase 1:

1) Correlation of the ex-vivo spectroscopy data with histological outcome

Phase 2:

1) Reduction of the false positive rate of WLE and AFI-III compared to WLE and

AFI-II.

2) Reduction of the false positive rate of WLE and AFI-II with NBI

3) Reduction of the false positive rate of WLE and AFI-III with NBI

4) Reduction of the false positive rate of WLE and AFI-III with in-vivo

spectroscopy

5) Correlation of the in-vivo spectroscopy data with histological outcome.

6) The amount of lesions detected with WLE and AFI III compared to WLE and

AFI II

Secondary outcome

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Study description

Background summary

Endoscopic surveillance of Barrett oesophagus (BO) patients is recommended to detect high-grade intraepithelial neoplasia (HGIN) or early cancer (EC) at a

curable stage. With standard endoscopy, however, it is difficult to distinguish areas with HGIN/EC. In the absence of visible lesions, random biopsies are obtained for histological assessment of neosplasia, but these random biopsies may miss dysplastic lesions (sampling error). The endoscopic detection of early neoplasia may be improved by the use of endoscopic tri-modal imaging (ETMI); a system that incorporates white light endoscopy (WLE) and autofluorescence imaging (AFI) for primary detection of early neoplasia and allows for targeted imaging of suspicious areas with narrow-band imaging (NBI). In a recent international multicenter study, AFI increased the sensitivity for detecting early neoplasia from 53% to 90% compared to WLE. Subsequent inspection with NBI of AFI-positive areas reduced the false-positive rate of AFI from 81% to 26%. Preliminary results of an international multicenter randomized cross-over trial also show that AFI increases the detection of early neoplasia with 40%, but again with a high false positive rate (i.e. do not contain neoplasia). The false positive rate was reduced from 72% to 47% with NBI, but at the expense of misclassifying 8 neoplastic lesions as unsuspicious. For the AFI III study the current AFI system is replaced for a new AFI III algorithm. Inspection with AFI III may be a better approach to detect early neoplastic lesions in the Barrett Oesophagus and to reduce the current high AFI false positive rate.
AFI and NBI are based on fluorescence spectroscopy, which measures the interaction between tissue and light. Every tissue has distinct fluorescence properties, thus by meticulously measuring the fluorescence spectra, one could possibly distuinguish between neoplastic and non-neoplastic tissue. However, the challenge is to uncouple the unspecific reemitted light from physiological fluctuation, from the specific scattering signal due to pathological processes. One of the possible solutions to this problem is a tunable, single wavelength laser. By tuning the wavelength, the specific fluorescence spectra corresponding to tissue characteristics can be optimized and thus specifically recognised. Adding in-vivo fluorescence to the AFI III system, may reduce the high AFI false positive rate compared to NBI inspection.

Study objective

Study phase 1: In patients with BO undergoing work-up endoscopy for early neoplasia, we aim to develop a classification to evaluate fluorescence spectroscopy of neoplastic and non-neoplastic lesions in Barrett epithelium, as used in phase 2.
Study phase 2: In patients with BO undergoing surveillance or work-up endoscopy for early neoplasia, we aim to evaluate if AFI III increases the accurary of detecting early neoplasia. Furthermore we aim to determine whether the addition of in-vivo fluorescence spectroscopy to the AFI III system further reduces the high false positive rate compared to NBI inspection.

Study design

For this prospective study a total of 50 patients will be included.

In phase 1 a total of 10 patients with proven HGIN or EC in a visual lesion will be included. During endoscopy the BO is examined with WLE to detect suspicious lesions, all findings are recorded. Then, the BO is inspected with AFI and the location, size and macroscopic appearance for additionally detected lesions are recorded. Visual lesions will be removed by endoscopic mucosal resection, according to current common therapeutic practice. Subsequently, the EMR specimen is placed on the ex-vivo spectroscopy set-up and measured, followed by corresponding biopsies of the measured areas. The biopsies and EMR specimens are then evaluated by the same expert gastro-intestinal pathologist to assess the presence of neoplasia. The histological data will be correlated to the fluorescence spectra. The measurement of fluorescence spectra does not influence the histological assessment of the EMR specimen by the pathologist.

In phase 2 of this study, a total of 40 patients will be included. 10 patients referred with HGIN.EC in a visual lesion, 10 patients with HGIN/EC without visual lesions, 10 patients with LGIN and 10 patients under surveillance for NDBO. During endoscopy the BO is examined with WLE to detect suspicious lesions, all findings are recorded. Then, the BO is inspected with AFI and the location, size and macroscopic appearance for additionally detected lesions are recorded, followed by inspection with NBI. Subsequently, the endoscope is replaced by the AFI III endoscope and the oesophagus is inspected with all modalities, followed by in-vivo fluorescence spectroscopy. A laserconducting fiberoptic probe, connected to the blue laser and a spectrometer, is passed through the working channel of the endoscope and positioned above the mucosa. Biopsies are then taken from all measured areas for histological correlation. The biopsies will be evaluated by the same expert gastro-intestinal pathologist to assess the presence of neoplasia.

Study burden and risks

Next to the general risks associated with upper endoscopy such as irritation of the throat by introduction of the endoscope, difficult swallowing and retrosternal pain, the use of ETMI for neoplasia detection and the addition of in-vivo fluorescence spectroscopy do not increase endoscopy risk. During endoscopic resection, delayed bleeding may occur in 3.3% of cases, usually easily manageable with endoscopic hemostatic techniques. Also, a perforation may occur in 2.4% of cases, usually manageable with endoscopic and conservative management.
In phase 1, there will be no extra burden for the patient. In phase 2, the extra burden for the patient will be the switch of endoscopes halfway the endoscopic procedure.

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

- Age > 18 years;
- BO with a minimal circumferential length of 3 cm;
- BO without dysplasia (NDBO), BO with LGIN, or patients with BO referred for endoscopic work-up of HGIN or EC;
- Signed informed consent

Exclusion criteria

- Prior history of surgical or endoscopic treatment for oesophageal neoplasia;
- Presence of erosive oesophagitis (Los Angeles classification *B);
- Inability to 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:	Pending
Start date (anticipated):	01-06-2010
Enrollment:	50
Type:	Anticipated

Ethics review

Approved WMO

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

ID: 21252
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL32287.018.10
OMON	NL-OMON21252